Statins Strife: Assessing the Expanding Pharmaceuticalisation of the Primary Prevention of Cardiovascular Disease

Tom Douglass BA (Hons), MA

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Abstract

In July 2014 the National Institute for Health and Care Excellence (NICE) published updated clinical practice guidance dramatically shifting the cardiovascular disease (CVD) prevention landscape in England. The most publicly and professionally visible aspect of this guideline was the recommendation to lower the primary prevention risk threshold from ≥20% risk of developing CVD over ten years to a ≥10% risk over ten years. This was an extremely significant development not least because it vastly expanded the numbers of people eligible to be offered CVD risk assessment and potentially advice on prophylactic measures against CVD – including, saliently, the offer a pharmaceutical solution. It has been estimated that this guidance makes millions of additional people in England eligible for the class of drugs called statins. To sociologically analyse this case, this thesis utilises the conceptual lens of pharmaceuticalisation – a process whereby human conditions, problems, capabilities (and beyond) are made increasingly amendable to intervention by pharmaceuticals. The aim of this thesis is to analyse crucial driving forces behind this decision and the subsequent implementation of the guideline, looking across multiple dimensions of pharmaceuticalisation, as well as to assess the overall extent to which pharmaceuticalisation is occurring in this case. The thesis explores the following overarching question: to what degree is the further pharmaceuticalisation of the primary prevention of CVD occurring and what are the driving forces? To analyse this question, this thesis presents empirical qualitative research drawing on multiple methods (documentary analysis, media analysis, and semi-structured interviewing). The thesis focuses on several key actors and subprocesses existing within the 'pharmaceutical regime' that can be implicated in driving, facilitating and/or potentially constraining the extent of the widening pharmaceuticalisation of the primary prevention of CVD. The pharmaceutical regime is a core conceptual aspect of pharmaceuticalisation and is necessarily concerned with the analysis of the driving forces and extent of pharmaceuticalisation. In analysing the overarching question, first, the creation of the opportunity for pharmaceutical deployment by NICE is analysed, examining how the influences of and regulatory dependency on the pharmaceutical industry are widening the opportunity for pharmaceuticalisation in this case. The role of the print news medium is also analysed. The research shows how portrayals of statins and usage expansion within the context of this case were controversy-oriented. Finally,

the understandings and approaches of GPs to the ≥10% threshold, another key actor in this case, are analysed – with the analysis highlighting the disparate manner in which GPs both understand the guidance and attempt to facilitate and guide the treatment of their patients. When considering multiple actors and competing driving forces within the pharmaceutical regime as a whole in this case, the analysis ultimately shows that pharmaceuticalisation is only partial in its overall extent. Critical and controversy-oriented newspaper coverage and evidence of resistance from GPs limits the extent of pharmaceuticalisation occurring in the case under study.

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Contents

Introduction

i.1 The Case of CG181

In July 2014, the National Institute for Health and Care Excellence (NICE) issued an update to its guidance on the assessment and reduction of cardiovascular disease and lipid modification: *Cardiovascular disease: risk assessment and reduction, including lipid modification'* (also known as clinical guideline (CG) 181, or more informally as the 'lipids guideline'). The most publicly and professionally visible aspect of this guideline was the recommendation to lower the primary prevention risk threshold from ≥20% risk of developing cardiovascular disease (CVD) over ten years to a ≥10% risk over ten years. This was an extremely significant development not least because it vastly expanded the numbers of people eligible to be offered CVD risk assessment and potentially advice on prophylactic measures against CVD, including, saliently, the offer a pharmaceutical solution. It has been estimated that lowering the risk threshold would make 4.5 million additional people in England eligible for the class of drugs called statins (NICE, 2014a; b). This is in addition to the millions of individuals already taking a statin at higher thresholds of risk and in the secondary prevention of CVD. Analysis has suggested that more than 30% of all adults aged 30-84 under this guidance would be deemed at significant enough risk of CVD to be eligible for a statin, with 95% of males and the majority of females aged over 60, and all men and women aged 75-84 being eligible for the drugs (Ueda, 2017). In the period since the guideline was established the actual numbers of prescriptions for statins has indeed risen – from 63 million units (individual pills) prescribed per year to more than 66 million units in 2016 in England (Health and Social Care Information Centre, 2016). The widening of the primary prevention threshold was by no means the only aspect of importance in the guideline, with other recommendations including, for example, formally changing the risk assessment tool utilised to assess patient risk (formally codifying in guidance QRISK2 rather other tools). The guideline on a more general level also acted to unify intersecting guidance on CVD and comorbidities (particularly diabetes). However, the primary prevention threshold was by far the largest aspect of change and arguably became its defining feature. But what drove this change?

CG181 has an identifiable timeline as far back as at least 2012[1] and seems to have been driven by two key factors. First, the widening generic availability of drugs within the statins class at the time of NICE's guideline development process, including the expiry of the patent for atorvastatin, previously marketed by Pfizer as *Lipitor* (in its patented lifetime, the world's most profitable drug). This drug became generic in the UK after its patent expired in 2012 (and thus was still on patent at the time the previous NICE guideline on the same topic was published in 2008), making it much less expensive at a cost of pence per day. This seems to have influenced, in line with procedures to regularly check and, where necessary, update guidelines, NICE's decision to begin in 2012 what was by their standards a relatively early full update of CVD prevention/lipid modification guidance. There was also developing evidence suggesting that the drugs had greater efficacy at lower thresholds of use in primary prevention than previously acknowledged. Rather than the ground-breaking addition of randomised controlled trial (RCTs) evidence, this was primarily secondary meta-analyses conducted by Cochrane (Taylor et al., 2013) and, importantly, the Cholesterol Treatment Trialists' Collaboration (CTT) (Baigent et al., 2010; CTT, 2012). The CTT was established in the 1990s with the goal of bringing together RCT data on statin therapy and cholesterol intervention to reliably assess with greater statistical certainty the efficacy of statins in various populations. Alongside the significantly lower cost of generic statins, this kind of analysis, which suggested benefit at lower levels of risk than codified in clinical practice guidelines, created an appetite for widened availability and should, as such, also be considered one of the core driving forces behind NICE's decision to update their guidance. Indeed, it is important to note that whilst conducting their own separate analysis, NICE strategically drew on the work of these other groups to assist with certain aspects of their analysis and cost utility modelling and/or to contextualise their evaluations.

However, whilst CVD causes 45% of all deaths in Europe (British Heart Foundation 2016), the establishment of this widened threshold of primary prevention ran contrary to the fact that some alternative analysis suggests that the safety and efficacy of statins may be questionable (see Abramson et al., 2013). Indeed, there have been concerns about pharmaceutical industry funding of research forming the evidence base

[1] This timeline stretches back even further. In the most obvious sense, the development of the statins evidence base is now three decades old; whilst previous evaluations of this evidence prior to CG181 by NICE occurred in the mid-2000s. See: Appendix 1.

and hidden trial data (Godlee 2016) – which are fairly well-established criticisms of the industry generally (Lexchin et al., 2003). Additionally, there were concerns that those on NICE's purportedly independent Guideline Development Group (GDG) might have links to the pharmaceutical industry (Wise 2014). Concerns surrounding promoting healthy lifestyles, or what might be termed lifestylism (Hansen and Easthope 2007) which refers to the emphasis on the individual responsibility for ensuring health through the adoption of 'healthy' lifestyle practices (e.g. diet, exercise, smoking cessation), also encircled the guideline's publication – notions which exists uneasily alongside widening deployment of statins to lower thresholds of risk (Polak, 2017). Though lifestyle recommendations were also made in CG181, with NICE suggesting that lifestyle risk factors should be modified alongside and/or prior to the initiation of a statin, the centrality of statins to NICE's recommendation was problematised in both professional circles and in the mass media on the grounds that it did not do enough to challenge unhealthy lifestyle practices. And indeed, as noted above, it is certainly the case that without the pricing and secondary evidence developments directly encircling the drugs themselves, the primary prevention risk threshold would not have altered.

Upon publication, this guideline was greeted by a wide ranging and multifaceted medical professional and academic dispute as well as public scrutiny (with a heavy volume of newspaper reporting). The flames for the latest, and arguably unparalleled round in debate and contestation about statins, were stoked initially in the recesses of the BMJ in October 2013 prior to the publication of the guideline. It was here that the publication of two controversial pieces of analysis concerned with the safety and efficacy of statins (Abramson et al., 2013) and the legitimacy of the cholesterol hypothesis (Malhotra, 2013) set in motion a dispute which was thrust into the British professional and public consciousness upon announcement of NICE's decision to widen the availability of the drugs.

It is important for the analysis presented later in this thesis for the reader to understand that NICE's guideline and this wider debate were initially separate developments (see in detail the timeline of events presented in Appendix 1). The papers published in the BMJ by Abramson et al, (2013) and Malhotra (2013), as well as subsequent objections to these papers by other academics and professionals were conflated (inappropriately in some ways) with the decision-making by NICE. As noted, NICE conduct their own appraisals and evaluations of evidence for the guidelines they

produce, and indeed, the Abramson et al. and Malhotra papers were not initially direct critiques of NICE's guideline work (though do discuss and critique similar guidance issued in the USA, and the same authors in later publications/documents do directly address NICE guidance). However, the decision to widen the primary prevention threshold thrust the issues presented in the BMJ papers into the public realm in Britain. In a spiralling manner, controversy associated with the critiques presented in the BMJ papers then served simultaneously to exacerbate interest in the updated NICE guidance. Without the shared timeframe this arguably would not have happened, or at least not to the same extent. Criticisms of the statins RCT evidence base are also applicable necessarily to NICE's work because they rely on the same evidence to conduct their health economic evaluations. Whilst this thesis explores these issues in much more detail in later chapters, the overall point here is that these events (as set out in more detail Appendix 1), though initially disparate are directly and indirectly interconnected and mutually exacerbating and are, as such, all part of what should be considered a unified case. Indeed, other actors, such as British news outlets (who widely reported the case) engaged with it as a unified case.

i.2 Analysing CG181 Sociologically: Why and How

CG181 is very clearly an example of the widening definitional expansion of what is considered a medical problem. The conceptual framework of medicalisation, which suggests such definitional and treatment expansion to be inherently social phenomena, could, as such, be employed to analyse the case. The concept of medicalisation has a long history within medical sociology and is arguably this sub-field's most well-known and most significant contribution – reaching far beyond even the disciplinary borders of more general sociology, permeating wider social sciences, such as anthropology (Bell and Figert. 2012), and even boasts evidence of engagement within medicine itself as well as at a broader cultural/societal level (Williams et al., 2017). Medicalisation means to define a social problem using medical terms and potentially to use medical means to treat or manage this problem (Conrad, 2005: 3). However, the centrality of developments and debate implicating the drugs themselves necessitates a sociological approach that sufficiently positions drugs as analytic entities in and of themselves (Williams et al., 2011a). Medicalisation with its much broader concerns, arguably lacks this necessary

specificity of focus. With some exceptions (e.g. Gabe, 1990; Gabe and Lipshitz-Phillips, 1984), only a small amount of medical sociological work until quite recently within or beyond the confines of the conceptual framework of medicalisation has devoted attention to pharmaceuticals in this way. The lack of specific focus on pharmaceuticals and, indeed, the actors that are driving widening usage has led medical sociologists to propose the distinct but interrelated concept of pharmaceuticalisation (Abraham, 2010a; Williams et al., 2011a). Pharmaceuticalisation is a sociological process that is defined by Williams et al. (2011a: 711) as the "transformation of human conditions, capacities or capabilities into opportunities for pharmaceutical intervention". At the most fundamental level, this concept suggests that pharmaceuticals, such as statins, are inherently social phenomena. How so? As Williams et al., (2011a) show, *interests and influences* are inherent in the development, testing, regulation, and promotion of drugs. At the same time pharmaceutical science and the use of pharmaceuticals are also heavily *mediatised.* Moreover, pharmaceuticals are a crucial feature in a landscape of *competing scientific/governing/professional/lay powers attempting to implement differing versions of healthcare* (see Gabe et al., 2012; Light 1997); whilst also unique *moral positions and identities* are constructed relative to the prescription and use of pharmaceuticals by professionals and patients. As this thesis will discuss, all of these aspects (and further) are apparent in the case under study. Indeed, this thesis examines the core driving forces and how the interaction between actors shapes the extent to which pharmaceuticalisation in this case is occurring. Specifically, the thesis examines the influences of the pharmaceutical industry on NICE's evaluative action; the coverage and framing of the case by the print news medium; and the prescribing behaviours and decision-making of GPs. To do this, this thesis deploys the work of Williams et al. (2011a) who have set out a conceptualisation of pharmaceuticalisation rooted in the notion of the pharmaceutical regime. This is a network of actors, sub-processes, organisations, cognitive structures and beyond that in various combinations and relationships facilitates (or constrains) the development and deployment of pharmaceuticals. The pharmaceutical regime suggests that to understand the widening use of medicines we need to look at the dynamic relationships, connections and networks that exists between organisations, actors and cognitive aspects. It directs analysis, as such, to exploration of driving forces and the extent of pharmaceuticalisation. To understand if, how and to what extent pharmaceuticalisation is occurring, analysis needs to look at movements in the

regime that open up opportunities for deployment and if and how this and other factors shape the manner these opportunities are understood, received and utilised.

Considering the definition of pharmaceuticalisation above, the prevention of CVD is arguably one of the archetypal examples of pharmaceuticalisation both in terms of constructing a condition/risk factor to treat (cholesterol) with drugs and subsequently the progressive widening of treatment thresholds where drugs can be used (Abraham, 2010b: 290). The case under study in this thesis is a continuation of this latter aspect in the sense that pharmaceuticalisation has already occurred to a certain level, but that further and widening pharmaceuticalisation appears to be occurring. However, though pharmaceuticalisation can occur at the same time as medicalisation, and in this sense may be partially contingent, it may also occur without any medicalisation. This thesis suggests that pharmaceuticalisation needs to thought of as operating on a spectrum. On the one end is an unmedicalised pharmaceuticalisation that operates largely beyond traditional medical spheres and/or without any transition in or application of a diagnostic category. On the other end of the spectrum is a more medicalised pharmaceuticalisation where medicalisation and pharmaceuticalisation are occurring together. The case under study can be thought of as a case of medicalised pharmaceuticalisation. This is in terms of pharmaceuticalisation occurring within traditional medical spheres and where new or widening diagnostic categories are interlinked with widening pharmaceutical deployment. Where a more medicalised form of pharmaceuticalisation appears to be occurring the decision to utilise the conceptual parameters of pharmaceuticalisation rather than medicalisation will reflect the primacy of pharmaceuticals within diagnostic transitions (or even where developments surrounding pharmaceuticals can be shown potentially to drive medicalisation). This is because the greater intensity and specificity of focus of pharmaceuticalisation on pharmaceuticals themselves and the actors which shape their deployment/consumption necessarily possesses greater analytic specificity than medicalisation (Coveney et al., 2011: 387; Williams et al., 2017).

In the case under study in this thesis, though the widening of diagnostic criteria is occurring, and as such, medicalisation is also occurring, the centrality of the drugs within the case suggests that pharmaceuticalisation is likely to have the most explanatory power due to its greater conceptual specificity. Whilst care needs to be taken not to inappropriately privilege or restrict analytical gaze to pharmaceuticals at the expense of the broader therapeutic landscape, it is also the case that appropriately appreciating

broader therapeutic landscapes can tell medical sociologists much about pharmaceuticalisation and its extent (Pollock and Jones, 2015). These are important aspects that will be given much more attention in Chapter One – but considering these initial discussions, and particularly the centrality of the notion of the pharmaceutical regime, the overarching question that this thesis investigates is: *To what degree is the further pharmaceuticalisation of the primary prevention of CVD occurring and what are the driving forces?* To answer this overarching question, as noted, above the thesis focuses on several actors and subprocesses of salience within the case – namely NICE (and its relationship with the pharmaceutical industry), the print news medium and GPs. The thesis, as such, examines three sub-questions to assess if these actors are driving widening pharmaceuticalisation and their role in the extent to which it is occurring. These actors were selected because, first NICE (potentially reflecting relationships with the pharmaceutical industry) was the actor that opened up the potential for widening deployment of statins. The print news medium heavily reported the case, can foster pharmaceuticalisation on a rhetorical level, and can figure within patient and public understandings of drugs. And GPs were selected because they are the gatekeepers to the use of statins and their role in decision-making about drugs retains significance. The thesis as such explores:

1. In what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?

2. How did the UK print news medium present and portray the potential widening usage of statins?

3. How do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk?

Before expanding these theoretical discussions and empirically justifying the above research questions in Chapters One and Two respectively, this introduction needs to explore some further general issues surrounding statins in the prevention of CVD, as well as NICE's nature, its processes and the role of its guidelines.

i.3 Statins and the Prevention of Cardiovascular Disease

CVD is a group of diseases of the heart and circulation (e.g. coronary heart disease, heart attack, angina, stroke) that all seem to be caused by build-up of fatty deposits known as atheroma (which includes lipids such as cholesterol) within artery walls. CVD is of significant interest to governments both because it is the leading cause of death globally (Unruh et al., 2016: 797), with 180,000 deaths from CVD occurring in England and Wales alone in 2010, and economically because significant proportions of healthcare budgets are spent on CVD care – in England, for example, CVD had cost the NHS more than £7000 million by the beginning of the current decade (NICE, 2014a: 5). The class of pharmaceuticals named HMG-CoA reductase inhibitors, or as they are more widely known, statins, are utilised to try to prevent CVD. An enormously profitable class of drugs whilst under patent after their emergence in the 1980s, the drugs attempt to prevent CVD, or in other words, CVD is pharmaceuticalised, in two ways. First, they may be used in primary prevention to prevent an event occurring in individuals defined as at risk. They may also be deployed in the secondary prevention of CVD where an individual has already had a cardiovascular event (such as a heart attack or a stroke) with the aim of preventing further disease complication or development (Unruh et al., 2016: 797-798). Both aspects were implicated in CG181. However, the use of the drugs in secondary prevention is less debated than in primary prevention – and, indeed, though evaluations were made by NICE in CG181 to assess the type and dose of statin that should be utilised in secondary prevention, the recommendation that everyone who has existing CVD begin taking a statin did not change in any radical manner. Statins lower levels of cholesterol, aiming to reduce low-density lipoprotein (LDL) cholesterol ('bad cholesterol'), an important risk factor for CVD. NICE guidance aims for a 40% reduction in non-HDL cholesterol level after three months of treatment (NICE, 2014a: 9) with ideal levels of 4 millimoles per litre (mmol/L) or less of non-HDL cholesterol. However, a complex picture of risk factors is additionally taken into account within risk calculation by tools such as QRISK2 (a cardiovascular disease prediction algorithm). CVD is strongly associated with age, mostly occurring in people older than 50. QRISK2 risk calculation also takes into account sex, family history, ethnicity, modifiable lifestyle risk factors such as smoking, blood pressure, and geographical factors such as whether an individual lives in the north or south of England (NCGC, 2014: 5). These risk factors are in part bound up together. For example, modifiable lifestyle risk factors contribute to cholesterol levels in most cases of high cholesterol (or hypercholesterolemia) (although there is an apparently

genetic variation called familial hypercholesterolemia), and broadly statins can be thought of as 'risk reducers' that are prescribed as a result of overall risk calculation and strategy. When looking at these factors, if the risk profile of an individual is 10% over ten years, this means that in the next ten years from a group of 100 similar people ten would have, for example, a heart attack or stroke. Supposedly, however, if all of those 100 took a statin four of those ten would be prevented from having that heart attack or stroke (NICE, 2014c). In CG181, NICE recommend atorvastatin 20mg as the particular type and dosage of statin that should be deployed to patients. This was because NICE's evaluations of existing evidence suggested that it was the best combination of dose (meaning supposedly lower chances of side effects) alongside greatest cholesterol reduction intensity. When considering these aspects in relation to cost, atorvastatin was considered by NICE to have the greatest clinical and cost-effectiveness.

As noted in the first section of this thesis, statins coexist in risk reduction, often uneasily, with lifestyle change, and in secondary prevention, with surgery (Pollock and Jones, 2015). Particularly in primary prevention, the emphasis is on joint management through pharmaceuticals and lifestyle together – though some argue the majority of reduction can be achieved by lifestyle changes alone (Abramson, et al., 2013). Statins are, of course, not the only drugs that feature in the prevention of CVD. Aspirin is used to prevent blood clots and a variety of blood pressure medications also exist. However, CG181 was concerned with making recommendations pertaining to blood lipids (and other guidance exists, such as CG127, produced by NICE on high blood pressure – see NCGC, 2011).

i.4 NICE: The Fourth Hurdle

NICE was introduced in 1999 under the New Labour government as part of broader developments in the UK and elsewhere concerned with disparities in care (or the so-called postcode lottery in healthcare access/delivery), modernisation, clinical governance, and particularly the evidence based medicine (EBM) movement (Harrison and Checkland, 2009: 126-127). The guiding rational behind EBM is that medical practice should be based on the effectiveness of interventions as established by the best quality evidence – moving away from individualised professional knowledge and clinical experience as guiding rationales. Medical knowledge is ranked into a hierarchy of

evidence with RCTs and systematic reviews at the top of this hierarchy (Knaapen, 2014: 823-824). EBM is also predicated on the notion that individual clinicians are insufficiently skilled or lack the necessary time to appropriately assess and incorporate such an approach without external guidance (Harrison and Wood, 2000). In these ways, clinical guidelines (in both the UK and elsewhere) hold appeal for governments as a tool for the rationing of increasingly scarce resources and addressing disparities in care, whilst they are also a clear representation of transitions away from reliance on individual authority, experience, discretion and decision-making towards standardisation, transparency, and accountability (Carlsen, 2010). The dominant model of EBM that has emerged has been termed scientific bureaucratic medicine (SBM) (Harrison et al., 2002).

The introduction of NICE created a 'fourth hurdle' body in the regulation of pharmaceuticals, adding an extra layer of cost-effectiveness evaluation on top of the regulation of quality, efficacy and safety by other drug regulatory bodies (Timmins et al., 2016). Ostensibly NICE represents transparency, accountability and rationality based on rigorous appraisal of evidence, and thus crowding out arbitrary and unscientific allocation of resources. This takes the form of clinical and economic evaluation of whether one intervention can be justified on the basis of expected costs over another or decision to do nothing in terms of health impacts. In other words, how well does treatment work relative to how much it costs the NHS? Health effects are expressed by quality adjusted life years (QALYs) which are equal to one year of life in perfect health. NICE declares an intervention cost-effective if an intervention is £20,000 or below per QALY (although this is flexible in some cases up to £30,000) expressed by the incremental cost-effectiveness ratio (ICER) a statistic which summaries cost-effectiveness. NICE produce both technology appraisals of the cost-effectiveness of interventions as well as guidance for a wide variety of topics using this ICER. Though they produce evaluations of technologies beyond pharmaceuticals, cost-effectiveness evaluations of pharmaceuticals are prominent and receive the most public attention (Brown and Calnan, 2010: 65).

The focus of this thesis is on the guidelines that NICE produce, although it is worth noting that there is some overlap between guidelines and technology appraisals. Indeed, in the case of CG181, this guideline updated and displaced both prior guidance and prior technology appraisals. Generally, guideline topics are referred to NICE by NHS England, except for cases where an existing guideline is being updated – which was the case for CG181. NICE begin reviewing their guidelines generally three years after publication and

the guideline development process can take two to three years. This involves collecting and collating all relevant information (including importantly any new evidence) and discussing the potential need for an update to an existing guideline with previous GDG members and stakeholders within the relevant disease area. NICE then decide if a full or partial update is required, if at all. Importantly, NICE do place emphasis on stability due to guidelines being hard to implement if there are constant changes to what is considered best clinical practice. However, CG181 was a relatively early full update owing particularly to changes in the costing of statins as more of the drug class became generic (including atorvastatin) since the publication of the predecessor to CG181. This meant a new scope was required. The scope establishes the clinical need, areas covered and clinical intent. This is then circulated to stakeholders. Stakeholders are organisations with an interest in or whom the guidance will impact – such as those whose care or practice is directly affected by the guideline and also includes the public sector, the third sector and commercial industries and manufacturers) and also involves the chair of the new GDG (with the rest of the GDG appointed later). From this point, the process is the same as that for any other new guideline. The National Clinical Guideline Centre (NCGC), a body who are commissioned to do the technical work (such as evidence reviews and associated health economic modelling) for NICE guidelines, first produce early draft review questions based on the issues identified in the scope. The newly appointed GDG then agree the suitability of the review questions, consider the evidence and analysis presented by the NCGC (and can ask for further evidence to be included or analysis conducted as they consider relevant), and then the GDG formulate the actual recommendations of the guideline. The GDG is comprised largely of specialists in the topic area but will include GPs and pharmacists, as well as patient and/or carer representation. A draft guideline is then produced and stakeholders again have opportunity to comment, this time on the full draft guidance. Commentary from stakeholders may then be incorporated before the final guideline is signed off by NICE's senior management, published and disseminated.[2]

i.5 Structure of the Thesis

[2] The guideline development process detailed above has changed in the years since the publication of CG181 but this was the process at the time CG181 was developed.

This introduction has outlined the parameters of the case under examination in this thesis and has offered some insight into the theoretical contours and empirical intentions. Building out of this, Chapter One takes as its main task the establishment of the conceptual parameters of pharmaceuticalisation. In doing this, Chapter One offers an analytical overview of the history of the concept of medicalisation as occurring over three phases. This endeavour allows the thesis to chart the development of thought on medicalisation in medical sociology that has ultimately resulted in the development of the contingent but also distinct concept of pharmaceuticalisation. This approach also helps to situate the distinction between medicalised and unmedicalised pharmaceuticalisation. Ultimately, the aim of this Chapter is to establish the utility and appropriateness of pharmaceuticalisation in the analysis of the case of CG181, and in particular, the pharmaceutical regime approach advocated by Williams et al. (2011a). It also explores how this approach features in and shapes the overarching research question of this thesis.

Chapter Two concerns itself with a more analytically and empirically oriented literature review of the sociology of pharmaceuticals. The chapter, as such, establishes the actors and relationships within the pharmaceutical regime of relevance in the case under study and the gaps in the empirical knowledge base that the thesis proposes to fill. These discussions are organised using the analytical dimensions established by Williams et al. (2011a) and focuses on regulators, the print news medium, and professionals and patients.

Chapter Three presents methodological discussions. It outlines the philosophical approach, discusses data collection, and outlines and justifies the specific methods and the approaches to analysing the data as presented in Chapters Four, Five and Six. The methodology employed in this thesis is multiple methods qualitative in nature.

Chapter Four, examines NICE's unique role as a fourth hurdle regulatory body within the process of pharmaceuticalisation, with a focus on the creation of the opportunity for the deployment of pharmaceuticals. In particular it examines how the influences of (and associated dependency on) the pharmaceutical industry serves to widen the use of even generic statins. Drawing on aspects of STS, this chapter examines the mechanisms built into the statins evidence base that exaggerate the efficacy and safety of the drugs, NICE's uniquely vulnerable position as a fourth hurdle regulatory body, whilst also considering the extent of the lack of independence of NICE's GDG. It is

argued that in these ways the influences of the pharmaceutical industry on the decision to widen the primary prevention threshold are apparent. This chapter is based on semi-structured interviews with GDG members and staff from NICE and the National Clinical Guideline Centre (NCGC) in combination with analysis of relevant documents. It explores the following research question: *in what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?*

Chapter Five considers the role of the print news medium as a driving force of pharmaceuticalisation and the impacts on its extent. This chapter takes the form of a media analysis, looking at the portrayals by the British print news medium of this case over two years. It is argued that this coverage was oscillating and controversy oriented. This chapter necessarily considers how the professional practices of journalists, particularly relating to newsworthiness, reflect but also shape and exacerbate uncertainty about the drugs, whilst at the same time creating a sense of unending deployment of pharmaceuticals. It examines the following research question: *how did the UK print news medium present and portray the potential widening usage of statins?*

In the final chapter, Chapter Six, the thesis turns to examine the role of General Practitioners (GPs). It is argued here that medical professionals have been decentred from analysis of medicalisation and, as such, pharmaceuticalisation. This, however, is problematic when considering the evidence of consumerism within healthcare, the unique professional identity of GPs and resistance to guidelines, and, indeed, what can be thought of as the distributed nature of medical decision-making. Based on twenty semi-structured interviews with GPs, this chapter considers their approaches to advising and facilitating the decision-making of patients. It considers if and how GPs approach decision-making with patients about the ≥10% primary prevention threshold, finding a stark disparateness between GPs. It ruminates, as such, on the pharmaceuticalised orientations of GPs, proposing a typology of prescribing behaviour, and the impacts this might have on the extent of pharmaceuticalisation occurring from the approaches, understandings and behaviours of professionals. It explores the following research question: *how do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk?*

The final chapter, Chapter Seven reviews the specific contributions to knowledge and looks in a more totalising way across the data to assess driving forces and the degree

of pharmaceuticalisation apparent in the case as an entirety, utilising the notion of the pharmaceutical regime to do so. It also considers the limitations of the research and opportunities for further research.

Chapter One: Conceptual Matters – Tracing the Intellectual Heritage of Pharmaceuticalisation

1.1 Introduction

The previous introductory chapter set out the case under study in this thesis and presented a rudimentary discussion of the theoretical and empirical parameters of the project, including introducing the concept of pharmaceuticalisation. It was briefly explained that pharmaceuticalisation is the primary conceptual lens through which this thesis analytically engages with NICE's decision to lower the primary prevention threshold for CVD from ≥20% risk over ten years to ≥10% risk over ten years, and in the process dramatically expanding the potential numbers of people eligible to take a statin.

This first substantive chapter turns now to a fuller discussion of the intellectual history underpinning the concept of pharmaceuticalisation and ultimately a thorough discussion and justification for the conceptual framework that is adopted by this thesis. In this regard, this chapter presents an overview of the history of 'medicalisation studies' – with the primary aim of highlighting the complex sociocultural assemblages and the interweaved development of sociological thought that has culminated in the conceptualisation by medical sociologists of the process of pharmaceuticalisation. In basic terms this chapter argues that there have been three phases of what we might think of as medicalisation theorising or "medicalisation studies". 'Phase One' or the 'The Orthodox Phase' (Williams 2001) which is defined by a radical critique of medicine's role in the management of deviance. 'Phase Two', or 'Beyond Orthodoxy and Biophysical Reality', which has not necessarily been labelled in the literature, though has been identified (see particularly Lupton, 1997; Williams, 2001; 2003), is comprised of a thornier/contested post-orthodox position where the medicalisation of all aspects of life rather than deviance is the key concern and where Foucauldian scholarship is influential. And finally, what this chapter calls 'Phase Three', 'Contestation and Contingency'. This phase is defined by a fundamental (re)evaluation of the concept and its explanatory power. Broadly speaking the debate moves through the first two phases as scholarship observes the initial cases of the medicalisation of deviant behaviour broaden into the medicalisation of everyday life alongside an increasingly contested healthcare landscape. The study of medicalisation also arguably becomes less overtly critical and

problematising over time. Though analysis of the medicalisation of everyday life continues within the third phase (and indeed aspects of criticism of the impacts of the process), the driving forces of medicalisation come under increased scrutiny and, for the first time, alternate concepts emerge that attempt to move beyond medicalisation or attempt to capture greater analytical specificity. The purpose of tracing the history of medicalisation is to situate its relationship with the more recent concept of pharmaceuticalisation and to ultimately defend the choice of pharmaceuticalisation as the conceptual framework adopted by this thesis (whilst acknowledging a certain level of contingency in the case under study which is a more medicalised form of pharmaceuticalisation).

1.2 Phase One: The Orthodox Thesis

Medicalisation has been one of the major conceptual and empirical interests in medical sociology since the late 1960s. It is defined as the process whereby human problems come to be regarded and treated as medical conditions (Conrad, 2007). In other words, it occurs when a medical frame is utilised to understand a particular problem. Debates surrounding medicalisation have a long history and charting a clear thought narrative and linearity is challenging because of the sheer diversity of thinkers who have contributed to the conceptual development of medicalisation. Whilst social constructionism, particularly in the extensive work of Peter Conrad (1975; 1979; 1992; 2005; 2007), has been key in defining the contours of the process, and as such, the conceptual endeavour attached to medicalisation, others including Illich (1975) (a sort of anarchic-libertarian) Marxists (Navarro, 1980; Taussig, 1980), feminists (Oakley, 1984; Reissman, 1989), Foucauldian-influenced (Armstrong, 1995), and postmodernists (Fox, 1999) have also weighed in on the debate. Partly reflecting this complex and variable sociological debate and contest, but also necessarily changes in the composition of medicine, and, indeed, wider society itself, it is vital to acknowledge that medicalisation has reshaped throughout its conceptual lifespan. Hence the development of the argument in this chapter that we might break down its intellectual history into three different periods of thought. First, what might be thought of as the 'orthodox' thesis (as Lupton, 1997 and Williams, 2001 have labelled it).

To appropriately situate the orthodox position, it is first necessary to discuss the foundations of the sociological study of deviance – which lie as far back as the work of Emile Durkheim (1895/1933). The ability to define and control deviance was a highly salient issue in the orthodox phase. Though not in the terms of medicalisation, and with medicine only, relatively speaking, in its professional infancy, Durkheim suggested that as societies mature from simple to complex that deviance management transitions from repressive to restitutive, which results not only in a change in how deviance is controlled but also how it is thought of and defined (Conrad and Schneider, 1980). Later, Parsons (1951), in his now classic functionalist account of the sick role, highlighted how the separation of intentional deviance (criminal) and unintentional deviance (sickness) were necessary with regard to appropriate disciplinary or treatment mechanisms. Criminals are punished, with an end goal of reshaping behaviour in line with convention, whilst sick people are treated with an end goal of removing the illness barriers to convention (Conrad and Schneider, 1980). For those that are ill, the existence of a sick role legitimises the 'deviant' behaviour of being sick, suggested Parsons. For society, this sick role helps to manage the potentially damaging and disruptive nature of sickness. The sick role has four parts, comprised of two accepted exemptions and two obligations. The sick individual (1) is exempt from normal responsibilities for the period of illness, and (2) is not held to be personally responsible for their illness. However, the individual (1) must understand that illness is an undesirable state and (2) that they are obligated to co-operate with relevant medical professionals to aid in their recovering to normal functioning.

Whilst hinting here at a social control dynamic at play, Parsons focused on the continuing functioning of society (and thus *necessity* of the sick role) rather than social critique – and as such it was left to subsequent scholars of a more critical persuasion to problematise medical social control and the notion that an objective medical reality exists independently from and outside of social relations (Williams 2003: 9-28). Although as Durkheim's and Parsons' observations hint at, medicine has long functioned as an agent of social control particularly through restoring individuals to normal social functioning, the necessity of this social critique was judged to reflect that for the first time medicine's sphere of social control was widening into potentially troubling grounds (Conrad and Schneider, 1980). Particularly because, as Conrad and Schneider (1980: 8) state, "the

greatest social control power comes from having the authority to define certain behaviours, persons, and things." And thus the concept of medicalisation was born.

The 'orthodox' thesis is comprised primarily of the scholarship of the 1970s and early 1980s, within which the roots of initial sociological conceptual interest in medicalisation are apparent. Taking a critical and problematising stance, scholars explored questions surrounding the reasoning and legitimacy of medicine's growth into an institution of social control, the power of medical professionals, and the institutional ability to define and control 'deviant' behaviours previously not defined within a medical frame (Conrad, 1975; Conrad and Schneider, 1980; Illich, 1975; Zola, 1972). At its most fundamental, medicalisation during this period of thought was conceived of particularly in terms of this third element, as occurring when a medical frame or definition is applied to understand or manage a particular issue (Conrad, 1992). Now very famously, Conrad and Schneider (1980) (see also Conrad, 1992) conceptualised medicalisation as (potentially) occurring across three distinct levels that may or may not involve professionals: the conceptual (use of medical vocabulary with few professionals involved), the institutional (organisational adoption of a medical approach often with non-medical personnel conducting the routine work), and the interactional (resulting from the doctor-patient relationship where physicians are necessarily involved). As Conrad (1992) reflects, this levelled distinction is important particularly in terms of locating what it is that the orthodox thesis can be said to be conceptualising, particularly in relation to the medical profession. The medicalisation critique was not necessarily a critique of the medical profession or their expansionist tendencies, despite some confusion about this over time (e.g. Strong, 1979). Though acknowledging the medical profession are very important, particularly in interactional medicalisation, and indeed often implement medical social control, medicalisation during this stage of thought as a concept is most concerned with definitional ability and subsequent application of a medical frame which can include the medical profession but may not.

Reflecting the importance of social constructionism to the conceptual development of medicalisation (Conrad, 1975; Conrad and Schneider, 1980; Zola, 1972), a key underpinning aspect in the orthodox account is that disease or illness are only recognised as such if they are regarded as an aberration from normal by a culture (Conrad and Schneider 1980). In other words, calling something an illness has impacts separate from any biological underpinning and may, as such, reflect the influence of

powerful social forces (Freidson, 1970; Zola, 1972), which, as noted, orthodox theorists sought to challenge, seeing medicalisation as a largely problematic process. In particular this was because, though medicine portrayed itself as supposedly objective and neutral, orthodox critics argued that medicine actually served to reinforce the moral order of society (Conrad and Schneider, 1980). Thus, the orthodox medicalisation thesis had at its core a concern with 'deviant' behaviours (such as, as highlighted by Conrad and Schneider (1980) alcoholism, childhood delinquency, child abuse, and hyperactivity, and for a period of time, homosexuality), and the shift in spheres of control of such phenomena from religion and law to medicine – in other words, from 'badness to sickness' (Conrad and Schneider, 1980). In essence, sociologists here desired to cast light on how certain issues or categories come to be defined, potentially illegitimately, as within the locus of medical control and treatment (Spector and Kitsuse, 1977). The reverse process of demedicalisation was also seen as possible (for example, homosexuality) but generally this was thought of as occurring sporadically.

The orthodox thesis emerged from the radical and emancipatory culture of the late 1960s and early 1970s, which, for a short time turned the world upside down, including medicine (Gabe et al., 2006). Indeed, Gerhardt (1989) suggested that medical sociologists, inspired and provoked by student revolution and demonstration in the late 1960s, began to see injustice and inequality as a cornerstone of academic concern and applied this to a critique of medicine. Beyond the disciplinary boundaries of sociology, in a similar period, certain radical critiques of medical activity were also emerging. The anti-psychiatry movement was particularly influential, where it was argued forcefully and critically that a dominant psychiatric lens was increasingly classifying normal every day behaviours and feelings into illness (Laing, 1960; 1961; Szasz, 1961 – see also Crossley, 1998). With this as backdrop, Zola (1972) and Illich (1975) most famously espouse what we now can think of as the critical and problematising tendencies of the orthodox medicalisation thesis. Zola suggested that an objective, scientific, supposedly morally neutral medicine was becoming the repository of truth, replacing or incorporating religion and law as the source of judgment. Zola (1972) suggested that the process whereby medicine was becoming this repository of truth and displacing other institutions of social control is an often low-key and potentially insidious process. In essence, the attachment of the labels 'healthy' and 'ill' becomes increasingly relevant to ever further elements of human life. Illich (1975) meanwhile wrote of the institution of

medicine as a nemesis of and threat to health. He saw industrial society as expropriating personal responsibility for health and as removing autonomy from the individual. As this radical, emancipatory context/time indicates, there was also emergent Marxist and feminist scholarship concerned with medicalisation. Taussig (1980) and particularly Navarro (1975; 1980) took issue with much of the framing of the social constructionist medicalisation critique and also the work of Illich (1975), suggesting that it had neglected to sufficiently engage with the role medicine played in reproducing capitalist power relations in society. Moreover, feminists (Ehrenreich and English, 1974; Oakley, 1984) have argued medicine to be a patriarchal institution that has used illness and disease definitions to subjugate and reinforce existing inequality between men and women – by emphasising female 'weakness' and 'illness susceptibility', as well as seizing control of areas such as pregnancy/childbirth.

Overall, the initial or 'orthodox' thesis (Lupton, 1997; Williams, 2003) of medicalisation had at its core a concern with the growing definitional and institutional power of medicine over matters of 'deviance', much of it seen as troubling and problematic. Scholars in this era of thought (roughly encompassing the time from the late 1960s to the early 1980s) promoted an inherently problematising, radical and emancipatory critique of medicine and medical professionals with a focus on restoring individual autonomy, challenging institutional definitional power and, to an associated degree, professional power. However, the concept did not (and could not) remain static.

1.3 Phase Two: Beyond Orthodoxy and Biophysical Reality

Beyond the 'orthodox' medicalisation thesis developed a thornier and more nuanced conceptualisation of medicalisation (Ballard and Elston, 2005), which can be said to represent social developments and sociological scholarship post the mid-1980s. This phase has been delineated in the work of Williams (2001; 2003) Lupton (1997) and the core distinction between this phase and earlier scholarship, as Conrad (1992) has acknowledged, is that medicalisation (and the sociological analysis of) increasingly included natural life processes as well as deviant behaviour. Intertwined with this, the presence of an applied Foucauldian (1973; 1979) critique also grew in salience. Whilst Foucault's initial work emerged at the same time as the orthodox scholars such as Illich and Zola, its impacts on medicalisation studies itself are perhaps more keenly felt slightly

later as a result of application by others (e.g. Armstrong, 1995). As Williams (2001: 147), states, the emergence of this more thorough critique seemed to strip away, or at least critically question, "former acknowledgment or acceptance of an underlying 'natural' or 'biophysical' reality…" which had always existed in the orthodox thesis. The medicalisation of everyday life beyond matters traditionally considered deviance, or the medicalisation of everyday life, and the problematizing of health as well as illness arose from a developing surveillance medicine (Armstrong, 1995: 395), where "the dissolution of the distinct clinical categories of healthy and illness… [establish] everyone within its network of visibility." In other words, with an increasing focus on lifestyle as impacting health and preventative medicine, 'health' as a category was inherently problematised – with bodies both healthy and ill simultaneously (Hughes 1994). Challenges from a variety of actors and angles to medical professional authority also began to emerge in this period. Healthcare as a landscape became increasingly contested and the balance shifted – a variety of actors that might be thought of as countervailing powers (Light, 1991; 1995) increasingly became important. Patients, for example, transitioned (at least to some degree) to consumers (Barker, 2008; Kroll-Smith and Floyd, 1997) with associated lessening knowledge disparities between patients/consumers and medical professionals. Indeed, it was argued that medical 'de-professionalisation' might be occurring (Haug, 1976), removing the high degree of clinical autonomy and the ability to self-regulate (Harrison, 2009; Harrison and Ahmad, 2000), reflecting broader trends of rationalisation and rejection of paternalistic professional control. Though the medical profession retained its grasp partially on a privileged position and autonomy, the golden age of doctoring (McKinlay and Marceau, 2002) was seemingly over (see Chapter Two for further on this debate).

In these ways medicalisation seemingly no longer reflected solely or at least primarily the role of the institution of medicine and medical professionals, but also, for example, how patients might be mobilised to act to promote awareness or progress in understandings of their condition (Figert, 1995), and importantly how other third party actors, such as the pharmaceutical industry might contribute to medicalisation (Conrad, 2007). The use of pharmaceuticals is certainly discussed as a part of the medicalisation puzzle in 'classic' medicalisation works (see Conrad, 1975; Conrad and Schneider, 1980)). However, related actors such as the pharmaceutical industry, were always of secondary analytical importance to the institution of medicine where they were

discussed (Conrad, 2007). At the same time, contrary to the orthodox thesis, there was a growing acceptance of the potential positives of medicalisation, particularly advances which had improved or saved the lives of patients (Kelly and Field, 1994).

As noted above, the developing 'thorniness' of the medicalisation debate at this time was perhaps most the result of the fact that Foucauldian scholarship was growing in importance in Anglophone medical sociology. Lupton (1997) provides a useful overview of the influence of Foucauldian thought on the conceptual understanding of medicalisation. Whilst Foucault himself did not speak in the language of medicalisation, above all else his scholarship influenced a realignment in conceptual understandings of power, which was in itself important for understandings of medicalisation. Whereas the institution of medicine had been lambasted and castigated for wielding a repressive power (Illich, 1975), Foucault (1973; 1979) suggested that power is a complex phenomenon that is not reducible to only one entity or set of actors. Rather it emerges and is propagated by a variety of social actors and institutions, and may be productive and positive, rather than solely repressive. Medicine is part of a wider system of disciplinary techniques in an expanding apparatus of control that are oriented towards moral regulation rather than more overt forms of violence or coercion – what he terms a panoptic system of surveillance. Power cannot be reduced to dualisms of state versus people, or a powerful medical profession versus patients/lay knowledges (Lupton 1995). Power does not simply constrain or dominate patients/citizens it works to shape/produce/make-up individuals who have a regulated autonomy/freedom. As such, as Lupton (1997: 99) observes, Foucauldian scholars see medicine as a disciplinary power. This scholarships suggests that medicine provides systems of knowledge/practice whereby we not only understand the body but that also shapes the way in which we experience it. Power relations "work in and through the human body" (Lupton, 1995: 5). In this sense, Foucauldian scholarship suggests that there is no biophysical or authentic body that exists beyond medical discourse – or in other words that the body is constructed through discourse and the clinical gaze of health professionals and other actors/entities (Lupton, 1997).

In the final decades of the twentieth century power/control became even further entrenched at the level of the individual, further widening the medical realm into every day aspects and spaces. Strategies for the individual to affect their own bodies in the name of health, or technologies of the self, become increasingly important (Rose, 1996:

1999). As such, this "fundamental remapping of the space of illness" and "the problematisation of the normal" (Armstrong, 1995: 395) occurring in the latter stages of the second half of the twentieth century, resulted in the distinction between health and illness taking on a new form in terms of a focus on prevention and the relationship between lifestyle and *risk* of disease. In other words, new truths and realities occurring at the site of and through the body have been opened up, and thus how we experience health and (potential) illness. In particular there was a greater focus on lifestyle choice in determining disease. This shift might be termed healthism (Crawford, 1980; 2006) or lifestylism (Hansen and Easthope, 2007) and central to this focus is a strong moral component/imperative to take responsibility for one's own health, or responsibilisation (Crawford, 2006; Rose, 1999). As Hansen and Easthope (2007: 56) state, "[u]nlike the traditional medical model of disease where understandings are limited to physical aberrations from 'normal', the focus on risk, future disease, individual behaviours mean that under a lifestyle approach almost every aspect of living is seen as health related." It is in this broader context of the medicalisation of everyday life that medical interest in cholesterol, lifestyle, CVD risk and the prevention of future CVD disease (despite lack of apparent illness) emerges (Greene, 2007). This way of thinking about disease causation emerged out of the broader influences of epidemiological multivariate analysis of chronic disease determinants, public health and government promotional activities, as well as increasing focus on risk in society.

However, one issue of conceptual significance here, particularly given the complexity of the debate, is what exactly medicalisation is, consists of or amounts to in this 'Phase Two' of medicalisation studies. Whilst Foucauldian scholarship is not necessarily couched in the terms of medicalisation[3], others such as Lupton (1997) highlight the importance of this type of scholarship for understandings of medicalisation. As Lupton (1997: 107) reflects, "from the Foucauldian perspective there are a number of inconsistencies and paradoxes that may be identified in the orthodox medicalisation critique." For example, in arguing anti-medicalisation, at least in the terms of lay people (re)gaining 'control' and autonomy over matters of health and illness, this may contradictorily expand medicalisation through encouraging and facilitating the development of medical knowledge in lay populations. Additionally, encouraging

[3] Armstrong in his 1995 paper only mentions the term once, and as noted Foucault did not use the term.

individuals to take responsibility for their health, through, for example, making preventative lifestyle choices such as those relating to diet, exercise, stress management, and/or not smoking, also seems to facilitate the expansion of the medical realm into everyday life. Equally, how can we de-medicalise society through the removal of medical professional/institutional power if power is so diffuse and health a social value? For example, health promotional activities are the result of complex processes of governmentality, (another key Foucauldian upon which the diffuseness of power relations is predicated). Power relations emerge from all areas of social life, and importantly includes self-governance and an 'imperative of health' (Lupton, 1995) following the internalisation of certain truths. As Lupton (1995: 9-10) states:

"In the interests of health one is largely self-policed and no force is necessary. Individuals are rarely incarcerated or fined for their failure to conform; however, they are punished through the mechanisms of self-surveillance, evoking feelings of guilt, anxiety and repulsion towards the self."

If and how this shift can be conceptually located relevant to medicalisation is a key issue in 'Phase Two'. Conrad (1992), for example, argues that categorising health behaviours as risks for disease is not medicalisation. He suggests that the term 'healthicisation' is a more accurate conceptualisation. Indeed, Conrad (1992: 223) argues, with "medicalisation, medical definitions and treatments are offered for previous social problems or natural events; with healthicisation, behavioral and social definitions are advanced for previously biomedically defined events (e.g. heart disease)." In other words, Conrad suggests that there is a distinction between biomedical causation and interventions, and lifestyle/behavior causation and intervention. "One turns the moral into the medical, the other turns health into the moral", Conrad (1992: 223) states.

However, this division might be argued to be an artificial and naïve one. Whilst a growing focus on the 'lifestyle model of disease' alongside the theory of specific etiology (to say nothing either about the emerging genetic model of causation) moves beyond the traditionally understood medical model, this can still be argued to advance and reflect medicalisation. It may be that "despite claims of being an alternative to traditional medical approaches to disease [lifestyle explanations] actually reflect a continuation and expansion of modernist and social-based medical explanation" (Hansen and Easthope, 2007: 52). Or as Turner (1992: 18) argued, "[t]he growing importance of preventative

medicine and the use of the concept of lifestyle to regulate… have meant that there is a *major intervention of medical ideas and practice into every day life* – through diet, exercise anti-smoking norms [and beyond]" (emphasis added). In this way, the lifestyle causation model of disease was argued by some to expand medicalisation in terms of increasing the sphere of medical intervention and concern to include healthy people (who might be thought of as pre-sick, and as such the possessors of 'virtual disease') (Hughes, 1994). Indeed, Crawford (1980) in writing on 'healthism' directly tied this concept to the medicalisation of everyday life. Meanwhile, Lowenberg and Davies (1994) debated whether increasing holistic health orientations that encompass lifestyle factors reflect medicalisation or demedicalisation. They considered three analytic dimensions including locus of causality (referring to growing emphasis on individual responsibility and lessening external absolution), status differentials (referring to lessening status gap between professional and patient), and growth of the pathogenic realm (referring to the extension of medical definitions, encompassing lifestyle factors). Whilst they argued that the connection between holistic conceptions of health and the first two analytical dimensions seems to reflect demedicalisation, the final dimension clearly reflects medicalisation. Pertinently, this final dimension reflects what Conrad himself (Conrad and Schneider, 1980), despite offering the alternative concept of healthicisation (Conrad, 1992), classically suggested was the most important factor of medicalisation – the ability to define, and thus socially control.

In the Foucauldian manner discussed above, Nettleton and Bunton (1995: 47) suggested that that the methods and techniques of lifestyle-oriented health promotion have fostered "an all-encompassing network of surveillance and observation." Armstrong (1995) similarly discussed the rise of 'surveillance medicine' alongside and to an extent as displacing hospital medicine as the hegemonic model of medicine. Surveillance medicine means an expansion of the clinical gaze into an "extracorporeal space – often represented by the notion of lifestyle – to identify the precursors of future illness" (Armstrong, 1995: 401). In adopting a lifestyle approach there is a growing penetration of the medical gaze into the everyday lifestyle choices of citizens (Lupton, 1997). As discussed above, this surveillance, due to the complex assemblages of power, also occurs at the level of self-surveillance, as well as at the state/institutional, as a result of the development of what might be thought of as the health promoting self (Nettleton and Bunton, 1995). In other words, citizens became the target of technologies of monitoring,

risk assessment and population level treatment interventions, which in turn make citizens aware, in these terms but also beyond, of their own potential contributions to their own health 'project' (Nettleton and Bunton, 1995). The risk calculation and prevention of CVD with statins is one of the clearest examples of this broader approach. As such, despite some conceptual difficulty in accounting for the growing focus on lifestyle risk, it seems that the more persuasive position within "Phase Two" was that an increasing focus on lifestyle (as part of a wider picture of complexity) reflected an expansion of the medical realm, and thus medicalisation.

1.4 Phase Three: Contestation and Contingency

In what remains of this chapter, it is argued that medicalisation scholarship has now entered a new phase that might be thought of as 'Phase Three', 'Contestation and Contingency' or potentially even 'Post Medicalisation'. Broadly speaking, in 'Phase Three' of medicalisation studies the key issue is the nature of and continuing relevance and utility of the concept itself in the context of major advances in biomedicine and biotechnology, including, for example, the vast development of the pharmaceutical industry. Very diverse philosophical positions concerning the nature of medicine/medical knowledge and corporeal reality also exist. Some have argued for an abandonment of the line of thinking proposed by medicalisation (Rose, 2007a); others have argued for a reformulation (Conrad, 2005; 2007); whilst there are those further still that have proposed new concepts that might can be thought of as partially complementary but also advocating a certain level of reformation (Clarke et al., 2003; Williams et al., 2011a). This debate about the contemporary nature and desirability of scholarship utilising the concept of medicalisation provides the distinctiveness for what this chapter distinguishes as Phase Three. Although, for example, alternate concepts such as healthicisation emerged in Phase Two, the debate before Phase Three never really involved serious evaluation of the continued utility and potential abandonment of the concept of medicalisation. Phase Three roughly refers to scholarship in the 2000s and 2010s, although the broader advances in biomedicine and biotechnology have their roots in the late 1980s. What is meant by this is that medicalisation scholarship in its own terms has only really begun to adequately grapple on a conceptual level with newer driving forces (such as the pharmaceutical industry) in this third phase of thought. There is some

older scholarship within a sociology of prescribing in particular that engages with the use of drugs but this was often conceptually divorced from medicalisation scholarship (e.g. Gabe, 1990; Parish, 1974 do not discuss medicalisation). This section of the chapter broadly concludes that, whilst we need to critically assess the continuing relevance of medicalisation, and indeed, move beyond it particularly in matters attached to analysis of pharmaceuticals, it is important to note that relations between medicalisation and emerging scholarship are "complex and contingent" (Williams et al., 2011a: 711) particularly in cases such as the one under study which can be thought of as a form of medicalised pharmaceuticalisation.

Medicalisation as a concept has since its inception been subject to scholarly critique. For example, surrounding the extent to which it is 'rampantly' occurring (Fox, 1977); of medical sociologists as no less imperialist than the institution of medicine itself (Strong, 1979); through to issues surrounding the regard, reliance, understandings and expectation lay individuals place on medical technologies (Williams and Calnan, 1996), and the particular dismissiveness of constructionist modes of thought surrounding biological realities and the positives and promises of bodies of knowledge such as medicine (Bury, 1986; Williams, 2001). However, Phase Three has resulted in the most sustained and thorough examination of the explanatory effectiveness of the concept.

Medicalisation due to its long history and overtly critical beginnings has significant intellectual baggage attached to it – and some have suggested that it is now a cliché of suspicion (Rose, 2007b). This critique certainly has its roots in aspects of 'Phase Two' (e.g. the problems with contending the de-medicalisation of society despite the diffuseness of power) but is most clearly articulated during Phase Three. Rose (2007a; see also 2007b) argues that medicalisation implies medical authority has extended beyond what is legitimate, that somehow to de-medicalise society is desirable – but arguing in this manner is of little help to social scientists in understanding why this has occurred or with what results. He calls for a deeper examination starting with an abandonment of the term, at least as it has been used. Rose suggests that medical meaning is entangled with the very form of our life and how we experience the world. Whilst medicalisation may be the beginning of analysis, it certainly should not be the conclusion because it lacks the depth to analyse the fundamental entanglement of medicine with who and what we are, the lack of a singular medical motive/boundary, or why it is better to live life in one definitional sense rather than another, whilst inferring passivity in those

who have become 'medicalised'. Whilst importantly Rose's work is influenced heavily by a Foucauldian emphasis on the inseparability of the way in which we live and understand life from the medical, importantly for the distinctiveness of this phase there is an emphasis (particularly in Rose, 2007a) uniquely on the abandonment of the concept.

Meanwhile, one of the most eminent and influential scholars of medicalisation, Conrad (2005; 2007), argues for a reconfiguration and development in understanding of the drivers of medicalisation without abandoning the term. Drivers now include, argues Conarad, the pharmaceutical industry as a key biomedical player alongside other biotechnology industries, consumerism and managed care. He argues that these changing drivers of medicalisation have served to reduce the influence of medical professionals, but that the broader underpinnings of the medicalisation thesis remain valid and important. Broadly he argues, then, that changes in medicine and society do not invalidate the premise of medicalisation, rather that there must be an appreciation of the shifting drivers of medicalisation.

More recently, Busfield (2017) offers a reassessment of the value of the concept of medicalisation. Her paper covers the history of the concept and utilises the space to address arguments from those who propose a displacement of the concept by alternative concepts (which are discussed below). She also discusses certain criticisms that might be posed against medicalisation, such as patient passivity, where she takes a similar perspective to Conrad (2005), emphasising shifting drivers, and medical imperialism, where she rejects the conflation with this and medicalisation (e.g. Strong, 1979). Busfield also criticises Rose (above) on medicalisation, arguing that there can be appropriate situations where challenging medicine's expansion into domains of life (e.g. sexuality) exists. Equally, she shows that much of the more recent analysis has not necessarily taken a problematising and negative stance against medicalisation, with much of the analysis focusing on description/explanation. Busfield concludes by arguing that the value of medicalisation remains, arguing that it is a process that is still occurring (e.g. the creation of new disorders such as 'gambling disorder' in psychiatry), whilst it also draws attention to social causes (rather than solely scientific), and particularly the actors that are driving medicine's expansion into every corner of life.

Nevertheless, others have argued for a more radical (re)framing of medicalisation (whilst still utilising similar terminology) in line with developments in bioscience and technological development. Clarke et al., (2003) have framed such notions as

biomedicalisation. The authors define biomedicalisation as the "increasingly complex multisited, multidirectional processes of medicalisation that are both being extended and reconstituted through the emergent social forms and practices of a highly and increasingly technoscientific biomedicine" (Clarke et al., 2003: 162). Importantly this reflects a transition from social control (as in medicalisation) over particular conditions to the potential for the transformation of bodies in and through biomedicalisation. They argue that the 'bio' in biomedicalisation reflects the developments and transitions made possible by various biological and medical sciences and technologies, ranging from genomics to transplant medicine. Biomedicalisation occurs across five dimensions: the political economic; risk and surveillance; the increasing technological nature of biomedicine; changes in biomedical knowledges; and the transformation of bodies.

So, in the midst of 'Phase Three', what are the defining features and debates of medicalisation scholarship? Certainly there can be no doubt that the concept of medicalisation has been problematised and challenged. The advent of the concept of biomedicalisation has been important (and indeed the Clark et al., 2003 paper is very widely cited) and has raised questions about the parameters and dimensions of medicalisation. However, it is not the intent of Clarke et al. (2003) to necessarily replace medicalisation (unlike Rose, 2007a) within the medical sociologist's 'conceptual toolkit' – rather to reframe the concept for the twenty-first century as a result of the vast reconstitution and reorganisation of biomedicine, whilst also leaving some space for the explanatory power of medicalisation. How much explanatory power their contentions have had in the fifteen years since the publication of paper is another matter – and it is here that they are joined in the 'toolkit' by the concept of pharmaceuticalisation.

1.4.1 Pharmaceuticalisation

The explanatory power of both medicalisation and biomedicalisation has been critiqued by those specifically concerned with the expanding usage of pharmaceuticals and the power, influence and wealth of the pharmaceutical industry in contemporary societies. As such, the concept of pharmaceuticalisation has been developed to grapple with a lack of specificity and focus on pharmaceuticals in other concepts (Abraham, 2009a; 2010a; Williams et al., 2009; 2011a). Pharmaceuticalisation is a sociological process that is defined by Williams et al. (2011a: 711) as the "transformation of human conditions,

capacities or capabilities into opportunities for pharmaceutical intervention". Williams et al. (2012) argue that pharmaceuticalisation is a more specific term than the 'catchall' term of biomedicalisation, whilst they also claim that the extent of the processes of biomedicalisation have been overestimated by Clarke et al., particularly when considering, for example, that the promises attached to genomic development and personalised medicine have as yet not come to fruition.

Pharmaceuticalisation is not a term that is completely new (the term was actually first used in anthropology by Nichter, 1989 as cited in Bell and Figert, 2012 and Gabe et al., 2015), although the term has only really entered widespread academic and particularly sociological usage since the late 2000s (Abraham, 2009a; 2010a; Fox and Ward, 2008; Williams et al., 2009). The sociological study of pharmaceuticals (see Chapter Two for greater analytical/empirical exploration of this subfield) has been somewhat limited prior to the twenty-first century. Some scholarship considered pharmaceuticals (e.g. ADHD drugs) under the auspices of medicalisation (Conrad, 1975; Conrad and Schneider, 1980), or, for example, as a 'social problem' (Gabe and Bury, 1988) but generally not with pharmaceuticals as the primary sociological focus themselves (Gabe et al., 2015). Perhaps the most significant body of medical sociological work on pharmaceuticals prior to the concept of pharmaceuticalisation has been within the sociology of prescribing (Parish, 1974; Gabe, 1990; Gabe and Lipshitz-Phillips, 1984). This body of work focused on the social factors shaping prescribing and did empirically engage with pharmaceuticals as analytic entities – though without the sophisticated conceptual apparatus offered by pharmaceuticalisation (see Chapter Two for further discussion of this body of work).

Increasing sociological interest in pharmaceuticals and pharmaceuticalisation (and questions about the conceptual scope of medicalisation) in the 2000s reflects the fact that prescription drug sales exploded in the latter stages of the twentieth century – globally sales amounted to over $466 dollars in 2003 (Busfield, 2006). The pharmaceutical sector has grown into a vastly significant global entity, and the industry has considerable power within healthcare scenarios and influence in national and global economies (Cockerham and Cockerham, 2010). The place of the pharmaceutical industry in contemporary medicine (and particularly the processes and techniques they draw on in attempting to expand the usage of pharmaceuticals) is explored far more thoroughly in the next chapter. However, it is possible here to illustrate the overall importance of

their position and the vast usage of medicines in contemporary western societies. At the end of the last decade, medicines "cost the National Health Service (NHS) in England over £7 billion every year… with the pharmaceutical industry the third most profitable industry in the UK economy behind tourism and finance" (Williams et al., 2009: 1). This is expanding year on year and currently exceeds £12 billion, with drug expenditures using up more than 10% of the total NHS budget (Maynard and Bloor, 2015). Indeed, Busfield (2010: 934) well summarises the vast expansion in the use of medicines:

> "In England, the number of prescribed medicines dispensed increased from an average of 8 per person in 1989 (Department of Health, 2001) to 16.4 in 2008 (NHS Information Centre, 2009) – a doubling over twenty years, with annual increases now running at around 4–5 percent. Spread evenly, this is well over one prescription per month for every year of a person's life, and does not take account of the enormous range of over-the-counter medications like pain-killers not requiring a prescription. Some types of pills have seen especially large increases. For instance, the use of statins to reduce cholesterol has been expanding rapidly, from 29.4 million prescriptions dispensed in England in 2004 to 52.4 million in 2008, at a cost of £594 million."

This is an interesting trend, and a potentially contradictory/paradoxical one in a context where, whilst sales have been expanding, pharmaceutical innovation has actually been declining (Abraham, 2010a; Light, 2010a). Whilst as this discussion indicates, the vast expansion of the use of pharmaceuticals is clearly vitally important to appreciate within the contexts of contemporary healthcare delivery, the reverse process of de-pharmaceuticalisation is also possible. As with de-medicalisation this is less common, but seemingly refers to either/or the removal of the opportunity for the use of a drug at the macro regulatory level, potentially the move towards alternate methods of treating a problem, or the decision by patents and professionals to discontinue use.

Busfield (2017), discussed above, argues that pharmaceuticalisation does not offer really anything beyond the conceptual parameters of medicalisation. However, she neglects two key aspects. Whilst not negating the nature of (bio)medicalisation as a driver of and/or related process to pharmaceuticalisation (Abraham, 2010a), pharmaceuticalisation as an explanatory framework copes better with the contemporary stature and importance of pharmaceuticals in healthcare due to its more precise/specific focus – doing different analytical work from medicalisation (Collin 2016; Coveney et al., 2011: 387; Williams et al., 2017). Indeed, it is important to note that the shared main

concern of social scientific interest in pharmaceuticals is to engage with drugs as analytic entities in and of themselves (Fraser et al., 2009) rather than as something representative of or subsumed within other processes such as medicalisation. Pharmaceuticalisation, as such, is necessarily attuned to assessing which actors and processes work towards expanding (or possibly constraining/contracting) drug usage. Equally delineations of pharmaceuticalisation thus far have sought to show that pharmaceuticalisation is a phenomenon potentially that may occur alongside but also beyond any problem becoming medicalised (i.e. the expansion of medical diagnosis) (Abraham 2010a; Williams et al., 2011a).

1.4.2 The Two Approaches to Pharmaceuticalisation

How have sociologists conceptualised the manner in which human 'problems' have become the target of pharmaceutical intervention? Two main conceptualisations and frameworks for analysis have been proposed in the literature. Both have been utilised in a significant amount of empirical work conducted within the field. Abraham (2010a) sets up his usage of the concept and his framework for analysis as concerned with assessing the 'real' impacts of pharmaceuticals – arguing that the necessity of expanding pharmaceuticalisation can and should be judged against whether or not it meets healthcare need, has efficacy, and is safe for patients. He begins with a different definition than the one by Williams et al (2011a) discussed earlier. Pharmaceuticalisation according to Abraham is "the process by which social, behavioural or bodily conditions are treated or deemed to be in need of treatment, with medical drugs by doctors or patients" (Abraham, 2010a: 604). Abraham argues that pharmaceuticalisation needs to be understood in relation to five main factors – biomedicalism, consumerism, industry promotion, de-regulatory state ideologies, and medicalisation itself. Abraham stresses the importance of understanding how the 'biomedicalism thesis', so pervasive in contemporary society, may be less important than the other four aspects individually or collectively as explanations of pharmaceuticalisation. Abraham argues that it is possible for pharmaceuticalisation to avoid the same clichés of critique and suspicion levelled at medicalisation because the claims of biomedicalism can be measured against the realities of pharmaceutical deployment in meeting health needs. Despite some closeness in terminology, Abraham here is referring not to the sociological concept of

biomedicalisation discussed by Clarke et al., (2003) but the ideological underpinning of contemporary biomedical drug development (in similar terms to what Busfield (2010) terms the 'progressive model'). He argues that in biomedical science, drug development is seen as the process of meeting objectively defined and established health problems, but in actuality, this is an inherently problematic assumption. Abraham argues that consumerism, state policies, and industry promotion actually serve to create and foster need, rather than meet need objectively existing beyond sociological variables. Whilst pharmaceuticalisation may be seen by those in science or the industry to be the necessary and natural progression to the meeting of health needs, Abraham establishes the importance of sociological variables in creating in some instances "false claims and expectations about the capacity of pharmaceuticals to meet those needs" (2010a: 617).

He argues that medicalisation (conceived here as a driving force of pharmaceuticalisation) may be a better explanation than biomedicalism. For example, in the case of ADHD where thresholds of what is considered 'normal' behaviour have been lowered so much that some studies suggested that 50% of all children could meet symptom criteria, or in the example of depression where doctors have been targeted to prescribed SSRIs after the 'Defeat Depression Campaign' facilitated by Royal Colleges in the 1990s. Rather than increasingly sensitive diagnosis in this example and others, pharmaceuticalisation is seemingly here driven by medicalisation due to the involvement of medical elites in establishing boundary changes and industry sponsored awareness campaigns. Abraham also discusses how consumerism may be a more persuasive driving force behind pharmaceuticalisation than biomedicalism. He identifies two types of consumer - access-oriented consumerism (e.g. campaigning for access to new drugs) facilitates pharmaceuticalisation whilst injury-oriented consumerism (e.g. legal action taken due to harm caused by drugs) potentially constrains pharmaceuticalisation. Though acknowledging the rise of the patient-consumer and consumerist principles within healthcare more generally, Abraham sets one caveat in particular as vital to understanding consumerism as a driving force – consumerism that aligns with the interests of industry is the consumerism that is generally successful in meeting its goals. Abraham, finally, discusses the persuasiveness of deregulatory ideology in driving pharmaceuticalisation. He notes that pharmaceutical product innovation has declined in the years that lifestyle and psychosocial areas have seen increasing pharmaceuticalisation. As such, pharmaceuticalisation cannot be explained by growth in

techno-scientific discovery/advance, or, as such, biomedicalism. This decline in innovation might be associated with de-regulatory tendencies within regulatory organisations from the 1980s onwards that have lessened the burden on the industry to be innovative, particularly because new drugs do not have to show therapeutic advance over existing drugs. This is ironic because arguments by industry and those in government for lessening the regulatory standards have been rooted in claims that overwhelming regulatory burdens have restricted innovation. These discussions in many ways build on his broader work in the sociology pharmaceuticals (explored more fully in Chapter Two). Elsewhere, but linking with his approach to pharmaceuticalisation, Abraham (2008a) argues for the necessity of a realist-empiricist philosophical foundation for analysis in the sociology of pharmaceuticals. This claim is built on an argument that the pharmaceutical industry, the state and patients have 'real' interests relating to the development, regulation and use of pharmaceuticals. His claim is that the pharmaceutical industry holds a 'real' interest in maximising profit, whilst patients have a 'real' interest in drugs that have efficacy and are safe, as do the state who also wish to maximise economic growth. Within a broader framework of inherent corporate bias in the regulation and development of pharmaceuticals, (Abraham, 1995; 2007; 2009b; Davis and Abraham, 2011), Abraham argues that a realist conception is necessary for sociologists to investigate in any meaningful way the manner in which the 'real' interests of the industry (and potentially the state) are prioritised over the 'real' needs of patients and the protection of the public.

Meanwhile, Williams et al., (2011a; 2011b) set out a more theoretically fluid conceptualisation and framework for analysis that is not tied to a realist philosophical position. These authors reject a grand synthesis in favour of an adaptable, eclectic, multilevel and multidimensional conceptual understanding so as to stimulate research with a variety of (interconnected) concerns. In doing so, and unlike Abraham, they do not set up their framework as a means to assert the validity of pharmaceuticalisation in any given case. It is also important to note that, continuing a previously established trend Williams and colleagues (2011a; 2017) view the term (and medicalisation) as neutral (perhaps due to concerns about exposure to Foucauldian and Rosian style critiques), rather than as overtly critical as in the initial development of medicalisation as a concept in the orthodox phase. It is sensitive to the potentially pervasive and problematic influence of the pharmaceutical industry, but also the benefits of pharmaceuticals in

alleviating human suffering. Williams and colleagues conceptualise pharmaceuticalisation as a "dynamic and complex heterogeneous socio-technical process that is part of what we might call a pharmaceutical regime" (Williams et al., (2011a: 711). Embodied by the chemistry technology of a pill, the notion of a pharmaceutical regime is vital to their framework, and itself refers to the networks of actors, institutions, cognitive structures and subprocesses involved in the development, dissemination and consumption of drugs. The focus of the concept of pharmaceuticalisation is, as such, to hone in on changes or developments within this pharmaceutical regime that are widening the use and pervasiveness of drugs in society. It is necessary as such for pharmaceuticalisation analysis to consider the dynamics and relationships between actors within this regime. Equally, the degree to which a problem is pharmaceuticalised is another key analytical point because it is likely that there are varying degrees of pharmaceuticalisation (potentially with co-existing therapeutic alternatives) variant case by case. Williams and colleagues allow for variations in the extent of pharmaceuticalisation and that different actors in the regime may simultaneously be working to expand and contract pharmaceuticalisation with varying successes and impacts over time. Their endeavour is also interdisciplinary and draws on Science and Technology Studies (STS) as well as medical sociology in constructing their conceptualisation. It is not made explicitly clear how the two are combined. But it might be assumed that by this they intend for pharmaceuticalisation to emphasise (ala STS) the interconnectedness of actors and entities in processes of pharmaceuticalisation, as well as the inseparability of social, political and cultural values and scientific endeavour – or the inseparability of technology and technological development from modes of living.

Williams et al. (2011a) highlight six dimensions of pharmaceuticalisation that are both interrelated and partially distinct from each other and that each in their own way may contribute to widening pharmaceuticalisation. In outlining six dimensions of pharmaceuticalisation the authors provide here an analytical framework. This, in other words, provides a number of areas of potential research terrain for empirical exploration each primarily implicating different actors (although acknowledging the potentially interconnected nature of actors and entities in processes of pharmaceuticalisation as part of the pharmaceutical regime). The first dimension is the redefinition and reconstruction of health problems as having a pharmaceutical solution, with the pharmaceutical industry identified as a key actor in widening markets (for their products). The authors

here broadly discuss the expansion of pharmaceutical markets worldwide since the 1980s with pharmaceutical companies vastly important in driving this process. This is in terms not only of developing new drugs, but also expanding the use of existing drugs (e.g. statins) and even creating new conditions to then provide treatments for. The second dimension is the regulation of pharmaceuticals. The focus here is on diminishing regulatory burden and regulatory dependence on the pharmaceutical industry, as well as the developing role of regulatory agencies in promoting innovation and the globalisation of western regulatory frameworks. The authors discuss in particular, drawing on Abraham (see 1995; 2008a), the often seemingly cosy relationships between industry and regulators that have led to concerns that regulators do not work in the interests of public health; reductions in the timescale of regulatory reviews; the pressures on regulators to promote rather than restrict innovation; and the harmonisation and globalisation of western models of regulatory activity (again intended to reduce regulatory rigour and review times). The third dimension articulated is the framing of health problems as having a pharmaceutical solution in media. Various forms of media are becoming increasingly important in the framing of pharmaceutical use, ranging from news reporting through to direct-to-consumer advertising (DTCA). Whilst media forms do not drive pharmaceuticalisation *per se* or drug availability, they can be important in celebrating or condemning (in different, even contradictory ways, varying by different types of pharmaceutical and even oscillating between the two over time) drug usage, expansion, and need through shaping/influencing lay patient and public understandings. This dimension can be read as being concerned both with the 'sense' of pharmaceuticalisation fostered in and by media and how these portrayals might also influence, shape or intercede with perspectives about drugs. The fourth theme put forward by Williams et al. is use of and understandings of medicines in everyday life and clinical encounters, by patients/lay individuals and doctors (who, the authors do note, retain a level of importance within medical decision-making). This dimension includes the understandings of and identities surrounding pharmaceuticals and the desire or resistance of lay individuals to consume pharmaceuticals, through to the mobilisation of patient groups to promote and provoke pharmaceuticalisation. The fifth theme is the use of drugs for non-medical purposes. Again in line with the consumerist tendencies of some lay individuals, drugs are being utilised for purposes of enhancement, both within the medical sphere but also illicitly beyond, for example, for cognitive enhancement in

healthy people. The final theme is the notion of pharmaceutical futures. The main crux of the authors' argument here is that pharmaceutical innovation and the promises of drug development, particularly in a wider biomedical context that includes weighty promises attached to the use of genetics to create a personalised medicine, are very important in shaping development initiatives, research and attracting funding in the present. Despite a reality of declining innovation every year, the expectations and hopes of actors from financers through to patients desiring a treatment for their particular condition are important in driving pharmaceuticalisation of the future.

These six dimensions can be viewed as delineating a variety of actors and subprocesses that operate as part of a broader network that these authors call the pharmaceutical regime. These six dimensions provide criteria upon which to judge which actors are driving (or indeed preventing/constraining/provoking resistance to) pharmaceuticalisation. It also provides criteria to establish the extent of pharmaceuticalisation in a given case (Williams et al., 2011a: 712). This can occur after analysing along which dimensions pharmaceuticalisation has expanded, contracted or where resistance is present. Dimensions of relevance in any given case of pharmaceuticalisation may differ and all six may not be actually relevant. In this sense, the exact composition of the pharmaceutical regime can be said to differ per case and, as such, it is the job of the analyst to decide which dimensions and associated actors are relevant to a particular case of pharmaceuticalisation. Once the dimensions of relevance have been decided, the framework provides the researcher with the ability to look across the actors implicated in specific dimensions and analyse which may be facilitating or constraining pharmaceuticalisation. The more facilitative that action, organisational/relational positioning, and/or cognition is in each dimension the greater the extent of pharmaceuticalisation will be overall. It is true that the authors do not explicitly set out exactly how the six analytic dimensions might be interconnected or interact with one another within the pharmaceutical regime of a particular case. This in one sense, though, is a strength in that an overly prescriptive approach may not be less well equipped to grapple with the specifics of individual cases.

1.5 Towards a Conceptual Framework

Recent work in the field suggests that medicalisation lacks the necessary level of analytical capacity and specificity to grapple with and explain contemporary developments – including, but not limited to, the explosion of pharmaceutical usage (both in and beyond prescription) and the vast influence of the pharmaceutical industry (see Chapter Two for further). The previous section explored the varying arguments for a reconfiguration of the concept and/or moving beyond it occurring in Phase Three. The medical realm and the driving forces behind its expanding boundaries have certainly reshaped and there has been a need for accompanying conceptual development. However, it seems that sociologists should be also cautious about abandoning the concept of medicalisation, particularly as the links between medicalisation and, for example, pharmaceuticalisation are "complex and contingent" (Williams et al., 2011a: 711). Both can occur at the same time through, for example, expansion in pharmaceutical deployment reflecting widening diagnostic criterion (Abraham, 2010a). Nevertheless, a conceptual assumption apparent in pharmaceuticalisation scholarship to date that is that pharmaceuticalisation has greater explanatory scope in matters pertaining to drugs than medicalisation or biomedicalisation (Coveney et al., 2011: 387; Williams et al., 2017), which is important for this thesis when considering the centrality of the drugs to the case (as outlined in the thesis introduction). Work on pharmaceuticalisation has also usefully identified key actors or sub-processes that might drive (or contract) the process, and can (depending on which approach is taken, see below) allow for assessments of validity or extent. As such, pharmaceuticalisation is the stronger conceptual approach in analysing the case of CG181.

However, as discussed in the previous section, there are competing conceptualisations and analytical frameworks for the exploration of pharmaceuticalisation. Both frameworks are highly valuable contributions to medical sociology and both have been widely cited (more than 300 times each). But which conceptualisation and analytical framework should underpin the empirical work explored in this thesis?

First, the conceptual notion of the 'pharmaceutical regime' proposed by Williams et al. (2011a) is useful and persuasive particularly in terms of overtly encouraging analysis to engage with the roles of multiple actors and the interconnected nature of pharmaceuticalisation. In grappling with the interplay between a variety of actors ranging from the pharmaceutical industry, the state, regulators, patients, professionals,

the media and beyond can highlight driving forces, the complex dynamics and relationships involved in expanding medicines usage, and importantly, the extent to which pharmaceuticalisation (and potentially de-pharmaceuticalisation) is occurring in any given case. In other words, what this framework can analyse is the degree to which it is occurring and how actors seek to drive or restrict pharmaceuticalisation in any given case. This conceptual approach, as concerned with driving forces and extent, is reflected in the choice of the overarching research question of this thesis: *to what degree is the further pharmaceuticalisation of the primary prevention of CVD occurring and what are the driving forces?* Importantly, the Williams et al. (2011a) conceptualisation and analytic framework allows sociologists to explore dynamics far beyond assessing the *validity* of cases of pharmaceuticalisation. This framework allows sociologists to explore potential positives or problems associated with pharmaceuticalisation, but it also arguably goes beyond this to enable a much clearer understanding than Abraham (2010a) of extent and the necessarily interconnected nature of action (at levels of drug development/market creation, regulation, dissemination, consumption and beyond) associated with the expanding use of medicines. Indeed, pharmaceuticalisation in a particular scenario may not be 'full' or complete. That is, there may be competing therapeutic alternatives in the broader landscape of the problem, or, indeed, resistance or rejection to pharmaceuticalisation by certain actors or entities along different dimensions (potentially simultaneously) for a general or case-specific reason. The notion of the pharmaceutical regime allows analysts to examine these manoeuvrings and, in the process, articulate whether actors are driving pharmaceuticalisation and the degree to which it is occurring when considering action in different dimensions. The actors of particular interest (NICE, print newspapers, and medical professionals) within the pharmaceutical regime specific to the case under study were outlined in the introduction to this thesis. Chapter Two will flesh out the empirical justifications for focusing on these actors and what they each contribute within the pharmaceutical regime of this case.

In addition to the utility of the pharmaceutical regime as a conceptual device, the work of Abraham is underpinned by a potentially constraining realist position that arguably limits its utility compared to the Williams et al. (2011a; 2011b) framework. The problem here is that in assessing the validity of biomedicalism as an explanatory force for pharmaceuticalisation this neglects that the way people think about or portray drugs can shape the actualities of use or future development and related notions of health and

illness (Williams et al., 2011b). In this way, newspapers are important. For example, (as will be explored in more detail in the next chapter) the print news medium has some ability to shape perceptions and use, potentially regardless of the realities of benefit or harm. Reporting on a wonder drug might result in expanding use or clamour by certain professional and patient groups, or might construct expectations about life saving potential. Equally, reporting on side effects in the newspapers, for example, might influence mass discontinuation of use or lessen professional willingness to prescribe. Both may be far from the realities of benefit or harm, and reflect more than anything journalistic practices and the nature of print news medium reporting in various ways (Williams et al., 2011b – see Chapter Two for further explorations of media and journalistic practices). However, impacts on pharmaceuticalisation are nevertheless apparent, for example, by imbuing drugs with a certain imagery or essence. Broadly, the media contains a set of actors which are not built into Abraham's framework and thus would be hard for analysis rooted in his work to grapple with. Moreover, Abraham's framework allows little room to analyse patient or professional *perspectives* about use. From Abraham's position drugs are either necessary or they are not, and this may capture something salient, but at the same time it can show little about how and why patients or consumers, and arguably professionals, desire, use or resist drugs in specific instances.

Due to utility of the notion of the pharmaceutical regime, the greater theoretical and philosophical fluidity offered by Williams et al. (2011a) and the broader analytical reach, this conceptualisation and framework for analysis of pharmaceuticalisation in the case under study in this thesis is preferred over Abraham's framework.

1.5.1 Medicalised and Unmedicalised Pharmaceuticalisation

Whilst the Williams et al. (2011a) conceptualisation of pharmaceuticalisation does not approach the process in specifically this way, this thesis argues that this conceptualisation of pharmaceuticalisation is sensitive to pharmaceuticalisation occurring on a spectrum or in different forms. Importantly, the interconnectedness between medicalisation and pharmaceuticalisation will be stronger and more contingent in some cases than in others. At one end is an unmedicalised pharmaceuticalisation that operates largely beyond traditional medical spheres and/or without any transition in or application of a diagnostic category. Drugs may be used, for example, beyond their

intended medical usage and outside of prescription for the purposes of cognitive enhancement. In this sense, medical professionals, medical settings and diagnosis are (largely) excluded from the process of unmedicalised pharmaceuticalisation. This end of the pharmaceuticalisation spectrum appears in some ways to be of greater interest to Williams and colleagues (2011a), reflecting the broader distinction between pharmaceuticalisation of this type and other concepts (and thus the concept's uniqueness) (Williams et al., 2017). However, it is important to be clear that these authors do not only limit their conceptualisation to this focus. They discuss how pharmaceuticalisation can occur both within and beyond traditional medical spheres and argue that the privileging of pharmaceuticals in and of themselves as analytic entities is also a significant contribution of pharmaceuticalisation (Coveney et al., 2011: 387; Williams et al., 2017). In this regard, this same cohort of scholars has very recently argued that the "value of pharmaceuticalisation is not solely do with those instances which extent beyond medicalisation but also those occurring *within* medicalisation" (Coveney et al., 2019: 269). Considering the scale of the use of pharmaceuticals prescribed by medical professionals, which in England includes 48% of the population taking at least one prescribed medicine in the last week (Moody and Mindell, 2017), the utility of the concept is clearly greater if it can incorporate pharmaceuticalisation within as well as beyond traditional medical spheres.

On the other end of the spectrum, then, is a more medicalised pharmaceuticalisation where medicalisation and pharmaceuticalisation are occurring together. This is in terms of pharmaceuticalisation occurring within traditional medical spheres and/or where new or widening diagnostic categories are interlinked with widening pharmaceutical deployment. Where a more medicalised form of pharmaceuticalisation appears to be occurring the decision to utilise the conceptual parameters of pharmaceuticalisation rather than medicalisation will reflect the primacy of pharmaceuticals (e.g. as a treatment) within diagnostic transitions, or even where developments surrounding pharmaceuticals can be shown potentially to drive medicalisation (e.g. through industry attempts to 'sell sickness' and create conditions that can be treated using pharmaceuticals). This is because the greater intensity and specificity of focus of pharmaceuticalisation on pharmaceuticals themselves and the actors which shape their use/deployment/consumption necessarily possesses greater analytic specificity than medicalisation (Coveney et al., 2011: 387; Williams et al., 2017).

Actors of importance within the pharmaceutical regime are likely to differ or have differential interactions with other types of actor depending on whether the particular case of pharmaceuticalisation is medicalised. Specifically, this thesis examines the influences of the pharmaceutical industry on NICE's evaluative action, the coverage and framing of the case by the newspapers, and the prescribing behaviours and decision-making of GPs. The empirical justifications for the choice of these actors will be explored more fully in Chapter Two. However, it is important to note that certain types of actors and the broader dimensions of pharmaceuticalisation within which they are operating may be differentially involved or of greater interest for analysts to focus on depending on what form of pharmaceuticalisation is under analysis. For example, regulatory practices, the perspectives of professionals and the dynamics of doctor-patient relationships, and/or how other dimensions (e.g. the mediatisation dimension) intercede with and influence more traditional medical settings and associated use of pharmaceuticals will be of greater interest to the analysis of the manoeuvrings of the pharmaceutical regime in cases of medicalised rather than unmedicalised pharmaceuticalisation.

The case under study in this thesis is a case of medicalised pharmaceuticalisation. Considering all of the discussions of the nature of medicalisation in this chapter, it is clear that medicalisation is occurring in terms of a widening diagnostic category which has been shaped institutionally by a regulatory body and defined in terms of and facilitated/necessitated by biomedical risk testing. Medical professionals are also the gatekeeper to treatment. This necessarily means that the pharmaceuticalisation of patients will occur in and from medicalised settings and interactions. Alongside the potential for the deployment of statins, CVD prevention also includes medicalised advice about lifestyle change, such as advice on exercise, diet, smoking, prior to and potentially in the place of a statin. However, the primary prevention part of the guideline development was driven by changes surrounding the drugs that reflected the influences of certain actors and necessitated/provoked action from others within the pharmaceutical regime. This can be interpreted as a continuation of what Greene (2007) suggests is the centrality of pharmaceuticals to fostering the legitimacy of treating risk and gradually widening the numbers of people to treat. And as Saukko et al. (2012: 562) summarise:

"Rather than the risk factor being identified first and treatment second, cholesterol gained traction as a risk factor only after the development of targeted drugs. This co-development of a risk factor and drugs has continued in the last decade, as the category of high cholesterol [and thus risk of CVD] has expanded to encompass increasingly lower levels of cholesterol [and thus lower levels of risk of CVD]"

The lowered primary prevention threshold established in CG181 is arguably a continuation of this trend, with the developments surrounding the drugs the primary reason that widening diagnostic/risk thresholds occurred. In other words, the drugs are the central analytic entity in this case, both in terms of widening the diagnostic threshold and, as explored in the introduction, in terms of being the central aspect of debate, comparison and professional and public visibility. As such, it should be analysed first and foremost as a case of pharmaceuticalisation – albeit a precise medicalised version of pharmaceuticalisation.

Considering these discussions, it is also worth noting that although CVD has already been pharmaceuticalised in both primary and secondary prevention, there is no reason why the regime approach cannot enable analysis to engage with case specific driving (or constraining) forces behind specifically the further and widening pharmaceuticalisation of CVD. Thus, it is possible to evaluate the extent to which further pharmaceuticalisation is actually occurring as well as potentially compare what the driving forces or constraints in specific dimensions to full pharmaceuticalisation may be in previous regulatory and usage contexts and in new and widening contexts.

1.6 Summary

This chapter has presented an analytical overview of the history of thought and theorising attached to medicalisation before providing justification for utilising the distinct but partially contingent concept of pharmaceuticalisation as the primary conceptual lens through which to analyse the case under study in this thesis. Three 'phases' of thought have been delineated. Whilst presenting such a complex body of literature in this way is necessarily imperfect (with each 'phase' possessing its own set of contradictions, disagreements and contestations), it is a strong way of highlighting the development of thought that has culminated in the concept of pharmaceuticalisation and takes inspiration from older work that has also viewed medicalisation as occurring in phases (Lupton, 1997; Williams, 2001; 2003). Pharmaceuticalisation has its own

complexities, not least in its contingent relationship with medicalisation and theoretical disputes between key contributors, but certainly scholarship on the concept so far has established (albeit loosely) a set of key actors/entities/processes which can be said to shape pharmaceuticalisation. The chapter proceeded to draw together the strands of pharmaceuticalisation scholarship, particularly utilising the work Williams et al. (2011a), to present a conceptual framework for analysing pharmaceuticalisation in CG181.

Moving forward, Chapter Two reviews the analytical and empirical work that has been produced exploring (directly and indirectly) the six analytical dimensions of pharmaceuticalisation as set out by Williams and colleagues. In doing this, the chapter assesses the gaps in the sociology of pharmaceuticals literature, particularly surrounding explorations of CVD pharmaceuticalisation. Chapter Two, as such, highlights an agenda for research, establishing the need for the empirical research presented later in the thesis as filling various scholarly gaps in the developing medical sociological knowledge base. It also complements the conceptual discussions in Chapter One by establishing actors and processes of relevance in this case.

Chapter Two: The Sociology of Pharmaceuticals (and Intersects)

2.1 Introduction

The previous chapter traced the intellectual history of what might be thought of as 'medicalisation studies', outlining the development of and transitions in the composition and focus of study in this area, as well as the emergence of parallel, and more specific concepts (particularly pharmaceuticalisation). It also provided an overarching conceptual framework for the empirical work contained within this thesis and a justification for approaching the case under study primarily through the lens of pharmaceuticalisation as conceptualised by Williams et al. (2011a). It also outlined the six analytical pathways specified by Williams et al. (2011a) as potential directions for empirical work concerned with the analysis of pharmaceuticalisation and, when looking across these dimensions, the conceptual value of the pharmaceutical regime. Building out of these discussions, Chapter Two takes a greater analytical and empirical focus, reviewing the work that has been conducted directly drawing on the concept of pharmaceuticalisation, as well as wider work on medicines that might loosely be associated within a sociology of pharmaceuticals – all tying back to CVD pharmaceuticalisation. As well as establishing gaps in the literature in this way, the chapter also argues for the potential intersection of certain wider literatures and theoretical directions in medical sociology with the analysis of pharmaceuticalisation. As such, the chapter weaves together analytical and empirical work directly assessing or that can be associated with pharmaceuticalisation, whilst also reviewing wider theoretical and conceptual aspects that can be complementary to analysing the analytical dimensions of pharmaceuticalisation as proposed by Williams et al. (2011a).

To begin, this chapter needs first to establish which dimensions of the Williams et al. (2011a) analytical framework are relevant to the widening availability and use of statins in the primary prevention of CVD as a case of pharmaceuticalisation. In doing this, the chapter can also show which specific actors, processes and dynamics are of most interest and comprise the pharmaceutical regime in this case – thus complementing the discussions at the end of the previous chapter. As noted in Chapter One, the notion of the pharmaceutical regime is central to the conceptualisation of pharmaceuticalisation as offered by Williams et al. (2011a). To understand if, how and to what extent pharmaceuticalisation is occurring, analysis needs to look at movements in the regime

that open up opportunities for pharmaceutical deployment and if and how this shapes the manner these opportunities are understood, received and utilised. As such, it is important to consider all potentially relevant actors and the interconnectedness of the dimensions of pharmaceuticalisation. Thus, the interest of this chapter is to highlight the need for further research in the individual dimensions whilst also focusing on the interconnected whole.

In terms of establishing what direction research on this case could take, immediately it is clear that the fifth and sixth dimensions of the framework are of limited relevance. The former of these reflects on trends towards the use of drugs for enhancement, such as the use of cognitive enhancement drugs to aid alertness and memory (see Vrecko, 2015) – which statins are not. The latter dimension is concerned with pharmaceutical futures and addresses the role of hope (for example, by patients – see Brown et al., 2015) and expectation as rhetorical devices in driving forward the processes of technological change (e.g. in attracting funding), even though the promises of a 'biotechnology revolution' have not, however, been reflected in pharmaceutical innovation. In the way that Williams et al. (2011a) set up this dimension, this also has limited relevance to statins as an existing and now (in the UK) generic class of drug. It has been suggested that widening the risk threshold where statins can be prescribed may also facilitate the expansion and normalisation of newly emerging lipids drugs (Unruh et al 2016). This is perhaps less well explained in this area by hope and expectation, however, and more so by other aspects discussed below (e.g. regulatory dependency). Additionally, the first dimension proposed by Williams et al. (2011), which refers to the role of the pharmaceutical industry in the reconstruction and reconfiguration of human problems as having a pharmaceutical solution, can also be argued to have only partial relevance to the case under study. As the chapter explores below, if and how industry influence and interests shape and intercede with regulator-driven pharmaceuticalisation is important to analyse. However, this chapter argues that due to the centrality of NICE in this case the conceptual and analytic approach needs to take a primarily regulatory focus.

This as such leaves three core potential research dimensions and associated types of actor that could be explored concerning the pharmaceuticalisation of CVD. 1) Regulatory bodies, closeness with the pharmaceutical industry and reductions in regulatory burden. 2) The media and pharmaceuticalisation – and how various forms of

media may create a 'sense' of pharmaceuticalisation, as well as potentially more directly promote or foster resistance to the use of pharmaceuticals. 3) The understandings and use of pharmaceuticals at the micro-level by patients and medical professionals. In what follows, this chapter will utilise these three dimensions as a structure, reviewing in turn literature corresponding with these dimensions and identifying gaps that justify the empirical work offered later in this thesis. The chapter begins by examining regulator-driven pharmaceuticalisation, necessarily examining the influences of the pharmaceutical industry on evidence available to regulators (with a particular focus on NICE's status as a 'fourth hurdle' regulatory body) and other connections/relationships that exist between industry and regulators. The chapter then in turn examines the role of media in processes of pharmaceuticalisation. And then, finally, the actualities of use and deployment of medicines at the micro-level by patients and professionals.

2.2 The Regulation and Evaluation of Pharmaceuticals

The second analytic dimension of pharmaceuticalisation outlined by Williams et al. (2011a) in their framework is concerned with the evolving relationships and roles of regulatory bodies. The authors outline three component parts to this dimension – reductions in regulatory hurdles and closeness with and dependency on industry, the role of regulatory bodies in encouraging innovation, and the globalisation of the western regulatory framework. The latter of these two aspects are of minimal importance to the case of widening use of generic statins as recommended by NICE. This section as such primarily focuses on this first component whilst also advancing discussion of the need for pharmaceuticalisation analysis to engage with NICE's role in the process of the evaluation of new and existing pharmaceuticals, which, as yet, has received limited attention by those exploring the concept.

To appropriately situate the work NICE does in the regulation and evaluation of pharmaceuticals, and its role here in pharmaceuticalisation, it is necessary first to consider the development and dissemination of pharmaceutical knowledge. Who develops the evidence that regulators consider and how? What processes or mechanisms might shape or influence the available evidence? The trialling of drugs is conducted by pharmaceutical companies themselves and those in their employ rather than by independent bodies (Angell, 2008). Companies design and construct trials in such a way

that minimises, or potentially cannot discover relevant harms of their drugs, whilst also importantly maximising evidence of benefit (Light, 2010a). As Light et al. (2013: 594) discuss, this can mean that patients most likely to experience side effects are excluded and drugs are tested on restricted populations (e.g. even though drugs may be used by the elderly, the elderly are often excluded from clinical trials). Equally, less common side effects, or those that take a longer period of time than observable by clinical trials to emerge are not easily recorded. Trials may not report on the actual benefits to the health or length of life of patients, whilst where drugs are compared against one another dosage levels may be selective, and trials may be ended early (Light et al., 2013; Will, 2010; see also Busfield, 2006). As Healy (2012) discusses, where clinical trials were once a means of weeding out ineffective treatments and to protect patients from the biases of the medical professional, they have become instead now a method to further the interests of the pharmaceutical companies that (largely) fund them.

Whilst as Will (2010) notes, suspicion of commercially funded research is nothing new, these well-known problems remain. As the AllTrials campaign indicates there is growing recognition of the problems of industry funded research, and particularly the non-registration of clinical trials. However, as many as 40% of clinical trials involving drugs in current use have never been registered (which includes making publicly available a trial protocol), and this number in itself says nothing of trials never registered and with no subsequent publications. This publication bias over time has deprived clinicians and patients of potentially necessary information when engaging in decision making about whether to prescribe or take a drug (Schafer, 2004). This is despite the emergence of public global registration through ClinicalTrials.gov in the early 2000s allowing retrospective registration. Even where trials occurring are prospectively registered, trialists are also often slow to provide summaries of results and full trial reports (needed for regulatory approval) are often not made publicly available (Rodwin, 2013b: 584). Equally, individual patient level data are generally not available for independent analysis or for the benefits of future research (see Godlee, 2016).

Moreover, there are potential issues in the systems of the dissemination of research that reflect the influences of the pharmaceutical industry – particularly the publication of research in academic journals. Indeed, industry funded studies are both more likely to be published in the first place and are potentially as much as four times more likely to report results favourable to the funding company than studies from other

sources (Brown and Calnan, 2013: 285; Lundh et al., 2012; Sismondo, 2008; Smith, 2005). Benefit of drugs are also exacerbated by the publication of the same trial data more than once. Multicentre trials, for example, allow data from different centres to be published separately in different journals or different combinations from across centres. Smith (2003; 2005) a former editor of the BMJ, and Horton (2004) current editor of the Lancet (see also Lexchin and Light, 2006) have suggested that journals serve as a marketing force for the pharmaceutical industry. The publication of industry funded trials is lucrative for journals, for example, with a company likely to purchase reprints for dissemination worth significant amounts of money to the functioning of the journal. Smith concludes his commentary with the argument that journals should not publish trials, rather journals should focus on critically describing the results with the trials themselves published on regulated websites – although this is something still yet to occur.

Ghost authorship, where scientific articles are not written by the person leading the paper, often using key opinion leaders (KOLs) with existing influence within the medical community, also may occur in the publication of medical research. It is unknown how extensive this may be, but there has been significant concern about the practice. Indeed, in the example of the menopausal hormone therapy treatment Prempro, producing company Wyeth utilised ghost-written publications to reduce concern about breast cancer risk, promote unsupported benefits and also promote unsupported off-label use in attempts to maximise markets for its use (Fugh-Berman, 2010).

However, ghost writing is only one aspect of 'ghosting'. It is important to appreciate that though trials are largely conducted by industry funded university researchers or increasingly through contract research organisations (CROs) (Healy, 2012: 99; Sismondo, 2009: 172; Sismondo and Doucet, 2010: 280), the pharmaceutical companies guide the research design, influencing the protocol and methods. In the case of CROs, the presence of reciprocity is an important aspect here because CROs rely on the business from industry for their existence (Rodwin, 2013a: 583) (further discussed below in discussions of ghost management). Meanwhile, there is significant institutional clamour to attract research funding or other forms of industry sponsorship, and university-based researchers may significantly rely on industry funding for career advance. Funding and sponsorship are likely to have subtle consequences, such as the development of long-standing relationships of mutual benefit, as well the creation of

positive perspectives about companies and their products (Sismondo, 2008). There have also been high profiles cases involving academics, such as that of Nancy Olivieri (a haematologist researching the drug deferiprone) and David Healy (a psychiatrist who problematised the adverse effects of SSRIs and the influence of industry on the available evidence), of hospital/university researchers being removed from positions and castigated in academic communities for speaking publicly about dangers to patients from (emerging) drugs. In these cases, the presence of research funding and broader institutional funding from pharmaceutical companies were significant components in the removal of employment and attempts to silence these academics (Schafer, 2004). This, as such, indicates that there may be difficulties associated with researchers engaging in whistleblowing activities when this negatively impacts powerful pharmaceutical industry funders. Sismondo and Doucet (2010) meanwhile, describe the 'ghost management' of medical research, employing the term to describe research situations where companies shape and control crucial steps in the research and dissemination process (see also Healy, 2012: 104-108). As Sismondo argues elsewhere, (2007: 1429) in extreme cases, "drug companies pay for trials by contract research organizations (CROs), analyse the data in-house, have professionals write manuscripts, ask academics [often KOLs] to serve as authors of those manuscripts [despite having minimal input], and pay communication companies to shepherd them through publication in the best journals." This 'publication planning', which involves a whole sub-industry of publication planner companies (with a history stretching back to the 1980s), is designed to extract the maximum value from the evidence and analysis, with the goal of establishing consistent drug profiles (Sismondo, 2009). In essence, this kind of medical research might be described as corporate science with the intention of marketing drugs and the process characterised as the 'trial journal pipeline' (Light et al., 2013). Journals also contain more overt marketing messages. Indeed, Collin and Otero (2015) offer a historical analysis of advertising in Canadian medical journals that suggest a high level of continuity concerning the utilisation of psychotropic drugs in the management of anxiety-depressive problems. This was despite paradigmatic shifts in the classification of psychiatric disorders and wider strife about the legitimacy of psychiatry over time, with this broader context potentially meaning that the continuity of messages held appeal for prescribing professionals.

These issues surrounding publication are important because medical journal publication legitimises emerging drugs and reifies existing medical knowledge, both of which impact how professionals (as readers of medical journals) facilitate the care of patients. Indeed, so called 'fourth hurdle' cost-effectiveness bodies such as NICE (Timmins et al., 2016) have no legal standing when it comes to accessing all existing evidence from pharmaceutical companies on a particular drug (Abraham, 2009a; Healy, 2012: 137). NICE only have access to published evidence or any evidence that companies or the regulatory/licensing body (assessing quality, safety and efficacy – in the UK, this is the MHRA) make available. When considering the problems with company involvement in trial design, and the systems of dissemination, having access to only published data inherently shapes the decisions that NICE make. As Abraham (2009a: 110-111) discusses, in the case of SSRI antidepressant usage in children which was initially considered safe by NICE on the basis of published evidence, NICE subsequently reversed this recommendation on the basis of accessing unpublished data and emerging concern that studies of a positive nature had been manipulated and data selectively released (Healy, 2012). Due to reliance on company produced RCT evidence, the production of guidelines can also help to create or foster legitimacy in support of new conditions. Healy (2012: 151-152) describes, for example, how NICE, trapped by reliance on published company RCT evidence which had trialled sedative drugs in children who were labelled as having bipolar disorder (despite conventional medical wisdom suggesting it had later onset) had little choice but to discuss it in related guidance. This guidance went some way in itself to endorsing and legitimising acceptance of childhood bi-polar disorder as a treatable condition in non-US contexts. The essence of this is that the existence of published RCT evidence goes some way to pulling a guideline into existence, and if a guideline is produced, the condition is assumed to have basis in reality. Further issues surrounding regulatory bodies are returned to below, but the core issue here is that fourth hurdle cost-effectiveness bodies can widen the use of medicines for existing conditions and confer legitimacy on emerging conditions and treatment, but this may be based on partial evidence due to dependence on industry for what is published. These issues, as such, hold significance in understanding the underpinning rationale behind the widened CVD primary prevention threshold established by NICE who necessarily have to utilise published evidence in the development of guidelines. A key concern for research, as such, is what issues can be identified with the published evidence and if and how NICE

themselves engage with the potential problems associated with industry produced RCT data.

The centrality of the industry in the development and dissemination of pharmaceutical knowledge should be clear from the above discussions. However, if the regulation of pharmaceuticals is independent and robust, surely evidential problems or biases will inevitably be exposed? The sociology of pharmaceuticals suggests, however, that regulation is rarely independent and that regulatory standards are deficient and have diminished rather than strengthened over time. Abraham has explored the history and politics of drug development and regulation through detailed case studies. However, perhaps his primary contribution to the field has been to establish the theory of corporate bias. Whilst this is a distinct contribution from his outline of pharmaceuticalisation, aspects indicative of corporate bias (such as lessening standards of regulation) are likely to have driven pharmaceuticalisation. Abraham (2008a: 873-874) views corporate bias as follows:

> the pharmaceutical industry was, and is, permitted to have privileged strategic access to, and involvement with, government regulatory policy over and above any other interest group; and more often than other factors, the industry was, and is, decisive in determining regulatory policy outcomes (or lack thereof). The regulatory state and the pharmaceutical industry work largely in partnership and behind a cloak of secrecy.

Rooted in an objective interest-driven realist framework against which the behaviour of actors can be examined, Abraham (2007; 2008a) suggests that patients have real interests in medicines having an optimal benefit-risk ratio, whilst industry has an objective interest in the maximisation of their profits. Turning to political sociology Abraham draws on aspects of regulatory capture (Bernstein, 1955) and corporatism to advance the notion of corporate bias. Regulatory capture suggests that regulatory agencies, whilst initially adversarial towards the regulated industry become captured by the industries they regulate. This may be the result of lobbying of government officials or as initial staff retire the development of a 'revolving door' where officials begin careers with industry before becoming regulators (and even subsequently moving back to industry). Regulatory capture is suggested to be cyclical where failures trigger public clamour for new or further aspects of regulation. Corporatist theory meanwhile assumes a regulatory state with its own interests. Rather than being initially adversarial, and subsequently passively defending industry after capture, there is more of a two-way

bargaining. Abraham argues that corporate bias, a variant of corporatism, better grapples with the nature of pharmaceutical regulation than regulatory capture (though aspects of regulatory capture are evident). This is particularly because the state has been at various points concerned with protecting its own interests independently. For example, the government produced a limited list in the mid-1980s which resulted in almost 2000 pharmaceuticals no longer being available on the NHS due to expense and therapeutic concerns. Importantly though, corporate bias has become neo-liberal corporate bias since the 1980s. Regulatory agencies have increasingly derived fees for their work from the drugs companies who have become customers (including the MHRA and more widely in the EU). Indeed, regulatory review times have steadily decreased as this is what the companies-as-consumers have clamoured for (Abraham and Lewis, 2000; Abraham, 2008a). Whilst the same companies-as-customer and regulatory fee issues do not apply to NICE in exactly the same way (particularly their guidelines), the institute has introduced in relatively recent time their single technology appraisals (STA) in addition to the multiple technology appraisals (MTA) (that look at a whole class of drugs rather than a single drug/technology). This has been aimed at reducing review times and seems to shift power towards the pharmaceutical companies who provide initial economic assessments, which often, and perhaps unsurprisingly, come in just under the upper QALY threshold for recommendation, suggesting cost-effectiveness but at a level that is the most profitable for the company (Timmins et al., 2016: 87-88).

Another important contribution in the work of Abraham relevant to understanding deficient and diminishing regulatory burden is that of the 'permissive principle' (Abraham, 2002; Abraham and Davis, 2009). This also potentially has more relevance to NICE's guideline development processes. Reflecting the entanglement of regulators with the industry they are regulating, the permissive principle in its application to the sociological analysis of pharmaceuticals is defined by the assumption that benefits are said to outweigh risks unless significant evidence of harm exists (Abraham, 2002: 20) and the "tendency to allow a drug on the market despite it not meeting established standards of efficacy or safety" (Abraham and Davis, 2009: 570). The opposite (though both could feature simultaneously in regulatory assessments) and traditional representation of clinical trialling and regulatory assessment, the precautionary principle, assumes that the tests are ones selected because they are most sensitive to assessing harm. As such, in applying critiques of permissiveness the burden

of proof falls on those of who perceive the drugs to be unsafe (Abraham, 2002). A precautionary approach is likely to require more significant evidence of benefit/safety, particularly where alternate treatments might already exist (both pharmaceutical and not) (Abraham, 2002). However, evidence suggests that the permissive principle has featured heavily in the regulation of various types and classes of pharmaceuticals over time (Abraham, 1995; Abraham and Sheppard, 1999) and often involves the violation of their own established technical standards (Abraham and Davis, 2009). In the case of triazolam (Halcion) a controversial hypnotic, in a US context in the 1990s Abraham (2002) shows how the permissive principle functions. For example, anecdotal evidence (despite lack of compelling RCT data) was utilised to confirm efficacy by expert committees at the Food and Drug Administration (FDA) and the Institute of Medicine, whilst simultaneously RCT evidence was required to confirm a lack of safety. Disjuncture or selectiveness between the use of evidence here, to the approval benefit of the drug, is suggestive of permissiveness. Overall, if benefit is assumed to outweigh risk, with a heightened burden on attempting to disprove benefit over risk, and/or some undermining of a body's own technical standards, the permissive principle, advanced by Abraham (2002) and Abraham and Davis (2009) in the STS tradition, can be said to have explanatory power.

Regulatory trust may be a key component underpinning permissiveness. In other work, Abraham (2008b) outlines two forms or norms of regulatory trust – investigative and acquiescent. Abraham suggests that in the countries such as the UK and the USA the underpinning norms of regulatory trust have shifted from investigative to acquiescent – that is, from norms that mean a thorough assessment of company data (and the anticipation of this by industry) to a greater sense that industry data will be accepted relatively uncritically. This, Abraham argues, reduces the incentives for companies to conduct adequate trials. Shifts in norms of regulatory trust are visible clearly in trends towards accelerated drug approvals (Davis and Abraham, 2011).

Having discussed the development and dissemination of pharmaceutical knowledge, the relationships between industry and regulators and deficient and diminishing regulatory standards at a general level, it is possible now to situate NICE in relation to these aspects and to establish gaps for further empirical research. As discussed in the early stages of this thesis, NICE is concerned with ensuring the cost-effectiveness of interventions that have already been given marketing approval

(assessing quality, safety and efficacy) (Timmins et al., 2016). Despite being a critical component in whether medicines are utilised in the NHS, the newer, additional layer, or so called 'fourth hurdle' (Crinson, 2004; Timmins et al., 2016) in the processes of regulating pharmaceuticals, that of cost-effectiveness evaluations embodied by NICE in the UK, has received very limited attention by research concerned with pharmaceuticalisation. In fact, NICE and similar bodies are absent from the Williams et al. (2011a) conceptualisation of pharmaceuticalisation. As discussed earlier in this chapter, this is despite problems associated with reliance on published evidence and the role that guidelines themselves play in establishing the legitimacy of a condition to treat within the mainstream medical consensus. Interestingly whilst bodies like NICE emerged ostensibly as a means to protect health services from the spiralling costs of pharmaceuticals (Timmins et al., 2016) and might be thought of as increasing regulatory burden overall, it is also clear that the pharmaceutical industry quickly saw the potential benefits of guidelines (Healy, 2012). Despite some debate at NICE about whether industry funded RCTs should be downgraded in the hierarchy of evidence to below that of independently funded RCTs, particularly following controversy surrounding SSRI antidepressants, no distinction is explicitly codified by NICE to guide evaluative procedures (Healy, 2012: 148). NICE have to manage significant levels of uncertainty and complexity in their guidelines and other appraisals, ranging from managing industry influences through to managing the sheer volume of data in many reviews. It is, as such, perhaps unsurprising that their evaluations are underpinned by 'system trust' (Luhmann, 1979) in the epistemic concreteness of biomedicine (regardless of funding source) and the systems of dissemination/publication to protect against bias in the evidence. Problematising industry data or publication bias would only serve to add additional layers of uncertainty to processes of evaluation (Brown and Calnan, 2013; Calnan et al., 2017).

Importantly Abraham (2009a) shows that in NICE's early years the overwhelming majority of drugs they reviewed achieved recommendation by NICE, which has continued to date (NICE, 2017). Whilst some of this reflects aspects already explored in this chapter (e.g. problems with published data or reliance on industry for evidence), the influence of broader social and political factors (which the pharmaceutical industry often exploit) can also undermine NICE's remit. This is because NICE exists in a polycentric regime (Black 2008) where regulators are themselves regulated by socio-political factors and

phenomena, particularly the pharmaceutical industry and the news medium (see below for discussions of media) (Brown and Calnan, 2010; 2013), whilst the government may also shape or undermine NICE's decision-making or processes as fits their own interests (Abraham, 2009a).

It is clear that a few notable controversies in the early years of the Institute seem to have set the tone for its existence and undermined its ability to provide any sort of strong resistance to the interests or influences of the pharmaceutical industry – and perhaps confirms the existence of corporate bias and/or the permissive principle. Abraham (2009a) discusses how the influenza drug *Relenza* produced by GlaxoWellcome was not recommended due to insufficient benefit. However, after threats to move premises out of the country and after 'new evidence' provided by the company was given to NICE, the Institute revised its recommendation so that it could be prescribed to certain at-risk individuals. Here, as discussed in this chapter, NICE were dependent on industry data, but additionally political and economic pressures, exploited by industry, seem to have impacted on their decision-making. Meanwhile, multiple sclerosis drug beta-interferon, a very expensive drug within the context of the NHS budget, was not recommended to be funded by the NHS. Appeals were made by various interest groups, including industry, but also, for example, industry-aligned patient groups who descended on parliament, though NICE ultimately upheld their decision. Under significant pressure, the government (with the Prime Minister Tony Blair becoming agitated) negotiated a 'risk sharing scheme' with the manufacturer to fund the drug, despite limited scientific evidence (Abraham, 2009a; Crinson, 2004; Timmins et al., 2016). In a more recent example, the government also stepped in on the issue of access to cancer drugs – extremely expensive drugs which often only extend life by a short period of time. NICE's established QALY threshold excluded at the time of evaluation, for example, kidney cancer drugs such as *Sutent*. Cancer is a disease with significant political capital, with issues surrounding denial of access rearing its head close to the 2010 General Election in the UK. The Cancer Drugs Fund was announced as a solution to the problem of accessing expensive cancer drugs. This fund was to the benefit of the pharmaceutical industry, undermined NICE's role, and actually meant a worse deal for the NHS all because it took the manufacturers' price rather than allowing NICE to alter its QALY threshold for cancer drugs and achieve discounts as resulting from existing access schemes/agreements (Timmins et al 2016). Importantly, the interplay and relationship between different

actors in the widening of the pharmaceutical regime (Williams et al (2011a) clearly emerges here.

There may also be conflicts of interest between those appearing on guideline development groups, who are often KOLs with numerous links to the pharmaceutical industry. The presence of such connections has been clear in a variety of different areas of medicine and guideline development almost since the inception of clinical practice guidelines (Healy, 2012). Whilst calls for greater transparency in medicine in recent times have emerged, with NICE themselves having a detailed declarations policy, due to the state of dependency on and interconnection with industry, it is difficult to appoint a truly industry-independent guideline committee. Indeed, as Moynihan and Cassels (2005) discuss (see also Moynihan et al., 2002), KOLs involved with cholesterol and CVD risk guidelines have had ties of various sorts to the pharmaceutical industry (e.g. paid consultant, speakers, or research funding). Evidence exists that older guideline writers (in the US context) had direct ties to statins manufacturers, and even in new guidelines the overwhelming majority of members had connections to the world's major drug companies, often having multiple ties (Unruh et al., 2016). Whilst a link between widening diagnostic categories and guideline developers with ties to industry is apparent (Moynihan et al., 2013), what is important here is not necessarily a directness of conflict of interest or intent to widen diagnostic categories or levels of acceptable usage to please companies. Rather, the shaping of long-standing relationships and the creation of a positive concept of industry and its products are subtler aspects impacting doctors and medical academics (Sismondo, 2008). Does a certain cosiness with industry result in a sufficiently critical eye applied to the evidence (particularly given the limitations of and problems with industry funded data)? Or perhaps it results in the recommendation of a drug treatment, such as statins, rather than more greatly emphasising alternate methods of reducing the risk of a heart attack (e.g. lifestyle changes)? Guideline production is only part of a broader systemic puzzle that has been explored in this chapter but is again indicative of dependency on and interconnection with industry systemically throughout medicine that can limit the effectiveness of regulation. Other medical sociological work of an observational nature has provided insight into some of the knowledge dynamics and the micro-level actualities of the production of guidelines (Knaapen et al., 2010; Moreira, 2005). However, the aims of these studies, far from the conceptual parameters

of pharmaceuticalisation, pay limited sustained or specific attention to how the pharmaceutical industry might be implicated in proceedings.

2.3 Regulators: Justifications for Further Research

The initial section of this chapter has discussed the second dimension of pharmaceuticalisation which identifies diminishing regulatory standards and the dependency of regulatory bodies on the pharmaceutical industry as potential drivers of pharmaceuticalisation. This section of the chapter first discussed the centrality of the pharmaceutical industry in the development and dissemination of pharmaceutical evidence and potential mechanisms and processes that might be involved in shaping knowledge and evidence. The purpose of these discussions was to highlight the nature of the evidence that regulators have to draw on in their work. Beyond the development and dissemination of pharmaceutical knowledge, this section then discussed how regulators themselves appear to lack independence from the pharmaceutical industry and concluded with discussions of NICE's specific regulatory positioning and potential vulnerabilities to the influences of the industry within the pharmaceutical regime.

Though the concept has sought to grapple with regulatory standards and the relationships between regulators and industry, there is little detailed analysis of NICE's role in the processes of pharmaceuticalisation (Williams et al, 2011a). This is despite the fact that NICE make funding decisions about which pharmaceuticals should be available within the NHS and create clinical practice guidelines that reify medical knowledge and shape the prescribing behaviours of physicians. Due to NICE's unique regulatory and organisational positioning, analysis needs to consider its relationships with, dependencies on and particular vulnerabilities to the influences of the pharmaceutical industry. More specifically, when considering movements in the pharmaceutical regime in this case, NICE are the actor that have opened up the opportunity for further pharmaceutical deployment by widening the primary prevention threshold where statins may be prescribed. Considering the discussions so far in this chapter, it is, as such, crucial for any research concerned with CG181 to consider if and how the pharmaceutical industry might have shaped the decision-making of the Institute. Specifically, research needs to concern itself with what problems in the statins evidence base reflecting the influences and interests of the pharmaceutical industry might exist that subsequently

shaped NICE's decision to widen the primary prevention threshold where statins can be prescribed. GDGs are also made up of researchers and medical professionals, many of whom have financial and research connections to the pharmaceutical industry. The issue here is a potential lack of independence between researchers and professionals and the creation of relationships and perceptions that lead to the promotion of the expansion of the availability and use of pharmaceuticals. This clearly reflects both the establishment of relationships between industry and KOLs designed to widen use of medicines, but also the inseparability of regulatory decision-making from industry. At the level of the guideline development group, can the influences of industry be established in terms of connections between members and industry that might lead to diminished regulatory burden or permissiveness?

As discussed in Chapter One, the overall aim of this thesis is to examine the degree of the further pharmaceuticalisation of CVD in this case and its driving forces. Considering the above discussions, to achieve this it is necessary to focus, first, on if and how the influences of and relationships with the pharmaceutical industry might be implicated in shaping and driving NICE's decision to open up the opportunity for widening medicalised pharmaceuticalisation. It is also necessary to look at how these aspects have shaped the extent to which further pharmaceuticalisation has occurred, examining, for example, whether existing evidence (potentially of different types) suggests that pharmaceuticalisation is justifiable, should have been restrained, or perhaps could have been even greater. This thesis, as such, pursues the following research question: *In what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?*

2.4 Media and Medicines

Though empirical attention has been devoted in varying degrees to all the dimensions identified by Williams et al. (2011a), by far the least attention appears to have been given within pharmaceuticalisation studies/the sociology of pharmaceuticals to the role of media. Indeed, in an introductory paper to a special issue on pharmaceuticalisation in *Social Science and Medicine*, Gabe et al. (2015) provide an overview of the 'pharmaceuticalisation studies' field, and of the six identified dimensions in Williams et al. (2011a), only media had received no analysis specifically of its own. Williams et al.

(2011a) argue that (in various formats) media is highly salient in processes of pharmaceuticalisation, and potentially processes of resistance to pharmaceuticalisation or even de-pharmaceuticalisation. In celebrating or condemning pharmaceutical developments, media may foster a sense of pharmaceuticalisation – of extent, desirability, necessity (Williams et al., 2008). Whilst media does not create or directly drive the development of new drugs or markets, it does, however, potentially facilitate and shape the extent of deployment, use, and understanding through certain framing methods, agenda setting, or promotional activities. The 'sense' of pharmaceuticalisation as portrayed in news coverage is in a way independently important in that it contributes to pharmaceuticalisation through disseminating ideas about scale, the desirability and necessity of drugs, operating on a rhetorical or conceptual level, but could also influence the behaviour of other actors within the pharmaceutical regime.

Though there was no analysis of media within the above special issue on pharmaceuticalisation, some analysis of media particularly in the broader sociology of pharmaceuticals does exist, however. As Dew et al. discuss (2016), 'media' is a highly heterogeneous entity in today's world and refers to a variety of mediums through which the processes of pharmaceuticalisation might be filtered and expand or contract. As such, before turning to examining the news medium (which as indicated earlier in the thesis was important in the context of this case), there is a need to explore work on media at a broader level. To begin, the impacts of advertising both to patients (Conrad and Leiter, 2008) and professionals (Collin and Otero, 2015) is potentially significant in pharmaceuticalisation. In New Zealand and the USA direct-to-consumer (DTC) advertising is a very significant vehicle for expanding the markets for medicines. The basic goal is to create a direct connection with consumers and encourage them to ask their doctor about a particular drug. DTC advertising is reminiscent of older forms of direct relationships between those producing drugs and their consumers, albeit utilising sophisticated advertising techniques and with a neoliberal flavour (Conrad and Leiter, 2008). As Lexchin (2006) discusses, DTC advertising has been very significant in widening, for example, the market for erectile dysfunction and the use of Viagra from only those with established medical problems (e.g. spinal cord damage) to a lifestyle drug that might be used by almost any man. In their marketing Pfizer have used images of young sportsmen, for example, to emphasise how almost anyone could benefit from enhancement from time to time. Evidence more generally exists to suggest that DTC

advertising has successfully broadened pharmaceuticalisation, including that associated with cholesterol reduction (Zachry et al., 2002; see also Angell 2004: 123-126), particularly because of increased patient demand (Frosch et al., 2007; Mintzes 2002; Mintzes et al., 2002;). Importantly, rooted supposedly in the empowerment of the lay actor, no longer passive recipients of medical advice, the consumer is encouraged to ask their doctor for a certain medication as a result of engagement with such advertising media (Seale, 2004). Though the only countries where DTC advertising is permitted is the US and New Zealand, elsewhere in the world pressure has been applied by industry to attempt to legalise it or at least to allow regulator-approved information to be disseminated online (Moynihan and Cassels, 2005; Mulinari, 2013). Beyond the US and New Zealand, evidence also suggests that companies may attempt to advertise more indirectly through sponsorship of public events and through press releases (Ham et al., 2008).

The internet meanwhile, which in some ways has provoked the occurrence of medicalisation and pharmaceuticalisation beyond professional spheres of influence, has combined interestingly with an increasingly active and 'expert' patienthood associated with seeking out health information and has blurred the boundaries between the cyber and the medical (Miah and Rich, 2008). More specifically, work has also shown how the internet may facilitate not solely information about but also access to drugs (Fox and Ward, 2008), potentially illicitly, and potentially undermining regulatory frameworks as a result of its borderless nature and the gatekeeping role of medical professionals (Fox et al., 2005b). A specific form of online media, social media, is becoming increasingly influential in today's world, utilised in innumerable ways on a vast scale. The internet has been pivotal in reshaping illness from a private experience to a public one, with social media being a particularly interactive and collaborative form through which this is occurring (Conrad et al., 2016). Online communities may provide the opportunity for users of certain drugs (such as weight loss drugs) to provide support and share experiences patient to patient, although this may have both aspects of empowerment and domination (Broom and Tovey, 2008; Fox et al., 2005a). Other online communities, such as those existing on pro-anorexia websites, may engage in communication and information sharing in the subversion of the dominant medical and social understandings of conventional usage of drugs, even to promote an anti-recovery perspective (Fox et al., 2005c).

At a more general level than pharmaceuticals, sociological explorations of media and health are more well developed (Nettleton, 2004; Seale, 2002; see also Dew et al., 2016). In constructing the self in late modernity one of the greatest repository of resources is certainly the mass media. Though appreciating the audience as active decoders who diversely interpret messages potentially in a way that does not align with the intentions of the producer (Hall, 1980) (although caution about audiences as always active is needed), Seale argues that "when people get sick, or make decisions about health, or visit their health service providers, or decide what to think and vote about health care policy and finance, their behaviour may be formulated in large part from resources drawn from various mass media" (Seale, 2004: 514). Media of different formats also offer a variety of experts and other actors a platform to debate issues (see Gabe and Bury, 1996: 458), although of course how exactly this is done, reflects the type and form (Dew et al., 2016; Gabe and Bury 1991: 452; Seale, 2002) as well as, where applicable, specific (journalistic) concerns about newsworthiness and balance. At the crux here, matters of health and illness are highly mediatised.

Turning specifically now to the news medium, whilst some evidence exists of declining circulation figures and falling advertising revenue (see Greenslade, 2016) for newspapers, they clearly do retain significant influence. For example, though the print newspaper sector in general has seen declining circulation in recent years, two of the UK's most popular tabloid newspapers nevertheless have print circulations of around 1.5 million, whilst broadsheet newspapers such as The Times have actually enjoyed rising sales figures of 9.2% (Greenslade, 2017). This is also to say nothing about the increasing popularity of accessing online material from the same national newspaper titles. Indeed, though far beyond the parameters of this thesis, in these tumultuous times of political upheaval there is evidence to suggest retention of significant influence on political attitudes (e.g. Reeves and de Vries, 2016). It is also clear that the news medium views matters of health an illness as a core issue:

> A day seldom goes by on which The New York Times fails to publish a health story; three to five stories are common, with one often appearing on the front page… [Whilst, also, t]he editor of one metropolitan newspaper told us that his paper's management had a list of five topics, one of which had to appear on the front page every day; health was on that list (Briggs and Hallin, 2016: 1).

Medical sociological work highlights the need to appreciate the journalistic practices that underpin newspaper framing of matters of health and illness. Research and analysis has established that the newsworthiness of stories is paramount for journalists (Henderson et al., 2014) who are motivated by a desire to keep and expand their audiences, potentially resulting in sensationalism and the fostering of an atmosphere of fear, danger, risk, uncertainty or excitement – which news medium portrayals of matters of health and illness can easily fit into (Seale, 2002: 40). A story may make the news if it has some closeness in resonance, is unexpected, is controversial or negative, relevant to the daily lives of the audience, and/or involving important sources such as experts (Seale, 2002: 39). News and other media organisations are driven by a desire to keep and expand their audiences and thus seek out ways of stimulating audiences. However, newsworthiness is a negotiated process (Conrad 2001) which draws upon and simultaneously shapes public opinion on a particular topic (Howarth, 2013). News coverage of a topic may also beget further news coverage for a certain period of time (Seale, 2002: 39) reflecting but also exacerbating public interest in or concern about an issue. Petts and Niemeyer (2004) have similarly suggested that the news medium act as active interpreters who seek to resonate with social preferences and concerns.

Seale (2002; 2004) discusses the narrative conventions utilised by producers of news and other media content, and that, through repeated exposure, media audiences themselves are well attuned to. These conventions necessarily underpin representations of matters of health and illness. First, oppositions are a common component – heroes and villains, safety and disaster, life and death. Sensationalism, or tabloidisation, may emerge particularly through the utilisation of opposites, for example, a new drug which is a lifesaving miracle drug, or the next potential thalidomide. This might lead to criticism of the news medium by those interested in health promotion or science communication about the 'truth' of reporting. But, of course, newsworthiness and even an entertainment angle is important in the news medium, potentially beyond concern for accuracy – and, indeed, the impacts of news medium reporting regardless of 'truth' value are interesting from a constructionist sociological standpoint anyway. Additionally, a degree of simplification is necessary to make complex information digestible. Novelty is also a salient aspect of reporting. But this simultaneously means that previously novel events (e.g. heart transplant) require a further angle to be newsworthy. 'Templates', where previous events are referred to as another "disaster in the same style as…" allow for the

easy import of existing stereotypes and judgments to an emerging story (see Kitzinger, 2000). The use of metaphors allows for oppositional comparison and similarly the import of familiar imagery (e.g. the use of war metaphors is identifiable across a variety of types of news, from sport to health) (see also Coveney et al., 2009: 488-489). Numbers are often used in creating oppositions and to exaggerate effects or emphasise uniqueness. Seale (2002; 2004) moreover identifies key themes/narratives that may emerge in news medium representations of health including: the dangers of modern life (e.g. stories generating fear – the harmful drug, for example); villains and freaks (e.g. threats to health by stigmatised communities and potentially manufacturers); victimhood (for example, stories of sick children); and professional and lay heroes (for example, stories of the patient-victim as rescued from illness, or the personal account of success over illness by the patient). There are also interesting oppositional tensions between professional and lay knowledges. For example, there is potentially a growing and greater tendency to reduce the professional to villain and the championing of the Every(wo)man in the context of a dangerous modern life. These aspects help to configure what it is about health and illness matters that is newsworthy, albeit within the context of some of the broader and more general journalistic concerns outlined above.

However, and as noted earlier, as with other forms of media, the news medium has received surprisingly limited empirical attention by medical sociologists specifically analysing pharmaceuticalisation. The dearth of empirical attention so far within pharmaceuticalisation studies given to the news medium is surprising, as the above discussions indicate, because of its potential importance in patient, public and potentially professional opinion on the promises and problems of matters of health and illness, including pharmaceutical developments and deployment (Seale 2002). Some older work from within the sociology of pharmaceuticals concerned with tranquilisers does engage with news medium portrayals and the influence of the medium within pharmaceutical controversies (Gabe and Bury, 1991; Gabe and Bury, 1996; Gabe et al., 1991). This, however, was long before delineations of pharmaceuticalisation. One paper that does discuss news medium impacts specifically with reference to pharmaceuticalisation, is Williams et al. (2008: 27). In the context of work on news medium constructions of the drug modafinil and the medicalisation/pharmaceuticalisation of sleepiness, Williams and colleagues argue that the medium in 'praising and/or criticising [pharmaceutical/biomedical developments] ... may (inadvertently) contribute to

[pharmaceuticalisation], diffusing information and raising awareness of pharmaceutical products in the public's mind, thereby facilitating their potential uptake in everyday/night life.' However, one recent paper focusing on audience reception suggests that news medium messages about pharmaceuticals are interpreted in diverse ways by audiences, significantly drawing on lay expertise and potentially with reference to personal experiences or knowledge of particular drugs (Gabe et al., 2017). The authors here discuss negative news medium coverage of the use of hypnotics observing that audiences nevertheless seemed often to respond to such coverage in line with pre-existing views, as reflexive users (Williams and Calnan, 1996), and that, as such, some degree of caution is necessary regarding the power of the news medium to promote de-pharmaceuticalisation – at least as applies to hypnotics. Whilst the Williams et al. (2008) paper above suggests that news medium coverage may figure in public perspectives, awareness and knowledge of pharmaceuticals, this latter study by Gabe et al. (2017) alerts analysts to the dangers of *overemphasising* the importance of news medium coverage on the configuration of audience perspectives.

One other important point that has been made in the limited literature on pharmaceuticalisation is that coverage of drugs tends to grow more critical over time, peaking at a certain point in time, before becoming more stable with considerations of risk and benefit (Gabe and Bury 1996; Williams et al., 2011a). The emergence of issues and problems, particularly the experience of side effects, tends to be important in coverage becoming more critical, even to the extent where, at a certain point in time, there may seem to be no conceivable benefit portrayed in reporting (Entwistle and Sheldon 1999). These observations are likely to be analytically relevant when considering the stage and state of reporting on statins, which are drugs that have been in existence for roughly 30 years (Greene 2007), and as such the opportunity has occurred for the emergence, for example, of concerns about and experience of side effects. Indeed, older analysis seems to indicate more positive portrayals of statins in news medium reporting with the majority of reporting not discussing adverse events (Moynihan et al., 2000). In the context of the case under study, is coverage still at peek levels of criticism or has it become more balanced?

Meanwhile, other analysis (also from beyond pharmaceuticalisation studies) suggests that it may be particularly salient for sociological research on medicines regulatory/evaluative bodies such as NICE, such as this thesis, to sufficiently concern

itself with media impacts on regulatory bodies. This is because such regulatory bodies exist in polycentric regimes (Black 2008) where regulators are themselves regulated by socio-political factors and phenomena. In particular, the news medium through the dissemination of values and beliefs tied to matters of health and illness may shape regulatory activity in cases where decision-making collides with medium-disseminated beliefs/values (Brown and Calnan; 2010; 2013). Indeed, Abraham (2009a) makes reference to the news medium and cases of influenza drug *Relenza* and of access to four Alzheimer's drugs. NICE had previously declared that for both treatment of influenza and of Alzheimer's the assessed drug treatments should not be funded by the NHS due to a lack of cost-effectiveness. However, surrounding media pressure built up (in alliance with other interest groups) and subsequently NICE revised their decision to fund drug treatment in these cases. Here the news medium reported on and exacerbated issues surrounding, for example, telling patients they could not access drugs until their condition was more advanced (Brown and Calnan, 2010). The news medium acts with the ability not only to disseminate information, but also to apply the weight of public pressure to widen or potentially constrain access to drugs when either position resonates with existing social values. Research such as that by Safer and Krager (1992) has shown (for a long time now) the damaging impact problematising reporting can have on prescription rates. Gabe et al. (2012), this time within the context of early stage breast cancer and access to drug Herceptin in the New Zealand regulatory context, also identify the role of media as salient in a case of pharmaceuticalisation (without using the concept). In this paper the authors argue that news about matters of health, particularly about health controversies, are always imbued with social and journalistic values (as explored above) and necessarily, as such, may act to influence and persuade the public about the merits of a case and the specific positions of different actors, such as regulators and the drug industry. This means that the news medium has the potential to act as a countervailing power to the pharmaceutical industry, for example, in reporting and constructing the case of the regulators against the manufacturer (as partially made up the corpus of reporting). Other work, such as Gabe and Bury (1996) on tranquiliser use, more clearly suggests this. Here, in the case of *Halcion*, the authors show how coverage of side effects was an influential factor in the regulatory decision to suspend the licence for the drug, or, in essence, to promote depharmaceuticalisation. In addition, Dew et al. (2017), who discuss controversy surrounding a new formulation of hypothyroidism drug

Eltroxin, which was considered to be bioequivalent to its predecessor yet was greeted by a voluminous increase in adverse drug reactions that were reported to regulators. These authors show how news medium reporting of adverse effects can heighten patient consciousness of a certain drug causing adverse events (and thus potentially reporting it to pharmacovigilance schemes, even independently of a medical professional). It also might shape professional willingness to accept this connection, or indeed, heighten the chance they make this connection independently of the patient (and thus report this in their professional capacity to pharmacovigilance schemes). These latter papers are congruent with the Williams et al (2011a) conceptualisation of pharmaceuticalisation where it is argued that media are far from captured puppets of the pharmaceutical industry, and though they may celebrate pharmaceutical developments, they may also potentially exacerbate and publicise medical controversy, and even condemn expansion. It seems, as such, that media have an important role to play both in macro-level regulatory decision-making about expanding drug regimes, as well as potentially as one aspect in the configuration of individual patient/consumer perspectives, albeit it in complex ways distributed over existing lay knowledge and interactions with human and non-human actors (Gabe et al., 2017; Rapley 2008).

Others such as Hallin et al. (2013) have suggested that health reporting has become increasingly politicised with the (partial) opening up of health to public debate and some associated transition in the conceptualisation and address of the audience. These authors suggest that audience come to be treated as active patient-consumers seeking out information to inform decisions about health, or potentially viewed as citizens judging the claims/actions of authorities and even participating in the debate. This is associated, saliently, with more critical and negative portrayals of biomedical developments and increased reporting of controversy and conflicts of interest in contemporary reporting than reporting in the middle of the twentieth century. Indeed, as the authors state in another paper (Briggs and Hallin, 2010: 161) "in framing health reporting as debate on controversial issues rather than transmissions of settled medical knowledge, journalists simultaneously portray health as part of the public sphere and introduce into health reporting many of the conventions of political reporting." The reporting of controversy reflects the emergence particularly of a 'public sphere model' of 'biocommunicability'. Though drawing significantly on the concept of biomedicalisation in outlining biocommunicability, the authors themselves do not set up an either/or

distinction between biomedicalisation and pharmaceuticalisation. As they explore in other work (Briggs and Hallin, 2016) they see pharmaceuticalisation as of significant importance to the broader processes of biomedicalisation, and even explore the concept in terms of its own independent importance in a chapter within this book length appraisal of the mediatisation of health. Biocommunicability refers to the manner in which communication about health, illness and medicine is structured, with variant models emphasising particular norms/assumptions about knowledge circulation, conceptualisation of the audience, and types of actor involved. Reporting may be modelled more traditionally (though still in existence e.g. in times of health crisis) in the medical authority model which disseminates expert knowledge to a passive audience. Reporting may also take the form of the patient-consumer model, which assumes the audience to be active seekers of information to help inform their decision-making about matters of health. The public sector model of biocommunicability conceptualises the audience as citizen who will engage in evaluation and judgement of the claims and activities of health authorities, as well as potentially enter into the debate in certain cases. This model has variants but perhaps the most interesting one in the context of the case under study in this thesis is the 'elite public sector' model. As Briggs and Hallin (2016) show, the type of reporting indicative of this sub-model largely focuses on information emerging from biomedical institutions, but also is rooted in the idea that debate within this specialized realm will be open to argument, contention and debate, and possibly subject to the corrupting influences of economic or political gain. The public, though with minimal voice in constructing this debate, does, importantly, act as judge.

2.5 Media and Medicines: Justifications for Further Research

Whilst a significant amount of medical sociological exploration of media does exist, there is limited empirical analysis of media, and particularly the news medium, specifically examining pharmaceuticalisation. As such, further empirical explorations of news medium engagement with and portrayals of drugs, including statins, are required to deepen understandings within pharmaceuticalisation analysis. In contributing to this, as well as contributing to the overarching research question of this thesis as concerned with driving forces and extent, this thesis pursues the following research question in Chapter Five: *how did the UK print news medium present and portray the potential widening*

usage of statins? In answering this question there are several aspects of analytical importance.

Analysis needs to concern itself with portrayals of statins, and potentially surrounding, complementary or juxtaposed treatment alternatives within the therapeutic landscape (Pollock and Jones, 2015). This is perhaps particularly salient when considering some of the above discussions about coverage becoming more critical and then stabilising over time (as drugs that have been in existence for three decades) or the now more generally controversy-oriented nature of medical reporting. Research needs to establish how statins are portrayed in the contemporary news medium and reflect on what consequences this might have. The 'sense' portrayed in news coverage is important in that it contributes to pharmaceuticalisation through disseminating ideas about, scale and the desirability and necessity of drugs. Pharmaceuticalisation can occur in this way on a conceptual or rhetorical level.

Portrayals of relevant actors are also of significance here, particularly how respective positions are relayed and shaped and whether actors in the pharmaceutical regime seek out media to make their case, attempt to influence audience understandings or even attempt to promote, reverse, challenge or defend regulatory decision-making. In this sense, as part of examining the pharmaceutical regime, it is necessary for analysis to reflect on media as one aspect in the 'regulation' of the regulators in cases where organisations, such as NICE, may be expanding the use of pharmaceuticals.

Coverage may also (partially) shape patient, public and potentially even professional perspectives on pharmaceuticals and subsequently influence pharmaceuticalisation, resistance to or depharmaceuticalisation at clinical or patient usage level. Though research should be careful not to overstate the importance of reporting in the configuration of audience perspectives (Gabe et al., 2017), newspaper coverage may nevertheless be one resource that influences perspectives or is taken into account when decision-making about statins is undertaken. Thus, it is important to understand the nature of the coverage to begin to understand how it might impact or influence pharmaceuticalisation in other dimensions. In this way, analysis of news reporting within cases of medicalised pharmaceuticalisation (rather than unmedicalised) is interested in if and how coverage can be located in the composition of doctor and patient understandings and subsequent decision-making. Though caution is certainly needed about overstating the importance of coverage in shaping and

configuring audience perspectives, evidence exists that there is some level of association between positive and negative reporting and varying levels of patient adherence (Nielsen and Nordestgaard, 2016). Work by Matthews et al. (2016) assesses the relationship between uptake and desistance of statins as a result of coverage of medical controversy, particularly surrounding the papers published in the BMJ (see introductory chapter and Appendix 1), associated with the case analysed in this thesis. The authors argue that newspaper coverage had identifiable impacts on the numbers of prescription statins stopped in the immediate period surrounding and after the reporting of events (as many as 200,000 patients), although they could find no difference in the initiation of new prescriptions. However, these authors are unspecific in their definition of the coverage, and arguably neglect to focus on all relevant coverage over time, and do not focus on reporting of the new ≥10% threshold or uptake by patients who qualify. Similarly, they provide no comprehensive analysis of the *types* of portrayal that might influence (in combination with existing lay knowledge or perspectives) decision-making about starting or stopping a statin. Qualitative medical sociological research can cast light on these issues.

How does the focus on newspaper portrayals of statins in the case under study contribute to answering the overarching research question of this thesis as concerned with driving forces and extent? If newspaper portrayals create a sense of necessity and desirability and positively frame those actors opening up opportunities for pharmaceutical deployment, then the news medium might be said to be a driving force of widening pharmaceuticalisation. The degree to which pharmaceuticalisation is occurring in a particular case will be higher if media is a driving force. In this sense, extent can be argued to reflect in one way the 'sense' of pharmaceuticalisation fostered. Not least this occurs if a positive sense of vast and unending pharmaceuticalisation at a rhetorical level is created. As noted, coverage may also have potential impacts on how audiences perceive and subsequently approach decision-making about pharmaceuticals, thus potentially shaping pharmaceuticalisation in other dimensions. Extent will also be higher in this way where coverage does not undermine or attempt to limit or challenge regulatory decision-making or the actions of those wishing to further pharmaceuticalisation more generally.

2.6 Patients and Professionals – Identities, Meanings, Understandings, Deployment and Use of Medicines

The final relevant dimension outlined in the analytical framework delineated by Williams et al. (2011a) is the role of patients and consumers in expanding the availability of pharmaceuticals, the meanings given to and use of medicines by patients and consumers, as well as pharmaceutical identities that are formed. As noted in Chapter One, Conrad (2005) in updating and contemporising his conceptualisation of medicalisation, views consumers as one of the driving forces of medicalisation. In this vein, Williams et al. (2011a) deepen the examination of the role of the consumer in the expanding parameters of the medical realm in proposing the examination of lay actors in driving pharmaceuticalisation and/or becoming pharmaceuticalised.

Some of the analytical interest in this dimension relates to relationships between the pharmaceutical industry and patients. Patient activism may be prominent in battling for widened or faster access to drugs, such as in the case of access to breast cancer drug Herceptin by women in the early stages of the disease (Gabe et al., 2012). Some work, from a position that might be referred to as disease-politics theory, has claimed, for example, that in the aftermath particularly of the AIDs crisis in the 1980s and the emergence of patient activism surrounding access to drugs, said patient activism was independently important in reshaping regulatory procedures and speed of approval. Although Williams et al. (2011a) make clear that the autonomous impacts of patient groups are still a point of argument, Abraham (2009a) argues, however, that the successes of patient groups are largely dependent on allegiance with the pharmaceutical industry – pointing towards the more limited successes associated with legal challenges (e.g. seeking compensation for harm) against the pharmaceutical industry. Rose (2013) meanwhile suggests that funding can foster a level of dependency that can bias the goals of patient activism or patient organisations towards that of industry.

Whilst patient groups (particularly in allegiance with industry) may be important actors in driving pharmaceuticalisation at the macro-level, for example, potentially through campaigning for access to drugs, this is an issue of minimal importance to this thesis. Indeed, the presence of consumer groups as driving the widening availability of statins in the case under study is not something that featured with any significance – although could be in other cases of medicalised pharmaceuticalisation. However, as also encompassed by this dimension of pharmaceuticalisation, an issue of interest and value in understanding and analysing the case under study is the everyday usage and

deployment of drugs, associated identities and underpinning perceptions, understandings and meanings given to medicines more generally by patients and arguably professionals.

Providing lay knowledge with a voice and a certain legitimation has been a key concern in medical sociology and there is a long tradition of the exploration of understandings, meanings, perceptions attached to health and illness by lay people (see for example, Calnan 1987). Across a diverse array of issues and diagnostic categories this body of literature within medical sociology is now vast and is well-trodden terrain. This tradition also includes engagement with the understandings attached to and the use of medicines by lay people. For example, Britten (1996) labels beliefs and actions surrounding medicines as either orthodox (rooted in medical opinion) or unorthodox (which includes a general aversion and emphasises a non-medical, problematising approach). Analysis has also suggested that there may be significant lay resistance to taking pharmaceuticals rooted in concern about the medicines themselves (particularly adverse effects), but also issues with regimens, identity and stigma (Pound et al., 2005) which might be said to be suggestive of some lay resistance to the seemingly boundless pharmaceuticalisation of society.

Drawing on this broader tradition concerned with lay understandings and experiences, this dimension of pharmaceuticalisation encourages further analysis of patient and consumer identities, understandings and use of pharmaceuticals. A clear example of empirical research investigating this dimension of pharmaceuticalisation, and one that deepens insights from older research, is Dew et al. (2015) who focus on the moral dimensions (e.g. responsibility, stigma, dependence) of the use of medicines by lay people. They suggest four positions or repertoires taken by patients/consumers reflecting varying degrees of what they term pharmaceuticalised governance, a concept which reflects situations where action is governed by pharmaceutical regimens and involves the construction/adoption of complex moral positions particularly surrounding responsibility. The four repertoires include: disordering society (active resistance, scepticism of the pharmaceutical industry and professionals, and pharmaceuticals as unable to tackle the social dimensions of disease); disordered self (a regretful dependence as a result of lack of self-responsibility for health); disordering substances (concerns about adverse consequences, including side effects but also on social roles, with costs and benefits weighed up uniquely in particular situations); and re-ordering

substances (drugs are morally neutral and use reflects natural need and compliance with external advice). These four repertoires reflect varying interpretations of the driving forces and legitimacy of pharmaceuticalisation and varying identities and degrees of independence from or dependence on pharmaceuticalised forms of governance.

Polak (2017), meanwhile (partially) building on the work of Dew et al. (2015) discusses the complex moral notions attached to being a statins user. She shows how statins have distinct moral notions attached to their use, requiring a complex balancing act between it being 'irresponsible' not to take a drug one 'needs' and a broader health promotion angle that emphasises how 'healthy living' can in itself reduce cholesterol/risk of heart attack without the need for a drug. This internal debate seems to give statins a relatively special status in analysis of the moral parameters of pharmaceutical use. This focus by Polak (2017) on the complex web of norms and morals that individuals balance in deciding whether to become pharmaceuticalised is important recent analysis. In focusing on identity construction and the morality of taking statins, Polak goes far beyond a broader range of studies that focus more limitedly on understandings of and decision-making by patients about statins (and subsequent treatment 'pathways') and associated understandings of cholesterol and risk assessment (Farrimond et al., 2010; Gale et al., 2011; Jovanovic, 2014; Polak, 2016; Saukko et al., 2012).

As part of a broader project on heart health, Will and Weiner (2015) explicitly link the use of statins to the conceptual underpinnings of pharmaceuticalisation (which Polak 2017 mentions but only in passing/indirectly through her use of the work of Dew et al., 2015). The specific angle Will and Weiner approach the topic is through the reclassification of a low-dose statin for sale over-the-counter (OTC) in the UK in 2005, as such, exploring the individual pharmaceutical consumer. The authors, first, conducted documentary analysis on policy, professional, and marketing narratives. They found that in policy discourses, the reclassification of statins was connected to rationales of self-care and individual health autonomy. The 'citizen-consumer' is encouraged to become involved in and knowledgeable about beneficial therapeutic care and preventions. It was expected that concerned citizen-consumers would engage with the newly classified product, seeking out testing by pharmacists to establish their risk profile (10-15% was deemed at enough risk to warrant low-dose OTC statins). However, in professional narratives, it was apparent that these consumerist tendencies were not thought of as beneficial, even if taking statins was. Patients, in these secondary professional narratives,

were framed as 'flawed consumers' who would make bad choices, such as taking too much medication or too little, or neglecting healthy lifestyle behaviours as a result of taking the drug. Professional narratives were framed in relation to the continuing need for prescription of statins and professional involvement. This is in contrast to the framing of consumers in marketing narratives, who were presented as rational, ordinary people, with the ability to weigh up pros and risks, who were doing their best in terms of lifestyle to stay healthy, but wanting to proactively utilise additional measures in ensuring a healthy heart. Though different in their emphasis, all three types of narrative assumed that there would be a market for the drugs. This did not, however, occur in actuality, and sales were very low. The authors also conducted interviews with the few individuals they could find who had engaged with OTC statins, who had begun and desisted, those who resisted statins completely (both OTC and prescription) and individuals who sought out alternate means of management. Perhaps the most important analytic element that emerges in this work is the role of the professional in pharmaceuticalisation. They stress the continued importance of professional prompting and advice to take medication, and in doctor identification of a problem in the first place, connecting the lack of professional involvement as a key element in a lack of consumer interest and construction of anti-pharmaceutical identities in the case of OTC statins. Importantly, Will and Weiner state:

> Though the literature on pharmaceuticalisation emphasises consumer demand and action, our data… suggest the continued importance of healthcare professionals both warranting drug use and advising on health. In contrast to the notions of resisting consumers and expert or compliant patients, we have suggested the idea of the activated patient or the primed consumer, who may wish to take control of managing aspects of their health following their own rationales, *but do so following professional prompting* (Will and Weiner, 2015: 287, emphasis added).

As will be important in the following section, that doctors and other health professionals retain value in patient decision-making is important analysis. This is not necessarily a completely unique finding in pharmaceuticalisation analysis, however. Though in a context of far greater severity and significant vulnerability (advanced stage cancer), Brown et al. (2015) suggest that trust in professional expertise (interweaved with other forms of trust and hope) is a crucial aspect in the engagement/desire to participate in experimental cancer drug trials. This is clearly a very different context to that of the use of statins in the primary prevention of CVD but nevertheless the importance of

professional expertise in decisions about becoming pharmaceuticalised emerges in this work. Whilst Williams et al. (2011a) do acknowledge that professional expertise retains a certain level of importance in the decision-making of patients and professionals, interestingly, however, this dimension is primarily oriented towards patients and consumers in the processes of pharmaceuticalisation.

The discussions in this section of the chapter have thus far highlighted the existence of a body of existing work and insight in the sociology of pharmaceuticals exploring patient perspectives on and the use of pharmaceuticals (including statins). It should be clear to the reader that, reflecting the prominence of the broader goal of legitimising and giving voice to lay knowledge and experience within medical sociology, the body of work on lay understandings and experiences of pharmaceuticals, and even of CVD medications, is very well developed. However, within pharmaceuticalisation studies less is known about other subprocesses and actors involved in medical decision-making and how this might shape particularly medicalised forms of pharmaceuticalisation. In the latter stages of the above part of this section this chapter has also highlighted the potential importance of medical professional expertise in decision-making about statins as well as a potential lack of consumerist impulse – at least within the prevention of CVD. Despite this, and partially reflecting the way that Williams et al. (2011a) approach this dimension of pharmaceuticalisation, the place of professional expertise in decision-making about drugs, including statins, has been given little empirical attention. This is despite the fact that a stratified professional expertise (even where this may be hard to divorce from the influences of the pharmaceutical industry) features significantly in the widening of pharmaceuticalisation at the macro-level (as discussions earlier in the chapter indicated, elite doctors feature in guideline development as KOLs). More importantly, though, for the purposes of this section of the chapter and the analysis presented later, the salience at the clinical level of 'rank and file' professionals' understandings and their place within decision-making about drugs has been given little detailed attention thus far in analysis of pharmaceuticalisation.

Perhaps one of the reasons the medical profession has been largely absent from initial conceptualisations of pharmaceuticalisation and subsequent empirical analysis is because the inherent involvement of doctors in the diagnosis and treatment of a condition has been already been encapsulated in a definitional and conceptual sense within the boundaries of medicalisation. The now classic conceptualisation of medicalisation as

occurring across three levels (conceptual, institutional, and interactional) by Conrad and Schneider (1980) (see also Conrad, 1992), though importantly not always requiring professional involvement, does necessarily involve the medical professional at the interactional level (though only potentially at the other two levels). Whilst this is important, it was also established in Chapter One that pharmaceuticalisation does different analytical work from medicalisation particularly in terms of its greater specificity of focus. In this sense, where the central analytical concern is pharmaceuticals, there is nothing precluding the analysis of the role of medical professionals in the process of pharmaceuticalisation – albeit a medicalised form of pharmaceuticalisation which the first chapter of this thesis uniquely defined and conceptualised.

One notable contribution to understandings of the role of professionals in the processes of pharmaceuticalisation is offered by Busfield (2010). Though Busfield does not use the term pharmaceuticalisation (in other work, as discussed in Chapter One, she has been critical of the utility of the concept – see Busfield, 2017), she does, however, explore the driving forces behind the vast expansion of medicines use. Alongside the pharmaceutical industry, governments, insurance companies, and the public, she argues that doctors are both important in the development of medicines (through work in academia, industry and clinical contexts), and as primary gatekeepers to prescription medications. In terms of the latter of these elements, three factors are established by Busfield (2010) as contributing to expanding use of medicines, at least some of which seems to be inherent to the role of the doctor – interventionism (or desire to provide help/treatment), imbalances in risk assessment, and limited knowledge of pharmacology. Interventionism, both in terms of altruistic desire to help and also appeasing supposedly consumerist patients, argues Busfield, means that a high proportion of doctor/patient interactions end with a prescription (potentially more than half). A prescription symbolizes an 'answer' to the problem and a way of bringing time-sensitive consultations to an end. Second, in judging the risk to a patient in terms of treatment or non-treatment, doctors simultaneously tend to err on the side of caution whilst also playing down the risks (e.g. side effects) of drug treatment. Finally, certain doctors (particularly non-specialists working in primary care) are often limited in their knowledge of pharmacology – with Busfield (2010) citing studies suggesting that many GPs admit that they do not have the expertise, ability or time to evaluate trial data on efficacy and safety.

Busfield's work here, however, arguably does not consider some of the micro-level and situational aspects unique to individual professionals and consultations or certain structural aspects that influence prescribing behaviour. However, work in the sociology of prescription does alert analysts to the broader array of beliefs and understandings evident at the micro-level in terms of individual understandings, beliefs and approaches, as well as other institutional, political and cultural factors influencing prescribing (Britten, 2001; 2008; Gabe, 1990; Gabe and Lipshitz-Phillips, 1984). This body of literature, which is mostly older and written prior to the development of the concept of pharmaceuticalisation is nevertheless necessary to consider because it highlights some of the factors shaping and influencing prescription by professionals, and thus is important to consider when analysing whether professionals are driving or limiting forces of the extent of pharmaceuticalisation in the case under study. The existence of this body of literature does not limit the value of focusing on professionals within the parameters of pharmaceuticalisation. Rather, it is argued by this thesis that the importance of some of the analysis offered by the sociology of prescribing (and other literature on professionalism) concerning professionals has been made peripheral in favour of a focus on consumerism within analysis of pharmaceuticalisation.

As shown by Gabe (1990) and Gabe and Lipshitz-Phillips (1984), it is clear that doctors bring different perspectives, beliefs and understandings about drugs to consultations with patients on general and drug-specific levels (reflecting concern, for example, about dependence or side effects) and may interact with patients in ways influenced by gender, class or ethnicity. The approach taken in the consultation and certain situational characteristics are also salient. They may decide it is necessary (or not) to explore broader therapeutic options or give greater or lesser weight to issues such as side effects. In consultations where difficult to define psycho-social symptoms are presented a prescription may help to reduce feelings of professional importance or inadequacy and perhaps help to avoid very lengthy discussion of symptoms and what they might mean. Workplace conditions, such as time-pressure in larger practices, might also mean that professionals take the 'easier' option to prescribe pharmaceuticals rather than explore potentially more difficult therapeutic alternatives, such as lifestyle changes. Educational, training or knowledge differences may also exist between younger and older professionals which might influence the approach taken.

Broader structural aspects are also important in shaping prescribing (Gabe, 1990). Cultural understandings of drugs at general and specific levels have shifted. In the latter stages of the twentieth century attitudes towards health and drugs have become less defined by enthusiasm and more by a pharmacological Calvinism (Klerman, 1972) – perhaps particularly in cases where narratives surrounding individual responsibility and lifestyle choice can be invoked in dichotomy with drugs. These notions are important in shaping both patient and professional understandings, beliefs and approaches. The political and economic climate in which prescribing takes place is also highly salient – with literature on professionalism also important here. On a general level doctors' ability to prescribe autonomously and using their own discretion has declined over time (Britten, 2001). On this final point, traditionally, as Willis (1989; 2006 – see also Coburn, 2006) argues, medical dominance of matters of health and illness and healthcare system occurred on three levels – over content of work (autonomy), over work of other healthcare occupations (authority), and over all matters of health in society (sovereignty). However, medicine has experienced a relatively sustained attack on its authority and claims to extraordinary trustworthiness. In the final decades of the twentieth century, all three levels identified by Willis (1989; 2006) of medical dominance over matters of health might be said to have been challenged. The creation of NICE, and the broader projects of modernisation and clinical governance in the UK in the 1990s clearly reflected, alongside the spiralling costs of healthcare in the Western world (Conrad et al., 2010), public dismay and calls for greater accountability, and associated government and professional concern with re-establishing public trust, following several high profile scandals (e.g. the Alder Hey organ scandal, the Bristol heart scandal, and the case of Dr Harold Shipman, a GP who mass-murdered patients) (Elston, 2009). These notions are indicative of broader trends that have been identified by sociologists in late modernity and neoliberal capitalism, including potentially an associated waning of deference to and scepticism of expert systems of knowledge, such as medicine, by lay people (Giddens, 1991).

The state and its actors (such as NICE) hold interest in achieving cost-effectiveness and in regulating the prescribing behaviours of the medical profession (e.g. in terms of standardisation) and have encroached on professional clinical autonomy. In the case under study, pharmaceuticalisation or at least the opportunity for pharmaceutical deployment is being driven by clinical practice guidelines produced by

NICE aimed at shaping the behaviour of GPs to achieve the greatest cost and clinical effectiveness. The broader model of healthcare that underpins this approach, scientific bureaucratic medicine (SBM), the dominant approach in the UK, (Harrison et al., 2002), assumes that valid evidence is obtained from expertly produced and accumulated research rooted in a hierarchy of evidence (with randomised control trials the gold standard). GPs in particular are viewed as too busy to access and/or insufficiently skilled to interpret and use this best available evidence in their practice. So this knowledge is disseminated to them through modes such as guidelines, with professional practice expected to be subsequently shaped/modified in line with the guidance (to the extent that it is appropriate to a particular consultation scenario, whilst not necessarily claiming to be universally applicable to all patients or determine clinical direction entirely). Knowledge generated and disseminated through an SBM model has facilitated the opportunity for treatment at a ≥10% risk threshold in the first place. This is supported by Freidson's (1994) later work who argued that professional re-stratification had occurred allowing the medical profession to retain power and influence, transforming some doctors into 'administrative elites' and 'knowledge elites' and other colleagues into the 'rank and file.' According to this perspective, though power differentials between the rank and file and the elite exist, the profession retains regulatory power over itself, with elite doctors increasingly shaping the development and design of mechanisms to influence practice of the rank and file as well as taking up managerial roles (Calnan, 2015), like 'poachers turned gamekeepers' (Checkland et al., 2009). This seemingly comes at the cost of some individual clinical autonomy for 'rank and file' doctors, but may be appealing on an abstract level for the professional as a whole in terms of establishing a market shelter (Freidson, 1994) from competition and retention of jurisdiction over a unique body of knowledge (Timmermans and Berg, 2003).

Movements towards standardisation, transparency and accountability might be said to have reshaped the constitution of medical professional identity itself – fostering a 'new professionalism', or an organisational professionalism (Evetts, 2011) rather than professionalism, as more traditionally conceived, as an occupational value differing from market and organisation (Freidson, 2001). Though there are aspects of continuity with professionalism as traditionally conceived, this new organisational professionalism includes lesser autonomy and greater standardisation of work practice and a move towards bureaucratic, hierarchical and performance management structures (Evetts,

2011). Elite professionals impose the limits of professionalism from above, rather than professionalism emerging from below (McClelland, 1990) which arguably characterised medicine's ascent to a dominant and powerful position, facilitating the 'golden age of doctoring' (McKinlay and Marceau, 2002). Other work has suggested that new breeds of doctors have emerged, exhibiting professional identities that balance the bureaucratic and governance protocols mandated from above, the pursuit of value for money, alongside the everyday practice of individualised patient care, acting as 'street-level bureaucrats' (Checkland, 2004), or 'neoliberal hybrids' (Checkland et al., 2009). It may be that some doctors have adopted market values to meet patient need without necessarily pursuing profit. However, others suggest that the idea of a new professionalism is problematic because there are aspects of both change and continuity (Evetts, 2009a; 2009b; 2011). Others further still seem to continue to speak about medical professionalism in more traditional terms, with high levels of clinical autonomy, power and strategic and stratified influence over governance mechanisms (Timmermans 2008a; 2008b). This said it does appear clear that medical professionals have adopted some organisational and market values, including adapting to budgetary constraints and meeting performance targets (Harrison and Ahmad, 2000). Managerialism, whilst complex, lacking a clear linearity in its development, and involving clinicians in hybrid roles, is also clearly a reality in the NHS (Dopson, 2009).

Indeed, GPs in particular do not seem to receive and utilise knowledge generated and disseminated through SBM in uniform ways. There is a significant body of literature in both the primary care and sociological literatures that suggests that clinical practice guidelines are not well followed by doctors, particularly GPs (Carlsen, 2010; Hansen et al., 2016). Why is this? The literature suggests that this seems to reflect conceptions of medical professional identity unique to the GP, with a significant emphasis on clinical discretion, experience and autonomy (Carlsen and Norheim, 2005) and a pronounced distinction between themselves and specialists that emphasises patient centred and holistic care (Checkland et al., 2008; Hansen et al., 2016). Armstrong (2002) argues that difficulties changing the clinical behaviour of GPs is the result of promotion of individual clinical autonomy, partially justified through and by a patient-centred approach, which flies in the face of the promotion of a collective professional autonomy predicated upon SBM. Clinical experience, and the associated cognitive familiarity with, for example, a drug treatment, seems as such to remain crucial in evaluating patient idiosyncrasies and

explains reluctance to follow clinical practice guidelines uncritically. The difficulty in applying population level 'collectivised expertise' in individual consultations (May et al., 2006) has also been highlighted in the existing sociological literature, particularly because it is emphasised that medical decision-making is a socially situated and complex process that is distributed across a variety of knowledges and interactions involving human and non-human actors (Clinch and Benson, 2013). As such, a broadly negative conception of clinical practice guidelines by some GPs (and other doctors), including of NICE guidelines specifically has been suggested in certain analysis (Spyridonidis and Calnan, 2011). It is useful to remember, however, the literature on medical professionalism (and understandings and implementation of guidelines) is a complex and at times contradictory body of literature with no overall agreement, perhaps because different researchers attend to different data (Timmermans 2008b). And indeed, other work, such as that of McDonald et al. (2009) has suggested that GPs increasingly see the benefits of guidelines in delivering quality care.

It is also necessary for this chapter to examine the nature of the doctor-patient relationship and particularly the extent to which patients figure as consumers in processes of medical decision-making and the form of the contemporary doctor-patient relationship. Undoubtedly the broader research agenda apparent in medical sociology concerned with lay perspectives, evaluations, meaning and use intersects to a certain extent with a broader debate within the discipline about the presence and extent of consumerism within medicine, an ideological discourse which suggests that health services should position informed choice as a central aspect in the design and delivery of care. Some analysis indicates that various governments in the UK since the 1980s, more or less motivated by neoliberal ideology, have been guided by the logic of consumerism in creating health policy and delivering care (Gabe, 2004; Gabe, Harley and Calnan, 2015; Krachler and Greer, 2015). Visible examples include the Expert Patient Programme and the marketisation and privatisation evident in the 2012 Health and Social Care Act. However, a language of partnership and shared decision-making has also been evident at the policy level (often sitting uneasily alongside certain more consumerist notions), and it is also unclear, as Will and Weiner's (2015) analysis is suggestive of, the extent to which patients possess the ability or desire to make choices about their health as informed and responsible decision-makers. Indeed, the majority of patients enter a medical consultation on an unequal footing often with minimal prior knowledge of what

treatments or procedures they may require (Gabe, Harley and Calnan 2015: 625). This asymmetry, despite decades of reform to equalise the consultation, may be inherent to the medical consultation (Pilnick and Dingwall, 2011). Patient dependency, vulnerability and the need for care also indicate the language of consumerism as it emerges at the micro-level, particularly in terms of emphasising patient choice, may be problematic (Nordgren, 2010). Additionally, despite certain narratives of declining trust in expert knowledge, it seems that patients in diverse healthcare contexts still seem to retain high levels of trust in clinicians. This may be more critical rather than unconditional but nevertheless remains high (Calnan and Rowe, 2008). It seems, as such, that consumerism, whilst powerful at the macro-level in terms of, for example, opening up the form/provider of healthcare to the forces of the market, at the micro-level, in the actualities of the medical consultation, is limited. Conceptualising patients as consumers also seems to neglect the complex range of actors, interactions (with both humans and non-humans) and knowledges, all in and beyond the consultation that shape medical decision-making (Rapley, 2008). Focusing only on the patient-consumer neglects the broader sociological picture of medical decision-making – and insufficiently grapples with networks of action and social relations that influence how doctors approach medical consultations and how patients respond to their work. Doctor-patient interaction is certainly one form of interaction and doctors the embodiment of certain knowledges that both feature in decision-making – and doctors' involvement in and facilitation of patient decision-making is itself distributed over a variety of evaluations including what is ethical, personalised to the patient and what the realities of healthcare organisational contexts are (Clinch and Benson, 2013). Further, doctors are themselves both trustees (with trust placed in them by patients) *and* trusters that are reliant on the action and knowledge of a variety of other actors, such as regulators, with trust used to bridge over complexity or uncertainty (Barbalet, 2009; Brown and Calnan, 2016). Both interpersonal trust, built on interaction, familiarity, competence and affect, and system trust, rooted in the continuing positive functioning of systems (Luhmann, 1979), is likely to be significant for medical professionals. Sociological research on the importance of trust in doctors by patients for the successful functioning of healthcare is well developed (Calnan and Rowe, 2008). However, what is less sufficiently acknowledged is the importance of other trust relations within medicine (Brown and Calnan, 2016; Gilson et al., 2005), including for medical professionals in other individuals encountered in the course of their work (such

as medical colleagues, managers, and even patients) as well as in organisational and systemic actors (Douglass and Calnan, 2016).

There is a long academic tradition in both medical and social scientific literatures of attempts to delineate the nature of the doctor-patient relationship. Parsons (1951) in his articulation of the sick role set out a paternalistic and one-sided doctor-patient relationship. However, the acknowledgment of mutuality in the relationship is not necessarily a new phenomenon or newly recognised/desired, with, classically, Szasz and Hollender (1956)(see also Szasz et al., 1958) setting out a three models of the doctor-patient relationship. Alongside the activity-passivity (doctor does something to patient) and guidance co-operation (doctor tells patients what to do) models, the authors also outline mutual participation (where doctor helps patient to help themselves) with this mutuality most clearly apparent in cases of chronic illnesses. Whilst certain aspects of this typology hold relevance (e.g. the emergency treatment of an unconscious patient can hardly involve mutuality), shared decision-making has become the dominant language of the medical encounter within the NHS. Others have suggested four models of the doctor-patient relationship: the paternalistic model, the informative model (professional provides all information so patient acting as consumer can select course of action), the interpretative model (acting as counsel to elucidate patient health values), and the deliberative model (the professional elucidates health values relevant to the scenario but also help select what is best) (Emanuel and Emanuel, 1992). From this typology, the authors suggest that the deliberative model is the most desirable model in the majority of scenarios. It is also apparent that this most clearly coheres with subsequent delineations of shared decision-making. Indeed, outlining the parameters, contours and nature of shared decision-making has, as such, been an important goal of academic analysis (one that reflects certain medical and social transitions but also reflects back on and shapes the nature of shared decision-making). Influentially, Charles et al. (1997) suggest that shared decision-making involves at least two participants, the sharing of information, both parties working towards consensus of treatment, and agreement on implementation of a treatment. Whilst respect for patient autonomy is a key medical ethical principle (Beauchamp and Childress, 2013), ideally it seems that shared decision-making should take into account 'broader' understandings of autonomy that is necessarily relational (Entwistle et al., 2012). Relational autonomy takes seriously how individuals are never truly autonomous and are in fact situated in a network of

relationships and social environments, including but not limited to health professionals (Entwistle et al., 2010). Broadly, as such, these discussions suggest that conceptualising patients as consumers seems to lack a certain awareness of the complex and necessarily relational/shared nature of medical decision-making.

2.7 Patients and Professionals: Justifications for Further Research

The discussions in this final section of the chapter implicates a number of potential directions for future research. At the most basic level, there is a gap in the existing literature for detailed analysis of the role of professionals in the processes of pharmaceuticalisation – actors who retain importance within cases particularly of medicalised pharmaceuticalisation. Not only is the body of work on lay experiences and understandings of pharmaceuticals very well developed, but other work, such as Will and Weiner (2015) in particular, highlights the problems with conceptualising patients as consumerist in the context of seeking pharmaceuticals in the primary prevention of cardiovascular disease. In analysing decision-making about statins in primary prevention we need to 'turn back' to the doctors to complete the picture of decision-making about drugs. Busfield's (2010) commentary indicates that GPs may fairly uncritically seek to prescribe. This is perhaps an overly simplistic view of the role of doctors and does not engage with the complex professional identities of professionals (perhaps particularly of GPs) and the dynamics of shared (and distributed) decision-making. The widened primary prevention threshold established by CG181 was also very controversial (with significant professional strife and newspaper attention). In the aftermath of the decision, it was claimed by a publication produced for GPs, *Pulse*, (Price, 2014) that based on a (non-representative sample) survey of GPs that two thirds would not be implementing the widened threshold. Whilst a far more rigorous social scientific approach to this phenomenon is required than this survey, other analysis does similarly suggest differences in perspective and approach to the primary prevention of CVD by GPs even at higher thresholds of risk (Clinch and Benson 2013). Indeed, Gale et al., (2011), have suggested that, even in the context of prior guidelines, GPs disagreed about the appropriate level of risk at which to initiate preventative treatment. The guideline at this time suggested ≥20% but Gale et al., show how some GPs preferred to start at <15% and others at <30%. GPs in other research have also seemingly varied in perspective on the

appropriateness of the level of risk (Barfoed et al., 2015). Meanwhile, Manca (2018), one of few (albeit it partial) examples of pharmaceuticalisation scholarship engaging with professional understandings, narratives and approaches, suggests different orientations amongst and as such, a certain degree of anxiety by some medical professionals both towards pharmaceuticalisation (particularly in the case of vaccines where widespread public uncertainty and controversy exists) and also the role of the pharmaceutical industry in production of knowledge.

At a basic level then, are GPs critically or uncritically implementing the widened threshold of primary prevention (if at all) and do differences exist in how they advise and/or facilitate patient decision-making about statins? Beyond this, what is the role of individual discretion in the framing, facilitation of decision-making and prescription of statins to patients at the lowered primary prevention threshold? What distributed factors at both institutional and interactional levels can be established that might shape or reflect professional implementation of this threshold? Analysis of these aspects is salient to understanding pharmaceuticalisation where conceptualising patients as consumers may be limited/problematic, and in this specific and controversial context. To grapple with these aspects, this thesis pursues the following research question: *how do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk?*

As with the other research questions defined in this chapter, exploration of this question forms part of the broader aim of this thesis. In simple terms, if GPs are broadly implementing the guidance then they can be considered to be a driving force of pharmaceuticalisation and the degree to which further medicalised pharmaceuticalisation is occurring will be higher. Whilst caution is needed in mapping GP understandings and approaches onto whether a patient ultimately becomes pharmaceuticalised, the involvement of the GP in decision-making about drugs is, as discussions in this chapter have highlighted, likely to hold a level of salience because professional perspectives and approaches retain value in decision-making about drugs where this occurs in traditional medical settings. Establishing the degree to which GPs are pharmaceuticalised in their orientation and approach is important as part of a broader picture of pharmaceutical decision-making. In turn it is possible then to analyse whether professional understandings of and approaches towards decision-making about statins are a facilitating or limiting force within the pharmaceutical regime.

2.8 Summary

This chapter has weaved together a variety of literatures important to understanding the analytical dimension of pharmaceuticalisation as proposed by Williams et al. (2011a). This chapter has argued the necessity of conducting further research on CVD pharmaceuticalisation, arguing for the need to consider three of the dimensions outlined by Williams et al. (2011a) (regulatory bodies, media and patients/professionals). Specifically, it has proposed a focus on NICE's decision-making (necessarily implicating the pharmaceutical industry), the print news medium, and, considering the well-trodden ground on lay and patient understandings/identities, the role of medical professionals. Each of these dimensions have been explored individually as corresponds with the data analysis presented later in this thesis. It will be clear to the reader that aspects of analytic importance are attached to each dimension independently. However, looking forward, it is important for the reader to also keep in mind that the notion of the pharmaceutical regime necessitates looking at the interconnectedness of all relevant actors/dynamics/dimensions as a whole when analysing the driving forces of and assessing the extent of pharmaceuticalisation. Whilst for the sake of clarity literature pertaining to each individual dimension of relevance has been examined relatively independently, the importance of the interconnectedness of the regime becomes important later in this thesis. Before any data analysis or discussion are presented, however, the next chapter, Chapter Three, considers the methodology utilised in the research presented in this thesis.

Chapter Three: Methodology

3.1 Introduction

This chapter details the methodological approach to the collection and analysis of the data subsequently presented in Chapters Four, Five and Six. The overall methodological approach taken in this thesis is qualitative in nature. The thrust of the approach can be summarised as such: data were collected using three different qualitative methods (documentary analysis, media analysis, and semi-structured interviews), with these data comprising four sets that were then thematically analysed. The aim of this chapter then is to provide a detailed justification for this overall approach. In doing this, the chapter begins with a discussion of the philosophical underpinnings of the research (which also further serves to clarify certain aspects of the conceptual approach outlined in Chapter One). It then moves to explore the research design of the project and the selection of the qualitative methodology. Subsequently the chapter moves to discuss the specific methods used, the underpinning rationale for the choice of methods, and the strengths and limitations of these methods as applies to this research project. The chapter then examines the overarching approach to data collection (which was iterative in nature) and the sampling procedures and access arrangements as pertains to specific aspects of the data collection. This is followed by a detailed description of the manner in which the data were analysed. The chapter finishes with an exploration of research ethics.

3.2 Philosophical Underpinnings

Social constructionism "emphasises the cultural and historical aspects of phenomena widely thought to be exclusively natural. The emphasis is on how meanings of phenomena do not necessarily inhere in phenomena themselves but develop through interaction in a social context" (Conrad and Barker, 2010: 67; see also Berger and Luckmann, 1966). As Chapter One discussed, constructionism in different forms has underpinned the study of medicalisation since its inception and can also guide explorations of the more specific process of pharmaceuticalisation when utilising the Williams et al. (2011a) framework (with philosophical criticisms of Abraham's work also offered in Chapter One). As Williams (2003: 9-28) discusses in *Medicine and the Body*, at

a certain point in the history of (medical) sociology the notion of biophysical reality was challenged, and in many ways abandoned, as the prominence of a Foucauldian position emerged in the study of medicalisation. This 'strong' constructionism, whilst also critical of the possibility of 'demedicalising' society presented by initial scholars writing about the process, challenged the idea of the "body and disease as existing as anything other than discursive entities" (Williams, 2003: 27). However, this strong constructionism in many ways can be said to suffer from the same problems as biological reductionism – with medical sociologists in some ways ironically advocating their own sort of 'imperialism' (with medical imperialism rallied against by the initial medicalisation scholars). In this way, a strong constructionism conflates the epistemological with the ontological, engaging in epistemic fallacy (see Bhaskar, 1998). The body is conflated with discursive constructions and the biological and the corporeal rendered unimportant (Williams, 2003: 22). Indeed, as Williams (2001) ponders, drawing on Strong (1979), Bury (1986) and others such as Craib (1997), strong social constructionism can problematically explain away the bodies of knowledge of other disciplines (for example, biomedicine) as social constructions – and as such, suggests that firm bodies of knowledge cannot and do not exist independently of the social. However, in questioning what a medical 'truth' is, in showing that medical knowledge is only relative and socially constructed, medical sociologists have fallen prey to their own argument. If medical knowledge is *only* relative and socially constructed then so too are the 'truths' of sociologists – and as such, with little of anything firm to say about anything 'real', we are left in an 'abyss' of relativism (Bury, 1986).

The key question for medical sociology, then, according to Williams (2003: 24) is how to go beyond the biological to sufficiently privilege the sociological without rendering unimportant bodily realities – a question that this thesis takes seriously. Whilst Williams here does not focus on pharmaceuticals in this work specifically, what he does offer is a way forward for medical sociology in resolving some of the above philosophical problems and contradictions and to bridge the divide between the social and the biological/chemical/natural. The proposal is the adoption of a weak variant of social constructionism that is attuned to disciplinary limitations and to a reality beyond only discourse that also allows enquiry to focus on the socially constructed *aspects* of health, disease, the body, or, as this thesis argues, the production/dissemination/use of pharmaceuticals without these weaker claims becoming necessarily all-encompassing

(Williams, 2003: 22). A weak variant of an avowedly social constructionist epistemological approach is defensible as long as it avoids the epistemic fallacy by acknowledging that the sociological is not the only valid body of knowledge, and thus avoids engaging in conflating what we know with how it is known (Williams, 2003: 27). Seemingly this can be done by also adopting a weak relativist ontology that allows for biological, chemical or otherwise natural realities to exist independently (to an extent) from the social, whilst also, for example, exploring how these realities may differ from biomedical knowledge claims about the extent of, for example, side effects in the real world compared to RCTs. Thus, in application to the study of pharmaceuticals, as well as investigating the manner in which the production and dissemination (including by lay sources) of medical knowledge reflects social contexts (Conrad and Barker, 2010: 73-74), medical sociologists need to acknowledge, for example, that such knowledge can be embodied in the chemical realities of drugs that can and do have real impacts on the human body (potentially both positive and negative). This philosophical position as taken by this thesis is one, as such, that is attuned to the long history of constructionist thought in medical sociology whilst also being sensitive to some of the limitations, particularly by avoiding sociological imperialism (as in Phase One medicalisation analysis) as well as the pitfalls of the strong variant.

It is true that in other work Williams (see Williams, 1999) advocates an avowedly critical realist position and that similarities between this and his 2003 work *Medicine and the Body* cited above exist. However, a careful reading shows that he stops short of declaring this book to be definitively critical realist sociology and can be read (see Chapter One of this work in particular) as a defence of a weak variant of social constructionism named as such. Unlike Williams' (1999) other work this thesis takes a weak constructionist position and avoids tying itself to critical realism particularly because of problems surrounding the avowedly transformative position espoused by critical realism (Hammersley, 2009). Critical realism can be argued to sit uneasily alongside the position of neutrality that pharmaceuticalisation analysis should begin from (Williams et al., 2011a), particularly in the way that it acts to both produce knowledge and simultaneously argue for social change. This approach, as such, can introduce bias, and, potentially illegitimately, shift social research from the endeavour of knowledge production about relevant social aspects to value judgment and configure it

as a political project (Hammersley, 2009: 7-8). Despite some philosophical similarities, opting for a weak social constructionism avoids this issue.

3.3 Research Design

One overarching aim of qualitative research is to explore the meanings and understandings attached by people to their social experience (Bryman, 1988: 61-62) whilst also situating these understandings contextually and with reference to the social structural aspects that give rise to or shape these meanings (Bryman, 1988: 63-64). This allows researchers to view and present the world through the eyes of those being studied, in the process often offering a voice to disparate worldviews, including potentially marginalised voices. Another aim is to examine the processual nature of social life, which allows analysts to elucidate processes shaping, surrounding or stemming from an event through observation, through retrospective recollection by relevant informants (using interviews) and/or through the use of documents to reconstruct events (Bryman, 2012: 402-403).

Reflecting these overarching aims and strengths, it is unsurprising that the majority of the studies thus far concerned with pharmaceuticalisation and in the broader sociology of pharmaceuticals have adopted qualitative designs. As explored in Chapter Two, a significant body of work exists, for example, on the understandings and meanings and subsequent identities that consumers and patients attach to medicines (e.g. Will and Weiner, 2015), whilst the processes that shape the regulation of new pharmaceuticals, for example, have also been widely studied (e.g. Abraham, 2002). Building on this existing body of qualitative medical sociological work on pharmaceuticalisation to analyse a new and unique case is, as such, entirely justifiable.

Equally, other critiques of the qualitative intellectual tradition presented above can be relatively easily addressed when designing and reporting qualitative work. Partially to provide a guard against criticisms of subjectivity, or, in other words, critiques suggesting that research began in an unfocused manner with an initially unspecific focus, whilst also relying too much on unsystematic personal views of the researcher about what is important, data were collected and analysed in a theoretically and conceptually informed way. Though as explored further below, an inductive design is reflected in the case study approach adopted by the research, as in Coveney (2010: 80) theory and

conceptualisation were used as guiding frames of reference. As well as the framework of pharmaceuticalisation, existing empirical/analytical contributions from literature were also used to guide the original analysis presented in this thesis as coheres with the said dimension(s) of pharmaceuticalisation under analysis (see Chapter Two). Meanwhile, protection against claims of a lack of transparency (and some protection thus against low levels of external reliability and research quality) in qualitative research can also be established by presenting a thorough account of the methodological steps and processes taken – which is the purpose of this chapter.

3.3.1 Case Study Design

As noted in Chapter Two, pharmaceuticalisation has been examined at both case specific, for example previous research on specific medicines such as statins themselves, and at a broader level (e.g. in terms of lay identities surrounding medicines use generally) in research analysing the process. However, whilst analysis of medicines at a general level is particularly helpful in developing typologies and conceptualisations of, for example, users (Dew et al., 2015), and has been particularly useful in terms of analysing the interests (Abraham, 1995) in the development and dissemination of pharmaceuticals, perhaps the most nuanced findings emerge from the exploration of case specific studies (e.g. Will and Weiner, 2015). Williams et al. (2011a: 711) themselves state that the "degree or extent to which [pharmaceuticalisation] is occurring remains open to empirical investigation on a case-by-case basis." Here these authors seem to encourage analysts to examine the extent of pharmaceuticalisation in individual cases. As such, the decision was taken by the researcher to interpret this quote in a way that meant examining the process of pharmaceuticalisation in one individual case – and as such adopt a case study design. Case studies at their simplest are detailed and analytically intensive studies of, for example, a singular community, organisation, person, family, or as in this research, a singular event and the directly related sub-events – with, importantly, the case itself the focus of analytical attention in and of itself (rather than, for example, location or setting) (Bryman, 2012: 66-68). The use of a case study design allows the researcher to delineate the unique nature of the specific case. Though the case will not be representative of or generalisable to all examples of expanding medicines usage, guideline development, newspaper reporting, or professional approaches/patient use, and as such perhaps has low external validity, it is able to highlight whether certain

aspects of a concept like pharmaceuticalisation hold true in that particular circumstance. It is not to represent the world that a case study attempts, but the case itself – and in the process can suggest complexities for further research and suggest the limits to theoretical claims (Stake, 2005: 460). Indeed, if the parameters of a conceptual framework have no explanatory power in a case that holds hallmarks to indicate that it should have explanatory power, then this can go some way to casting doubt on explanatory credibility overall. This said, rather than in the sense of sample-to-population generalisability, single case study research can offer analytic transferability – or in other words, ideas at more abstracted levels that can apply in other situations other than the original case (Yin, 2013: 325-326). In this sense inductive reasoning, where specific insights can inform more general conclusions, is necessarily present in case study design.

3.4 Choice of Methods: Rationale and Collection Process

A multiple qualitative methods approach was taken in this research. Three different methods were drawn on resulting in four different datasets. Two of these datasets, documents and semi-structured interviews with NICE/GDG/National Clinical Guideline Centre (NCGC)[4] participants (or 'NICE-related' informants) were combined in the analysis of the following research question: in what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?
Next, a media analysis of newspaper reporting was conducted in answering: how did the UK print news medium present and portray the potential widening usage of statins? Finally, data comprised of semi-structured interviews with GPs were analysed in answering: how do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk? This section now discusses the rationale for this approach, provides a justification for the methods chosen and discusses issues of sampling, access and the data collection process.

Before proceeding with specifics, it is worth outlining the overall approach taken to the collection and collation of the data which was iterative in nature. The process began by collating the documents pertaining to the case under exploration in this thesis. This

[4] This is a body that NICE subcontracts the technical work of guideline development to.

first step allowed the researcher to establish all events and aspects of relevance. Initially a 3.5 year time limit parameter stretching from June 2012 to December 2015 was established, with the researcher initially deciding to limit collating to relevant documents produced in that time because this initially seemed to capture all of NICE's development activities, which had begun in 2012 and concluded in 2014, with time included after the publication of the guideline allowing for any relevant commentary to emerge on the decision. However, this proved to be problematic as developments directly relevant to the case and to sufficiently understanding its dimensions continued in 2016 (see Appendix 1) at the same time as analysis of the data were under way. Eventually the researcher concluded the collation of further documents for analysis in December 2016. This was justified on grounds that with the progression of time that debate concerned with statins was becoming less directly tied specifically to NICE's decision. It was also justified on grounds of time limitations inherent to PhD study and funding deadlines. It also became clear in the process of collation that at the other end of the time parameter, June 2012, whilst adequate to capture the majority of directly applicable documents, could not capture everything – for example, documents relating to NICE's previous guideline on the topic (CG67) published in 2008. As such, special dispensation was made for certain documents pertaining to that guideline as well as other documents (such as Cochrane and CTT publications) that, it became clear, were salient/necessary to include in the analysis to understand NICE's evaluative work sufficiently (e.g. they were discussed or referenced in other documents). However, the bulk of the documents collated came from the June 2012-December 2016 time period.

Whilst this was ongoing, print news medium reporting of this case was also collated. Concurrent collation of these forms of data was iterative in nature. News medium reporting alerted the researcher to potentially important developments whilst the document analysis also helped to establish the time parameters to be applied to the collation of print news medium reports. It was clear that it was only necessary to focus on news medium reporting between October 2013 and October 2015 to capture reporting directly of relevance to the case under study in this thesis (because subsequent developments were not necessarily reported or the thrust of the reporting was too far removed from the original case).

Though the case overall was developing at the same time as the collection of data, the bulk of the documents and reporting relevant to the case were collated and the initial

stages were under way prior to interview data collection. As such, the initial stages of document analysis in particular helped to guide the approach to the semi-structured interviews with NICE-related informants and GPs. For example, it helped guide questioning to GPs about specific aspects of implementation and allowed comparison between these answers to the actualities of the guideline. The interview data also iteratively shaped the analysis of the documents (and newspaper reporting) because aspects of importance not necessarily initially understood by the researcher came to light in the interview data. A good example of this being a scenario analysis[5] undertaken during the course of the GDG that was only minimally explored in documentation and thus was difficult to understand prior to the interviews with NICE-related informants (discussed in Chapter Four).

3.4.1 Documents: Rationale, Sampling, Selection and Collation

Documents can provide critical insight into a wide variety of social phenomena, including the processes of decision-making (Altheide and Schneider, 2013: 55-56). Documents are widely used resources in sociological research which is concerned with analysing meaning in the content and language of documentation (Prior, 2016). In this research, documents were analysed in combination with semi-structured interview data to analyse NICE's guideline development process and to examine how influences on evidence and/or guideline development processes by the pharmaceutical industry may be established in widening the usage of medicines. As a method, documentary analysis has already been used in the sociology of pharmaceuticals to similar ends in the analysis of the development and regulation of pharmaceuticals (Abraham, 1995).

A progressive theoretical sampling strategy as discussed by Altheide and Schneider (2013: 55-60) was employed in the selection of documents. This approach suggests that document selection needs to be guided by the conceptual or theoretical parameters of a project, but that also relevant documents are established and collected over time as understanding of a problem or case emerges. It may be necessary to begin analysis and then collect further documentation to confirm or complicate particular issues. Conducting document analysis in this manner is particularly well suited to

[5] This was where cost-effectiveness was examined and affirmed in the hypothetical scenario that 10% of people ceased taking a statin and another 10% switched to a different and lower intensity statin/dosage.

collecting documents that present different orientations towards an issue/dimension – which in the case of this thesis was concerned particularly with how the pharmaceutical industry's influence might (or not) manifest itself in NICE's decision-making. In this way it was crucial to the analysis to collect a wide range of documents from different sources that would aid in understanding how this influence might manifest. Necessarily documentation produced by NICE themselves would likely resist delineating certain external influences on their work, which other documents, however, might bring to light. Documents were accessed online through systematic searching of regulatory, academic and medical professional online platforms and resources. Altheide and Schneider (2013: 113-114) argue that whilst the internet has vastly expanded access to documentary data and even created new forms of data for analysis, it is very important to immediately download and store documents (and other potential research artefacts) when they are accessed via the internet. There may be a tendency to assume that the material will remain online and can be accessed in the same way in the future. However, resources might be taken down, URL links may cease to work, or aspects of the documents may be changed. Whilst this is likely to be a particular problem with user-generated content (e.g. on social media), due to the fact that all documentary data were collected via the internet for this research, this approach to collation of documents was taken in this research too (despite not utilising new media such as social media within the document analysis). The researcher produced both a physical and digital archive of all the documents for the analysis. In total 190 documents were established from three (loose) categories of source. In what follows below, the chapter presents the types of documents that were collated, analysed and the underpinning rationale for the inclusion of these documents. The notion of 'categories of source' is used here to assist with presenting the types of material used but was only loosely pre-defined prior to data collection.

The process of establishing the dataset for the documents began with collecting documents produced by NICE pertaining to the guideline development, including the full guideline itself, and other documents such as appendices and meeting minutes. These documents can be grouped together as 'regulatory' documents. NICE's website provides a vast array of resources that provide significant detail of the processes they use in their various evaluations at a general level, whilst also providing a large volume of documents detailing the specifics of individual guideline development, the evidence used, and the specific history associated with the development of a particular guideline, as, indeed, they

did for CG181. The researcher only included documents specifically pertaining to CG181 in the analysis, but other documents (e.g. on how guidelines are developed and other manuals) were read thoroughly to understand NICE's guideline development process. In total 14 documents from this category were sampled. These kinds of state/regulatory documents have been used widely by Abraham throughout his career to understand and assess how interests might shape scientific findings and regulatory approvals (see for example Abraham and Lewis, 2000). In essence, these documents are interesting sociologically not because they capture reality but because of the potential sources of influence or bias that they might reveal (Bryman, 2012: 550). Documents of this type necessarily involve portrayals of events and the self-presentation of the organisation, and thus should not be treated as evidence of exactly what they purport to document (Atkinson & Coffey, 2011; Bowen, 2009: 33). As such, it is necessary to take a critical approach in that such documentation provides evidence of an organisation's own perspective and what they might hope to be thought of as doing (Atkinson and Coffey, 2011; Bryman, 2012: 555). The development of a critical approach to NICE's self-reporting of its own guideline development in this way was facilitated by analysing documents from the following two categories of source.

The researcher also collated data from 'academic' sources. It became clear to the researcher that there was a large volume of debate occurring in the BMJ and the Lancet, some of it directly in opposition to the other journal (both are high profile medical journals) about expanding the use of statins in primary prevention. The data collected from these sources are essentially academic argument about the merits of expanding statins use and ranged from peer reviewed journal publications, medical opinion pieces, letters to the editor (though excluded rapid responses due to high volume of data and lack of editorial or peer review oversight thus making it difficult to ascertain the quality of the commentary). As discussed in the above section, this all came from the time period of June 2012-December 2016 and was located by searching for 'statins' within the internal search engines of these journals and then reviewing whether the article related to widening statins usage in this case. This data were sought because it assisted the researcher with assessing potential issues and problems within the statins evidence base and included a variety of commentary on the decision to widen the availability of the drugs by NICE. The initial searching prompted the researcher to collect publications produced by Cochrane and the CTT. It was clear these were actors of importance that had

both produced influential meta-analyses and systematic reviews of the whole of the statins evidence base (and, indeed, both are cited by NICE in their guideline as part of the evaluations and in support of their conclusions). As these two actors in particular were identified as important in other documents, as noted above, the researcher included documents published beyond the initial time period of June 2012 to December 2016. Cochrane for example had published two separate reviews of statins in primary prevention (Taylor et al., 2011; 2013). In 2011 they had declared that their review of the evidence suggested that expanding the use of statins to people at lower levels of risk than codified in existing guidance would be problematic, whilst their 2013 review concluded in the opposite manner. There was also some correspondence between the CTT and Cochrane following the 2011 review (primarily the CTT disagreeing with the conclusions of the 2011 Cochrane review) that Cochrane had made publicly available and was also included in the analysis. A 2010 CTT (Baigent et al., 2010) paper was also included in the documents analysed. Documents relevant to the departure of a GDG member were also included beyond the initial timeframe.

As part of understanding the case as a whole and contextualising various aspects of the data, the researcher also read a number of other papers that have been published in the last thirty years from statins RCT evidence, other observational evidence, and other relevant material (e.g. papers about new generations of drugs) so as to fully understand the evidence NICE had drawn on (or not) in its systematic review of evidence. However, due to practical considerations these papers were not formally analysed as part of the documentary analysis, rather just used to shape researcher understanding. Equally, for the purposes of this project it was of greater analytical salience to analyse commentary looking at the evidence base as whole and, for example, the limitations inherent to the overall evidence base and/or commentary on NICE's processes (particularly because the majority of the statins RCT evidence is concerned with secondary rather than primary prevention). In total then 145 documents from this category were sampled and analysed.

Finally, the researcher collated documents produced by what can be thought of as medical professional sources. There is an issue of crossover with some of the above 'academic' category (e.g. some of the commentary in the BMJ was written by professionals). However, for clarity a distinction is made here between publications in journals/scientific sources and material gained from elsewhere. As such, this category includes various forms of professional commentary on the case. For example, stakeholder

review of the draft version of the guideline (e.g. by the Royal College of General Practitioners). NICE also made publicly available correspondence (two letters and subsequent replies) the Institute received from a leading group of medical professionals who criticised the evidence upon which the decision to expand the primary prevention threshold was made. In total 31 documents from this category were sampled.

3.4.2 Print News Medium Reports: Rationale, Sampling, Selection and Collation

Coveney (2010: 84) discusses how there is no unified approach to conducting media analysis, with researcher interest, relevance, time period selection and retrievability crucial in what becomes a research document and shapes any emergent analysis. It is as such necessary to detail these criteria. As discussed in Chapter Two, the news medium is a crucial site of dissemination and debate about scientific developments, and thus is a potential influencer of public opinion, whilst potentially also having a conceptual role in creating a 'sense' of scientific progress and, as such, the pharmaceuticalisation of everyday life (Williams et al., 2008). Print newspapers were selected as the particular form of media to analyse primarily because the coverage by print newspapers of this case was the most sustained. In a practical sense, print news was also the easiest to collate and collect and, considering the time and funding considerations attached to doctoral study, did not require transcription (compared with TV or radio, as examples).

The decision was taken before the collection of newspaper data or the documentary data to analyse reporting separately from other forms of documents. As will already be apparent to the reader, this decision was driven primarily by the theoretical parameters of pharmaceuticalisation, which highlights media as a unique dimension for analysis (Williams et al., 2011a). 170 print news medium articles were selected for inclusion in the analysis based on the fact that they had been published in national UK newspapers in the period between October 2013 and October 2015. The whole of a newspaper article was considered the unit of analysis. This data were collected using the LexisNexis database, a database used by other researchers with similar interests (Williams et al., 2008) to access reporting because it has a database of almost every news article published in the UK. All print news medium material was downloaded from the LexisNexis database immediately upon access and was stored in both digital and physical forms (to avoid loss of access and facilitate analysis). Articles of all types (including

opinion pieces but excluding letters) were included if they were judged to have made reference to 'statins' within the context of the parameters of this case and the expanding usage threshold (rather than broader reporting, with relevance established with reference to the document analysis and timeline of events detailed in Appendix 1), and at least one of the following search phrases: 'NICE' 'BMJ', 'side effects', 'controversy'. The sample comprises eight national newspapers (and where reporting was evident, their Sunday sister publications): The Guardian and The Observer; The Times and the Sunday Times; The Daily Mail and Mail on Sunday; The Daily Express and The Sunday Express; The Mirror and The Sunday Mirror; The Daily Telegraph and The Sunday Telegraph; The Sun; and The Independent (which subsequently became an online only paper but was still produced in print during the time period under study). Similar to Williams et al. (2008), this was carried out with knowledge of circulation, readership, orientation and style of the news outlets, with the established sample inclusive of diverse political and tonal orientation. The researcher was alerted to the existence of online news content during data collection, but such data (e.g. MailOnline content) were not included in the dataset. Though it is also important to note that people do increasingly consume news online, it seemed that, based on comparison in the early stages of sampling, that online news content and print versions of a story (from the same outlet – e.g. the Guardian and the Guardian's website), at least in the context of the case under study, were often very similar in terms of content. It is also important to note sufficient risk of CVD (as established by NICE's guidance) is strongly associated with older age. Older people (particularly 65 plus) are the group most likely to consume news via newspapers (Ofcom, 2017). Thus, the place of newspaper coverage in decision-making about statins holds potential salience in this sense (though it is not the intent of this thesis to establish audience impacts, only the nature of the coverage). In addition, if online news content were included, why should non-newspaper sources such as online BBC News not also be included in the sample? Due to these considerations the decision was made to focus only on print newspaper reporting.

3.4.3 Semi-Structured Interviewing: Rationale, Access, Sampling and Collection Processes

In-depth interviewing is perhaps the most widely used method in qualitative research and is in the most basic sense, a conversation oriented at exploring an individual's

account of social phenomena (Green and Thorogood, 2004: 79-81). The emphasis in in-depth interviewing is on the interviewee's perspective and their account of lived experience (Seidman, 2006: 9-10). This allows for rich detailed answers and descriptions that offer crucial insight into what the participant views as important about social phenomena (Bryman, 2012: 470-471). These aspects meant that qualitative interviewing was an appropriate method to use in this research across two different sample populations. First, it allowed NICE-related informants the chance to provide perspectives on and understandings of the guideline development process and the evidence upon which this decision was made, doing justice to their lived experience of the guideline production and the meanings they attached to their involvement. Alongside the use of documentary data this allowed the researcher access to a wide variety of perspectives and thus afforded the ability to present an informed and fair account of the production of the guideline. It also allowed the researcher to explore how GPs perceived the widened primary prevention threshold and how they understood their approach to its implementation and the facilitation of patient decision-making.

However, the qualitative interview is not a homogenous entity and does exist in different forms. The decision to use semi-structured interviewing in both sample populations rather than unstructured interviewing was chosen because of the conceptual foundations of the project and the specific dimensions of pharmaceuticalisation and associated research question the researcher desired to investigate when interviewing each sample. As such, the researcher already had a set of topics that were important to address. As with Coveney (2010: 91-92) it was a concern, as such, that using a completely unstructured approach would mean neglecting certain topics of salience to understanding the dimensions of pharmaceuticalisation as apparent in this case. Semi-structured interviewing, however, also afforded the interview process a degree of flexibility to explore further topics of interest as they emerged, allowing participants the chance to present what they believed to be important.

Debates exist about the kinds of knowledge claims that can be made from this kind of interview data. It has been suggested that data derived from qualitative interviewing provides idealised accounts that are not necessarily relatable to what a person actually believes or how they behave (Murphy et al., 1998: 105). Equally there is an issue of whether meanings presented in an interview are ever stable and in some way representative of a verifiable internal (perspectives, beliefs) or external (actions taken)

reality (Dingwall, 1997: 38; Murphy and Dingwall, 2003). In other words, an interview might be seen as an exercise in impression management where interviewees seek to present themselves in a particular manner which is socially acceptable, even in the case of failures (e.g. as competent or moral actors) (Murphy and Dingwall, 2003: 95-96). From this perspective, interviews can be seen themselves an example of interaction and thus social phenomena to be studied. This perspective is not universally shared, however. Others suggest that accounts by interviewees can be both resource *for* analysis and topic *of* analysis (Hammersley and Atkinson, 2007: 97-98). This debate about the knowledge claims that can be made using interview data has not yet been definitively resolved. Whilst the discussion in the paragraph prior to this one indicates the approach taken in this thesis sides more with the second position, that interview data can tell us something about the phenomena being described, it is nevertheless clearly important to be aware of the potential problems of 'impression management' in accessing some sort of internal or external reality possessed or purported by the participant as represented by the interview data that emerges. During the (systematic) thematic analysis of the interview data (see section 3.6 below for a broader discussion) the researcher analysed the data with an awareness of the potential for the presence of said impression management. As an example, the coding process unveiled how, in places, the talk of some of the GPs interviewed was oriented towards presenting a sense of a detailed knowledge of the specifics of the guideline (despite this guideline being only one small element of the practice of GPs) potentially to legitimise their particular clinical approach and/or to convince the interviewer of the value of their contribution to the research.

Before looking at certain specifics of the sample-specific data collection, it is also important to note that in both sample populations the semi-structured interviewing was conducted both in person and via the telephone. The need for telephone interviews was primarily a practical necessity in both sample populations. The NICE-related interviewees were elite individuals positioned variously around the UK and were also generally time-scarce. As such, due to the cost pressures inherent to a limited research funding budget attached to a doctoral scholarship and the need to interview these individuals with the potential for short notice change of schedule, telephone interviews were necessitated for six of nine interviews conducted in this group. The remaining three interviews were conducted at the NICE offices in London or in places of employment. In the second interview sample (GPs), cost implications were less pressing as distance was

less of a problem (the researcher and participants were all located in the south of England). However, eight of twenty GPs interviewed wished to conduct their interview via telephone because of time pressures associated with primary care and the need to conduct the interview, as such, during times outside of work hours. Whilst the researcher stressed a preference for in person interviews, both were offered so as to maximise potential sample size. The remaining twelve interviews with GPs were conducted in primary care facilities.

There may be limitations to using telephone interviews, such as problems with recording, problems with building rapport with the participant and the lack of non-verbal communication. However, as Bryman (2012: 488) discusses, there is no reason necessarily why telephone interviews cannot yield the same quality data as in person interviews. Indeed, no problems were encountered with recording the interviews which were all able to be transcribed without issue, and no notable differences were recorded between telephone and in-person data with regards to content, context, richness of description, length of responses to particular questions or overall length of interview (indeed, in the GP sample, the longest interview was one conducted via telephone). The researcher also spent time prior to the start of the recorded interview attempting to build rapport with the participant in the same 'getting-to-know-you' manner that in-person approaches enjoy. Other research within medical sociology has also employed a mix of in-person and telephone qualitative interviewing to access time-pressured and elite individuals (Brown et al., 2016).

3.4.3.1 GDG/NICE/NCGC Interviewees

The research successfully negotiated access to interview six members of the GDG, one member of NICE's senior management staff, and two members of the NCGC that worked on CG181 (n=9). Sampling was necessarily purposive in nature because the aim was to interview GDG members and staff that had worked on the production of the guideline to understand the processes and problems with detail. It is important to note that by the eighth interview little new about guideline development processes and use of evidence was emerging in the data, and arguably as such, saturation was achieved. This suggests that the small sample size and the lack of access to everyone involved in the guideline development did not restrict access to relevant information. Connections between NICE

and the University of Kent were already established as a result of, at that time, ongoing research being conducted on NICE's technology appraisal processes (subsequently published: Brown et al., 2016; Calnan et al., 2017). Whilst the processes under study here are different, and thus the relevant personnel are also different, this connection meant that the researcher and supervisory team were able to gain referral to management personnel involved specifically in NICE's guideline development. A member of NICE's senior management, who also participated in the research, gave permission for the researcher to invite relevant NICE and NCGC staff to participate.

It appeared initially that there were 18 potential interviewees. However, the first issue with this number of potential participants was that two of the technical members from the NCGC had moved on to new employment and it proved difficult to locate contact information. The second issue was that one member of the GDG had died, and another, it was suggested, should not be contacted because this member had been enforced into leaving the GDG due to a dispute about conflicts of interest emerging mid-way through the guideline process. Though the researcher did wish to interview this GDG member, ultimately it was necessary to respect the wishes of NICE's senior management. Thus, in actuality, there was a potential sample size of 14. Eleven of the fourteen potential participants responded to an invite but it was only possible to set up nine interviews. Of the nine interviews, the longest interview was 100 minutes and the shortest was 45 minutes.

A topic guide was used in the interviews which varied slightly depending on the professional expertise and type of participant. However, all interviews followed the same overarching format (with more or less emphasis on certain aspects depending on particular expertise): Interviews began by exploring the professional background and expertise of the participant, the role they undertook in the development of the guideline and, for members of the GDG, why they had applied to be involved with this guideline. Interviews then moved to discuss core issues grouped under: the development process; strengths and limitations of the evidence; the therapeutic landscape; and the future. Appendix 8 details the topic guide used.

As noted, the documentary analysis and an analysis of interviews with NICE-related informants were combined in a triangulated approach. Interviewees were perhaps likely to have a one-side (likely uncritical) view of the guideline (though to produce a fair and nuanced analysis it was of course necessary to take into account these

perspectives). Documents meanwhile, whilst offering insight into the nature of the potential influences of the pharmaceutical industry on the statins evidence base and a diverse range of commentary on widening the usage of the drugs (which was valuable in understanding of all of the dynamics at play), only offered limited insight into the actual guideline development process. Indeed, as noted in a prior section, interview data were invaluable in, for example, clarifying the nature of the scenario analysis (discussed earlier) that was carried out within the development process but that was only briefly detailed in the guideline itself.

3.4.3.2 GP Interviewees

Access to GP interviewees for the study was negotiated in one Clinical Commissioning Group (CCG) in the south of England. Relationships at the University of Kent facilitated the establishment of a connection with a member of this CCG's board. This board member, who was also a GP, was interested in the proposed research and offered to help negotiate access to GPs within the CCG. The prominent position of this board member meant that he was familiar to and had well developed existing relationships with many of the GPs working within the CCG. This board member, as such, acted as a gatekeeper to accessing GP interview participants. This individual also participated in a pilot study interview, with the aim both of giving the board member a greater understanding of the research that they were subsequently going to promote within the CCG, as well as to help establish strengths and weaknesses within the interview topic guide. Some minimal changes primarily to the ordering of the questioning to avoid repetition and to aid clarity were made following the pilot interview.

Data collection here began with the aim of interviewing between 15 and 20 GPs, with the caveat that data collection would continue until saturation had been achieved. An email advertisement was sent to every GP working within the CCG (more than 60) by the CCG board member. The response was initially muted with only several participants, but as was agreed with the ethics committee and the NHS (see the final section of this chapter), several further emails were sent over a period of nine months. A purposive sampling approach was taken. At the most basic level, qualification to participate was based on being a GP currently working within the CCG with an aim of recruiting an even split of male and female GPs. More particularly, the researcher set out to establish a

sample diverse in terms of levels of clinical experience. The rationale here was that differences in clinical experience might shape how GPs approached the use of guidelines (due to the clash between clinical experience and guidelines noted in other research discussed in Chapter Two). Age was initially predicated to be a good indicator of years of clinical experience. However, due to potential issues with undergoing medical education and training later in life (as, indeed was the case for one GP in the sample), it was necessary to be more specific. As such, a sampling frame was established relating to years of clinical experience (early or later career), with the aim of interviewing between seven and ten GPs with ten or less years clinical experience as a GP. The sampling also ultimately benefitted from elements of snowballing with GPs on four occasions recommending and asking particularly younger colleagues if they would consider participating. Ultimately twenty GPs were interviewed. Twelve were female and eight were male, with seven having ten or less years of experience. One was 60 years or older; six were 50-59 years; seven were 40-49 years old; and six were 30-39 years old. 14 were partners in their practice, 2 were salaried GPs, 3 were GP registrars, and 1 was a locum. The longest interview was 80 minutes and the shortest was 25. Appendix 10 details the social and personal characteristics of the GPs and links into the analysis presented in Chapter Six.

A potential weakness in the sampling approach used in this study is the focus on only one CCG. The CCG in question did not have a specific stance evident at board level concerning CG181 (this was confirmed by the GP gatekeeper who was also a board member). It was evident, however, that (a minority of) CCGs in other parts of England have produced publicly available documentation concerning how this guideline (as a large-scale change) was to be specifically approached. As such, it is conceivable that this kind of added layer of governance at the CCG level might have shaped how GPs approached the guideline. However, whilst it might have improved the external validity of the research (as well as potentially adding a comparative element) to have collected data in two or more CCGs, evidence also exists to suggest that GPs are heterogenous and individualistic even in the age of clinical practice guidelines (Armstrong, 2002; Spyridonidis and Calnan, 2011). As such, it was unclear what benefit the research would have gained from interviewing across multiple CCGs. As such, and also reflecting practical concerns about access in CCGs where no prior contacts existed, the decision was taken to collect data in only one CCG.

As with NICE-related informants above, a semi-structured interview topic guide was utilised. Interviews were structured around the following overarching sections: NICE and guidelines; general understandings of CVD prevention and the therapeutic landscape; framing and implementation of CG181; and driving forces. The topic guide utilised following the pilot is detailed in Appendix 9.

3.5 Data Analysis

All data in this thesis were analysed thematically. Despite its very wide use across a broad variety of social science disciplines, until relatively recently thematic analysis has been fluidly and inconsistently demarcated. However, thematic analysis received a robust delineation by Braun and Clarke (2006). These authors set out a theoretically and philosophically flexible framework or toolkit that researchers, if following it diligently, can draw on to produce nuanced and sophisticated analysis of data in a wide variety of types of research project, including within the sociology of health and illness (Braun and Clarke, 2014). They propose a six phase/stage model.

Phase one is concerned with establishing familiarity with the data, which involves reading through thoroughly at least once the data to be analysed as well as generating initial notes and ideas. The transcription of data (e.g. interview data) can arguably be incorporated within this phase of analysis and might even be thought as a crucial part of it. Phase two is concerned with generating initial codes. Coding is concerned with identifying interesting features of the data at the most elemental level, with individual codes then grouped together to form themes (Braun and Clarke, 2006: 88). Where portions of the data were similar to previously coded aspects of the data, the researcher used the same coding so as to facilitate ease and clarity of grouping into themes. Codes were developed 'inclusively' with a focus on appropriately appreciating segments of data within the context of the writing or talk within which these segments appear (Braun and Clarke, 2006: 89). It is possible that coding might have focused on smaller segments of data in certain aspects of the data but this then runs the risk of misrepresenting the true meaning of the data. Phase three is concerned with assessing the relationships between codes. In essence it is the first phase of the interpretation of the data. The goal of this phase of the analysis is primarily to group all codes into initial themes. Phase four involves reviewing candidate themes – or in other words, assessing the viability of these

thematic groupings. Reading the coded segments of data grouped together here allows the analyst to establish whether the candidate themes have enough data supporting them, whether themes are interrelated and can be collapsed together and ensuring that coded segments of data cohere with the rest of the group. Braun and Clarke argue that phase four itself has two levels. Level one is concerned with ensuring that coherent patterns emerge *within* themes. If this is the case the analyst can proceed to the next level. Level two looks at the thematic representations of the whole dataset – do the themes represent the meanings evident in the data or the part of the data that is the focus of concentration (though of course what is considered accurate representation will depend on, for example, theoretical approach). It is necessary during level two to re-read the data as a whole to assert that everything of relevance has been captured by the existing themes. If something has been missed or meanings are displaced it may be necessary to return to phase two and recode all or portions of the data. Phase five begins when the 'thematic map' of the data successfully passes the tests of the two levels in phase four. It is concerned with defining and refining themes. In essence, the analyst needs to finalise accurate names for the themes, ensuring that these names clearly alert readers to what aspects of the data the theme captures. It may also be necessary here to establish subthemes – which are mainly used to structure or improve the clarity of large or complex themes. Subthemes are established here as part of a process of refining the overall theme. Most importantly within this phase, the analyst needs to write thorough analysis that identifies what the theme captures, why this is so, what is of interest about a theme, and how it relates to the overall 'story' captured by the analysis as a whole. The final phase, phase six, involves writing up. The analysis of the data are finalised here, telling the 'story' of the data as a whole in a way that is compelling and in a manner that demonstrates the validity of the data. As such, the aspect of most importance in this phase is balancing providing sufficient evidence of the theme within an analytical narrative that does more than simply describe the data – in other words, it must provide a substantive argument.

In Appendix 3 are two randomly selected segments of data with attached annotations showing the finalised codes applied to the data and the thematic grouping of these codes. This segment is taken from the analysis of the newspaper reporting but the process is typical of all of the analysis presented in this thesis. This appendix offers insight into the coding process (particularly in terms of what and how much data are reflected

in a code and subsequent theme) and to offer some indication of the rationale for how codes were translated into themes. All of the codes generated and their position within themes are also provided in Appendix 2.

In what follows the chapter now offers specific insights into core aspects of theme formation in the analysis of different datasets all conducted using the Braun and Clarke (2006) framework detailed above. All data were analysed using a combination of manual/physical and computer assisted approaches. Coding and theme formation was discussed with the supervisory team attached to this thesis, particularly in phases two through four. These team discussions arguably served to improve the internal reliability of the project building in an inter-observer consistency (Bryman, 2012: 390). It is important to note that familiarity with all the data (phase one) was gained by reading and rereading data throughout the data collection phase, and then each set of data were read through again in its entirety before beginning separate phases of the analysis of each set of data. As noted towards the beginning of this chapter, the overall procedure taken in the analysis of the data began with thematic analysis of documentary and newspaper data but thereafter the analysis was iterative.

3.5.1 Analysis of Documents and Interviews with NICE-Related Informants

As discussed, analysis of documents and analysis of interviews with NICE-related informants was combined. Initial coding of the documents had begun prior to even beginning the interviews. However, once interview data collection was finalised and interview data were subsequently coded, the datasets were integrated and treated as one for theme formation. The thematic analysis of these two sets of data focused primarily on specific aspects of the data that implicated the potential influences of the pharmaceutical industry both in terms of the existing statins evidence base but also on NICE's regulatory/evaluative activity as applies to primary prevention. This was guided by the theoretical parameters of the second dimension of pharmaceuticalisation and the existing empirical evidence (as was detailed in Chapter Two). This selective focus also partly reflected the fact that certain documents (for example, the full 302-page guideline for CG181 – see NCGC, 2014), though necessary to consider, were vast and in places irrelevant to the specific focus of this thesis. Interviews also included a lot of procedural explanations and other contextualising, only some of which were relevant to the focus of

the research. As such, part of phase one of the thematic analysis as applies to the NICE-related analysis was to establish aspects of the data that were relevant to the research. Initially nine candidate themes were established from the coded data. However, during phase four of the analysis this was honed to five (that are presented in Chapter Four within two overarching sections).

3.5.2 Analysis of Newspaper Reports

The newspaper thematic analysis was analysed with a particular focus on the role of media in creating a 'sense' of the pharmaceuticalisation of everyday life (Williams et al., 2008) as well as if and how reporting is celebratory or condemnatory (Williams et al., 2011a) with associated potential impacts on the understanding and uptake of drugs. The analysis of newspaper reporting considered the entirety of all individual reports as potentially relevant, particularly due to the centrality of pharmaceuticals to the reporting on the case. It may have been possible to adopt alternate analytic techniques, perhaps particularly discourse analysis in the analysis of print news reporting. However, when considering the desire to analyse the pharmaceutical regime the researcher made the decision that the data should be analysed in a singular way to enable the researcher to look across the data with a totalising and potentially comparative analytic gaze. Equally, certain forms of discourse analysis, such as critical discourse analysis with its focus on coercive language as a reflection of ideology and power might also be said to be incompatible with the commitment to neutrality in the conceptualisation of pharmaceuticalisation by Williams et al. (2011). Thematic analysis is an appropriate analytic technique to analyse newspaper reporting in itself anyway because it allows access to the complexities of reporting and distinctions between type of newspaper/authorship or over time, more so than other analytical techniques (e.g. content analysis), allowing researchers to deconstruct notions of media as a homogenous entity (Beharrell, 1993; Bryman, 2012: 552-553).

Once familiarity with the data were sufficiently achieved the researcher coded all of the data and then initially grouped codes into five candidate themes. During phase four, one of these themes, 'Professional Disunity' was removed because, after recoding, it was clear that in actuality this theme was more accurately dispersed across three of the remaining four themes (though it was not assumed before beginning recoding that these

segments of the data would necessarily fit within existing themes). During phase five, the analyst developed subthemes for the four emerging overarching themes to improve the clarity of the analysis based on clear sub-thematic groupings that emerged within the data. Each subtheme incorporated several of the finalised codes.

3.5.3 Interviews with GPs

The analysis of GP data was guided by interest in the ways in which doctors understand the guideline and statins, as well as how they approach, contribute to, and facilitate the decision-making of patients. Though theoretically and empirically pharmaceuticalisation has neglected the role of medical professionals, wider theorising and empirical work suggests that medical professionals must be brought back into focus to more fully understand decision-making surrounding drugs, particularly because such decision-making is a shared activity, with interesting complexities surrounding professional identity and consumerism also arguably necessitating analytical attention in the processes of pharmaceuticalisation. Of all the analysis conducted for this thesis, the analysis of GP interviews was arguably the most protracted. The researcher spent more time in phase four of the data analysis here than with either of the previous two parts of the overall data analysis. The key issue here was a significant crossover between themes and difficulties disentangling subtly related aspects. Ultimately the research achieved sufficient heterogeneity between themes by (partially) grouping codes in themes based on differences between understandings and the actualities of practice. Ultimately three themes were honed and finalised. As with the media analysis these themes were also further honed to include subthemes with the primary goal of increasing clarity and allowing for emphasis on thematic positions and orientations apparent in the talk of GPs to emerge.

3.6 Reflexive Considerations

Reflexivity is the process of critical self-evaluation/appraisal and continual internal dialogue about the positionality of the researcher and how this shapes research processes and outcomes (Berger, 2015). At the core of reflexivity is the aim of increasing the accuracy, credibility and thus trustworthiness of the research through accounting for

the researcher's beliefs, values and biases (Cutcliff, 2003; Buckner, 2005). In this way it enhances the quality of the research in that it shows how researcher positioning and their interests arguably shape all aspects of the research (Jootun et al. 2009). Reflection on problems encountered during the course of research also encourages transparency about the research design and analysis.

First then, it is important to position the researcher socially and professionally relative to the research area and participants. As Berger (2015) shows, the social positioning of the researcher can shape research in terms of access and in terms of what informants may be willing to share with someone of different social positioning and with a different worldview to their own. Though medical training/background was apparent in the supervisory team for this project (and thus inevitably held some level of influence on the analytical focus of this doctoral research), the researcher himself is not a health professional and has not received medical education/training. Though the aims and questions of medical/health research and sociological research are distinct, it is nevertheless possible that a researcher with an educational background, training and/or experience in sociology *and* medicine might have collected and analysed data relevant to the overarching aims of this project with differential emphases. For example, in data collection and/or analysis of GP approaches to consultations about statins at the ≥10% threshold potentially this combined background might have led a different researcher to see or privilege dynamics apparent in the talk of the GPs not necessarily apparent to a sociologist without formal medical training (and perhaps particularly specialism in general practice). More importantly, the relationship between a researcher with a medical background might have resulted in a different researcher-participant relationship and rapport. Perhaps, for example, certain dynamics of decision-making might have been left unexplained, differential language used, or greater clinical depth explored in the interview (e.g. due to perception of comprehension). Though lack of medical background did not prevent initial access to the sample of GPs, which was relatively straightforward to establish as a result of the gatekeeper GP, it is worth noting that it was necessary to be patient and to ride out short periods of frustration during times of minimal potential-participant response in this segment of the research.

Status differentials between the student-researcher and the elite medical professionals and researchers serving on the GDG may also have impacted on the interview data collected. Differential status and some intimidation (alongside concern to

retain access to the sample) were keenly felt by the researcher particularly prior to and in the interviews with NICE participants. This was so much so that the researcher felt nervous prior to interviews with elite medical professionals. Status differentials arguably manifested in the collected data in terms of it being uncomfortable for the researcher to pursue or follow up, for example, critical questioning concerned with the statins evidence base where a strong initial rebuttal was evident. Though there is no overt verbal evidence in the data, it is also possible that across the interview samples, status as a student researcher may have limited what participants wished to reveal because, for example, of perceptions of the rigour or potential impacts of doctoral research (particularly relative to the participants' professional prominence).

Access to regulatory bodies that may be driving/facilitating pharmaceuticalisation is also in itself a difficult task. Concern about retention of access featured in the research presented in this thesis. In this regard, the researcher felt a level of caution reflecting the wish to not have access to NICE-related participants removed by pursuing *excessively* critical lines of questioning particularly concerning the statins evidence base or the guideline development that might be perceived to be critical of NICE in particular. It is true that NICE-related participants were certainly more sceptical than the GPs of the motivations behind the research. This seemed to reflect perceptions of the sociological nature of the research and of its epistemic differences to biomedical knowledge as well as some concern that the researcher may have been motivated by a pre-existing anti-statins agenda (which manifested itself primarily in the conversations prior to agreeing to interview). The latter wariness might have reflected the fact that the guideline and members of the GDG had been subject to criticism in professional and popular spheres and partially impacted the ability of the research to access a larger sample than the 9 interviewees. There were also some attempts amongst NICE informants to frame alternate discourses and interpretations of the evidence as inferior to their own work or rooted in misunderstanding. Participation in the research might have been seen as opportunity by some NICE-related participants to 'correct' public and professional criticisms and supposed misunderstandings or at least to explain why these alternative interpretations/narratives might be wrong. Rather than defensiveness, however, this may simply have reflected their own confidence in the work they had conducted, or at least as reflecting their epistemic position.

It is also worth reflecting here on the context of the case under study. At the time of research design and data collection the case was still ongoing and new debate about it was emerging. It was challenging to keep abreast of a case that was changing at the same time as data were being collected. Also, though the analytical focus of the research lies with other actors, the fact that the research occurred at the early stages of the implementation of the guidance also made it hard to establish connections with enough GPs who were willing and able to provide access to patients who qualified at the new primary prevention threshold.

It is also important to note some of the overarching difficulties apparent when conducting research on pharmaceuticals and the specific actors and sub-processes composing the pharmaceutical regime. These issues were necessarily present in the design of the research presented in this thesis. For example, as reflected in a lack of existing research, it is likely to be extremely difficult to gain access to pharmaceutical companies and pharmaceutical scientists developing and trialling drugs to collect primary sociological data of how companies construct markets for their drugs (both present and past). Even if access were to prove possible for sociologists of pharmaceuticals there may conceivably be significant scepticism or wariness from those working in the industry about the nature of the research that might limit its progress, continuation or depth. As such, medical sociological research has often engaged in historical or secondary methodological approaches when analysing particularly the construction of markets for drugs by the industry (e.g. researching advertising – see Collin and Otero, 2015). It may be possible, as Sismondo (2009) has been able to do, to access primary data for certain parts of the process of the construction of markets for drugs, such as publication planning conferences (which were publicly accessible even though the nature of publication planning is backstage). But as Sismondo (2009: 173) notes, he did not feel able to collect certain types of data (e.g. interview data) because it was felt that detailed discussions of his academic background and the backstage nature of the work of publication planners would make honest questioning and representations by both parties impossible. Sismondo's work here, as such, highlights just some of the methodological and even ethical difficulties inherent in navigating researching the pharmaceutical industry.

As discussed earlier in this chapter, documentary evidence is one potential way around access and representation problems relating to the industry and regulators, (and

has been used in the extensive research on the pharmaceutical industry and regulators by Abraham and others – e.g. Abraham, 1995). In the research presented in this thesis, documentary data did allow the researcher to counterbalance the perspectives presented in the interviews by NICE-related participants and examine potential problems with the statins evidence base that might have acted in a way to critique or challenge the understandings of and work done by NICE-related research participants. However, as discussed in Chapter Two, even secondary data (e.g. academic publication of trial data or reports sent to regulatory bodies) may have significant limitations or may not be available at all. The point here overall then is that when researching pharmaceuticals and the pharmaceutical regime, and as was the case in the research presented in this thesis, there are significant constraints on access to, the form and availability of sociologically pertinent data that necessarily impact methodological choices and the quality of the data collected.

3.7 Ethics

This research underwent Research Ethics Committee review at the University of Kent in 2015 receiving a favourable recommendation to proceed with the interviews of human participants. The aspects of the research pertaining to medical professionals within NHS roles also underwent local Research Management and Governance (RM&G) review by the NHS. University ethics approval is all that is required to achieve RM&G approval for research with NHS professionals, rather than ethical approval by an NHS research ethics committee. Full ethical approval from an NHS research ethics committee is only required for research involving patients not solely professionals. The research was designed and conducted with reference to research ethics guidelines created and disseminated by the British Sociological Association (see British Sociological Association, 2017).

Collection/Storage of Data: Audio recording took place for all participants (following signed and expressed permission). Once an interview was complete this was uploaded to a university-owned PC for transcription purposes and deleted from the recording devices. Physical copies were also produced to aid the analysis that were stored in a secure locker at the University of Kent. All physical interview transcriptions were destroyed at the end of the analysis process.

Informed consent: Informed consent "implies two related activities: participants need first to comprehend and second to agree voluntarily to the nature of their research and their role within it" (Israel and Hay, 2006: 61). This necessitates ensuring that participants have both capacity to consent and are provided with relevant materials to understand the research prior to beginning their participation. The main ethical issue here was ensuring that participants were fully informed about the nature of the research. This said, informed consent can be slightly problematic because it is necessary to calculate and gauge what is necessary for participants to understand the nature of the research and their participation in it whilst at the same time not giving so much away that particular responses are necessarily invoked. All participants were provided with a participant information form prior to their interview which provided them with some basic background information, the intent of the research, indicated the way in which the data would be analysed and used, but did so in a way that did not lead them to produce particular lines of response (see Appendices 6 and 7). All participants signed a consent form prior to the interview taking place which was used to assert that they were aware of the nature of the research, right to withdraw at any time, consent to audio recording, and the manner in which data derived from the interview would be used. The researcher also verbally confirmed that the participant understood the nature of their participation before the interview started as well as that they were happy to have their interview digitally recorded. All participants were also offered the chance to have a full transcription of their interview (though none ultimately took up this offer) and a report of relevant findings has also been made available to all participants.

Confidentiality and Anonymity: Confidentiality and anonymity during all research process stages (beginning with transcription/storage, data analysis, writing up and beyond) was assured to all interview participants. All interviews were anonymised during the transcription phase (meaning that information that might lead to identification was removed/redacted and every name and location were anonymised). Participants were given randomly assigned code names/numbers (e.g. NICE1; GP1) based on which part of the study they were involved in. The research concerned with NICE's guideline development processes had to take into account the fact that the names of everyone involved in the guideline is published by NICE and is public knowledge. It was necessary, as such, to indicate to participants that anonymity for their participant

could clearly only be guaranteed to a certain level. Participants were, of course, aware of the public nature of their role in the development of the guideline, so this was not reported by any participant to be a problem. To help with preserving a certain level of anonymity for the participants from the GDG/NCGC this research refers to all participants by the code name NICE1, NICE2 (and so on) and does not explicitly differentiate between types of involvement in the guideline development (e.g. chair of GDG, or senior management figure).

3.8 Summary

This chapter has provided a detailed overview of the qualitative methodology employed in this thesis. It began with an explanation of the philosophical underpinnings of the project. It then moved to explore the research design and the underpinning rationale for the qualitative methodology. Subsequently the chapter moved to discuss the types of methods utilised to collect the four datasets, sampling and access arrangements, the underpinning rationale for the choice of methods, and some strengths and potential problems with these methods in their application within this research project. The chapter then followed this up with a detailed exploration of the dynamics of thematic analysis and its application, reflexive considerations, before finishing with a discussion of ethical principles.

Moving now into the second half of the thesis, Chapters Four-Six are concerned with presenting the thematic analysis of the collected data and each answer one specific research question detailed throughout the first half of this thesis. As such, Chapter Four presents the analysis of documents and interviews with NICE-related informants. Chapter Five is concerned with the media analysis. Finally, Chapter Six offers the analysis of the interviews with GPs. Chapter Seven looks across the datasets and discusses them with reference to the pharmaceutical regime.

Chapter Four: The Influence of the Pharmaceutical Industry in the Development of CG181

4.1 Introduction

This chapter presents the joint thematic analysis of nine interviews with relevant informants (including six guideline development group (GDG) members, one member of NICE's senior management team, and two National Clinical Centre (NCGC) employees working on the guideline) and thematic analysis of 190 documents directly pertaining to or surrounding the guideline[6]. This chapter addresses the research question: *In what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?* In answering this question, the chapter is structured around two overarching sections: 'the influences of the pharmaceutical industry on the evidence base', and 'the guideline development group and the pharmaceutical industry'. In doing this, it is necessary to draw on aspects of STS to 'open the black box' of statins as a technology and assess how certain mechanisms in the initial scientific fact-making (Latour, 1987) might serve to exacerbate efficacy and diminish concerns about safety – with this evidence necessarily informing the basis of historical regulation but also, as in this case, for further (re)evaluations serving to widen availability and usage.

In analysing if and how the influences of the pharmaceutical industry emerge in this case, this chapter offers insight into the second dimension of pharmaceuticalisation as outlined by Williams et al. (2011a). This regulatory dimension is concerned with closeness between and dependency on the pharmaceutical industry by regulators. NICE are the regulatory actor that have opened up the opportunity for further pharmaceutical deployment by widening the primary prevention threshold where statins may be prescribed. This dimension of pharmaceuticalisation suggests that it is, as such, crucial for any research concerned with such regulatory activity to consider if and how the pharmaceutical industry might have shaped the decision-making of, in this case, NICE. Specifically, the research concerns itself with if there may be mechanisms built into in the statins evidence base reflecting the influences and interests of the pharmaceutical industry that subsequently shaped NICE's decision to widen the availability of statins. It

[6] Appendix 3 provides references for the quoted/referenced documents that formed part of the thematic analysis. Other references that were not formally analysed but drawn on in support of certain arguments are included in the reference list.

also considers whether, at the level of the guideline development group, if and how the influences of and associated dependency on industry might be established in terms of connections between elite researchers and professionals involved in the guideline development and industry.

In service of the overarching research question of this thesis as concerned with driving forces and extent, this chapter uniquely captures the interactions between NICE and the pharmaceutical industry within the pharmaceutical regime of the case under study. In particular, this chapter assesses if and how industry influence and regulatory dependency drive widening pharmaceuticalisation in the area of CVD. It also considers whether the extent of the opportunity for further pharmaceuticalisation opened up by CG181 is justified by the existing evidence. Pharmaceuticalisation is approached initially as a neutral process here (Williams et al., 2011a) whilst also being guided by the available evidence in subsequently establishing strengths or problems associated with the process within the regulatory dimension.

Before presenting the analysis, it is important to note that, in response to the framing of the research question at the heart of the chapter, it might immediately be counter-argued that four of the five statins with UK marketing authorisation were at the time of the GDG generic – off-patent (thus dropping to a cost of pence a day) and with seemingly little financial gain on offer to the industry and the original manufacturers (e.g. Pfizer, the patent holders of *Lipitor*, generically available as atorvastatin). The fifth (rosuvastatin) was also not recommended other than in extreme circumstances where other statins are not having the desired impacts or are causing side effects (and has itself gone off-patent in years immediately after the guideline was published). How and why would manufacturers want to influence decision-making about generic drugs? One answer to this question might be that the decision taken by NICE to widen the primary prevention threshold has supposedly made as many as 9 million people eligible to be offered the drugs in primary prevention (Ueda et al., 2017), drugs which are prescribed on the assumption that they will be taken for the rest of that individual's life, rather than for a limited time as might be the case for acute conditions. In recent years, other western countries (such as the US) have also reduced risk thresholds to similarly low risk thresholds where the drugs can be offered (Unruh et al., 2016). Again this opens up many millions of potential patients who become eligible to be offered statins. Whilst statins will never hold the same value to the pharmaceutical industry as they did in the 1990s and

2000s, there is clearly still benefit in the expansion of primary prevention markets in the 2010s and beyond (Unruh et al., 2016) (e.g. for generic manufacturers), perhaps particularly in a broader context of declining innovation in the industry and the end of the age of the blockbuster drug. However, this chapter will argue that this line of argument has limited value when considering the evaluations conducted by NICE for CG181. It argues that, in particular, this points towards a directness of interest and influence. This thus misses the issues of real sociological salience here – particularly surrounding the construction of the evidence base on statins, the subtle influences on and long term relationships between industry and influential researchers and professionals (such as those on the GDG), as well as the future of cholesterol reduction and CVD prevention.

4.2 The Influences of the Pharmaceutical Industry on the Statins Evidence Base

4.2.1 Benefit in Primary Prevention

As discussions in earlier sections of this thesis have highlighted (see also Appendix 1), a significant and polarising debate occurred within the medical community surrounding NICE's decision to widen the primary prevention threshold and the benefits of statins in low risk populations. Debates about efficacy are of course not divorced from safety (particularly because the presence of side effects may be deemed more or less tolerable if significant benefit can be established) but for the sake of clarity this chapter discusses the safety profile of statins in the next section. The first part of the analysis in this theme begins with some qualifications about NICE's processes of evaluation and certain aspects of conflation and inaccuracy of commentary that were made in the wider context of the case (and which was, for example, reported in newspaper coverage). It is important to note that in the context of the case as a whole, consternation emerging from the publication of the BMJ papers, particularly that written by Abramson et al. (2013), was in certain ways inappropriately conflated with what NICE had done during their evaluations. Though NICE's decision to widen the primary prevention threshold thrust this pre-existing dispute into the public realm, and indeed, these disputes necessarily cast light onto NICE's decision-making in terms of more general issues (e.g. the limitations of the available data necessarily utilised by NICE), qualification is needed here. Abramson

et al. (2013) produced a critical reanalysis of a CTT meta-analysis that in itself was published in 2012. Abramson and his colleagues suggest in their BMJ paper that in reanalysing the CTT data there were no reductions in all-cause mortality from statins and that CTT analysis had utilised 'softer' outcomes (which supposedly suffers from bias resulting from unblinding[7]) in asserting the benefit of statins in primary prevention. Based on this, Abramson et al. criticised any movement to widen risk thresholds upon which statins could be prescribed. Following this, certain subsequent commentary within medical circles conflated the meta-analysis work conducted by the CTT with the subsequent recommendations made by NICE to widen the primary prevention threshold. For example, commentary in the BMJ suggested:

> The Cholesterol Treatment Trialists (CTT) Collaboration is the major source of data used by NICE, with commercial secrecy agreements. The latest reviews by NICE and the Cochrane group rely on the private 2012 meta-analysis from the CTT for all the data (McPherson, 2014)

Whilst the above quote correctly identifies the influence of CTT publications on vastly different results and analysis by Cochrane in 2011 and 2013 on statins in primary prevention (see timeline of events in Appendix 1), NICE conducted their own evaluations for the purposes of CG181. This conflation is perhaps surprising particularly when considering that NICE's (very well-known) remit is concerned with cost-effectiveness, whilst this was not the primary goal of CTT analysis (who as a collaboration have been concerned particularly with demonstrating the benefit of LDL cholesterol reduction regardless of baseline risk) or the Cochrane Review. Correspondence made public by Cochrane makes clear that the CTT complained to Cochrane about their 2011 review which problematised the use of statins in low risk populations and criticised the lack of inclusion of a paper published by the collaboration in late 2010. Indeed, the vastly different analysis presented in the 2013 Cochrane Review is explicitly contextualised throughout the paper with reference to the findings of the CTT (reflecting both pressures emerging from private communication, which was subsequently made public, as well as emerging publications by the collaboration). Whilst these emerging analyses figured in

[7] Unblinding in the allocation of treatment in statins clinical trials is evident. Bias occurring from unblinding is evident in the evidence base where individuals with lower total and LDL cholesterol have been allocated to the statin arm of trials. Abrahamson et al. (2013) argue that his serves to improve the appearance of levels of 'soft' outcomes (such as revascularisation).

NICE's decision to review and update its previous guidance with what became CG181, importantly it produces its own evidence reviews (for statins here, systematic reviews of the published RCT data) in response to its own review questions. Indeed, NICE's evaluations for both guidelines and technology appraisals involve a great degree of complexity (Brown et al., 2016; Calnan et al., 2017), and in this case, for example involved an examination of the available published evidence to evaluate which statin held the greatest clinical and cost-effectiveness. Importantly, also, data analysed for this chapter suggests that NICE were interested in harder outcomes in establishing benefit (such as cardiovascular death) than that included in CTT analysis, which in evaluating the benefits of LDL cholesterol reduction has included softer outcomes under the composite outcome of 'major vascular events'. This emerged in both the interview and document analysis:

> Heart attack deaths and strokes are very hard outcomes. What we were very clear on in this guideline was that we were not going to base results on treatments that *just* lower your cholesterol or have soft outcomes, rather those that have been proven to save lives (NICE7).

> The GDG did not consider that the use of a surrogate outcome – evidence of LDL-cholesterol lowering – was sufficient to make a recommendation for statin treatment (NCGC, 2014: 189).

However, NICE do draw on the 2013 Cochrane analysis to support recommendations, and particularly importantly, seem to draw numbers needed to treat (NNT) figures directly from this analysis (itself clearly influenced by the CTT analysis). The NNT figures suggest the likelihood at population level of a particular cardiovascular event occurring in people with a certain level of risk when a statin is taken compared to not taking one. At a 10% 10 year risk, NICE's analysis suggests that treating 100 people for ten years will prevent four cardiovascular events. However, it can be quite difficult to compare data from different studies with each other due to differences in risk in studies, duration of follow up, and importantly the way that outcomes may be differentially grouped and reported. This latter aspect meant that though NICE themselves calculated individual outcomes across the published evidence (e.g. myocardial infarction), it was assumed that this would underestimate the benefit of statins because of differences in the reporting of combined outcomes in these data. As such, existing NNT analysis by Cochrane (which has its basis in analysis done by the CTT) figured prominently in NICE's recommendation as a way around this. However, composite outcomes themselves may

be presented in such a way that exaggerates benefit. For example, (as noted in the critical 2011 Cochrane analysis) in publications of the MEGA (pravastatin) trials utilised in their systematic review by Cochrane in 2013 data, fatal and non-fatal events were provided together but not separately, so it was hard to establish whether an individual had had a non-fatal event followed by a fatal event, in the process potentially exaggerating benefit.

It is worth noting here that the CTT, though receiving no funds directly itself from the pharmaceutical industry is part of a broader unit at the University of Oxford (the CTSU) which receives millions in industry funding, including in the past specifically for research on statins and other cholesterol-lowering drugs, whilst the CTT is also comprised of the trialists of the drugs themselves – and as such can hardly be considered independent analysts[8]. However, the NNT figures are less a direct reflection of pharmaceutical influence via the CTT as was inferred in a broader sense by some of the commentary in this case (e.g. the above quote from a letter by McPherson et al.), but instead are symptomatic of broader issues with the evidence base on statins that may have shaped individual and composite outcomes NNT figures (i.e. as the second Cochrane analysis in 2013 present them) to appear more beneficial than they are.

Indeed, almost every RCT of the more than thirty (eleven in primary prevention) that NICE included in their systematic review as concerned with lipid therapy for this guideline had pharmaceutical industry funding. These trial data come from a wide timeframe ranging from the early 1990s to the late 2000s – importantly in the main from time periods when statins with marketing authorisation in the UK were under patent. In the 2011 Cochrane Review (which, compared to the subsequent 2013 review, took a problematising stance on statins in low risk patients in primary prevention), it was stated that:

> Caution also needs to be taken regarding the fact that all but one of the trials had some form of pharmaceutical industry sponsorship. It is now established that published pharmaceutical industry-sponsored trials are more likely than non-industry-sponsored trials to report results and conclusions that favour drug over placebo due to biased reporting and/or interpretation of trial results. In primary prevention where world-wide the numbers of patients eligible for treatment are massive, there might be

[8] No total level of funding received by CTSU from the pharmaceutical industry is publicly available. However, as an example of the significance of the level of funding the unit receives, recently the CTSU received £96 million funding from pharmaceutical company Merck Sharpe & Dohme for the study REVEAL which considered LDL cholesterol-lowering benefit of anacetrapib alongside statins (Thompson et al., 2014). Published in 2017, the results of this trial were favourable for the company.

motivations… to [establish, for example, through the use of] composite outcomes and early stopping… results that clearly support intervention (Taylor et al., 2011: 11-12).

The CTT has received patient-level data from most major statin trials that must be held in "strict confidence". Only the drug companies, trialists and CTT have had access to the primary data, meaning medical journal editors, peer reviewers, Cochrane reviewers and even guideline writers have had to rely on unverified analyses of almost exclusively commercially funded clinical trials (Malhotra, et al., 2016: 15).

These quotes capture much of importance for the purposes of this section of the chapter. The overwhelming majority of evidence from RCTs drawn on in secondary analysis and by NICE has been funded by the pharmaceutical industry, who, as explored in Chapter Two, may utilise various mechanisms to cast their drug in the best light, maximising evidence of benefit. Equally, no independent eyes have ever had access to these data. Individual patient data (which paints a clearer picture of benefit because it avoids problems with selective reporting and composite outcomes, as discussed above) has never been made available for independent analysis to calculate benefit. The BMJ and its editor Fiona Godlee, in the aftermath of NICE's decision to widen the primary prevention threshold, has established a campaign to facilitate access to these individual patient data. Whilst also, as indicated in analysed documents, an independent committee established by the BMJ to assess the retraction of the Abramson et al. and Malhotra papers critical of the utility of statins, as part of its overall conclusion suggested that much of the consternation over statins reflects the fact that no independent body has ever had access to individual patient data and that releasing this would serve to clarify the overall picture of benefit and harm. NICE, though they attempted to, did not gain access to these individual level data for the purposes of CG181 and as such had to rely solely on the published evidence and secondary commentary by Cochrane. The CTT (who have access to these individual patient data) supposedly had attempted to facilitate access to these data, but time constraints at NICE's end of things had prevented this. As discussed further in the next section time constraints reflected the need to contact all individual trialists to gain access to all available data (due to commercial agreements) and it was also not clear which data (particularly on adverse effects) would be available even if they were successful.

Various mechanisms have been utilised in statin clinical trials to exaggerate benefit that even access to individual patient level data may not overcome. One example is the premature conclusion of trials:

[There is evidence some trials] were prematurely stopped because significant reductions in primary composite outcomes had been observed… the benefits of the reductions seen in a composite outcome of major cardiovascular events and specific endpoints at two years into the trial were considered sufficient to stop the trial…Early stopping of trials is of particular concern because in this and other situations early stopping may lead to an over-estimation of treatment effects (Taylor et al., 2011: 11).

And pre-randomisation screening of participants:

…the benefit of statins found in clinical trials may be exaggerated because prerandomisation screening procedures include monitoring for compliance with therapy (Abramson et al., 2013).

These kinds of mechanisms, as such, may distort the true benefit of the drugs (particularly NNT) – which then distorts the cost-effectiveness analysis as conducted by NICE, with statins appearing potentially more effective within the context of QALY calculations than they actually may be. As such, the influences of the pharmaceutical industry, who have funded the overwhelming majority of the research and the existing evidence, necessarily shaped NICE's lowered primary prevention threshold in CG181 in this way.

4.2.2 The Safety Profile of Statins

If the benefits of expanding the use of statins in primary prevention can, as above, be questioned, this, as such, intensifies the spotlight on what might go wrong from taking the drug. As has been made clear above, in terms of analysis specifically of the actualities of NICE's evaluations, the critiques posed by Abramson and colleagues of the work of the CTT, despite much conflation in professional and public debate between the two, is again only partially applicable to NICE's work because they do their own statistical evaluations concerned with cost utility. To reiterate, NICE, though drawing on the work of the CTT or Cochrane to support their recommendations in certain places, at no point did they base their recommendations *directly* on meta-analyses of trial data conducted by others (though it these external analyses were importance in the appetite for widening the threshold and as supporting references throughout the development and production of the guideline), as was claimed by some. However, as above, analysis of broader

commentary again highlights the issues that exist in the published data that the GDG subsequently reviewed in making their recommendations.

As noted above, almost all of the RCT data NICE utilised in their recommendations were funded by the companies whose drugs were being trialled. This trial data suffers from a number of problems pertaining to safety that reflect the influences of the pharmaceutical industry. The quotes below capture the key ways in which industry sponsored clinical trials attempt to minimise adverse events from statins, such as selective inclusion of participants in trials, and potentially fail to measure or report the adverse events that do emerge:

> Possible mechanisms by which adverse effects might be minimised in clinical trials include exclusion of up to 30% of patients with comorbidities (such as liver, kidney, muscle or inflammatory diseases), pre-randomisation run-in periods in which people who fail to tolerate statins are excluded, 10% dropout rates, failure to assess for specific potential adverse events (like [muscle pain] or cognitive changes), and under ascertainment and selective reporting of adverse events (including serious adverse events) (Abramson et al., 2013: 3).

> …clinical trial populations studied in pre-marketing trials are highly selected. For example, industry sponsored trials include pre-randomisation run-in periods where those individuals who fail to tolerate statins in addition to placebo non-compliers are excluded. RCT patients therefore do not often represent the true population, many of which have multiple co-morbidities, that will actually take the drugs in the real world. Such RCTs may thus seriously underestimate adverse effects such as muscle pain or cognitive impairment and also fail to detect drug interactions, e.g. amlodipine and statins (Malhotra et al., 2015: 6).

There is, as these quotes indicate, a very significant concern that the populations studied in RCTs do not reflect the heterogeneity of the populations that will take the drugs in the real world. Indeed, despite the fact that this threshold meant that almost all men over the age of 60 and women over the age of 75 (Ueda et al., 2017) would reach a risk level of 10% primarily as a result of age alone this population have largely been excluded from RCTs.

> …the majority of trials excluded people aged over 75 years. Only 2 studies were identified specifically in adults older than 65 years, and people aged over 85 years were excluded. (NCGC, 2014: 196)

Vastly widening the use of the drug in the elderly may run contrary to the fact that presence of polypharmacy and comorbidities potentially increase the extent of adverse effects in older people (factors that are part of the reason for exclusion in the first place). Equally age may heighten the impact of more minor side effects (e.g. increasing frailty). This exclusion of the elderly (even despite very limited evidence in the 'old old') is an issue of sensitivity for NICE. NICE's Citizens Council, which provides a public perspective on issues of ethical/moral salience, definitively decided more than ten years ago that age alone should not result in the exclusion of a person from access to treatment. Whilst as such, NICE's decision to not restrict usage of drugs in elderly populations, particularly for people aged over 75, reflects this social value judgment (Will, 2009), the fact that so little evidence exists necessarily reflects industry attempts to cast their drug in the most beneficial light by trialling the drug in younger populations (Angell, 2009). NICE recommend expanding the reach of risk assessment from 74 in the previous guidance (CG67) to 84 in CG181. This is argued to be reflection of the greater sensitivity of the now recommended risk assessment tool QRISK2. NICE recommend a cautious consideration of risk and benefit (primarily in reducing the risk of myocardial infarction), but importantly the guideline vastly expands the numbers of older people eligible to take the drug, despite limited evidence in this population, significant uncertainty, and the potential for widening the incidence of adverse events.

An associated issue is that trials are generally set up to assert efficacy against placebo and investigate only major safety issues, excluding more minor problems such as myalgia (muscle pain) or cognitive changes which may, however, be important in patient adherence. RCTs are of course necessarily far shorter in duration than the amount of time that drugs such as statins (lifelong) for chronic illnesses will be taken for (Busfield, 2006). As such, other forms of evidence might provide a more detailed picture of the safety profile of a drug over time. In a safety update produced by the MHRA (the result of medical and public scrutiny in the months after NICE's issuance of the draft of CG181 in February 2014) it was admitted that RCTs had deficiencies in asserting the levels of adverse effects of statins:

Large clinical trials also showed that statins are generally well tolerated by most people who take them. Safety was carefully monitored in these trials by comparing statin side effects with those reported for placebo treatment. **However, these trials were general aimed at establishing efficacy. Specific suspected side effects were not investigated as the main outcomes of these trials, so this data is not enough to establish the**

safety profile of statins. Some side effects only become apparent when medicines are used in the community… Data from clinical practice can help identify side effects occurring in these situations (MHRA, 2014 – bold emphasis not in the original document)

At the crux of the matter then, these mechanisms make it difficult to establish a reliable figure of adverse event levels (either for those already prescribed a statin or to facilitate prediction in wider populations, such as at 10% risk) for specific side effects or overall levels. This is because the trial participants are likely to be significantly less heterogeneous than the wider population due to for example, screening for comorbidities, multiple medications, or those who fail to adhere during pre-randomisation (perhaps due to adverse effects such as musculoskeletal pain), whilst the RCTs have generally not been designed to investigate adverse events as the primary focus in the first place. It is clear from the analysed materials in this chapter that even if NICE had been successful in negotiating an agreement with the CTT to access individual patient trial data, the CTT themselves, even as the major meta-analysts of statins data, did not have all data on adverse events, particularly beyond the major ones of concern (for example, cancer) because simply it had at that point never been sought and not included in published material – although even this information would have aided NICE's analysis. The CTT announced plans only in 2015 to access, collate and analyse all patient level data on *all* adverse events (more than six months after the publication of CG181). Collins and colleagues at the CTT subsequently published a paper in the Lancet asserting the safety and efficacy of statins in September 2016. However, the efforts by the CTT to collate data on adverse events and, indeed, wider efforts, to collect further data on muscle related side effects (such as the *StatinWISE* trial at The London School of Hygiene and Tropical Medicine) are still ongoing. And as discussed above, and despite a public campaign by the BMJ, there has been no commitment by the CTT to make data available for independent assessment at the time of writing (apparently due to commercial agreements).

The lack of availability and/or independent scrutiny of these RCT data has led critics to cite observational work which suggests more significant levels of adverse events than that reported or recorded by RCT data or subsequent meta-analysis of this data by, for example, the CTT. Observational data are also much more contemporary than RCT evidence, particularly in terms of the type of people who will take the drug. A widely debated adverse event is that of muscle pain:

…a cross sectional analysis from the National Health and Nutrition Examination Survey database shows that the prevalence of muscle pain in statin users is 50% greater than in non-users. In absolute terms, this increase in muscle pain is 100 times greater than that reported in clinical trials—53/1000 patients, Number Needed to Harm (NNH)=19. A retrospective cohort study that included 13 626 people taking statins and 32 623 controls found a greater incidence of musculoskeletal disorders overall and injuries in those taking statins (odds ratio 1.19, 95% confidence interval 1.08 to 1.3 and 1.13, 1.05 to 1.21, respectively). The NNH for musculoskeletal disorders and injuries in people taking statins were 47 and 37, respectively (Abramson et al., 2013: 2).

The now well known 'hierarchy of evidence', where RCT data and systematic reviews are considered the gold standard, and cross sectional and other observational evidence considered of much lower quality, featured heavily in debates about expanding the use of statins in the aftermath of NICE's decision – and was drawn on in defending the safety profile of statins. One key issue was that of ascertainment – for example, the attributing of musculoskeletal pain to a statin where, in actuality, causation cannot necessarily be established and may reflect other factors. Indeed, Sir Professor Sir Rory Collins of the CTT in correspondence made publicly available by the BMJ surrounding the publication of the Abramson et al., and Malhotra papers, was highly critical in this way of analysis drawing on observational data and the suggestion of discrepancies between levels of adverse events recorded in these data compared with RCT data. Indeed, in a 2016 paper on the matter, Collins and colleagues argue that:

The only adverse events shown definitely to be caused by statin therapy—ie, are adverse effects of statins—are myopathy (specifically defined as muscle pain or weakness combined with large increases in blood concentrations of creatine kinase) and diabetes, although it is likely that the risk of haemorrhagic stroke is also increased. Typically, treatment of 10 000 patients for 5 years with an effective statin regimen… would be expected to cause about 5 extra cases of myopathy (one of which might progress to rhabdomyolysis), 50–100 cases of diabetes, and 5–10 haemorrhagic strokes. Statin therapy may also cause symptomatic adverse events (e.g. muscle pain or weakness) in up to 50–100 patients per 10 000 treated for 5 years (Collins et al., 2016: 2553).

However, despite these assertions, the issue of industry influence on the available RCT data remains. Indeed, reflecting on his involvement in a paper concerned with assessing levels of side effects that can be attributed to a statin and the issue of the nocebo effect (where being told an adverse event might happen results in said event happening), Goldacre in the quote below (from a letter published in the BMJ) suggests that the key

issue in the debate about statins and side effects must be that of pharmaceutical industry influence on the clinical trials and what is reported in publication.

…our meta-analysis looked at side effects in randomised trials of statins and found that many, such as muscle aches, were reported to an equal degree by participants taking a placebo. Those side effects may therefore be partly non-pharmacological, and due to negative expectations, or the "nocebo" effect, as has been shown in research on other drugs… Unfortunately, although our methods were sound, the reliability of our findings is… undermined by the poor reporting of side effects in clinical trials reports in academic journals (Goldacre, 2014: 1).

Importantly there are problems with the ability of RCTs *and* observational work to capture the true extent of side effects. However, as is consistent with the way NICE grade the quality of evidence, NICE draw on published RCT and secondary analysis evidence in their cost-effectiveness analysis about statins. The key issue for the purposes of this chapter is, as such, the problems stemming from industry influence on the creation of the evidence base necessarily feeds into NICE's decision-making about expanding the availability of statins in primary prevention. This said, there was level of awareness at NICE about the limitations of RCT evidence on safety (though the drugs were not considered dangerous).

Anyone who prescribes statins knows that people can get muscle pains. And yet the placebo trials suggest that it is no more common than with placebo. That just feels odd to most people, I have to confess that. So a detailed examination of what material there was on adverse effects was important because as you may know there is still ongoing work by Rory Collins and others on what material was disclosed and what may not have been disclosed when the trials were originally published (NICE2).

As such, NICE's health economic modelling built in certain provisions to ensure cost-effectiveness even despite higher levels of adverse events than suggested by RCT evidence (where it existed), checking if cost-effectiveness could still be assured at ≥10% risk even if certain percentages of patients stopped taking their statin or switched to a lower intensity statin.

A scenario analysis was… carried out considering the impact if a greater rate of adverse events in high-intensity treatment caused some people to cease taking statins or to change to a lower intensity. This found that high-intensity treatment would still be cost-effective compared to medium-intensity treatment if 10% of people taking high-intensity statins ceased treatment and another 10% switched to a medium-intensity

statin, demonstrating that the results are insensitive to the rates of adverse events over a very wide range of possible rates (NCGC 2014: 175)

[We asked would these percentage levels] make a difference to the cost-effectiveness and the answer was no… even if the difference was as high as 10% and therefore having to stop taking statins, it is still cost-effective it does not change the fundamental result (NICE7).

However, it was not completely clear from the data why or how these particularly figures of 10% discontinuation and 10% switching rates had been decided to be appropriate. In terms of the former, the drug information for atorvastatin, for example, suggests that 1 in 10 people may experience side effects. Clearly this was felt to be high, however by guideline developers, and there was no indication in the data analysed for how/why the 10% switching figure had been decided upon.

Although side effects are fairly common, I mean compared with other medicines anything like 10% is quite a high rate of side effects (NICE7).

And ultimately, the utility of observational evidence was problematised:

We did have quite a lengthy group debate during the guideline group sessions about whether we should be using more observational data to look at adverse events. But there was a distinct sense that we need to be really careful about doing that because of the degree of bias that enters into trying to interpret that kind of data. That is if you tell people they are going to get muscle aches well probably will come back with muscle aches (NICE8).

Whilst, as this quote captures, caution may be needed about establishing causation of side effects, and/or the influence of side effects on adherence, particularly as established by observational research, the usage of these scenario levels which were rooted in expert opinion to assess cost-effectiveness seems to be at odds with other suggested levels. Indeed, levels of adherence to statins, potentially as a result of side effects, seems to be significantly lower than that anticipated/acknowledged by NICE:

A recent systematic review confirms this—only 49% (95% CI 48.9% to 49.2%) of patients were adherent at one year on the basis of observational data, whereas RCTs report that 90.3% (89.8% to 90.8%) continue to be adherent. RCTs of adherence enhancing strategies show a substantial reduction in adherence (<50%) between six and 24 months. Although adherence is only a marker for adverse effects and patients discontinue for other reasons, this problem needs to be further explored… (Fahey and Smith, 2014: 1).

Interestingly, also, Professor Collins from the CTT has a patent for a genetic test that supposedly identifies those likely to be susceptible to side effects.

Professor Collins filed a patent in 2009 for a test that identifies a gene that makes patients more likely to suffer muscle pain with statins. The test, branded as StatinSmart, had until recently been sold directly to the consumer in the USA on a website that claimed up to 29 per cent of statin users will suffer muscle pain, weakness or cramps. Although Professor Collins said the 29 per cent figure was "misleading", Boston Heart Diagnostics, the American company granted an exclusive licence for Collins's patent, stood by its claims. It cited a US task force on statins safety that concluded randomised controlled trials "had major limitations" because patients with side-effects were often excluded (Malhotra et al., 2016: 16).

As will be apparent to the reader, the 29% figure suggested above is starkly different to the 50-100 per 10,000 suggested by Collins et al. in a previous quote above. Indeed, if levels of side effects and subsequent adherence are widely variant from NICE's scenario levels, it is not clear whether the expansion of the primary prevention threshold will actually be cost-effective due to the population level impacts of the drugs, undermining the purpose of their evaluations. Equally, of course, expanding the use of statins might cause harm to patients, or at least encourage some dismissiveness amongst medical professionals about patient concerns with potential or emerging harms (Will, 2014). NICE recommends that professionals attempt to establish a maximum tolerable dosage and can prescribe a lower intensity statin than that of atorvastatin 20mg as the primary recommendation (which is considered high intensity whilst also being low dosage) if this is necessary. The option also exists, recommended in the guideline, for clinicians to utilise creatine kinase testing to identify myopathy and thus the risk of this significant harm, and the guidance suggests that physicians explore with patients other causes of existing or emerging muscle pain before and after prescribing. But this focus on achieving utilisation of a statin (which is also supported by NICE's attempts to get the ≥10% threshold included in the QOF), or at least identifying significant harm, is not necessarily sensitive to patient concerns or complaints (where for example raised creatine kinase is not evident) that the drugs are causing muscle pains or having other effects (Will, 2014), and as such, patient centred care.

Overall, the key issue for the purposes of this chapter is the uncertainty surrounding side effects that necessarily reflects the purposeful influences of the

pharmaceutical industry on the design of the clinical trials with the intention of maximising evidence of benefit and minimising evidence of harm. Independent analysis of industry-sponsored patient level data, as called for by the BMJ, could allow for the verification of the low levels of side effects as supposedly evident in RCTs. But even if this ever occurred, it may not be able to account for the various mechanisms designed to minimise the occurrence of side effects in the first place. Evidence from RCTs concerned with the side effects of statins is at best limited and it is very hard to establish reliable levels, despite the scenario analysis carried out by NICE in establishing cost-effectiveness, which seemed to be partially rooted in expert option about side effects levels and some existing drug information. It is interesting that NICE utilised such a scenario analysis that at best seems to be an estimation particularly surrounding switching to a lower intensity statin (and not grounded clearly in RCT evidence or secondary analysis of this evidence) rather than use observational evidence to inform their evaluations. Rather than being precautionary particularly in the face of uncertainties about harm and side effects, NICE's approach seems to be guided more by permissiveness where benefit is assumed to outweigh risk (with only RCT evidence seriously entertained) (Abraham, 2002). Indeed, in the use of a scenario analysis there was clear permissiveness in the approach to adverse events – that these could not be more significant than suggested by the very limited RCT evidence and existing drug side effect information (Abraham, 2002). It is true that NICE are bounded by certain time constraints both in terms of the decision to update guidance and the nature of the actual development processes in the GDG. However, negotiating/waiting for access to individual patient data (despite potential limitations) provided by the CTT before widening the primary prevention threshold, or even establishing the paucity or lack of collated individual patient data on all adverse events (and thus delaying or not recommending widening treatment) would have been more indicative of a precautionary approach. This is particularly important when considering that NICE's remit, as concerned with cost-effectiveness, is also potentially undermined by permissiveness because of vast uncertainties in establishing the actualities of side effect and adherence levels that on a population level could vastly skew their cost-effectiveness modelling.

The discussions throughout the two themes so far of the ways in which the industry has shaped evidence about benefit, side effects and of disparities between types of evidence is of vital importance here in analysing NICE's decision-making and

pharmaceuticalisation. The data suggest that the influences of the pharmaceutical industry during the initial production of knowledge in the RCTs importantly then contributes to the further misshaping of medical knowledge and practice. In this case, the reliance on industry data, even where these data are two decades old and the drugs subsequently have become generic, continues to (re)shape the production of guidelines upon which many medical professionals rely – and, as such, the pharmaceutical industry indirectly influences the opportunities for further pharmaceuticalisation of CVD, as has occurred in this case. This is despite the potential for harm to patients, or at least physician indifference to side effect claims by patients, and even the lack of robustness of NICE's cost-effectiveness analysis that could undermine the role of the institute. Whilst the cost-effectiveness of atorvastatin (the ultimately recommended statin) appeared to be significantly below NICE's £20,000 per QALY cost-effectiveness threshold, and indeed, was potentially cost-effective down to a lower risk threshold of 7%, the discussions so far have indicated how the influences of and dependency on the pharmaceutical industry serve to undermine these calculations and their reliability.

4.3 The Guideline Development Group and the Pharmaceutical Industry

4.3.1 The GDG and Connections to Industry?

It was claimed (at an abstracted level) by critics of CG181 that financial connections existed between members of the guideline development group (ranging in a typical manner for these sorts of connections from research funding and advisory work through to speaker and conference fees).

> We are… seriously concerned that 8 members of NICE's panel of 12 experts for its latest guidance have direct financial ties to the pharmaceutical companies that manufacture statins (Thompson et al., 2014: 4)

The above quote captures the essence of the debate here and seems to indicate a potential opportunity for the influence of the pharmaceutical industry to emerge. As becomes clear in chapter five, this issue of GDG financial connections, inspired in actuality by this section from this letter by Thompson et al. letter, was picked up on by and widely reported by the British newspapers. But to what extent does the above quote capture the problem? Well, research suggests that financial connections between guideline group members and

the pharmaceutical industry can be associated with the widening of diagnostic categories, and as, such the expansion of markets for drugs (Unruh et al., 2016).

What is important here is not the types of connection or of any individual benefit to GDG members, but rather that connections exist between GDG members and the pharmaceutical industry at all. Dependency on and connection to the pharmaceutical industry across the knowledge development process (Cosgrove and Wheeler, 2013; Light et al., 2013). Clinical practice guidelines of course hold a very significant place in the delivery of contemporary healthcare and become vulnerable to the influences of industry due to the increasingly common partnerships in research between academics/professionals and industry as one step in the broader process of pharmaceutical knowledge creation. Clamour for transparency in the medical sphere in recent times reveals connections in research and practice but it does not actually remove the problem – it simply translates the problem from one of secrecy bias to openness bias (Cosgrove and Wheeler, 2013). This means that it is difficult to hide such an interest, but at the same time it does not resolve the issue. As such, where relationships exist between guideline developers and the pharmaceutical industry the question is arguably less about direct influence and more about the more subtle and potentially inevitable inability of researchers and professionals to sufficiently problematise the involvement and practices of the industry in the trialling and construction of the evidence base on drugs.

It does hold true in this case, as per NICE's declarations of interest policy, that in terms of admittance to the GDG, direct financial involvement with research or other activity directly pertaining to the drugs under consideration is not permitted by NICE. Rather than companies specifically manufacturing statins (past or present), the figure of 8 of 12 group members with financial connections more accurately refers to the pharmaceutical industry in a general rather than specific sense – and as noted above this reflected a variety of connections. In this way the above quote from Thompson et al. is slightly misleading in its phrasing, but does capture correctly the existence of connections to the pharmaceutical industry more generally. There was unlikely ever to be any direct financial benefit for any members of the GDG from widening the use of generic statins even if they had had direct connections. [REDACTED]

As one GDG member remarked about discussions with colleagues after the publication of the draft guideline:

We had a sort of joke about it that [we] were supposed to have made loads of money or something. Not true, absolutely not true. Completely unfair (NICE5).

However, the point is that where researchers or medical professionals are so intertwined with industry at a variety of levels the key question is whether they can they ever be truly neutral, and avoid sensitivity to industry interests or possess sufficient critical distance to give appropriate weight to precautionary evaluation in the light of uncertainty? Indeed, influences on researchers can be quite subtle, involving long term relationships (even career long) and the creation of positive attitudes that lead them to promote industry interests in research and beyond (Sismondo, 2008) even without necessarily believing that is what they are doing. In this sense, a lack of precautionary action from GDG members, many of whom had long standing relationships with the pharmaceutical industry, is certainly evident in discussions earlier in this chapter surrounding the limitations of side effect data.

Further to this, and in its own way in support of the above discussions, it was suggested by an informant from within NICE's senior management that if the guideline group had been appointed in 2016 rather than four years previously, the composition of the GDG would have been different.

With hindsight, though the committee and the chair were selected in line with the interests policy at the time I think [NICE] should have recognised that it would be seen as a bigger issue than [they] thought it would be…. And with hindsight and under current practice we wouldn't have appointed all of those people to the committee. There was a view among some of our developers that leading researchers should be on committees [but this is not the view necessarily taken in senior management now]. Their value is in what they publish not in what they think it means… so [in recent times they've] tended to move towards people who are more generalist who, and well there would have been more GPs on this committee under our current arrangements. It was relatively diverse but the interpretation of the evidence was dominated by the experts, such as the chair, well, and [the] other specialists (NICE2).

And that a change of chair policy had also occurred, removing any connection to the research area:

Um [NICE] have changed [the] conflict of interest policy in the light of the experience particularly with this guideline. So the chairs now can have no specific interests at all. So most of the chairs are not experts in that field any more (NICE2).

This can be read as NICE attempting to reduce or even resist the potential influences of the pharmaceutical industry on, or at least, reflecting its place within a polycentric regulatory regime (Brown and Calnan, 2013), media criticism of its guideline processes, and as such, a partial move towards investigative norms of regulatory trust rather than acquiescent (Abraham 2008b) (the latter of which seems to have underpinned pharmaceutical regulatory processes under neoliberalism). However, this can also be read as tacit admittance that organisational mechanisms were at less than ideal standards – and more fruitful for shaping by industry influence than at present and more acquiescent in trusting industry produced knowledge than now. And of course, even these mechanisms do not remove dependency on industry in the creation of medical knowledge at the level of research.

Whilst the discussions in this section have thus far been relatively abstracted, the chapter now turns to examine two particular examples of emergent influences from within the pharmaceutical sector that may have featured in and influenced the proceedings of and decision by the GDG to widen the availability of statins in primary prevention. The first of these discussions complements the above theme concerned with the influences of and dependency on the pharmaceutical industry at the level of the GDG, providing one example of the uncertainties inherent where relationships with industry exist. The second example moves to examine the case of [REDACTED] (who was not interviewed as part of this research), examining non-disclosure of relevant research interests and emerging commercial interests. This theme explores a more direct visible example of unethical individual behaviour and profit motive within the GDG, with impacts both on CG181 as well as the future of CVD prevention.

4.3.2 The Next Generation of Drugs

Analysis of the declarations of interest documentation for the GDG suggests that four members of the panel were involved with PCSK9 inhibitors, an emerging class of injectable drugs that alongside statins also lower LDL cholesterol. Whilst this new class drugs were not under consideration in this guideline (indeed, one example of this class, evolocumab, marketed as *Repatha* by Amgen, was only given European and FDA regulatory approval after the publication of this guideline) there is evidence that the

connections between the GDG and the future of lipids medications also yielded opportunity for industry influence to emerge.

> [S]ome members of the guideline panel are also involved in next generation, more expensive, cholesterol lowering drugs, which are not yet on the market. If cholesterol lowering becomes established in low risk people, the indications for these new cholesterol lowering drugs such as… PCSK9 inhibitors will probably expand as well. (Thompson et al., 2014: 4)

The argument captured in the above quote is that industry influence was salient in an indirect manner on the decision by the GDG to widen treatment thresholds. The establishment of treating a wider number of people with lower levels of risk and more moderate levels of cholesterol might legitimise the use of newer drugs in such populations – and, indeed, three members of the committee had connections to the creator of *Repatha*, including ongoing advisory work and future work (at that time) on a clinical trial of a PCSK9 (seemingly in patients with familial hypercholesterolemia rather for more general marketing approval). However, NICE's current technology appraisal published in 2016 (TA394) only recommends the use of *Repatha* in primary prevention in cases of familial hypercholesterolemia where a maximum tolerated dose of statins has not had the desired impacts on lowering LDL cholesterol (NICE, 2016). Additionally, controversy surrounding impacts on mortality impact has also emerged in more recent times (Schmidt, 2017). This said, *Repatha* has been tested in individuals who also take a statin and it largely seems to be seen as an addition to rather a than replacement for a statin. Equally, the impacts on LDL cholesterol reduction beyond that offered by statins alone have been emphasised by the industry-funded FOURIER trial on *Repatha* (Sabatine et al., 2017). This is compatible with a broader agenda surrounding benefits of the reduction of LDL cholesterol regardless of baseline (indeed, heavily emphasised by the CTT) and new drugs with potency in LDL lowering may come to be seen as increasingly necessary in the pursuit of this agenda (Unruh et al., 2016). These arguments are, as such, suggestive that the above quote captures something of salience.

There are problems with an argument that suggests some sort of overt intent to influence NICE recommendations by certain members of the GDG on behalf of drugs such as PCSK9s that at the time did not even have marketing authorisation. However, as discussed above, widening the market for cholesterol reduction is unlikely to be damaging to the discussed next generation of drugs. Indeed, Unruh et al. (2016: 800) note

that with patent protection for statins expired, the scramble for the next blockbuster drug in this area is significant because of the renewed patent protection offered and associated higher prices for medicines to be taken life-long. Members of the GDG were involved with Amgen on work on PCSK9s (albeit it in different populations) at the same time as Amgen were seeking marketing approval for *Repatha*. As such, this discussion again is indicative of closeness between the GDG, the regulatory state, where this connection was not envisioned as a sufficient conflict to preclude inclusion in the GDG, and the pharmaceutical industry. Again, as explored in the previous section, the importance of subtle influences of the pharmaceutical industry on researchers and KOLs cannot be discounted (Sismondo, 2008; 2013). Did a sufficiently critical distance exist in this case? Connections existed despite the potential associated with normalising the treatment of wider numbers of people not considered to be sick at the same time as industry desire to find the next cholesterol blockbuster drug also exists. Whilst only time will be able to show the extent to which *Repatha* and other newer cholesterol lowering drugs are deployed, this example cannot be discounted in any thorough analysis of industry influences on this guideline, however indirect and/or opaque it may have been. At the very least this example provides weight to the more general discussions of the connections between members of the GDG and the pharmaceutical industry and the associated problems of permissiveness and acquiescence. Some sort of directness of intention to widen future markets for *Repatha* through the manipulation of this guideline is undoubtedly an overstep, but again relationships existed, and ones, indeed, within the same field of research.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

4.4 Discussion

This chapter has explored the second dimension of pharmaceuticalisation as established by Williams et al. (2011a), focusing specifically on NICE's regulatory connections with and possible dependency or reliance on industry. Analysis of NICE's role in the process of pharmaceuticalisation presented here is unique within pharmaceuticalisation studies. The Institute has surprisingly been ignored in existing pharmaceuticalisation conceptualisations and empirical scholarship despite its fourth hurdle function evaluating which medicines should be funded by the NHS and in shaping the clinical activity of medical professionals through its guidelines. The focus on NICE broadens understandings within pharmaceuticalisation studies of this regulatory dimension by illuminating how NICE's specific organisational positioning means that the influences of and dependency on the pharmaceutical industry shape its regulatory work. The question at the heart of this chapter was 'in what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry?' In answering this question, this chapter has shown that, first, NICE are reliant on efficacy and safety data (or the lack of) produced and published by the pharmaceutical industry that they then apply in decision-making about cost-effectiveness. In this case reliance on existing published evidence (much of which was used to create the initial markets for statins) continues to shape the appearance of utility and safety even upon reassessment of the evidence by NICE. Mechanisms built into the RCT evidence base by the pharmaceutical industry have served to foster further pharmaceuticalisation of CVD years after the initial markets were opened up. Secondly, GDGs are made up of researchers and medical professionals, a large proportion of whom have financial and research connections to the pharmaceutical industry generally and even the specific manufacturers of CVD medicines. The main issue here is a potential lack of independence between researchers and professionals and the creation of relationships and perceptions that can be argued to have featured in promotion of the expansion of the availability and use of statins. The

inseparability of regulatory decision-making from and dependency on industry clearly emerges in both of these ways.

Exploring these aspects further now, first, in line with evidence base and dependency problems established in other work (e.g. Abraham, 2009a; Light et al., 2013; Healy, 2012; Sismondo, 2007), the analysis suggested that the influences of the pharmaceutical industry are visible in terms of the reliance almost completely on industry funded published data and secondary meta-analyses/systematic reviews[9]. Generic drugs present lessening costs to healthcare institutions, but cost utility analysis also necessarily takes into account evidence of clinical benefit (will it be effective for the cost) and safety when expanding availability to a wider population. Significantly, as such, this chapter has engaged in 'opening the black box' of statins as a technology and assessing how certain mechanisms in the initial scientific fact-making (Latour, 1987) serve indirectly to continue to widen pharmaceuticalisation even though the drugs are now generic. Whilst the cost-effectiveness of atorvastatin (the ultimately recommended statin by NICE) appeared to be significantly below NICE's £20,000 per QALY cost-effectiveness threshold, and indeed, was argued to be potentially cost-effective down to a lower risk threshold of 7% risk over ten years, the chapter indicated how uncertainties surrounding efficacy and safety stemming from industry influence on the evidence in the creation/establishment of markets for the drugs (Williams et al. 2011a) raise doubts about these claims to cost-effectiveness and thus reliability of the recommendations. Problems in the evidence reflecting the influences of the pharmaceutical industry cumulatively mean that arguably cost-effectiveness cannot be definitively established. Importantly, uncertainties surrounding benefit and safety (as stemming from the influences and deliberate practices of the pharmaceutical industry) would not even exist in the first place if the trialling of the drugs had been independently conducted, rather than by industry (Light et al. 2013), or at least, considering budgetary constraints, with greater transparency and reporting. The types of issues identified in this chapter reflect the centrality of the pharmaceutical industry across the processes of drug development, knowledge production, regulation and beyond. However, this is a systemic issue that has

[9] Secondary analysis also shows evidence of industry connections as a result of reliance on what is already published as well as a lack of independency from industry by the bodies conducting the secondary analysis, e.g. the CTT.

been identified far beyond only statins and CVD medications (Light et al., 2013; Rodwin, 2013a, b; Cosgrove and Wheeler, 2013).

This chapter also considered the approach to the evaluation of the evidence within the GDG. The closeness of the GDG to the industry, a longer standing issue in cholesterol/CVD guideline production (Moynihan and Cassels, 2005; Unruh et al., 2016), is unlikely to have been consistent with establishing a precautionary approach to widening the use of statins in primary prevention. Whilst no direct connections exist to statins manufacturers, the key concern, however, is whether sufficient critical distance and willingness to engage with the potential limitations of the industry funded RCT evidence and secondary analysis was evident in the GDG, particularly given coexisting and long-standing relationships and more subtle influences that create positive perceptions of industry drug development and products (Sismondo, 2008). There was little problematising of published RCT data nor the second of two of Cochrane's systematic reviews of published evidence by NICE, despite this being a significantly different analysis than Cochrane themselves had published only two years previously (the first suggesting little evidence of benefit even at higher thresholds of risk than ≥10% risk). There were also limited attempts to access individual patient data.

Interestingly, the guideline group did problematise the use of independent observational evidence in evaluating potential adverse events in the light of minimal RCT evidence. This led the group, as such, to conduct a scenario analysis (rooted in the expert opinion of the GDG) that supposedly avoided the problems of observational data but in itself had none of the supposed rigour of review of RCT evidence. Observational evidence (though with its own problems), if utilised, seems likely to have cast doubt on the expansion of statins in primary prevention, so, in this context, the utilisation of a scenario analysis despite its own lack of rigour and the preference for expert opinion/analysis rather than observational data were permissive choices. The lack of credibility or even availability of evidence on side effects is indicative of the influences of industry on the existing evidence. But the preference in the GDG for confidence that side effects could not be more significant than suggested by the very limited RCT evidence and existing drug side effect information, and an associated reluctance to use observational data in this example and thus, instead, the conducting of a scenario analysis, also raises questions about the more subtle influences on the GDG and the impacts of a lack of any real independence. In all of these ways decision-making in this case is consistent with growing

permissiveness in regulatory practice, because benefit was simply assumed to outweigh harm (Abraham, 2002; Abraham and Davis, 2009). It is also consistent with less critical and investigative and more acquiescent forms of regulatory trust (Abraham, 2008b) which interestingly applies to NICE here as much as more traditional regulatory bodies. Abraham argues that more investigative forms of trust incentivise companies to conduct better trials. This is of limited value in explaining regulatory trust as it applies to this case of generic drugs and fourth hurdle bodies, however, because few recent RCTs have or will be conducted on the now generic statins. The nature of acquiescent norms of trust as it applies to NICE in the production of its guideline here refers to a more general approach where industry evidence is trusted and potentially insufficiently problematised, and an approach where rather than delaying a decision until all potential relevant data can be gathered (e.g. access to individual patient data) favourable evaluations occur without this access. The emphasis placed on quickness of regulatory review/evaluation times over the interests of patients is also indicative of the theory of corporate bias (Abraham, 2008a).

[REDACTED]

The overall aim of this thesis to examine the degree of the further pharmaceuticalisation of CVD in this case and its driving forces. This chapter highlights that whilst NICE through its evaluative regulatory activity is the actor within the pharmaceutical regime that is directly responsible for the further pharmaceuticalisation of CVD, the influences of the pharmaceutical industry, though mostly subtle and indirect, are identifiable despite the generic status of the drugs. The extent to which pharmaceuticalisation in a given case or in a given disease area is occurring reflects if and how it expands or contracts along multiple dimensions and as involving the behaviours and interactions of multiple actors after the opportunity for intervention has opened up (or widened as in this case) – and this thesis begins to unpick these dynamics in the remaining chapters. However, when reflecting on the degree to which the further pharmaceuticalisation of CVD is occurring, it is possible to discuss whether the extent of pharmaceuticalisation established in CG181 can be said to be justified by the statins evidence base and, in this case, regulatory rigour. It is true that the GDG did discuss even greater pharmaceuticalisation along the lines of age rather than more complicated form of QRISK2 risk testing and rejected it. However, the evidence presented in this chapter suggests that the extent of the further pharmaceuticalisation established by CG181 nevertheless lacks precaution and is unjustified when taking into account efficacy and safety issues minimised in the published evidence and as treated permissively and with acquiescent trust by NICE.

Chapter Five: The Mediatisation of CVD Pharmaceuticalisation – Oscillation and the Exacerbation of Controversy

5.1 Introduction

This chapter presents the findings from the thematic analysis of newspaper reporting of the widening CVD primary prevention threshold established in NICE CG181 and the surrounding debates, commentary and context. The research question at the centre of this analysis is: *How did the UK print news medium present and portray the potential widening usage of statins?* It is the aim of this chapter, as such, to analyse the role of the print news medium as a relevant actor within the pharmaceutical regime (and part of the third dimension of pharmaceuticalisation identified by Williams et al., 2011a). The chapter focuses on the role of print newspapers in framing and (re)shaping debates and discourses surrounding the decision to lower the primary prevention threshold and potentially widen the usage of statins. The purpose of this chapter is to examine portrayals of the necessity and desirability of pharmaceuticalisation and establish the 'sense' of pharmaceuticalisation fostered. Pharmaceuticalisation within the mediatised dimension, at a conceptual, rhetorical or sensory level, can be said to be occurring when, for example, newspaper coverage organises and frames a drug or case positively, with limited critical engagement and uncertainty present and/or with an emphasis on extent. Coverage will also cohere with the interests of other actors within the regime who are fostering or facilitating pharmaceuticalisation. Once this 'sense' is established it may also possible to ruminate on the actualities of the impact of coverage as it reflects back on and potentially provokes action, interactions or responses from the other actors within the regime.

It is important that research does not overstate the importance of newspaper coverage in the configuration of audience perspectives (Gabe et al., 2017), particularly because this thesis does not present data concerned with audience perspectives, only the thematic intricacies of reporting. However, analysis suggests that news coverage is an important source of health information for lay audiences. Audiences can and do use this health information when constructing health-related identities (Seale, 2002) and media-disseminated information does figure within medical decision-making when decision-making is (accurately) conceptualised as being distributed over a number of forms of

knowledge and interaction (Rapley, 2008). It is, as such, important to consider the nature of the coverage as a basis to contextualise other research that has suggested impacts on (de)pharmaceuticalisation from the news coverage of the case under study (Matthews et al. 2016) and as a basis to facilitate further sociological research comparing thematic intricacies with audience reception and medical decision-making.

In terms of the selection of this as a case to report, it is not that the print news medium clearly engages in the promotion of a dominant position or agenda here, but that journalists' engagement with this case seems to reflect its controversial and thus newsworthy nature. It reflects significantly events in the wider context of the case, but which importantly are always tied back to the expansion in availability of the drugs, such as emerging professional opinion, debate and contestation, research updates, and even political intervention. Broadly, in the early stages (with the tide beginning to turn in roughly March or April 2014), critical medics and researchers were presented positively. After criticisms of the BMJ publications emerge, however, these individuals are presented as having (potentially) inflicted damage on the health of patients through misinformation. Meanwhile, NICE and those involved in the construction of secondary analysis of the database (such as Professor Rory Collins from the CTT) were initially presented as excessively pedalling pharmaceutical cures without concern for side effects and patient health, but this also at least partially reshapes in reporting as 'evidence' emerges declaring statins to be safe drugs and as a countercriticisms of the critics position emerges. Journalistic concern with newsworthiness is important to the 'journey' of the story here because, as Seale (2002) notes, once a story is established as news this often begets further coverage of associated developments, and tangentially related stories, until the enthusiasm for the story diminishes. Importantly for the analysis presented in this chapter, negative or controversial stories are newsworthy. Where pharmaceuticals are central to newsworthy medical controversy, the size of the impact or the personalisation of, for example, dangers to patients from side effects have independent significance, but also importantly figure as part of an implied critique of the authority of the medical professional, their fallibility and the contestability of the body of medical knowledge.

Before presenting the analysis, it is important to note, also, as Figure 1 below makes clear, that there is no stark *thematic* distinction between tabloid publications, middle-market publications, and purportedly higher quality broadsheet publications

included in the analysis. However, it is clear (again, see Figure 1) from the numbers of reports and the minimal presence in (such as the Sun) or absence of some British tabloids (e.g. the Daily Star) from the dataset, that this was a case more of interest to the middle-market and broadsheet British newspapers.

5.2 Framing and (Re)Shaping CVD Pharmaceuticalisation: Emerging Themes

Considering the general thrust of the approach to the news stories discussed above, four themes emerged from the analysis of newspaper reporting – size and significance; side effects: dangers to patients; violations and uncertainty in the evidence base: conflicts of interest; and the relative positioning of statins and lifestyle. Figure 1 presents the occurrence of the themes as they appear in each of the print news outlets.

5.2.1 Figure 1: Distribution of Newspaper Themes

N=170	Telegr-aph *N=30*	Guard-ian *N=17*	Indep-endent *N=12*	Mirror *N=10*	Daily Expre-ss *N=29*	Daily Mail *N=39*	Times N=30	Sun N=3
Size and significance	25	15	10	7	27	35	22	2
Side effects	23	15	9	7	22	33	23	1
Violations and uncertainty	18	14	7	4	11	15	8	1
Relative positioning	11	7	3	3	8	17	9	-

5.3 Size and Significance

The first theme emerging from the analysis of the newspaper reporting on this case pertains to the *size and significance* of the changing primary prevention threshold and the widening usage of statins. This was the most prevalent theme, appearing in 143 reports. This theme emerged in several interconnected subthemes: the vast numbers of people who potentially qualify for statins under the new threshold and the extent of the numbers of people already using the drug; the size and significance of the numbers of people with or at risk of cardiovascular disease in the UK and the scale of the health impact attached to widening the use of statins; and the extent of the financial impact of widening statins usage. Though controversy is not clearly present in this particular theme, these thematic aspects cohere with some of what Seale (2002) suggests makes a story newsworthy anyway – because they are aspects personalised to the everyday experiences of readership and offer superlatives in terms of numbers of people and impact.

5.3.1 Numbers and Types of People

Numbers (particularly very large or very small) are deployed in reporting because they appear objective and fact based (Seale, 2002: 38) and as a result they work to emphasise the 'reality' of the scale and significance of the subject of reporting. Journalists reporting on the widening primary prevention threshold place emphasis on large numbers of potential new patients, whilst also touching on the types of people that will be/are implicated (particularly in terms of age). For example, The Daily Mail note the vast numbers of people being made eligible for statins by the change:

> In July, the health watchdog NICE changed its advice to encourage GPs to prescribe the drugs to anyone with a 10 per cent chance of having a heart attack. It means 17million adults… are now eligible to take statins (Spencer, The Daily Mail, 24th September 2014).

The Guardian and the Mirror below similarly make comment on the size and extent of the numbers of people implicated, although further fostering a sense of the vastness of the

prevalence and use of the drug in the UK by referring to the numbers already using the drug at prior risk threshold levels:

Draft guidance from the National Institute for Health and Care Excellence (Nice) has recommended that everybody with a risk as low as 10% over 10 years (rather than 20% as now) should be eligible for statins from their GP. About 7 million middle-aged people are now taking a daily statin and the regulator's proposed guidance could extend that to 5 million more (Boseley, The Guardian, 13th June 2014).

Seventeen million people will be offered statins to cut heart attacks and strokes under radical new NHS guidelines out today. Doctors previously prescribed the drugs only to those with a 30% or greater risk than normal of heart disease within a decade. This was lowered to 20% in 2005 - but now medics are to hand pills to those with just a 10% risk. The move will increase the number of patients eligible for the cholesterol-busting drugs from 12.5 million (Gregory, The Mirror, 18th July 2014)

The focus on relative expansion here, with the change presented as potentially almost doubling usage levels, powerfully creates a sense of the size and significance of the change – as well as seemingly unending pharmaceutical deployment in the fight against CVD. Whilst there are some problematising aspects here, for example, the use of "just a 10% risk" by The Mirror journalist, in other instances journalists more explicitly problematise the size and significance of the change in terms of the low risk of patients. For, example, other articles refer to the UK as the 'statins capital' of Europe or in other similar terms, such as 'statins island', and is seemingly tinged with some negativity about the state of the health of the UK population. These kinds of phrases operate uniquely to emphasise the vastness of the threshold change and the widening usage of statins within the particular context of the UK. For example:

The new rules would make at least 10million patients eligible for anti-cholesterol drugs, securing Britain's place as the statins capital of Europe (Hope, The Daily Mail, 12th February 2014).

And in an opinion piece:

I have to admit, though, that the story that gets me right where I live (temporarily, West 24th Street) is the news from "Statin Island"… This is NICE's proposal that 12 million extra Britons should routinely be given statins if they have a 10 per cent chance of getting heart disease within 10 years (Woods, The Telegraph, 15th February 2014).

The reporting here additionally engages with the age profile of people who are likely to qualify.

> The majority of men aged over 60 and women over 65 will be offered the drugs by their GPs, even if they only have a one in 10 chance of developing cardiovascular disease within a decade. Among all adults, four in 10 will be told they should take them (Knapton, The Telegraph, 18th July 2014).

This quote from the Telegraph reflect an association between increased risk of CVD and growing older (as, indeed, is built into the QRISK2 assessment tool), but it also creates the sense that age alone is enough to qualify an individual for statins. On the one hand this might be seen as normalising and destigmatising the use of statins; but it also serves to create doubt about the necessity or legitimacy of the use of the drug if almost every individual by virtue of their age alone should be using the drug to prevent CVD. The latter sense is arguably more powerful here – particularly because of the framing of the situation as "*even if they only have a one in ten chance of developing cardiovascular disease*". These quotes also have a similar relationship with gender – fostering a sense that pharmaceuticalisation is more likely for older men than older women.

5.3.2 Scale of CVD Problem

Another element pertaining to size and significance emphasised in the body of reporting is that concerned with the large numbers who die from cardiovascular disease in the UK. These debates are more neutrally framed than some of the aspects in the previous subtheme and are arguably aimed at providing insight into the rationale for widening usage. The Sunday Times, for example, emphasises the status of CVD relative to mortality rates:

> Cardiovascular disease is still the country's biggest killer, claiming about 180,000 lives a year (Summers, The Sunday Times, 18th May 2014).

As does the Guardian:

Cardiovascular disease is still the leading cause of deaths in the UK, responsible for one in every three, even though the numbers have halved since the 1970s and 1980s. In 2010, around 80,000 deaths were caused by cardiovascular disease and 49,000 by strokes (Boseley, The Guardian, 12th February 2014).

Reporting also touches on the scale of the numbers of lives widening the use of statins potentially might save – emphasising size in terms of sheer numbers and slightly more opaquely the significance of life saving potential. This emphasises (relatively uniquely in the reporting as a whole) a more positive side to the widening use of the drugs, drawing more on interpretations of impact evident in commentary by (or at least sources sympathetic to) NICE. The Express, states for example:

If everyone eligible took the drugs, between 20,000 and 50,000 deaths could be prevented every year, it is claimed (Willey, The Express, 24th September 2014).

The Mirror reports similar statistics:

The National Institute for Health and Care Excellence has calculated the change will save 50,000 lives a year (Gregory, The Mirror, 18th July 2014).

5.3.3 Financial Cost

This positivity is also partially reflected in discussions of cost. Journalists discuss the size and significance of the costs associated with widening usage. The presentation of cost is often juxtaposed (even in the same reporting) in terms of the overall costs to the NHS (which initially appear large) and the everyday costs on an individual patient level. At the crux of the debate here is whether it is cost effective to expand statins usage compared with treatments after actual cardiovascular events. Generally, the dominant notion is that due to the patent for the drugs having expired they are now cost-effective, despite the large initial outlay necessary from the NHS budget. Despite notions of cheapness and limited cost, this is indicative of the broader theme of size and significance because the focus here (both explicitly and implicitly) is often on the scale of the costs to the NHS *without* widening the usage of statins.

The drugs are now off-patent and therefore cheap. Nice says if 80% of the 4.5 million newly eligible take them, the cost to the NHS will be £52m, which is small in the context of the savings from heart attack and stroke treatment (Boseley, The Guardian, 18th July 2014).

The message surrounding cost, however, is not uniformly reported. The Mirror, for example, in two different reports present quite different messages:

Prof. Simon Capewell, an expert in clinical epidemiology at Liverpool University, said: "The recent statin recommendations are effectively condemning all middle-aged adults to lifelong medications of questionable value. "They steal huge funds from a cash-strapped NHS" (McKeown, The Mirror, 16th June 2014)

The cost argument doesn't really stand up either. By normal standards, statins are cheap and effective. They already save the NHS untold millions by averting heart attacks and strokes and NICE calculates at least 20,000 deaths could be averted (Routledge, The Mirror, 25th July 2014).

The Times uniquely present the impacts on primary care resources, although ultimately emphasising the cost-effectiveness of expanding usage of the drugs relative to treating cardiovascular events:

NICE conceded that "there is insufficient capacity within existing primary care resources to meet the increase in demand". Its models suggested that more statins would still be good value even if 25 per cent more GP appointments were needed at a cost of hundreds of millions of pounds (Smyth, The Times, 19th July 2014).

5.4 Side Effects: Dangers to Patients?

The next theme emerging from the data is that of 'side effects: dangers to patients?'. Side effects were a prominent concern in the newspaper reporting on the decision to widen the usage of statins, significantly reflecting professional uncertainty and debate about the extent of occurrence and the potential for harm reflecting the widening usage of the drugs (particularly where benefit might be questioned). There was focus in the newspaper reporting on the types of side effects experienced and the numbers of individuals who might be impacted by side effects; side effect risk versus health benefi§t of the drug for patients; and patient stories of side effects. The unique focus of this theme is on aspects

of reporting where the orientation is on the consequences of side effects rather than where the emphasis is on problems, for example, in the underpinning evidence base (this focus and distinction is further elaborated in discussions of the third theme below).

It has been highlighted in the literature that media coverage of drugs tends to grow more critical over time, peaking at a certain point in time, before becoming more stable with considerations of risk and benefit (Gabe and Bury, 1996; Williams et al., 2011a). The emergence of issues and problems, particularly the experience of side effects, tends to be important in this as criticism builds, even to the extent where there seems no conceivable benefit portrayed in reporting (Entwistle and Sheldon, 1999). How can these arguments be located relative to the stage and state of media reporting on statins (at least in this specific case)? Statins are drugs that have been in existence for quite some time now, and as such the opportunity has occurred for the emergence of concerns about and experience of side effects but has the stage of reporting arrived at a stable consideration of risk and benefit? The subthemes discussed below indicate that there is certainly consideration of both benefit and risk in reporting when considered as a whole, but that this tended to oscillate over time as the dynamics of this particular case reshaped and that the coverage was still more negative than positive.

5.4.1 Types of Side Effect and Extent of Occurrence

In the most straightforward sense, elements of print newspaper reporting indicative of this theme refer to the types of side effects associated with statins and ruminate on the numbers of patients who might experience side effects (both amongst those already taking them and in the new cohort). Print news coverage identifies several types of potential side effect. For example:

> In rare cases, statins can affect the liver. In about one in 10,000 cases they can cause rhabdomyolysis, a serious kidney disease. There can also be muscle weakness. But many people complain of effects such as nausea, muscle pain, fatigue, erectile dysfunction and stomach problems (Boseley, The Guardian, 22nd March 2014b).

There is also engagement with estimates of the numbers of people who have experienced or might experience a side effect from a statin. However, in the quotes below, though clearly reflecting the time of reporting and associated stage of the debate about this case,

even in the same print publication (The Telegraph), there is no agreement on the extent of occurrence of side effects associated with statins:

> Studies have suggested that up to one in five patients taking statins suffers some kind of ill-effect, including muscle aches, memory disturbance, cataracts and diabetes (Donnelly, The Telegraph, 12th February 2014).

> Most commonly, according to NHS Choices, these include muscle and joint pain, but also nose bleeds, a sore throat, runny or blocked nose, headache, nausea, constipation, diarrhoea, and flatulence; as many as one in 10 are said to be susceptible to a side-effect. Anecdotally, the most common moan from statins users appears to be "brain fog" – fuzzy thinking and memory loss (Lambert, The Telegraph, 16th May 2014).

5.4.2 Side Effect Risk Versus Drug Benefits

Newspaper reporting also makes reference to the level of risk associated with side effects relative to the benefits of taking the drugs. Reporting here reflects debate and contest amongst professional and other interest groups about the likelihood of benefit to patients relative to risk of side effect harm. Whilst this also obviously reflects concerns with level of efficacy, the framing of this concern is generally presented relative to side effect risk, with a comparative focus, either explicitly or implicitly, on numbers needed to treat relative to numbers needed to harm. The print newspaper reporting shifts (at various times and with varying degrees of balance) between reporting statins to be lacking necessary efficacy relative to side effects and declaring statins safe *and* beneficial. There is a rough divide identifiable between early reporting (pre April 2014) and later reporting, but this is imperfect as a means to capture the direction of reporting which is oscillating throughout the sample. Whilst reporting on the debate and uncertainty, and particularly professional disunity and conflict, acts to create a sense of doubt about statins benefit relative to risk, it cannot be said that the news print medium holds a fixed, or seemingly coherent position here. These notions are not dissimilar to that identified by Barry and Busch (2010) who in the context of news reporting on antidepressant usage in children also noted journalistic engagement with drug risk versus benefit, and though engaging with both sides, reporting offered no overall impression of risk or benefit outweighing the other.

Indicative of reporting that is problematising, The Times explicitly refers to the relative risk-benefit levels. First, in an expert opinion piece from a doctor (Dr Porter),

which also includes advice to patients about the necessity and desirability of the threshold change:

Using the current 20 per cent risk threshold it is estimated that about 35 people will need to take a statin for five years to prevent one of them developing cardiovascular disease. Over that same period 1 in 40 taking the drugs will develop a statin-induced cataract, about 1 in 100 will have liver problems, and 1 in 400 will develop kidney failure. Reducing the threshold to just 10 per cent will mean more people will have to be treated to save a life, but the odds of a serious side effect like kidney failure remain exactly the same, shifting the risk-benefit ratio towards risk… (Porter, The Times, 25th March 2014).

Other reporting in the Daily Mail, is similarly problematising:

Millions of healthy Britons are about to be given statins needlessly and exposed to debilitating side effects which include muscle pain and diabetes, leading doctors warn (Borland, The Daily Mail, 11th June 2014).

As noted, however, reporting on notions of side effects and relative benefit partially reflects emerging opinion and debate amongst professionals and researchers. As such, with varying degrees of balance, reporting later in the overall context of the case partially undermines some of the claims in earlier reporting and moves to partially assert the safety of statins, although with no clear firm resolution to the matter and without ever fully removing side effect uncertainty. The Telegraph, for example, engage with the positive side of the expanding usage debate, and as such, notions of high relative benefit and low risk to patients:

Many cardiologists have backed the plans, with a panel of six leading doctors claiming "the jury is no longer out" about the benefits of the drugs in preventing strokes and heart attacks, compared with risks which they said had been falsely overstated (Donnelly, The Telegraph, 10th July 2014).

The Daily Mail meanwhile base an article around comments made by a prominent cardiothoracic surgeon and statins advocate, who is shown to be very positive about the benefits of statins relative to risks even beyond the extent of deployment desired by the NICE guideline.

Sir Magdi said he believed statins should be available from chemists without prescription and that everyone over 40 should take them. He said that side-effects pale into insignificance when compared with the benefits and not to make use of what we have is lunacy (Macrae, The Daily Mail, 19th May 2014).

However, as we can see from the quote below, also from the Daily Mail, reporting is oscillating in nature, partially reflecting professional debates and contest in the wider context. This quote reflects coverage of the publication of a journal paper (towards the end of the period under study in this chapter) by statins critics involved in some of the initial challenges to NICE's decision to lower the primary prevention threshold. The oscillating tendencies of newspaper portrayals reflecting the case itself are particularly visible in the use of the phrase 'reignites the debate'.

Healthy patients given statins are more likely to suffer side-effects than they are to gain any benefits, doctors warn… The warning, made last night in an editorial in medical journal Prescriber, reignites the debate over statins, the most widely prescribed drugs in the UK and taken by up to ten million Britons. Fewer than one in 200 of the healthy patients who take them benefit, the authors said (Spencer, The Daily Mail, 7th September 2015).

It can be seen from the quotes presented in this sub-theme that newspaper reporting on side effects has no clear or fixed position. Reporting shifts its emphasis and holds varying degrees of balance throughout the period under study depending on emerging medical opinion and debate. The newspapers approach the controversy with their own aims, particularly concerning newsworthiness – which emerges perhaps most clearly when professional knowledge can be problematised or where controversy is present (Briggs and Hallin, 2016; Seale, 2002). Indeed, whilst the newspapers promote no absolutely clear position on the actualities of side effects and relative benefits of the drug (though the negative outweighs the positive), what is clear, however, is an emphasis in reporting on professional disunity – which is most clearly encapsulated by a Daily Mail headline using a military/battle metaphor similar to that observed in other analysis (Hilton et al., 2010; Seale, 2002), entitled "Statins Wars" (22nd July 2014). Other work by Macintyre et al. (1998) has highlighted 'division amongst experts' as one of five key themes emerging from their analysis of media representations of food scares. Rather than a single theme in the analysis contained within this chapter, however, professional debate and disunity intercedes with and is in evidence in varying ways throughout (as will become clear) the three of four latter themes presented in this chapter. Sometimes this is explicit in the form of news reports presenting conflicting positions and direct arguments between those

involved in the debate. It is also more implicitly evident in terms of the oscillating focus of reporting when looking at newspaper publications over the period under study.

5.4.3 Patient Stories of Side Effects

A final element within the broader side effects theme is that of patient and professional stories and anecdotes about statins side effect. For example:

> June Browning, 66, a retired paediatrician from Angus, has been taking statins for four years, after her GP prescribed them when she developed mild angina. She said: "When an exercise test proved I had some mild heart disease, my doctor prescribed statins straight away. I certainly wouldn't do without them. I've had none of the joint pains or muscle aches that some people have described." Others, however, have complained of significant side effects. Sonya Young, 52, from Buckinghamshire, was put on statins by her GP after finding that her cholesterol was too high. She says she suffered severe side effects, including pain in her arm and neck, memory loss, blurred vision, nausea, dizziness and tinnitus. She said the symptoms stopped when she stopped taking the drugs. "The joint pain decreased and my brain fog lifted. I would say since I stopped taking them I've got my life back" (Summers, The Times, 18th May 2014).

A journalist from the Mirror interestingly also shares his own experiences with readers, attempting to positively shape perception, drawing powerfully on his wish that the drugs could have been used to save his father:

> I wish statins had been available many years ago. My father died of a heart attack aged 54 and his father similarly at 56. High blood pressure runs in the family and if they'd had statins (and hadn't smoked) they would probably have lived much longer. I've taken them for more than a decade with no noticeable side effects and I encourage older people to ask for them (Routledge, The Mirror, 25th July 2014).

It can be seen from these quotes that the reporting engages with the actual experiences of patients and journalists-as-patients (including types of side effect), both positive and negative, even in the same piece. Particularly in the first quote, this serves again to enforce uncertainty about statins and side effects, rather than being overtly celebratory or condemnatory, although it also powerfully serves to personify some of the side effects experienced by patients. This latter remark resonates with Gabe et al. (1991) who suggest that issues surrounding pharmaceutical usage as a public problem are made graspable by journalists (or so is the assumption of journalists) through vivid personal

descriptions. The second quote above is more overtly celebratory, but when placed in the context of the reporting overall is a relatively rare occurrence.

5.5 Violations and Uncertainty in the Evidence Base: Conflicts of Interest

A third theme emerging from the analysis of the corpus is concerned with problems within the statins evidence base. At the heart of matters here is the role of the pharmaceutical industry, associated financial connections/conflicts of interest, and, as such, the potential for violations in and uncertainty surrounding the evidence base (upon which the decision to widen and expand the usage of statins was based). Reporting where this theme appears refers primarily to notions of financial connections between the NICE GDG and the pharmaceutical industry, and the potential for more indirect forms of financial self-interest by the pharmaceutical industry in the actual development and creation of the evidence base.

It is important to note that debates and uncertainty about the reliability and validity of the evidence base refer partially to concerns about side effects. However, in distinction to the quotes presented as indicative of the theme of side effects (where the emphasis is on types of side effect, relative benefit, and patient and professional stories of side effects), the emphasis in quotes indicative of this theme of violations and uncertainty is on problems associated with the role of the pharmaceutical industry in the construction and evaluation of the evidence base (including concern with efficacy as well as side effects). Conflicts of interest are at the heart of this theme, particularly pertaining to the connections and influence of the pharmaceutical industry. It is here that the thematic distinction between the two exist.

5.5.1 Financial Connections Between NICE and Industry

The quotes below are indicative of the general concern with potential financial connections between NICE as a supposedly independent evaluative and regulatory body and the pharmaceutical industry. This focus emerges particularly following the first of two open letters written by high-profile statins critics from within the medical profession itself. However, the Sunday Express seems initially to have raised the issue – although it only becomes more widely reported following the first letter. Broadly, the implication is

that financial connections between those on the supposedly independent guideline development group for this decision and the industry may have swayed the decision-making to expand the usage of statins. Indeed, below the financial ties between NICE guideline group members and industry are made out to be 'close':

Some critics accused NICE's guideline group of close ties with the pharmaceutical industry (Boseley, The Guardian, 18th July 2014).

Other reporting emphasises the same point:

The National Institute for Health and Care Excellence (NICE) stands accused of allowing itself to be influenced by the drug companies, which will make huge profits from treatment. NICE should only rely on impartial advice and that does not seem to be the case here (Anon, The Sunday Express, 2nd March 2014).

More specifically, journalists also refer to the individuals on NICE's guideline panel against whom the claims of financial connections have been made, the types of activity individuals received payment for, and the names of pharmaceutical companies with links to members of the committee.

Concerns have been raised that eight of the 12-strong panel recommending widespread use of statins have financial links to the pharmaceutical companies that manufacture them.
They include Dr Anthony Wierzbicki, chairman of the NICE panel and a heart disease specialist at Guys and St Thomas' Hospital in London, who has ties to six firms, including Pfizer, Sanofi and Aventis, which sponsored his research into cholesterol-lowering drugs (Anon, The Daily Mail, 11th June 2014).

A Sunday Express investigation has discovered eight out of 12 members of the Nice panel which drew up the guidance have financial ties to companies that make statins... The financial ties are declared in an appendix to the new draft Nice statins guidance and include payments for speeches, lectures or to attend conferences which can reap thousands of pounds per hour. It also includes salaries for involvement in clinical trials of new statin-style drugs, which can amount to tens of thousands of pounds a year, payment for drug company advisory roles, and in one case a sponsorship of a work post (Johnston, The Sunday Express, 9th March 2014).

Interestingly here the Sunday Express in the above quote, acting in an investigative capacity, overtly attempt to influence the debate. This is a particularly interesting finding concerning media within the processes of pharmaceuticalisation and is indicative of a public sector model of biocommunicability. In the Observer, an opinion piece meanwhile

by statins critic Aseem Malhotra suggests that it is not necessarily that the panel did anything overtly wrong, but that the sense of conflicts of interest damages both NICE's ability to fairly regulate and patient perception of the statins evidence base. Indeed, the headline of the piece is:

Is the failure of health regulation damaging our well-being?

Before Malhotra summarises the concern well:

[There are]…major concerns over the impartiality of the guideline development group on statins, with eight of the 12 members declaring financial ties to companies manufacturing statins and related drugs. There is no suggestion that the panel acted in any improper way. However, when confidence in an organisation such as NICE is imperative, it is essential there should be no perceptions of conflicts of interest. The systems for selection of panellists, the scrutiny of evidence and the methodology and openness of the consultation need to be beyond reproach (Malhotra, The Observer, 1st February 2015).

There is a focus here on potential loss of public confidence in the impartiality of NICE and its ability to evaluate evidence fairly and with patients and the NHS in mind. Importantly though, through the act of reporting this potential issue this at the same also serves to help foster this concern and uncertainty. This quote is particularly interesting in this sense because it is from a piece published relatively late in the overall context of the case. The continuing focus in the news coverage on the matter as something worth engaging with, and importantly, not resolved, operates as such to emphasise the potential for a violation in the evidence base – thus problematising (and potentially constraining) pharmaceuticalisation.

Following a second open letter by largely the same group of statins critics, reporting also touches on the involvement of MPs in the case. This works to emphasise the seriousness of the allegations against NICE – that, as above, it has not acted impartially and fulfilled its duty as an evaluative body designed to protect the financial interests of the NHS or the health interests of patients.

MPs will consider claims that the NHS body for rationing drugs is "not fit for purpose" after guidance that said statins should be given to 12million people.

The Commons health select committee will today examine calls for the National Institute of Health and Care Excellence (Nice) to change its operation, after its panels were accused of holding "conflicts of interests" and being too close to drugs companies (Malnick and Donnelly, The Telegraph, 22nd October 2014).

However, reporting often includes a degree of balance – of both sides of the debate. In the case of this subtheme, however, this does not operate sufficiently to challenge notions of financial links between NICE panellists and industry, but rather seems to reflect journalistic concern with balanced reporting, even where some articles are themselves specifically addressing the problems of conflicts of interest. It may also reflect the newsworthy nature of contest and disagreement between influential medical professionals, medical academics and regulators. Journalists generally draw on defensive quotes from NICE's Professor Mark Baker. For example, in the Sunday Express:

Mark Baker, director of NICE's Centre for Clinical Practice, said: "Our committees are made up of clinicians, patients and others with the skills necessary to help interpret sometimes complex data. All of them have to declare any interests they may have and they are not allowed to receive income from the pharmaceutical industry or any other vested interest for the year before the start of the guideline or at any time during the development of the guideline. However guideline groups must be professionally credible and we can't exclude people simply because they have at some time in the past participated in commercial trials or advised companies. None of the committee members has put their names to the recommendations to make money for themselves" (Johnston, The Sunday Express, 29th June 2014).

In this way, journalists reported NICE's defence of its practices in this case. The focus is on NICE's conflict of interest procedures being followed and a defence of the integrity and quality of the panel. There is a rejection of any significant or direct financial connections, and a claim that prior connections do not shape decision-making and are justifiable in the search for a panel sufficiently qualified and 'credible' to evaluate the data.

However, pieces published in the Times and the Telegraph, unique in the corpus, focus on the case of the member of the guideline group who had not been prevented from participating in the evaluative process despite, as it was later revealed, having financial interests.

NICE said that one member of the statins guidance panel was separately asked to resign over a conflict of interest. David Wald, a consultant cardiologist, was a founder of a company that sells a pill combining a statin with drugs to reduce blood pressure. Dr Wald denied NICE's claim that he had not disclosed his

interest before joining the panel and said he was unfairly excluded (Malnick and Donnelly, The Telegraph, 22nd October 2014).

The reporting (stemming from a time slightly after the main events of the case) of this individual's conflict of interests acts further to problematise the reported claims made by those from or sensitive to the position of NICE that conflict of interest procedures stopped individuals from entering positions of influence in the first place. Again, the newsworthiness nature of controversy and the fallibility of medical knowledge is the primary concern for journalists here.

5.5.2 Manipulation and Misrepresentation of Data

Reporting indicative of the overall theme of violations and uncertainty in the evidence base also includes discussions of potential industry influence on the creation of the evidence base underpinning the new threshold and subsequent secondary analysis of the data by industry aligned groups (primarily the CTT). However, the newspapers also report on counter-arguments from the CTT and NICE about the strength of the evidence base, and counter-criticisms about the vested interests and misrepresentation of data by statins critics. Again, reporting reflects professional divide and debate, although here about the validity and reliability of the supporting evidence base rather than the specific influences and interests of guideline group members. And as throughout this chapter, reporting has varying degrees of balance reflecting the emerging and developing professional opinion. On the one side of things, news reporting engages with the issue of hidden data and the influence of the pharmaceutical industry on the development and secondary assessment of the evidence base. The Express reports the first of two letters written by high profile medical professional statins critics:

Today, in an open letter to the Health Secretary, nine leading medics say it is a step too far. They want the National Institute for Health and Care Excellence, which issues guidance on what drugs doctors should prescribe, to refrain from final recommendations until "hidden" data on the adverse effects is released (Sheldrick, The Express, 11th June 2014).

The journalist here engages with one of the elements in particular in this letter, disseminating the notion that the database upon which the decision to widen the threshold for statins usage may not include all the available evidence – that the

pharmaceutical industry, who is responsible for funding the research and the creation of the evidence base, may have concealed data about the extent of side effects. The Independent similarly draw on this letter, disseminating the position of the critics that the plan to widen the usage of statins should be halted until independent researchers can examine all relevant data:

The doctors want the new guidance withdrawn until all data from statins trials is made available to "credible researchers" (Cooper, The Independent, 11th June 2014).

Earlier reports drawing on contestations stemming from the two BMJ articles and surrounding debate, as well as other commentary from critics, also suggest that the extent of side effects is concealed in company-funded trials. For example:

Company-funded studies show side effects in less than one per cent of patients. Independent studies show them in at least 20 per cent. Inquiries have suggested adverse effects can be minimised in drug company trials by excluding patients if they fail to tolerate statins during "run-in" periods or if they have certain pre-existing health problems. Opponents of statins also claim some side effects such as muscle pain or confusion are not included in drug company reports (Johnston, The Sunday Express, 2nd March 2014)

The Guardian also suggest manipulation of trial data by the pharmaceutical industry because of financial interests, arguing that only the industry-aligned CTT have seen pertinent patient level data (rather than meta-analyses), not NICE. It is also suggested that even the CTT have not seen all the trial data:

Collins and his team at Oxford University's clinical trials service unit are the only investigators who have seen the full patient-level data for some - but not all - of the statins trials. They formed the Cholesterol Treatment Trialists Collaboration to monitor and analyse statins data over the years. His critics point out that drug companies have helped fund his work (Boseley, The Guardian, 13th June 2014)

A similar notion, following the announcement that the CTT will re-examine statins data, is drawn upon in the Sunday Express:

"Manufacturers should release all their trial data on statins for scrutiny." British Medical Journal chief Fiona Godlee added: "This is a concern. We assumed all the possible side effects had been assessed. This is not the case." Oxford University Professor Rory Collins, whose research concluded the drug was safe, will head the new research team (Johnston, The Sunday Express, 15th February 2015).

The focus, however, is not solely on the concealment of data pertaining to side effects, there are also concerns about data on more general issues of efficacy and patient benefit. For example, from the Telegraph:

…recent academic papers have questioned the widespread use of statins, claiming that they cause harmful side effects and do not cut death rates (Malnick, The Telegraph, June 11th 2014).

A similar sense surrounding is also invoked in this Guardian quote, this time focusing on the issue of medicalising the population unnecessarily:

Dr Fiona Godlee, editor of the BMJ, said major issues that deserved public debate had been raised in the papers - particularly the potential medicalisation of a large proportion of the population and the lack of access to data held by drug companies (Boseley, The Guardian, 22nd March 2014a).

However, news reporting also engages with those defending the integrity of the evidence base and, importantly within the overall theme, counter-criticisms of the critics themselves as misrepresenting and manipulating data. Naturally this includes the use of NICE as a source and the rejection of the claims from statins statistics surrounding safety and efficacy:

In response to the criticisms, NICE said there was "no credible argument against [statins'] safety and clinical effectiveness" for patients with a 10 per cent risk (Cooper, The Independent, 11th June 2014).

However, more interestingly, reporting draws on the views of Professor Rory Collins (either implicitly or explicitly) who in is his role as CTT director attempted to defend the widening threshold and criticise supposed misrepresentations of benefits and 'real world' side effect data at existing thresholds of use (in which he successfully lobbied to have statements in the BMJ about side effects retracted). The crux of the issue is examined here in the Daily Mail:

A leading medical journal overstated the dangers of taking statins by up to 20 times, it was claimed last night. The British Medical Journal has now withdrawn statements published last year that said the cholesterol-lowering drugs cause side effects in one in five patients, but has not retracted the articles. A leading statins researcher [Professor Rory Collins], who says the figure is one in 100, called the claims a huge error' that will cause unnecessary deaths'. It is feared the BMJ articles could discourage patients from

taking the life-saving medicines, which are prescribed to millions in the UK (Hope, The Daily Mail, 16th May 2014).

The Telegraph meanwhile, declares statins 'safe' as a result of the acknowledgment and retraction of the publication of erroneous statistics in the BMJ:

Statins are now deemed safe following an acceptance last week by the British Medical Journal that it had published flawed research overestimating the side-effects of the drugs taken by more than seven million people in the UK to reduce cholesterol. The research had prompted headlines last year because it claimed that 18-20 per cent of patients suffered debilitating side-effects, including muscle cramps and lethargy. This claim has now been withdrawn by the authors (Pemberton, The Telegraph, 19th May 2014).

The sense fostered in these quotes is one that statins critics have themselves engaged in misrepresentation and have promoted erroneous statistics lacking in reliability or validity. The focus here is also on the damage that the promotion of such claims might do to patient health, and potentially cause deaths that would have been preventable – not just at the new threshold but also beyond. Indeed, a similar sense is invoked in the following quote from the Telegraph (and several other outlets), but this time the journalist powerfully and evocatively draws on a quote comparing the misrepresentation of statins side effects statistics to the MMR vaccine controversy (another case where an influential journal paper suggested, as it turned out, erroneously that the vaccine was linked to autism).

Sir Rory Collins, professor of medicine and epidemiology at Oxford University, said lives could be lost as a result of health professionals misleading people over the safety of the cholesterol-reducing drugs in an echo of the MMR vaccine controversy. The statins expert said he was particularly concerned over the way the subject has been covered in the British Medical Journal (BMJ), which published papers by two critics claiming statins caused harmful side effects and did not reduce mortality. "It is a serious disservice to British and international medicine," he said. He claimed the articles were probably killing even more people than were harmed as a result of the divisive paper on the MMR vaccine by Andrew Wakefield. "I would think the papers on statins are far worse in terms of the harm they have done," he said (Edgar, The Telegraph, 22nd March 2014).

Overall, then, this theme is indicative of reporting of concern, uncertainty and debate about the use of and evaluation of evidence as presented by the print news medium. In the first subtheme the message is more overtly negative in terms of portrayal and without

significant engagement with counter argument (though NICE representatives are quoted). However, as with the previous theme of side effects, professional debate and contest underpins much of the newspaper reporting in the second subtheme concerned with the wider evidence base. This is reflected well in this further quote from The Times:

> And the balloon has gone up. Not just gone up, but exploded. Something I have heard described as "statin wars" has broken out in the medical profession, leaving patients and the public utterly bemused (Aaronovitch, The Times. June 19th 2014)

Interestingly, as explored above, later in the case, a 'critique of the critics' emerges, with powerful suggestions that the statins critics themselves have propagated, promoted and repeated problematic statistics. At a certain point in the case those defensive of NICE's decision-making actively seek to challenge negative coverage and attempt to use media in the promotion of a certain angle which restores a degree of credibility in popular opinion about statins, the widening usage threshold, and the underpinning evidence base. Collins (and others) begin to appear, purposely it would seem, in newspaper reporting in response to criticism and critical reporting of the decision to widen the primary prevention threshold in the initial stages after the decision was announced – and it appears Collins in particular seeks out media coverage to redress the balance of public opinion. The comparison to MMR, for example, seems a deliberate ploy to associate with and discredit statins critics in the same way as Andrew Wakefield (the author of the controversial MMR paper). It can be seen in other quotes more that there are implicit attempts to scientifically discredit the critics by referring to 'prejudice belief, and anecdote' as underpinning their criticisms:

> Giving statins to millions of healthy people is similar to vaccinating them, and critics of widespread use rely on "prejudice, belief and anecdote", heart experts claimed (Anon, The Times, 2nd July 2014).

Nevertheless, as with the previous theme, there is no overall clear message – and indeed reporting oscillates over time. However, even where the attention turns to a 'critique of the critics' the dominant earlier idea of evidence base contamination by a powerful pharmaceutical industry with significant influence and vested interests never completely disappears. This is particularly because this type of quote is framed as a response to those issues and the debate ongoing. Overall though, the news medium is certainly no mere

puppets here of any group and have an oscillating message, with journalistic concern with newsworthiness arguably underpinning this oscillation (particularly the emphasis on medical controversy and 'war' within the profession). However, there is a clear acknowledgement by those external to the media involved in the case of the power of the news medium in shaping and influencing popular opinion about medical developments and uptake of drugs.

5.6. Relative Therapeutic Positioning of Lifestyle Change and Statins

The final theme emerging from the corpus of newspaper articles is that pertaining to notions of lifestyle change as a preventative measure and the positioning and perceived desirability relative to statins. The reporting coalesces around a debate about the emphasis given to lifestyle change at the new lowered risk threshold relative to statins. As with the previous two themes this partially reflects professional and academic debate and contest in the wider landscape and context. Three positions are evident in the reporting, the first two of which encapsulate the bulk of the data: that lifestyle changes should be encouraged instead of statins for individuals qualifying at the new threshold; statins and lifestyle change should be utilised as preventative strategies in a combined therapeutic landscape by individuals qualifying at the new threshold; and more minimally in the corpus, that statins are beneficial in primary prevention independent from lifestyle at the new threshold.

5.6.1 Lifestyle Change Instead of Statins: Too Many Drugs

This first position generally reflects reporting of the perceptions of statins critics' concern with the development and is more greatly identifiable in the earlier stages of the case. Indicative of this position is the following from a debate piece published in the Daily Mail, between two doctors who offer contrasting opinions (Dr Maholtra here criticises the development).

> The next big decrease in deaths from heart attacks won't be brought about by doling out statins but by doing battle with the biggest and still growing health problem that we, in common with other Western nations, face: obesity. Being overweight and having a poor diet causes more serious health problems than alcohol and smoking put together, with obesity associated with such serious conditions as type 2 diabetes,

high blood pressure, cancer and cardiovascular disease. My biggest worry about statins is that people will see them as a magic pill that allows them to tuck into three pizzas a night and umpteen hamburgers with impunity. But they aren't. People who want to take care of their health, need to make changes themselves. Make… lifestyle changes and whatever NICE says you won't need those statins at all (Malhotra and Baigent, The Daily Mail, 13th February 2014).

The focus in this quote is the idea that statins give patients an 'illusion' of protection, meaning thus that they may neglect lifestyle elements (particularly in this quote in terms of dietary changes). A similar sense is invoked by the Times, who draw on the opinion of a Dr Porter:

My… concern with lowering the threshold is that too many people regard statins as a substitute for healthy diet and lifestyle modification, rather than as a supplement to such changes. I would rather my patients lost weight, exercised more, ate healthily, stopped smoking and drank in moderation than took a statin (Porter, The Times, 25th March 2014).

Drawing on a journal paper critical of the lowered statins threshold, the focus in the Telegraph is similar, but with a slightly more overt emphasis on the notion that CVD is the consequence primarily of lifestyle choices surrounding diet, exercise and smoking and thus is best prevented by making lifestyle changes.

…Dr Malhotra and Prof. Capewell suggest that patients at low risk of disease would be better off given advice to improve their lifestyles, given that 80 per cent of heart disease is linked to diet, smoking or lack of exercise (Anon, The Telegraph, 20th Jan 2015).

The same notion is also put forward in these quotes from two pieces in the Guardian, creating a sense that the guidelines are too drug-centric rather than addressing the root of the problem, unhealthy lifestyles:

They are also concerned that GPs will hand out pills instead of tackling the root causes of heart attacks and strokes by encouraging people to stop smoking, reduce their drinking, eat more healthy food and take more exercise (Boseley, The Guardian, 12th Feb 2014).

This second quote from The Guardian from a piece published at a later time, though acknowledging NICE's emerging defence of the changing threshold in terms of it being a balanced therapeutic landscape (see second subtheme below), also emphasises concern

from professionals in primary care that the emphasis is too much on drugs at the expense of lifestyle.

People who turn up in GP surgeries with raised cholesterol are often unfit rather than unwell. They have lifestyle issues, including inactivity and being overweight. NICE's guidance says doctors should support patients in changing their lifestyle first and offer statins only if they and the patient think it appropriate, but some GPs fear there will be pressure to put more people on pills (Boseley, The Guardian, June 13th 2014).

Reporting indicative of this element of the theme, overall, emphasises a something resembling the moral perspective indicative of lifestylism (Hansen and Easthope, 2007) or healthism (Crawford, 1980). As such, the emphasis is on individual responsibility for making healthy lifestyle choices, and as such, not relying on drugs to prevent health problems.

5.6.2 Combined Therapeutic Landscape

The combined landscape position reflects newspaper engagement with and quotation of those defending the guideline change and NICE themselves. Drawing on figures showing falling CVD death rates and the opinions of a Professor Weissberg, this quote from the Times is indicative of this position:

Data gathered by the charity showed that deaths from cardiovascular disease among people under 75 had dropped from about 260 people per 100,000 in 1970 to just under 60 per 100,000 in 2009. "That has not happened by accident," Professor Weissberg said. "It is because people have stopped smoking, take more exercise and take better drugs." He added: "If you really want to tackle heart disease, if you want to eradicate it, it has to be a combination of medication and lifestyle" (Elks, The Times, 27th December 2013).

Similarly, in the other half of the debate piece in the Daily Mail (discussed above), Dr. Baigent discusses the preventative benefits of statins and lifestyle changes in a combined therapeutic alliance:

Others have suggested that there are better ways of cutting cholesterol advising patients to eat healthily and exercise more. I am all for such lifestyle changes, but it doesn't have to be one thing or the other. I say that you can lose weight and take statins and get even more benefit by doing both (Malhotra and Baigent, The Daily Mail, 13th February 2014).

The print news medium also significantly engages with the defence by NICE of their threshold change. For example:

NICE says the draft guideline does not propose that GPs automatically prescribe pills. Baker says doctors and patients should explore the options for stopping smoking, losing weight, eating more healthily, drinking less alcohol and becoming more active" Baker said (Boseley, The Guardian, June 11th 2014).

Spokespeople for NICE, as well as others supporting the widening use of statins, are quoted as emphasising the importance of seeing the change as a unified landscape. This is evident in this quote below from the Sunday Express:

A spokesman for NICE said: "Drug therapy plays a key role in the management of people with high cholesterol levels and this is properly reflected in the draft guideline which provides clear advice on the most cost-effective drugs, based on the best available research evidence. However, and just as importantly, the guideline also recommends that standard models of care should include advice and support in lifestyle changes for both primary and secondary prevention of heart disease" (Johnston, The Sunday Express, 2nd March 2014).

5.6.3 Independent Statins Benefit

Finally, there is some minor engagement in the news reporting with the idea that statins can be beneficial independent from lifestyle change. Compared with the occurrence of the other two positions presented within this theme, this third position is rarely promoted in and of itself – even if it is assumed to exist in the wider context of the case by those promoting an anti-statins approach to managing CVD risk. However, journalists do draw on quotes emphasising the usefulness of statins for people in certain populations. For example:

Maureen Talbot, senior cardiac nurse at the British Heart Foundation, said: "Two thirds of the adult population in Britain have elevated cholesterol. “Statins have been a great tool for doctors to help people who can't lower their cholesterol level and therefore their risk of a heart attack or stroke, with positive lifestyle changes" (Donnelly, The Telegraph, 26th December 2013).

This quote here seems to emphasise that there are individuals who cannot make positive lifestyle changes or who have tried and not succeeded significantly enough, and for these people, statins are independently beneficial/positive. Whilst these types of individual are not detailed, one might assume it refers to the very elderly or physically impaired that

may struggle to exercise, for example. Potentially there may also be a genetic angle here too, where genetically high cholesterol levels are not necessarily the result of lifestyle factors, and thus are not necessarily vastly impacted by lifestyle changes. The quote creates a sense that some individuals are 'justified' in using statins independently from lifestyle changes (although the genetic aspect is likely to be of limited importance at 10% risk in reality). This mirrors notions of responsibility relating to familial hypercholesterolemia (genetically high cholesterol levels) identified by patients (Weiner, 2009). The second quote below adds a different dimension to this:

> You can lower cholesterol by not smoking, eating healthily and exercising, but, say statins advocates, that's hard for most people. "It is very difficult to change lifestyle and produce substantial reductions in risk factor levels. If you have the non-meat, non-dairy diet of the rural Chinese from some time ago, you have the kind of cholesterol levels you are born with," Collins said. "To get people to change their diet to get the cholesterol levels of a Chinese peasant is pretty tricky, whereas a statin will do that and it is pretty clean and effective" (Boseley, The Guardian, 22nd March 2014b).

The journalist here quotes Sir Professor Rory Collins (CTT director) who suggests that within the context of contemporary societal arrangements (seemingly due to contemporary diets) it is very difficult for lifestyle changes to have the desired impact – and thus a statin is independently desirable. Societal dietary arrangements are thus cast in a problematic light (potentially referring to powerful food industries or the more general culture of consumption), and drug treatment framed as an effective solution within the context of complex broader societal assemblages. There is a subtle sense here that society is oriented problematically in terms of levels of food consumption (rather than in terms of health inequalities/socioeconomic factors) and thus pharmaceuticals are necessary to redress this balance.

From these discussions, overall, the print news medium debate and discuss three identifiable positions that present statins relatively to lifestyle change as preventative measures against CVD. Much of the reporting is focused on the first two positions concerned with lifestyle promotion over statins, or statins and lifestyle within a combined landscape, but a (minor) third position suggests statins can have independent benefits also exists within the corpus. Inherent in the three subthemes are issues surrounding professional debate and uncertainty about whether expanding statins usage is necessarily best for patient health. Reporting framing the first position coalesces around whether or not expanding statins usage sufficiently engages with the root cause

of CVD, whether the focus is too drug-oriented, and sends out the wrong message to patients. However, reporting also discusses whether CVD primary prevention is inherently a unified therapeutic landscape, and that the first position includes confused critics. Indeed, NICE are quoted as defending the changing threshold through claims that this is not just about statins, but that lifestyle is equally, if not more important.

5.7 Discussion

This chapter has discussed newspaper reporting of the widening primary prevention threshold and thus the wider availability of statins (and the surrounding events in the case). In this way it has explored the place of the print news medium within the pharmaceutical regime and, as such, the mediatisation dimension of pharmaceuticalisation outlined by Williams and colleagues. This chapter has explored the question of: *how did the UK print news medium present and portray the potential widening usage of statins?* It has argued that presentations and portrayals in reporting coalesced around four themes: size and significance; side effects: dangers to patients; violations and uncertainty in the evidence base: conflicts of interest; and the relative positioning of statins and lifestyle. Though reporting arguably is more significantly negative and problematising than positive and celebratory across these themes, it is oscillating with no firm or fixed message and the stage of the medical/scientific debate in the case overall influenced the tone of the reporting at various points. Overall, the portrayal of the widening pharmaceuticalisation of CVD in print newspaper reporting can be said to be one of vast expansion but also of significant uncertainty about the safety and necessity of the (potential) widening use of statins.

The key element in the newspaper reporting of this case, overall, and a unifying element across the majority of themes explored, is the portrayal of statins expansion as causing great professional disunity and dispute and the association of the drugs with significant uncertainty and controversy. Research by Macintyre et al. (1998) has highlighted 'division amongst experts' as one of five key themes emerging from their analysis of media representations of food scares. Rather than a single theme in the analysis contained within this chapter, however, professional debate and disunity intercedes with and is evident in varying ways throughout particularly the themes of side effects and violations and uncertainty in the evidence base. Gabe et al. (2012) suggest

that media serve as a forum where professional debate and consternation occur in the public eye, with the news medium simultaneously amplifying and (re)shaping the debate with one eye, for example, on newsworthiness. The newsworthiness of the story is also enhanced when the authority of medical professionals/knowledge can be questioned and problematised (Briggs and Hallin, 2016; Seale 2002), and this seems to at least partially explain the high level of newspaper interest in this case. Controversy is a key aspect of contemporary medical news reporting generally (Hallin et al., 2013) and the presence of it in this case is seized upon and amplified by the newspapers whilst setting up the audience as judges of the merits of the case and positioning of particular actors. As discussed by Gabe and Bury (1996), lay publics have become less trusting as they have become increasingly aware that a definitive medical perspective does not necessarily exist and that experts disagree. The mediatisation of a fractured medical perspective and expertise undermines medical authority and is one source alerting the lay public to the fact that expert knowledge has become chronically contestable (Giddens, 1990). The act of reporting professional dispute contributes in itself to the controversy and to the uncertain conditions within which regulatory and importantly doctor-patient decision-making about statins exists. Whilst audience interpretations cannot be known from the data presented in this chapter, the result of the presence of professional dispute, and the lack of ability to definitively resolve it, serves to imbue statins thematically with uncertainty – and thus the sense of further pharmaceuticalisation fostered is of the uncertainty of benefit, risk and necessity. Whilst audience perspectives are configured in diverse ways drawing on various forms of knowledge and experience, this sense of pharmaceuticalisation fostered in coverage is more compatible with encouraging depharmaceuticalisation (as has been shown to have occurred by Matthew et al., 2016) and constraining further pharmaceuticalisation at this new threshold.

Focusing on each theme in turn, first, a 'size and significance' theme emerged from the data, reflecting several (partially interconnected) subthemes: numbers and types of people, the size of the CVD problem, and financial cost. For some time, medical sociological researchers have identified this kind of notion in reporting on pharmaceuticals – for example, with a theme emerging in the work of Gabe et al. (1991) on media portrayals of tranquiliser dependence entitled "scale of the problem" (Gabe et al., 1991: 335). The most salient aspect in this theme is that the emphasis on the size and significance of the change fosters a sense of vastly expanding and almost unending

pharmaceuticalisation of CVD. The sense fostered overall is one where the size of the change, in terms of the numbers of people this includes, is presented as vast (potentially excessive), but at the same time is one which is open potentially to significant benefits in reducing high rates of CVD, particularly when considering the cost-effectiveness of the off-patent drugs. Relative to the other themes explored in this chapter, however, certainly this theme reflects the least controversy-oriented portrayals by the print news medium when reporting on this case. Williams et al. (2008) in a paper on media portrayals of the wakefulness drug *Modafinil* argue that the newspapers contribute to the pharmaceuticalisation of everyday life by creating a sense of seemingly unending pharmaceutical deployment and use. Whilst the authors provide this argument as a general analytical point, this role is most evident in elements of reporting indicative of and referring to the size and/or significance attached to the potential widening of use of statins. Journalists in this way creates a sense of large scale pharmaceutical deployment in the area of cardiovascular disease.

The second theme that emerged from the analysis was that of side effects: dangers to patients. This had three component parts, including the type and extent of occurrence of side effects, side effects risk versus benefits, and patient stories of side effects. In terms of the theme overall, the presentation of the necessity and desirability of pharmaceuticalisation relative to potential increases in experiences of side effects, as such, is not necessarily problematised here by the newspaper, though at times of course there is a significant element of this, particularly early in the reporting. The print news medium, however, through reporting the risk of side effects and disseminating professional disunity about side effect risk (both in individual articles and over time), serves powerfully to create a sense of doubt and uncertainty, rather than necessarily outright commendation or condemnation, about the impacts of statins side effects and the relative benefit of the drugs to patients. Of course, all drugs have listed side effects, but the media, as an important source of health information for patients (Seale, 2004), potentially have a significant role to play in the association or reinforcement of particular drugs, such as statins, with uncertainties about side effects through the act simply of reporting and debating issues, regardless of the realities of the situation. Indeed, other work by Dew et al. (2017) suggests that reporting of side effects can heighten consciousness and the attribution by patients or professionals of certain problems experienced by patients to the drugs. Reporting of the risk of side effects from a drug by

the news medium, particularly where there is no clear resolution to the matter, may create anxieties that shape the actualities of uptake, resistance, or statins desistance. A high volume of reporting stressing uncertainty in this way in this case, could go some way to explaining the more general statins discontinuation rates suggested by Matthews et al. (2016). The reporting may not necessarily always be negative or condemnatory, but the fact that, for example, side effect risk and statins are *associated* in reporting in such a significant and high profile way serves to imbue the drug with uncertainty that could feature in decisions to stop new initiations as well as encouraging people to discontinue out of apprehension of future experience of side effects or harm. Again, it is important to stress that the configuration of patient perspectives about pharmaceuticals reflects diverse and various knowledge and experiences. However, understanding the thematic intricacies of the reporting contextualises the discontinuation rates following an intense period of reporting noted by Matthews et al. (2016) and can serve as a basis for further research exploring if and how exactly news coverage features in the configuration of patient perspectives and subsequent decision-making and action.

The third theme emerging from the analysis of the data was that of violations and uncertainty in the evidence base, which had two aspects: financial connections between NICE and industry and manipulation and misrepresentation of the evidence base. The corrupting influence of economic gain is clearly a highly newsworthy aspect, with the newspapers here unveiling the issue and then amplifying it over time in alliance with certain critical and influential medical professionals. Whilst some of this reporting was relatively inaccurate in terms of the actualities of the conflicts of interest present in NICE's evaluative activity, the sense created here in a large part of the reporting was that of a corrupted decision to widen the usage of statins. As part of this other actors within the pharmaceutical regime, particularly NICE, but also the pharmaceutical industry and elite medical professionals were framed negatively and as unnecessarily furthering pharmaceuticalisation. Though these aspects remain pertinent in the reporting and never completely disappear, interestingly at a certain point in the case, representatives of NICE and the CTT seem to seek out coverage to quash conflicts of interest stories and present positive portrayals of statins (in terms of both efficacy and safety). A comparison made by NICE representatives and allies to the MMR vaccine seems a deliberate ploy to associate and discredit statins critics in the same way as the author of the controversial MMR paper has been. The news medium are certainly no mere puppets in this context

(Williams et al., 2011a), but this is a clear acknowledgement of power held by actors like newspapers in shaping and influencing discourse and popular opinion about medical developments and associated institutions (Brown and Calnan, 2010; 2013). This also points towards a role for the news media as a countervailing power (as Gabe et al., 2012 suggest), interestingly in this case often challenging but also at other times supporting pharmaceuticalisation and in (partial) allegiance with different actors as the case oscillates.

The final theme reflected concerns in the newspaper reporting with the relative and appropriate therapeutic positioning of statins and lifestyle change. The overall framing is one where there is no substitute for making healthy lifestyle choices – reflecting notions of what has been called elsewhere pharmacological Calvinism (Klerman 1972), a societal attitude that values 'working hard' for a desired goal rather than taking a pharmaceutical shortcut, and certainly individualised orientations to health associated with healthism (Crawford, 1980) or lifestylism (Hansen and Easthope 2007). Newspapers or other forms of media have not created this discourse, and indeed their engagement with the relative positioning of statins and lifestyle involves, to a large extent, reporting professional opinion (although some journalists offer their own opinions and interpretations largely pro-lifestyle change). However, they certainly contribute to (re)framing and relating this type of discourse to the debate about widening primary prevention CVD thresholds drawing on pre-existing social values of individual responsibility for health. Broadly then, the newspaper coverage takes a lifestyle frame (Clarke, 2005; Rozanova, 2006) where emphasis is on individual responsibility for health, rather than a more objective biomedical frame that portrays illness (or potential illness) as the result of morally neutral bodily breakdown – where conceivably pharmaceutical treatment might be more favourably framed. The two frames are perhaps less clear cut than Clarke (2005) and Rozanova (2006) distinguish (lifestyle practices and risk have been (bio)medicalised), but a lifestyle focus certainly contains a more overtly moral element. This particular aspect of reporting might be said to pose problems for the clarity of the three models of biocommunicability (Briggs and Hallin, 2016), with this aspect of reporting potentially indicative in different ways of all three identified models. It might be viewed as a medical-authority model dissemination where patients are instructed as to what is best for their health. It might, however, also be a patient-consumer model in that it addresses patients as (potentially) active and asserts the need

to take responsibility for one's own health. However, debate also emerges about whether statins are even necessary if problematic lifestyle aspects can be sufficiently modified and, as such, is indicative of a public sector model that casts the audience as judge of the merits of the positions of particular actors. In this way, and, indeed, when taken as one aspect of a controversial case as a whole, this aspect of reporting can more strongly be said to be indicative of the public sector model of biocommunicability. Pollock and Jones (2015) meanwhile, have suggested that an understanding of CVD pharmaceuticalisation necessarily requires engagement with the wider therapeutic landscape in which pharmaceutical treatment takes its place. The importance of this point is clear here in newspaper portrayals, where CVD pharmaceuticalisation is framed as inferior to, or at least as no substitute for lifestyle change. The lifestylism (Hansen and Easthope 2007) apparent in the reporting here arguably contributes to the medicalisation of everyday life through the ever-widening dissemination and promotion of medically oriented understandings of healthy living – interestingly, potentially at the expense of the pharmaceuticalisation of everyday life which is presented as inferior (Coveney et al., 2019: 269).

The final chapter of this thesis engages in a detailed examination of the manoeuvrings and interactions between actors within the pharmaceutical regime of this case. However, the portrayals examined in this chapter indicate that, when considering the overarching research question of this thesis as concerned with extent and driving forces, the print news medium acts as a constraining force of pharmaceuticalisation. The coverage reflects, shapes and in a sense organises uncertainty surrounding the drugs and in much of the reporting creates a sense that the necessity and desirability of the widened threshold is low, with significant risks, and potentially reflects corrupt influences and low-quality evidence. Portrayals of other actors within the pharmaceutical regime also necessarily oscillate as the dynamics of the debate shift and reshape but uncertainty reflected in and exacerbated by the coverage about the presence of the influence and interests of the pharmaceutical industry on NICE's decision never disappears from the coverage. The coverage overall can be said to be in greater disharmony with the interests of other actors within the pharmaceutical regime that are attempting to widen pharmaceuticalisation.

This will be returned to in the final chapter, but overall the degree to which the further pharmaceuticalisation of CVD is occurring is necessarily lower as a result of the

exacerbation of uncertainty evident in the coverage. The 'sense' of the necessity and desirability of pharmaceuticalisation is partially independent from the actualities of impacts on prescription levels or regulation within the pharmaceutical regime. At this sensory or conceptual level, more complete cases of pharmaceuticalisation will be mediatised with less uncertainty present and coverage will cohere more clearly throughout with the positions of other actors within the regime who are fostering or facilitating pharmaceuticalisation than occurs in the coverage of the case under study. Whilst being careful not to be cavalier about particularly the configuration of audience perspectives (particularly as this thesis does not present analysis of audience reception) the nature of news coverage and the 'sense' created is also of course of greater compatibility with constraining the pharmaceuticalisation of and/or facilitating depharmaceuticalisation in patients. However, there are further questions to be asked here that cannot be definitively resolved by the data presented in this chapter about how exactly the thematic intricacies and 'sense' of pharmaceuticalisation established in this chapter might be interpreted by and reflected in the action of other actors within the regime. In particular, further research is necessary to establish how the thematic intricacies of newspaper reporting figure exactly within medical decision-making about statins and the configuration of patient perspectives on the drugs. This and other remaining questions will be returned to in the final chapter of this thesis.

Chapter Six: Disparate and Distributed – The Understandings and Approaches of GPs to CVD Pharmaceuticalisation

6.1 Introduction

This chapter details the thematic analysis of interviews with twenty GPs. The question this chapter addresses is: *How do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk?* At the heart of this chapter, as such, is analysis of the manner and the degree to which GPs are implementing the guidance and whether uniformity or disparateness amongst GPs can be established. As established in Chapter Two, the underpinning justification for analysing the role of GPs reflects the fact that the influence and importance of medical professionals has been problematically decentred in pharmaceuticalisation analysis and largely ignored as an actor within the pharmaceutical regime, arguably to the detriment of its conceptual scope and analytical insight. Within a context where patients still clearly value professional advice and recommendation and where medical consumerism seems to be limited (Will and Weiner, 2015), there is a clear need to assess professional perspectives and the ways in which doctors approach, contribute to, and facilitate the decision-making of patients. Medical professionals most be brought back into focus to more fully understand patient decision-making surrounding drugs, particularly because such decision-making is a shared activity and can be seen as relationally autonomous rather than viewed as divorced from external influences. More generally there is also a wealth of evidence that has been accumulated by medical sociologists about lay understandings and experiences even within the sociology of pharmaceuticals.

The analysis of interviews with GPs is presented in three overarching themes: Use of Guidelines and Other Knowledges; Treatment Orientation; and Evaluations of Relevant Information. As such, the chapter begins with an examination of the manner in which GPs perceive and use guidelines and knowledge generated and disseminated via scientific bureaucratic medicine (SBM) particularly compared to emphasis placed on the importance of their own clinical experience and discretion. The chapter then examines how this relates to and impacts on the implementation of relevant components of CG181. The chapter then discusses differential approaches to treatment orientation, which

though reflective of perspectives on/use of guidelines is analytically distinct in capturing differing understandings and approaches to facilitating the decision-making of patients about statins, particularly in terms of the moral and ethical aspects present in the talk. The final theme presented in the chapter necessarily complicates the previous discussions, highlighting how ethical and personalised patient evaluations feature in the presentation of 'relevant' information to patients – though suggesting overall that disparate approaches amongst GPs can be identified.

6.2 Use of Guidelines and Other Knowledges

In this first theme, the chapter focuses on how GPs perceive and approach the use of NICE guidelines, and the specific form of knowledge it embodies, in their practice. Knowledge generated and disseminated through an SBM model has facilitated the opportunity for treatment at a ≥10% risk threshold in the first place. However, GPs do not receive and utilise knowledge generated and disseminated through SBM in uniform ways (Carlsen, 2010; Carlsen and Norheim, 2005; Checkland et al., 2008; Hansen et al., 2016). As such, it is important to begin with establishing the perspectives and use of NICE clinical practice guidelines, whilst also drawing on if and how GPs have utilised knowledge specific to CG181.

In the data analysed there was a pronounced distinction between GPs positively and negatively viewing NICE guidelines, with an associated connection between those GPs who spoke more positively about NICE guidance and those who saw the widened threshold as a beneficial decision, or at least, a decision that they were largely uncritical of or pragmatic about. Importantly, GPs who were critical of guidelines were also generally critical of the widened primary prevention threshold (although this was a more complex picture because attached to some of the negativity about guidelines were potential medico-legal implications). In the data in this theme, it very clearly emerges that the ways in which GPs engage with the ≥10% risk threshold reflects existing understandings of and engagements with SBM. Understandings of and use of guidelines reflected individual clinical experiences, knowledge, training, and willingness to draw on and trust knowledge indicative of an attempt to govern and standardise their practice.

6.2.1 The Acceptance and Necessity of the Scientific-Bureaucratic Model

The first thematic position that emerged from analysis of portions of the data pertaining to GP perspectives on NICE guidelines was of acceptance of and need to conform practice to the SBM model of medical practice – although of course without using this social scientific conceptualisation of the process. This position reflects the perceptions primarily of GPs who were judged to have spoken positively about the role of NICE guidance (13/20) in contemporary primary care. GPs within this thematic position here can be thought of as accepting of the logic of the scientific-bureaucratic model of evidence-based practice. NICE guidelines, though as part of a broader decision-making process, were seen by GPs here as the "gold standard" (GP3) and the best available and should be followed (where appropriate). For example:

I find them enormously helpful. They are a good resource, I rarely go against them… Of course I would discuss it with the patient … But yeah generally they are the best evidence and guidelines available if they cover an area in the UK (GP12).

Acceptance of the logic of a scientific-bureaucratic model, and as such, NICE guidelines, more specifically was rooted in perceptions of the contemporary circumstances of general practice – of GPs as gatekeepers with a very broad range of health problems to face and a high workload. The perceived necessity of a uniform approach, and the difficulties that would be experienced in achieving this uniformity without NICE, also emerged as of salience. These two elements clearly emerge in the quote below:

I think they are very important actually. We were are working in a very broad sense. We are gatekeepers, we never have a clue what is coming through the door and we have to know a little bit about everything. I think that is actually quite difficult… If we didn't have some guidance in certain areas to follow it would be quite tricky to have a uniform approach to things and I think we need some backup in certain areas to be able to practice in the best way that we can (GP13).

The difficulties of practicing without NICE guidance and evaluative activity was also articulated by GP5:

I am thoroughly in favour of NICE and I am very glad about their existence; and I think it would be very difficult to practice with the huge amount of evidence in modern medicine, the huge wealth of data, if you didn't have NICE there to do it. So yes thoroughly in favour of NICE guidance (GP5).

This GP here emphasises how he values NICE guidance in terms of the management of large quantities of research evidence and the impossibility of the task for an individual GP to make sense of it all and deliver best practice. Meanwhile, the importance of uniformity also emerged for other GPs.

I see it as trying to make sense of a sophisticated modern health service and trying to make sure that nobody is doing anything that sort of are crazy or even dangerous. The evidence these guidelines are based on is the best evidence we have so we should try to follow it (GP6).

Here the focus for this GP was on uniformity in ensuring dissemination of best practice and the associated issue of ensuring patient safety. It was, however, emphasised across those that spoke positively about NICE guidance that it was guidance and not a mandate. This was where clinical judgment and discretion became important in terms of applying guidelines to individual patients. However, the emphasis in much of the talk was that that was the intent of guidelines in the first place – to guide practice but in a manner that complemented patient centred care.

… they obviously do… distil, theoretically at least, best practice on specific topics into, hopefully, a reasonably understandable form which can help to guide us into the most appropriate treatment for common conditions. And, I suppose, they're always designed with the ideal world and the ideal patient in mind. But… that's where the clinical judgement comes in with deciding whether that applies to the patient in front of you or not (GP18).

For these GPs, overall then, guidelines were the embodiment of best evidence, that without, they themselves as individual GPs could never hope to collate and utilise without NICE, with these guidelines informing practice to the greatest possible degree and with the greatest possible uniformity that was appropriate to individual clinical scenarios. As a result, in terms of CG181, this was reflected in the fact that the vast majority of GPs here were positive about the widened primary prevention threshold and the widened availability of statins as a result of this.

I mean somebody who has got a 20% risk and had it for a few years is likely to have really furred up arteries. If you can get them on a statin at [lower] risk a couple of years earlier, then that can only be beneficial (GP3).

More specifically, the population level approach necessitated in the treatment of risk of CVD (and indicative of SBM due to being rooted in RCT data and disseminated by guidelines) was positively viewed. This kind of GP saw the change as having potentially beneficial impacts on the levels of cardiovascular events in the population and which necessarily shaped considerations of benefit even in individual consultations.

…my outlook on the usefulness of these in a broader sense, and therefore the driver of my individual patient pathway for these things is, you know, does include consideration of population level benefits. And I suppose for me statins are like vaccines for me, to a certain extent….The whole vaccination schedule is population driven and most of those patients aren't going to benefit from what we're giving them. Statins, you know, there is a population level aspect to consider as well as the individual patient (GP18).

In addition, though concerns about the adverse effects of statins had featured prominently in professional and popular discourse surrounding this guideline, these GPs (though aware of these debates) generally saw statins to be as a safe drug, largely reflecting their views of the underpinning evidence and the logics of SBM.

I've seen significant morbidity from people who are convinced that stains are doing them harm. I think illogically. Very occasionally you see significant harm from a statin, but very rarely in my experience and that is supported by the available evidence that we have (GP12).

Here the GP suggests that concerns about side effects were not reflected in the best available evidence. Meanwhile, the talk of another GP suggested that general positivity about SBM knowledge was reflected in the specifics of their practice resulting from CG181.

I think as this guideline makes clear it is important to really be sure that the drugs are causing the problem, particularly with muscle pain. You need to talk with the patient to establish if there might be any underlying causes for you know muscle pains. And in the unlikely event it is the statin we could lower the dose or change the statin (GP6).

Here the approach of this GP very clearly mirrors the approach to the identification and management of side effects apparent in the guideline and thus is indicative of the utilisation of knowledge generated and disseminated through SBM.

6.2.2 Clinical Autonomy and the Rejection or Resistance to Collectivised Logics

However, other GPs (7/21) stressed a greater emphasis on the negative elements of NICE guidance. In particular here, the notion that NICE guidelines were 'dictum from above' and actively devalued or had the potential (if a doctor too rigidly attempted to follow them) to devalue individual discretion and clinical autonomy, with similar perspectives amongst 'rank and file' doctors suggested in other research (Spyridonidis and Calnan, 2011). This, as such, was used as a basis to criticise the value of the scientific-bureaucratic model of evidence-based practice. These elements can be seen in the quotes below, where both GPs make powerful comparisons to 'trained monkeys', and describe their discretion and training/experience as like a 'sense':

…training and clinical experience has got to count for something hasn't it? Increasingly the experience side of it is being devalued. Erm before long they will be training monkeys to do our job, or certainly machines. If you take the sort of sixth sense out of it then you know what are we there for? (GP8).

You know, like with everything you can go from one extreme to the other and you know a monkey can follow a guideline… I don't think there are many doctors nowadays where practice is not evidence based. But um the best doctors, I think, use various different sources of evidence. NICE guidelines have become the predominant method of getting a flow of where you might head. But um it can take away from decision-making if you allow it to and that can be problematic because we've been trained to have a particular sense of things (GP11).

As such, due to devaluing clinical experience, scientific-bureaucratic of medicine was for this type of GP of limited acceptability – a point articulated clearly by GP1:

… my personal view is that the particular and so called evidence-based medicine on which guidance is based has limited value in that I think that evidence-based decision making should take into account evidence-based medicine in the sense of NICE, but also the patients' wishes… but also long term clinical experience and professional knowledge. The experience of a GP is vital in the quality of the decision that is made (GP1).

It was also suggested that NICE guidelines did not necessarily translate well into real world consultations and were created with some sort of ideal patient in mind rather than the one in front of them.

I do not necessarily think that they are always in the individual patient's benefit. Erm so I will discuss it with the individual patients but we won't necessarily adhere to them… It's not so much that I object to their use, what I object to is the one size fits all. Patients are individuals and a set of very rigid guidelines are you know do not suit individual patients. Erm so you know if they were just guidelines it would be fine but they sort of but they are marketed as very dogmatic rules that could lead to us being sued (GP8).

For this kind of GP then, in contrast with their colleagues above, there was a clear clash between what guidelines intended (operating with population level focus) and the real patient sat in front of them. The most salient point here is that guidelines were thought to devalue professional discretion, experience and knowledge, but due to the individualised experiences and needs of patients, these aspects was in fact perceived as inherent necessities. In contrast to some of their colleagues above, guidelines were perceived as a threat to clinical autonomy and experience (for example due to attached medico-legal pressures, as expressed by GP8 in the final line of the above quote) rather than as something that could be easily navigated and/or was part of a positive and complementary overall decision-making package. A scientific-bureaucratic model might have some value but only if clinical autonomy and their own knowledge and experience was afforded the appropriate standing, particularly as allowed GPs to tailor advice to the individual patient in front of them. Certain GPs, as such, here seemed to be comfortable practicing outside of NICE guidance. Others seemed to be resentful of guidelines and how this, as they perceive it, diminishes individual clinical autonomy/experience, and indeed, the potential medico-legal implications. The implications for the implementation for CG181 were, as such, more complex for this problematising group of GPs than the first group of GPs detailed above. Indeed, one GP (GP1) from the sample had been completing ignoring CG181.

I haven't been applying the 10% level guidance [partly] because I have a very liberal view of guidelines (GP1).

This GP also went on to problematise specific aspects of the population level approach of CG181 and as such SBM knowledge.

I think in this case it is a [question] of at what point they are recommended. And actually whether we are treating a lot of people unnecessarily to reduce one event. So the case of numbers needed to treat. I don't

know what the numbers would be if we are looking at reducing the QRISK to the 10% threshold. So erm yeah if we are having to treat 200 with the view of reducing one cardiovascular event or separate vascular incidents, you know a lot of people get side effects with statins therefore it would be questionable at this level… I think I'd have to see a stronger argument for benefit before subjecting patients to likely risk of side effects. … I think we are broadly beginning to fiddle around the edges of benefit. Kind of, we have tackled the low hanging fruit (GP1).

Here this GP suggests that a population approach may have no benefit for particular patients and may as such needlessly expose patients to side effects from statins. Similar perspectives from GPs critical of NICE guidance were also identifiable:

…in my mind the numbers needed to treat kind of balance better at the 20% than they do at the 10%. You have to treat vastly more people to reduce one person from having a heart attack or a stroke. So you know obviously in terms of the population as a whole you know if you are a strategist, a health strategist you see this as a very viable sensible thing….But as a GP you kind of think 'ughhh' when you know that a good 20% do get statins side effects, whether they recognise them or not – in terms of fatigue, energy levels, ability to think, muscle aches and so on and so forth, particularly because we have to treat maybe 100 people to prevent one death (GP17).

Here GP17 discusses how the lower risk threshold, from their perspective, does not balance as well as the prior threshold, that this threshold is potentially too low because, again, the risk of side effects does not seem to be justifiable relative to benefits to individual patients. Other aspects of the talk of GPs critical of guidelines cohered with emphasis in the case under study in this thesis with the problems of widening pharmaceuticalisation seemingly of age alone.

I am uncomfortable that we might be putting [elderly] people on statins, this is something potentially encouraged by the guideline, when as far as I know there is a lack of evidence and the studies haven't been done in that age group... they may be on multiple medications or you may, well at a certain point you've got to ask what is the point? (GP20).

The emphasis on the particular scenario of the patient in front of the GP as opposed to the population level approach was again significant here, with people in their 80s and 90s being picked out as a clear example of the potential pitfalls and problems with SBM knowledge and an associated lack of patient centeredness – and as such, a reluctance to consider initiating a statin in the elderly. The concern here was that even though risk

testing was extended by this guideline up to age 84, an individualised focus was needed in elderly populations due, for example, to the lack of evidence and the potential problems of polypharmacy. For certain elderly people, potentially with a limited number of years remaining, the question was also whether they would actually get any benefit whilst introducing the risk of side effects.

However, only GP1 had been completely ignoring the lowered primary prevention threshold. Other critical GPs had been discussing risk testing and reduction with patients who had a risk level between 10% and 19% mostly because they felt legally pressured to record they had done so or (more commonly) duty bound as part of facilitating informed patient decision-making to conduct risk testing and discuss treatments options with patients. As is explored later in the chapter, however, there was a particularly pronounced emphasis by this kind of GP on engaging with lifestyle changes rather than utilising a statin to lower risk which was partially rooted in dissatisfaction with a population level, collectivised rationale and the greater individualised benefits from lifestyle changes than a statin. The implications for understanding the implementation of the ≥10% primary prevention threshold, and indeed, pharmaceuticalisation here, are that GPs with this kind of understanding appeared to be less likely to positively greet the change, potentially practice outside/ignore it (as GP1 had been doing) and seemed most likely to interpret the guideline and practice in such a way that reflected a high degree of clinical autonomy as relates to the individual patient and their specific health scenario (e.g. relating to age).

6.2.3 The Salience of (Dis)trust in NICE?

GP perceptions of guidelines at a general level, as well as the way they reported they perceived and were implementing the widened primary prevention threshold in CG181, also reflected the degree to which they trusted NICE and their evaluation of evidence. Trust emerged as important both in terms of evaluating, where GPs felt they could, the trustworthiness of actors and evidence base, and where GPs felt they could not, to bridge over uncertainties stemming from their own knowledge and or expertise constraints. What is interesting here, however, is that doctors are both trustees (with trust placed in them by patients) *and* trusters that are reliant on evaluative activity and knowledge created by bodies such as NICE, implicating a chain of trust (Brown and Calnan, 2016).

As such, system trust (Luhmann, 1979) by GPs in bodies such as NICE is crucial to decision-making and individual patient-doctor interactions, forming part of both the knowledge base upon which patients place trust in doctors (relative to the types of advice/information/perspective given), as well as potentially forming part of the picture of if and how doctors trust (or not) their own competencies (self-trust), patients, colleagues, and other systemic aspects (Douglass and Calnan, 2016). Pharmaceuticalisation as such is predicated on this chain of trust and necessarily the level of system trust placed in NICE by GPs.

When focusing specifically on evaluative work and recommendation done by NICE for this guideline, two positions emerged in the first group of GPs described above. One narrative from GPs in this group was of an almost unconditional trust being placed in NICE's evaluations conducted for CG181. Due to the generic status of the drugs and their familiarity prescribing statins there was no reason to consider the widened primary prevention threshold problematic.

There's always gonna be those that that wonder 'well how many more people does that bring into the treatment threshold and how much more money is that gonna cost the NHS?... That's not unreasonable to think I suppose. But the drugs are generic now and their benefits are well established (GP3).

However, another view of NICE guidelines also existed in this first group of GPs identified above. Indeed, other GPs seemed to trust in NICE as a way to navigate (humble) concerns about their own lack of speciality and thus abilities to make sense of the underpinning or any developing research evidence. In this narrative, NICE were considered to be producing guidelines developed by elite experts on a particular topic. In some of the talk here, GPs juxtaposed expert knowledge and evaluation with their own generality. As such, trust in research and evaluative expertise was grounded in notions that GPs, evaluating themselves, lacked a speciality, potentially sufficient and sophisticated knowledge in line with current research developments, and/or the ability to evaluate said research evidence. For example:

As a GP I don't think I have any particular expertise and I have a lot of faith in the people who develop the guidelines… as having more knowledge about a particular topic than I do, do you know I want mean? So you know, whilst it is quite nice to have free range to do whatever you like, I'm happy that the people who

develop the guidelines are in inverted commas experts and as such they are generating good advice if that makes sense (GP7).

However, in the second group of GPs detailed above, those critical of the utility of guidelines, the evidence of trust in NICE was more limited. Interestingly there was pronounced uncertainty about nefarious influences from the pharmaceutical industry on NICE's evaluations for CG181. For this kind of GP, it was the case that a lack of system trust, or distrust in NICE reflected the inability of NICE supposedly to resist structural failures surrounding publications.

I think they [NICE] are probably responding to research evidence here – but only some of the research is published and available for NICE to draw on in their processes (GP1).

Uncertainty about motives and the potential influences on decision-making by actors such as the industry, that could not be resolved by trust, was one clear element in why these GPs had problematised the changing threshold and had concerns particularly about offering/prescribing statins at ≥10% risk.

However, interestingly, for one GP, it was suggested that the knowledge constraints that applied in certain areas of their practice did not apply to cardiovascular disease and statins, making them personally more evaluative of this decision, which in some respects made trust in external bodies and process for this GP less salient. Indeed, this GP was happy to accept the presence of NICE guidance and the logics of SBM as one influence on their decision-making at a general level, but was critical of CG181.

I suppose statins is something I know a bit more about than say cancer drugs. The things I know less about I will take more on trust. I think the things I know more about I have read other things which may, you know, throw a different light on it, the numbers needed to treat, the statistics about patients that do and do not take their statin, the numbers of patients who get side effects.... Kind of you know put the whole NICE guidance into a different perspective… it's weird though isn't it? That I trust more on something I know less about. I use the guidance more because I need to trust the experts' opinion more (GP17).

6.2.4 Interactions with Colleagues

It emerged in 11 of the interviews that GPs suggested they had spoken with colleagues at their practice or more broadly in the CCG about the widened primary prevention

threshold. Certain aspects of the talk of GPs highlighted the importance of the professional knowledges of colleagues in shaping subsequent decision-making by GPs. It was clear that such interactions were important in terms of shaping subsequent perceptions and practice and could be either affirmative or challenging to existing conceptions of and action resulting from the guideline. Interactions were both informal (such as brief chats with trusted friends or colleagues over morning coffee) as well as more formal in nature (such as team/practice meetings).

…well I think there was one colleague in particular who I respect er who erm felt this was a big change but was probably the right thing that we should be doing. [As a result] I started to ok think this is probably what we should be doing (GP12).

This GP had been initially reticent about the widened primary prevention threshold but suggested that following this discussion with a trusted colleague, had shifted perspective and had moved to alter practice to accommodate the changed threshold, including offering a statin. Another GP suggested similarly:

Yeah certainly in our clinical meeting it was discussed. Well I've been at this practice now for 12 years, even in the 12 years I've noticed that the number of patients with heart disease has dropped because, you know you can't doubt that, and it has got to be statins – you know maybe we are being more rigorous with our management of hypertension and the other risk factors – but it has got to be good medical treatment that is doing it. We seemed to agree on that point, and you know this maybe causing us some more work, but it broadly being a good thing that patients consider statins at this risk (GP16).

Meanwhile, a GP critical of the widened threshold also reported speaking to colleagues about the threshold change but with a different emphasis:

I remember speaking to several of them about this… and as they were quite annoyed or negative about it that was probably important on… my initial thoughts on it probably looking back (GP20).

This time, however, the result was one more of affirmation of a problematising position. Colleagues shared a similarly sceptical initial view to GP20 and this had contributed to solidifying this perspective for this GP. Another GP suggested similarly here:

Um yeah, we meet together and have coffee in the mornings and all of us poo-hooed it in all honesty. Didn't think to highly of it and didn't think it was realistic… it just seemed like yet another ridiculous nonsensical dictum from above. You know at ground level. That's how it felt at the time I think. And so we were all a little bit disparaging about it. I don't think, certainly as a practice, I don't think we've suddenly put a whole cohort of people on statins. That hasn't happened at all (GP17).

In this quote GP17 suggests that a practice-wide negativity about the guideline shaped individual resistive practice.

Additionally, a further critical GP had been involved in discussions with practice colleagues about the reluctance of patients in the initial months after the confirmation of the guideline change to take up a statin. They had debated whether this was something reflecting a particular way that they as professionals might be talking about primary prevention at ≥10%.

Yes we did [meet about it]. It was one of the guidelines we spoke about in the surgery, a few times actually. And I think we all agreed that you have to be counselling patients. You know so over the 10% risk um and I think we spoke about it for when the guideline had been out for a little while that we were finding it harder to convince people who had 10% risk that they needed a statin and maybe that was our pre-conceived ideas and our use of language in discussing the risk. And that maybe we needed more balance (GP14).

Whilst this GP remained negative about widening the primary prevention threshold she reported that her approach to the threshold had softened and was now more balanced in how patients were counselled. Despite continuing reticent, the importance of interaction with colleagues, which was in this case evaluative over time, contributed to the practice and decision-making of this GP. These discussions indicate the importance of the professional knowledges of colleagues in shaping subsequent decision-making by GPs in ways that might have been complementary or problematising of SBM knowledge, highlighting the diverse and distributed nature of knowledge use underpinning the implementation of the ≥10% risk threshold.

6.3 Treatment Orientation

The analysis of the data also suggested that were some stark differences in perspectives on and approach to the therapeutic landscape at the ≥10% threshold. Whilst as noted above, this partially connects and reflects the above discussions about use/approach to

guidelines themselves (most clearly a pronounced focus on making lifestyle changes seemed to cohere with a scepticism about guidelines), there were also aspects that emerged from the data that were at least partially divorced from these considerations and stand as important analytical insights on their own. Patient identities and moral positions constructed relative to being a pill-taker (and indeed, statins-taker) have been discussed in the sociology of pharmaceuticals and in the analysis of pharmaceuticalisation (Dew et al., 2015; Polak, 2017). Interestingly, in the data presented in this section, there is evidence of moral aspects shaping the way in which *GPs* approach the treatment landscape and consultations with patients. This is particularly in terms of the sense of holding responsibility to foster patient self-responsibility for healthy living. It is interesting given the focus on patient identity construction in Williams et al. (2011a) and in related discussions of diverse moral positioning taken about medicines by patients in subsequent empirical work (Dew et al., 2015) that moral aspects featured in differential ways in the talk of GPs. This is both in terms of how this shaped the way GPs approach consultations with patients and also, potentially, in terms of how this contributes to patient identity construction and moral understandings of pharmaceuticals. It is, however, beyond the scope of this chapter to do more than ruminate on the potential connections between moral aspects evident in the talk of GPs and how patients morally position themselves and conceive of statins.

Three clear orientations (other than for the one GP who had not at all been implementing the guideline) towards treatment pathway emerged from the analysis: unified therapeutic landscape; promoting lifestyle changes; and independent statin benefit. Moral aspects were not clear in all of the talk but do feature particularly in the final two of these orientations.

6.3.1 Unified Therapeutic Landscape

GPs (9/20) saw the ≥10% in terms of a unified therapeutic landscape and emphasised the necessity for (typical) patients of making lifestyle changes prior to and subsequently alongside taking a statin. This is well captured by the following quotes:

> I wouldn't automatically just go for lifestyle and leave it at that nor would I automatically go to a statin. If someone had that kind of risk I would always suggest to them a three month trial. Or even a six months trial before we think about going on a tablet (GP16).

I think for most people I think it is important that we tackle that [lifestyle] side of things first. Because I think they can be complacent. Some people think if we put then on a statin they think 'oh that is fine' but it never is fine. It has to be done in conjunction with lifestyle changes (GP10).

Meanwhile, in the following quote from GP18, the overarching essence of what can be thought of the position of presenting a unified therapeutic landscape, of a balance between statins and lifestyle change, clearly emerges, with the GP emphasising "I don't view it as lifestyle versus statins."

I think, I suppose, I don't view it as lifestyle versus statins. When I have a discussion about CVD risk here lifestyle is always one of the first things I talk about and I do very much encourage them to have a healthy lifestyle as well as statins. I will always say, you know, my phrase always goes along the line of well we should be thinking about starting a statin which will help to lower your risk of a heart attack and stroke, but this isn't instead of making lifestyle changes. It should be as well as, and you should have a healthy diet, regular exercise, healthy weight anyway. It should be in addition to that (GP18).

In the latter part of this quote GP18 emphasises here that statins should be seen as an addition not a replacement to making lifestyle changes. In a further similar example, the following GP emphasises that it would be to no benefit to a patient to take a statin if they persisted with unhealthy lifestyle practices, particularly smoking. Statins are seen by this GP as having benefit but only in addition to lifestyle changes:

From my perspective if someone smokes there is hardly any point in someone taking a statin, you know what I mean? It would be irresponsible of me to just prescribe a statin and not try to help with them smoking. You might make a tiny dent in their risk comparative to what stopping smoking will do you know what I mean… I don't for one second think that statins should replace lifestyle. You know it should be lifestyle first, statins are only an adjunct to lifestyle change… in the 10-20% risk area I'm not always saying have a statin, I'm saying lets see what happens if we you know we can stop the smoking, do some more exercise etc and see if risk can come below the 10% threshold that way and have another look in a few months (GP7).

GP3 held a similar view, as can be seen below. When discussing with a patient risk reduction, particularly because of an expectation of a negative reaction to the idea of a statin, this GP introduced all of the options within the therapeutic landscape concurrently so as to "sell it" to the patient most effectively.

I frame it as 'there are some things that will help bring risk down, lifestyle changes, and medications we can offer that will help, including a statin.' That is an easier way to sell it if you are trying to sell it. Part of a suite of things that we are trying to do (GP3).

The quotes presented above suggest clearly that GPs here in this category seemed to focus on the preventative benefits that would come from unified engagement. There was also a sense, however, more implicit in the data, that moral baggage attached both to their own role in facilitating statins-taking as well as the moral positioning of the patient in becoming a statins taker, was diminished if lifestyle changes were also attempted/made. For example, as the quote from GP7 indicates, who makes reference to it being 'irresponsible' not to engage with the smoking habit of a patient, a sense of responsibility to facilitate lifestyle changes rather than only prescribe drugs is evident.

6.3.2 Promoting Lifestyle Change: Individual Responsibilities and Overall Health Benefit

Another group of GPs (6/20) suggested that they actively attempted to promote lifestyle change in place of a statin where risk level was between 10% and 19%. It was not necessarily that these GPs would not offer or prescribe a statin at this threshold (particularly when deferring to a patient centred model of care), but these GPs advised and emphasised to patients the benefits of lifestyle changes to a much greater extent than they promoted a statin. For example, in the below from GP11, this GP emphasises that "we want to prevent [taking a statin] if we can").

You know I try to motivate them and say there are things we can do, you know we can support you in diet and exercise and stopping smoking being the number one thing that we focus on in the first consultation and then get them back in a few weeks or months to see how they are doing. I say to them we'll do their weight and see if they can lose a couple of pounds even. You know try to increase the motivation to do something. I'd say you know there are guidelines that suggest you should be on some medicines now because of the cholesterol and the diet and that kind of thing. But I generally say we want to prevent that if we can, let's try and reduce risk through some lifestyle changes… I think the guideline is very heavy towards the medication. Although there are obviously the lifestyle measures, it is more you know once they are at 10% you should be thinking about a statin (GP11).

This category of GP were more clearly motivated by a moral imperative surrounding looking after one's own health. This clearly emerges in this quote:

> Of course one of the biggest difficulties with [statins], um we have become a nation that relies on tablets rather than rather than taking any personal responsibility for our lifestyle. The risk of statins is that people carry on living the same lifestyle of over-eating of over-drinking, not doing exercise. And just popping pills… So personally I do think um reducing the QRISK to 10% where you consider a statin is kind of you know is a difficult one because that includes a whole category of people who I think should really be working on lifestyle big time… rather than just reaching for a pill because all it is doing it encouraging them, these people, to reach for a pill, and not take lifestyle change seriously (GP17).

As well as emphasising the responsibilities for one's own health (which is evident again in the below quote), there was also a holistic emphasis by this kind of GP, or at least, a focus on the general health of patients. Whilst statins were seen as rooted in cholesterol reduction, the benefits for patient health in a general sense as resulting from lifestyle changes was emphasised. As can be seen in the quote below, this focus on the broader health of patients was part of the justification for GPs promoting lifestyle in place of, or at least with far more emphasis than the need for a statin.

> My problem is that it is just medicalising everything, giving out pills for everything, rather than, you know, it is just that people need to eat better, exercise more and take responsibility for living healthily – a balanced lifestyle. That for me is far more important than the use of a statin. I wish there was more investment in public health in that sense rather than this kind of focus on statins. People get so much more from a healthy lifestyle than they do from any specific benefits from a statin (GP20).

Interestingly GP20 here, a GP very negative about the changed threshold, also went on to suggest that the whole threshold reflected age more than anything else and as such even lifestyle changes may not be possible or particularly beneficial, though she would discuss particular strategies and changes as were relevant to a patient (e.g. smoking).

These GPs overall were not averse to more forcefully promoting a statin beyond the 10-19% category but, as can be seen in the quotes presented here, these GPs saw lifestyle changes as superior to statins at the ≥10% threshold and held clear views problematising 'popping pills' (GP17) and lack of individual responsibility for health instead of making lifestyle changes.

6.3.3 Independent Statin Benefit and Moral Neutrality

Other GPs (4/20) placed significantly more emphasis in their framing to patients on the importance of a statin relative to the benefits from lifestyle change. There was a clear acceptance by GPs in this category of the ≥10% threshold, its necessity and that it was a risk level that required the application of treatment. And in this way, the drugs were morally neutral application of the best available evidence. GPs in this category, as such, spoke about the clear evidence-based benefits of a statin, and the potentially less evidence-based benefit of lifestyle changes:

> You see there's some evidence that even a low dose statins is extremely effective in prevention. So even if a patient is not very tolerant and they are taking a low dose of something they are still getting an awful lot of protection. Erm it's much less clear, apart from smoking, how much say weight loss, or exercise has an impact…. They are complementary but independent of too. So a fat person [sic] taking statins is potentially less at risk than a thin person not taking a statin (GP6).

The greater evidence-based benefit of statins was used as justification by this GP for the earliest possible initiation of a statin. For another GP emphasising the importance of statins here, it was also not necessarily that statins had greater health benefit over lifestyle change factors, but that the necessity of a statin at ≥10% risk reflected societal forces, potentially beyond the control/influence of the GP, thus encouraging and/or necessitating prescription. A GP here suggested that the structure of society was set up in such a way that facilitated and perpetuated unhealthy lifestyles, and statins were a necessary (if partially unfortunate) solution to this. This seemed to partially make patient use of statins morally neutral in the view of this GP, whilst also meaning it was necessary and legitimate for them to prescribe (providing a sort of moral absolution for the GP too). Indeed, this attitude amongst some GPs about prevention (that there was only so much that they could do, with a greater focus on structural conditions necessary) seems to have been in existence for quite some time (Williams and Calnan, 1994: 377-379).

> Well lifestyle choices have a huge impact, do a lot of exercise, doesn't smoke, healthy lifestyle you know. Then they are much less likely to get cardiovascular disease. But that is influenced so much by culture, structure of society, which is nothing to do with their GP. Lifestyle change is hard to make and keep up. How important is it? Well it is hard to assess actually and to keep up. For a GP… verging on the impossible…

Statins, I can do. That's why I prescribe. It's easy for me whereas getting someone to change their lifestyle is difficult and often unrewarding (GP12).

In a way the GPs with this position, despite all positively discussing the benefits of SBM, might be seen as not being guideline based in their practice. The guideline suggests that there should be an attempt to optimise lifestyle factors (if relevant) prior to initiating a statin. These GPs however indicated that they would discuss the benefits of initiating a statin immediately. As was the case with GP12, this might occur alongside encouragement to optimise lifestyle choices where possible but the perceived difficulties in having sufficient success with lifestyle change prompted this GP to discuss initiating statins with patients almost immediately once risk was established. Importantly, in contrast to the previous group of GPs, statins were morally neutral and reflected the application of best evidence and/or structural components beyond the control of GP or patient.

As will become clear in later discussions in this chapter, the placing of a GP within one of these three positions does not *necessarily* mean that that is how they subsequently approached a consultation with a patient. As is discussed below, GPs emphasised the need to personalise the discussions with patients in terms of the specific scenario faced by that patient and indeed across the interviews almost every GP emphasised the importance of facilitating informed patient decision-making and the need to resist paternalistic approaches. However, these three positions are how GPs characterised their desired outcome for consultations with 'typical' patients – though of course, there are diverse factors shaping if patients become pharmaceuticalised. Clearly as the dominant language in the NHS is of shared decision-making and that patients still value professional expertise in decision-making about CVD prevention (Will and Weiner, 2015), these distinct positions are important to consider in the process of pharmaceuticalisation. Particularly for GPs emphasising lifestyle changes this often went hand in hand with concern about the benefit to individual patients versus the risks of exposing them to side effects as well as translating collectivised rationale into individual consultations.

6.3.4 Decision-Making Over Time

However, it is necessary to complicate the above discussions. It is important to note that decision-making about whether or not to initiate a statin in primary prevention is not an isolated one-off decision. Decision-making about a statin is distributed potentially over time, multiple consultations (including medication reviews after initiation), and potentially multiple professionals. As GP9 below shows, decision-making following initiation of a statin is an ongoing phenomenon, in that patients may return as a result of side effects or report stopping or desire to stop during medication review.

…[they] come back in and say I'm having side effects and I don't want to take it, so then we re-evaluate and talk about what we can do (GP9).

More interestingly, however, the three positions presented above continue to hold some explanatory power here even when acknowledging that decision-making is not contained within a single space and time. For example, GP11, who was one of the professionals with a 'promoting lifestyle change' approach, suggested that:

…what I worry about with statins with the new guidelines because we identify people at risk. For the most part we'll all be at risk at some point or another and it is my question is if we start offering statins at such a low point are we almost giving them a reason not to change their lifestyle well I've got a tablet that can sort it out anyway you know. So if they come back and if there has been some progress even minimal I'll keep encouraging it without [the statin] and maybe they come back again (GP11).

In this quote it emerges that the decision-making about a statin is distributed over different consultations following a period of lifestyle change, which reflecting the position of this GP is then potentially expanded. Though this GP also spoke about having had a patient who had come back and requested and was prescribed a statin following a lack of motivation and success in changing her lifestyle, the salience of the specific approach to the therapeutic landscape nevertheless emerges.

Meanwhile, decision-making involving GPs who held a more balanced perspective were distributed differently over consultations:

If they tell me they are doing as much exercise as they can I don't feel right in saying you cannot have a statin. But it is something that I do think about. I wouldn't automatically just go for lifestyle and leave it at that nor would I automatically go to the pills. If someone had that I would always give them a three month trial… before we think about… a tablet (GP16).

A lot of patients who are negative about statins say well I'll go away and I'll lose weight and I'll stop eating cheese, and I'll do this and I'll do that and then can we recheck it in six months? And I'm like yeah we can do that. But what I find people fall into two camps, they either tighten everything up and it does actually make a difference to their cholesterol and it changes their QRISK and they don't need one anymore. Or they whether they do or don't, they say they they've done everything they can and it makes no difference, and perhaps then they have one [a statin] (GP13).

A different orientation from GP11 above to treatment clearly emerges in these two quotes. The GP in the first quote shows how decision-making is distributed over time and separate consultations but in a way that is suggestive of a balanced orientation towards treatment, with a distinct period of lifestyle change before the statin becomes something to consider. The GP in the second quote suggests with more complexity that she is happy to be guided by patients' successfulness with lifestyle changes, and if this is not to sufficient levels will suggest a statin is necessary.

However, by contrast is this quote from a GP positioned with a more pro-statins orientation towards treatment:

If they want to I will say absolutely, have a really good go with diet and lifestyle, get your diet down to a healthy level, go the gym regularly, let us review it in six months. Hopefully things are gonna go well but I'll say you may still find that despite your best efforts you are still at sufficient risk of cardiovascular disease and maybe we need to revisit then a statin (GP18).

Here this GP suggests that he introduces the idea of the likelihood of still being sufficiently at risk to warrant a statin even where patients suggest they would like to have a chance to change aspects of lifestyle. The decision is still distributed over time and separate consultations but with a different emphasis – an emphasis that suggests that even with significant effort to make changes to lifestyle a statin is still likely to be necessary if the patient wants to manage their risk sufficiently.

6.4 Evaluation of Relevant Information: Ethical and Personalised Evaluations

Though the above theme captures much of importance in terms of the approach preferred by GPs within the context of shared decision-making about the therapeutic landscape at this level of risk, further qualifications and complexities emerged in the data.

Clinch and Benson (2013) have suggested that GPs facilitate patient involvement through the selection and ordering of relevant information, involving multiple types of 'evaluation' – and which, it seems, is in itself distributed over and reflective of various existing knowledge and interactional events (such as those detailed above). In the interviews conducted for this thesis, it was apparent that treatment decision-making at the ≥10% risk threshold was also distributed across a number of evaluations that GPs conducted prior to and within the context of consultations. These evaluations informed what was considered to be relevant information and its presentation to patients. This thesis argues that 'relevant' information provided about the ≥10% threshold was evaluated and offered in terms of whether, first, it was ethical (such as giving the patient the ability to make a 'fully informed' decision), and/or through a process of personalisation (whereby GPs evaluated personal information about the patient and offered treatment based on this, such as about perceived severity of risk).

6.4.1 Ethical Evaluations

It was clear that GPs in the sample undertook a variety of evaluations about what was considered relevant information to a patient that can be thought of as ethical evaluations – ranging from whether or not it was ethical to 'worry' patients by consulting with them about this primary prevention threshold in the first place, to what information was considered relevant in the promotion of the ethical principles of beneficence and nonmaleficence.

Near universally, the GPs emphasised the importance of being patient centred and of mutual shared decision-making in their approach to treatment at the ≥10% risk threshold. This meant, of course, finding out what patients felt about the ability and necessity of making lifestyle changes and their desire to take a statin. The guideline uses wording that suggests that statins should be 'offered' and not mandated, and that the wishes of an informed patient should be at the centre of decision-making. Broadly in line with this, and the ethical principle of informed decision-making, GPs across the sample spoke about the importance and centrality of involving patients in decision-making about treatment.

…it is patient choice. It's a balance, you can't be paternalistic, but you've got to try and guide people to the best of your ability (GP11).

However, though GPs universally emphasised the importance of patient choice when explicitly asked about it, other elements of their talk suggested this was complex in a bioethical sense. For certain GPs problematising of the widening primary prevention threshold there was apparent concern, creating an interesting bioethical dilemma, about whether a ≥10% primary prevention threshold was an appropriate threshold for intervention and thus 'relevant information'.

I've found it hard to even talk to patients…. Some of them will worry… why would I want to make them worry when I don't really believe they are significantly at risk of an event? (GP20).

In this quote, this GP expressed a concern that telling patients about their risk at this threshold, and thus conferring liminality somewhere between sick and healthy (Scott et al., 2005), would cause patients unnecessary stress, worry, and potentially contradicting the medical ethical principle of nonmaleficence, which is the intentional avoidance of harm (Beauchamp and Childress, 2013).

A further ethical dilemma surrounding evaluation of what constitutes relevant information also emerges in a different and slightly more obscure way – in terms of whether GPs decided to tell patients that the ≥10% threshold represented (at the time of data collection) a recent change. Indeed, GPs had varying orientations to and rationales for whether they explained to patients that this threshold represented a change in policy. Whilst this may only be a small element of some consultations with patients, what is important here is the disparities between GPs in their approaches again. Differential framing by GPs here means that patients have more or less access to relevant understandings/perspectives/knowledge, which in turn *may* feature in how they understand risk and therapeutic options. It was seen by some GPs as relevant information, and for others, as something unimportant to patient-centred care and decision-making, despite the controversial nature of the change and the potential pertinence of information, for example, that less than two years previously patients would not have been offered a statin.

For some GPs a changing guideline was not really seen as relevant to patient-decision making and/or that patients would not be interested in this fact.

T: Do patients know that something has changed in terms of NICE guidance?
GP2: I'm not sure they really understand there has been a shift here.
T: So it's not part of your conversations?
GP2: I don't bring that up. I don't say look it used to be 20% but we've brought this down. I just say that look you fall into the threshold where we would normally offer cholesterol lowering medication.

I do not say anything about changing guidelines to them, I suppose I don't tend to see it as particularly relevant to them what the previous guideline used to say. I think that the current guidelines are the ones that we are following and they are the best practice at the moment (GP18).

For GPs thinking in this way, it was only seen as necessary to explain to patients who had been told during a previous assessment that CVD risk and/or cholesterol were unproblematic, thus causing them to question whether their health had become worse. For example:

I think it depends if they have been told before that they haven't needed anything. So I think most people haven't got a clue, they haven't heard of it I don't think patients know anything about the guideline… So they don't really understand it, but they might say if you suggest a statin oh I was fine before – then I go into a discussion about them [NICE] lowering it (GP7).

For one GP, it was apparent that there was a conscious decision not to talk about the fact that the threshold had changed:

I personally only say that if they were someone who previously were in the 10-19% and were told that they were fine. I would probably only bother to say that if they were in that. I would still say that as it is over 10% then we need to address it but I wouldn't say that has recently changed… It would just give them more reason to protest (GP13).

This GP, who was more uncritical of the new threshold than others in the sample, suggests that discussing this change is likely to lead to patient protest, and thus did not offer the information. In some senses this might be thought of as ethically problematic in terms of facilitating informed decision-making.

Other GPs, however, had more actively discussed the change of threshold with patients – with a suggestion that it was ethically necessary to provide this information.

You know a year ago or however long it was, two years ago we were saying it was 20% and I think that immediately sets a different tone to the conversation really doesn't it… [that in some ways] for us [as GPs] perhaps we feel that we would be more willing to accept it at 20% risk than below (GP14).

It was clear, as such, in the talk of certain GPs, that by presenting information to patients about the changing threshold, having evaluated that this was necessary, there was an explicit acknowledgement that this information could shape decision-making about statins, and as such, was ethically necessary in terms of making patients aware of surrounding debates. It was also important ethically in that it facilitated informed decision-making in the face of potential patient confusion. Whilst the importance of this element of GP practice is unlikely to have purchase in a long term sense (as this guideline becomes older), there was a clear disparity apparent here in GP practice in the 18-24 months between guideline publication and data collection. Interestingly, there was some connection in the talk of certain GPs here that indicated that whether or not this was considered relevant information was predicated upon GP perspectives/approaches to this guidelines as discussed earlier in the chapter. GP14, for example, a critical and problematising GP of this change, had spoken about this guideline representing a change as a way to give patients some indication that this was not an immutable law nor something this GP felt was completely necessary even though this approach was more broadly justified in terms of facilitating informed decision-making.

6.4.2 Personalised Evaluations

In presenting advice to patients about therapeutic pathways, GPs also drew on evaluations of the personal circumstances of the individual patient. Indeed, reflecting the guideline (and previous iterations), GPs also placed more stress on the importance of a statin when there were comorbidities in existence (such as diabetes or hypertension), where there was a family history of CVD, or where there were particularly abnormal cholesterol levels. There is some overlap here with the first overarching theme presented in this chapter. However, the difference lies in the emphasis within the talk between guidelines at a more abstracted level and here in this theme on the actualities of consultations with patients. This personalised emphasis on the recommendation of a statin when these kinds of factor were present was evident across the sample of interviewed GPs.

I certainly would be recommending certain people with a diabetic diagnosis or other comorbidities to consider statins, or where there is a very strong family history of heart disease or stroke (GP1).

You know if they had a strong family history and a high cholesterol and led a very stressful lifestyle I'd be far more worried about them and perhaps discuss it more strongly (GP17).

GPs also placed differential personalised emphasis on particular elements of a patient's lifestyle considered problematic, such as smoking, as was evaluated as relevant to the individualised context of the patient. Some GPs also seemed to draw on what they knew about the patient's overall life. GP15 suggested that for many people, including at 10%, it is hard to make lifestyle changes due to various social arrangements and commitments, reflecting the structure of society – thus prompting this GP to offer a statin earlier in the process and more forcefully to patients.

I still think that people should try to make lifestyle changes but you've also got to be realistic sometimes when they are working long hours or something, and thus I often just say "we should really strongly think about a statin because your risk falls within the problematic range"… You can lecture people until you are blue in the face about exercise, diet, whatever, but realistically they are living lives that they are struggling with… sometimes you know that you are not going to get through to somebody about lifestyle, they are talking about work you know, on the road by 6, up at 5, home by 8 (GP15).

For GP15 there is a clear focus here on what might be achievable for patients based on the particular circumstances of the patient, whilst also filtering this advice through personal perceptions and orientations to treatment, in this case, as a GP who believes strongly in the utility of statins.

Interestingly, for patients without additional issues such as comorbidities or a strong family history, risk level relative to therapeutic pathway was also personalised. In essence, for four GPs in the sample, the closer the patient was to 20% the more likely they were to emphasise the need for a statin, whilst closer to 10% risk they would advise patients with more emphasis on lifestyle change. This is particularly interesting compared to the actualities of the guideline where there is no distinction made between risk reduction strategies at different risk levels within the overall threshold. The essence of this subtheme is well captured by the extract below:

I definitely do think the figure makes a difference to how I would behave in the consultation… if they were on 19% I would be much more keen to talk seriously with them into a statin. If they were 11% then I would probably have a more heart hearted effort at a statin (GP13).

It was also emphasised that in terms of QRISK2 calculations, above 15-17% lifestyle change was unlikely on its own to reduce risk sufficiently, and certainly not out of the ≥10% threshold. This provided justification for other GPs to more forcefully promote and advise patients to take a statin and start more immediately.

I tend to look at the numbers and put them through the QRISK2 calculator. I don't tend to say to patients I don't think this will work. I say this is what I think is feasible in terms of lifestyle change, this is what your score will be if this happens and it's up to them. I might say I think that's reasonable because we might be able to do well here, but if it is still gonna be well above 15 then I tend to say "we'll try to make these changes, but we can start you on a statin if you want to now rather than waiting" (GP7).

For these GPs the way in which emphasis was given to particular therapeutic pathways seemed to reflect, as such, a personalised evaluation of the level of risk. However, interestingly this emerged amongst particular GPs with a balance orientation to treatment who elsewhere in their talk had also identified as having some uncertainty about the widened threshold. This suggests that whilst personalised in framing, this also reflected perceptions about the necessity of a statin at the ≥10% threshold. This was partially resolved by placing a greater emphasis on the drug nearer to what was the previous risk threshold of 20%. This was particularly the case for GP13, who also partially resolved uncertainty (that in actuality stemmed from broader commentary and argument in the context of this case) through deference to and trust in NICE, as well as this greater emphasis on statins closer to the 20% risk.

6.5 Discussion

This chapter has presented the thematic analysis of semi-structured interviews with twenty GPs, analysing their perceptions, approaches and the aspects and influences that shape their involvement in decision-making about CVD primary prevention at the ≥10% threshold as established by NICE in CG181. At the heart of this chapter was the following question: *How do GPs understand the ≥10% primary prevention threshold and the utility*

of statins, and what shapes if/how have they have been implementing guidance about this level of risk? This chapter has presented three overarching themes (with specific subthemes emerging within these overarching themes) in answering this question: use of guidelines and other knowledges; treatment orientation; and evaluations of relevant information.

This chapter has considered the role of doctors within the pharmaceutical regime and has enlarged and complicated understandings of the clinical dynamics of pharmaceuticalisation. This has expanded understandings of the fourth dimension, relating to the use of medicines, of the Williams et al. (2011a) conceptualisation of pharmaceuticalisation. In particular, this has been done through highlighting the dynamics involved in the configuration of GP understandings, prescribing behaviour and approaches to CVD pharmaceuticalisation – aspects which arguably have been made peripheral in the pharmaceuticalisation literature to date. In other words, the analysis has revealed the understandings and approaches of GPs within the process of pharmaceutical decision-making about statins, with this role important to understand particularly because it has been shown in other research that patients value the input of professionals during decision-making about statins initiation (Will and Weiner, 2015). Overall, GPs displayed disparate understandings of the utility of CG181 and the place of statins in the CVD therapeutic landscape. If and how GPs had been implementing the guidance was dependant on their understandings of and approaches to SBM and other forms of knowledge, the moral qualities of treatment, and their evaluations of what was relevant information. In this regard, what emerges overall as of most salience in this chapter is the complicated dynamics involved in GP involvement in decision-making about statins at the ≥10% primary prevention risk threshold. It is clear that GP implementation of the guidance and involvement in/attempts to facilitate patient decision-making involve assemblages of professional, contextual, and individual factors reflecting various interpretations and use of various knowledges, orientations, interactions, and forms of evaluation. These factors simultaneously reflect and shape the extent to which GPs are pharmaceuticalised in their approach to treatment. After discussing all of these factors, towards its end this chapter sets out a typology that captures the pharmaceuticalised orientations of GPs.

GPs, as one actor within the pharmaceutical regime (Williams et al., 2011a), exist in disparate and often uneasy relationships with other actors and processes of the

pharmaceutical regime (e.g. knowledge generated and disseminated through SBM/NICE guidelines). This is despite certain other analysis that has painted a picture of GPs as uncritically contributing to the widening use of pharmaceuticals as solutions to health problems (Busfield, 2010). Busfield discusses how three factors (seemingly inherent, at least partially, to the social role of the doctor) have contributed to the vast expansion of the use of medicines in recent decades – interventionism (desire to provide a solution); imbalances in risk assessment (playing down risks); and limited knowledge of pharmacology. Busfield's analysis can partially explain some of the interview data analysed and presented in the chapter in terms of some GPs positively receiving and implementing the widened threshold. However, across particularly the first of these two factors the interviewed GPs were highly disparate in their approach to the pharmaceuticalisation of the primary prevention of CVD. As the section analysing GP orientations towards treatment indicates, the initiation of a statin as indicative of 'interventionism' was heavily resisted by six GPs who preferred their patients to have a significant prior attempt at lowering risk through making lifestyle changes. Indeed, there was little indication that these GPs in the 18-24 months between the publication of CG181 and data collection had prescribed statins to many patients at all within a 10%-19% risk. Additionally, in the talk of these critical GPs, the risk of subjecting patients to side effects for minimal benefit was a significant concern at the 10% risk threshold, suggesting that in contrast to Busfield's argument, a number of GPs actually significantly problematised the risks of the drugs, particularly because of population level benefit logic (rather than individual patient benefit) underpinning the primary prevention of CVD. As such, the data analysed and presented in this chapter suggests that there is greater complexity attached to the role GPs place in the use of medicines and the degree to which they might be thought of as 'pharmaceuticalised' in their approaches towards treating patients (at least it applies to the primary prevention of CVD).

As discussed in the previous chapter concerned with the print news medium, Pollock and Jones (2015) have argued that the analysis of CVD pharmaceuticalisation must be contextualised relative to the broader therapeutic landscape. Sufficiently appreciating this point necessarily means engaging with, as highlighted by the sociology of prescribing, the cultural context within which medical decision-making is taking place (Gabe et al., 1990). In particular, issues surrounding individual responsibility for health and certain related moral notions attached to the use of pharmaceuticals and if and how

these aspects figured in how GPs perceived and approached this treatment threshold, and thus pharmaceuticalisation. For certain GPs, particularly those who composed the individual statins benefit treatment orientation, the drugs were seen as morally neutral and their widening use was the result of the application of the best available evidence. There was also a certain resignation by GPs in this category that lifestyle changes were likely to be very hard for patients to make sufficiently, rooted both in past experiences and perceptions of the structure of society. However, for many of the GPs outside of this treatment orientation the drugs were imbued with moral baggage. At the root primarily of concern was the 'unnecessary' utilisation of pharmaceuticals where healthy lifestyle practices could be adopted to mitigate risk and their own professional responsibility to encourage healthy lifestyles. Certainly for those GPs who were characterised in the promoting lifestyle orientation there was a pronounced narrative of lifestylism (Hansen and Easthope, 2007) which diminished the desire to pharmaceuticalise patients. In this regard, these GPs wanted a more extensive medicalisation due to moral (and health) superiority through medically promoted lifestyle change actually at the expense of pharmaceuticalisation (Coveney et al., 2019: 269). Polak's (2017) work highlights the complex moral positions patients take on statins use. The findings of this chapter confirm that GPs also possess complex and disparate understandings that reflect moral positions pertaining to their own responsibilities and perceptions of individual patient responsibility for health that influence treatment orientation. GPs themselves, of course, do not exist in a social vacuum and the line between medical knowledge and social emphasis on individual responsibility is blurred (Hansen and Easthope, 2007). These positions are important to appreciate though because GPs' perspectives (at least as far as they allow them to emerge in consultations) may be one aspect in the configuration of patient's own moral positioning on treatment. Though, of course, caution is necessary here because this chapter has only presented data on professional perspectives and not the understandings of patients or observations of the doctor-patient relationship – with further work required in this regard (see Chapter Seven).

These treatment orientations coalesced with broader approaches to the use of guidelines and professional identity as well as evaluations of ethical practice and the evaluation of the personal circumstances of patients. In the first overarching theme, a problematising orientation taken towards NICE guidelines by a minority group of GPs were evident in the data, a theme which is broadly in line with sociological literature

concerned with the understandings and implementation of clinical practice guidelines (Spyridonidis and Calnan, 2011). However, a larger group of GPs did see the value of the knowledge produced and disseminated through guidelines, in a way not dissimilar to that articulated by Mcdonald et al. (2009), and this was reflected in the fact that the majority of the GPs interviewed had been attempting to implement the guideline. The divide between GPs concerning clinical practice guidelines evident in the data has not necessarily been articulated in the same way in other studies, although when looking at the literatures on professionalism and professional identity overall divergent positions are apparent. Nevertheless, there were clear examples from the data of how understandings of and aspects of professional identity were relevant to understanding the clinical dynamics of pharmaceuticalisation. GP1, for example, had been completely resisting the implementation of the guideline and had not been conducting risk testing or discussing the therapeutic landscape with his patients – and thus the pharmaceuticalisation of these patients would not occur. One of the factors underpinning this was a very negative view of NICE guidelines. Experience level and number of years in clinical practice also figured (with the lesser experienced members of the sample often describing problems justifying decision-making outside of guidelines and their more limited knowledge and experience bases). Greater experience levels coalesced with greater comfort in practicing outside of the guideline. For other problematising GPs, a rejection of the collectivised population level logic underpinning the preventative use of statins was compatible with a lifestyle focus (and the perception of the supposedly greater individualised benefit) that also featured for this kind of GP. The holistic emphasis of general practice (Hansen et al., 2016), or at least a focus on overall patient health, also emerged here through an attempt by this kind of GP to appreciate and maximise the overall health of their patients.

Meanwhile, the acceptance of the logic of SBM and a high level of system trust (Luhmann, 1979) in NICE and was more likely to coalesce with a strong emphasis in the talk of GPs on the benefits of statins (either independently or as part of a therapeutic alliance with lifestyle changes). The importance of trust for other actors in healthcare (beyond patients and their trust in professionals) emerges here (Brown and Calnan, 2016; Douglass and Calnan, 2016; Gilson et al., 2005). Trust was placed in NICE and their evaluative activity particularly to bridge over aspects of uncertainty and where knowledge constraints were acknowledged/evident. It is important to note here,

however, that this research only focused on certain specific aspects of one guideline and even in this limited scenario, it was clear that not every GP, even those welcoming the change had a detailed knowledge of all relevant aspects of the guideline. For example, it is not clear from the data that all GPs were knowledgeable about the targeted total cholesterol level reduction (set in CG181 as 40% reduction over three months). So whilst the 10% threshold, as the aspect of the guideline most professionally and publicly disseminated and discussed, was well known and had been thoughtfully considered, certain related specifics had not necessarily been considered to the same extent. As such, some cautiousness is required in terms of the extent that specifics of the knowledge generated and disseminated via SBM that has been translated into clinical practice.

It is also clear that decision-making about statins at the 10% risk threshold was distributed over certain evaluations made by GPs relating to ethical practice and patient circumstances. As such, the strongly oriented approaches of specific GPs were not a display of what might be conceptualised as traditional professional power. Indeed, it was clear from aspects of the talk in the vast majority of the GP interviews that they attempted to order and present information to patients in ways that related to the specific circumstances of the patient and in this way meaningfully attempt to engage patients in decision-making in a similar way to that observed by Clinch and Benson (2013). However, some of these aspects were indicative of broader orientations towards knowledge or treatment particular to the individual GP. For example, whether primary prevention was deemed ethical, or the particular level of risk even within the 10-19% threshold where it was seen as more or less crucial to offer and advise patients of the necessity of a statin.

Armstrong (2002) suggests that the problem with attempting to alter GP behaviour through guidelines is that it may take a significant amount of time to cognitively adjust to new drugs (or wider applications), partly reflecting, as such, the persistence of individual clinical autonomy, rooted in individual experience. Over time the ≥10% threshold may become normalised, perhaps particularly reflecting positive experiences (e.g. minimal evidence of increasing prevalence of side effects). However, at the time of the interviews with GPs, this change was still relatively new, and as such, the lack of positive feedback and experience could explain the negative faction of GPs in the sample (particularly because some of these negative GPs also suggested in their talk that the 20% threshold had been much more reasonable, thus indicating that they were not

necessarily adverse to primary prevention in itself). This temporal aspect to decision-making in itself is another important aspect to appreciate. And in this way, and indeed more broadly, Rapley's (2008) model of distributed decision-making holds explanatory power here. Whilst Rapley (2008) looks at medical decision-making overall, with a particular emphasis on how decision-making is an ongoing process for patients much of which occurs beyond the time and place confines of the medical consultation, it is clear that the involvement of GPs in the processes of decision-making is also distributed potentially over a variety of knowledges, orientations and evaluations which themselves exist in but also beyond individual consultations and could evolve over time. Rapley's work (see also Clinch and Benson, 2013) also encourages medical sociologists to consider how even the small aspects of interaction with doctors and beyond may shape decision-making (indicating the importance of, for example, whether GPs told patients about the threshold change being new). Whilst other analysis has simplified the positioning of doctors within the pharmaceutical regime (particularly Busfield, 2010), detailed examination of the distributed nature of GP involvement in decision-making highlights, at least in the case under study in this thesis, how this is anything but simplistic, with particular approaches to decision-making about statins reflecting a combination of factors.

6.5.1 Typology of Pharmaceuticalised Orientations

It is clear that depending on the particular ways knowledge, interactions, orientations and evaluations are distributed and applied, in terms of the pharmaceuticalisation of the primary prevention of CVD, a typology of how pharmaceuticalised GPs are in their approach to the primary prevention of CVD at ≥10% risk can be established. In what follows, this chapter connects the thematic discussions presented above to three typological positions. Variant on the ways the themes presented in this chapter (use of guidelines and other knowledges, treatment orientation, and evaluations of relevant information) were intertwined, this typology is comprised of 'Advocative GPs', 'Pragmatist GPs' and 'Resistive GPs'. Appendix 10 notes the professional and social characteristics of the GP participants and places each GP in one of the following typological positions, as well as allowing the reader to contextualise quotes presented earlier in the chapter.

Advocative GPs (4/20) can be thought of as the most positive and emphasising of the benefits of a statin within the <10% threshold. This was even to the extent that they thought that statins could be beneficial independent from and beyond the impacts of making lifestyle changes. Statins were also seen as morally neutral and their widening usage the reflection of the best available evidence. The practice of this group of GPs was shaped by SBM, and they emphasised the importance of SBM. However, advocative GPs also went beyond the guideline in forthright emphasis on statins, without necessarily vocalising that they understand that this was actually in a sense a violation of the guideline. Interestingly, this strong sense of the beneficial nature of statins in this group of GPs was not clearly related to social or professional characteristics – with this type the most heterogenous particularly in terms of career stage and experience. This type of GP displayed high levels of system trust in NICE's evaluations of evidence, particularly due to the generic status of the drugs. They were also likely to have had positive interactions with colleagues about statins at this new threshold of risk. Moreover, decision-making with patients was likely to be distributed across fewer consultations with an earlier emphasis on statins. They were also unlikely to ethically problematise the primary prevention threshold and tried to minimise talk of threshold change/statins controversy. Overall, this group were pharmaceuticalised in their outlook on and approach to the threshold change.

Pragmatist GPs (9/20) were more rounded in their assessment of the widening primary prevention threshold, and at times displayed some uncertainty about benefit and the risk of side effects. However, this group did broadly display trust in NICE. Though GPs of this type emphasised different positive and negative elements, GPs here seemed to practice the most closely to the guideline in terms of having a balanced understanding of the therapeutic landscape and encouraging patients to take a period of lifestyle change prior to and continuing healthy living alongside a statin. This group were also more likely to be younger and less experienced professionals. Lesser clinical experience and the greater prominence of EBM within their medical education compared with older colleagues was likely to be important in this group's practice being most clearly guided by SBM and thus CG181. Decision-making with patients was reported to be distributed over several months and several consultations, including a period of lifestyle change first, and then the

recommendation of a statin if the necessary cholesterol/risk reduction was not made (taking a unified approach to the therapeutic landscape). However, interestingly this type of GP was the most likely to emphasise the need for a statin earlier when a patient's risk level was closer to the older 20% risk threshold. On an ethical level, it was considered a violation not to tell patients that they had a risk level considered problematic and not to engage them in discussion about treatment options and the dynamics of the threshold. Overall, this group were pharmaceuticalised in their outlook but there was a pronounced wariness about patients taking a statin without making changes where necessary to lifestyle behaviours – with the moral baggage attached to statins diminished (for both themselves and their patients) if lifestyle changes were attempted prior to and alongside statins-taking.

Resistive GPs (7/20) were very critical about the benefit of and need for the new primary prevention threshold. GPs in this category ranged from those suggesting they reluctantly discussed with patients risk at this threshold, with a very heavy emphasis on making lifestyle changes instead of a statin, to two GPs in the category who saw the whole threshold as problematic and flawed, and were either not holding discussions with patients at all and/or saw any intervention at this threshold (including lifestyle changes) as largely unnecessary and reflective more of age than anything requiring treatment. This group were the most emphasising of the importance of individual professional experience/knowledge and most likely to practice outside of guidelines. As such, the majority of this group were older and the majority had between 15 and 25 years clinical experience. As part of this they also displayed low trust or distrust in relevant systemic actors. This group held pronounced ethical concerns about the threshold and about making patients worry 'unnecessarily'. They also considered informing patients about the threshold change as a recent change to be ethical practice, but it was clear that this was often deployed to attempt to diminish positive perspectives about the necessity of the guidance and statins. Where GPs here were engaging with the guidance, decision-making was distributed over the longest period of time with the most time allowed for attempts at lifestyle changes. Statins had the most significant moral baggage for this group of GPs – and emphasis was placed on not using drugs to treat problems of lifestyle. GPs of this type also reported negative and condemnatory interactions with colleagues about the guideline. Overall resistive GPs can be said to be the least pharmaceuticalised

in their outlook on the threshold change, with a small number displaying a near completely unpharmaceuticalised outlook in their approach to typical patients.

The value of this typology is that it provides clear indication of the disparate understandings of and approaches to pharmaceuticalisation displayed by GPs and the array of factors that feature in how they approach decision-making and consultations with patients. This said, it is important to note that contemporary medical decision-making is a nuanced phenomenon. In this regard, this typology should not be read as indicating (the return of) paternalism within the doctor-patient relationship nor that the understandings and approaches displayed by GPs translate linearly into patient understandings and decision-making. Indeed, particular aspects of decision-making were evident across the typology of GPs proposed in the typology. As in Clinch and Benson's (2013) work, there was a clear attempt by the majority of GPs to involve patients in decision-making about their own preventative treatment. For example, GPs other than particularly one resistive GP, who were implementing the threshold stressed the need to not be paternalistic and to listen to the wishes of the patient, even where they also offered a recommendation. Indeed, GP11, a resistive GP very problematising of the threshold, reported a case where a patient had come back after attempting to make lifestyle changes, unsuccessfully so in the mind of the patent, and so in consultation with the patient, GP11 prescribed a statin. This is a clear indication that it is necessary to be wary of ascribing too much significance to the understandings and approaches of GPs in terms of the configuration of patient perspectives. Indeed, as Rapley (2008) alerts us, professional knowledge and interaction are part of a broader picture of medical decision-making that includes diverse sources of information and interaction.

However, the specific positions of GPs on this threshold change and the associated perceptions of statins emerged more forcefully in the ways GPs reported they approached consultations with patients than it has done in other work which has looked at decision-making at the previous and less professionally and publicly controversial ≥20% risk threshold (Clinch and Benson, 2013). Particularly those with stronger positions on the utility of statins or lifestyle change might be thought of more as, either intentionally or not, engaging in broader forms of shared decision-making where the GPs were willing to offer their advice, act as friend or teacher, rather than neutrally present the options (Entwistle et al., 2012). Importantly GPs at the polar ends of the typology

were more likely to limit or emphasise particular options presented to patients (e.g. by not even discussing the need for a statin). As patients still value professional advice (as Williams et al. 2011a note), and evidence suggests that consumerist impulses in preventative CVD treatment are low (Will and Weiner, 2015), this will clearly shape the treatment pathways patients are aware of, understand or even that are open to them. Overall then, it is important to understand how GPs approach decision-making in this sense, whilst also not *necessarily* ascribing the beliefs and approaches of professionals to how patients themselves understand pharmaceuticalisation or if they become pharmaceuticalised or not. Professionals feature importantly with the pharmaceutical regime of cases of particularly medicalised pharmaceuticalisation, but diverse factors shape patient decision-making. There are further questions and agendas for research to establish in this area, particularly surrounding establishing the manner in which professional approaches and clinical dynamics translate into if and how patients become pharmaceuticalised. This will be returned to in the final chapter of this thesis.

Overall, in terms of the overarching research question of this thesis, are GPs a driving force of pharmaceuticalisation and how do they shape the extent of its occurrence in the case under study? The disparate approaches evident in the data analysed in this chapter suggest that GPs are not universally a driving force of pharmaceuticalisation in the case under study. It is true that a greater proportion of GPs can be positioned within a typological position that coheres with expanding pharmaceuticalisation. This includes 'Advocative' GPs who were in certain ways practicing outside of the guidance with a pronounced and forthright emphasis on the relative necessity and quick initiation of a statin. Nevertheless, there was a group of GPs that were resistant to pharmaceuticalisation (with a small number even declining to implement the guidance) within the sample that necessarily places limits on the extent of pharmaceuticalisation occurring at the lowered CVD primary prevention threshold.

Chapter Seven: Discussion – Looking Across the Pharmaceutical Regime

7.1 Introduction

The purpose of this final chapter is to undertake an overview of the data analysis, draw together the findings presented in the three analysis chapters and establish an answer to the overarching question posed by this thesis: to what degree is the further pharmaceuticalisation of the primary prevention of CVD occurring and what are the driving forces? In doing this, this chapter considers the dynamics and manoeuvrings of the pharmaceutical regime in the case under study and considers the explanatory power of the conceptualisation of pharmaceuticalisation as proposed by Williams et al. (2011a). In the final stages, this chapter considers some of the limitations of the research presented in this thesis and discusses the important remaining questions left in its wake.

7.2 Summary of the Data Analysis and Contributions to Knowledge

Before looking at the pharmaceutical regime of the case under study in its interconnected and totalising way, and thus establish overall conclusions particularly about the extent of pharmaceuticalisation, it is necessary to summarise the dimension-specific findings from the data analysis with a focus particularly on driving forces. The previous three chapters have presented the data analysis of the role of three core actors (NICE, newspapers and GPs) in the pharmaceutical regime implicated in driving, facilitating or potentially constraining the extent of the widening pharmaceuticalisation of the primary prevention of CVD.

Chapter Four discussed the creation of the opportunity for pharmaceutical deployment by NICE (as operating within the regulatory dimension of pharmaceuticalisation) and the associated influences of and dependency on the pharmaceutical industry that have shaped the opportunity for the further pharmaceuticalisation of CVD. The question, as such, at the heart of this chapter was: in what ways may NICE's decision to widen the availability of statins have been influenced by the pharmaceutical industry? In answering this question, it was shown that, first, NICE are reliant on published efficacy and safety data (or the lack of) produced and published by the pharmaceutical industry that they then apply in evaluations of cost-effectiveness.

In this case reliance on existing published evidence (much of which was used to create the initial markets for statins) continues to shape the appearance of utility and safety even upon reassessment of the evidence by NICE and acts to continue to further pharmaceuticalisation. Secondly, there was evidence of a lack of independence between the prominent researchers and professionals involved in the development of the guideline and the pharmaceutical industry. The inseparability of regulatory evaluation from the influence of and dependency on industry was clearly shown to emerge in both of these ways.

Overall, this focus on NICE's regulatory activity broadens understandings within pharmaceuticalisation studies of the regulatory dimension. It does this by illuminating how the influences of the industry pervade NICE's evaluative activity and shows how its specific organisational positioning means that the influences of and dependency on the pharmaceutical industry are difficult for the Institute to avoid or resist. Despite its fourth hurdle function, the institute has largely been ignored in pharmaceuticalisation scholarship before this research. Whilst NICE do not grant marketing approval for drugs (which is done in the UK by the MHRA) they are highly significant in deciding which and to what extent drugs are utilised and funded within the NHS. In distinct ways from other regulatory bodies, permissiveness (in terms of the uncritical assumptions of benefit and safety and how associated cost effectiveness was assured through the scenario analysis) and corporate bias (particularly in relation to speed of regulatory approval over patient interests) have shaped the widening availability of drugs as resulting from NICE's evaluative/regulatory activity. The analysis of NICE's role in the process of pharmaceuticalisation is itself in these ways, at least to date, a unique contribution within pharmaceuticalisation studies.

The findings of Chapter Four are also timely in the context of current policy attempts (e.g. the AllTrials initiative and 'Sunshine' laws) to reduce, or at least make more transparent, the influences and interests of the pharmaceutical industry on the development and dissemination of pharmaceutical knowledge. In this regard, retrospective registration of all clinical trials (and thus transparency of methodology) as well as the availability of individual patient data would have strengthened NICE's evaluative work and potentially altered the nature of their guidance.

Chapter Five discussed the print news medium within the process of pharmaceuticalisation. The specific research question central to this chapter was: how

did the UK print news medium present and portray the potential widening usage of statins? It was argued that portrayals in reporting coalesced around four themes: size and significance; side effects: dangers to patients; violations and uncertainty in the evidence base: conflicts of interest; and the relative positioning of statins and lifestyle. The newspaper portrayals analysed indicated that the print news medium acts more as a constraining force of pharmaceuticalisation in the case under study. The coverage reflected and reshaped uncertainty and controversy surrounding the drugs and in much of the reporting created a sense that the necessity and desirability of the widened threshold was low, with significant risks, and potentially reflecting corrupt influences and low-quality evidence. Portrayals of other actors within the pharmaceutical regime also necessarily oscillated as the dynamics of the debate shifted and reshaped but uncertainty reflected in and exacerbated by the coverage about the presence of the influence and interests of the pharmaceutical industry on NICE's regulatory action never disappeared. The coverage overall can be argued not to cohere with the interests of other actors within the pharmaceutical regime that are attempting to widen pharmaceuticalisation.

Chapter Six, discussed the perceptions and approaches of GPs to the ≥10% threshold, highlighting the disparate manner in which GPs reported that they understood the guidance and attempted to facilitate and guide the treatment of their patients. It analysed the perceptions and approaches of GPs in decision-making about CVD primary prevention at the ≥10% threshold as established by NICE in CG181. At the heart of this chapter was the following question: How do GPs understand the ≥10% primary prevention threshold and the utility of statins, and what shapes if/how have they have been implementing guidance about this level of risk? It was shown that GPs displayed disparate understandings of the utility of CG181 and the place of statins in the CVD therapeutic landscape. If and how GPs had been implementing the guidance was variant on their understandings of and approaches to SBM and other forms of knowledge, the moral qualities of treatment, and their evaluations of relevant information. Variant on how these aspects were distributed, a threefold typology of the pharmaceuticalised orientation of GPs was established (Advocative, Pragmatist and Resistive). Overall, this analysis has expanded understandings of the fourth dimension of the Williams et al. (2011a) conceptualisation of pharmaceuticalisation. It is true that it cannot be known from the data presented what the impacts are exactly of the perspectives and approaches

of GPs on if patients became pharmaceuticalised. However, the analysis offers insight into an important actor within the process of pharmaceutical decision-making – particularly when this is conceptualised as distributed over and involving a number of relevant actors, interactions and knowledge. The thesis highlighted distinct approaches, framing and certainly differences in the treatment options offered to patients that could feature as part of a distributed collection of factors in how patients understand the drugs and if they become pharmaceuticalised. Doctors' advice is still valued by patients (Will and Weiner, 2015) and, as such, it is necessary to understand their perspectives and clinical approaches within the pharmaceutical decision-making picture. Overall, the disparate approaches evident in the data analysed suggest that GPs cannot be considered universally to be a driving force of pharmaceuticalisation in the case under study, though more GPs had pharmaceuticalised orientations.

On a broader level, this thesis offers one of the most comprehensive accounts of one case of (medicalised) pharmaceuticalisation and the multiple dimensions along which it expands and/or contracts available within pharmaceuticalisation studies to date. The notion of the pharmaceutical regime is a central part of the Williams et al. (2011a) conceptualisation and directs analytical attention to the driving forces and the extent of pharmaceuticalisation. The importance and utility of the pharmaceutical regime lies in its emphasis on the interconnected nature of the dimensions of pharmaceuticalisation and its relevant actors. Some other analysis, though not in a thesis or book length appraisal, does look in a limited way across the regime and considers the multiple component parts in the expansion of medicines use (Collin and Otero, 2015). However, most other analysis is more clearly focused on one dimension (e.g. Dew et al., 2015) and/or certain closely interrelated components (e.g. Britten et al., 2015; Brown et al., 2015; Vrecko, 2015; Will and Weiner, 2015) of pharmaceuticalisation rather than placing this dimension within its much broader network. Indeed, not all work that has drawn on the Williams et al. (2011a) framework has clearly tied its analysis into examining the pharmaceutical regime, with some empirical papers not even using the term (e.g. Vrecko, 2015). Other work within the sociology of pharmaceuticals beyond pharmaceuticalisation studies does also attempt to take a more totalising view (Busfield, 2010; Gabe et al., 2012) particularly by drawing on the theory of countervailing powers (Light, 1997; 2010b). However, analysing at length the contingencies between and complexities of the multiple component parts in the expansion of statins availability with

direct reference to the pharmaceutical regime within a single disease area has been a unique contribution of this thesis. As the case under study highlights, whilst pharmaceuticalisation might be expanding in one dimension, in other dimensions there can be significant resistance to, constraints on pharmaceuticalisation and even depharmaceuticalisation. Empirically privileging one dimension will, as such, result in misleading evidence about the extent of pharmaceuticalisation and serve to diminish the importance of the presence of competing actors within the pharmaceutical regime.

7.3 Looking Across the Pharmaceutical Regime

As discussed, the pharmaceutical regime suggests that to understand the widening use of medicines we need to look at the dynamic relationships, connections and network that exists between organisations, actors and cognitive aspects. To understand if, how and to what extent pharmaceuticalisation is occurring, analysis needs to look at movements in the regime that open up opportunities for deployment and if and how this and other factors shape the manner these opportunities are understood, received and utilised. In this vein, this thesis has attempted to look across the spectrum of the regime, analysing, in this case, the regulatory creation of the opportunity for the further deployment of statins through to the portrayals of, approaches to and deployment of medicines.

As established, the three analysis chapters in this thesis each offer their own important analytical findings in understanding if and how pharmaceuticalisation is occurring in and across different dimensions. However, utilising the idea of the pharmaceutical regime allows this thesis to explain and analyse the driving forces behind the widening opportunity for the use of statins in this case and the subsequent reception and utilisation of this widening opportunity in order to make a judgment about extent. Or in other words, the extent to which networks and relationships between actors and organisations cohere (or not) and facilitate (or not) the wider use of drugs in this case. The case under study in this thesis and the dynamics of the pharmaceutical regime can be broken down as follows. NICE's guideline has opened up the opportunity for pharmaceutical deployment. This, however, reflects networks and connections with the pharmaceutical industry. Though direct interest is largely negligible in this case, the positioning of NICE in their guideline production necessitates reliance and dependency on industry for the available evidence. Mechanisms and practices utilised by the

pharmaceutical industry during the development of pharmaceutical knowledge have served to exaggerate the appearance of benefit and minimise evidence of side effects. Similarly, relationships between the pharmaceutical science community and industry make it difficult to establish a truly independent guideline development group for the evaluation of this evidence (potentially meaning, for example, that limitations of the evidence are not seriously considered). In this case, these aspects of influence and dependency have coalesced to drive the widening availability of statins – though there were also attempts to establish an even wider preventative treatment threshold based solely on age.

However, though the widening opportunity for pharmaceutical deployment has occurred at the regulatory level, the way this has been received and subsequently utilised in wider professional and public spheres is, in this case, anything but uncritical and uniform. The potential for the widened usage of statins provoked significant scrutiny and critique in popular discourse and from medical communities. This reflects concern about the construction of the evidence base but also broader societal and moral values about the use of drugs to treat problems stemming from 'unhealthy' lifestyles. The print news medium, reflecting their own priorities, and, as such, particularly the newsworthiness of medical professional strife and disagreement, have amplified and exacerbated the controversy. This in turn, has acted at a rhetorical level to enforce the notion of the rampant pharmaceuticalisation of society, though also concerns about the use of drugs to treat unhealthy lifestyles. And though this cannot be established from the data presented (with methodological reflection required here – see limitations section below), it also may have had (and continue to have) impacts on if and how patients use the drugs (see Matthews et al., 2016). Moreover, the prescription of the drugs by GPs is highly disparate. This lack of uniformity reflects a variety of diverse organisational factors and cognitive aspects that impact if and how GPs (who act as gatekeepers of pharmaceuticalisation) approach and attempt to facilitate decision-making. The distributed nature of decision-making over various knowledges, evaluations and interactions, and as such, the overall pharmaceuticalised orientation of GPs, which though not considered properly to date within the context of the pharmaceutical regime, features as one aspect, in a more broadly distributed picture of decision-making, in certainly if and how patients are offered and prescribed a statin.

As this discussion indicates, the extent of pharmaceuticalisation clearly reflects an overall network of organisations, actors, and aspects of cognition. Indeed, if healthcare is viewed as an arena of competing and contending organisations and actors all attempting to establish their vision of healthcare delivery (Light, 1997), interestingly in this case, the print news medium and GPs seem to act at least partially as a countervailing power (Light, 1997; 2010b) to NICE (and as such to the pharmaceutical industry). The degree to which these actors take up this mantle is greater, it seems, than it is in other cases where commercial interests seem to have won out (Busfield, 2010; Gabe et al., 2012) (with commercial interests having little direct importance in this case, of course). Though these actors do not prevent the expansion of the opportunity for pharmaceutical deployment in this case, they have certainly limited its extent to date. Additionally, and importantly, the narrative of individual responsibility for living healthily holds a fairly unique level of importance in the analysis of statins. Lifestyle change and associated moral narratives/understandings exist outside of the pharmaceutical regime but they uniquely intercede with and shape the regime and its actors in this case, highlighting the importance of looking at the expansion and potential contraction of pharmaceuticals as part of broader therapeutic landscapes (Pollock and Jones, 2015). Overall, though the pharmaceuticalisation of the primary prevention of CVD is expanding overall, when looking across the case as a totality, and when looking at different dimensions of pharmaceuticalisation, there are aspects of resistance in both rhetorical and clinical ways that indicate that pharmaceuticalisation is constrained overall here.

7.4 The Explanatory Power of Pharmaceuticalisation

As discussed above, this thesis has established underappreciated actors in the Williams et al (2011a) pharmaceuticalisation conceptual framework and in the subsequent empirical work utilising their framework that has required further exploration. However, this thesis has also established, alongside the body of other empirical work already available in pharmaceuticalisation studies, that the conceptualisation and analytical framework of pharmaceuticalisation offered by Williams et al. (2011a) offers a strong, dexterous and diverse framework for analysing the widening use of medicines. Of the three dimensions of pharmaceuticalisation established as relevant to the case of medicalised pharmaceuticalised under study in this thesis, it was possible for the

empirical research presented in this thesis to examine the explanatory power of the contentions of each dimension, whilst also identifying new empirical directions and findings. Even where actors such as NICE have been ignored in the pharmaceuticalisation literature, the dimensions of the framework have sufficient depth and articulate and capture core issues in such a way that it was possible to reorient, for example, the regulatory dimension to focus on a new actor whilst tying into broader issues identified in the dimension e.g. of dependency on the pharmaceutical industry.

As was explored above, the research showed the existence of regulatory closeness to and dependency on the pharmaceutical industry. It also highlighted the oscillating tone and nature of news coverage – and though creating a sense of rampant widening availability and use of statins also fostered uncertainty and controversy. The thesis, though focusing on professionals rather than patients, has also shown how identities and moral positions are developed and adopted relating to pharmaceuticals. As part of this, it has also broadened understandings of the clinical approaches and professional dynamics involved in widening pharmaceuticalisation – with professionals, though under-appreciated, nevertheless noted by Williams et al. (2011a) as retaining importance in decision-making about drugs. Such aspects as explored in this thesis are core component parts of the three relevant dimensions of pharmaceuticalisation established by Williams et al. (2011a).

However, some caution about the generalisability and suitability of this study for evaluating the conceptualisation and empirical framework offered by Williams et al. (2011a) is necessary. Though the same group of scholars has recently made clear that pharmaceuticalisation can grapple with expanding medicines use in both medicalised and unmedicalised contexts (Coveney et al., 2019), as discussed in Chapter One, there are important distinctions between medicalised and non-medicalised pharmaceuticalisation – most notably the different types of actors that are implicated. As such, this thesis can only provide empirical verification of the dimensions and regime approach of the Williams et al. (2011a) framework within the context of medicalised pharmaceuticalisation.

7.5 Limitations and Opportunities for Further Research

As this chapter makes clear, the approach taken in this thesis has successfully allowed for an examination of the overarching research question as concerned with driving forces and extent within and across multiple dimensions of pharmaceuticalisation. In addressing the actor-specific sub-research questions, it has also contributed to understandings of previously peripheral actors within the process. However, this section of the chapter considers certain limitations to the research presented in this thesis, the potential for future research that may be able to address some of these limitations, as well conceptual considerations and research necessary to fill remaining knowledge gaps that exist in the general body of work on pharmaceuticalisation.

This thesis has been concerned with the overarching aim of examining the driving forces and extent of the further pharmaceuticalisation of CVD. But are there limitations to this conceptual approach? This aim reflects the centrality of the notion of the pharmaceutical regime and the dimensional approach to the conceptualisation of pharmaceuticalisation as presented by Williams et al. (2011a). As the authors themselves state (Williams et al., 2011a: 721) "the extent of pharmaceuticalisation will…vary from case to case and depends on the context and the interplay between particular sets of actors in any one case." Their framework, in other words, intends analysis to explore how action in relevant dimensions of their six dimensions of pharmaceuticalisation shapes the overall extent of its occurrence. However, from the existing body of pharmaceuticalisation literature and the dynamics highlighted by this thesis, it is not clear that there can ever be a case of 'full' or 'complete' pharmaceuticalisation. Indeed, research within the sociology of pharmaceuticals, even in work prior to the delineation of pharmaceuticalisation, has consistently identified constraints and different forms of resistance to pharmaceuticalisation in specific and general cases across different dimensions (see Gabe et al., 2012; Pound et al., 2005), and even within different CVD regulatory and usage contexts (Will and Weiner, 2015). This thesis has also itself identified aspects of resistance through detailed consideration of the diverse factors that comprise disparate professional understandings and approaches to further CVD pharmaceuticalisation. Some of these aspects (e.g. resistance to use of clinical guidelines) have reach far beyond CVD pharmaceuticalisation and reflect the perspectives and actions of a professional group who have otherwise been largely assumed to foster pharmaceuticalisation (Busfield, 2010). But how significant is this issue of the potentially necessarily incomplete extent of pharmaceuticalisation? The Williams et al. (2011a)

framework does not debate or rule out that the pharmaceuticalisation of a case or disease area could be full or complete. If and when conceptual advancement occurs (the authors have more recently themselves discussed the possible need for a pharmaceuticalisation 2.0 – see Gabe et al., 2015), the question of whether a disease area can ever be fully pharmaceuticalised could certainly be given more consideration. This could be considered as part of a broader reassertion of the centrality and importance of the notion of the pharmaceutical regime so that more empirical work, as noted earlier, utilises the regime approach and examines multiple dimensions and their relationships between dimensions when analysing cases of pharmaceuticalisation. However, as the framework stands, this issue of necessarily limited extent is far from fatal. Looking across the dimensions of the pharmaceutical regime and assessing the potential and variable expansion and/or contraction of pharmaceuticalisation in relevant dimensions will successfully expose differential degrees of pharmaceuticalisation across these dimensions in specific cases/disease areas. Exploring the extent of pharmaceuticalisation thus remains an important empirical aim and can illuminate how pharmaceuticalisation might be expanding and/or contracting across multiple dimensions and the overall extent, though perhaps necessarily partial, that this amounts to.

Beyond these conceptual concerns, this thesis has some empirical limitations. First, the research, though employing document analysis, might have interviewed more widely than solely NICE-related participants for the analysis presented in Chapter Four. It might have interviewed both prominent statins critics and prominent researchers involved with the construction of the evidence base over time to explore further its nature and search for any insights not available in published literature and documentation. Clearly also an ethnographic study of the process of developing CG181 would also have allowed the researcher access to the dynamics of guideline development and to further evaluate, for example, the considerations given to the limitations of the statins evidence base. This was not possible because the researcher had not yet begun this doctoral research. Going forward, as NICE reassess their guidance and potentially further widen CVD pharmaceuticalisation, with wider use of statins and/or other drugs, observational research of this process would be a strong addition to the pharmaceuticalisation literature allowing primary access to the dynamics of guideline development.

The analysis of newspaper reporting and the understandings and approaches of GPs are valuable contributions to understandings of CVD pharmaceuticalisation and help fill in the picture of decision-making about statins. However, from the data collected and the analysis presented, it is not possible to connect the rhetorical aspects of pharmaceuticalisation in the newspaper reporting or the understandings and approaches of professionals to how newspaper coverage or clinical dynamics were received by and impacted on patients. In this regard, the understandings of the dynamics of the pharmaceutical regime in the case under study remain partial. In short, the inclusion of patient perspectives (or even a more generalised lay voice) would have helped facilitate the linking of the dimensions of pharmaceuticalisation within the pharmaceutical regime and thus in examining the extent of the further pharmaceuticalisation of CVD.

The decision not to collect data on patient understandings, identities and usage and particularly about if and how doctors featured in their decision-making about statins at the new lowered threshold was partly enforced by access issues and the demands of the high volume of other evidence considered within this thesis. However, as has been explored at length this decision also reflected the need to redress the analytical focus which has largely excluded professionals from the analysis of pharmaceuticalisation despite evidence suggesting they retain their importance in the shaping of patient decision-making about statins (Will and Weiner, 2015). Whilst a significant body of work already exists on patient identities, understandings and usage of drugs in medical and sociological literatures, and, indeed, on statins specifically (Polak, 2017; Will and Weiner, 2015), it would nevertheless have been insightful to explore if and how exactly professional advice featured in patient (distributed) decision-making about statins. What remains missing is analysis of if and how exactly professionals feature in the development of patient understandings of pharmaceuticals and the decision to become and remain pharmaceuticalised. The research in this thesis has shown the disparate approaches taken by GPs, but further research is required to establish the actualities of the impacts on patient decision-making (which is likely to be distributed across a wider variety of factors (Rapley, 2008)). It seems likely that in a context of continuing trust, albeit conditional trust, in professionals (Calnan and Rowe, 2008) and muted consumerist tendencies in CVD prevention (Will and Weiner, 2015), that disparate professional approaches and pharmaceuticalised orientations will have differential impacts on patient

decision-making. Nevertheless, empirical verification is required to assess this professional positioning in the configuration of understandings, identities and use. Further research would need to take the form of interviewing patients about the influence of their doctor within the picture of decision-making about drugs. Though methodologically challenging, observational work of the doctor-patient relationship (perhaps in combination with qualitative interviewing) would also allow unique exploration of the clinical dynamics involved in pharmaceuticalisation. It would enable analysis of if and how the reported approaches of GPs emerge in consultations and the place of professional pharmaceuticalised orientations in decision-making about statins.

Another limitation of the research is the lack of audience perspectives on the newspaper coverage analysed. From the data presented the research is unable to connect the themes identified in the data analysis to the impacts on audience reception (particularly by patients or future patients) and thus the impacts of the coverage on understandings and use. Whilst this thesis has revealed the state and stage of newspaper coverage of statins, understanding of the pharmaceutical regime in the case under study remains partial in this way. To complete understandings of the dynamics and manoeuvrings of the pharmaceutical regime and thus to assess more effectively the extent of the further pharmaceuticalisation of CVD, alongside professional impacts on patient understandings and use of statins, further research should examine the place of newspaper and other media representations within the configuration of perspectives about statins. In particular, how do lay audiences interpret the historical coverage examined in this thesis and/or any further coverage of statins and the CVD therapeutic landscape? This could be done alongside the recommended exploration of the doctor-patient relationship to analyse if and how clinical and media coverage features in the decision-making of patients about statins – and in this way complete understandings of the dynamics and interweaved nature of the pharmaceutical regime in this case.

It may also have been prudent to focus on a wider variety of news reporting and other media. Whilst the focus solely on the print news medium has allowed a detailed examination of the media form that covered relevant events to the most significant extent, wider media coverage of this case and surrounding events was also evident and important. Indeed, radio coverage was quite pronounced and featured live debates between opposing camps which in itself actually stimulated further newspaper coverage. Whilst it is unclear that the thematic intricacies would have dramatically altered, it would

have allowed this research to offer a fuller understanding of the mediatisation dimension of the pharmaceutical regime. Indeed, audience consumption of media is, as Seale (2002: 25) suggests, intertextual. By this he means that audience consumption of media is not limited to one story from one medium at a time but is interweaved with a variety of other stories and forms of media. As discussed, this thesis has looked at the thematic intricacies of media portrayals rather than attempting to assess impacts on audiences. However, further research on media and pharmaceuticalisation could attempt to evaluate how different mediums cohere, are interpreted by audiences and, as such, contribute to the configuration of perspectives, necessarily taking into different types of and forms of stories and portrayals about specific drugs but also pharmaceuticals on a more general level. Pharmaceuticalisation analysis also needs to turn to social media to examine the ways new media platforms might be used to share information and offer advice or gain/provide support about pharmaceuticals as well as cohere with or challenge other forms of media. For example, does social media provide a platform to challenge or promote use of statins? Social media (and health information more generally gained from the internet) could also be analysed in relation to patient decision-making about statins and its prominence relatively speaking to interactions with and advice from professionals.

7.6 Concluding Comments

Overall, the primary prevention of CVD has become further pharmaceuticalised – not only in terms of the widened availability but also, as detailed earlier in this thesis, in terms of actually rising numbers of prescriptions of statins since the guideline confirmation, from 63 million units to 66 million units prescribed (Health and Social Care Information Centre, 2016). This research has shown evidence of pharmaceuticalised orientations in a significant group of the sample of GPs interviewed. However, whilst the pharmaceuticalisation of the primary prevention of CVD is expanding overall, when looking across the case as a totality and looking at different dimensions of pharmaceuticalisation there are aspects of resistance in both rhetorical and clinical ways that suggest that pharmaceuticalisation is constrained in these dimensions and thus overall here. This thesis has unpicked some of the forces at play here and has examined the extent of the pharmaceuticalisation of the primary prevention CVD by looking across

what Williams et al. (2011a) call the pharmaceutical regime. Whilst each individual analysis chapter (Chapters Four, Five and Six) has provided insight into the different potential aspects, dimensions and drivers of pharmaceuticalisation, unlike some of the existing analysis of the concept this thesis has, by focusing on different actors in a single case, attempted to look across the networks and relationships that bind organisations, actors and associated cognitive structures together in driving and producing this overall extent of pharmaceuticalisation.

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Appendix 1: Timeline of Events

Date	Event	Date	Event
January 2006	NICE publish technology appraisal 94 establishing the cost effectiveness of statins in primary prevention when a ten year ≥20% primary prevention risk is evident.	May 2008	NICE publish clinical guideline 67 which codifies in clinical guidance the use of statins when CVD risk is ≥20% in primary prevention.
January 2011	A Cochrane review challenges evidence of benefit and cost effectiveness of statins in those with a risk less than 20%. Importantly this did not include a late-2010 meta-analysis by the Cholesterol Treatment Trialists Collaboration (CTT).	February-March 2011	Prof. Collins from the CTT complains to Cochrane about the non-inclusion of the 2010 meta-analysis evidence and about misleading press releases indicating that statins in low risk individuals might do more harm than good.
May 2012	A further CTT meta-analysis published in *The Lancet* suggests statins significantly reduce all-cause mortality and major vascular events in those at low risk.	August 2012	Final NICE guideline scope published for CG181
September 2012	First NICE CG181 GDG meeting held	January 2013	A further Cochrane review is published in 2013 which includes four further clinical trials and the 2012 meta-analysis by the CTT. The conclusion supports the widening of statins to lower risk patients (including ≥10% risk over ten years) without increasing risk of harm.
October 2013-December 2013	Two papers are published in the BMJ, the first by Abramson et al, who dispute the benefits of statins on mortality rates. The second, an 'Observations' piece by Malhotra, suggests issue with the saturated fat and heart disease connection. They also quote observational work	November 2013	Final GDG meeting held

	suggesting that almost 1 in 5 statins users experience side effects. In response, Prof. Collins complains to Fiona Godlee, editor in chief at the BMJ, to complain about 'misleading' claims in the Abramson et al and Malhotra papers days previously and argues that the papers are guilty of rounding up of an adverse effects figure from an observational study from 17.4% to 1 in 5. Collins is offered the chance to formally publish a paper with these complaints, but this is never acted on.		
November 2013	US guidelines produced by expert panels from the American Heart Association, American College of Cardiology and the Obesity Society recommend broadening the primary prevention of CVD to those with a 7.5% ten-year risk (albeit calculated in a different manner than proposed by NICE below).	February 2014	NICE release a draft of their guideline for consultation by stakeholders – announcing publicly for the first time the intention to halve the primary prevention threshold where statins can be offered, from ≥20% to ≥10% risk over ten years. This is accompanied by a high volume of news medium reporting of this case that continues into the autumn.
March 2014	A paper is published in the European Journal of Preventive Cardiology suggesting adverse effects happen just as often on placebo as compared with statins. However, one of the authors, Goldacre, later clarifies these claims following some misreporting, asserting that this result reflects poor reporting of adverse effects in journal publication of trial data.	March 2014	Prof. Rory Collins of the CTT publicly accuses the BMJ of endangering patients with false claims (in the Abramson et al and Malhotra papers) about the safety of statins.

March and April 2014	Correspondence marked 'not for publication' by Collins, continues with BMJ editor Fiona Godlee. Collins continues to dispute the accuracy of adverse effects statistics – suggesting that due to it being an observational study rather than an RCT, there is no evidence to suggest that the noted adverse effects in this study relate to a statin.	May 2014	The BMJ publishes corrections to the misquoted side effects figure in the Abramson and Malhotra articles.
May 2014	An Independent Statins Review Panel is announced to consider whether one or both articles should be retracted and to review the BMJ's publication process.	June 2014	An open letter to NICE is published urging withdrawal of impending guidance until data are made independently available.
July 2014	NICE publish the final guideline CG181 replacing CG67 and TA94.	August 2014	The Independent Statins Review panel decides, as per Committee on Publication Ethics code, that the Abramson et al and Malhotra papers do not need to be retracted. The panel also adds to calls for data to be made available for independent review.
October 2014	Pulse magazine (a publication aimed at GPs) release a survey of more than 560 GP respondents suggesting that 66% are refusing to prescribe statins at the ≥10% risk threshold recommendations.	October 2014	CTT members write to Committee on Publication Ethics (COPE) (who's retraction policy was the standard utilised by the Independent Statins Review panel established by the BMJ) to complain about the BMJ's handling of the Abramson et al and Malhotra papers and overall editorial policy (correspondence between the CTT and the BMJ via COPE continues throughout 2015).
January 2015	NICE releases the 2016/2017 Quality and Outcome (QOF) indicators for stakeholder consultation (QOF is an incentive scheme aimed at standardising care	February 2015	The CTT announce their intention to publish new analysis of statins safety data. This includes requesting unreported/published data that the CTT has thus far not had access to.

	and rewarding contractors for high quality care). Included in this consultation document are two proposed indicators to incentivise the prescription of a statin when a patient also has additional risk factors of diabetes and/or hypertension (QOF IND 10/QOF IND 11).		
February 2015	Chief medical officer for England writes to the Academy of Medical Sciences asking for review of drug evaluation, citing statins as a key example of public trust in science being damaged.	June 2015	NICE decides it will include QOF indicators that reward the treatment of patients in the ≥10% risk threshold with statins. This is despite significant consternation during the consultation period from the Royal College of General Practitioners (RCGP) and the General Practitioners Committee (GPC) and GP members of the Indicator Advisory Committee (IAC). An indicator is also included that rewards lifestyle advice in this patient population.
August 2015	NICE decides not to include an indicator in the QOF incentivising GPs at the ≥10% risk threshold after negative feedback from medical professional stakeholders. However, NICE suggests they will look at pilot schemes to test indicators relating to the ≥10% threshold.	April 2016	COPE writes to the CTT, drawing a line under the matter, suggesting that the BMJ had acted appropriately in the correction of misquoted side effects figures and in making alterations to its editorial policy.
September 2016	A review paper is published by the CTT in The Lancet univocally asserting statins benefits outweigh risk of harm. However, the CTT still do not have access to all patient level side effect data, access to which is still being negotiated.	September 2016	Several pieces are published in the BMJ again calling for statins data to be made publicly available for independent scrutiny.

November 2016	A paper by Malhotra et al is published in *Prescriber* calling into question some of the analysis published in September by the CTT, maintaining early critiques (e.g. by Abramson et al 2013) of efficacy, side effects, and the influence of the pharmaceutical industry.

Appendix 2: List of Codes

All codes presented in alphabetical order within their themes and subthemes

Chapter Four Codes:

The Influences of the Pharmaceutical Industry on the Statins Evidence Base

Benefit in Primary Prevention

Access to and type of evidence used – benefit
CTT influence/presence
Conflation with NICE's evaluative work – benefit
Difficulty/problem in the evidence base or its interpretation
Generalised technical/procedural talk – benefit
Mechanisms shaping appearance of benefit
NICE processes and intended outcomes – benefit
Quality and development of evidence base – assured in participant talk
Statins beneficial – assured in participant talk

The Safety Profile of Statins

Access to and availability of evidence - safety
Adherence and ensuring cost-effectiveness
Conflation with NICE's evaluative work – safety
Generalised technical/procedural talk – safety
Levels and types of side effects
NICE processes and intended outcomes – safety
Mechanisms in and limitations of all evidence – safety
Statins not unsafe – assured in participant talk

The Guideline Development Group and the Pharmaceutical Industry

The GDG and Connections to Industry?

Financial or other benefits to GDG members
Industry connections – type/nature
Industry direct gain from this guideline
Nature of evidence appraisal
Nature of GDG process
Public misrepresentation
Robustness of NICE's declarations of interest policy
Subsequent changes to NICE policy

The Next Generation of Drugs

GDG members concurrently involved with industry developing new CVD drugs
LDL cholesterol-lowering agenda
New drug not displacing statins
Normalising low risk means broader use of new drugs
Not violating declarations of interest – lack of direct connection to statins
Searching for next blockbuster drug
Success of new drugs

[REDACTED]

[REDACTED]

Chapter Five Codes:

Size and Significance

Numbers and Types of people
Age
Gender
Halving risk threshold
Large scale expansion
Large scale with many millions of existing patients

Scale of CVD Problem
CVD levels/morality rates
Lives saved

Financial Cost
Low cost that is good for the NHS
Low cost to the NHS
Use of clinical time and resources
Value questionable

Side Effects: Dangers to Patients?

Types of Side Effect and Extent of Occurrence
Numbers experiencing side effects
Types of side effect

Side Effect Risk Versus Drug Benefits
Poor relative benefit
Positive relative benefit
Professional disunity – side effects

Patient Stories of Side Effects
Personal and family experiences of side effects – negative
Personal and family experiences of side effects – positive

Violations and Uncertainty in the Evidence Base: Conflicts of Interest

Financial Connections Between NICE and Industry
Defence of NICE/GDG
GDG connections to pharmaceutical industry
Public and government confidence
Removal of GDG member
Professional disunity – integrity of NICE/GDG

Manipulation and Misrepresentation of Data

Countercriticism - misrepresentation by statins critics
Expert defence of statins and evidence base
Impacts (data manipulation/misrepresentation)

Pharmaceutical industry manipulation of the evidence
Professional disunity – evidence base

Relative Therapeutic Positioning of Lifestyle Change and Statins

Lifestyle Change Instead of Statins: Too Many Drugs
Morally problematic because encourages pills instead of lifestyle changes
Not tackling CVD causes
Wrong patient message

Combined Therapeutic Landscape

Actualities of evidence and NICE guidance on combined approach
Lifestyle changes and drugs complementary
Not a substitute

Independent Statins Benefit
Hard to achieve sufficient lifestyle changes
Statins justified/necessary in some cases

Chapter Six Codes:

Use of Guidelines and Other Knowledges

The Acceptance and Necessity of the Scientific-Bureaucratic Model
Acceptance of population-level benefit logic
Based on best available evidence – guidelines in general
Broad nature of general practice – guidelines in general
Clinical judgement important in application of guidance
High volume of evidence
Presentation of knowledge of specifics of CG181
Statins safe as confirmed by best available evidence
Uniformity in practice – guidelines in general
Widening use of statins will be beneficial

Clinical Autonomy and the Rejection or Resistance to Collectivised Logics
Clinical discretion and clinical autonomy devalued by guidelines
Concern about evidence – use in elderly
Concern about population level logic – balancing individual benefit and potential for harm
Importance of clinical experience
Individual circumstances – guidelines not translating
Medico-legal concerns
Practicing outside of guideline
Reluctantly following the guideline

The Salience of (Dis)trust in NICE?
Familiarity with prescribing statins
Motives and influences of pharmaceutical industry
No profit motive – drugs generic
Own ability/knowledge to evaluate evidence
Trust in specialists/experts
Trust in NICE's processes

Interactions with Colleagues
General reflection on practice with colleagues

Negative interaction with colleagues
Positive interaction with colleagues
Reflection on CVD/treatment landscape with colleagues

Treatment Orientation

Unified Therapeutic Landscape
Complimentary benefit
Combined approach convincing to patients
Lifestyle changes prior to statins
Statins not a replacement for lifestyle changes

Promoting Lifestyle Change: Individual Responsibilities and Overall Health Benefit

Broader health benefits from lifestyle changes
Guideline drug centred
Statins encourage lack of self-responsibility for health
Support patients to change lifestyle to avoid statins – professional responsibility

Independent Statin Benefit and Moral Neutrality
Application of best available evidence – morally neutral
Benefits of lifestyle changes not necessarily clear
Considers practice to be following the guideline
Difficulties associated with making lifestyle changes
Social structures shaping lifestyle choices
Statins independently beneficial

Decision-Making Over Time
Lifestyle change successes – evaluate over time
Review of adherence and tolerance distributed over time
Statins still likely to be necessary even after period of lifestyle change

Evaluation of Relevant Information: Ethical and Personalised Evaluations

Ethical Evaluations
Do not want to cause emotional harm to patients
Ethics of discussing recent guidance change
Necessity of shared decision-making – ethical practice

Personalised Evaluations
Importance of level of risk within threshold shaping treatment approach
Individual health circumstances of the patient shapes treatment approach
Prior knowledge about patient drawn on
Relevant lifestyle factors of the patient shapes treatment approach

Appendix 3: Approach to Theme Development

Sample 1 The Guardian, 11th June 2014:

The eight doctors say they do not believe the benefits of statins outweigh the side effects. – *Poor relative benefit,* ***Side Effects: Dangers to Patients? (Side Effect Risk Versus Drug Benefits)***

The doctors point out that all the trial data comes from pharmaceutical industry trials, which have not been put in the public domain. The over-dependence on industry data raises concerns about possible biases. Extensive evidence shows that industry funded trials systematically produce more favourable outcomes than non-industry sponsored ones, they write. – *Pharmaceutical industry manipulation of the evidence,* ***Violations and Uncertainty in the Evidence Base: Conflicts of Interest (Manipulation and Misrepresentation of Data)***

NICE says the draft guideline does not propose that GPs automatically prescribe pills. Barker says doctors and patients should explore the options for stopping smoking, losing weight, eating more healthily drinking less alcohol and becoming more active. – *Lifestyle changes and drugs complementary,* ***Relative Therapeutic Positioning of Lifestyle Change and Statins (Combined Therapeutic Landscape)***

Sample 2 The Daily Mail, 18th July 2014

The known side effects include type 2 diabetes and severe muscle pain – *Types of side effect,* ***Side Effects: Dangers to Patients? (****Types of Side Effect and Extent of Occurrence)*

and there is also evidence that patients regard the pills as an excuse to lead unhealthy lifestyles. – *Morally problematic because encourages pills instead of lifestyle changes*, **Relative Therapeutic Positioning of Lifestyle Change and Statins (*Lifestyle Change Instead of Statins: Too Many Drugs)***

Guidelines issues by NICE today tell GPs to consider prescribing statins to anyone with a 10 per cent risk of developing heart disease within a decade (generally people over 40). Currently, they are offered to patients with a 20 per cent risk. – *Halving risk threshold,* ***Size and Significance (Numbers and Types of People)***

NICE estimates that between five and ten million adults are currently taking the drugs although 12.5 million are eligible – *Large scale with many millions of existing patients,* ***Size and Significance (Numbers and Types of People)***

But under the new guidelines another 4.5 million would qualify. This means that 17 million adults - nearly of the 37 million adults in Britain - would either be on statins or offered them. – *Large scale expansion,* ***Size and Significance (Numbers and Types of People)***

…Professor Mark Baker, director of the Centre for Clinical Practice at NICE, said: 'Statins are safe and effective – *Positive relative benefit* ***Side Effects: Dangers to Patients? (Side Effect Risk Versus Drug Benefits)*** and now they are cheaper, it is a good deal for more people to have access to them under the NHS – *Low cost that is good for the NHS,* ***Size and Significance (Financial Cost)***

The overwhelming body of evidence supports their use, even in people at low risk of cardiovascular disease –. The effectiveness of these medicines is now well proven. *Expert defence of statins and evidence base*,

Violations and Uncertainty in the Evidence Base: Conflicts of Interest (Manipulation and Misrepresentation of Data)

and their cost has fallen – *Low cost to the NHS,* ***Size and Significance (Financial Cost)***

Appendix 4: Quoted Documents from Analysed Documents (Chapter Four)

Abramson, J.D., Rosenberg, H.G., Jewell, N. and Wright, J.M. (2013) Should people at low risk of cardiovascular disease take a statin. *BMJ, 347: f6123.*

Collins, R., Reith, C., Emberson, J., Armitage, J., Baigent, C., Blackwell, L., Blumenthal, R., Danesh, J., Smith, G.D., DeMets, D. and Evans, S. (2016) Interpretation of the evidence for the efficacy and safety of statin therapy. *The Lancet, 388(10059): 2532-2561.*

Fahey, T. and Smith, S.M. (2014) Retraction of statins article is not in the public interest: better characterisation of benefits and risks is crucial. *BMJ, 348: g4028.*

Goldacre, B. (2014) Meta-analysis of side effects of statins shows need for trial transparency. *BMJ, 348: g2940.*

Malhotra, A., Abramson, J., de Lorgeril, M. and Sultan, S. (2016) Opinion: More clarity needed on the true benefits and risks of statins. *Prescriber, 27(12): 15-17.*

Malhotra, A., Apps, A. and Capewell, S. (2015) Maximising the benefits and minimising the harms of statins. *Prescriber*, *26(1-2): 6-7.*

McPherson, K. (2014) Concerns about the latest NICE draft guidance on statins. BMJ, 349: g4130

McPherson, K. et al. (2014) NICE should be independently investigated in relation to its systems designed to deal with conflicts of interest of its guideline development group panels. [Online] Available at: https://www.nice.org.uk/Media/Default/NewsItem/NewsArticleImage/Letter-Mulholtra-et-al-to-HSC.pdf. [Accessed 7th May 2017]

Medicines and Healthcare Regulatory Agency (MHRA) (2014) Statins: benefits and risks. [Online] Available at: https://www.gov.uk/drug-safety-update/statins-benefits-and-risks. [Accessed 1st June 2017]

National Clinical Guideline Centre (NCGC) (2014) Lipid Modification [Online] Available at: https://www.nice.org.uk/guidance/cg181/evidence/lipid-modification-update-full-guideline-pdf-243786637 [Accessed June 5th 2017].

Taylor, F., Ward, K., Moore, T.H., Burke, M., Davey Smith, G., Casas, J.P. and Ebrahim, S. (2011) Statins for the primary prevention of cardiovascular disease. *Cochrane Database, 1(1) DOI: 10.1002/14651858.CD004816.pub4*

Thompson, R. et al. (2014) Concerns about the latest NICE draft guidance on statins. [Online] Available at: https://www.nice.org.uk/Media/Default/News/NICE-statin-letter.pdf. [Accessed 7th May 2017]

[REDACTED]

Appendix 5: Quoted Newspaper Reports from Analysed Data (Chapter Five)

Aaronovitch, (2014) Taking statins won't make me a couch potato. *The Times*, 19th June 2014.

Anon, (2015) Apples or nuts as effective as statins. *The Daily Telegraph*, 20th January 2015.

Anon (2014) Be wary of statins pressure. *The Sunday Express*, 2nd March 2014.

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Appendix 6: NICE Participant Information Sheet

Purpose of the Research

The purpose of this PhD research is to explore the development, implementation and understandings of recent National Institute for Health and Care Excellence (NICE) guideline (CG181) on cardiovascular disease risk assessment and reduction, including lipid modification, instigated in 2014. With a particular focus on notions surrounding primary prevention, members of the guideline development group for CG181 and members of NICE staff with a role related to or in the production of the guideline are being asked to participate in an interview so as to examine the processes of development surrounding the guideline, the use of evidence, the place of statins in the preventative therapeutic landscape at the new 10% risk threshold, and the understandings of uncertainty/controversy surrounding CG181. In other parts of the research, the extent to which the new guideline has thus far impacted on and been utilised in the actualities of clinical activity is also being analysed.

Benefit of the Research

The study will be beneficial because it will:

- **Highlight in detail the processes of NICE guideline development and the specifics of CG181. This will be of interest to the sociological community and the general public.**
- **Highlight the underpinning rationale for expanding the primary prevention risk threshold by those involved in the development of the guideline, the use and strength of the evidence, and the intended therapeutic balance between statins and lifestyle change**
- **Provide evidence into the extent of implementation of the guideline by GPs (the analysis of which can be made available for NICE's use)**

Research Organisers

Interviews with GPs will form part of the doctoral research of PhD candidate Tom Douglass in the School of Social Policy, Sociology and Social Research (SSPSSR) at the University of Kent. The research is being supervised by Professor of Medical Sociology Mike Calnan and Dr. Joy Zhang both of SSPSSR at the University of Kent. **The researcher has accepted no attached external funding for the project or has any financial ties to any entity, reflecting the fact that this research is being conducted for the purposes of doctoral studies**.

What's Involved?

The duration of participation in the research will be one roughly 45-60 minute qualitative interview conducted at the discretion and convenience of the participant. This can take place either in person in time and place convenient to the participant or via the phone. **The interview will be audio recorded for the purposes of data collection and analysis (with permission).** Participants will be given a period prior to the commencement of the research to (re)consider their participation and ask any questions.

Do I have to take part?

It is entirely up to you to decide whether to join the study and you are free to withdraw at any time, without giving a reason and without consequence. Before you make a final

decision, the researcher will describe the study and go through this information sheet. If you agree to take part, you will then be asked to sign a consent form.

Ethical Clearance and Confidentiality

The research follows all ethical protocols set out by the SSPSSR department at the University of Kent, and the British Sociological Association. The research has received clearance through the SSPSSR Research Ethics Committee.

Following data collection all interviews will be anonymised and no personally identifiable data is retained or utilised in the study or saved afterwards. It is important to note that, though all responses will be treated anonymously and should not be identifiable to anyone but the researcher, certain members of staff at NICE and those involved in the guideline development group can be considered public figures. Thus, whilst no names, identifiable job descriptions or specifics of involvement will be listed at any point, it may still be possible for readers with specialist knowledge to ascertain which participants have been interviewed. By signing the consent form you declare that you accept this scenario.

During the course of the research, the data will be stored on secure servers at the University of Kent and no one but the research team will be allowed access to the data. Following the completion of the research all electronic recordings will be destroyed and transcripts will be archived securely.

Feedback

The researcher is happy to provide anonymized interview transcripts as well as copies of resulting publication upon request. The researcher is also willing to prepare a short report or presentation on the implementation of the guideline by GPs, if sufficient interest is declared by NICE or anyone involved in the development of CG181.

Contact Details

Any questions about the research can be submitted to:

- Tom Douglass via email on td216@kent.ac.uk.
- Professor Mike Calnan on M.W.Calnan@kent.ac.uk.

If you remain unhappy and wish to complain formally contact:

- The University of Kent's Director of Research Services, Simon Kerridge via email on directorofresearchservices@kent.ac.uk, who will conduct an investigation and respond.

Thank you for reading this information sheet and considering participation in the research.

Appendix 7: GP Participant Information Sheet

Purpose of the Research

The purpose of this PhD research is to explore the framing, perceptions, clinical approach, and understandings of the therapeutic aims presented in recent National Institute for Health and Care Excellence (NICE) guideline (CG181) surrounding lipid modification and the primary and secondary prevention of cardiovascular disease, instigated in 2014. With a particular focus on notions surrounding primary prevention, GPs are being asked to participate in an interview so as to examine expert understandings of the latest guideline, how statins are located in the wider therapeutic landscape relating to cardiovascular disease, as well as to assess the extent to which the new guideline has thus far impacted on and been utilised in the actualities of clinical activity.

Issues for Exploration and Benefit of the Research

This research will give GPs a platform to present their understandings of a variety of issues relating to CG181. The issues explored will include the utilisation of statins, how statins relate to issues surrounding lifestyle choice/change, the role of relations of trust, perceptions of using pharmaceuticals for low risk primary prevention, approach to consultations with patients and the role of clinical governance and performance management techniques as relating to the case study.

The study will be beneficial because it will:

- **Highlight GP understandings of and the extent of engagement with statins for CVD prevention at the new lower risk threshold and beyond**
- **How statins for prevention are understood and located by GPs in the wider therapeutic landscape (particularly in relation to lifestyle alteration)**
- **The potentially mediating role multidirectional trust (at a variety of levels) plays in the process and the importance of professional expertise in facilitating certain treatment pathways**

Research Organisers

Interviews with GPs will form part of the doctoral research of PhD candidate Tom Douglass in the SSPSSR department at the University of Kent. The research is being supervised by Professor of Medical Sociology Mike Calnan and Dr. Joy Zhang both of SSPSSR at the University of Kent. **The researcher has accepted no attached external funding for the project or has any financial ties to any entity, reflecting the fact that this research is being conducted for the purposes of doctoral studies**.

What's Involved?

The duration of participation in the research will be one roughly 30-45 minute qualitative interview conducted at the discretion and convenience of the GP. This can take place either in person in time and place convenient to the GP or via the phone. **The interview will be audio recorded for the purposes of data collection and analysis (with permission).** GPs will be given a period prior to the commencement of the research to (re)consider their participation and ask any questions about the research.

Do I have to take part?

It is entirely up to you to decide whether to join the study and you are free to withdraw at any time, without giving a reason and without consequence. Before you make a final decision, the researcher will describe the study and go through this information sheet. If you agree to take part, you will then be asked to sign a consent form. You will be given a copy of the signed consent form and this information sheet to keep.

Ethical Clearance and Confidentiality

The research follows all ethical protocols set out by the SSPSSR department at the University of Kent, the British Sociological Association, and the NHS. The research has received clearance through the SSPSSR Research Ethics Committee. The research has also undergone examination by local NHS Research and Development as is required for research involving NHS professionals.

Following data collection all interviews will be anonymised and no personally identifiable data is retained or utilised in the study or saved afterwards. You or your responses will not be in any way identifiable to anyone but the researcher. During the course of the research, the data will be stored on secure servers at the University of Kent and no one but the research team will be allowed access to the data. Following the completion of the research all electronic recordings will be destroyed and transcripts will be archived securely.

Feedback

The researcher is happy to provide anonymised interview transcripts as well as copies of resulting publication upon request. The researcher will also write a report and offer to present research findings at relevant professional meetings.

Contact Details

Any questions about the research can be submitted to:

- Tom Douglass via email on td216@kent.ac.uk.
- Professor Mike Calnan on M.W.Calnan@kent.ac.uk.

If you remain unhappy and wish to complain formally contact:

- The University of Kent's Director of Research Services, Simon Kerridge via email on directorofresearchservices@kent.ac.uk, who will conduct an investigation and respond.

Thank you for reading this information sheet and considering participation in the research.

Appendix 8: NICE Interview Topic Guide

BACKGROUND

Professional role/expertise

Understanding of the role of NICE guidelines in clinical practice

Understanding of NICE processes of guideline development, GDG selection

Specific role of participant

Relationship of NICE guidance with other forms of guidance

CG181 DEVELOPMENT PROCESS/PRIORITIES

Involvement in the production of other guidelines

If so, CG181, typical?

Driving forces and priorities of guideline

Disagreement or disharmony in the production of CG181

STRENGTH/LIMITATIONS OF EVIDENCE

Amount of evidence

Pharmaceutical industry involvement in evidence base

Lack of safety data

Importance of and trust in CTT

Effectiveness of conflict of interest procedures at NICE

Concerns about widening primary prevention

Reaction from public/professionals

THERAPEUTIC LANDSCAPE

Intended balance between statins and lifestyle changes

Professional and patient understanding of balance

FUTURE/LOOKING FORWARD

Impacts of the guideline on health/NHS

Improvements that could be made to process of guideline development

Anything that could have been done differently

Changes/updates to CG181 in the future

Appendix 9: GP Interview Topic Guide

NICE BACKGROUND AND GUIDELINES

Understandings of NICE guidelines

Necessity of following NICE guidelines

Importance in practice?

Managing volume of evidence

CVD BACKGROUND

Statins utility (general level)

Statins already overprescribed?

Importance of lifestyle relatively

FRAMING, UNDERSTANDING AND IMPLEMENTATION OF CG181

Understanding of priorities of guideline

Impacts of professional/public controversy in wider context of case

Enacting the guideline?

Risk testing

Therapeutic balance

Therapeutic advice to patients

What do patient want?

DRIVING FORCES

NICE as trustworthy?

Understandings of role of pharmaceutical industry

Strength of evidence

Quality and outcomes framework and this guideline

Impacts of the guideline

Appendix 10: GP Sample Characteristics

GP ID	*PERSONAL/PROFESSIONAL CHARACTERISTICS [Format: gender; age; approx. (nearest 5) years in practice; position]*	*TYPE*
GP1	Male; 50s; 20; Partner	Resistive
GP2	Female; 50s; 20; Partner	Pragmatist
GP3	Male; 40s; 5; Registrar	Pragmatist
GP4	Female; 30s; 5; Registrar	Pragmatist
GP5	Male; 50s; 25; Partner	Pragmatist
GP6	Male; 60s; 30; Locum	Advocative
GP7	Male; 40s; 10; Partner	Pragmatist
GP8	Female; 50s; 25; Partner	Resistive
GP9	Female; 40s; 10; Partner	Pragmatist
GP10	Female; 30s; 10; Salaried	Pragmatist
GP11	Female; 30s; 5; Registrar	Resistive
GP12	Male; 50s; 20; Partner	Advocative
GP13	Female; 30s 10; Partner	Pragmatist
GP14	Female; 40s; 20; Partner	Resistive
GP15	Female; 40;15; Partner	Advocative
GP16	Female; 40s; 20; Partner	Pragmatist
GP17	Female; 50s; 25; Partner	Resistive
GP18	Male; 30s; 5; Partner	Advocative
GP19	Male; 30s; 5; Salaried	Resistive
GP20	Female; 40s; 15; Partner	Resistive

Appendix 11: List of Acronyms

CCG – Clinical Commissioning Group

CG181 – NICE Clinical Guideline 181: Cardiovascular Disease: Risk Assessment and Reduction, including Lipid Modification

CTT – The Cholesterol Treatment Trialists Collaboration

CVD – Cardiovascular Disease

EBM – Evidence-based Medicine

GDG – Guideline Development Group

KOL – Key Opinion Leader

MHRA – Medicines and Healthcare Regulatory Agency

NCGC – National Clinical Guideline Centre

NICE – National Institute for Health and Care Excellence

QALY – Quality Adjusted Life Year

RCT – Randomised Controlled Trial

SBM – Scientific Bureaucratic Medicine