Psychiatric Genomics and Mental Health Treatment: Setting the Ethical Agenda

*Forthcoming in *American Journal of Bioethics*

Mental illnesses have a substantial impact on global population health. Mental, neurological, and substance-use disorders, which include schizophrenia, depression, and dementia, account for 13% of the global burden of disease (Patel 2013) and this is predicted to rise to 15% by 2020 (WHO 2001). Depression is currently the third largest contributor to the disease burden (Patel 2013) and is projected to be the second largest contributor after ischaemic heart disease by 2020 (WHO 2001). Comorbid conditions often mean the successful treatment of physical illnesses, such as HIV / AIDS, cancer, diabetes, heart disease, will hinge on the effective treatment of mental illness (Prince 2007). Funding of mental health care treatment and research is problematically scarce, as research investment and service provision consistently fail to meet demand. In the UK alone the wider economic cost of mental illness is £105bn annually (Campion et al, 2012), and, in the US, this figures is estimated to be $467bn (Insel 2015), with half of US residents in need of mental health care not being served at all (Lewis-Fernandez et al 2016). Yet a report by the mental health charity MQ revealed that only 5.5% of the UK research budget is spent on mental illness in comparison to 19.6% on cancers, translated to £9.75 invested in research per person affected by mental illness compared to £1571 spent on cancer research per patient (MQ Transforming Mental Health 2015). In the US, the National Institute of Mental Health revealed that in 2006 average expenditure for per person for mental disorders was $1591 compared to $5167 for those with cancer (NIMH, Average Expenditures per Person [1996 vs. 2006]). Moreover, between 2009 and 2011, the National Alliance on Mental Illness reported cumulative cuts of more than $1.8bn from state budgets for mental health services for children and adults living with mental illness (NAMI 2011).

Chronic underfunding as well as limited progress and outcome data in relieving the global burden of mental health has fuelled the re-prioritisation of existing research and treatment strategies (Bhui 2016). Since 2008 the National Institute of Mental Health has prioritised a research agenda that focuses on biogenetic causes for normal and abnormal brain function, emphasising that mental disorders should be thought of as ‘developmental brain disorders’ (Insel 2009). This agenda channels recent developments in psychiatric genomics which examine the genetic causes for certain neurological traits and utilise larger, population-based studies to analyse the prevalence of human genomic variation to detect risk susceptibility towards certain mental disorders (Merikangas 2003, McClellan and King 2010, Gratten 2014). Preventative measures can then be recommended, either through lifestyle changes or targeted psychotropic drug treatments (Seretti and Fabbri 2013). The explanatory, predictive, and preventative possibilities of genomics may encourage a more personalised approach to medicine which enables patients to make health

choices that are more closely tailored to their individual circumstances, thus placing psychiatric genomics research at the forefront of improving mental health outcomes (Insel 2009).

With this growing genomic revolution in psychiatry comes shifting normative parameters for appropriate clinical interventions for mental disorders. Thus far, the ethical discourse has focused overwhelmingly on the challenges arising in conducting psychiatric genomics research (Biesecker and Peay 2003, Mathieu et al 2013), or on rehearsing well-recognised issues that arise when applying clinical genetics practice or direct-to-consumer genetic tests within the mental health context (Appelbaum 2004, Hoop 2008, Newson 2009, Bunnik et al 2012, Hoge and Appelbaum 2014). Yet, as we go on to show, there are significant ethical challenges in translating the findings of these research activities into the clinical and public health contexts.[1] In this paper, we establish an ethics agenda for psychiatric genomics as it relates to both these contexts: we review the main translational challenges, identifying and reviewing three distinct ethical concerns, before outlining a novel research agenda to tackle these issues. Section I examines concerns around genetic essentialism which could inadvertently exacerbate stigma against individuals with mental disorders. Section II discusses the promises of genomic medicine, which raises potential therapeutic consequences of 'genetic responsibility', explored in Section III. Section IV probes how individualised genomic medicine and public health applications of genomic research could together divert attention away from ethical examination of key environmental and systemic factors which contribute to mental illness. Section V outlines the need for an interdisciplinary, clinical ethics research agenda to examine the impact of the genomic revolution on mental disorders research and treatment. We further suggest that biogenetic and genomic research into mental disorder must work in concert with ethically informed, evidence-based therapeutic interventions which do not lose sight of the individual situated within unique environmental circumstances.

I. Genetic Essentialism and Stigma

Biogenetic and genomic research has been used in public health strategies that advocate for greater parity between physical and mental illnesses and to combat stigma (Angermeyer et al 2011). Stigma remains a major barrier to help-seeking behaviour by individuals with mental disorders, as well as their social inclusion within the broader community. Recent anti-stigma initiatives have likened mental illness to a 'broken leg' (Lucy 2012) and other physical illnesses, such as diabetes and cancer (National Alliance for Mental Illness 2009, 1997). Thomas Insel, Director of the National Institute of Mental Health, refers to mental disorder as a 'brain disorder',

[1] The way we use 'public health' in this paper is related, but not co-extensive, with population health research, the latter of which refers to clinical studies that involve the creation and analysis of large-scale, epidemiological datasets. More specifically, we utilise the term 'public health' to denote the practices and strategies used to translate scientific data (including population-wide genomic research) into practical health interventions, for individuals or at-risk population groups.

or ‘disorders of specific brain circuits’ (TedBlog 2013). These campaigns stress that the individual is not to blame for their mental illness and, in theory, biogenetic explanations help reduce attributions of voluntary choice, culpability and guilt; challenging the view that personal weaknesses and failings cause mental disorder, social exclusion and rejection of those who have mental illnesses should decrease as a result (Angermeyer et al 2011).

However, this hypothesis has not been borne out in practice. The dubious success of biogenetic explanations to combat stigma is attributable to the ways in which assumptions about *genetic essentialism* can sometimes accompany these popular translations of research (Rüsch et al 2010): ‘In a genetic-essentialist view, we are our genes’ (Phelan et al 2013). In this context, genetic essentialism is grounded in the belief that genes determine our species-membership, and our individual identity and characteristics. There are two critical features embedded within a genetic essentialist view: (i) gene determinism (the notion that genes cause species/group/individual characteristics); (ii) categories of homogeneity and difference (the notion that genes underline the distinctions and commonalities amongst us). For example, if genomic research indicates that racial groups differ based on their genes; from a genetic essentialist perspective, then, genes construct individuals as part of a homogenous racial group whilst separating them from other racial groups.

It is important to recognise that genomic research in the scientific field denies essentialist claims, highlighting instead the challenges in clinical and public health translation from ‘bench to bedside’, and from ‘bedside to practice’. Weak rather than strong genetic explanations of mental disorders dominate research results, and complex genotype-phenotype relationships directly contradict genetic essentialist beliefs (Dar-Nimrod and Heine 2011, Rose 2015, Schizophrenia Working Group 2014). Most people conducting research in psychiatric genomics acknowledge the importance of the gene-environment interaction in the aetiology of mental disorders, particularly in two key dimensions (Rutten et al 2013, Uher 2014): first, socio-economic and familial determinants are found to contribute to mental health in important ways. Country of birth, gender, poverty, adverse childhood experiences and stress, can all make individuals vulnerable to disorders (Saxena 2007, Hatzenbuehler et al 2013, Barnett et al 2012, Ehlert 2013, Read and Bentall 2012). Second, research into epigenetics highlights how environmental factors shape gene expression dynamically (Zhang and Meaney 2010, McGowan and Szyf 2010, Sonuga-Barke 2010), further indicating the possible *reversibility* of epigenetic functions (Hunter 2012, Kubota et al 2012). According to Zhang and Meaney, ‘environmentally driven changes in neuronal transcriptional signals could potentially remodel the methylation state of specific regions of the DNA [… which] could, in turn, prove essential for sustained alterations in synaptic function’ (Zhang and Meaney 2010). Thus, research into the macro- to micro-level causes of mental disorder, from global health factors to individual epigenetic responses, all emphasise the close

synergy between environment and genetic influences, such that 'the effects at one level can be only be understood within the context of the other' (Zhang and Meaney 2010).

Yet, popular translations of genetic and genomic research have mixed results: on one hand, these can evoke essentialist views, leading to negative effects for people with mental illness within society: the notion of the human genome as the essence of human life and nature, ascribed with a causal agency that seems to function independently of an individual's will, has gained popular traction (Dar-Nimrod and Heine 2011). Scientific findings are translated as confirming strong genetic explanations for mental disorders, suggesting that assumptions of genetic essentialism are difficult to displace (Dar-Nimrod and Heine 2011). On the other hand, it is shown that public perception about genetic essentialism is decidedly more complex, contradictory, and non-uniform, with numerous factors influencing public attitudes toward genetics, such as educational levels, social and cultural context, gender identity, perceived personal benefits and harms, and applicable practical, clinical and research uses (Condit 2010, Condit 1999). Indeed, analogies of a genetic 'blueprint' are often understood in a probabilistic, non-absolute rather than deterministic manner (Condit 1999, Condit et al 2001).

Condit's research rightfully draws attention to much needed nuance to the issue of genetic essentialism in the public translation of scientific findings. There are nonetheless important ethical consequences which remain from the ways that biogenetic approaches shape understandings of mental disorder and those diagnosed with these disorders. Importantly, Condit does not examine the consequences of biogenetic explanations in the mental health context, though her survey of linkages between race-targeted genetic interventions and health do indicate an increase in lay perceptions of genetic determinism and race-based discrimination even as such strategies are considered useful in accelerating practice-based applications of genomics by medical researchers (Condit and Bates 2005). This dual-edged sword emerges likewise in the mental health context, perhaps understandably given that both ideas of race and mental illness have pre-existing, value-laden connotations which likely impact the interpretation of genetic explanations in such contexts (Condit and Bates 2005). On one hand, it can be seen that biogenetic explanations of mental illness help mitigate public perceptions of personal responsibility, yet simultaneously the same explanations can deepen stigma of individuals with mental disorders in other worrying ways. For example, studies have repeatedly indicated that biogenetic attributions of mental disorder heighten public perceptions of immutability, dangerousness, otherness, and unpredictability, exacerbating social distance and discrimination as a result (Read et al 2006, Schomerus et al. 2014, Pescosolido et al 2010).

These translational issues are not isolated solely to public perceptions but affect diagnosed individuals and their self-perceptions in problematic ways. As well as worsening social stigma, biogenetic framing of mental illness has been shown to generate *self*-stigmatising, negative attitudes amongst individuals diagnosed with mental disorders (Lebowitz and Woo-kyoung 2014,

Rüsch et al 2010). Contrary to the anti-stigma initiatives, isolating the disorder within one's inherited genes, brain, or body, can heighten subjective feelings of guilt, blame, and shame. For example, biogenetic framing of depression, eating disorders, schizophrenia has been shown to entrench assumptions about persistence, chronicity, and prognostic pessimism (Deacon and Grayson 2009, Easter 2012, Lebowitz et al 2013, Rüsch et al 2010). Individuals diagnosed with schizophrenia quite understandably prefer psychosocial as opposed to biogenetic interpretations of their disorder, given that genetic and genomic foci in mental illness has tended to perpetuate public and self-stigma (Holzinger et al 2003). As we will see in the next section, the ethical consequences of genetic essentialist assumptions are not confined to stigmatising ways of understanding mental disorder, but generate pressing ethical issues surrounding its treatment at the clinical level.

II. The Promises of Genomic Medicine

Regardless of its questionable success as an anti-stigma tool, genomics is increasing in prominence due to its potentially transformative approach towards the clinical treatment of mental disorders. The complex aetiology of mental disorders has meant that treatments are often reactive as opposed to proactive. Most individuals are diagnosed and treated once behavioural symptoms of mental disorder emerge, often in an acute phase. As Insel explains, '[t]he good news stories in medicine are early detection and early intervention. If we waited until the heart attack, we would be sacrificing 1.1 million lives every year in this country to heart disease. That's precisely what we do when we decide that everyone with one of these brain disorders has a 'behavioral disorder' – we wait until the behavior becomes manifest' (TedBlog 2013). But genomic medicine can potentially apply the same preventative strategies in place for certain physical illnesses to the domain of mental health care so that interventions take place *prior* to the development of acute behavioural symptoms.

Genomic medicine applies an informational model to ensure that treatment is 'predictive, preventative, personalised, and participatory' (Hood 2011). Using genome-wide associations generated through large population-wide sample collections, genomic medicine can start to identify possible ways to assess and help prevent the development of potential health risks. Molecular markers help indicate early stages of a disease even before symptoms appear. As the Personalized Medicine Coalition state, genomic medicine signals a movement away from reaction to prevention (PMC 2014). Genomic medicine is also 'personalised' in that interventions are intended to be adapted specifically to the genetic make-up of particular individuals. Such personalisation does not necessarily mean new treatments, devices, or drugs that are created specifically for the individual. Rather, clinicians classify individuals into smaller superfamilies or subpopulations with particular molecular markers to indicate (i) reactions to particular

pharmacological treatments and (ii) susceptibility towards certain diseases. In this way, genomics helps concentrate or 'stratify' preventative or therapeutic interventions to those who will benefit (Juengst et al 2012). That clinicians can treat individuals with more precision and fewer side effects as a result of enhanced knowledge about potential reactivity to certain pharmacological treatments does not encourage a more participatory clinical model, since patients still rely on the clinician's expertise. Rather, greater patient participation and individual responsibility emerges with the potential for genomics to identify disease susceptibility. Patients are encouraged to be proactive in informing themselves about their genetic data, making lifestyle, treatment, and health care choices to compensate for genetic risks, and seeking access to appropriate treatments (PMC 2014). The use of genomic data in treating mental disorders can therefore potentially empower patients to make better informed, responsible, autonomous decisions towards their mental health.

But the discourse of empowerment and participation in genomic medicine raises two key ethical issues when applied to treating mental disorders. First, how personal, genetic responsibility is framed requires closer scrutiny, particularly as it could potentially undermine psychosocial therapeutic approaches and the clinician-patient therapeutic alliance: well-recognised features of contemporary mental health practice that are beneficial to patients. Second, the application of genomics to broader public health interventions risks shifting attention away from critical analyses of ways in which inequitable socio-economic, political, and cultural structures can directly impact on mental health care. We discuss these in turn in the next two sections.

III. Recovery and Genomic Responsibility

Closer examination of the narrative of individual empowerment in genomic medicine reveals a double-edged sword: on the one hand, the deterministic bias within genetic essentialism can lead to *subjective* resignation or fatalism towards one's biology, undermining the discourse of individual empowerment within genomic medicine (Lebowitz 2014). There has been a paucity of research focusing on the subjective impact of biogenetic explanation amongst those with a clinical diagnosis of mental illness in contrast to the number of studies exploring the complex picture underlying public perceptions of genetic determinism. As one of the first studies in this area, Easter's 2012 qualitative analysis probed subjective interpretations of biogenetic attributions for eating disorders. Her results confirmed the results of other quantitative studies indicating that, whilst blame and guilt for the disorder diminished when biogenetic explanations were adopted, so too did self-perceived agency in the recovery process. One patient in Easter's study speculated that biogenetics would have 'been an enabler' for disordered behavior, whilst another stated that it would encourage her to say, '"Oh, I can't control this as much. Because, it's biological. It's in my genes. So therefore I can't control it"' (Easter 2012). What these statements reveal is that these deterministic attitudes may not be isolated to *genetic* causal explanations, but likewise

emerge from the *genomic* focus on pathophysiology to identify an individual's risk probabilities of developing certain mental disorders. That particular mental disorders are thought to be heritable could contribute to views that certain outcomes are predetermined, leading to a sense of genetic fatalism. Risk *susceptibility* comes to mean risk *inevitability*, irrespective of their environment or behaviour, thus perpetuating a self-fulfilling prophecy which may inhibit help-seeking behaviour (Phelan 2006, Easter 2012). Prognostic pessimism rather than optimism tends to accompany genetic essentialist assumptions amongst those diagnosed with mental disorder, thereby reducing the motivation to actively engage and contribute to the therapeutic alliance in treatment. Both optimism and active involvement in treatment has been shown to be crucial to constructive outcomes and effective recovery from mental disorder (Meyer et al 2002, Horvath and Luborsky 1993).

On the other hand, with genomic medicine comes a heightened sense of subjective genetic responsibility, as individuals are expected to become informed and act appropriately based on such knowledge revealed through genomic testing. Novas and Rose explain:

> In this process, the subject of the genetic consultation was increasingly addressed as an autonomous individual making informed and responsible choices in a process of self-actualization. This was the individual who was confronted with the range of new choices that developments in bio-medicine had placed before them. Such individuals had to make complex decisions concerning their own life and the lives of their actual or potential off-spring in the light of new genetic knowledges, and in the light of a range of new techniques such as prenatal testing, pre-implantation diagnosis and the abortion of foetuses thought to carry, or potentially to carry, genetic pathologies. The good subject of the genetic consultation thus becomes the individual who will modify their lifestyle responsibly in relation to their genetic risk. […] Thus we can see that the subject that is fabricated in the contemporary genetic consultation is not merely a subject at genetic risk, but also a responsible subject who exercises choice wisely. (Novas and Rose 2000)

In this way, the responsible self in the age of genomic medicine is modelled after the 'rational consumer' who is 'enterprising, prudent, encouraging the conduct of life in a calculative manner by acts of choice with an eye to the future and to increasing personal well-being and that of the family' (Novas and Rose 2000). This model of responsible selfhood encourages individuals to *prevent* the onset of illness through proactive pharmacological treatments, pre-emptive interventions, lifestyle changes, as well as creating an obligation to act in relation to one's family and future, especially since genetics stress heritability of disease from one generation to the next (Novas and Rose 2000). Responsible individuals would volunteer and choose to undergo genetic testing and counselling should other family members have heritable conditions. At present, no

clinical genetic tests can reliably predict whether one will develop serious mental illness, such as bipolar disorder and schizophrenia. Genomic testing can, at best, calculate probabilities of one developing a particular condition based on large population-wide samples (Hippman et al 2013). Some progress has been made in identifying risk alleles (Schizophrenia Working Group 2014) though these are currently too uncertain or poorly understood to assist in genetic counselling (Gershon and Alliey-Rodriguez 2013, Hippman et al 2013). There is nonetheless growing focus on ways that genetic counselling may enable individuals to equip themselves with genomic information about their and their family's risk of developing certain mental disorders (Inglis et al 2015, Gershon and Alliey-Rodriguez 2013).

This model of the self as 'rational consumer' is deeply contestable from an ethical perspective. Of particular importance for our discussion is the way in which its implicit notion of subjective responsibility impacts on the individual's self-understanding as well as the clinician-patient relationship. On the surface, the development of genetic testing and counselling has also been accompanied by the language of autonomy and 'non-directiveness' which means that decisions should be made by the patient based on his or her own values and beliefs. At a deeper level, however, the individualistic turn in genomic medicine suggests that the treatment encounter has an *instrumental function* for the patient: all the necessary information is supplied to the rational consumer/patient, and they make appropriate, prudent decisions based on the probability of risks (Harvey 2010, Juengst et al 2012). This shifts focus away from the treatment itself to how an individual *responds to information*.

In the first place, genomic medicine could potentially narrow the scope of treatments towards mainly pharmacological interventions. Studies have revealed two trends: first, genetic results for a modifiable medical risk or diagnosis have been shown to alter perceptions about how the condition is to be effectively controlled, towards drug-based interventions as opposed to equally, if not more, efficacious behavioural or environmental change (Marteau et al 2004). Second, clinicians were more likely to push for pharmaceutical drug treatment as opposed to psychotherapy when disorders could be attributable to biogenetic causes (Lebowitz and Woo-kyoung 2014). Moreover, individuals could be held accountable for making imprudent, irresponsible, choices following genomic testing. Even as genomic medicine increasingly offers patient-centred choices, there are implicit pressures to be 'prudent'. Should they 'resist their making up as health-creating persons and fail to make the 'right', healthy choices', then they are 'marked out as irresponsible and hence unfit to be self-governing citizens' who may even relinquish their right to healthcare (Harvey 2010). These issues raise further concerns as to whether a genomic approach to mental disorder risks (i) overemphasising pharmacological treatments and (ii) fetishizing a punitive concept of responsibility which, rather ironically, contributes to the blaming, stigmatising attitudes towards those with mental illness. Studies indicate that genetic explanations of mental disorder tend to increase stigma of the disorder and

social isolation and distance of the individual in public perceptions, and more crucially, reduce empathy, understanding, and patience amongst mental health clinicians (Lebowitz and Woo-kyoung 2014). This latter finding is significant, given the importance of a strong, therapeutic alliance between clinician and patient for treatment adherence, social inclusion, and long-term recovery prospects. In sum, with genetic essentialist assumptions, individuals with mental disorders are feared and separate; without them, they are potentially culpable and blameworthy for failing to be proactive in preventing the onset of their disorder.

These problems are symptomatic of a lack of clarity surrounding the compatibility of genomic treatment approaches to current evidence-based, psychosocial treatments for mental disorder. The concept of genomic responsibility is vulnerable to instrumentalising and oversimplifying the therapeutic encounter (Drake et al 2009), and thus conflicts with recovery-oriented, psychosocial interventions in problematic ways. Genomic medicine assumes that individuals have, or are willing to gain, insight into their potential health and associated risk-factors; it assumes that the internal resources typical of the rational consumer are readily available to agents. But these assumptions are questionable for a number of reasons. First, insight might be lacking, simply because behavioural symptoms for certain disorders are often triggered by adversity and stress, combined with subjective difficulties adapting (what researchers call 'resilience') (Davydov et al 2010). Moreover, these assumptions disregard the fact that much of the therapeutic process is aimed towards *precisely* the development of greater subjective insight, self-understanding, self-acceptance, and adaptive agency. In this sense, psychosocial treatments are often reactive, but they also have *intrinsic and developmental*, rather than simply instrumental, functions.

This is captured well in Easter's study when one woman describes the pitfalls of biogenetic explanations of eating disorders:

> I feel like that would lead to people judging you…Like it being an inherent part of you. And just people labelling you as, "Oh. That person is a bulimic person." … it would just kind of in the back of people's heads teach them to make snap judgments about bulimia. And just assume that there's an easy cure… Like it's like a shot. You get a shot. And you're cured. Or just something like that. But bulimia you don't cure it like that. It's thought patterns. And it takes a long time to cure. You have to re-train yourself how to think. And you also have to re-train your behavior how to eat. And it takes time. (Easter 2012)

Moreover, whilst psychotropic drugs have been shown to be beneficial for schizophrenia, research has indicated the importance of accompanying psychosocial interventions in order to address residual impairments in social functioning and help with medication adherence (Bustillo et al 2001, Turkington et al 2006, Westermann et al 2015, LeVine 2012). Psychosocial therapeutic

approaches utilise narrative validation, encourage experiential reflection, and engage in constructive questioning in order to cultivate healthy internal resources amenable towards treatment adherence, long-term recovery, and better social integration. Recognition of an individual's unique characteristics and life experiences is vital for the success of this therapeutic process (LeVine 2012). The interaction requires sustained personal engagement, levels of trust, where therapists are thought to be genuine, non-judgemental, and interested in the unique experiences of the individual (Jung 2015). This enables individuals to situate their disorder within a broader biographical narrative, to help make sense of the self and at times, participate in the reparation of the fractured self through altering ways of thinking, behaving, perceiving others and the world (Singer 2013). In this respect, the therapeutic process itself cumulatively and constitutively facilitates greater self-understanding, empowering individuals so they can assume an active role towards recovery. In treating a variety of disorders, such as depression, eating disorders, personality disorders etc., psychosocial approaches stress the importance of understanding environmental, experiential causes, so that individuals are equipped with adequate coping mechanisms and volitional agency, whilst eschewing self-blaming, self-stigmatising narratives which could undermine these developing volitional skills. In this way, treatment is often a difficult process but also contributes to individuals' sense of achievement, particularly when they recover.

Thus, treatment of mental disorder requires personalised medicine, but not in the way that is championed by genomic medicine. Whereas the personalised dimension of genomic medicine stresses general lifestyle advice and guidance about probable risks based on one's genetic makeup, the general and reductive nature of these therapeutic engagements can undermine the recovery goals of self-understanding and volitional control. The complex aetiology of mental disorders means personalised treatment must consider the complex dynamic between environmental, experiential, and biological factors.

IV. The Importance of Environment in the Public Health Prevention of Mental Disorders

The individualised focus of genomic medicine increasingly makes mental disorder and its treatment a *personal* issue. Though this personalised focus of genomic medicine has been thought to conflict with traditional public health approaches (Khoury 2011), there has been a growing move to explain and justify the central role of public health as a mediator between research and practice at the clinical level. Recent public health approaches work in concert with genomics, integrating and applying large-data, genome-wide association studies and epidemiological analyses to identify key strategies to improve public and individual health (Khoury 2016). Researchers have set the following translational agenda for public health: 1) ensure that genomic technology has a net positive health impact on the at-risk population groups and to serve as an

unbiased intermediary between stakeholders in practice; 2) utilise data collection on health impact to assess the added value or disvalue of personal genomic tests and applications; 3) evaluate population health data sets and determine the benefits of using genomic tools to aid additional data collection on health impact (Khoury 2011). In principle, then, public health approaches have a critical translational role in terms of guiding the future use and application of genomic data for personalised, individual treatment for mental disorder (Gill et al 2010, Moore et al 2011).

But there are ethical concerns associated with this agenda. According to the World Health Organisation, 'mental health and mental illness by and large are viewed as residing outside the public health tradition', largely due to its multifactorial causes which require vectors of health and illness to be conceived more as a spectrum rather than dichotomy (WHO 2001). The difficulty in integrating the mental health agenda within public health has contributed to the continuing lack of parity between mental and physical treatments. It is unclear whether the increasing genomic focus in public health can help address this challenge adequately. In the context of mental disorder, the dual shift towards (i) personalised genomic medicine; (ii) integrating genomics into public health approaches, could together inadvertently shift focus away from the necessary amelioration environmental factors which impact on mental illness. From one direction, genomic medicine 'relocat[es] responsibility for health care away from social and political realms and onto the shoulders of patients', further 'individualising' responsibility for health (Juengst et al 2012). From the other direction, the increasing focus on genomics in public health approaches risks side-lining the socio-cultural-economic aspects of mental disorder further. Yet, numerous studies indicate that barriers to mental and physical health treatment parity relates strongly to environmental issues of surrounding societal stigma, unequal distribution of wealth and resources, and gender inequality. Alongside biological factors, research has revealed that socio-economic factors can also be important contributors to both childhood and adult mental health illnesses. One review study further found that children from socioeconomically disadvantaged families were two to three times more likely to develop mental health problems compared to more advantaged families (Reiss 2013, Shonkoff et al 2012). Links between children developing psychosis or schizophrenia and low socioeconomic households have also been shown (Wicks et al 2005). And, whilst the connection between exposure to physical or sexual childhood abuse and adult psychopathology is well established, there has been indication that this correlation is even stronger in women than in men (MacMillan et al 2001). For example, gender-specific issues, such as violence against women, economic deprivation, limited control over reproductive health, and cultural values were likewise revealed to be important factors in postnatal depression in Goa (Patel et al 2002). Research into epigenetics further substantiates the important influences of *both* biological and environmental factors, where the close interplay between genetic predisposition and socioeconomic and cultural context has been shown to determine the epigenetic expression of genes, and subsequently the onset of mental illness (Zhang and Meaney 2010).

This observation should give rise to caution when promoting the individualised discourse of genomic medicine in its present form within public health forums. In the first instance, the areas of empowerment associated with this type of medicine remain largely unavailable to individuals in certain circumstances: genomic testing and prevention does little to address the deep ethical and political issues associated with children who grow up in socioeconomically deprived families, or women who experience sexual and physical abuse. The discourse of individualised, personalised genomic medicine is risky in that it potentially restricts the focus of public health interventions to the level of whether individuals have access to genomic testing, diverting attention away from pressing systemic issues surrounding gender and socioeconomic inequality which, as major causes of mental illness, demand closer critical ethical scrutiny. Whilst the WHO is optimistic that a public health approach can help achieve the goals of improving global mental health and parity between physical and mental health treatments (WHO 2001), the complexity and depth of this challenge demands an increasingly multifaceted approach which goes *beyond* genomics – one which draws upon normative resources from clinical ethics and political philosophy, as well as those embedded within social scientific research and public health strategies.

V. *Priorities for Future Research*

It is clear that the genomic revolution is becoming increasingly important in the field of mental health as it promises to inform the development of new ways to help prevent and treat mental disorders. Public health approaches have begun to integrate this research into their policy recommendations. This is evidence of a genuine attempt at translating genomic research to the 'bedside' and clinical practice. However, if this research is to be translated in ways that are appropriate and most likely to accrue the putative benefits offered by genomic evidence, the process of translation needs to be complemented by ethics research to examine its potential impact on individuals with mental illness, and how any ethical concerns may be addressed. The discussion above suggests four areas should be prioritised in such ethics research:

1) *Translation*: There needs to be effective, bi-directional translation between genomics and genetics research and mental health practice. Public health approaches are increasingly asserting their role in disseminating and functioning as the mediator of the impact of genomic research on care and treatment pathways for people with mental disorders. But deeper ethical reflection must accompany this chain of communication – from scientific research to public health policy to clinical practice – so that ethical issues which emerge from the clinical practical level of mental health treatment likewise inform the distinct (but sometimes overlapping) agendas of public health and population health genomic research. Clinical ethics research into this process of translation is

necessary to ensure that public health disseminations and clinical interventions (i) mitigate genetic essentialist assumptions and challenge stigma towards particular diagnoses; (ii) maintain the personalised nature of therapeutic engagement with individuals and their particular experiences; (iii) keep sight of crucial socioeconomic structures which require reform to better prevent the development of mental disorders.

2) *The Relationships between Genetic and Psychosocial Models*: Further work needs to be done to examine the complementarity between genomic approaches (including genetic counselling) and approaches shaped by psychosocial models of mental disorder. This is not to suggest that genetic contributions are innately questionable – indeed, the consensus is that further understanding of the genomic basis of serious mental illnesses, particularly in the field of epigenetics, could do much to enhance pre-existing evidence about the close interaction between genetic predisposition, psychological development, and environmental context. However, more research is needed to explore the precise subjective impact of biogenetic attributions, particularly on its impact on conceptions of selfhood, responsibility, and agency which may have important consequences on the therapeutic alliance. Additional work should clarify and critically analyse the differences and similarities between these two approaches, as well as consider ethical issues surrounding the clinical division of labor, addressing practical questions such as whether genetic risk counsellors should liaise with, or themselves be trained to provide, psychotherapeutic treatments.

3) *Clinician-Patient Relationship*: The advent of genomic medicine and its integration in public health approaches generate key ethical questions about the changing nature of the clinician-patient relationship and the therapeutic encounter. There needs to be further ethical examination of what these changes mean to individuals seeking mental health treatment and the normative foundation of the therapeutic alliance which aids successful recovery of mental disorder. Indeed, the genomic revolution may reset the ethical parameters for clinical interventions. Further research is needed to explore how these genomic approaches work at the clinical, therapeutic level, and to ensure that these approaches are ethically sound.

4) *Funding and Resource Allocation*: Mental health research and treatments are critically underfunded in many countries. The growing prioritisation of genomic research and therapies in mental health therefore requires ethical scrutiny and careful justification (Lewis-Fernandez et al, 2016). Further research needs to examine how governments, public health bodies, and mental health agencies should balance the funding demands for innovative genomic medicine and severely under-resourced psychosocial therapies.

Conclusion

Growing developments in genomics has meant their increasing application mental health. Whilst this has some potential benefits there are challenges. If the benefits of genomics for mental health are to be realised and the pitfalls avoided, these challenges, many of which are ethical, need to be identified, analysed and addressed. In this paper we have identified a number of ethical challenges and set out an agenda for a programme of ethics research to complement scientific/clinical research in genomics.

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