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Danish validation of the Multimorbidity Treatment Burden Questionnaire (MTBQ) and findings from a population health survey: a mixed-methods study

Marie Hauge Pedersen, Polly Duncan, Mathias Lasgaard, Karina Friis, Chris Salisbury, Finn Breinholt Larsen

ABSTRACT

Objective To validate the Danish Multimorbidity Treatment Burden Questionnaire (MTBQ) and obtain a population-based evaluation of treatment burden.

Design Mixed-methods.

Setting Danish population-based survey.

Participants Translation by professional translators and an expert group. The scale was tested by 13,407 participants (aged ≥25 years) in treatment.

Measures The 10-item MTBQ was translated into Danish using forward-backward translation and used in a large population health survey. A global MTBQ score was calculated and factor analysis and Cronbach’s alpha assessed dimensional structure and internal consistency reliability, respectively. Spearman’s rank correlations between global MTBQ scores and scores of self-rated health, health-related quality of life and the number of long-term conditions, respectively, assessed construct validity. MTBQ scores were grouped into four categories (no, low, medium, high burden) to assess interpretability and population-based evaluation of treatment burden.

Results The scale showed high internal consistency (α=0.87), positive skewness and large floor effects. Factor analysis supported a one-dimensional structure of the scale with a three-dimensional structure as a less parsimonious alternative. The MTBQ score was negatively associated with self-rated health (r=−0.45, p<0.0001) and health-related quality of life (r=−0.46/−0.51, p<0.0001), and positively associated with the number of long-term conditions (r=0.26, p<0.0001) and perceived stress (r=0.44, p<0.0001). Higher treatment burden was associated with younger age, male sex, high educational level, unemployment, being permanently out of work, not living with a spouse/cohabitant, living with child(ren) and long-term conditions (eg, heart attack, stroke, diabetes and mental illness).

Conclusion The Danish MTBQ is a valid measure of treatment burden with good construct validity and high internal reliability. This is the first study to explore treatment burden at a population level and provides important evidence for policy makers and clinicians about sociodemographic groups at risk of higher treatment burden.

INTRODUCTION

Treatment burden is defined as patients’ perception of the effort required to look after their health and the effect of this on their everyday life. Given the current disease-centred approach to healthcare, patients are often required to attend separate appointments, adopt lifestyle changes, self-monitor medical conditions and take complex combinations of medications. This can create considerable workload for patients, which may result in high treatment burden, particularly for patients with multimorbidity (multiple long-term conditions) and patients lacking the capacity or support to align their treatment with other roles and responsibilities in life. A Danish ethnographical study suggested that patients with multimorbidity experienced difficulties in organising their treatment around their family life, social life and work life, and in setting goals and agendas with health professionals.
Due in part to the world’s ageing population, the prevalence of multimorbidity is increasing. It has now become the norm rather than the exception that patients presenting to general practice have multimorbidity, and healthcare systems are struggling to cope with the complexity. As a result, there is a growing expectation that patients self-manage their health conditions, which may lead to high treatment burden, potentially resulting in poor treatment compliance and low health-related quality of life.

Evaluating the level of treatment burden in the general population may be used as a performance measure of how well the healthcare system responds to the population’s needs while respecting their functioning and well-being. Moreover, a study of treatment burden at the population level may identify subgroups at risk of poor outcomes who feel overwhelmed by their treatment and have problems with compliance, and therefore may benefit from less disruptive treatment. To measure the burden of treatment at the population level and to better understand the relationship between treatment burden, demographic factors and health measures, a validated generic measure of treatment burden is essential.

In recent years, five generic measures of treatment burden (not specific to a particular health condition) have been developed but none of these measures have yet been translated into Danish. We evaluated these five measures and found the Multimorbidity Treatment Burden Questionnaire (MTBQ) to be most suitable for use in a comprehensive population survey as it included key aspects of treatment burden and was concise with simple wording. The MTBQ is a 10-question measure of treatment burden developed and validated in a UK study of 1546 older adult participants (mean age 71 years) with three or more long-term conditions. The MTBQ was validated as part of the 3D Study, a randomised controlled trial within primary care in England and Scotland. In the UK, the scale has demonstrated good content and construct validity, reliability and responsiveness to change. The aspects of treatment burden captured by the MTBQ includes medications, healthcare appointments, lifestyle changes, self-monitoring and having to rely on help from family and friends. These aspects are relevant to evaluate in a Danish context where the healthcare system is highly specialised with treatment regimens across specialties, sectors, and public and private healthcare providers, affecting many individuals with one or more conditions. We, therefore, considered the MTBQ a generic measure of treatment burden applicable to all persons in treatment although the scale was originally developed for individuals with multimorbidity.

The aims of this study were: (1) to translate the MTBQ into Danish; (2) to validate the psychometric properties of the Danish version of the MTBQ in a general population of individuals in treatment; and (3) to describe the relationship between treatment burden, sociodemographic factors and health measures at a population level. As far as we are aware, this is the first study to explore population-level associations between treatment burden and population characteristics.

METHODS

Study design and data collection

The study was based on cross-sectional data from the 2017 Danish population-based health survey named ‘How are you?’. Denmark has approximately 5.7 million inhabitants and is divided into five administrative regions. This study comprised data from one of these regions: the Central Denmark Region. Approximately 23% of the Danish population resides in this region, which has a demographic composition similar to that of the total Danish population. The survey consisted of a random sample drawn from the Danish Civil Registration System using the unique personal identification number assigned to all Danish residents. A total of 44658 individuals aged 25 years and older were invited to participate in the survey (February–May 2017).

A total of 28627 individuals (64%) responded to the questionnaire (web or postal). To identify participants in treatment, we used the following question as selection criteria: ‘Do you receive treatment or take medication for one or more conditions, or do you attend rehabilitation or regular check-ups?’ (yes/no). Respondents who reported to be in treatment were included in the study population and asked to complete the MTBQ. In total, 13407 individuals in treatment comprised the study population for this study (online supplemental appendix A).

The MTBQ

In the original English MTBQ, individuals were asked how much difficulty they have with different aspects of treatment. Overall, the 10 questions covered the aspects of medication (three questions), self-monitoring (one question), contact with health professionals (three questions), obtaining information (one question), implementing lifestyle changes (one question) and relying on help (one question). Each question was scored from 0 (not difficult or does not apply), 1 (a little difficult), 2 (quite difficult), 3 (very difficult) to 4 (extremely difficult). A global score was calculated by taking an average of the questions answered and multiplying this by 25 (range 0–100). Participants were excluded if more than 50% of the answers were missing. To assess the interpretability of the questionnaire, the global MTBQ scores greater than 0 were grouped into tertiles resulting in four categories: no burden (score 0), low burden (score ≤1), medium burden (score 10–22) and high burden (score ≥22).

Sociodemographic factors

The following sociodemographic factors were included: sex, age, country of origin, deprivation level (register data), educational level, cohabitation status (living with a spouse/cohabitant or not), and living with child(ren) aged 0–15 years or not (survey data). Denmark was defined as country of origin if respondents had at least
one parent who was both a Danish citizen and was born in Denmark. Deprivation level was estimated for each of the 638 parishes in the Central Denmark Region based on the percentage with low educational level, the percentage people of working age without employment, and mean personal income. Using latent profile analysis, we categorised parishes into five classes. Parishes belonging to class one had the highest social ranking, whereas parishes belonging to class five were the most deprived. Respondents were asked about their highest level of completed school education and any further higher level of education. Using education nomenclature (International Standard Classification of Education) from Statistics Denmark, we categorised educational level as low (1–10 years of education), medium (11–14 years) and high (≥15 years).

Employment status was defined by three categories: employed or student, unemployed (temporary or long term) and permanently out of work (disability pension, early retirement pension and old age pension) (combination of survey data and register data on receiving public benefit during the past year).

Long-term conditions and multimorbidity
Information on long-term conditions was collected using a revised version of a disease checklist recommended by the WHO for health surveys. Respondents were asked about 17 long-term and potentially fatal and/or debilitating conditions (table 1). They were recorded as having a condition if they currently had the condition or if they had previously had the condition and still experienced after-effects. When defining multimorbidity, we grouped some of the conditions together due to similarity in their risk factors or treatment regimens (table 1). The variable indicates the minimum number of long-term conditions as respondents may have had other conditions than these 17 specific conditions.

Measures of health status
From survey data, we collected information on self-rated general health (single question; five-point Likert scale), health-related quality of life (The Short Form (12) Health Survey (SF-12) V.2: Physical Component Summary and Mental Component Summary scores; calculated from 12 questions including the self-rated general health question; standardised (mean=50; SD=10) higher score indicated better health-related quality of life), and perceived stress (Perceived Stress Scale 10-item version; ranging from 0 to 40; higher score indicated higher stress).

Statistical analysis
Descriptive statistics of participant characteristics were generated for the study population. We tested the psychometric properties of the questionnaire against the minimum standards set out by the International Society for Quality of Life Research (ISOQOL). The analysis plan and results are described in relation to ISOQOL’s six recommended standards, and the Strengthening the

| Table 1 | Participant characteristics (participants in treatment aged 25+ years at the time of the 2017 ‘How are you?’ survey, Central Denmark Region, n=13407) |
|-----------------|---------------------------------|
| **Sociodemographic factors** | n | %* |
| Mean age (SD), years | 59 | 16.0 |
| Age, years (missing data: n=0; 0%) | | |
| 25–34 | 802 | 9 |
| 35–44 | 1368 | 12 |
| 45–54 | 2350 | 18 |
| 55–64 | 3142 | 21 |
| 65–74 | 3612 | 23 |
| 75–84 | 1720 | 13 |
| 85+ | 413 | 4 |
| **Sex (missing data: n=0; 0%)** | | |
| Female | 7370 | 54 |
| Male | 6037 | 46 |
| **Country of origin (missing data: n=0; 0%)** | | |
| Denmark | 12815 | 92 |
| Other | 592 | 8 |
| **Educational level (missing data: n=363; 2.7%)** | | |
| Low (0–10 years) | 2387 | 21 |
| Medium (11–14 years) | 7336 | 54 |
| High (15+ years) | 3321 | 25 |
| **Employment status (missing data: n=161; 1.2%)** | | |
| Employed or student | 5843 | 43 |
| Unemployed | 828 | 8 |
| Permanently out of work | 6575 | 49 |
| **Living with spouse/cohabitant (missing data: n=247; 1.8%)** | | |
| No | 3318 | 32 |
| Yes | 9842 | 68 |
| **Living with child(ren) aged 0–15 years (missing data: n=1570; 11.7%)** | | |
| No | 9815 | 82 |
| Yes | 2022 | 18 |
| **Deprivation level (missing data: n=0; 0%)** | | |
| 1 Least deprived areas | 1251 | 13 |
| 2 | 3784 | 28 |
| 3 | 3766 | 25 |
| 4 | 3966 | 27 |
| 5 Most deprived areas | 640 | 8 |
| **Self-reported long-term conditions (missing data: n=57; 0.4%)** | | |
| Cardiovascular disease (one or more) | 5471 | 39 |
| Hypertension | 5163 | 36 |
| Angina pectoris | 500 | 4 |
| Heart attack | 355 | 3 |
| Stroke | 488 | 4 |
| Diabetes | 1602 | 12 |
| Cancer | 876 | 6 |
| COPD and/or asthma | 2131 | 17 |

Continued
Continued

| Condition                          | n  | %  |
|-----------------------------------|----|----|
| COPD                              | 1110| 8  |
| Asthma                            | 1419| 11 |
| Allergy                           | 2721| 21 |
| Osteoarthritis                    | 4701| 34 |
| Rheumatoid arthritis              | 1358| 11 |
| Osteoporosis                      | 1078| 9  |
| Slipped disk or other back disorder | 2802| 22 |
| Mental illness                    | 1982| 17 |
| Migraine or frequent headache     | 2273| 18 |
| Tinnitus                          | 2372| 17 |
| Cataract                          | 1065| 8  |

No of self-reported long-term conditions † (missing data: n=57; 0.4%)

| No         | n  | %  |
|------------|----|----|
| 0          | 1230| 9  |
| 1          | 3403| 26 |
| 2–3        | 5992| 44 |
| 4+         | 2725| 21 |

Mean no of self-reported long-term conditions (SD)

| Condition                          | Mean no of self-reported long-term conditions (SD) |
|-----------------------------------|--------------------------------------------------|
| Health measures                   |                                                  |
| Mean self-rated health score (SD)‡ (missing data: n=202; 1.5%) | 2.98 0.9 |
| Mean PCS score (SD)§ (missing data: n=0; 0%) | 45.20 11.4 |
| Mean MCS score (SD)§ (missing data: n=0; 0%) | 47.39 11.1 |
| Mean PSS score (SD)§ (missing data: n=169; 1.3%) | 13.08 7.5 |

*Weighted to represent the population of the Central Denmark Region, aged 25+ years, in treatment.
†Number of self-reported conditions from a list of 17 conditions asked in the survey. When counting the number of conditions in an individual, conditions with similar risk factors and treatment regimens were grouped and only counted once. Hence, if a person had asthma and COPD, it was counted as one condition in that individual. Likewise, if a person had any combination of hypertension, heart attack and angina pectoris, it would only count as one condition in that individual. Respondents included in the analyses may have had other conditions than the 17 conditions asked in the survey.
‡Single question: ‘In general, would you say your health is: excellent (5), very good (4), good (3), fair (2), poor (1)?’
§Based on the SF-12 V.2 questionnaire.

Conceptual and measurement model

Conceptual framework, translation and pretest of the questionnaire

The original MTBQ was developed using the treatment burden framework developed by Eton et al. A purpose of this study was to validate a Danish translated version of the MTBQ in a general population.

The translation from English into Danish were conducted in the following steps. Step 1: The MTBQ was forward translated into Danish by a professional native Danish registered translator, bilingual in English and Danish. Step 2: An expert group that comprised seven native Danish speakers, bilingual in English and Danish, reviewed the translation. The expert group had a background in questionnaire design, public health, health communication, anthropological fieldwork, multimorbidity research and nursing. Step 3: A blinded independent back translation was undertaken by a professional native English speaker, bilingual in Danish and English. Step 4: The expert group compared the backward version with the original English version.

Establishment of content validity was out of scope for this paper. However, a pretest was conducted to test the Danish translation of the MTBQ (including the purpose-maid treatment question) for inclusion in a large population survey, including the comprehensibility of the question formulations, and if the page layout was intuitive and functional. The pretest included two steps: First, 10 patients (native Danish speakers in a cardiac outpatient clinic; aged 18–90 years) were asked to fill out the questionnaire. Second, comprehensibility, meaningfulness, wording clarity and functionality of the layout was discussed through face-to-face interviews (online supplemental appendix B).

Question properties

Question properties were examined focusing on missing data, ‘does not apply’ responses and response distribution.

Dimensionality

In accordance with previous studies of treatment burden measures, we used factor analysis to assess dimensionality. To test whether the one-dimensional structure of MTBQ discovered by Duncan et al. could be found in the Danish version of MTBQ, we estimated a confirmatory factor model (CFA) with one factor using maximum likelihood with Satorra-Bentler (SB) adjustments to account for non-normal data. Online supplemental analysis was conducted to investigate whether the fit of this model could be improved by including more factors. The specification of the number of factors, and which variables loaded onto which factor, was informed by exploratory factor analysis (details included in online...
supplemental appendix C). As recommended by Hoyle and Panter, model fit of CFA was evaluated with a range of fit indices including the $\chi^2$, the root mean square error of approximation (RMSEA), the standardised root mean square residual (SRMR), the comparative fit index (CFI) and the Tucker-Lewis index (TLI). RMSEA $\leq 0.06$ was interpreted as a close fit, while RMSEA $\leq 0.08$ was interpreted as an acceptable fit. A non-significant $\chi^2$ and a value of SRMR $\leq 0.08$ were taken as an acceptable fit, while for the CFI and the TLI a value of $\geq 0.95$ was taken as an indicator of good fit.

Reliability
Cronbach’s $\alpha$ was calculated to assess internal consistency reliability with a score of 0.7–0.9 being deemed acceptable.

Validity
Construct validity
The survey respondents rated each treatment aspect by level of difficulty (not difficult, a little difficult, quite difficult, very difficult, extremely difficult and does not apply). To ensure findings were comparable with other studies, the questions were scored as in the original UK validation study: from 0 (not difficult or does not apply) to 4 (extremely difficult). A global score was calculated by taking an average of the questions answered and multiplying this by 25 (range 0–100). Participants were excluded from the analysis if more than 50% of the answers were missing.

Based on the findings of prior studies, four prespecified hypotheses were tested to examine construct validity: first, a negative association between treatment burden and self-rated health; second, a negative association between treatment burden and health-related quality of life; third, a positive association between treatment burden and the number of self-reported long-term conditions; and fourth, a positive association between treatment burden and perceived stress. Spearman’s rank correlation ($r_s$) was used to test the hypotheses because of the ordinal scoring of the measures, and Cohen’s rule of thumb was used to interpret the magnitude of the associations (ie, $r_s\leq 0.11$ ‘small’; $r_s=0.31$ ‘medium’; $r_s=0.51$ ‘large’).

Responsiveness
As the study was based on cross-sectional data, it was not possible to assess responsiveness to change.

Interpretability of scores
For the sake of comparison, we applied the same threshold scores as in the original UK study, that is, no burden (score 0), low burden (score <10), medium burden (score 10–22) and high burden (score $\geq 22$). Across these categories, we compared participant characteristics (eg, age, sex, educational level, deprivation level, long-term conditions) and health measures (eg, self-rated health, health-related quality of life). Associations between treatment burden and participant characteristics were tested using logistic regression models that accounted for the ordered nature of the four category groupings of the MTBQ score. Standard ordered logit models, however, assume proportional odds, which empirically have been shown to be violated frequently. We, therefore, used partial proportional odds models with which the proportional odds assumption could be tested using Wald tests and any possible violations could be adapted in the models.

When testing violations of the proportional odds assumption, we used a 1% significance level, as recommended, to minimise the significance of substantively trivial violations due to our large sample size. We also estimated the models adjusted for age, sex, country of origin, educational level, employment status, marital status, living with child(ren) aged 0–15 years, deprivation level, individual long-term conditions and multimorbidity.

Demands on respondents
The effort required of respondents to complete the MTBQ questionnaire was assessed during the patient interviews in the pretest and by analysing the proportion of missing responses in the ‘How are you?’ survey.

Patient and public involvement
There was no patient or public involvement in the design of the study.

RESULTS
The participants were characterised by a mean age of 59 years, a small majority of women (54%), more than 9 out of 10 having a Danish origin, and more than half having a medium level of education (table 1). Almost half were permanently out of work and 43% were employed or studying. The large majority were living with a spouse or cohabitant (68%) and only a small proportion were living with child(ren) aged 0–15 years (18%). Around one-third were living in the most or second-most deprived areas and two-thirds had two or more long-term conditions. A global MTBQ score was calculated for 13,229 (99%) individuals.

Conceptual and measurement model
Conceptual framework, translation and pretest of the questionnaire
The MTBQ was translated into Danish in a thorough process that ensured that the meanings of the original questions were retained and easy to understand. During the process, the expert groups review of the translation resulted in changes to make the language slightly more informal. The comparison of the original English version and the backward translated English version showed good agreement and resulted in few minor changes of the Danish version. The pretest indicated that the questions were meaningful and easily understandable with clear formulations and satisfactory wording, but a clearer page layout of the ‘Does not apply’ response option was requested (online supplemental appendix B). The final Danish version was included in the ‘How
are you?’-questionnaire 2017, p.8, under the headline ‘Behandling’ (‘Treatment’).36

Question properties

The proportion of missing data for each question was less than 3% (table 2). Responses were positively skewed and high floor effects (60%–84%) were found for all questions. Furthermore, the global MTBQ score was positively skewed with 39% of participants scoring 0 (online supplemental appendix D). The highest proportion of ‘does not apply’ responses (41%) was seen for question 10.

Dimensionality

In the CFA analyses, the indices were ambiguous about the fit of the one-dimensional SB-adjusted model with no correlated errors (table 3). The χ² test was statistically significant, but it is well known that the test may be significant in large samples even though the magnitudes of model-data discrepancies are slight. This finding should, therefore, not lead to rejection of the model.37 38 However, CFI (0.895) and TLI (0.865) did not indicate acceptable fit, whereas RMSEA (0.057) and SRMR (0.051) did indicate good fit. The standardised factor loadings ranged from 0.52 to 0.77 (all p<0.05) (online supplemental appendix E). Inspection of the modification indices revealed several correlated error terms, which is not that surprising since some of the questions covered the same underlying aspects (eg, use of medication). Allowing for a few correlated errors based on theoretical judgement markedly improved the model fit (table 3), supporting the unidimensionality of the MTBQ. In this case, the factor loadings ranged from 0.53 to 0.75 (all p<0.05).

In online supplemental appendix C, the exploratory factor analysis indicated the possibility of three factors. Based on this, a three-factor CFA was estimated. Factor 1, termed ‘Medication and self-monitoring’, included four items (nb. 1, 2, 3, 4), factor 2, termed ‘Healthcare contacts and health information’, included four items (nb. 5, 6, 7, 8) and factor 3, termed ‘Coping ability’, included two factors.

Table 2 Responses to the Multimorbidity Treatment Burden Questionnaire (n=13407)

| Question                                                                 | N     | Not difficult n (%) | A little difficult n (%) | Quite difficult n (%) | Very difficult n (%) | Extremely difficult n (%) | Does not apply n (%) | Missing data n (%) |
|-------------------------------------------------------------------------|-------|---------------------|-------------------------|-----------------------|-----------------------|--------------------------|---------------------|------------------|
| 1. Taking lots of medications                                           | 13172 | 7840 (58)           | 1946 (15)               | 441 (4)               | 193 (2)               | 64 (1)                   | 2688 (20)          | 235 (2)          |
| 2. Remembering how and when to take medication                          | 13209 | 9518 (70)           | 1468 (12)               | 260 (2)               | 149 (1)               | 70 (1)                   | 1744 (14)          | 198 (1)          |
| 3. Collecting prescription medication                                   | 13170 | 9775 (72)           | 1229 (10)               | 295 (3)               | 166 (2)               | 139 (1)                  | 1566 (12)          | 237 (2)          |
| 4. Monitoring your medical conditions (eg, checking your blood pressure or blood sugar, monitoring your symptoms, etc) | 13112 | 7520 (55)           | 1409 (11)               | 343 (3)               | 156 (2)               | 113 (1)                  | 3571 (28)          | 295 (2)          |
| 5. Arranging appointments with health professionals                     | 13150 | 8627 (64)           | 1350 (11)               | 379 (3)               | 159 (1)               | 137 (1)                  | 2498 (19)          | 257 (2)          |
| 6. Seeing lots of different health professionals                        | 13083 | 6707 (49)           | 1512 (12)               | 486 (4)               | 239 (2)               | 180 (2)                  | 3959 (30)          | 324 (2)          |
| 7. Attending appointments with health professionals (eg, getting time off work, arranging transport, etc) | 13088 | 7863 (58)           | 1439 (12)               | 436 (3)               | 256 (2)               | 151 (1)                  | 2943 (23)          | 319 (2)          |
| 8. Obtaining clear and up-to-date information about your condition       | 13084 | 8460 (62)           | 1710 (14)               | 551 (5)               | 262 (2)               | 185 (2)                  | 1916 (15)          | 323 (2)          |
| 9. Making recommended lifestyle changes (eg, diet and exercise)         | 13087 | 5494 (40)           | 2842 (21)               | 1224 (10)             | 563 (5)               | 375 (3)                  | 2589 (20)          | 320 (2)          |
| 10. Having to rely on help from family and friends                        | 13134 | 4980 (37)           | 1398 (12)               | 606 (5)               | 335 (3)               | 278 (2)                  | 5537 (41)          | 273 (2)          |

*Population-weighted proportions.
items (nb. 9, 10). Overall, the results indicated that the three-factor CFA could be an alternative to the one-factor model with some improvements in model fit and small increases in factor loadings.

Reliability
The internal consistency of the scale was high with a population-weighted Cronbach’s alpha of 0.87.

Validity
Construct validity
As expected, treatment burden correlated negatively with self-rated health (medium) and health-related quality of life (medium with physical health and large with mental health) and positively with the number of self-reported conditions (small) and perceived stress (medium) (table 4).

Responsiveness
Not applicable.

Interpretability of scores
Table 5 shows that the odds for perceiving higher treatment burden was highest among the youngest individuals (age 25–34 years) and decreased markedly until the age of 75–84 years after adjusting for sex, country of origin, educational level, employment status, cohabitation status, living with child(ren) aged 0–15 years, deprivation level, long-term conditions, and multimorbidity. The adjusted odds for higher treatment burden were also increased for males, individuals of Danish origin, highly educated individuals, unemployed individuals and those permanently out of work, individuals not living with a spouse or cohabitant, individuals living with child(ren) aged 0–15 years, individuals not living in the highest or lowest deprived areas, and for 13 specific long-term conditions (exceptions were asthma, allergy, tinnitus and cataract) with the highest odds seen among those affected by heart attack, stroke, diabetes and mental illness. Furthermore, the odds for higher treatment burden increased with the number of long-term conditions and with lower self-rated health, lower physical and mental health, and higher perceived stress. Six variables in the adjusted models did not fulfil the proportional odds assumption. For these variables, different ORs for no, low and medium treatment burden, respectively, were estimated (see table 5 and online supplemental appendix F for details).

Demands on respondents
During the translation process, great emphasis was put on ensuring that the wording was easy to understand and informal in a Danish context while retaining the original content of each question. In the test phase of the Danish version, none of the ten patients had difficulty understanding and answering the questions. Furthermore, the proportion of missing survey data for each question was less than 3% and a global MTBQ score was calculated for 99% of the participants, despite the fact that the ‘How are you?’ questionnaire is very comprehensive.

Sensitivity analyses
Overall, the sensitivity analyses supported the conclusions from the main analyses. Compared with the full sample, a small decrease was seen in the restricted sample (participants...
Table 5  Participant characteristics by treatment burden categories (participants in treatment aged 25+ years at the time of the 2017 ‘How are you?’ survey, Central Denmark Region, with a global MTBQ score)

| Treatment burden (score)* | N | None (0) | Low (<10) | Medium (10-22) | High (≥22) | Unadjusted OR (95% CI)† | Adjusted OR (95% CI)‡ |
|---------------------------|---|----------|-----------|---------------|------------|-----------------------|----------------------|
| Participants (n, (%))     | 13229 | 5470 (39) | 4066 (30) | 2233 (18) | 1460 (13) |                       |                      |
| Sociodemographic factors  |  |          |           |              |            |                       |                      |
| Mean age (SD), years      | 13229 | 62 (15) | 58 (16) | 55 (16) | 53 (16) |                       |                      |
| Age, years (%):           |  |          |           |              |            |                       |                      |
| 25–34 (ref.)              | 799 | 24       | 31       | 24       | 22       |                       |                      |
| 35–44                     | 1359 | 25       | 30       | 25       | 20       | 0.93 (0.78 to 1.12)   | 0.82 (0.68 to 1.00)  |
| 45–64                     | 2333 | 31       | 32       | 20       | 17       | 0.72 (0.61 to 0.85)   | 0.54 (0.45 to 0.66)  |
| 55–64                     | 3122 | 39       | 32       | 19       | 11       | 0.49 (0.42 to 0.57)   | 0.34 (0.28 to 0.42)  |
| 65–74                     | 3569 | 54       | 29       | 11       | 6        | 0.26 (0.22 to 0.30)   | 0.15 (0.12 to 0.19)  |
| 75–84                     | 1661 | 52       | 27       | 12       | 8        | 0.29 (0.24 to 0.35)   | 0.14 (0.10 to 0.18)  |
| 85+                       | 386  | 32       | 25       | 22       | 22       | 0.83 (0.63 to 1.08)   | 0.41 (0.29 to 0.57)  |
| Sex (%):                  |  |          |           |              |            |                       |                      |
| Female                    | 7258 | 39       | 30       | 18       | 13       | 1.01 (0.94 to 1.09)   | 0.84 (0.77 to 0.92)  |
| Male (ref.)               | 5971 | 39       | 30       | 18       | 13       |                       |                      |
| Country of origin (%):    |  |          |           |              |            |                       |                      |
| Denmark (ref.)            | 12647 | 40       | 31       | 18       | 12       |                       |                      |
| Other                     | 582  | 33       | 24       | 20       | 23       | 1.32 (1.08 to 1.61)§  | 0.75 (0.59 to 0.96)§ |
| Educational level (%):    |  |          |           |              |            |                       |                      |
| Low (0–10 years)          | 2315 | 39       | 28       | 18       | 16       | 1.17 (1.05 to 1.29)   | 1.11 (0.98 to 1.25)  |
| Medium (11–14 years) (ref.) | 7279 | 41       | 30       | 17       | 12       |                       |                      |
| High (15+ years)          | 3310 | 37       | 33       | 19       | 11       | 1.19 (1.08 to 1.31)§  | 1.31 (1.17 to 1.47)§ |
| Employment status (%):    |  |          |           |              |            |                       |                      |
| Employed or student (ref.) | 5820 | 37       | 32       | 19       | 11       |                       |                      |
| Unemployed                | 822  | 18       | 28       | 25       | 28       | 2.78 (2.37 to 3.26)   | 1.58 (1.34 to 1.87)  |
| Permanently out of work   | 6441 | 45       | 28       | 15       | 12       | 0.71 (0.65 to 0.77)§  | 1.22 (1.06 to 1.40)  |
| Living with spouse/cohabitant (%): |  |          |           |              |            |                       |                      |
| No                        | 3261 | 33       | 30       | 20       | 17       | 1.59 (1.46 to 1.73)   | 1.44 (1.31 to 1.58)  |
| Yes (ref.)                | 9748 | 43       | 30       | 16       | 11       |                       |                      |
| Living with child(ren) aged 0–15 years (%): |  |          |           |              |            |                       |                      |
| No (ref.)                 | 9732 | 42       | 30       | 17       | 12       |                       |                      |
| Yes                       | 2014 | 28       | 31       | 23       | 18       | 1.76 (1.59 to 1.94)   | 1.16 (1.01 to 1.33)  |
| Deprivation level (%):    |  |          |           |              |            |                       |                      |
| 1 Least deprived areas (ref.) | 1234 | 43       | 31       | 17       | 9        |                       |                      |
| 2                         | 3737 | 39       | 32       | 17       | 12       | 1.19 (1.05 to 1.35)   | 1.20 (1.04 to 1.39)  |
| 3                         | 3717 | 40       | 29       | 18       | 14       | 1.26 (1.10 to 1.43)   | 1.21 (1.04 to 1.40)  |
| 4                         | 3917 | 39       | 30       | 18       | 14       | 1.28 (1.12 to 1.45)   | 1.17 (1.01 to 1.36)  |
| 5 Most deprived areas     | 624  | 32       | 28       | 22       | 18       | 1.77 (1.46 to 2.14)   | 1.13 (0.90 to 1.40)  |
| Self-reported long-term conditions (%):¶ |  |          |           |              |            |                       |                      |
| Hypertension              | 5100 | 39       | 31       | 18       | 12       | 0.98 (0.91 to 1.06)   | 1.27 (1.14 to 1.43)  |
| Angina pectoris           | 491  | 21       | 25       | 27       | 27       | 2.67 (2.19 to 3.24)   | 1.77 (1.39 to 2.25)  |
| Heart attack              | 351  | 21       | 27       | 23       | 28       | 2.54 (2.01 to 3.20)   | 2.05 (1.57 to 2.70)  |
| Stroke                    | 480  | 26       | 22       | 21       | 31       | 1.85 (1.46 to 2.39)§  | 2.21 (1.71 to 2.85)  |
| Diabetes                  | 1580 | 26       | 32       | 23       | 19       | 1.84 (1.65 to 2.06)   | 2.24 (1.94 to 2.58)  |
| Cancer                    | 862  | 33       | 34       | 17       | 16       | 1.25 (1.08 to 1.45)   | 1.59 (1.32 to 1.92)  |

Continued
with ≥2 long-term conditions) in the proportion of ‘Does not apply’ responses (9%–35% vs 12%–41%), in the total floor effects (55%–82% vs 60%–84%) and in the global MTBQ score of 0 (37% vs 39%). In contrast to the original analysis, country of origin, living with child(ren) under the age of 16 and 4+ long-term conditions (reference: 2–3 long-term conditions) were not significantly associated with increased treatment burden, whereas the most deprived area was (reference: least deprived area).

**DISCUSSION**

In this study, we applied meticulous methods to translate and validate a Danish version of the MTBQ using data

| Table 5 | Continued |
| --- | --- |
| **Treatment burden (score)** | **Unadjusted OR (95% CI)** | **Adjusted OR (95% CI)** |
| N | None (0) | Low (<10) | Medium (10–22) | High (≥22) | **None (0)** | **Low (<10)** | **Medium (10–22)** | **High (≥22)** |
| COPD | 1085 | 27 | 30 | 23 | 20 | 1.82 (1.60 to 2.08) | 1.74 (1.48 to 2.06) |
| Asthma | 1404 | 31 | 31 | 22 | 16 | 1.45 (1.29 to 1.63) | 1.06 (0.92 to 1.23) |
| Allergy | 2702 | 33 | 31 | 20 | 16 | 1.40 (1.28 to 1.53) | 0.94 (0.82 to 1.06) |
| Osteoarthritis | 4639 | 36 | 30 | 19 | 15 | 1.25 (1.16 to 1.35) | 1.24 (1.10 to 1.40) |
| Rheumatoid arthritis | 1340 | 28 | 27 | 22 | 22 | 1.94 (1.70 to 2.20) | 1.52 (1.30 to 1.78) |
| Osteoporosis | 1057 | 35 | 29 | 19 | 16 | 1.25 (1.09 to 1.44) | 1.35 (1.13 to 1.60) |
| Slipped disk or other back disorder | 2773 | 27 | 30 | 23 | 20 | 2.01 (1.83 to 2.20) | 1.53 (1.36 to 1.73) |
| Mental illness | 1964 | 16 | 26 | 27 | 30 | 4.11 (3.70 to 4.56) | 2.61 (2.27 to 3.00) |
| Migraine or frequent headache | 2252 | 25 | 27 | 24 | 24 | 2.44 (2.20 to 2.70) | 1.37 (1.20 to 1.57) |
| Tinnitus | 2342 | 37 | 29 | 19 | 15 | 1.17 (1.06 to 1.29) | 1.02 (0.90 to 1.17) |
| Cataract | 1045 | 39 | 28 | 17 | 16 | 1.06 (0.92 to 1.23) | 1.11 (0.93 to 1.32) |

No of self-reported long-term conditions (%)**

| | N | 0 (ref.) | 1 | 2–3 | 4+ | Mean no of self-reported long-term conditions (SD) |
| --- | --- | --- | --- | --- | --- | --- |
| Mean self-rated health score (SD)**† † | 13032 | 13180 | 1.9 (1) | 2.3 (2) | 2.7 (2) | 3.3 (2) |
| Mean PCS score (SD)**§§ | 13229 | 13229 | 51 (9) | 46 (10) | 41 (11) | 34 (10) |
| Mean MCS score (SD)**§§ | 13229 | 13229 | 53 (8) | 48 (9) | 42 (10) | 35 (10) |
| Mean PSS score (SD) | 13112 | 13112 | 10 (6) | 12 (7) | 16 (7) | 21 (7) |

Bold values indicate statistical significance at the 5% level.

*Population-weighted means, SDs and proportions.
† Adjusted for age, sex, country of origin, educational level, employment status, marital status, living with child(ren) aged 0–15 years, deprivation level, individual long-term conditions and multimorbidity.
§ The variable does not fulfil the proportional odds assumption in the ordered logit model at a 1% significance level. The regression coefficient (and OR) is, therefore, allowed to vary in the partial proportional odds model. The results can be seen in online supplemental appendix F.
†† The reference group for each self-reported long-term condition is the group of individuals without that specific condition. For example, for individuals with diabetes the reference group is those individuals without diabetes.
** Number of self-reported conditions from a list of 17 conditions asked in the survey. When counting the number of conditions in an individual, conditions with similar risk factors and treatment regimens were grouped and only counted once. Hence, if a person had asthma and COPD, it was counted as one condition in that individual. Likewise, if a person had any combination of hypertension, heart attack and angina pectoris, it would only count as one condition in that individual. Respondents included in the analyses may have had other conditions than the 17 conditions asked in the survey.
† † The scores of health measures are included in the regression analyses as continuous variables. Hence, the ORs represent the odds of a higher level of treatment burden category versus the current or lower level treatment burden category for a one-unit increase in the health measure score.
‡‡ The scores of health measures are included in the regression analyses as continuous variables. Hence, the ORs represent the odds of a higher level of treatment burden category versus the current or lower level treatment burden category for a one-unit increase in the health measure score.

COPD, chronic obstructive pulmonary disease; MCS, Mental Component Summary; MTBQ, Multimorbidity Treatment Burden Questionnaire; PCS, Physical Component Summary; PSS, Perceived Stress Scale.
from a large population health survey, which provided a population-based evaluation of treatment burden. The results indicate a high-quality Danish version that is easy to understand with satisfactory psychometric properties. The percentage of missing data for each question was small (<3%) despite the Danish survey being very comprehensive, but the floor effects of each question were high (60%–84%). There was evidence of high internal consistency and good construct validity and confirmatory factor analyses supported the unidimensionality of the scale, although online supplemental analysis indicated that a three-dimensional scale may be an alternative or complement to the one-dimensional scale.

At the population level, we found positive associations between treatment burden and a broad range of sociodemographic factors and health measures, including younger age, being male, being highly educated (compared with medium educational level), being unemployed or permanently out of work, not living with a spouse or cohabitant, living with child(ren), low self-rated health, poor health-related quality of life and high perceived stress. Also, most of the included long-term conditions were associated with higher treatment burden with the strongest associations being found among those affected by myocardial infarction, stroke, diabetes and mental illness; the odds for high treatment burden increased with the number of long-term conditions.

A key strength of our study is its use of a thorough translation process. This process included using the forward-backward translation method and pre-testing the translated version to ensure a high-quality translation. Another major strength was the use of a large population health survey with a high response rate, yielding a large study population, demonstrating that the MTBQ is suitable for evaluation of treatment burden in the general Danish population in treatment despite being developed for individuals with multimorbidity. Moreover, the use of register-based information allowed for weighting of the data. Therefore, the findings of the study are likely to be representative of the general Danish population (aged 25+years) in treatment. A further strength of the study is that the MTBQ questionnaire was developed using the same conceptual framework as the Patient Experience with Treatment and Self-management (PETS) treatment burden measure. Triangulation of findings across studies, cultures and healthcare systems strengthens the growing body of evidence about treatment burden and associated factors.

There are some limitations. First, to test construct validity, we tested prespecified hypotheses of associations between the MTBQ and selected health measures. Ideally, we would have included direct measures of treatment burden, such as number of tablets, complexity of medication regimen, and number of appointments with different health professionals. Additionally, it would have been preferable to include a comparative measure of treatment burden (eg, the Healthcare Task Difficulty or the Treatment Burden Questionnaire). This was precluded due to length limitations in the comprehensive population survey. Also, information on specific types of mental illness was not included in the survey data. Linking to register data on medical information could meet some of these limitations but this was out of scope for this study. Second, it was not possible to calculate the Spearman’s rank correlations or to use the CFA models with SB adjustments using weighted data, which may reduce the generalisability of those findings. However, the weighted partial proportional odds models supported the associations between treatment burden and the health measures. Third, the responsiveness of the MTBQ was not assessed due to the data being cross-sectional, and therefore, no conclusions about temporality or causation can be made. Fourth, establishment of content validity was out of scope for this study. However, there is no reason to think that the range of topics which were important for patients in Denmark would be any different from those in the original validation study in the UK. Additionally, the pretest of the Danish MTBQ indicated good content validity.

In addition to the above limitations, there are some considerations regarding the original English MTBQ. First, as in other treatment burden measures the rating scale is not balanced, but concentrates on the dimension of ‘difficulty’. A balanced scale would include the dimension of ‘easy’ as well. This may affect the respondents’ perception when answering the questionnaire. Second, in the scoring of the MTBQ the response options ‘Not difficult’ and ‘Does not apply’ was equated, potentially affecting the score distribution. Given the large floor effects, a revised approach to these considerations may be investigated in future research. Third, the applied threshold values for interpretability is based on a purely statistical criteria and not a clinical anchor, which would be relevant to identify in order to increase the clinical significance of the burden levels.

In accordance with our findings, previous studies have found that high treatment burden was associated with young age, an increasing number of long-term conditions, low health-related quality of life, poor self-rated health, mental illness, stroke and diabetes. However, the reported positive association with male sex was not found in any of these previous studies. It is also noteworthy that Duncan et al found no associations between high treatment burden and physical medical conditions, in contrast to this study. This difference may be due to our large sample size, giving sufficient power to detect significant associations even for less frequently occurring physical conditions. However, treatment regimens for specific conditions may also differ between the UK and Denmark, which may contribute to differences in the perceived treatment burden for those conditions. Additionally, in the UK study the conditions were obtained from medical record data, whereas for this study they were self-reported, which may contribute to the different findings. The positive association between treatment burden and high educational level (compared with medium level) is not a common finding of previous
studies either. This association may relate to high expectations among the highly educated to themselves, to the life they want to live and to treatment and the healthcare system.

High floor effects similar to those found in this study have previously been found in other studies of generic treatment burden measures. However, both floor effects and positive skewness of the single questions and the global MTBQ score were more pronounced in this study than in the UK study. One reason for this difference is that this study included participants taking treatment for one or more long-term conditions (mean age 59 years), whereas the UK study included a less well-studied population whereby participants had three or more long-term conditions (mean age 71 years). Sensitivity analyses showed a reduction in the ‘Does not apply’ answers and overall floor effects when the analysis was restricted to people with two or more long-term conditions, though the differences were small compared with the original findings. This indicates that the observed floor effects are primarily explained by respondents not feeling burdened by their treatment or experiencing that particular treatment task. It may not be surprising that many individuals do not have a problem with all included aspects. However, even having a large burden from one or two aspects can represent an important burden. Another possibility is that individuals most overwhelmed by their treatment may not have the capacity to fill out the comprehensive survey, thereby enhancing the skewed distribution of treatment burden if the weighting does not fully account for the possible response bias. Hence, the reported treatment burden distribution may be viewed as a conservative estimate of patient-perceived treatment burden in the general population. Also, even though high floor effects are common to treatment burden measures, the measures still show robust and meaningful relationships with other person-centred and patient-reported outcomes, supporting their usability. Nevertheless, different ways to address the issue of high floor effects will be explored in subsequent research.

When assessing dimensionality of a scale, optimisation of statistical fit should in general be balanced against parsimony where only factors that represent a considerable proportion of the variation in the data should be retained. The results from the main analyses support the possibility of using the Danish MTBQ as a one-dimensional measure of (overall) treatment burden across the different aspects of treatment burden. The advantage of this is a parsimonious description of the data, which has implications for use and interpretation. On balance we recommend a one-dimensional structure for the Danish MTBQ. We recognise, however, that there are advantages to having sub-dimensions, namely the ability to identify specific aspects of treatment that are particularly burdensome, which may be more difficult to identify when the MTBQ is used as an overall one-dimensional scale. We, therefore, recommend that subdomain analyses of specific aspects of treatment burden are explored in future research.

To the best of our knowledge, this is the first study to translate and validate a Danish version of a generic treatment burden measure. It is also the first study to assess sociodemographic factors and health measures associated with treatment burden at a population level, providing important evidence to policy makers and clinicians about groups of patients who are most likely to experience high treatment burden (eg, younger people, unemployed, individuals with childcare responsibilities). We recommend further validation to assess the responsiveness of the MTBQ in a Danish context and to assess the use of the MTBQ in a clinical setting, including identification of clinically relevant threshold values to identify patients with high, medium and low treatment burden, respectively, as well as establishing content validity. Also, subsequent research is planned to evaluate treatment burden using a more comprehensive list of long-term conditions drawing on medical register data. Additionally, research into the effects of different multimorbidity patterns on treatment burden is planned to strengthen the understanding of particular burdensome disease combinations for use in the planning of courses of treatment and healthcare system organisation.
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ORCID iDs
Marie Hauge Pedersen http://orcid.org/0000-0001-8472-0555
Polly Duncan http://orcid.org/0000-0002-2244-3254
Chris Salisbury http://orcid.org/0000-0002-4378-3960
Finn Breinholt Larsen http://orcid.org/0000-0002-6848-123X

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