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Treatment burden in Multiple Long-Term Conditions: a mixed-methods study protocol

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Abstract

Background: Treatment burden represents the work patients undertake because of their healthcare, and the impact of that effort on the patient. Most research has focused on older adults (65+) with multiple long-term conditions (MLTC-M) but there are more younger adults (18-65) living with MLTC-M and they may experience treatment burden differently. Understanding experiences of treatment burden, and identifying those most at risk of high treatment burden, are important for designing primary care services to meet their needs.

Aim: To understand the treatment burden associated with MLTC-M, for people aged 18-65 years, and how primary care services affect this burden.

Design & setting: Mixed-methods study in 20- 33 primary care practices in two UK regions.

Method: i. In-depth qualitative interviews with adults living with MLTC-M (approximately 40 participants) to understand their experiences of treatment burden and the impact of primary care; with a think-aloud aspect to explore face validity of a novel short treatment burden questionnaire for routine clinical use (STBQ) in the initial 15 interviews. ii. Cross-sectional patient survey (approximately 1000 participants) with linked routine medical record data to examine the factors associated with treatment burden for people living with MLTC-M, and to test the validity of STBQ.

Conclusion: This study will generate in-depth understanding of the treatment burden experienced by people aged 18-65 years living with MLTC-M, and how primary care services affect this burden. This will inform further development and testing of interventions to reduce treatment burden, and potentially influence MLTC-M trajectories and improve health outcomes.

Introduction

Multiple long-term conditions (multimorbidity or MLTC-M, defined as the existence of two or more long-term conditions) affects approximately 1 in 4 of the UK population, is associated with reduced quality of life and increased hospital admissions [1, 2] and accounts for over half of the costs of primary and secondary care [3]. MLTC-M is more prevalent, and occurs at a younger age, in more deprived areas, contributing to health inequalities [3-5]. MLTC-M disproportionately affects those living in areas of socio-economic deprivation and minority ethnic groups [6]. Most research on MLTC-M has included patients aged over 65 years, however, almost a third of people with four or more conditions are under this age [7].

Treatment burden represents the work that patients undertake because of their healthcare, and the impact of that effort on patients [8, 9]. Younger populations may experience different challenges that affect their treatment burden. Interventions focused on younger populations have the potential, through addressing treatment burden at an earlier stage, to influence trajectories of MLTC-M [10]

United Kingdom (UK) National Institute for Health and Care Excellence (NICE) MLTC-M guidance for [11] recognises the need to reduce treatment burden [12]. However, no existing interventions have shown convincing reduction of treatment burden for people living with MLTC-M [13-15].

Few qualitative studies have investigated the experience of treatment burden for people with MLTC-M in primary care [16, 17]. A recent systematic review of the impact of interventions on patient-

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reported burden of treatment included 11 studies, only one of which focussed on people living with MLTC-M [14]. Available measures of treatment burden are too time consuming to be used in routine clinical practice to identify patients at risk of being overburdened by the demands of their healthcare. The multimorbidity treatment burden questionnaire (MTBQ) is a validated measure developed to capture the effort required to manage MLTC-M [7]. It has been used to evaluate treatment burden in two UK surveys, largely focused on people in older age groups, and more affluent / minimally diverse populations [7, 18]. Each of these studies has evaluated the performance of a different single-item measure alongside the MTBQ; these had limited sensitivity and positive predictive value [18, 19]. Practical ways of measuring treatment burden in routine primary care practice would be valuable, enabling identification of people who are more likely to be over-burdened.

To our knowledge, no studies have explored the impact the organisation of primary care services has on the treatment burden experienced by people with MLTC-M. This protocol describes a mixed-methods study. The overarching aim is to understand the treatment burden associated with MLTC-M for people aged 18-65 years, and how primary care services affect this burden, in order to inform service design. We will:

1a) explore, in-depth, their experiences of treatment burden and its impact;
1b) explore the face validity of a short treatment burden screening questionnaire (STBQ).
2a) examine the factors associated with treatment burden for adults living with MLTC-M;
2b) test the validity of the STBQ for routine clinical use.

Method

Concurrent mixed-methods study including qualitative and quantitative components, and stakeholder engagement (Figure 1).

[insert figure 1 here]

Theoretical Framework

The cumulative complexity model [20] is used as a theoretical framework for the study. It describes the balance between the workload that an individual experiences because of their healthcare, and the capacity they have to manage that workload.

Definition of multimorbidity

We will use the 20-condition Cambridge multimorbidity score to identify eligible participants [4, 21]. We will develop GP electronic record searches, based on the published code sets to identify people with two or more of these 20 conditions.

Participants Adults (18-65 years) with two or more long-term conditions.

We will exclude people with dementia, those lacking capacity to consent, people receiving palliative care, and nursing home or care home residents.

Inclusivity

People from ethnic minority groups are likely to report poorer health outcomes and experiences of accessing health services than their white-British counterparts [6]. They are often under-represented in research, limiting the relevance and generalisability of results.

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We will seek to increase participation of people from ethnic minority groups and socio-economically disadvantaged communities. All participant materials will be translated and back-translated into commonly spoken languages in the study areas. Interpreters will be available for interviews.

Qualitative study

Design

Semi-structured qualitative interviews with adults living with MLTC-M exploring objectives 1a,b.

Sampling

We will recruit up to eight primary care practices across two geographical areas. Participants will be purposively sampled to achieve maximal variation in practice-level deprivation and rurality; patient age, gender, ethnicity, employment status, being a carer, and type of MLTC. Invitations will be sent to eligible patients identified by electronic record searches in participating practices. Interested people will contact the study team to arrange an interview in-person, by telephone or videocall. Fully informed consent will be taken at the time of the interview (written or audio-recorded).

Data collection

Topic guides have been developed and piloted with input from the PPI (patient and public involvement) group. In-depth interviews will focus on patients' experiences of MLTC-M burden and their capacity to manage the workload. We will explore how different health conditions interact how the experience of burden changes with time and circumstances; how patients navigate primary care services, and the impact of health services on MLTC-M burden and capacity. Interviews will be audio-recorded, professionally transcribed, anonymised, and managed in NVivo 12.

Up to 15 initial interviews will explore participants' thoughts about the STBQ. Participants will be asked to think aloud [22] as they complete the measure, including commenting on the layout and wording, and discussing the reasoning behind their questionnaire responses. These interviews will be carried out in blocks of 3-5. At the end of each block, the data will be reviewed and the questionnaire modified.

Participating patients will be offered a £25 shopping voucher.

Analysis

Analysis will involve two stages.

Objective 1a,b. Data analysis will be thematic [23], conducted by the interviewers, members of the research team and up to two public contributors from the PPI group. Analysis will begin with line-by-line coding, followed by discussion to agree the coding frame. Transcripts will be coded by one researcher, and a randomly chosen sample will be reviewed independently by a second researcher. The researchers will initially identify themes, which will then be discussed with other members of the research team. Analysis will continue alongside data collection, allowing the topic guides to be modified to respond to findings. Up to two members of the PPI group will be invited to contribute to the analysis by (i) being involved in a facilitated discussion in which codes are developed and researcher interpretations of the data checked; (ii) using selected extracts from transcripts to sense-check, refine and expand themes.

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Objective 1b. Framework analysis [24] will be conducted to analyse the think-aloud interviews. The researchers will summarise the data within a framework matrix, based on the different aspects of the questionnaire. The final version of the STBQ will be used in the survey.

Sample size and participant recruitment will be determined based on the concept of information power [25]. Our analysis is informed by established theory, interviews will be focused on the research questions, and we anticipate participants will have rich experiences relevant to the research question. These factors will increase the information power of our sample. Sufficient information power will be achieved when the sample is deemed to have addressed the study's research questions (we estimate 30-40 interviews).

Quantitative study

Design

Cross-sectional patient survey and analysis of linked routinely collected GP record data, addressing objectives 2a, b.

Sampling

We will sample up to 25 primary care practices across two geographical areas in England, aiming to recruit 50% of practices from Index of Multiple Deprivation (IMD) deciles 1-5 [with one being most deprived and 10 least deprived] and at least 6 practices in deciles 1-3. Practices will run electronic searches to identify eligible patients, and will invite a random sample of up to 500. Sample size calculation is presented in Table 1.

[insert table 1 here]

Data collection

i. Survey

The measures included in the survey are described in Table 2.

[insert table 2 here]

ii. Medical records

Survey respondents will be asked to consent to access to their medical records. For consenting participants, the following data will be collected and linked to the survey data for analysis: age, sex, individual-level deprivation, number and type of long-term health conditions, number of prescribed medications, and number and type of consultations in general practice. In addition, we will collect anonymised data on the age, sex, deprivation level and number of long-term conditions of all patients invited to complete the survey, facilitating comparison with the respondent sample.

Data management and analysis.

Data will be managed in a REDCap database and analysed using Stata 17. Unclear questionnaire data will be treated as missing. Descriptive analyses will report MTBQ, PROMIS 10 and PCPCM by the other variables of interest.

Regression analyses**:** We will investigate the association of MTBQ scores with the variables of interest. We will explore three types of regression models: logistic regression where MTBQ scores are dichotomised into those with and without high burden; ordinal logistic regression where the MTBQ score is categorised into different levels of burden, and linear regression with the global

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MTBQ scores as a continuous measure. Initially we will assess each of the variables of interest in univariate models and will then build multivariable models using stepwise methods. Multicollinearity will be assessed using variance inflation factors and we will consider non-linear associations for numeric variables. Depending on missing data we will carry out complete case analyses and also imputed analyses. The results from the linear regression will be presented as primary results with the rest as a sensitivity analyses dependent on testing the assumptions in the regression models.

More details are available in Supplementary Material 1.

STBQ validation: Different versions of the STBQ will be explored through inter-item correlations, internal consistency (Cronbach's alpha), and comparison of the association between the STBQ with high treatment burden as measured by the MTBQ using the receiver operator characteristic curve and diagnostic parameters: sensitivity, specificity, positive and negative predictive values. We aim to achieve the shortest possible questionnaire that has a high sensitivity.

Stakeholder engagement

We will hold three workshops in the two study sites. An early workshop will engage a diverse group of people living with MLTC-M in discussions about the content of the interviews and survey. In two late workshops we will engage with stakeholders representing patients, primary healthcare services, commissioners and policy makers to identify the implications of our research findings.

Patient and Public Involvement

Our PPI group of eight members with lived experience of MLTC-M contributed to the development of the research questions, the study protocol, study documentation, and the design of the survey and qualitative topic guide. They will be involved in the analysis of the qualitative data, interpretation and dissemination of the study findings.

Discussion

This study uses qualitative interviews with patients, and a cross-sectional patient survey linked to routine data to understand treatment burden experienced by people 18-65 years living with MLTC-M, and the ways in which the organisation of primary care services affects? this burden. Through the qualitative research we will use the cumulative complexity model to understand how and why treatment burden affects younger people and how workload and capacity interact [20]. Through the cross-sectional survey with linked routine data we will identify the factors associated with treatment burden, and associations between treatment burden and quality of life. Finally, we will seek to validate a short treatment burden measure for use in routine clinical care. We will produce practical recommendations for how primary care services can reduce treatment burden experienced by people 18-65 years living with MLTC-M. This will lead to further development and testing of interventions to reduce MLTC-M burden, with the potential to influence MLTC-M trajectories and improve health outcomes.

References

1. Huntley, A.L., R. Johnson, S. Purdy, J.M. Valderas, and C. Salisbury, Measures of multimorbidity and morbidity burden for use in primary care and community settings: a systematic review and guide. Ann Fam Med, 2012. 10(2): p. 134-41.
2. Agborsangaya, C.B., D. Lau, M. Lahtinen, T. Cooke, and J.A. Johnson, Health-related quality of life and healthcare utilization in multimorbidity: results of a cross-sectional survey. Qual Life Res, 2013. 22(4): p. 791-9.
3. Stafford, M.S., A. Thorlby, R. Fisher, R. Turton, C. Deeny, S., Understanding the health care needs of people with multiple health conditions. 2018, The Health Foundation.[accessed 06 June 2023]; Available from: https://www.health.org.uk/publications/understanding-the-health-care-needs-of-people-with-multiple-health-conditions.
4. Barnett, K., S.W. Mercer, M. Norbury, et al., Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet, 2012. 380(9836): p. 37-43.
5. Salisbury, C., L. Johnson, S. Purdy, J.M. Valderas, and A.A. Montgomery, Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. Br J Gen Pract, 2011. 61(582): p. e12-21.
6. Verest, W., H. Galenkamp, B. Spek, et al., Do ethnic inequalities in multimorbidity reflect ethnic differences in socioeconomic status? The HELIUS study. Eur J Public Health, 2019. 29(4): p. 687-693.
7. Duncan, P., M. Murphy, M.S. Man, et al., Development and validation of the Multimorbidity Treatment Burden Questionnaire (MTBQ). BMJ Open, 2018. 8(4): p. e019413.
8. Eton, D.T., D. Ramalho de Oliveira, J.S. Egginton, et al., Building a measurement framework of burden of treatment in complex patients with chronic conditions: a qualitative study. Patient Relat Outcome Meas, 2012. 3: p. 39-49.
9. May, C.R., D.T. Eton, K. Boehmer, et al., Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness. BMC Health Serv Res, 2014. 14: p. 281.
10. Stokes, J., B. Guthrie, S.W. Mercer, N. Rice, and M. Sutton, Multimorbidity combinations, costs of hospital care and potentially preventable emergency admissions in England: A cohort study. PLoS Med, 2021. 18(1): p. e1003514.
11. Multimorbidity: clinical assessment and management, in NICE guideline [NG56]. 2016, National Institute for Health and Care Excellence: United Kingdom.[accessed 06 June 2023]; Available from: https://www.nice.org.uk/guidance/ng56/resources/multimorbidity-clinical-assessment-and-management-pdf-1837516654789.
12. Valderas, J.M., J. Gangannagaripalli, E. Nolte, et al., Quality of care assessment for people with multimorbidity. J Intern Med, 2019. 285(3): p. 289-300.
13. Smith, S.M., E. Wallace, T. O'Dowd, and M. Fortin, Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database Syst Rev, 2021. 1(1): p. CD006560.
14. Lesage, A., B. Leclere, L. Moret, and C. Le Glatin, Decreasing patient-reported burden of treatment: A systematic review of quantitative interventional studies. PLoS One, 2021. 16(1): p. e0245112.
15. Smith, S., Wallace, E., Clyne, B., Boland, F., Fortin, M., Interventions for Improving Outcomes in Patients With Multimorbidity in Primary Care and Community Setting: A Systematic Review. 2021, Research Square.
16. Demain, S., A.C. Goncalves, C. Areia, et al., Living with, managing and minimising treatment burden in long term conditions: a systematic review of qualitative research. PLoS One, 2015. 10(5): p. e0125457.

17.   Rosbach, M. and J.S. Andersen, Patient-experienced burden of treatment in patients with multimorbidity - A systematic review of qualitative data. PLoS One, 2017. 12(6): p. e0179916.

18.   Morris, J.E., P.J. Roderick, S. Harris, et al., Treatment burden for patients with multimorbidity: cross-sectional study with exploration of a single-item measure. Br J Gen Pract, 2021. 71(706): p. e381-e390.

19.   Hounkpatin, H.O., P. Roderick, S. Harris, et al., Change in treatment burden among people with multimorbidity: a follow-up survey. Br J Gen Pract, 2022. 72(724): p. e816-e824.

20.   Shippee, N.D., N.D. Shah, C.R. May, F.S. Mair, and V.M. Montori, Cumulative complexity: a functional, patient-centered model of patient complexity can improve research and practice. J Clin Epidemiol, 2012. 65(10): p. 1041-51.

21.   Payne, R.A., S.C. Mendonca, M.N. Elliott, et al., Development and validation of the Cambridge Multimorbidity Score. CMAJ, 2020. 192(5): p. E107-E114.

22.   Willis, G., Cognitive Interviewing: A Tool For Improving Questionnaire Design. 2005. 352.

23.   Clarke, V. and V. Braun, Thematic analysis. The Journal of Positive Psychology, 2016. 12(3): p. 297-298.

24.   Gale, N.K., G. Heath, E. Cameron, S. Rashid, and S. Redwood, Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol, 2013. 13: p. 117.

25.   Malterud, K., V.D. Siersma, and A.D. Guassora, Sample Size in Qualitative Interview Studies: Guided by Information Power. Qual Health Res, 2016. 26(13): p. 1753-1760.

26.   Health Measures: Transforming How health is Measured. [accessed 2021 18.6.2021]; Available from: https://www.healthmeasures.net/explore-measurement-systems/promis.

27.   PROMIS Global-10. [accessed 2021 18.6.2021]; Available from: https://www.codetechnology.com/promis-global-10/.

28.   Etz, R.S., S.J. Zyzanski, M.M. Gonzalez, et al., A New Comprehensive Measure of High-Value Aspects of Primary Care. Ann Fam Med, 2019. 17(3): p. 221-230.

29.   Morris, N.S., C.D. MacLean, L.D. Chew, and B. Littenberg, The Single Item Literacy Screener: evaluation of a brief instrument to identify limited reading ability. BMC Fam Pract, 2006. 7(1): p. 21.

30.   Salisbury, C., M.S. Man, P. Bower, et al., Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach. Lancet, 2018. 392(10141): p. 41-50.

Table 1. Power for total sample size of 1000, baseline risk of high burden 20% and risk of high burden 30% in group with characteristic of interest.

	Prevalence of patient characteristic of interest [a]						
	0.2	0.25	0.3	0.35	0.4	0.45	0.5
POWER	84.4%	89.2%	92.1%	93.8%	94.9%	95.4%	95.6%

[a]For example, patient living in a deprived area

Table 2. Survey measures

Concept	Measure	Description
Socio-demographic data	Age, gender, ethnicity and employment status	Participants are asked to describe: • age • gender • ethnicity (selecting from the list provided here: https://www.ethnicity-facts-figures.service.gov.uk/style-guide/ethnic-groups) • employment status
Health status	a. PROMIS 10 [26, 27] b. Self-reported long-term conditions	a. A validated 10-item person-centered measure of health and functioning for people with long-term conditions. The questions are a better fit for our purposes than those included in, for example, the SF-12. b. One question asks the participant to list the conditions they believe they have, that have or will last longer than 6 months
Treatment burden	a. The multimorbidity Treatment Burden Questionnaire (MTBQ) [7] b. Novel short treatment burden questionnaire (STBQ)	a. The MTBQ is a concise, simply-worded set of questions to measure treatment burden in people with MLTC-M. In this study, we will use the 13-item questionnaire. b. Building on previous work to develop a single question screening measure for treatment burden [18] we have developed, with PPI input, the STBQ. It includes two questions: one - to screen for high treatment burden, and one – to understand what they find difficult from a range of options. The STBQ has been developed for use in clinical practice, rather than as a research tool. It may be revised in response to feedback from initial qualitative interviews.
Primary care experience	PCPCM [28]	The PCPCM focuses on the patient's access to care, relationship with the doctor / practice, and ability to reach health outcome goals. It comprises 11 items that form an evaluation of access, continuity,

		comprehensiveness, coordination, advocacy, family and community context, and goal-oriented care.
Health literacy	SILS [29]	A validated single-item screening instrument, designed to identify patients with limited reading ability who need help reading health-related materials.
Healthcare use	Healthcare Use [30]	We will include five questions, adapted from Salisbury and colleagues [30], asking whether participants have recently stayed at an NHS hospital, visited A&E, and taken time off work to attend hospital and GP appointments.
Other		We may additionally include a small number of questions from other validated questionnaires if it is apparent from stakeholder work or initial qualitative work that any issues create treatment burden for patients which are not already included in the other data sources proposed.

Figure 1. Study flowchart.

Workshop 1 (months 0-8) Face-to-face or virtual workshops with patient stakeholders To inform content of qualitative interviews / review survey materials

Qualitative patient interview study(months 1-25)	Cross-sectional patient survey (months 1-28)
Recruitment of primary care practices (n= up to 8)	Recruitment of primary care practices (n = up to 25)
Practices search electronic records to identify eligible participants, and send invitations by post and SMS.	Practices search electronic records to identify eligible participants; send invitations by post and SMS (first and reminder)
Initial patient interviews (n = up to 15) and rapid analysis to inform the survey	Survey completion (n = 1000)
Additional patient interviews (n = up to 25)	Extraction of routinely collected medical record data
Data transcription and Interview analysis (n= approximately 40 interviews)	Data input and analysis

Mixed methods analysis

Workshops 2 and 3 (months 22-24) Face to face or virtual workshops with patient stakeholders to discuss the implications of the study findings

Writing up study reports