BMJ Open

A systematic review of patient-reported measures of treatment burden in stroke.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-029258
Article Type:	Research
Date Submitted by the Author:	18-Jan-2019
Complete List of Authors:	Gallacher, Katie I; University of Glasgow, Institute of Health and Wellbeing Quinn, Terry; University of Glasgow, Cardiovascular and Medical Sciences Kidd, Lisa; University of Glasgow Eton, David; Mayo Clinic, Elliot, Jennifer; University of Glasgow Johnston, Natalie; University of Glasgow Erwin, Patricia; Mayo Clinic College of Medicine Mair, Frances; University of Glasgow, General Practice and Primary Care
Keywords:	Stroke < NEUROLOGY, treatment burden, patient-centred care, patient-reported measure, systematic review

A systematic review of patient-reported measures of treatment burden in stroke.

Katie Gallacher – Institute of health and Wellbeing, 1 Horselethill Road, Glasgow, G12 9LX, University of Glasgow, katie.gallacher@glasgow.ac.uk, 0141 330 8323 (corresponding author)

Terence J Quinn – Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Scotland

Lisa Kidd – Nursing and Healthcare, University of Glasgow, Glasgow, Scotland

David T Eton – Department of Health Sciences Research, Mayo Clinic, Rochester, US

Jennifer Elliot - Institute of Neuroscience & Psychology, University of Glasgow, Glasgow, Scotland

Natalie Johnston - Institute of health and Wellbeing, University of Glasgow, Glasgow, Scotland

Pat Erwin - Department of Health Sciences Research, Mayo Clinic, Rochester, US

Frances S Mair - Institute of health and Wellbeing, University of Glasgow, Glasgow, Scotland

3040 words

Abstract

Objectives

Treatment burden is the workload of healthcare for people with long-term conditions (LTC) and its impact on wellbeing. A method of measurement is required to identify those experiencing high burden and to measure intervention efficacy. Our aim was to identify, examine and appraise validated patient reported measures (PRMs) of treatment burden in stroke. Here, stroke serves as an exemplar LTC of older adults.

Design

A systematic review of published studies that describe the development and validation of PRMs measuring treatment burden in stroke survivors. We searched MEDLINE, Embase, CINAHL, PsycINFO electronic databases. Limitations: publication January 2000-2018 inclusive. Screening, data extraction and quality appraisal were conducted by two independent reviewers. Content of the PRMs were compared to a published taxonomy of treatment burden. Quality appraisal was conducted using ISOQOL standards.

Setting

No restrictions were set based on clinical setting or geographical location.

Results

From 3368 articles, 5 relevant PRMs were identified: Two stroke specific (Satisfaction with Stroke Care questionnaire (SASC) and The Stroke Patient-Reported Outcome Measure (Stroke-PROM)); the others were generic but validated in stroke (The World Health Organisation Quality of Life-100 (WHOQOL-100); The Patient's Questionnaire on Participation in Discharge Planning (P-QPD); The Chao

Perception of Continuity scale (Chao-PC)). None comprehensively measured treatment burden. Examples of omitted burdens included: developing coping strategies, risk factor modification, returning to driving. The most notable issue regarding quality appraisal was that three PRMs lacked any underpinning conceptual framework relevant to the sample.

Conclusions

There is a need to develop a comprehensive PRM of treatment burden for use in stroke, with potential for use in other older populations.

Strengths and limitations of this study

First systematic review to examine patient-reported measures of treatment burden in stroke, an important aspect of patient care.

Thorough literature search of four major electronic databases and reporting as per PRISMA guidelines.

Exclusion of non-English language papers and publication pre-2000 (the latter due to the rapidly evolving nature of stroke management over recent decades).

Treatment burden is a recently recognised and multi-faceted barometer of quality of care, making searches challenging.

Paper

INTRODUCTION

Stroke is a common condition of older adults, in Europe the incidence of stroke increases by a factor of 100 between the ages of forty and eighty[1]. Stroke treatments, particularly newer rehabilitative therapies, are often complex with multiple interacting components or people involved in their delivery. Multidisciplinary therapy and early discharge from hospital are now recommended in guidelines and these are becoming more commonplace in practice[2 3]. Engaging with and accessing such treatments, however, can demand considerable time and effort from stroke survivors, and this can be difficult for those who are older or frail.

Our previous qualitative research and systematic review demonstrated that people who have had a stroke can feel overwhelmed by managing their recovery and that this is exacerbated when health services are fragmented and lacking in a person-centred approach [4 5]. Treatment burden is defined as the workload of healthcare for people with long-term conditions and its impact on wellbeing [5 6]. It is becoming increasingly recognized by governing bodies and clinical guidelines as an important barometer of quality of care requiring attention [7]. Healthcare workload encompasses all tasks relating to health including those recommended by health professionals and those required to maintain or improve health status [8]. Through our previous research we created a taxonomy of treatment burden in stroke and a conceptual model [4 5], the latter is shown in Figure 1. Our research showed that treatment burden is not purely dependent on volume of healthcare work; the way that services are planned, delivered and co-ordinated also influences the perceived burden felt by an individual [5]. For example, poor co-ordination or communication

between healthcare providers can result in duplication or omission of important aspects of care. Capacity to manage healthcare workload will vary greatly between individuals due to personal abilities and circumstances, therefore two people with the same treatment workload may cope very differently [5 8].

Treatment burden is important because it may reduce quality-of-life and result in non-adherence to recommended treatments, resulting in suboptimal health-related outcomes and wasted health-service resources [9]. For example, intentional and non-intentional non-adherence to medications may result because of an excessively complex or poorly planned medication regime [10]. Consideration of treatment burden is particularly important in older people who may have a decreased ability to self-manage health due to physical, cognitive and emotional difficulties. To date, treatment burden has been under researched [4 11] and may not be adequately considered by clinicians involved in the provision of care for older people with long-term conditions.

Stroke can be used as an exemplar long term condition for describing treatment burden. It is common in older adults [1], often occurs in the context of other comorbidity[12] and can result in complex physical and cognitive impairments[13]. In previous work we created a conceptual model of treatment burden in stroke through qualitative systematic review and analysis of interviews with stroke survivors [4 5]. This provided important insights into the lived experience of treatment burden in this group and highlighted the need for a method to quantify this burden. There are many potential applications of a tool that measures treatment burden. It could enable clinicians to identify those experiencing high levels of burden and to identify those in greater need of intervention such as additional support with self-management. It could facilitate inclusion of treatment burden as an outcome in clinical trials of stroke

therapies alongside measures of efficacy to ascertain if treatments are not simply effective but likely to be *manageable* for older, frailer patients in a 'real world' setting. Lastly, measurement of treatment burden would allow analysis of the effectiveness of interventions aimed at decreasing burden.

Treatment burden is experienced on an individual level, therefore a patient-reported measure (PRM) is the best approach to measurement. A PRM is a report of the patient's health experience that comes directly from the patient, without interpretation of the response by anyone else [14]. It is a common and useful way to measure experiences or outcomes that require information direct from the patient, for example quality-of-life or satisfaction with health services. To help clinicians and researchers choose which of the many available PRMs to use, The International Society for Quality of Life Research (ISOQOL) has published a set of standards that can be used in the quality appraisal of PRMs [14].

The aim of this systematic review is to collate and appraise published, validated PRMs of treatment burden in stroke. We were particularly interested in content of the tool, the extent to which the PRMs aligned with our previously developed conceptual model of treatment burden in stroke [4 5] and the quality of the supporting research[14].

METHODS

We followed PRISMA [15] guidance in the design, conduct and reporting of our review (Appendix 1). A protocol was developed and is available at https://www.crd.york.ac.uk/prospero/. All aspects of screening and data extraction were performed by two independent reviewers (KG, TQ, LK, JE, NJ, DE) with recourse to a third arbitrator as necessary (FM).

Searching strategy

An initial scoping search was carried out to identify relevant terms and phrases which would be used in the formal electronic search. This consisted of a preliminary search of personal files; MEDLINE via Ovid; and the use of the 'related articles' function in PubMed. A formal search strategy was then created with an information scientist (PE). We used a concepts-based approach to design the search syntax, using validated search filters where available. The concepts were: stroke; treatment burden; and patient-reported measure. The full search strategy can be found in Appendix 2. Databases searched were: MEDLINE (Ovid), Embase (Ovid), CINAHL (EBSCO), PsycINFO (EBSO) from 2000 up to and including January 2018. PRMs predating 2000 were deemed to be irrelevant to the current experiences of stroke survivors due to considerable changes in stroke management over recent decades.

Screening

Papers found were uploaded to a web-based systematic software programme DistillerSR (Evidence Partners) to facilitate screening and data extraction. Inclusion criteria are shown in Appendix 3.

Consistent with a prior systematic review of treatment burden measures[11], potentially relevant scales were assessed at the level of individual items or domains. Items in each measure were scrutinized to ascertain if they were consistent with the definition of treatment burden outlined in the inclusion criteria (which is in line with the taxonomy of treatment burden and conceptual model created in our previous research) [4 5]. If less than 50% of items in the PRM reflected treatment burden, then it was excluded. An exception to this was the presence of an independently scorable item or subscale that was deemed relevant, regardless of size. If a study

had used a potentially relevant PRM but no information on development or validation was given in that paper, then the original development paper was sought and examined. If the original development paper was published pre-2000 but the PRM had been used in a published study after that date, then the PRM was included. References of included papers were scrutinized for relevant articles and the above process repeated until no new titles were found.

Data extraction and evidence synthesis

The data extraction and quality appraisal form is provided in Appendix 4. Data extracted were: descriptive data about the study (e.g. sample size and details of participant characteristics); items relating to treatment burden; and information on PRM development or validation including psychometric testing. Content of the items on treatment burden were mapped to the taxonomy of treatment burden created in our previous work [4 5]. This was undertaken to ascertain which aspects of treatment burden were included in the PRMs and to scrutinize if any burdens were omitted. Quality appraisal was conducted using ISOQOL standards [14] as a reference. ISOQOL standards include: whether the PRM was developed from a conceptual framework; reliability (how much it is free from measurement error); content validity (whether it measures what is relevant and important to the patient); construct validity (whether it measures what it purports to measure); responsiveness (whether it can detect changes over time); interpretability of scores (whether scores are meaningful to those using it); and patient and investigator burden (how difficult it is to use). We did not create a summative quality score and did not exclude papers due to perceived risk of bias; rather it served as a point of discussion.

RESULTS

Screening

The PRISMA diagram of included studies is shown in Figure 2. The database search yielded 3368 articles, of which 120 were retrieved for full-text review. The text of a further 21 papers, which were identified through reference list searching or were the original validation studies of PRMs identified within the full text papers, were also fully reviewed.

Identified PRMs

Five papers were identified that each described the development or testing of relevant PRM [16-20] and were included in the review (Table 1).

Table 1 – Included PRMs

Name	Country of study	Purpose of PRM	Structure of PRM	Maximum score	Items relevant to treatment burden	Treatment burden in PRM
SASC	UK	Patient satisfaction with stroke services	2 domains (inpatient, outpatient), 13 items	39	12	Interactions with healthcare staff (kindness, personal care, communication); information provision about illness /services available after discharge; type, amount and adequacy of hospital treatments and therapies; preparation for return home; access to social and medical support in the community; adequacy of outpatient and ambulance services.
Stroke-PROM	China	Effects of stroke on patients participating in drug trials	4 domains (physical, psychological, social, therapeutic), 46 items	230	4	Satisfaction with effects of treatments and services received.
WHOQOL-100	Turkey	Quality of life	6 domains, 24 facets, 100 items	500	4	Accessibility and quality of health and social care.
P-QPD	Sweden	Patient perceived involvement in discharge planning	3 subscales (information, medical treatment, goals and needs) 14 items	56	14	Information provision on illness / tests /examinations /treatments /medication/ rehabilitation; ability to ask questions; ability to participate in discussions about treatments /goals/social support/ rehabilitation needs after discharge; participation in working out discharge plan.
Chao-PC		Patient perceived continuity of care	2 domains, 23 items	115	17	Doctor's knowledge of past medical history and family; location of medical care; continuity of doctor; fragmentation of care; relationship with doctor; communication with doctor; access to other specialist; emergency care; trust in doctor.

The Satisfaction with Stroke Care (SASC) questionnaire[16] was developed to measure stroke survivor's satisfaction with inpatient and outpatient health and social care services; twelve out of thirteen items measure treatment burden. This PRM was originally developed and validated in a sample of stroke survivors. The Stroke Patient Reported Outcome Measure (Stroke-PROM)[17] was developed for use as an outcome measure in stroke drug trials and measures the effects of stroke and its treatments on an individual. Only four out of forty-six items are relevant to treatment burden, but this was an independently scorable domain on satisfaction with treatments. This PRM was developed and validated in a sample of stroke survivors. The other three measures were originally developed in non-stroke populations and subsequently validated in stroke survivors. The World Health Organisation Quality of Life-100 (WHOQOL-100)[18] is aimed at measuring quality of life and four out of its one hundred items are relevant; they measure accessibility and quality of health and social care and constitute an independently scorable domain. The Patient's Questionnaire on Participation in Discharge Planning (P-QPD)[19] measures perceived patient involvement in the discharge planning process, all items are relevant to treatment burden, and all focus on the discharge process. The Chao Perception of Continuity scale (Chao-PC)[20] has twenty three items; seventeen of which measure treatment burden, all items focus on continuity of care.

Details of the participants included in each study are given in Appendix 5. Four of the studies reported a mean age over sixty years [16 18-20], the other stated that 48% were between forty-five and sixty-five and that 40% were sixty-five years or over [17]. Two studies were conducted in the UK (SASC and Chao-PC)[16 20], both were community-based with a majority of white participants. The other studies were conducted in China (Stroke-PROM)[17], Sweden (P-QPD)[19] and Turkey[18]

(WHOQOL-100). All studies included a balanced mix of men and women. Level of participant education varied between studies, the Chinese sample had the highest [17] and one of the UK samples had the lowest [20].

Content of the PRMS

Table 2 shows the aspects of treatment burden included in and missing from the PRMs found. All aspects of treatment burden found within the included PRMs fell inside our previously published conceptual framework and taxonomy.

Table 2 – Our taxonomy of treatment burden in stroke. Aspects of treatment burden not included in any of the PRMs found are shown in red

Type of treatment burden	Healthcare workload	Care deficiency
Making sense of stroke management and planning care	Understanding symptoms, investigations, treatments, risk factors. Information gathering. ***Taking responsibility for health management.*** Goal setting & prioritising. ***Problem solving.*** ***Managing uncertainty.*** ***Maintaining motivation.*** ***Developing coping strategies.*** ***Coping with negative emotions.***	Lack of information provision & poor signposting. Information hard to understand. Poorly timed information. Not enough verbal information. Information not tailored to individual. Lack of support with care planning.
Interacting with others	Seeking advice or help from health and social care professionals. ***Gaining emotional and practical support from friends, family, fellow patients.*** ***Strained relationships due to treatments.*** ***Protecting carers from stress.*** ***Dealing with stigma e.g. of walking aids.***	***Misdiagnosis.*** Paternalism from HPs. Lack of empathy from HPs. Mismatch in ideas between patient and HP. ***Poor access to a GP.*** Poorly co-ordinated care. Poor continuity. ***Poor communication from GP.***
Enacting management strategies	Undergoing acute care. Inpatient rehabilitation. Discharge process. Community rehabilitation. Attending outpatient appointments Taking medications. ***Risk factor modification.*** ***Managing co-morbidities.*** Adaptations to home. Organising and receiving home care. ***Return to driving and employment.*** Using mobility aids. ***Managing finances.*** ***Enacting coping strategies.*** ***Using alternative therapies.***	***Waiting times for inpatient tests.*** Unpleasant ward. Poorly supported discharge. ***Poor GP follow up.*** Lack of help with transport to appointments. Complicated medication regimes. Poor access to home adaptations and walking aids. Substandard home care. ***Poor access to driving assessment.*** ***Complicated benefits system.*** ***Lack of psychological support and support groups.***
Reflecting on management	Attending review appointments. Joint healthcare decisions with HPs. ***Reflecting on progress.*** ***Deciding on adherence to HP advice.*** ***Keeping up to date with new treatments available.*** ***Managing worry about another stroke.***	***Poor short-term follow up for milder cases.*** ***Poor long-term follow up for all.***

Quality appraisal

A detailed account of quality appraisal is given in Table 3. The two PRMs that were developed in stroke populations (SASC and Stroke-PROM)[16 17] were both developed from qualitative work relevant to the sample i.e. in stroke survivors. The WHOQOL-100 had been originally developed from qualitative work undertaken in non-stroke populations and did not include any qualitative research examining stroke survivors' experiences. It was unclear if the Chao-PC or the P-QPD had been developed from any underpinning qualitative work with stroke survivors or drew on any conceptual model.

Table 3 – Quality appraisal of included papers using ISOQOL standards as a reference

Patient reported measure	Developed from qualitative work relevant to sample?	Reliability	Content validity	Construct validity	Responsive-ness	Interpreta-bility	Feasibilty
SASC	Patient / health professional interviews; literature search.	Internal consistency: Cronbachs alpha = 0.86 for hosp satisfaction and 0.77 for home satisfaction. Test-retest: weighted kappa = good reliability for 11 questions. Mean difference on test-retest = 0.59 (SD2.40) hospital satisfaction; 0.32(SD=2.1) home satisfaction.	By post - 28 then 23 participants	Principle components analysis revealed 2 factors. High correlation between hosp satisfaction and other FACES satisfaction measure (r-0.67; p<0.00005). No strong correlations found between hospital satisfaction and measures of function or quality of life. Weak negative correlation found with the Geriatric Depression score (r= -0.26; p-0.0015). No strong correlations found between home satisfaction and other measures apart from a Nottingham extended ADL scale (r=0.30; p=0.00098).	Not tested.	High score = greater satisfaction Score if answering 'satisfied' to all questions: hospital satisfaction =16/24 Home satisfaction =10/15	Response rate to postal questionnaire 87%

Stroke-PROM	Patient / health professional interviews; literature search.	Internal consistency: Cronbach's alpha = 0.905 for the total score and for the four domains it ranged from 0.861 to 0.908. No test-retest.	By referring to literature, consulting questionnaires , interviewing patients and consulting with patients, physician experts and 1 psychometric expert. Confirmed using the CV1 .	Confirmatory factor analysis: index of fit met the standard requirements. Discriminant validity: modified Rankin scale assessed disability and scale could differentiate between healthy controls and stroke patients with diff degrees of disability.	Not tested.	Higher score = more positive responses.	Response rate, completion rate were over 97%. Time to completion 8.9 mins.
WHOQOL-100	Expert review and focus groups but not stroke survivors specifically (results not given).	Internal consistency: Cronbach's alpha for relevant domain (environment) = 0.92 Test-retest not done in stroke survivors and not given.	Yes but not in stroke survivors and results not given	Convergent validity, correlations found between WHOQOL 100 and SF36. Fair to good for relevant domains.	Not in stroke patients and results not given.	Higher = better QOL	Long – 100 items.
P-QPD	Unclear.	Internal consistency: Cronbach's alpha = Information 0.82; Goals Needs 0.87; Medical treatment 0.66.	Face validity established with "patients and experts"	Factor analysis (3 factors extracted); Comparisons of scores across known-groups - subscale differences found on age, length of hospital stay, ADL (independent vs.	Not tested.	Higher =greater participation	Not discussed.

		No test-retest.		dependent). No diffs based on gender, education, living arrangement, or prior experience of stroke.			
Chao PC	Unclear.	Internal consistency: Cronbach's alpha ranged from 0.7 to 0.76 for interpersonal trust, interpersonal knowledge, and provider consistent care. No test-retest.	Face to face delivery of questionnaire for 110 participants.	Exploratory factor analysis: 3 factors supported (interpersonal trust, interpersonal knowledge, provider consistent care). Known-groups validity comparing distress and disability groups -- no significant differences in scores identified.	Not tested	Hither = better continuity.	Low response rate in postal questionnaire. Deemed not easily transferrable to a UK setting without further modification

Regarding reliability, all PRMs had been tested for internal consistency and all were found to be suitably reliable (Cronbach's alpha >0.70). Only one study provided information on test-retest reliability (SASC)[16], assessed by weighted kappa in a sample of 21 patients who repeated the PRM two weeks after the original mailing. Eleven out of the thirteen items had a weighted kappa ≥0.3 and the authors reported that cut-off as acceptable.

Content validity had been assessed in all studies, although in the case of the WHOQOL-100[18] this was not with stroke survivors and the SASC[16] had not been tested face-to-face. All studies had assessed construct validity using various methods including factor analysis, correlations with other PRMs and known-groups validity. Results are detailed in Table 3.

None of the studies had tested for responsiveness to change but this was deemed appropriate as none were measuring outcomes longitudinally.

Regarding interpretability, all papers described the meaning of high and low scores but only one described a cut off (SASC)[16].

Three studies (SASC, Stroke-PROM and Chao-PC)[16 17 20] reported that they assessed participant burden by analysing response rates; the two with high response rates were deemed to have low burden (SASC, Stroke-PROM)[16 17] and the other was deemed not easily transferrable to a UK population without further modification as the response rate had been poor (Chao-PC)[20]. No studies assessed investigator burden i.e. ease of use for the researcher using the PRM.

DISCUSSION

PRMs found

We found five PRMs that measure treatment burden in stroke. All had been tested in older stroke survivors in a mix of hospital and community settings within developed countries. One PRM was aimed at measuring patient satisfaction (SASC)[16] and this covered the most aspects of treatment burden out of the PRMs found however many treatment burdens were missing. Two PRMs focussed on important but limited aspects of treatment burden: continuity of care (Chao-PC)[20] and participation in discharge planning (P-QPD)[19]. The other two (WHOQOL-100 and Stroke-PROM)[17 18] are longer measures that included a small minority of items that were relevant to the issue of treatment burden and independently scorable. In summary, none of the published PRMs comprehensively measured treatment burden in stroke.

During quality appraisal, the most notable weakness was that the three studies that involved validation of PRMs originally developed in non-stroke populations (Chao-PC, P-QPD, WHOQOL-100)[18-20] did not describe any qualitative work underpinning their use in stroke survivors. Additionally, the lack of assessment of content validity or consideration of feasibility of the WHOQOL-100 results in uncertainty about whether this long 100-item measure is suitable in a stroke population who are typically older and potentially cognitively impaired, frail or easily fatigued. Only one PRM (SASC)[16] provided a cut off score, this was for 'satisfactory treatment'. None of the studies were longitudinal therefore none assessed responsiveness, however testing of this would be required if longitudinal measurement was an intended future use of the PRM, such as in a clinical trial. One measure (Chao-PC)[20] was deemed by the authors as unsuitable for use in a UK population due to the low response rate to mailings, assumed to be due to some items not being relevant to those receiving healthcare in the UK. This was because

the items did not distinguish between primary and secondary care and so could be confusing to the patient.

Strengths and limitations

Our search was limited to English language papers which could be viewed as a limitation, although there is increasing evidence that this may have little effect [21]. Exclusion of papers published pre-2000 could also be viewed as a limitation however this was chosen due to the rapidly evolving nature of stroke management over recent decades. One paper published before 2000 was included because the PRM identified had been used in subsequent studies after that date [22]. Searching for papers that examine treatment burden is challenging because it is a relatively new concept that is multi-faceted. To combat this, we clearly defined treatment burden prior to the start of our review based on our previous qualitative work [4 5].

How results fit in with current literature and future research

Treatment burden is a relatively new concept in the medical literature, with robust qualitative work giving us a better understanding of the patient experience of this phenomenon in stroke and other patient groups [4-6 23 24]. Despite this, we still need to understand more about the relationship between treatment burden and health-related outcomes; how burden changes over the patient journey; and whether we can lessen treatment burden through altering the way that healthcare is provided. To examine these areas, quantification of treatment burden is required, yet this is not straightforward. Treatment burden is more than simply healthcare workload, it is a complex interplay of healthcare systems, individuals and their social networks that results in a feeling of encumbrance if demand outweighs personal resources [5 8].This has the potential to lead to disengagement from health services, wasted

resources and worsening health outcomes, particularly in vulnerable groups such as those who are older, frail, socioeconomically deprived or socially isolated [25].

Treatment burden has received attention from researchers interested in individual conditions [26] and from those interested in studying people with multiple long-term conditions [6]. PRMs have recently been developed for use in the latter population [27-29]. There is overlap between these generic treatment burden PRMs and our taxonomy of treatment burden in stroke, however many stroke-specific burdens are omitted such as robotic upper limb neurorehabilitation, speech and language therapy, management of visual problems and vocational rehabilitation. There is good evidence that stroke survivors obtain better health-related outcomes in treatment pathways designed specifically for stroke survivors [30] and therefore their healthcare experience is likely to be different. In this systematic review we chose to exclude PRMs that have not been validated in stroke survivors because current guidance for PRM selection indicates that it is desirable that chosen PRMs be validated in a sample relevant to the population in question [14]. This means that PRMs developed for use in non-stroke populations risk omitting important stroke-specific burdens that arise due to stroke-specific treatments and the complex nature of stroke-related impairments. Additionally, stroke survivors are typically older individuals who may have cognitive impairment, visual difficulties or aphasia that can make completion of a PRM challenging. It is vital that when PRMs are developed for use in older populations that careful attention is paid to usability in this group.

In conclusion, we found no comprehensive PRMs of treatment burden that had been validated in a stroke population. Further research to develop and validate a new PRM of treatment burden in stroke would be important to enable new insights into

quality of care. Such a tool could also be of value for use in other older populations with similar healthcare challenges.

ACKNOWLEDGEMENTS

None

AUTHOR CONTRIBUTIONS

KG, TQ, DE and FM contributed to the design of the project. PE created the search strategy and conducted the search. KG, TQ, LK, DE, JE, NJ and FM screened papers, extracted and analysed data. KG drafted the paper and all authors reviewed drafts and approved the final version.

COMPETING INTERESTS

The Author(s) declare(s) that there is no conflict of interest'

FUNDING SUPPORT

The Stroke Association TSA 2017/01

REFERENCES

1. Bejot Y, Bailly H, Durier J, et al. Epidemiology of stroke in Europe and trends for the 21st century. Presse medicale 2016;45(12 Pt 2):e391-e98
2. Royal College of Physicians. Stroke Guidelines 2016. https://www.rcplondon.ac.uk/guidelines-policy/stroke-guidelines. Accessed 10th January 2019.
3. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke 2016;47(6):E98-E169
4. Gallacher K, Morrison D, Jani B, et al. Uncovering Treatment Burden as a Key Concept for Stroke Care: A Systematic Review of Qualitative Research. PLoS Med 2013;10(6)
5. Gallacher KI, May CR, Langhorne P, et al. A conceptual model of treatment burden and patient capacity in stroke. Bmc Family Practice 2018;19
6. Eton DT, Ridgeway JL, Egginton JS, et al. Finalizing a measurement framework for the burden of treatment in complex patients with chronic conditions. Patient Relat Outcome Meas 2015;6:117-26
7. NICE. Multimorbidity: clinical assessment and management, 2016. https://www.nice.org.uk/guidance/ng56 Accessed 10th January 2019.
8. May CR, Eton DT, Boehmer K, et al. Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness. BMC Health Serv Res 2014;14:281
9. May C, Montori VM, Mair FS. We need minimally disruptive medicine. BMJ 2009;339:b2803
10. Chambers JA, O'Carrol RE, Hamilton B, et al. Adherence to medication in stroke survivors: A qualitative comparison of low and high adherers. Br J Health Psychol 2010:592-609.
11. Eton DT, Elraiyah TA, Yost KJ, et al. A systematic review of patient- reported measures of burden of treatment in three chronic diseases. Patient Relat Outcome Meas 2013;4:7-20
12. Gallacher KI, Batty GD, McLean G, et al. Stroke, multimorbidity and polypharmacy in a nationally representative sample of 1,424,378 patients in Scotland: implications for treatment burden. BMC Med 2014;12:151
13. Stroke Association. State of the nation - Stroke statistics, 2018. https://www.stroke.org.uk/resources/state-nation-stroke-statistics. Accessed 10th January 2019.
14. Reeve B, Wyrwich K, Wu A, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. Qual Life Res 2013;22(8):1889-905
15. PRISMA. Transparent reporting of systematic reviews and meta-analysis, 2009. http://www.prisma-statement.org/. Accessed 10th January 2019.

16. Pound P, Gompertz P, Ebrahim S. Patients' satisfaction with stroke services. Clin Rehab 1994;8:7-17

17. Luo YH, Yang J, Zhang YB. Development and validation of a patient-reported outcome measure for stroke patients. Health Qual Life Outcomes 2015;13

18. Unalan D, Soyuer F, Ozturk A, et al. Comparison of SF-36 and WHOQOL-100 in patients with stroke. Neurology India 2008;56(4):426-32

19. Almborg AH, Ulander K, Thulin A, et al. Patients' perceptions of their participation in discharge planning after acute stroke. J Clin Nurs 2009;18(2):199-209

20. Hill KM, Twiddy M, Hewison J, et al. Measuring patient-perceived continuity of care for patients with long-term conditions in primary care. BMC Fam Pract 2014;15:191

21. Morrison A, Polisena J, Husereau D, et al. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int* J Technol Assess Health Care 2012;28(2):138-44

22. Sulch D, Melbourn A, Perez I, et al. Integrated care pathways and quality of life on a stroke rehabilitation unit. Stroke 2002;33(6):1600-04

23. Sav A, Sav A, endall E, et al. 'You say treatment, I say hard work': treatment burden among people with chronic illness and their carers in Australia. Health Soc Care Community 2013;doi: 10.1111/hsc.12052.

24. Gallacher K, May C, Montori VM, et al. Understanding Treatment Burden in Chronic Heart Failure Patients. A Qualitative Study. Ann Fam Med 2011;9(3):235-43

25. Mair FS, May CR. Thinking about the burden of treatment. BMJ 2014;349:g6680

26. Kahn LS, Vest BM, Madurai N, et al. Chronic kidney disease (CKD) treatment burden among low-income primary care patients. Chronic Illn 2015;11(3):171-83

27. Eton DT, Yost KJ, Lai JS, et al. Development and validation of the Patient Experience with Treatment and Self-management (PETS): a patient-reported measure of treatment burden. Qual Life Res 2017 doi: 10.1007/s11136-016-1397-0

28. Tran VT, Harrington M, Montori VM, et al. Adaptation and validation of the Treatment Burden Questionnaire (TBQ) in English using an internet platform. BMC Med 2014;12:109

29. Duncan P, Murphy M, Man MS, et al. Development and validation of the Multimorbidity Treatment Burden Questionnaire (MTBQ). BMJ Open 2018;8(4):e019413

30. Langhorne P, Williams BO, Gilchrist W, et al. Do stroke units save lives? Lancet 1993;342(8868):395-8

Figure legends

Figure 1 – Conceptual model of stroke treatment burden. The arrows represent the possible pathways between components that stroke patients may follow. The 'enacting management strategies' component has four subcomponents. Reproduced with permission from Plos Med [4] (Creative Commons Attribution-Non Commercial 4.0 License)

Figure 2 – PRISMA flow chart

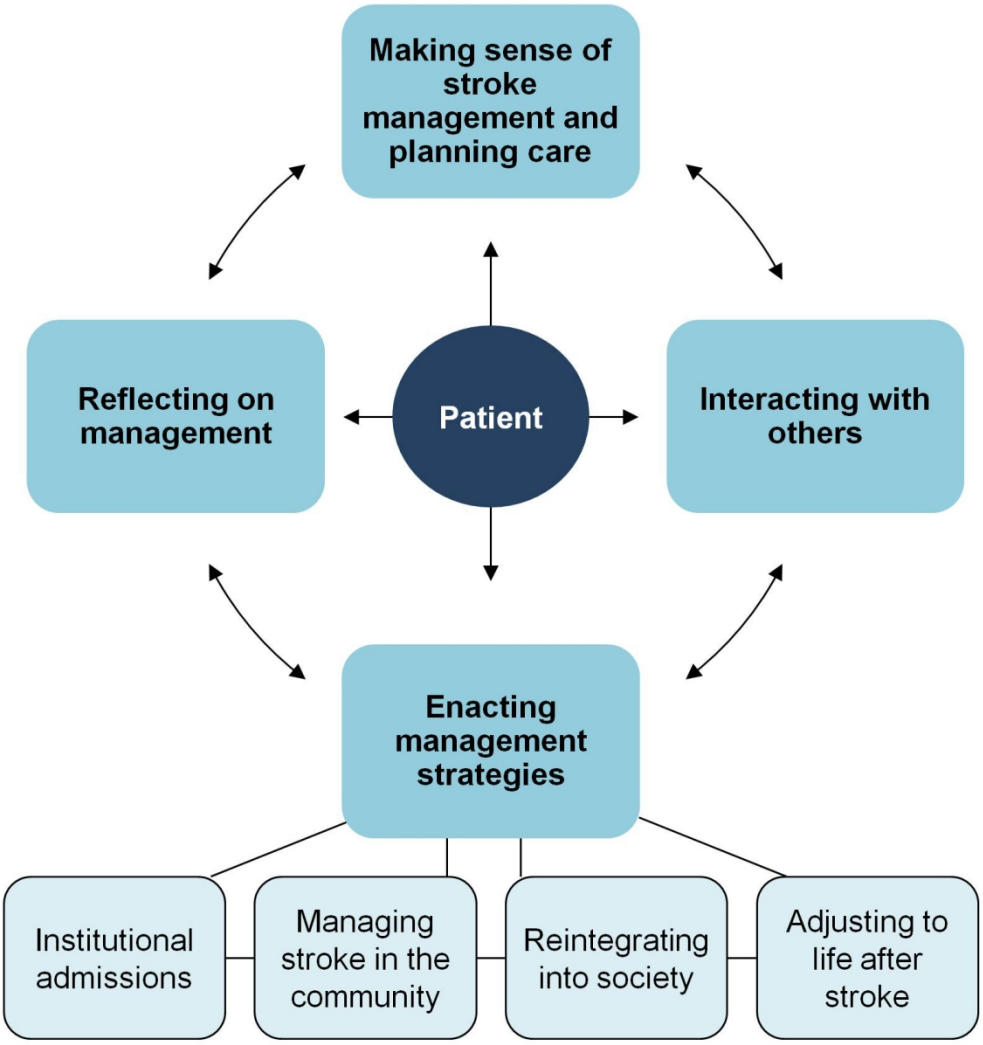
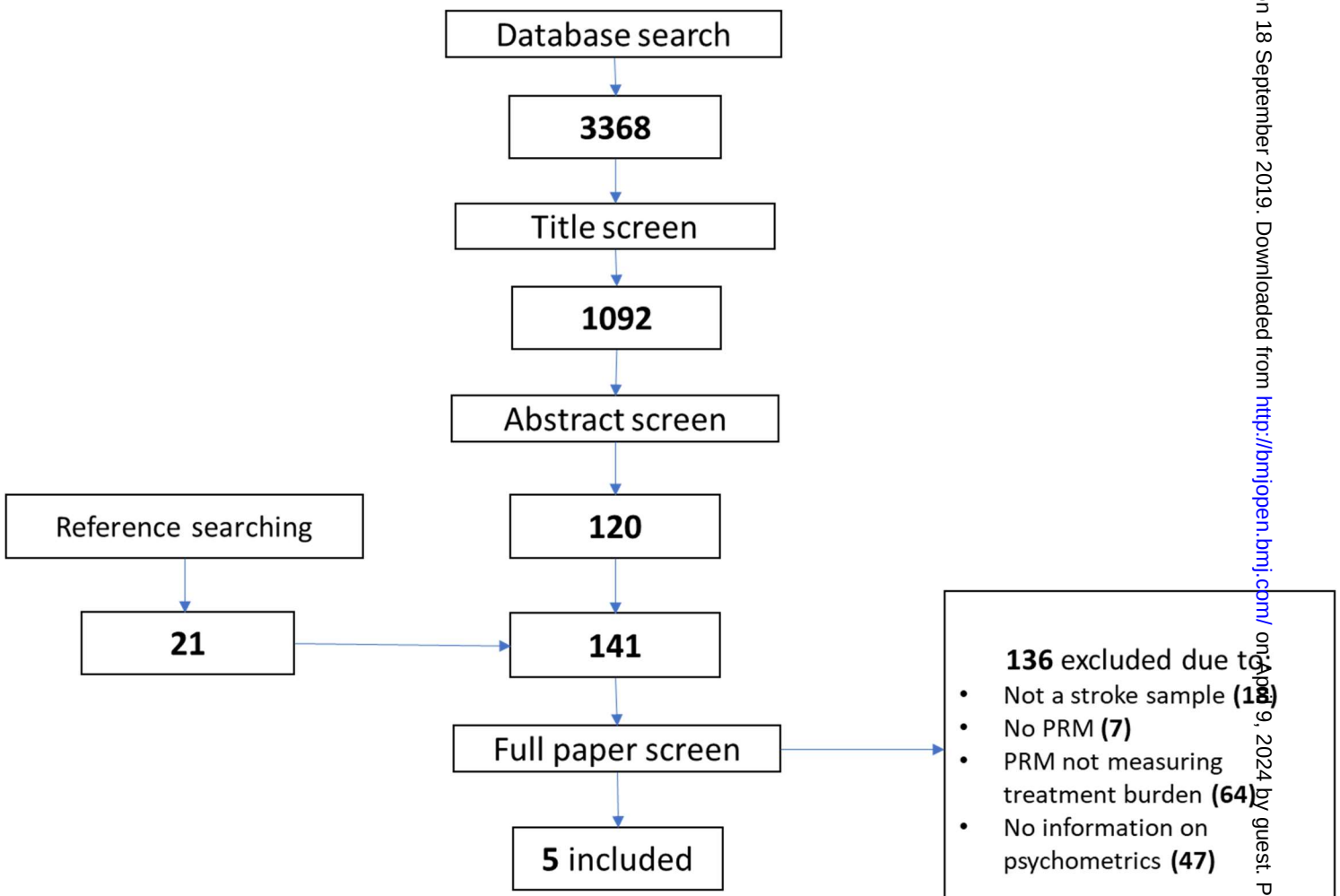


Figure 1 - Conceptual model of stroke treatment burden. The arrows represent the possible pathways between components that stroke patients may follow. The 'enacting management strategies' component has four subcomponents. Reproduced with permission from Plos Med [4] (Creative Commons Attribution-Non Commercial 4.0 License)

135x142mm (300 x 300 DPI)



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Appendix 3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	14
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 and flowchart
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and Appendix 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix 2 – Search strategy

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search history sorted by search number ascending

1 Stroke/ or Stroke Rehabilitation/

2 (cva or "cerebrovascular accident*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 8382 Advanced

3 exp brain infarction/

4 exp brain ischemia/

5 Intracranial Hemorrhages/

6 exp "intracranial embolism and thrombosis"/

7 ((subarachnoid or brain or intracranial or cerebral or cerebrovascular or intracerebral) adj3 (embol* or thrombo* or infarct* or h?emorrhag* or isch?emi*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

8 or/1-7

9 8 or stroke*.ti.

10 9 and "patient reported".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

11 9 and (prom or proms).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12 9 and ((qualitative* or "focus groups" or interview* or questionnaire* or survey* or measur* or scale* or subscale* or item* or domain* or trial* or observation* or "cross section*" or rate* or rating or tool*1 or instrument* or assess* or evaluat* or cohort*).mp. or exp cohort studies/ or randomized controlled trial.pt.)

13 (self adj report*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

14 (patient adj2 (reported or centered or centred or education* or preference* or experience* or satisfaction* or counsel* or perception or perceived)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

15 (patient adj2 (engag* or participat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

16 12 and (13 or 14 or 15)

17 10 or 11 or 16

18 (complex* adj3 (regimen* or treatment* or therap* or intervention*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

19 17 and 18

20 drug administration schedule/ or adheren*.mp. or nonadher*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

21 guideline adherence/ or *lifestyle/ or *activities of daily living/ or *absenteeism/ or *quality of life/ or *patient compliance/ or *treatment refusal/ or *self care/ or *self administration/ or *patient participation/ or patient education as topic/

22 (disrupt* or barrier* or noncomplian* or compliant).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

23 (daily or everyday or disablity* or disabled or support*).mp. or office visits/ or "appointments and scheduling"/ or empower*.mp. or "out of pocket".mp. or financial*.mp. or paperwork.mp. or overwhelm*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

24 transportation/ or driving.mp. or distance.mp. or *educational status/ or health literacy/ or demands.mp. or social support/ or life change events/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

25 *income/ or *costs of illness/ or *fear/ or *pain/ or *poverty/ or anxiety.mp. or skipped.mp. or *exercise/ or *health care costs/ or exp *prescriptions/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

26 17 and (20 or 21 or 22 or 23 or 24 or 25)

27 17 and (burden* or workload).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

28 17 and (deficien* or limitation* or difficult* or isolat* or dependen*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

29	19 or 27 or 28
30	limit 29 to (english language and yr="2000 - 2018")
31	remove duplicates from 30

Appendix 3 – Inclusion / exclusion criteria

INCLUSION CRITERIA
Types of studies English language. From any geographical location. Publication 2000 and onwards. Describes the development, validation or use of a patient-reported measure of treatment burden in stroke - this includes full measures, scorable scales within measures and other scorable components like single items.
Types of participants Adults (>18 yrs) Diagnosed with at least one stroke, including ischaemic, intracerebral haemorrhage or subarachnoid haemorrhage.
Types of outcome measures Treatment Burden • Sense-making and planning e.g. goal setting • Interacting with others e.g. accessing care • Enacting management strategies e.g. taking medications • Reflecting on management e.g. monitoring progress
EXCLUSION CRITERIA
Types of studies Grey literature / not published in a peer reviewed journal. Studies that have not developed, validated or used a patient-reported measure of treatment burden. Studies that do not provide any psychometric characteristics of the measure. Studies that describe a product or device-specific patient preference or satisfaction measure. Studies that are not an original research study.
Types of participants Children (<18 yrs). No CVA diagnosis (e.g. diagnosis of TIA, subdural haematomas, infarction / haemorrhage due to infection or tumour, cerebral palsy or any other neurological deficit). Mixed groups of participants e.g. patients and carers or health care providers, unless results from patients are explicitly separate from other participants.
Types of outcome measures Measures that are not patient-reported. Burden on health services / systems or health professionals. Economic burden at a society level e.g. costs to government or councils. Carer burden.

Appendix 4 – Data extraction form

Data extraction
Sample size
Mean / median age and age range (please specifiy if mean or median)
Number of male and female participants
Socioeconomic status of participants
Ethnicity of participants
Level of disability / activities of daily living of participants
Setting
Other participant info given
What is the purpose of the PRM?
What is its structure e.g. number of domains, subdomains, items
What aspects of treatment burden are covered? E.g. one item on info seeking, one item on medications…
Quality appraisal
Was the measure developed from concepts developed in qualitative work (in a previous study or this one)?
Was the above qualitative work done relevant to the current sample?
Did the above qualitative work include a conceptual model?
Was reliability tested?
How was reliability tested and and what was the result?
Was content validity tested?
How was content validity assessed and what was the result?
Was the population that content validity was tested in similar to the current sample?
Was justification for the recall period given?
Was construct validity assessed?
How was construct validity tested and what were the results?
Was responsiveness tested?
How was responsiveness tested and what was the result?
Was interpretability of scores tested?
How was interpretability of scores measured and what was the result?
Has the measure been translated? If so into what language?
Has it been evaluated in this new language?
Has patient and investigator burden been considered?
Was this an issue?

Appendix 5 - Participant details

PRM	Sample size	Setting	Age	% male	Education level	Ethnicity
Satisfaction with Stroke Care questionnaire (SASC)	149	Community	Mean 71	50%	Not given	80% white; 7% black Caribbean; 5% Bangladeshi, 2% black African, 2% Indian, 2% Pakistani, 1% other Asian, 1% not completed
Stroke Patient Reported Outcome Measure (Stroke-PROM)	475	Community and hospital	11.6%≤45; 48.4%45-65; 40%≥65	60%	38.5% primary school or lower; 30.3% junior high school; 18.5% senior high school; 12.6% college or higher	Not given
World Health Organisation Quality of Life-100 (WHOQOL-100)	70	Hospital	Mean 60.16 (SD 11.30)	61%	67.1% primary school graduates or less educated; 40% were retired.	Not given
Patient's Questionnaire on Participation in Discharge Planning (PQPDP)	188	Hospital	Mean 74 (SD 11.2)	56%	75% elementary school; 19% sec/high school; 6% university	Not given
Chao Perception of Continuity scale (Chao-PC)	168	Community	Mean 67.65 (SD 12.54)	58%	79% <16 yrs; 14.3% <18 years; 6% >18 yrs	98.2% white British

BMJ Open

A systematic review of patient-reported measures of treatment burden in stroke.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-029258.R1
Article Type:	Research
Date Submitted by the Author:	11-Jul-2019
Complete List of Authors:	Gallacher, Katie I; University of Glasgow, Institute of Health and Wellbeing Quinn, Terry; University of Glasgow, Cardiovascular and Medical Sciences Kidd, Lisa; University of Glasgow Eton, David; Mayo Clinic, Elliot, Jennifer; University of Glasgow Johnston, Natalie; University of Glasgow Erwin, Patricia; Mayo Clinic College of Medicine Mair, Frances; University of Glasgow, General Practice and Primary Care
Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Neurology
Keywords:	Stroke < NEUROLOGY, treatment burden, patient-centred care, patient-reported measure, systematic review

A systematic review of patient-reported measures of treatment burden in stroke.

Katie Gallacher – Institute of Health and Wellbeing, 1 Horselethill Road, Glasgow, G12 9LX, University of Glasgow, katie.gallacher@glasgow.ac.uk, 0141 330 8323 (corresponding author)

Terence J Quinn – Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Scotland

Lisa Kidd – Nursing and Healthcare, University of Glasgow, Glasgow, Scotland

David T Eton – Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota, USA

Jennifer Elliot - Institute of Neuroscience & Psychology, University of Glasgow, Glasgow, Scotland

Natalie Johnston - Institute of Health and Wellbeing, University of Glasgow, Glasgow, Scotland

Pat Erwin - Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota, USA

Frances S Mair - Institute of Health and Wellbeing, University of Glasgow, Glasgow, Scotland

Abstract

Objectives

Treatment burden is the workload of healthcare for people with long-term conditions (LTC) and its impact on wellbeing. A method of measurement is required to identify those experiencing high burden and to measure intervention efficacy. Our aim was to identify, examine and appraise validated patient reported measures (PRMs) of treatment burden in stroke. Here, stroke serves as an exemplar LTC of older adults.

Design

A systematic review of published studies that describe the development and validation of PRMs measuring treatment burden in stroke survivors.

Data sources

We searched MEDLINE, Embase, CINAHL, PsycINFO electronic databases.

Eligibility criteria

Studies published between January 2000 and 12th April 2019 inclusive, in English language. No restrictions were set based on clinical setting or geographical location.

Data extraction and synthesis

Screening, data extraction and quality appraisal were conducted by two independent reviewers. Content of the PRMs were compared to a published taxonomy of treatment burden. Quality appraisal was conducted using International Society for Quality of Life Research (ISOQOL) standards.

Results

From 3993 articles, 6 relevant PRMs were identified: Three were stroke specific: The Satisfaction with Stroke Care questionnaire (SASC); The Stroke Patient-Reported Outcome Measure (Stroke-PROM); and The Barriers to Physical Activity after Stroke scale (BAPAS). Three were generic but validated in stroke: The World Health Organisation Quality of Life-100 (WHOQOL-100); The Patient's Questionnaire on Participation in Discharge Planning (P-QPD); and The Chao Perception of Continuity scale (Chao-PC). None comprehensively measured treatment burden. Examples of omitted burdens included: developing coping strategies, managing finances, and returning to driving. The most notable issue regarding quality appraisal was that three PRMs lacked any underpinning qualitative research relevant to the sample.

Conclusions

There is a need to develop a comprehensive PRM of treatment burden for use in stroke, with potential for use in other older populations.

294/300

Strengths and limitations of this study

The first systematic review to examine patient-reported measures of treatment burden in stroke, an important aspect of patient care.

Thorough literature search of four major electronic databases and reporting as per Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Exclusion of non-English language papers and publication pre-2000 (the latter due to the rapidly evolving nature of stroke management over recent decades).

Treatment burden is a recently recognised concept influencing quality of care and quality of life, making literature searches challenging.

Paper

INTRODUCTION

Stroke is a common condition of older adults, in Europe the incidence of stroke increases by a factor of 100 between the ages of forty and eighty[1]. Stroke treatments, particularly newer rehabilitative therapies, are often complex with multiple interacting components or people involved in their delivery. Multidisciplinary therapy and early discharge from hospital are now recommended in guidelines and these are becoming more commonplace in practice[2 3]. Engaging with and accessing such treatments, however, can demand considerable time and effort from stroke survivors, and this can be difficult for those who are older or frail.

Our previous qualitative research and systematic review demonstrated that people who have had a stroke can feel overwhelmed by managing their recovery and that this is exacerbated when health services are fragmented and lacking in a person-centred approach [4 5]. Treatment burden is defined as the workload of healthcare for people with long-term conditions and its impact on wellbeing [5 6]. It is becoming increasingly recognized by governing bodies and clinical guidelines as an important barometer of quality of care requiring attention [7]. Healthcare workload encompasses all tasks relating to health including those recommended by health professionals and those required to maintain or improve health status [8]. Through our previous research we created a taxonomy of treatment burden in stroke and a conceptual model [4 5], the latter is shown in Figure 1. Our research showed that

treatment burden is not purely dependent on volume of healthcare work; the way that services are planned, delivered and co-ordinated also influences the perceived burden felt by an individual [5]. For example, poor co-ordination or communication between healthcare providers can result in duplication or omission of important aspects of care. Capacity to manage healthcare workload will vary greatly between individuals due to personal abilities and circumstances, therefore two people with the same treatment workload may cope very differently [5 8].

Treatment burden is important because it may reduce quality-of-life and result in non-adherence to recommended treatments, resulting in suboptimal health-related outcomes and wasted health-service resources [9]. For example, intentional and non-intentional non-adherence to medications may result because of an excessively complex or poorly planned medication regime [10]. Consideration of treatment burden is particularly important in older people who may have a decreased ability to self-manage health due to physical, cognitive and emotional difficulties. To date, treatment burden has been under researched [4 11] and may not be adequately considered by clinicians involved in the provision of care for older people with long-term conditions.

Stroke can be used as an exemplar long term condition for describing treatment burden. It is common in older adults [1], often occurs in the context of other comorbidity[12] and can result in complex physical and cognitive impairments[13]. In previous work we created a conceptual model of treatment burden in stroke through qualitative systematic review and analysis of interviews with stroke survivors [4 5]. This provided important insights into the lived experience of treatment burden in this group and highlighted the need for a method to quantify this burden. There are many potential applications of a tool that measures treatment burden. It could enable

clinicians to identify those experiencing high levels of burden who may need additional support with self-management. It could facilitate inclusion of treatment burden as an outcome in clinical trials of stroke therapies alongside measures of efficacy to ascertain if treatments are not only effective, but *manageable* in older, frailer patients in the 'real world.' Lastly, measurement of treatment burden would allow analysis of the effectiveness of interventions aimed at decreasing burden.

Treatment burden is experienced on an individual level, therefore a patient-reported measure (PRM) is the best approach to measurement. A PRM is a report of the patient's health experience or experience with healthcare that comes directly from the patient, without interpretation of the response by anyone else [14]. It is a common and useful way to measure experiences or outcomes that require information directly from the patient, for example health-related quality of life or satisfaction with health services. To help clinicians and researchers select which PRMs to use in a given setting, The International Society for Quality of Life Research (ISOQOL) has published a set of standards that can be used in the quality appraisal of PRMs [14].

The aim of this systematic review is to collate and appraise published, validated PRMs of treatment burden in stroke, including discrete portions of PRMs that measure burden (e.g., scales, scorable single items). We were particularly interested in content of the tool, the extent to which the PRMs aligned with our previously developed conceptual model of treatment burden in stroke [4 5] and the quality of the supporting research[14].

METHODS

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [15] guidance in the design, conduct and reporting of our review (Appendix 1). A protocol was developed and is available at https://www.crd.york.ac.uk/prospero/. All aspects of screening and data extraction were performed by two independent reviewers (KG, TQ, LK, JE, NJ, DE) with recourse to a third arbitrator as necessary (FM).

Searching strategy

An initial scoping search was carried out to identify relevant terms and phrases which would be used in the formal electronic search. This consisted of a preliminary search of personal files; MEDLINE via Ovid; and the use of the 'related articles' function in PubMed. A formal search strategy was then created with an information scientist (PE). We used a concepts-based approach to design the search syntax, using validated search filters where available. The concepts were: stroke; treatment burden; and patient-reported measure. The full search strategy can be found in Appendix 2. As 'Patient-reported measure' is not a recognised subject heading, 'patient reported outcome measure' was utilised and in addition 'patient reported' was entered as a textword or subject heading or author keyword. Databases searched were: MEDLINE (Ovid), Embase (Ovid), CINAHL (EBSCO), PsycINFO (Ovid) from 1st January 2000 up to and including 12th April 2019. PRMs predating 2000 were deemed to be irrelevant to the current experiences of stroke survivors due to considerable changes in stroke management over recent decades.

Screening

Papers found were uploaded to a web-based systematic software programme DistillerSR (Evidence Partners) to facilitate screening and data extraction. Inclusion criteria are shown in Appendix 3.

Consistent with a prior systematic review of treatment burden measures[11], potentially relevant scales were assessed at the level of individual items or domains. Items in each measure were scrutinized to ascertain if they were consistent with the definition of treatment burden outlined in the inclusion criteria (which is in line with the taxonomy of treatment burden and conceptual model created in our previous research) [4 5]. If less than 50% of items in the PRM reflected treatment burden, then it was excluded. An exception to this was the presence of an independently scorable item or subscale that was deemed relevant, regardless of size. If a study had used a potentially relevant PRM but no information on development or validation was given in that paper, then the original development paper was sought and examined. If the original development paper was published pre-2000 but the PRM had been used in a published study after that date, then the PRM was included. References of included papers were scrutinized for relevant articles and the above process repeated until no new titles were found.

Data extraction and evidence synthesis

The data extraction and quality appraisal form is provided in Appendix 4. Data extracted were: descriptive data about the study (e.g. sample size and details of participant characteristics); items relating to treatment burden; and information on PRM development or validation including psychometric testing. Content of the items on treatment burden were mapped to the taxonomy of treatment burden created in our previous work [4 5]. This was undertaken to ascertain which aspects of

treatment burden were included in the PRMs and to scrutinize if any burdens were omitted. Quality appraisal was conducted using ISOQOL standards [14] as a reference. ISOQOL standards include: whether the PRM was developed from underpinning qualitative research ; reliability (how much it is free from measurement error); content validity (whether it measures what is relevant and important to the patient); construct validity (whether it measures what it purports to measure); responsiveness (whether it can detect changes over time); interpretability of scores (whether scores are meaningful to those using it); and patient and investigator burden (how difficult it is to use). We did not create a summative quality score and did not exclude papers due to perceived risk of bias; rather it served as a point of discussion.

Patient and public involvement

The Research Advisory Group that guides this programme of research includes four stroke survivors or carers of stroke survivors. Their input has helped to guide the aims, objectives and methods of this study. Additionally, the results of this study were presented to three individuals with cardiovascular disease and discussed in a focus-group setting which informed our discussion in the paper.

RESULTS

Screening

The PRISMA diagram of included studies is shown in Figure 2. The database search yielded 3993 articles, of which 184 were retrieved for full-text review. The text of a further 21 papers, which were identified through reference list searching or were the original validation studies of PRMs identified within the full text papers, were also fully reviewed.

Identified PRMs

Six papers were identified that each described the development or testing of a relevant PRM [16-21] and were included in the review (Table 1).

Table 1 – Included PRMs

Name	Country of study	Purpose of PRM	Structure of PRM	Maximum score	Items relevant to treatment burden	Treatment burdens in PRM
SASC[16]	UK	Patient satisfaction with stroke services	2 domains (inpatient, outpatient), 13 items	39	12	Interactions with healthcare staff (kindness, personal care, communication); information provision about illness /services available after discharge; type, amount and adequacy of hospital treatments and therapies; preparation for return home; access to social and medical support in the community; adequacy of outpatient and ambulance services.
Stroke-PROM[17]	China	Effects of stroke on patients participating in drug trials	4 domains (physical, psychological, social, therapeutic), 46 items	230	4	Satisfaction with effects of treatments and services received.
BAPAS[18]	France	Patient perceived barriers to regular physical exercise after stroke	2 subscales (behavioural barriers, physical barriers), 14 items	70	7	Information provision; transport problems; lack of motivation; fear of another stroke; fear of falling; lack of finances; activity not suited to individual (patient not sporty).
WHOQOL-100[19]	Turkey	Quality of life	6 domains, 24 facets, 100 items	500	4	Accessibility and quality of health and social care.
P-QPD[20]	Sweden	Patient perceived involvement in discharge planning	3 subscales (information, medical treatment, goals and needs), 14 items	56	14	Information provision on illness / tests /examinations /treatments /medication/ rehabilitation; ability to ask questions; ability to participate in discussions about treatments /goals/ social support/ rehabilitation needs after discharge; participation in working out discharge plan.

Chao-PC [21]	UK	Patient perceived continuity of care	2 domains, 23 items	115	17	Doctor's knowledge of past medical history and family; location of medical care; continuity of doctor; fragmentation of care; relationship with doctor; communication with doctor; access to other specialist; emergency care; trust in doctor.

The Satisfaction with Stroke Care (SASC) questionnaire[16] was developed to measure stroke survivor's satisfaction with inpatient and outpatient health and social care services; twelve out of thirteen items measure treatment burden. This PRM was originally developed and validated in a sample of stroke survivors. The Stroke Patient Reported Outcome Measure (Stroke-PROM)[17] was developed for use as an outcome measure in stroke drug trials and measures the effects of stroke and its treatments on an individual. Only four out of forty-six items are relevant to treatment burden, but this was an independently scorable domain on satisfaction with treatments. This PRM was developed and validated in a sample of stroke survivors. The Barriers to Physical Activity after Stroke scale (BAPAS) [18] was developed to measure the perceived barriers to regular physical exercise after a stroke. It was developed and validated in stroke survivors and seven out of fourteen items were deemed relevant to treatment burden. The other three measures were originally developed in non-stroke populations and subsequently validated in stroke survivors. The World Health Organisation Quality of Life-100 (WHOQOL-100)[19] is aimed at measuring quality of life and four out of its one hundred items are relevant; they measure accessibility and quality of health and social care and constitute an independently scorable domain. The Patient's Questionnaire on Participation in Discharge Planning (P-QPD)[20] measures perceived patient involvement in the discharge planning process, all items are relevant to treatment burden, and all focus on the discharge process. The Chao Perception of Continuity scale (Chao-PC)[21] has twenty three items; seventeen of which measure treatment burden, all items focus on continuity of care.

Details of the participants included in each study are given in Appendix 5. Five of the studies reported a mean age over sixty years [16 18-21], the other stated that 48%

were between forty-five and sixty-five and that 40% were sixty-five years or over [17]. Two studies were conducted in the UK (SASC and Chao-PC)[16 21], both were community-based with a majority of white participants. The other studies were conducted in France (BAPAS)[18], China (Stroke-PROM)[17], Sweden (P-QPD)[20] and Turkey[19] (WHOQOL-100). All studies included a balanced mix of men and women. Level of participant education varied between studies, the Chinese sample had the highest [17] and one of the UK samples had the lowest [21].

Content of the PRMS

Table 2 shows the aspects of treatment burden included in and missing from the PRMs found. All aspects of treatment burden found within the included PRMs fell inside our previously published conceptual framework and taxonomy.

Table 2 – Our taxonomy of treatment burden in stroke. Aspects of treatment burden not included in any of the PRMs found are shown in red

Type of treatment burden	Healthcare workload	Care deficiency
Making sense of stroke management and planning care	Understanding symptoms, investigations, treatments, risk factors. Information gathering. ***Taking responsibility for health management.*** Goal setting & prioritising. ***Problem solving.*** ***Managing uncertainty.*** Maintaining motivation. ***Developing coping strategies.*** Coping with negative emotions.	Lack of information provision & poor signposting. Information hard to understand. Poorly timed information. Not enough verbal information. Information not tailored to individual. Lack of support with care planning.
Interacting with others	Seeking advice or help from health and social care professionals. ***Gaining emotional and practical support from friends, family, fellow patients.*** ***Strained relationships due to treatments.*** ***Protecting carers from stress.*** ***Dealing with stigma e.g. of walking aids.***	***Misdiagnosis.*** Paternalism from HPs. Lack of empathy from HPs. Mismatch in ideas between patient and HP. ***Poor access to a GP.*** Poorly co-ordinated care. Poor continuity. ***Poor communication from GP.***
Enacting management strategies	Undergoing acute care. Inpatient rehabilitation. Discharge process. Community rehabilitation. Attending outpatient appointments / therapies. Taking medications. Risk factor modification. ***Managing co-morbidities.*** Adaptations to home. Organising and receiving home care. ***Return to driving and employment.*** Using mobility aids. ***Managing finances.*** Paying for treatments. ***Enacting coping strategies.*** ***Using alternative therapies.***	***Waiting times for inpatient tests.*** Unpleasant ward. Poorly supported discharge. ***Poor GP follow up.*** Lack of help with transport to appointments. Complicated medication regimes. Poor access to home adaptations and walking aids. Substandard home care. ***Poor access to driving assessment.*** ***Complicated benefits system.*** ***Lack of psychological support and support groups.***
Reflecting on management	Attending review appointments. Joint healthcare decisions with HPs. ***Reflecting on progress.*** ***Deciding on adherence to HP advice.*** ***Keeping up to date with new treatments available.*** Managing worry about another stroke.	***Poor short-term follow up for milder cases.*** ***Poor long-term follow up for all.***

Quality appraisal

A detailed account of quality appraisal is given in Table 3. The three PRMs that were developed in stroke populations (SASC, Stroke-PROM and BAPAS)[16-18] were developed from qualitative work relevant to the sample i.e. in stroke survivors. The WHOQOL-100 had been originally developed from qualitative work undertaken in non-stroke populations and did not include any qualitative research examining stroke survivors' experiences. It was unclear if the Chao-PC or the P-QPD had been developed from any underpinning qualitative work with stroke survivors, however development of the Chao-PC was underpinned by Banahan's conceptual model of continuity of care[22 23].

Table 3 – Quality appraisal of included papers using ISOQOL standards as a reference

Patient reported measure	Developed from qualitative work relevant to sample?	Reliability	Content validity	Construct validity	Responsiveness	Interpretability	Feasibility
SASC	Patient / health professional interviews; literature search.	Internal consistency: Cronbachs alpha = 0.86 for hosp satisfaction and 0.77 for home satisfaction. Test-retest: weighted kappa = good reliability for 11 questions. Mean difference on test-retest = 0.59 (SD2.40) hospital satisfaction; 0.32(SD=2.1) home satisfaction.	By post - 28 then 23 participants.	Principle components analysis revealed 2 factors. High correlation between hosp satisfaction and other FACES satisfaction measure (r-0.67; p<0.00005). No strong correlations found between hospital satisfaction and measures of function or quality of life. Weak negative correlation found with the Geriatric Depression score (r= -0.26; p-0.0015). No strong correlations found between home satisfaction and other measures apart from a Nottingham extended	Not tested.	High score = greater satisfaction Score if answering 'satisfied' to all questions: hospital satisfaction= 16/24 Home satisfaction= 10/15	Response rate to postal questionnaire 87%.

				ADL scale (r=0.30; p=0.00098).			
Stroke-PROM	Patient / health professional interviews; literature search.	Internal consistency: Cronbach's alpha = 0.905 for the total score and for the four domains it ranged from 0.861 to 0.908. No test-retest.	By referring to literature, consulting questionnaires, interviewing patients and consulting with patients, physician experts and 1 psychometric expert. Confirmed using the CV1 .	Confirmatory factor analysis: index of fit met the standard requirements. Discriminant validity: modified Rankin scale assessed disability and scale could differentiate between healthy controls and stroke patients with diff degrees of disability.	Not tested.	Higher score = more positive responses.	Response rate, completion rate were over 97%. Time to completion = 8.9 mins.
BAPAS	Patient interviews and health professional expert panel.	Internal consistency: Cronbachs alpha = 0.86. Test retest: Intraclass correlation coefficient model 2,1 = 0.91 (95% CI 0.79-0.97).	Panel of experts in the field and 10 patients.	Principal component analysis with number of factors fixed at 8 - showed original structure (BAPAS-27) was replicated in the final BAPAS scale. The 8 factors explained 84% of total variance of the BAPAS scale. Also assessed the proper construct of the BAPAS scale - 2 factors were obtained that explored	Not tested.	Higher score = more barriers.	Time to complete if naïve = 4 mins.

				physical dimensions and 2 that explore behavioural. A 2 part scale was constructed (physical and behavioural). Criterion validity tested using correlation with mRS score: r=0.65 (p<0.001).			
WHOQOL -100	Expert review and focus groups but not stroke survivors specifically (results not given).	Internal consistency: Cronbach's alpha for relevant domain (environment) = 0.92 Test-retest not done in stroke survivors and not given.	Yes but not in stroke survivors and results not given.	Convergent validity, correlations found between WHOQOL 100 and SF36. Fair to good for relevant domains.	Not in stroke patients and results not given.	Higher = better QOL	Long - 100 items.
P-QPD	Unclear.	Internal consistency: Cronbach's alpha = Information 0.82; Goals Needs 0.87; Medical treatment 0.66.	Face validity established with "patients and experts".	Factor analysis (3 factors extracted); Comparisons of scores across known-groups - subscale differences found on age, length of hospital stay, ADL (independent vs. dependent). No diffs based on gender, education, living arrangement, or prior	Not tested.	Higher =greater participation.	Not discussed.

		No test-retest.		experience of stroke.			
Chao PC	Unclear.	Internal consistency: Cronbach's alpha ranged from 0.7 to 0.76 for interpersonal trust, interpersonal knowledge, and provider consistent care. No test-retest.	Face to face delivery of questionnaire for 110 participants.	Exploratory factor analysis: 3 factors supported (interpersonal trust, interpersonal knowledge, provider consistent care). Known-groups validity comparing distress and disability groups - no significant differences in scores identified.	Not tested	Higher = better continuity.	Low response rate in postal questionnaire. Deemed not easily transferrable to a UK setting without further modification.

Regarding reliability, all PRMs had been tested for internal consistency and all were found to be suitably reliable (Cronbach's alpha >0.70). Only two studies provided information on test-retest reliability (SASC and BAPAS)[16 18]. The SASC study assessed this by weighted kappa in a sample of 21 patients who repeated the PRM two weeks after the original mailing [16]. Eleven out of the thirteen items had a weighted kappa ≥0.3 and the authors reported that cut-off as acceptable. The BAPAS study repeated the measure in 21 participants after 4-6 days and found good reproducibility with an intra-class coefficient (ICC) of 0.9 [18]. However, authors note the short interval between test and retest therefore the possibility of recollection bias.

Content validity had been assessed in all studies, although in the case of the WHOQOL-100[19] this was not with stroke survivors and the SASC[16] had not been tested face-to-face. All studies had assessed construct validity using various methods including factor analysis, correlations with other PRMs and known-groups validity. Results are detailed in Table 3.

None of the studies had tested for responsiveness to change but this was deemed appropriate as none were measuring outcomes longitudinally.

Regarding interpretability, all papers described the meaning of high and low scores but only one described a cut off (SASC)[16].

Three studies (SASC, Stroke-PROM and Chao-PC)[16 17 21] reported that they assessed participant burden by analysing response rates; the two with high response rates were deemed to have low burden (SASC, Stroke-PROM)[16 17] and the other with a low response rate (Chao-PC) was deemed not easily transferrable to a UK population without further modification due to the structure and content of its

items[21]. Two studies reported time to complete the measure (Stroke-PROM and BAPAS) [17 18]. None assessed investigator burden i.e. ease of use for the researcher using the PRM.

DISCUSSION

PRMs found

We found six PRMs that measure treatment burden in stroke. All had been tested in older stroke survivors in a mix of hospital and community settings within developed countries. None of the PRMs found had been developed to comprehensively evaluate treatment burden and none of the included studies were aimed at doing so. Rather, they were aimed at assessing related concepts or narrow aspects of treatment burden. One PRM, which was developed before treatment burden had been conceptualised in the medical literature, was aimed at measuring patient satisfaction (SASC)[16] and this covered the most aspects of treatment burden out of the PRMs found however many treatment burdens were missing. Three PRMs focussed on important but limited aspects of treatment burden: barriers to participation in physical activity (BAPAS) [18], continuity of care (Chao-PC)[21] and participation in discharge planning (P-QPD)[20]. The other two (WHOQOL-100 and Stroke-PROM)[17 19] are longer measures that included a small minority of items that were relevant to the issue of treatment burden and independently scorable. In summary, none of the published PRMs comprehensively measured treatment burden in stroke.

During quality appraisal, the most notable weakness was that the three studies that involved validation of PRMs originally developed in non-stroke populations (Chao-PC, P-QPD, WHOQOL-100)[19-21] did not describe any qualitative work

underpinning their use in stroke survivors. Additionally, the lack of assessment of content validity or consideration of feasibility of the WHOQOL-100 results in uncertainty about whether this long 100-item measure is suitable in a stroke population who are typically older and potentially cognitively impaired, frail or easily fatigued. Only one PRM (SASC)[16] provided a cut off score, this was for 'satisfactory treatment'. None of the studies were longitudinal therefore none assessed responsiveness, however testing of this would be required if longitudinal measurement was an intended future use of the PRM, such as in a clinical trial. One measure (Chao-PC)[21] was deemed by the authors as unsuitable for use in a UK population due the structure and content of the items. For example, . items did not distinguish between primary and secondary care and so could be confusing to a UK patient.

Strengths and limitations

Our search was limited to English language papers which could be viewed as a limitation, although there is increasing evidence that this may have little effect [24]. Exclusion of papers published pre-2000 could also be viewed as a limitation however this was chosen due to the rapidly evolving nature of stroke management over recent decades. One paper published before 2000 was included because the PRM identified had been used in subsequent studies after that date [25]. Searching for papers that examine treatment burden is challenging because it is a relatively new concept that is multi-faceted. To combat this, we clearly defined treatment burden prior to the start of our review based on our previous qualitative work [4 5].

How results fit in with current literature and future research

Treatment burden is a relatively new concept in the medical literature, with robust qualitative work giving us a better understanding of the patient experience of this phenomenon in stroke and other patient groups [4-6 26 27]. Aspects of care that stroke survivors describe as particularly burdensome include information provision about stroke treatments, care co-ordination and the process of transitioning from hospital into the community[4 5]. These are examples of areas that would benefit from measurement and intervention to lessen treatment burden. Despite this, we still need to understand more about the relationship between treatment burden and health-related outcomes; how burden changes over the patient journey; and whether we can lessen treatment burden through altering the way that healthcare is provided. To examine these areas, quantification of treatment burden is required, yet this is not straightforward. Treatment burden is more than simply healthcare workload, it is a complex interplay of healthcare systems, individuals and their social networks that results in a feeling of encumbrance if demand outweighs personal resources [5 8].This has the potential to lead to disengagement from health services, wasted resources and worsening health outcomes, particularly in vulnerable groups such as those who are older, frail, socioeconomically deprived or socially isolated [28].

Treatment burden has received attention from researchers interested in individual conditions [29-32] and from those interested in studying people with multiple long-term conditions [6]. PRMs have recently been developed for use in the latter population [33-35]. There is overlap between these generic treatment burden PRMs and our taxonomy of treatment burden in stroke, however many stroke-specific burdens are not represented in the generic measures such as, robotic upper limb neurorehabilitation, speech and language therapy, management of visual problems and vocational rehabilitation. There is good evidence that stroke survivors obtain

better health-related outcomes in treatment pathways designed specifically for stroke survivors [36] and therefore some of their healthcare experiences are likely to be different. In this systematic review we chose to exclude PRMs that have not been validated in stroke survivors because current guidance for PRM selection indicates that it is desirable that chosen PRMs be validated in a sample relevant to the population in question [14]. This means that PRMs not developed for use in stroke specifically may not fully represent all treatment burdens encountered by stroke survivors. Additionally, stroke survivors are typically older individuals who may have cognitive impairment, visual difficulties or aphasia that can make completion of a PRM challenging. It is vital that when PRMs are developed for use in older populations that careful attention is paid to usability in this group.

In conclusion, we found no comprehensive PRMs of treatment burden that had been validated in a stroke population. Further research to develop and validate a new PRM of treatment burden in stroke would be important to enable new insights into the quality of care and quality of life of stroke survivors. Such a tool could also be of value for use in other older populations with similar healthcare challenges.

ACKNOWLEDGEMENTS

Research Advisory Group stroke survivors / carers of stroke survivors: Roger Lambert, Tim Morrow, David Jones, Moira Campbell. Focus group members: Roger Lambert, David Jones, David Brooks.

AUTHOR CONTRIBUTIONS

KG, TQ, DE and FM contributed to the design of the project. PE created the search strategy and conducted the search. KG, TQ, LK, DE, JE, NJ and FM screened

papers, extracted and analysed data. KG drafted the paper and all authors reviewed drafts and approved the final version.

COMPETING INTERESTS

Dr Katie Gallacher and Dr Terry Quinn received funding from The Stroke Association to complete this work. Dr Quinn received a grant from BMZ/Pfizer and payment from BMS / Pfizer and Bayer for educational activities outside the submitted work. Prof Mair received payment for educational activities from Janssen outside the submitted work.

FUNDING SUPPORT

The Stroke Association TSA 2017/01

The Stroke Association TSA LECT 2015/05

DATA SHARING STATEMENT

No new data were created from this study.

REFERENCES

1. Bejot Y, Bailly H, Durier J, et al. Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med* 2016;45(12 Pt 2):e391-e98
2. Royal College of Physicians. Stroke Guidelines 2016. https://www.rcplondon.ac.uk/guidelines-policy/stroke-guidelines. Accessed 1st July 2019.
3. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 2016;47(6):E98-E169
4. Gallacher K, Morrison D, Jani B, et al. Uncovering Treatment Burden as a Key Concept for Stroke Care: A Systematic Review of Qualitative Research. *PLoS Med* 2013;10(6)
5. Gallacher KI, May CR, Langhorne P, et al. A conceptual model of treatment burden and patient capacity in stroke. *Bmc Fam Pract* 2018;19
6. Eton DT, Ridgeway JL, Egginton JS, et al. Finalizing a measurement framework for the burden of treatment in complex patients with chronic conditions. *Patient Relat Outcome Meas* 2015;6:117-26
7. NICE. Multimorbidity: clinical assessment and management, 2016. https://www.nice.org.uk/guidance/ng56 Accessed 1st July 2019.
8. May CR, Eton DT, Boehmer K, et al. Rethinking the patient: using Burden of Treatment Theory to understand the changing dynamics of illness. *BMC Health Serv Res* 2014;14:281
9. May C, Montori VM, Mair FS. We need minimally disruptive medicine. *BMJ* 2009;339:b2803
10. Chambers JA, O'Carrol RE, Hamilton B, et al. Adherence to medication in stroke survivors: A qualitative comparison of low and high adherers. *Br J Health Psychol* 2010:592-609.
11. Eton DT, Elraiyah TA, Yost KJ, et al. A systematic review of patient- reported measures of burden of treatment in three chronic diseases. *Patient Relat Outcome Meas* 2013;4:7-20
12. Gallacher KI, Batty GD, McLean G, et al. Stroke, multimorbidity and polypharmacy in a nationally representative sample of 1,424,378 patients in Scotland: implications for treatment burden. *BMC Med* 2014;12:151

13. Stroke Association. State of the nation - Stroke statistics, 2018. https://www.stroke.org.uk/resources/state-nation-stroke-statistics. Accessed 1st July 2019.

14. Reeve B, Wyrwich K, Wu A, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. *Qual Life Res* 2013;22(8):1889-905

15. PRISMA. Transparent reporting of systematic reviews and meta-analysis, 2009. http://www.prisma-statement.org/. Accessed 1st July 2019.

16. Pound P, Gompertz P, Ebrahim S. Patients' satisfaction with stroke services. *Clin Rehab* 1994;8:7-17

17. Luo YH, Yang J, Zhang YB. Development and validation of a patient-reported outcome measure for stroke patients. *Health Qual Life Outcomes* 2015;13

18. Drigny J, Joussain C, Gremeaux V, et al. Development and Validation of a Questionnaire to Assess Barriers to Physical Activity After Stroke: the Barriers to Physical Activity After Stroke Scale. *Arch Phys Med Rehabil* 2019 doi: 10.1016/j.apmr.2018.12.034

19. Unalan D, Soyuer F, Ozturk A, et al. Comparison of SF-36 and WHOQOL-100 in patients with stroke. *Neurol India* 2008;56(4):426-32

20. Almborg AH, Ulander K, Thulin A, et al. Patients' perceptions of their participation in discharge planning after acute stroke. *J Clin Nurs* 2009;18(2):199-209

21. Hill KM, Twiddy M, Hewison J, et al. Measuring patient-perceived continuity of care for patients with long-term conditions in primary care. *BMC Fam Pract* 2014;15:191

22. Chao J. Continuity of care: incorporating patient perceptions. *Fam Med* 1988;20(5):333-7

23. Banahan BF, Jr., Banahan BF, 3rd. Continuity as an attitudinal contract. *J Fam Pract* 1981;12(4):767-8

24. Morrison A, Polisena J, Husereau D, et al. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care* 2012;28(2):138-44

25. Sulch D, Melbourn A, Perez I, et al. Integrated care pathways and quality of life on a stroke rehabilitation unit. *Stroke* 2002;33(6):1600-04

26. Sav A, Kendall E, McMillan SS et al. 'You say treatment, I say hard work': treatment burden among people with chronic illness and their carers in Australia. *Health Soc Care Community* 2013;doi: 10.1111/hsc.12052.

27. Gallacher K, May C, Montori VM, et al. Understanding Treatment Burden in Chronic Heart Failure Patients. A Qualitative Study. *Ann Fam Med* 2011;9(3):235-43

28. Mair FS, May CR. Thinking about the burden of treatment. *BMJ* 2014;349:g6680

29. Kahn LS, Vest BM, Madurai N, et al. Chronic kidney disease (CKD) treatment burden among low-income primary care patients. *Chronic Illn* 2015;11(3):171-83

30. Eton DT, Anderson RT, Cohn WF, et al. Risk factors for poor health-related quality of life in cancer survivors with multiple chronic conditions: exploring the role of treatment burden as a mediator. *Patient Relat Outcome Meas* 2019;10:89-99

31. Lorenz EC, Egginton JS, Stegall MD, et al. Patient experience after kidney transplant: a conceptual framework of treatment burden. *J Patient Rep Outcomes* 2019;3(1):8

32. Rogers EA, Yost KJ, Rosedahl JK, et al. Validating the Patient Experience with Treatment and Self-Management (PETS), a patient-reported measure of treatment burden, in people with diabetes. *Patient Relat Outcome Meas* 2017;8:143-56

33. Eton DT, Yost KJ, Lai JS, et al. Development and validation of the Patient Experience with Treatment and Self-management (PETS): a patient-reported measure of treatment burden. *Qual Life Res* 2017 doi: 10.1007/s11136-016-1397-0

34. Tran VT, Harrington M, Montori VM, et al. Adaptation and validation of the Treatment Burden Questionnaire (TBQ) in English using an internet platform. *BMC Med* 2014;12:109

35. Duncan P, Murphy M, Man MS, et al. Development and validation of the Multimorbidity Treatment Burden Questionnaire (MTBQ). *BMJ Open* 2018;8(4):e019413

36. Langhorne P, Williams BO, Gilchrist W, et al. Do stroke units save lives? *Lancet* 1993;342(8868):395-8

Figure legends

Figure 1 – Conceptual model of stroke treatment burden. The arrows represent the possible pathways between components that stroke patients may follow. The 'enacting management strategies' component has four subcomponents. Reproduced with permission from Plos Med [4] (Creative Commons Attribution-Non Commercial 4.0 License)

Figure 2 – PRISMA flow chart

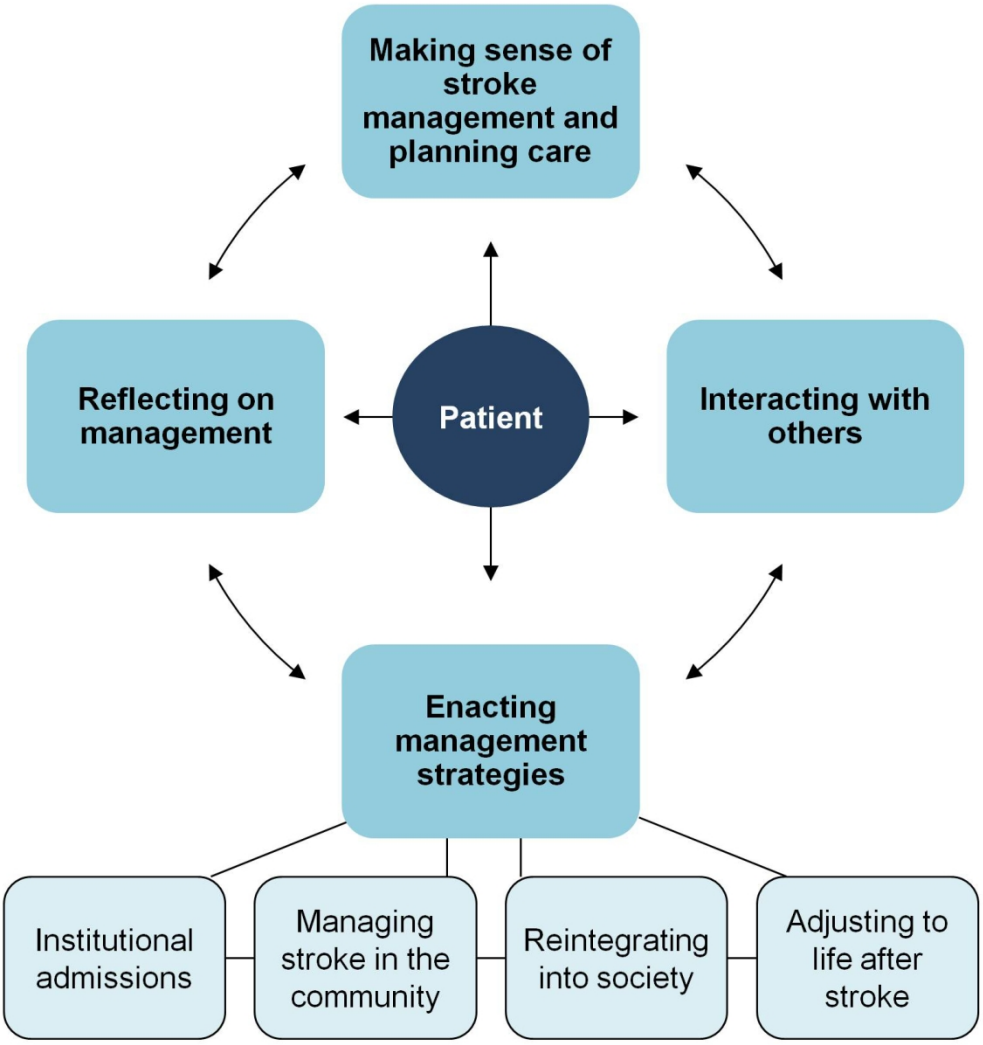
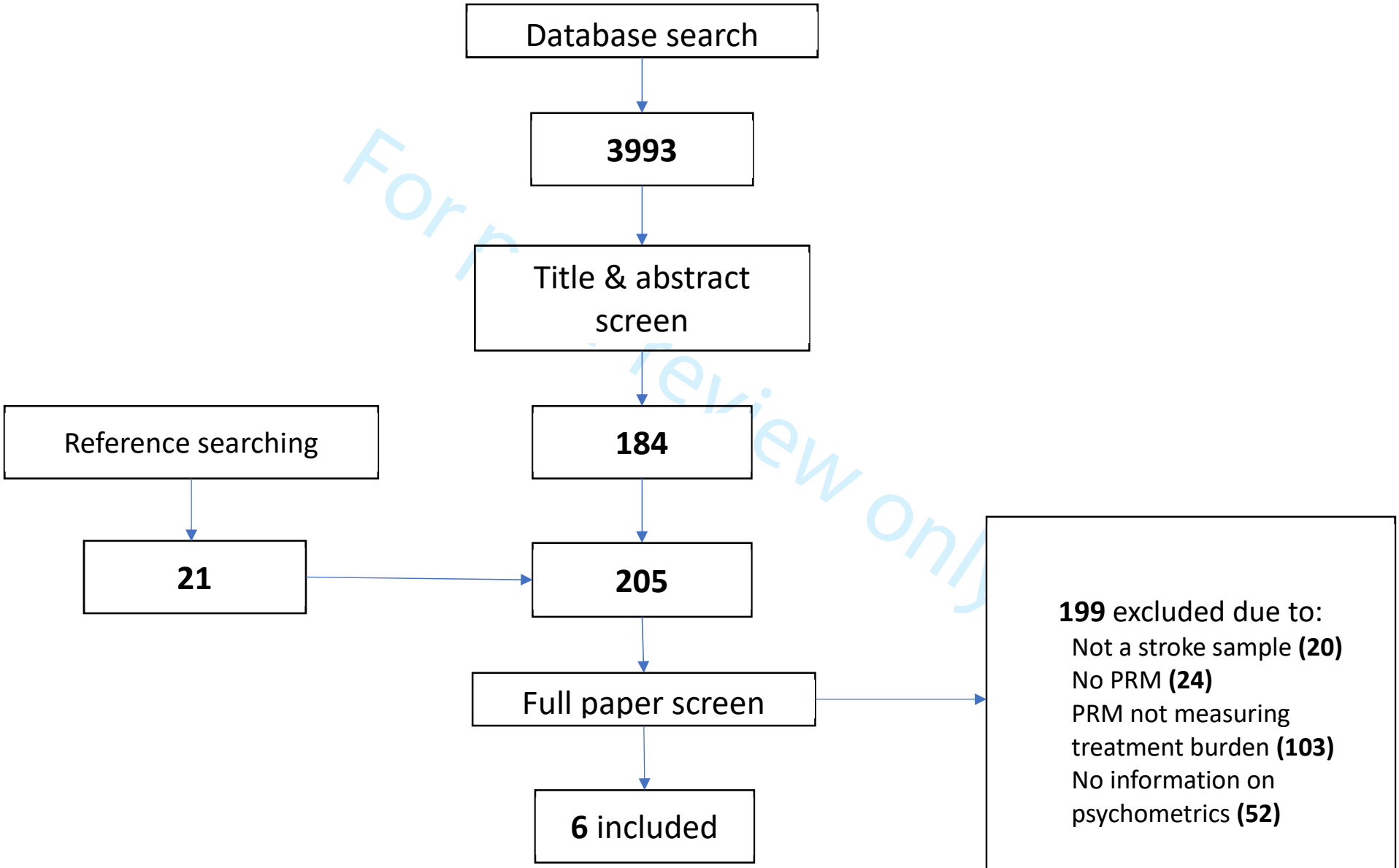


Figure 1 - Conceptual model of stroke treatment burden. The arrows represent the possible pathways between components that stroke patients may follow. The 'enacting management strategies' component has four subcomponents. Reproduced with permission from Plos Med [4] (Creative Commons Attribution-Non Commercial 4.0 License)

135x142mm (300 x 300 DPI)



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Appendix3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9 and flowchart
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 and Appendix 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21 and Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13 and Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	25
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	26

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

For more information, visit: **www.prisma-statement.org**.

Appendix 2 – Search strategy

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search history sorted by search number ascending

1 Stroke/ or Stroke Rehabilitation/

2 (cva or "cerebrovascular accident*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 8382 Advanced

3 exp brain infarction/

4 exp brain ischemia/

5 Intracranial Hemorrhages/

6 exp "intracranial embolism and thrombosis"/

7 ((subarachnoid or brain or intracranial or cerebral or cerebrovascular or intracerebral) adj3 (embol* or thrombo* or infarct* or h?emorrhag* or isch?emi*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

8 or/1-7

9 8 or stroke*.ti.

10 9 and "patient reported".mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

11 9 and (prom or proms).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12 9 and ((qualitative* or "focus groups" or interview* or questionnaire* or survey* or measur* or scale* or subscale* or item* or domain* or trial* or observation* or "cross section*" or rate* or rating or tool*1 or instrument* or assess* or evaluat* or cohort*).mp. or exp cohort studies/ or randomized controlled trial.pt.)

13 (self adj report*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

14 (patient adj2 (reported or centered or centred or education* or preference* or experience* or satisfaction* or counsel* or perception or perceived)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

15 (patient adj2 (engag* or participat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

16 12 and (13 or 14 or 15)

17 10 or 11 or 16

18 (complex* adj3 (regimen* or treatment* or therap* or intervention*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

19 17 and 18

20 drug administration schedule/ or adheren*.mp. or nonadher*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

21 guideline adherence/ or *lifestyle/ or *activities of daily living/ or *absenteeism/ or *quality of life/ or *patient compliance/ or *treatment refusal/ or *self care/ or *self administration/ or *patient participation/ or patient education as topic/

22 (disrupt* or barrier* or noncomplian* or compliant).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

23 (daily or everyday or disablity* or disabled or support*).mp. or office visits/ or "appointments and scheduling"/ or empower*.mp. or "out of pocket".mp. or financial*.mp. or paperwork.mp. or overwhelm*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

24 transportation/ or driving.mp. or distance.mp. or *educational status/ or health literacy/ or demands.mp. or social support/ or life change events/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

25 *income/ or *costs of illness/ or *fear/ or *pain/ or *poverty/ or anxiety.mp. or skipped.mp. or *exercise/ or *health care costs/ or exp *prescriptions/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

26 17 and (20 or 21 or 22 or 23 or 24 or 25)

27 17 and (burden* or workload).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

28 17 and (deficien* or limitation* or difficult* or isolat* or dependen*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

29	19 or 27 or 28
30	limit 29 to (english language and yr="2000 - 2018")
31	remove duplicates from 30

Appendix 3 – Inclusion / exclusion criteria

INCLUSION CRITERIA
Types of studies English language. From any geographical location. Publication 2000 and onwards. Describes the development, validation or use of a patient-reported measure of treatment burden in stroke - this includes full measures, scorable scales within measures and other scorable components like single items.
Types of participants Adults (>18 yrs) Diagnosed with at least one stroke, including ischaemic, intracerebral haemorrhage or subarachnoid haemorrhage.
Types of outcome measures Treatment Burden • Sense-making and planning e.g. goal setting • Interacting with others e.g. accessing care • Enacting management strategies e.g. taking medications • Reflecting on management e.g. monitoring progress
EXCLUSION CRITERIA
Types of studies Grey literature / not published in a peer reviewed journal. Studies that have not developed, validated or used a patient-reported measure of treatment burden. Studies that do not provide any psychometric characteristics of the measure. Studies that describe a product or device-specific patient preference or satisfaction measure. Studies that are not an original research study.
Types of participants Children (<18 yrs). No CVA diagnosis (e.g. diagnosis of TIA, subdural haematomas, infarction / haemorrhage due to infection or tumour, cerebral palsy or any other neurological deficit). Mixed groups of participants e.g. patients and carers or health care providers, unless results from patients are explicitly separate from other participants.
Types of outcome measures Measures that are not patient-reported. Burden on health services / systems or health professionals. Economic burden at a society level e.g. costs to government or councils. Carer burden.

Appendix 4 – Data extraction form

Data extraction
Sample size
Mean / median age and age range (please specifiy if mean or median)
Number of male and female participants
Socioeconomic status of participants
Ethnicity of participants
Level of disability / activities of daily living of participants
Setting
Other participant info given
What is the purpose of the PRM?
What is its structure e.g. number of domains, subdomains, items
What aspects of treatment burden are covered? E.g. one item on info seeking, one item on medications…
Quality appraisal
Was the measure developed from concepts developed in qualitative work (in a previous study or this one)?
Was the above qualitative work done relevant to the current sample?
Did the above qualitative work include a conceptual model?
Was reliability tested?
How was reliability tested and and what was the result?
Was content validity tested?
How was content validity assessed and what was the result?
Was the population that content validity was tested in similar to the current sample?
Was justification for the recall period given?
Was construct validity assessed?
How was construct validity tested and what were the results?
Was responsiveness tested?
How was responsiveness tested and what was the result?
Was interpretability of scores tested?
How was interpretability of scores measured and what was the result?
Has the measure been translated? If so into what language?
Has it been evaluated in this new language?
Has patient and investigator burden been considered?
Was this an issue?

Appendix 5 - Participant details

PRM	Sample size	Setting	Age	% male	Education level	Ethnicity
Satisfaction with Stroke Care questionnaire (SASC)	149	Community	Mean 71	50%	Not given	80% white; 7% black Caribbean; 5% Bangladeshi, 2% black African, 2% Indian, 2% Pakistani, 1% other Asian, 1% not completed
Stroke Patient Reported Outcome Measure (Stroke-PROM)	475	Community and hospital	11.6%≤45; 48.4%45-65; 40%≥65	60%	38.5% primary school or lower; 30.3% junior high school; 18.5% senior high school; 12.6% college or higher	Not given
Barriers to Physical Activity after Stroke (BAPAS)	109	Community	Mean 60.6 (SD 12.8)	63%	Not given	Not given
World Health Organisation Quality of Life-100 (WHOQOL-100)	70	Hospital	Mean 60.16 (SD 11.30)	61%	67.1% primary school graduates or less educated; 40% were retired.	Not given
Patient's Questionnaire on Participation in Discharge Planning (PQPDP)	188	Hospital	Mean 74 (SD 11.2)	56%	75% elementary school; 19% sec/high school; 6% university	Not given
Chao Perception of Continuity scale (Chao-PC)	168	Community	Mean 67.65 (SD 12.54)	58%	79% <16 yrs; 14.3% <18 years; 6% >18 yrs	98.2% white British