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Patient experiences of the burden of using medicines for long-term conditions and factors affecting burden: a cross-sectional survey

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Abstract

Many patients find using medicines burdensome. This paper reports the types of issues people experience with medicines, using a validated measure of medicines burden, and the factors associated with high burden. The cross-sectional study involved patients presenting prescriptions at pharmacies or awaiting appointments at GP practices or out-patient clinics, during October 2015 to December 2016. Adults using at least one regular medicine were asked to complete the Living with Medicines Questionnaire V3 (LMQ-3). The LMQ-3 contains 41 statements rated on a 5-point scale (strongly agree to strongly disagree), with higher scores indicating greater burden, plus a visual analogue scale for self-reporting of overall perceived burden (VAS-burden). For a sub-sample, access to their medication record was requested, facilitating calculation of the complexity of their medicine regimen using the Medicine Regimen Complexity Index (MRCI). Of 1,888 questionnaires distributed, 684 were returned (36.2%) and medication records obtained for 163. The median number of medicines respondents reported using was 4 (range 1 to 26). Two-thirds (418; 67.0%) used medicines more than once daily, 67 (10.1%) required assistance with medicines and 189 (28.3%) paid a prescription charge. LMQ-3 scores showed a strong positive relationship with VAS-burden scores ($r=0.547$; $p<0.001$). LMQ-3 and VAS-burden scores were lower in older age groups, but both increased with increasing number of medicines and dosing frequency. LMQ-3 score was positively related to MRCI score ($n=163$; $r=0.217$; $p=0.005$), whereas VAS-burden was not. Older respondents reported lower burden in most domains. Higher numbers and frequency of medicines, paying prescription charges, needing support and deprivation increased burden across multiple domains. Factors strongly associated with high LMQ-3 scores were: needing support, high dosing frequency and unemployment. Interventions seeking to reduce medicines burden should consider targeting individuals who need support with using medicines, use at least four medicines, more than twice daily and/or pay prescription charges.

Key words: long-term conditions, medicines, patient perspectives, treatment burden, regimen complexity

What is known

- Using medicines for long-term conditions can be burdensome to some individuals and the burden is multi-dimensional.
- Medicines burden is an important factor in patients' experiences of using medicines but has not been measured in general populations.
- Factors associated with high levels of medicines burden could include regimen complexity, which increases with the number of medicines.

What this paper adds

- Medicines burden increases with both number of medicines and regimen complexity, but older individuals report lower burden.
- Needing assistance with using medicines is associated with high burden and paying prescription charges increases burden, particularly in the unemployed.
- Health professionals should consider different aspects of the medicine use experience when reviewing patients' regimes for managing long-term conditions.

Introduction

Polypharmacy, the use of multiple medicines in individuals, is increasing globally, fuelled by ageing populations and increases in non-communicable chronic diseases (Barrett *et al.* 2016). Many patients find using several medicines for long-term conditions burdensome and this burden is multi-dimensional, affected by multiple factors such as medicine formulation, regimen, adverse events, social burden and experiences of healthcare (Krska *et al.* 2013, Mohammed *et al.* 2016, Sav *et al.* 2013 a,b). Polypharmacy is also of growing concern among health professionals and initiatives to reduce over-prescribing are increasing (Bokhof & Junius-Walker 2016, Cooper *et al.* 2015). Polypharmacy is associated with various adverse outcomes, including increased hospitalisation, cognitive impairment, falls and drug interactions (Maher *et al.* 2014, Guthrie *et al.* 2015, Dalwhani *et al.* 2017).

A recent study involving 5,213 patients over 60 years old, found that almost a third used five or more medicines regularly and that increasing polypharmacy was associated with decreasing socioeconomic status (Dalwhani *et al.* 2017).

In 2012 approximately 15 million people in England had a long-term condition, using 70% of the health budget, with higher prevalence in older people and those of lower socioeconomic status (Department of Health, 2012). Estimates suggested in 2018 2.9 million people (4.4%) would have three or more long-term conditions; actual data show 26 million have at least one (PSNC, 2017). A new study estimates the proportion with at least four conditions will be 17% by 2035, being much higher in the elderly (Kingston *et al.* 2018). The requirement for a much greater focus on the management of multi-morbidity is thus clear. National guidance on managing multi-morbidity, issued by the National Institute for Health and Care Excellence in 2017, stated that the overall demands of medicine-taking, or 'pill burden' being unacceptable to the patient is a form of 'problematic polypharmacy' (NICE, 2017). These and other national guidelines (Royal Pharmaceutical Society, 2013) advocate person-centred care, which requires that clinicians determine patients' experiences of using medicines. A patient-reported measure of medicine burden is also essential for assessing the value of interventions aimed at reducing problematic polypharmacy.

The Living with Medicines Questionnaire (LMQ) (Krska *et al.* 2017), developed from the patient perspective, covers eight domains of medicine burden: relationships with health professionals, practical difficulties, interference with daily life, lack of effectiveness, side effects, general concerns, cost and lack of autonomy (Katusiime *et al.* 2018). The LMQ version 3 (LMQ-3) has undergone psychometric testing, has been translated into several languages (Zidan *et al.* 2016) and is being used in both cross-sectional and intervention studies in a number of countries. The instrument could be used to identify those at highest risk of problems from medicine burden who could potentially benefit from interventions, but for this purpose, a cut-point for high burden is needed. The extent to which people experience burden from medicines has not yet been reported, nor have the different aspects of medicine-related burden experienced by different sub-populations. Large-scale surveys are required, ideally involving a wide demographic, and conducted in primary care, where most medicines are used, which would also enable comparisons across countries.

The aims of this study were: i) to quantify the types of issues people experience with medicines which contribute to overall burden, and ii) to assess the socio-demographic- and medicine-related characteristics which are associated with negative experiences of medicine use and high levels of burden.

Methods

Ethical approval

Approval was obtained from the National Research Ethics Service (Ref: 15/SC/0505) together with relevant research governance approvals. Data were collected between October 2015 and December 2016.

Settings

The study was conducted in South-East England in three types of settings: community pharmacies, GP practices and outpatient waiting areas of one local general hospital. These were used to maximise the severity of illness and thus medicine experiences and to capture those who use prescription and delivery services, hence may not visit GPs or pharmacies, in out-patient settings.

Twenty community pharmacies and 20 general practices were selected from NHS Choices website, located in areas with different degrees of deprivation across Kent and Medway. All were contacted in writing inviting them to permit questionnaire distribution from their premises to patients waiting for prescriptions or appointments. A multiple pharmacy company was approached seeking agreement for provision of participants' patient medication records (PMRs), in addition to questionnaire distribution, to enable the complexity of medicine regimens to be calculated without respondents needing to provide full details themselves. Six pharmacies and five general practices agreed to questionnaire distribution only and six further pharmacies, located in areas of differing deprivation, also agreed to provide PMRs with patient consent. A local general hospital out-patient department agreed to permit questionnaire distribution to patients in waiting areas. Seven different out-patient clinics were used, to ensure variation in type of medical conditions and medicines use experiences.

Participant recruitment

Potential participants were adults (18 years or older), using at least one prescription medicine for any long-term disease/condition, living in England. Exclusion criteria were: self-reporting as too unwell or unable to complete the questionnaire (for example because of severe dexterity problems), unable to read English and using only acute prescription medicines.

The study used convenience sampling, approaching as many as possible potential participants present on the day at the time of questionnaire distribution. Patients presenting prescriptions at pharmacies or awaiting appointments at GP practices or out-patient clinics were screened verbally for eligibility and, if eligible, invited to participate. All were provided with free-post envelopes allowing return of the completed questionnaire by post, with the option to complete it while waiting.

In the six community pharmacies which agreed, potential participants were also asked for written consent for the pharmacist to provide an anonymised copy of their PMR for the previous six months. The PMR was anonymised and linked to returned questionnaires using individual codes.

Instruments

The LMQ-3 is a self-completion questionnaire which includes 41 Likert-type statements rated on a 5-point scale (strongly agree to strongly disagree), within eight domains (Katusiime *et al.* 2018). Domain scores are summed to produce a total scale score (total LMQ-3 score) depicting the overall level of medicine burden (range 41 to 205), with higher scores reflecting higher medicine burden. A 10cm visual analogue scale ranging from 0 “no burden at all” to 10 “extremely burdensome” allows self-reporting of overall perceived burden (VAS-burden). A free-text question allows respondents to add further details of their medicine use experiences. Basic demographic characteristics, together with details of the number, type and frequency of use of medicines are also collected.

The 65-item Medicine Regimen Complexity Index (MRCI) quantifies the complexity of any given regimen, by giving higher weightings to dosage forms with complex administration modes, higher dosing frequency and more additional directions (George *et al.* 2004), thus higher MRCI scores indicate greater complexity. Researchers applied this instrument to the regimens derived from PMRs for individual patients.

Data analysis

Data were entered into IBM SPSS (version 22) and subjected to quality checks. Missing data were excluded from analyses (pairwise and/or listwise deletion). Postcodes were used to obtain indices of multiple deprivation (IMD quintiles) using the English IMD 2015 <http://geoconvert.mimas.ac.uk/>. Respondent age and number of medicines were categorised to facilitate sub-group and regression analysis.

Cronbach’s alpha was calculated for the eight LMQ-3 domains to demonstrate scale reliability. Simple descriptive statistics quantifying self-reported experiences with medicine use are reported as proportions of respondents who strongly agreed/agreed, had neutral responses and disagreed/strongly disagreed with each statement. Free-text comments were analysed thematically using a framework approach based on the eight domains of the LMQ-3 and quotations selected which illustrated the burdens experienced within each domain. Medicine regimen complexity was calculated using the method described by George *et al.* 2004. Relationships between characteristics and medicines burden were explored using t-tests or ANOVA for LMQ-3 scores and Mann-Whitney U or Kruskal-Wallis tests for VAS-burden scores. Correlations between number of medicines, LMQ-3 total and domain scores, VAS-burden and MRCI scores were assessed using Spearman’s correlation coefficient. A p value of <0.001 was selected as demonstrating statistical significance, due to the number of tests performed. Standard multiple linear regression (forced entry) was used to explore predictors of overall medicine burden using LMQ-3 total scores (Field, 2013).

Results

Response rates

A total of 1,888 questionnaires were distributed and 684 returned (36.2% response rate). Response rates varied slightly by recruitment source: 80 (36.4%) were returned from GP practices, 275 (29.4%) from out-patient clinics and 329 (44.9%) from community pharmacies. Missing data was low for individual LMQ-3 statements and most demographic characteristics, however 67 (9.9%) did not provide a full postcode and a further 6.7% postcodes could not be matched to a deprivation level. All LMQ-3 statements were completed by 523 respondents which, after allowing for missing demographic data, provided >99% power for multiple regression analysis, using key variables. There were 163 respondents who also gave permission for their PMR to be used to calculate regimen complexity.

Demographic characteristics of the sample

Half the respondents were female (343; 53.2%), the majority were of white ethnicity (596; 89.6%) (Table 1); ages ranged from 18 to 92 years with over two-fifths aged 65 years or over (277; 41.9%). Nearly half the respondents were retired (332; 49.8%). In comparison to the local population the sample was older, the proportion of white ethnicity was slightly lower, and the proportion retired was much higher (Office for National Statistics, 2011).

<<INSERT TABLE 1>>

The median number of medicines respondents self-reported using was 4 (n=652; range 1 to 26). Hyperpolypharmacy (10 or more medicines) was reported by 9.0% (59). Almost all used oral solid dose formulations, with 166 (25.2%) also using other formulations. Two-thirds (418; 67.0%) reported using a medicine more than once daily. Sixty-seven (10.1%) required assistance with using medicines and 189 (28.3%) paid a prescription charge (Table 1).

Effect of socio-demographic characteristics and medicines use on burden

The LMQ-3 total scores were normally distributed: mean 99.7 (S.D. 19.8), range 50 to 173 (maximum possible range 41 to 205). VAS-burden scores were skewed towards the lower end of the scale, with 107 (16.0%) indicating they perceived no burden at all (VAS-burden=0.0). Despite this, the VAS-burden scores showed a strong positive relationship with LMQ-3 total scores (Spearman's $r=0.547$; $p<0.001$).

Neither LMQ-3 total scores nor VAS-burden scores showed any differences dependent on gender, educational level or ethnicity. LMQ-3 scores showed a significant trend towards lower perceived burden in older age groups (Table 2). Unemployed respondents had higher LMQ-3 scores than employed or retired respondents and scores increased with higher levels of deprivation, though this did not reach statistical significance. LMQ-3 score increased with both increasing number of medicines and increasing dosing frequency, but not with formulations used. Respondents needing support with using medicines and those paying prescription charges had higher LMQ-3 scores than those who were independent or received free medicines.

<<INSERT TABLE 2>>

More respondents aged 65 or over self-reported no or low VAS-burden than younger respondents. Other factors affecting self-reported burden (Table 2) showed a similar pattern of characteristics to LMQ-3 total scores, with two exceptions: formulation was not related to LMQ-3 total score and deprivation level showed no clear relationship with VAS-burden score (Table 2).

LMQ-3 scores within the highest quartile of the distribution were categorised as indicating high burden (score >110), while those with scores <88 were categorised as having no burden. Respondents with scores falling in the high burden quartile were significantly more likely to be younger than 65, use medicines more than once daily, require help with using medicines, be unemployed or pay prescription charges (Table 3). The median VAS-burden score for these respondents was 5.25, significantly higher than for respondents in the lowest quartile (0.5) or two middle quartiles (1.7) ($p < 0.001$).

<<INSERT TABLE 3>>

Our a priori hypotheses were that several aspects of medicine burden would relate to age, medicine regimen complexity (numbers, type, frequency) and the need for support using medicines, and that employment status, paying prescription charges and deprivation may affect cost burden (George *et al.* 2004, Sawicki *et al.* 2009, Sav *et al.* 2013, Mohammed *et al.* 2016, Vijan *et al.* 2005).

The number and frequency of medicines used, needing assistance with medicines, paying a prescription charge and age affected scores across multiple domains (Table 4). Deprivation status affected fewer domain scores, employment status only one, while gender, type of medicine, educational status and ethnicity had no significant effect on any domain. Factors affecting any domain were entered into multiple regression analysis which showed that high LMQ-3 total scores were predicted mostly by frequency of medicine use and needing assistance with medicine use, with deprivation status and paying a prescription charge having some effect (Table 5). The number of medicines, age and employment status did not predict higher burden.

<< INSERT TABLES 4 and 5>>

Regimen complexity and burden

For the 163 respondents who completed all LMQ statements and also gave consent for their PMR to be provided, MRCI scores were calculated, which provided a composite measure of medicine number, frequency and formulation.

These data also enabled comparison with the respondents' self-reported number of medicines ($r=0.779$). Within this sub-population, LMQ-3 total score was weakly correlated with both the number of medicines (Spearman's $r=0.194$; $p=0.012$) and MRCI score (Spearman's $r=0.217$; $p=0.005$), although self-reported burden (VAS-burden) was not related to MRCI score (Spearman's $r=0.017$; $p=0.798$). LMQ domains covering interference with daily life ($r=0.266$; $p < 0.001$), general concerns ($r=0.231$; $p=0.001$), side effects ($r=0.162$; $p=0.015$) and cost burden ($r=0.161$; $p=0.022$) showed some association with medicine regimen complexity.

Experiences with medicines, in eight domains

The responses to all 41 statements are shown in Table 6 within the eight domains, along with Cronbach's alpha values. Example results from each domain are described below along with quotations which illustrate these findings.

<<INSERT TABLE 6>>

Practical difficulties

Over 10% reported difficulties getting prescriptions from the doctor (91; 13.4%), getting medicines from the pharmacist (63; 10.8%) or both (38; 5.6%), while 102 (15.0%) put a lot of planning and thought into using their medicines. Higher LMQ-3 scores in this domain indicate more practical problems with the day-to-day management of medicines. Interestingly although domain scores increased with increasing frequency of daily use and needing help with managing medicines, they were higher among respondents aged below 65 years than for older respondents (Table 4). The quotes below illustrate the type of practical problems relating to access affecting working age respondents;

"I run out of meds because I cannot see the doctor, I run out of meds because I cannot get to the chemist. When I change to a different doctor (i.e. I move home) it takes me a long time to get my GP prescribing medicines that my consultant wants me to take... I have to buy medicines on the internet...I can't get medicines prescribed long term for my medical conditions that last for years but come and go." (female, age 54, 6 medicines)

"GP management insist all prescriptions are requested in person at the surgery, the opening times are incompatible with my work hours. Fortunately ...pharmacist has a collection service, so is able to request, collect and dispense on my behalf." (female, age 47, 1 medicine)

Cost-related burden

Although the cost of prescription medicines was not burdensome for the vast majority, and the response to cost-related statements was lower than for the other domains, 137 (27.2%) worried about paying for their medicines, 81 (12.7%) agreed they had to pay more than they could afford and 52 (8.0%) agreed they had to choose between medicines and basic essentials. Scores for this domain were significantly higher, indicating greater cost-related burden, in respondents paying prescription charges (Table 4). Not surprisingly, retired respondents reported lower cost burden (4.96 ± 2.27) compared to those employed (7.22 ± 3.04) or unemployed (7.93 ± 2.38). Respondents aged over 65 also reported lower cost burden (Table 4), while greater cost burden was also associated with higher deprivation status.

The different circumstances which contributed to cost burden are illustrated by these examples:

"Paying for them [prescription medicines] is my biggest problem/worry. I am long term sick and unable to work. Yet don't qualify for free prescriptions. Long term illness should qualify in England." (female, age 39, 3 medicines)

"Currently out of work. I am finding it difficult to pay for 5 different drugs. However I do not wish to be a burden on the government by signing on and claiming benefits" (male, age 34, 5 medicines)

Lack of perceived effectiveness

The vast majority of participants felt that their medicines were working (501; 76.5%) and prevented their condition getting worse (535; 78.8%). Indeed several expressed gratitude, while others indicated the overwhelming benefits:

"As my AEDs [medicines] help control my seizures I am very grateful that they exist. And I just live with the side effects as seizures are harder to have to deal with." (female, age 37, 5 medicines)

"Medications ...are the reason I'm still with the living. Obviously at times I become concerned at the amount I take, then I remember the alternative." (male, age 75, 10 medicines)

However, some (75; 11.1%) were dissatisfied with the effectiveness of their medicines, or felt they did not live up to expectations (53; 7.8%). Higher scores in this domain, indicating less satisfaction with medicine effectiveness, were found in respondents of younger age, using medicines three or more times daily, paying for prescriptions and needing support with medicines (Table 4).

“Have no effect on the amount of pain I am in, which makes my life revolve around pain & depression”
(female, age 63, 16 medicines)

“Not very effective at helping but have been told I cannot try others as the alternatives are not on the NICE list.” (female, age 48, 7 medicines)

Relationships with health care professionals relating to medicines

While most participants reported good communication and relationships with health providers, in terms of their medicine use experiences, some judged that doctor(s) did not listen to their opinions (107; 15.7%). A fifth did not get enough information about medicines from their doctor (140; 20.6%). Younger respondents again showed higher scores than older respondents in this domain, indicating poorer quality relationships while needing help with medicines also resulted in higher scores (Table 4). Many respondents provided additional comments, illustrating their concerns about poor oversight by and lack of trust in doctors:

“Not enough thought is put into side effects of medication and long term effects of constantly being on medication. Doctors have a very much reactive attitude to the future effects and in my experience can rarely be bothered to make you aware of side effects. Their attitude is to take it or leave it but it’s not always such a black or white answer for the patient.” (male, age 34, 2 medicines)

“I don’t feel that I have a GP that I can talk to or who believes or supports me. I have no faith in them now.”
(female, age 54, 9 medicines)

General concerns about using medicines

Over half of participants were concerned about long-term effects of using medicines (369; 54.4%). Other concerns related to potential drug-drug interactions (137; 20.2%) and wanting more say in the brands of medicines used (181; 26.7%), possibly based on experiences with switching brands. Several factors affected this domain, in which higher scores indicate more concerns (Table 4).

“I take many medications for several conditions and I am not sure they always take interactions into account and have had a few reactions to medications...” (female, age 46, 10 medicines)

“I had been stable on a branded medication for over 10 years, but they have just discontinued it. So now I feel anxious that this latest generic will put me back to square one.” (female, age 55, 5 medicines)

Side effects experience

A substantial proportion agreed that they experienced bothersome side effects (120; 17.9%) and that side effects interfered with day-to-day life (130; 19.2%). Indeed 128 (19.0%) agreed that side effects were worse than the problem for which they used medicines. Scores within this domain were higher in those using more medicines, three or more times daily and needing support with medicines (Table 4).

"I am concerned by side effects. Also taking a diuretic is not ideal as I am out working. On the road - no access to a loo. Side effects are the problem of most concern." (female, age 60, 4 medicines)

One participant hinted at the burden resulting from prescribing cascades resulting from medicines being prescribed to counteract side effects of others, a known contributory factor to polypharmacy;

"I worry on a daily basis about the strong side-effects of prednisolone; the personality changes also affect everyone around me. It is annoying because of one medicine I have to take several others to counteract those side-effects..." (female, age 54, 5 medicines)

Interference with day-to-day life

Interference with social or leisure activities was reported by 112 (16.5%) and with daily tasks by 92 (13.6%). Medicines were also perceived to affect social relationships (78; 11.5%) and sexual lives (95; 14.4%). Higher scores in this domain, indicating greater interference with daily life, were related to both number and frequency of medicines use, higher deprivation status and unemployment. Higher scores were also found in younger respondents and people needing support with using medicines (Table 4).

"[Medicines] they make me tired, meaning that I can't get out a lot, have a social life or do a lot of activities. They also make me dizzy, so I often find it hard to be fully focused and present during conversations, making social interaction sometimes challenging... I find it hard to remember to take them and to fit this into whatever activity I am doing, but this isn't really something I can avoid so I just have to get used to it." (female, age 18, 1 medicine)

A few described social stigma associated with using medicines, particularly younger respondents:

"I have to carry a glucose test kit, insulin pen, needles and sugar for hypos. It's often hard to carry the supplies discreetly thus advertising my condition which undermines confidence at times." (male, age 34, 2 medicines)

"Possibly the largest burden is the social effect of sometimes having to take them in public (feelings of shame/guilt/furtiveness at being obviously 'on painkillers', and having to answer questions about what I've just taken)." (female, age 28, 8 medicines)

Patient autonomy/control over their regimens

Many participants reported limited empowerment to alter their medicine regimes to suit their lifestyle. While only 140 (20.8%) agreed they could change their medicine dose, half (244; 50.7%) felt able to change administration times. However, 181 (26.8%) felt they had no choice in whether or not to take their medicines at all. Scores in this domain were highest, indicating lack of autonomy, in respondents who were older, taking more than four medicines and paying for prescriptions (Table 4).

"I am not given choices on medicines and treatments available to treat my symptoms." (female, age 46, 10 medicines)

"Nobody likes to take medicine. But in the circumstances I have to take them to keep myself well under doctors instructions." (male, age 71, 8 medicines)

Discussion

This study reports the burden associated with medicines, measured using the LMQ-3, experienced by a sample of patients from one region of England, using medicines for long-term conditions. It also demonstrates that regimen complexity is, as anticipated, positively associated with burden.

Effect of regimen complexity on medicines burden

Increases in both number of medicines and frequency of daily use were associated with higher overall burden. Formulation type was only associated with self-reported VAS-burden, not LMQ-3 total scores, but contributed to overall complexity of individual medication regimens assessed using the MRCI, which was positively related to burden in a sub-sample of respondents. Other studies have shown that frequency and formulation can affect treatment burden in specific conditions, including diabetes and cystic fibrosis (Sawicki *et al.* 2009, Vijan *et al.* 2005). Medicines complexity may be linked to adherence (Mansur *et al.* 2012) or re-hospitalisation (Willson *et al.* 2014), therefore complexity could prove useful for identifying patients who could benefit from interventions (Hirsch *et al.* 2014). However it must be recognised that even one medicine may prove burdensome for some individuals, as our data shows and has been suggested by others (Mohammed *et al.* 2016, Zarowitz 2011).

Effect of age on medicines burden

Perhaps surprisingly, older people perceived themselves as having lower burden; LMQ-3 total scores, self-reported VAS-burden and all domain scores except autonomy were lower in those aged 65 or over than in younger respondents. It may be that for older individuals medicines are not viewed as a 'burden', but rather a 'necessity' to get through life; several expressed gratitude for the benefits they bring. There may be several explanations for this. Older people may have been taking regular medicines for longer than younger people, thus could have developed routines for managing medicines over lengthy periods. Most older people were retired, therefore medicines would not disrupt work patterns and they may experience fewer interference with social activities than younger people. Older people do not pay prescription charges, hence perceive no cost burden. They may have established better relationships with healthcare professionals or be reluctant to complain. Side effects may have been eliminated or become accepted over time, or weighed against perceived benefits in terms of increased lifespan or symptom reduction. It is of course possible that the lower perceived burden among older people is due to social desirability bias, however the questionnaire was anonymous and returned mainly by post. Alternatively the older population in our sample may under-represent those who are more ill, such as the housebound. It is however interesting that other work using the same instrument in different populations reports similar findings (unpublished data), while a trend showing lesser burden with increasing age was shown among respondents to the Treatment Burden Questionnaire (Tran *et al.* 2012). High satisfaction with health care and a tendency to report positive experiences has also been found in older people (Bowling *et al.* 2012). Further work is needed to determine why older people perceive low medicines burden and if the experiences reported here are typical.

Other factors affecting burden

Unemployment and paying prescription charges were associated with higher overall burden and, not surprisingly, cost burden was most common among those paying prescription charges. Over a quarter of respondents indicated some degree of cost-burden. Although only 10% of prescription items dispensed in England require a co-payment,

long-term condition are increasingly being diagnosed in younger people who therefore incur these charges. A recent large survey (n=5612) found that the cost burden incurred can lead to non-adherence, with consequences of poorer health outcomes and/or impact on daily lives (Prescription Charge Coalition, 2017). Requiring support with using medicines increased burden in multiple domains. The extent to which support is required with using medicines among home-dwelling individuals in England is not known and is not routinely recorded. However, there are 5.8 million informal carers in England and Wales (ONS, 2011) the majority of whom manage medicines as part of their activities (Francis *et al.* 2006). Therefore further work is required to clarify how the need for support, which varies in nature, affects perceived burden.

Domains of medicine burden

All aspects of medicines burden are experienced by some individuals. Statements covering general concerns showed the highest level of agreement, while relationships with health professionals generated the highest number of comments. Side effects and interference with daily life increased with both number and frequency of medicines use, whereas practical difficulties increased only with frequency.

Lack of autonomy/flexibility to vary regimens may not be perceived as a burden by many, but for some the effort of maintaining strict adherence to prescribed regimens may represent loss of independence, freedom and/or spontaneity (Demain *et al.* 2015). Encouraging autonomy in fitting medicines around daily lives without loss of clinical benefit may reduce perceived medicine burden and encourage persistence with long-term medicines (Mohammed *et al.* 2016; Ridgeway *et al.* 2014). Learning more about the individual experience of using medicines, through instruments such as the LMQ-3, could assist health professionals in providing individually tailored, person-centred care. Such tailoring is advocated by national guidance (NICE, 2017) and has the potential to increase patients' sense of autonomy.

The findings support recent reviews of qualitative studies, exploring patient perspectives of treatment and medicine burden, which show that medicine use can disrupt activities, work and relationships, cause social stigma and have undesirable physiological consequences (Demain *et al.* 2015, Mohammed *et al.* 2016). An individual's perception of treatment burden may be affected by how their regimen fits within their personal life situation. However, as our qualitative data show, beliefs about the necessity of using medicines, an important aspect of medicines use (Horne *et al.* 2013), also impact on perceived burden. Each individual must weigh up their concerns about risks, actual side effects, the effort involved in managing medicines and any potential disruption to daily life against the multiple benefits derived from medicines.

Relevance to policy and practice

Several instruments measure satisfaction with medicines (Katusiime *et al.* 2016) which we have found is negatively correlated with medicines burden (Katusiime *et al.* 2018). Few other instruments measure burden; one measures overall treatment burden (Tran *et al.* 2012), others focus on burden in specific medical conditions (Eton *et al.* 2013) but cover limited aspects of medicines use. As our data show, there is a large range of issues which face people using regular medicines, not adequately covered by the limited aspects of medicines included in the Treatment Burden Questionnaire (Tran *et al.* 2012) or in disease-specific measures. Medicines burden is multi-factorial (Mohammed *et*

al. 2016), as illustrated by the variation in domain scores within the LMQ-3 instrument. Moreover, there is a need for a generic medicines burden measure which is relevant to a diverse population, given the increasing prevalence of multi-morbidity and polypharmacy. We believe this instrument could prove useful in identifying those with high burden who may benefit from intervention to help reduce this. Our data show that over 50% of those who were unemployed and people who needed support with using medicines had high burden, as did over 40% of those who had to use medicines three or more times a day and over 30% of those who were aged below 65, used more than four medicines or paid prescription charges. The findings are of relevance to those seeking to develop or deliver interventions aiming at reducing medicines use (deprescribing) in line with current policies and guidelines (Royal Pharmaceutical Society, 2013; NICE, 2017). Assessment of medicine burden may prove useful in helping to identify those potentially likely to benefit from such interventions.

Strengths and limitations

The sample size was sufficient to enable the exploration of demographic and medicine characteristics in relation to medicines burden, however we used convenience sampling, and our results must be viewed in this light. The sample was derived from only one region of England, thus may not represent experiences more widely, therefore larger studies using random sampling are required. The questionnaire was only available in English and its length may have contributed to the response rate (36%), which was, however, relatively high given the direct distribution method used. Potential participants with cognitive impairment may have had problems in its completion and may have not responded. Those who did respond may have had more medicine-related issues than non-responders, and the distribution method precluded housebound individuals and those using prescription medicines delivery services, who may be more likely to have such issues. Despite the known limitations of convenience sampling and the relatively low response rate, the sample was diverse in terms of age, deprivation status and number of medicines used and was large enough to conduct the analyses with high power. Respondents were generally older than the local general adult population and more were retired, which is not unexpected, since medicines use, a requirement for inclusion, increases with age.

Although permission to access PMRs and calculate MRCI scores was sought only for a sub-set, the data obtained enabled confirmation of the contribution of medicine-related factors high burden. The PMR also facilitated a check on self-reported numbers of medicines used, although dispensed medicines may differ from actual use. All analyses were of necessity based on respondents' self-reporting of the numbers, frequency and formulations of medicines used and demographic details. Deprivation status was only available for 83% of the sample.

Conclusion

Responses to the LMQ-3 in this English population of regular medicine users revealed a diverse range of issues contributing to medicines burden. Medicine users who pay prescription charges, use more than four medicines, use medicines more than twice daily and need support with using medicines have the highest burden. Current policy in England has a distinct focus on people with long-term conditions (NHS England, 2014), and guidance advocates providing individually tailored care for those using at least ten medicines or using fewer with an increased risk of adverse events, including those having difficulty managing their treatment (NICE, 2017). Our results suggest the need to assess the degree of burden perceived by individuals using relatively few medicines but with other factors

contributing to medicines burden and that the targeting of interventions seeking to reduce medicines burden should also consider these individuals. Although our study found that older people reported lower levels of medicines burden than younger people, further work is needed to determine whether this is replicated elsewhere and reasons for this finding.

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Table 1 Socio-demographic and medicine-related characteristics of LMQ respondents (n=684*)

Socio-demographic characteristics		Frequency (%)
Gender (n= 645)	Female	343(53.2)
	Male	302(46.8)
Age (year) (n = 661)	18-29	65(9.8)
	30-49	113(17.1)
	50-64	206(31.2)
	65-79	215(32.5)
	80 or over	62(9.4)
Education level (n=639)	School	248(38.8)
	Technical college/Apprenticeship	205(32.1)
	University	136(21.3)
	Other	50(7.8)
Employment status (n=666)	Employed	236(35.4)
	Unemployed	74(10.8)
	Retired	332(49.8)
	Full-time student	23(3.5)
Ethnicity (n= 665)	White	596(89.6)
	Asian/Asian British	21(3.2)
	Mixed	12(1.8)
	Black/African/Caribbean	31(4.7)
	Other	5(0.8)
Deprivation level (n=567)	1 (Highest)	103(18.2)
	2	125(22.0)
	3	80(14.1)
	4	140(24.7)
	5 (Lowest)	139(21.0)
Medicine-related characteristics		Frequency (%)
No. of medicines (n=652)	1-4	389(59.7)
	5-9	204(31.3)
	10 or more	59(9.0)
Formulation used (n = 659)	Tablets/capsules	450(68.3)
	Other formulations	43 (6.5)
	Both types	166 (25.2)
Frequency of use (n = 664)	Once per day	246(37.0)
	Twice per day	190(28.6)
	Three times per day	84(12.7)
	More than 3 times per day	64(9.6)
	Other times**	80(12.0)
Managing medicines (n=663)	No (Autonomous)	596(89.9)
	Yes (Requires assistance)	67(10.1)
Paying for prescriptions (n= 667)	No	478(71.7)
	Yes	189(28.3)

* missing data were excluded from this analysis, numbers of respondents are provided for each characteristic

** includes medicines used when required (prn), different days of the week, every fortnight, monthly, three months and every five years

Table 2 Demographic and medicines use characteristics on LMQ-3 total scores and VAS scores

Characteristic		N	Mean LMQ-3 total score (95%CI)	p-value	N	Median VAS score (95%CI)	p-value
Gender	Female	266	100.4 (95.6; 100.8)	0.208	336	1.6 (1.2; 2.0)	0.593
	Male	233	98.2 (98; 102.9)		298	1.6 (1.2; 2.0)	
Age (years)	18-29	56	100.8(95.6; 105.8)	<0.001	64	2.65 (1.6; 3.9)	<0.001
	30-49	104	105.6(101.5; 109.8)		112	3.0 (2.0; 4.6)	
	50-64	167	102.2(99.3; 105.4)		205	2.0 (1.6; 2.5)	
	65-79	150	92.5(89.9; 95.2)		210	0.9 (0.6; 1.0)	
	80 or over	33	97.5(91.8; 103.0)		60	1.0 (0.5; 1.6)	
Employment	Employed	207	107.6(98.9; 104.2)	<0.001	233	2.0 (1.6; 2.6)	<0.001
	Unemployed	60	114.7(109.5; 120.3)		74	4.75 (3.0; 5.8)	
	Retired	222	94.0(91.9; 96.3)		323	1.0 (1.0; 1.3)	
Deprivation level	1 (Highest)	79	103.0(99.1; 107.1)	0.012	103	1.6 (1.0; 2.3)	0.314
	2	95	101.6(95.6; 105.6)		123	1.5 (1.0; 3.0)	
	3	63	100.1(95.5; 104.4)		77	1.2 (0.8; 2.0)	
	4	104	95.9(92.8; 99.1)		137	1.8 (1.2; 2.2)	
	5 (Lowest)	92	94.9(90.6; 98.7)		116	1.2 (1.0; 2.0)	
No. of medicines	1-4	319	97.2(95.3; 99.3)	0.001	387	1.5 (1.1; 1.8)	0.007
	5-9	145	103.9(99.8; 107.2)		197	2.0 (1.3; 2.5)	
	≥ 10	36	104.1(97.6; 110.7)		58	3.0 (1.3; 5.0)	
Frequency of use	Once daily	202	94.8(92.5; 96.9)	< 0.001	241	1.2 (1.0; 1.6)	<0.001
	Twice daily	139	99.0(95.9; 102.2)		185	1.3 (1.0; 1.7)	
	Three times/ day	52	110.9(104.7; 117.6)		84	2.7 (1.6; 4.0)	
	≥ 4 times daily	53	109.1(102.6; 115.1)		62	4.85 (2.2; 5.5)	
Formulations	Oral solid dose	350	99.6 (97.4; 101.5)	0.994	442	1.45 (1.1; 1.6)	0.004
	Other	33	99.7 (92.7; 106.8)		42	2.0 (1.0; 4.8)	
	Both	124	99.5 (95.8; 103.7)		163	2.2 (1.9; 3.0)	
Managing medicines	Independent	465	98.1(96.4; 99.9)	< 0.001	587	1.6 (1.3; 1.9)	0.001
	Requires help	46	116.4(110.0; 120.1)		64	4.0 (1.4; 5.4)	
Paying for prescriptions	No	350	97.3(95.3; 99.4)	< 0.001	468	1.3 (1.0; 1.6)	0.004
	Yes	139	104.6(101.4; 107.7)		187	2.3 (2.7; 3.5)	

Table 3 Demographic and medicines use characteristics of respondents with high burden (n=123)

Characteristic		Proportion with high LMQ-3 total score (n)	p-value
Age (years)	18-29	32.1 (18)	0.001
	30-49	31.7 (33)	
	50-64	27.5 (46)	
	65-79	11.3 (17)	
	80 or over	15.2 (5)	
Employment	Employed	25.6 (53)	<0.001
	Unemployed	58.3 (35)	
	Retired	12.6 (28)	
Deprivation level	1 (Highest)	25.3 (20)	0.018
	2	25.3(24)	
	3	25.4 (16)	
	4	13.5 (14)	
	5 (Lowest)	20.7 (19)	
No. of medicines	1-4	19.7 (63)	<0.05
	5-9	30.3 (44)	
	≥ 10	30.6 (11)	
Frequency of use	Once daily	13.4 (27)	< 0.001
	Twice daily	25.2 (35)	
	Three times daily	40.4 (21)	
	≥ 4 times daily	43.4 (23)	
Managing medicines	Independent	20.2 (94)	< 0.001
	Requires help	54.3 (25)	
Paying for prescriptions	No	20.3 (71)	0.004
	Yes	30.7 (50)	

Table 4 Effect of key factors on individual domain scores with higher scores indicating greater burden (n=684, missing data excluded from all analyses)

Factor		Mean domain score (maximum possible score)							
		Relationships (25)	Practicalities (35)	Lack of effect (30)	Side effects (20)	Concerns (35)	Cost (15)	Interference (30)	Autonomy (15)
Age (years) ¹	18-29	12.5	16.0	13.8	9.2	19.3	7.9	13.2	9.2
	30-49	13.0	15.9	14.2	9.9	20.8	7.6	14.4	9.5
	50-64	12.1	15.0	14.2	9.6	20.3	6.9	13.8	10.2
	65-79	11.1	13.5	12.6	8.8	18.5	5.1	12.2	11.0
	80 or over	11.0	14.5	13.1	8.8	19.1	5.4	13.4	10.9
	P value	<0.001	<0.001	<0.001	0.012	0.001	<0.001	0.001	<0.001
Number of medicines ²	1-4	12.0	14.5	13.5	8.8	19.0	6.6	12.4	10.0
	5-9	11.8	15.0	13.5	9.9	20.4	6.2	14.2	10.8
	≥ 10	11.8	15.7	14.2	10.7	20.8	5.9	16.3	10.8
	P value	0.759	0.09	0.414	<0.001	0.003	0.103	<0.001	<0.001
Frequency of use ³	Once daily	11.6	13.9	13.0	8.6	18.8	6.5	11.8	10.5
	Twice daily	11.6	15.0	13.3	9.3	19.7	6.3	13.1	10.3
	Three times/ day	12.4	16.0	14.2	10.8	21.5	6.7	15.8	10.2
	≥ 4 times daily	12.7	16.5	15.3	10.5	20.9	6.4	16.3	9.8
	P value	0.107	<0.001	<0.001	<0.001	<0.001	0.740	<0.001	0.293
Paying for prescriptions ⁴	No	11.5	14.4	13.2	9.2	19.3	5.7	13.2	10.6
	Yes	12.8	15.7	14.4	9.6	20.5	8.2	13.5	9.5
	P value	<0.001	0.001	<0.001	0.182	0.009	<0.001	0.418	<0.001
Managing medicines ⁵	Independent	11.8	14.5	13.3	9.0	19.3	6.4	12.9	10.3
	Requires help	13.0	17.4	15.5	11.6	21.9	6.8	16.9	10.6
	P value	0.013	<0.001	<0.001	<0.001	<0.001	0.440	<0.001	0.290

1 – higher burden scores in those aged below 65 for relationships, practicalities, lack of effect, cost and interference, lower burden scores for autonomy

2 – higher burden scores in those using more medicines for side effects, interference and autonomy

3 – higher burden scores in those using medicines more frequently/day for practicalities, lack of effect, side effects, concerns and interference

4 – higher burden scores in those paying for prescriptions for relationships, practicalities, lack of effect, cost and autonomy

5 – higher burden scores in those who need support with using medicines for practicalities, lack of effect, side effects, concerns and interference

Table 5 Standard multiple linear regression analysis of medicine-related and socio-demographic factors associated with medicine burden (N = 436)

	B-values	Std. Error	Beta	95% confidence intervals for B		t	p-value
Constant	141.728	8.855		124.311	16.006	<0.000	159.145
Number of medicines	0.549	0.307	0.099	-0.156	1.785	0.075	1.153
Frequency of use*	3.862	1.036	0.199	1.825	3.729	<0.001	5.899
Paying for prescriptions	-6.015	2.486	-0.145	-10.905	-2.420	0.016	-1.125
Managing medicines*	-13.945	3.723	-0.186	-21.268	-3.746	<0.001	-6.622
Age	-0.098	0.085	-0.082	-0.266	-1.143	0.254	0.070
Deprivation	-1.826	0.684	-0.133	-3.171	-2.672	0.008	-0.482
Employment	-1.853	1.567	-0.090	-4.935	-1.182	0.238	1.229

R Square= 0.208; Adjusted R Square = 0.191; *p-value < 0.001

Table 6 Responses to individual statements in the LMQ-3 (N=684 Missing data excluded from analysis)

Statements in their respective domains	Agree/ Strongly Agree %(n)	Disagree/ Strongly Disagree %(n)	Neutral opinion %(n)
Practical difficulties (7 items; $\alpha = 0.671$)			
I find getting my prescriptions from the doctor difficult.	91(13.4)	506(74.7)	80(11.8)
I find getting my medicines from the pharmacist difficult	73(10.8)	530(78.3)	74(10.9)
I am comfortable with the times i should take my medicines	573(84.3)	53(7.8)	54(7.9)
I am concerned that I may forget to take my medicines	170(25.2)	248(58.4)	111(16.4)
I have to put a lot of planning and thought into taking my medicines.	112(16.5)	427(63.0)	139(20.5)
It is easy to keep my medicines routine	541(79.4)	53(7.8)	87(12.8)
I find using my medicines difficult	30(4.5)	588(87.6)	53(7.9)
Perceived effectiveness (6 items; $\alpha = 0.748$)			
I am satisfied with the effectiveness of my medicines.	490(72.5)	75(11.1)	111(16.4)
My medicines prevent my condition getting worse	535(78.8)	56(8.3)	88(13.0)
My medicines live up to my expectations	460(67.5)	53(7.8)	168(24.7)
My medicines allow me to live my life as I want to	468(69.2)	74(10.9)	134(19.8)
My medicines are working	501(76.5)	34(5.2)	120(18.3)
The side effects are worth it for the benefits I get from my medicines	272(40.8)	103(15.5)	291(43.7)
Communication/relationships with HCPs (5 items; $\alpha = 0.786$)			
I trust the judgement of my doctor(s) in choosing medicines for me.	502(73.7)	69(10.1)	110(16.2)
My doctor(s) listen to my opinions about my medicines	410(60.1)	107(15.7)	165(24.2)
My doctor takes my concerns about side effects seriously.	373(55.3)	77(11.4)	224(33.2)
I get enough information about my medicines from my doctor(s)	405(59.6)	140(20.6)	135(19.9)
The health professionals providing my care know enough about me and my medicines	421(62.9)	101(15.1)	147(22.0)
Cost-related burden (3 items; $\alpha = 0.787$)			
I worry about paying for my medicines	137(27.2)	330(53.6)	149(24.2)
I sometimes have to choose between buying basic essentials or medicines	52(8.0)	520(79.5)	82(12.5)
I have to pay more than I can afford for my medicines.	81(12.7)	406(63.7)	150(26.5)

Table (continued) Statements in their respective domains	Agree/ Strongly agree %(n)	Disagree/ Strongly Disagree %(n)	Neutral opinion %(n)
Concerns about medicine use (7 items; $\alpha = 0.783$)			
I worry that I have to take several medicines at the same time	137(20.2)	385(56.9)	155(22.9)
I would like more say in the brands of medicines I use	181(26.7)	237(34.9)	260(38.3)
I feel I need more information about my medicines	188(27.8)	317(46.8)	172(25.4)
I am concerned about possible damaging long-term effects of taking medicines	369(54.4)	195(28.8)	114(16.8)
I am concerned that I am too reliant on my medicines	289(42.6)	218(32.1)	172(25.3)
I am concerned that my medicines interact with alcohol	340(50.9)	116(17.3)	212(31.7)
I worry that my medicines may interact with each other	216(31.9)	287(42.4)	174(25.7)
Side-effect-burden (4 items; $\alpha = 0.846$)			
The side effects I get are sometimes worse than the problems for which I take my medicines	128(19.0)	386(57.2)	161(23.9)
The side effects that I get from my medicines interfere with my day to day life	130(19.2)	422(62.3)	125(18.5)
The side effects I get from my medicines are bothersome	120(17.9)	446(66.5)	105(15.6)
The side effects I get from my medicines adversely affect my wellbeing	76(11.4)	484(72.6)	107(16.0)
Interference to day-to-day life (6 items; $\alpha = 0.813$)			
My medicines interfere with my social or leisure activities	112(16.5)	483(71.1)	84(12.4)
Taking medicines affects my driving	66(9.9)	498(75.1)	99(14.9)
My medicines interfere with my social relationships	78(11.6)	510(75.4)	88(13.0)
Taking medicines causes problems with daily tasks	92(13.6)	514(76.5)	67(9.9)
My medicines interfere with my sexual life	95(14.4)	428(64.8)	138(20.9)
My life revolves around using medicines	189(30.0)	380(56.2)	107(15.8)
Autonomy/control (3 items; $\alpha = 0.614$)			
I can vary the dose of the medicines I take	140(20.8)	424(63.1)	108(16.1)
I can choose whether or not to take my medicines	181(26.8)	393(58.1)	102(15.1)
I can vary the times I take my medicines	244(35.9)	311(45.8)	124(18.3)