


PROTOCOL

Open Access



# Quality and acceptability of patient-reported outcome measures used to assess fatigue in axial spondyloarthritis (axSpA): a systematic review (protocol)

Nathan A. Pearson<sup>1\*</sup> , Jonathan C. Packham<sup>2</sup>, Helen Parsons<sup>3</sup> and Kirstie L. Haywood<sup>1</sup>

## Abstract

**Background:** The prevalence of axial spondyloarthritis (axSpA) is estimated between 0.15 and 1.2%, with many of those patients experiencing severe fatigue. Current axSpA assessment guidance recommends use of a single-item visual analogue scale for fatigue severity. However, concerns have been raised about the ability of such a limited assessment to identify patients with major fatigue, to detect important change in fatigue or to reflect the multi-dimensional nature of fatigue. The proposed systematic review will identify and evaluate the quality and acceptability of single- and multi-item patient-reported outcome measures (PROMs) used to assess fatigue in axSpA, seeking to make recommendations for the 'best' measures for research and/or clinical practice.

**Methods/design:** The review will seek to include published studies which report evidence of the development and/or measurement and/or practical properties of clearly defined and reproducible measures of fatigue following completion by patients with axSpA. Five major databases will be searched from 1980 to August 2017: MEDLINE (OVID), EMBASE (OVID), PsycINFO (OVID), World of Science and CINAHL. Study methodological quality will be assessed against the COnsensus-based Standards for the selection of health Measurement INSTRUMENTS (COSMIN) checklist. The measurement and/or practical properties of reviewed measures will be assessed against current international standards. A short list of the 'best'-quality PROMs will be produced. The review will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Discussion:** This study will provide the first robust and transparent evaluation of patient-reported measures of fatigue used in the axSpA population, synthesising evidence of quality, relevance and acceptability. The review will benefit patients, clinicians, health professionals and researchers wishing to enhance axSpA-fatigue assessment in routine practice, service evaluation and research. The findings will impact future research which seeks to better understand the nature of axSpA fatigue and evaluate the relative benefit of fatigue-management strategies.

**Systematic review registration:** PROSPERO [CRD42016042271](https://doi.org/10.1186/1745-7189-4-2271)

**Keywords:** Quality, Acceptability, Fatigue, Ankylosing spondylitis, Axial spondyloarthritis, Measurement, Musculoskeletal disorders, Systematic review

\* Correspondence: [n.pearson.1@warwick.ac.uk](mailto:n.pearson.1@warwick.ac.uk)

<sup>1</sup>Royal College of Nursing Research Institute, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK  
Full list of author information is available at the end of the article



## Background

Axial spondyloarthritis (axSpA) is an inflammatory disease that primarily affects the spine and pelvis, impairing mobility to the detriment of the patient's physical well-being [1]. It is characterised by widespread back and joint pain and stiffness [2]. axSpA and ankylosing spondylitis (AS) are two facets of a single disease distinguished by whether radiographic sacroiliitis is observable by X-ray examination (AS) or not (axSpA) [2]. Up to 75% of axSpA patients report experiencing fatigue [3–7], and for many, this is both severe and frequent [7]. Patients with AS have highlighted the relative importance of seeking to better understand the fatigue associated with their illness [8], underlining the need for an appropriate fatigue assessment that really captures what matters to patients. As exemplified in rheumatoid arthritis (RA), a review of methods of fatigue assessment [9] and qualitative research with patients highlighted both the multi-faceted nature of RA fatigue [10] and the inadequacy of current methods of assessment. The result was the development of a patient-reported outcome measure (PROM) specific to RA fatigue—the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAFF-MDQ) [11, 12]. PROMs are single- or multi-item questionnaires which seek to provide a patient-derived assessment of how they feel, what they can and cannot do and how well they are living their lives as a consequence of their health and associated health care [13].

Current assessment guidance for AS exists in the form of a core outcome set (COS) [14]. The COS provides guidance for the minimum number of outcomes to include in future clinical practice and clinical trials: that is, pain, stiffness, function, global wellbeing and spinal mobility [14, 15]. A recent update recommends the assessment of fatigue severity with a single-item visual analogue scale (VAS) [16]. However, evidence from a large UK cohort of AS patients highlighted significant limitations with a single-item assessment of fatigue, including the failure to identify some patients with major fatigue, to detect important change in fatigue, to reflect the multi-dimensional nature of fatigue or to detail the nuances of fatigue essential to driving tailored healthcare.

A growing number of multi-item fatigue-specific (for example, the Multidimensional Fatigue Inventory (MFI-20) [17] and Fatigue Severity Scale [18]) and condition-fatigue-specific (for example, the BRAFF-MDQ [12] and Functional Assessment of Cancer Therapy scale [19]) PROMs are now available. This growth in availability reflects the importance of capturing the multi-faceted, often condition-specific, nature of fatigue [20] and the importance of seeking to reflect the outcomes that really matter to patients [21]. However, it is unclear how well these measures perform in the axSpA population; it cannot be assumed that the measurement and practical properties of measures are

consistent across different patient populations. Confidence in the use of PROM-based assessment is underpinned by evidence of performance in the population of interest [22], and structured reviews of PROM quality and acceptability provide essential evidence to inform selection.

The proposed systematic review will evaluate the quality (measurement properties), relevance (measures what is important) and acceptability (simplicity and convenience) of clearly defined and reproducible multi- and single-item PROMs which purport to measure fatigue and have been completed by the axSpA population. A short list of 'best' measures of fatigue for use with the axSpA population will be developed to inform recommendations for use in both routine clinical practice and research.

## Method/design

The review will include published studies reporting evidence of the development, measurement and/or practical properties of clearly defined and reproducible measures of fatigue evaluated following completion by patients with axSpA. The review will be completed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [23].

Study methodological quality will be assessed against the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines [24, 25]. The measurement and/or practical properties of included measures will be assessed against a transparent appraisal framework informed by current international standards for PROM quality [22, 26–29].

## Search strategy

A comprehensive search strategy will be developed using Medical Subject Headings (MeSH) and free text searching to reflect four key characteristics [26, 30, 31]: (1) population—axSpA, (2) construct—fatigue, (3) type of assessment—patient-reported measures and (4) measurement properties (a modified version of a sensitive search filter and accompanying exclusion filter) [30] (example search in Additional file 1: Appendix 1).

Following the review of titles and abstracts of included studies, a further 'named measure' search will be developed and applied with search terms developed as above to reflect (1) population—axSpA, (2) construct—fatigue, (3) named fatigue measures and (4) measurement properties.

The search strategy will be modified for each of the following databases: MEDLINE (OVID), EMBASE (OVID), PsycINFO, World of Science and CINAHL. Searches will be run from 1980 to August 2017.

### **Stage 1: Identifying evaluative studies of PROM-based fatigue assessment in axSpA**

The search strategy will use MeSH, keywords and synonyms to identify studies of adult patients with axSpA where the concept of fatigue is assessed. To ensure maximal sensitivity, a wide range of terms will be used to reflect the target patient sample (axSpA) and fatigue. A modified filter describing measurement and assessment will be used to identify studies using PROMs (original filter developed by the PROM group and Knowledge Centre, Department of Public Health, University of Oxford). Terms describing the measurement evaluation will be searched for using a modification of the COSMIN filter [30]. The recommended COSMIN exclusion filter will be added to the search string [30].

Titles and abstracts will be reviewed for inclusion by one reviewer (NP); a second reviewer (KH) will independently review a 10% subset of randomly selected titles and abstracts and agreement checked [32, 33]. A third independent reviewer (JP) will resolve any differences regarding eligibility. Reference lists of included articles will be screened for additional articles. The reason(s) for any full-text exclusions will be recorded.

### **Review inclusion/exclusion criteria**

#### **Study inclusion**

Studies will be included if they (i) include a clearly identifiable and reproducible PROM-based assessment of fatigue; (ii) the study reports evidence of the development and/or evaluation (practical or measurement properties) of the PROM following completion by members of the axSpA population; and (iii) the study has been published, peer-reviewed, is available as a full text and is written in English. Studies will be excluded if they are (i) available as abstract only; (ii) the assessment of fatigue is not patient-reported, clearly identifiable or reproducible; (iii) the study simply describes use/application of a PROM without further evidence of measurement/practical properties; (iv) the measurement and/or practical properties cannot be extracted specific to the axSpA population; or (v) the study has not been published, peer-reviewed or is not available in English.

All abstracts that include patients with psoriatic arthritis (PsA) will be screened by a consultant rheumatologist (JP) and included if a subset of patients is clinically defined as having axSpA and separately reported.

#### **PROM inclusion**

PROMs will be included if (i) they are fatigue specific: both multi-item and single-item measures will be included and (ii) fatigue is assessed as a separate domain within a multiple domain assessment (e.g. SF-36 Vitality [34]). Assessments of fatigue will not be included if they are (i) clinician-reported or (ii) a non-PROM-based assessment.

### **Stage 2: Identifying studies using named PROM-based fatigue measures in axSpA**

The search strategy will use the search filters developed in stage 1 for population (axSpA), construct (fatigue) and measurement properties (COSMIN filter). In addition, a named measures search filter will be developed and added to the search string to identify single- and multi-item measures used in axSpA fatigue assessment. All identified titles and abstracts will be extracted, and any duplicates between stage 1 and 2 searches will be removed. Title and abstract screening will follow the same procedure outlined for the stage 1 search (see stage 1), and the same eligibility criteria will be applied.

#### **Data extraction and appraisal**

Data extraction will be informed by previous reviews [35, 36] (see Additional file 1: Appendix 2) and the requirements of the COSMIN checklist [24, 25]. COSMIN provides a transparent appraisal system that is internationally developed. The checklist contains quality criteria for evaluating ten measurement properties—validity (content, structural, construct, criterion, cross-cultural), reliability (internal consistency, test-retest, measurement error), responsiveness and interpretability. This review will consider all evidence of measurement evaluation that relates to fatigue-specific measures only.

Data extraction will capture (1) study information (population, definition of fatigue, language) and (2) PROM-based information. PROM-based evidence of measurement properties will include validity (structural, content and face, construct, criterion, longitudinal), reliability (inter- or intra-rater, test-retest, internal consistency, measurement error), responsiveness (criterion or construct-based) and interpretability (minimal important change, smallest detectable change, response shift). Evidence for the practical properties of PROMs will include acceptability (relevance) and feasibility. The extent of patient involvement as active research partners in PROM development, evaluation and/or application will be sought [37].

Study methodological quality for each reported measurement property will be assessed using the COSMIN checklist 4-point scale (i.e. poor, fair, good, excellent) [24, 25]. Two reviewers (NP and KH) will independently undertake data extraction and apply the COSMIN checklist on a randomly selected 10% subset of included papers. Any disagreements are resolved through discussion with a third reviewer (JP or HP).

#### **Data synthesis**

Data synthesis will seek to contextualise evidence of the reported measurement and/or practical properties alongside the methodological quality of the study. As per earlier reviews, data synthesis will consider (i) study methodological quality (COSMIN scores), (ii) the number of studies

reporting evidence per fatigue measure, (iii) the results for each practical and measurement property per measure, and (iv) consistency between evaluations [35]. Data synthesis will report two pieces of information. First, measurement property quality will be categorised as adequate (+), not adequate (-), conflicting (+/-) or unclear (?). Second, the strength of evidence for the quality of each measurement property reviewed will be categorised as 'strong', 'moderate', 'limited', 'conflicting' or 'unknown' [32, 35].

Following data synthesis and item-content comparisons, PROM recommendations will be informed by (1) whether and to what extent essential domains of fatigue identified—as per the RA-fatigue model—are reflected within the PROM (content validity), (2) the availability of adequate evidence of minimally important measurement properties—validity (structural and construct) and reliability (internal consistency and test-retest), and (3) an evidence base that is minimally judged to be of moderate quality.

## Discussion

Awareness of the importance of fatigue in inflammatory conditions has grown over the past decade [20]. Whilst patients report fatigue as one of the key symptoms of their condition, there is limited evidence of an improved understanding of fatigue in axSpA and its impact on patients' lives [3, 38, 39]. Moreover, growing evidence suggests that the experience of fatigue is not homogeneous across conditions [10, 40] and hence a generic approach to assessment may miss important aspects of fatigue for particular patient groups.

This study will provide the first robust and transparent evaluation of patient-reported measures of fatigue used in the axSpA population, synthesising evidence of quality, relevance and acceptability. The findings of this review will inform the selection of patient-reported fatigue assessment, thus impacting future research which seeks to better understand the nature of axSpA fatigue. Improving the assessment of fatigue in routine practice, service evaluation and research will enhance our understanding of the way in which fatigue impacts upon the lives of people with axSpA, and the way in which their fatigue responds to fatigue-management strategies.

## Additional file

**Additional file 1:** Appendix 1. Search strategy. Appendix 2. Quality criteria to appraise reported measurement properties [28, 36]. (DOCX 25 kb)

## Abbreviations

AS: Ankylosing spondylitis; axSpA: Axial spondyloarthritis; CINAHL: Cumulative Index to Nursing and Allied Health Literature; COS: Core outcome set; COSMIN: COnsensus-based Standards for the selection of health Measurement INstruments; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROM: Patient-reported outcome measure; RA: Rheumatoid arthritis

## Funding

This work was supported by the National Ankylosing Spondylitis Society (NASS) grant number WAR1.

## Authors' contributions

KH is the guarantor of the review. NP drafted the manuscript. Eligibility criteria and data extraction criteria were developed by all authors. NP and KH developed the search strategy. KH and HP provided outcome measurement expertise. KH and JP provided expertise on axial spondyloarthritis, including ankylosing spondylitis. All authors reviewed the manuscript, provided feedback and approved the final version.

## Ethics approval and consent to participate

Not applicable (protocol)

## Consent for publication

Not applicable (protocol)

## Competing interests

The authors declare that they have no competing interests.

## Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## Author details

<sup>1</sup>Royal College of Nursing Research Institute, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK. <sup>2</sup>Institute of Applied Clinical Science, Keele University, Staffordshire, UK. <sup>3</sup>Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, UK.

Received: 6 February 2017 Accepted: 17 July 2018

Published online: 07 August 2018

## References

- Raine C, Keat A. Axial spondyloarthritis. *Medicine*. 2014;42:251–6.
- Poddubnyy D. Axial spondyloarthritis: is there a treatment choice? *Ther Adv Musculoskelet Dis*. 2013;5:45–54.
- Calin A, Edmunds L, Kennedy LG. Fatigue in ankylosing spondylitis—why is it ignored? *J Rheumatol*. 1993;20:991–5.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol*. 1994;21:2286–91.
- Jones SD, Koh WH, Steiner A, Garrett SL, Calin A. Fatigue in ankylosing spondylitis: its prevalence and relationship to disease activity, sleep, and other factors. *J Rheumatol*. 1996;23:487–90.
- Ward MM. Health-related quality of life in ankylosing spondylitis: a survey of 175 patients. *Arthritis Care Res*. 1999;12:247–55.
- Haywood KL, Packham JC, Jordan KP. Assessing fatigue in ankylosing spondylitis: the importance of frequency and severity. *Rheumatology (Oxford)*. 2014;53:552–6.
- National Ankylosing Spondylitis Society: NASS Research Priorities 2013–2018. 2013. <http://nass.co.uk/research/nass-research-priorities/>. Accessed 21 Sept 2016.
- Hewlett S, Dures E, Almeida C. Measures of fatigue: Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional Questionnaire (BRAFMQ), Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scales (BRAFNRS) for severity, effect, and coping, Chalder Fatigue Questionnaire (CFQ), Checklist Individual Strength (CIS20R and CIS8R), Fatigue Severity Scale (FSS), Functional Assessment Chronic Illness Therapy (Fatigue) (FACIT-F), Multi-Dimensional Assessment of Fatigue (MAF), Multi-Dimensional Fatigue Inventory (MFI), Pediatric Quality Of Life (PedsQL) Multi-Dimensional Fatigue Scale, Profile of Fatigue (ProF), Short Form 36 Vitality Subscale (SF-36 VT), and Visual Analog Scales (VAS). *Arthritis Care Res*. 2011;63(Suppl 11):263–86.
- Hewlett S, Cockshott Z, Byron M, Kitchen K, Tipler S, Pope D, et al. Patients' perceptions of fatigue in rheumatoid arthritis: overwhelming, uncontrollable, ignored. *Arthritis Rheum*. 2005;53:697–702.
- Nicklin J, Cramp F, Kirwan J, Urban M, Hewlett S. Collaboration with patients in the design of patient-reported outcome measures: capturing the experience of fatigue in rheumatoid arthritis. *Arthritis Care Res*. 2010;62:1552–8.

12. Nicklin J, Cramp F, Kirwan J, Greenwood R, Urban M, Hewlett S. A cross-sectional study to evaluate the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional questionnaire, visual analog scales, and numerical rating scales. *Arthritis Care Res.* 2010;62:1559–68.
13. Haywood KL, Wilson R, Staniszewska S, Salek S. Using PROMs in healthcare: who should be in the driving seat—policy makers, health professionals, methodologists or patients? *Patient.* 2016;9:495–8.
14. van der Heijde D, Bellamy N, Calin A, Dougados M, Khan MA, van der Linden S. Preliminary core sets for endpoints in ankylosing spondylitis. Assessments in Ankylosing Spondylitis Working Group. *J Rheumatol.* 1997;24:2225–9.
15. van der Heijde D, Calin A, Dougados M, Khan MA, van der Linden S, Bellamy N. Selection of instruments in the core set for DC-ART, SMARD, physical therapy and clinical record keeping in ankylosing spondylitis. Progress report of the ASAS Working Group. Assessments in ankylosing spondylitis. *J Rheumatol.* 1999;26:951–4.
16. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis.* 2009;68(Suppl 2):1–44.
17. Smets EM, Garssen B, Bonke B, De Haes JC. The multidimensional fatigue inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res.* 1995;39:315–25.
18. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol.* 1989;46:1121–3.
19. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol.* 1993;11:570–9.
20. Hewlett S, Choy E, Kirwan J. Furthering our understanding of fatigue in rheumatoid arthritis. *J Rheumatol.* 2012;39:1775–7.
21. Staniszewska S, Haywood KL, Brett J, Tutton L. Patient and public involvement in patient-reported outcome measures: evolution not revolution. *Patient.* 2012;5:79–87.
22. Streiner DL, Kottner J. Recommendations for reporting the results of studies of instrument and scale development and testing. *J Adv Nurs.* 2014;70:1970–9.
23. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8:336–41.
24. Terwee CB, Mokkink LB, Knol DL, Ostelo RW, Bouter LM, de Vet HC. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. *Qual Life Res.* 2012;21:651–7.
25. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol.* 2010;63:737–45.
26. De Vet HC, Terwee CB, Mokkink LB, Knol DL. *Measurement in medicine: a practical guide.* Cambridge: Cambridge University Press; 2011.
27. Haywood KL, Staniszewska S, Chapman S. Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review. *Qual Life Res.* 2012;21:35–52.
28. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol.* 2007;60:34–42.
29. US Food and Drug Administration Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Rockville: Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research; 2009. <https://www.fda.gov/downloads/drugs/guidances/UCM193282.pdf>.
30. Terwee CB, Jansma EP, Riphagen II, de Vet HC. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. *Qual Life Res.* 2009;18:1115–23.
31. Terwee CB, Prinsen CA, Ricci Garotti MG, Suman A, de Vet HC, Mokkink LB. The quality of systematic reviews of health-related outcome measurement instruments. *Qual Life Res.* 2016;25:767–79.
32. Haywood KL, Colin SM, Crawley E. Assessing severity of illness and outcomes of treatment in children with chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review of patient-reported outcome measures (PROMs). *Child Care Health Dev.* 2014;40:806–24.
33. Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. *Resus.* 2015;88:150–7.
34. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30:473–83.
35. Elbers RG, Rietberg MB, van Wegen EE, Verhoef J, Kramer SF, Terwee CB, et al. Self-report fatigue questionnaires in multiple sclerosis, Parkinson's disease and stroke: a systematic review of measurement properties. *Qual Life Res.* 2012;21:925–44.
36. Conijn AP, Jens S, Terwee CB, Breek JC, Koelemay MJ. Assessing the quality of available patient reported outcome measures for intermittent claudication: a systematic review using the COSMIN checklist. *Eur J Vasc Endovasc Surg.* 2015;49:316–34.
37. Haywood KL, Colin SM, Crawley E. Assessing severity of illness and outcomes of treatment in children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME): a systematic review of patient-reported outcome measures (PROMs). *Child Care Health Dev.* 2014;40:806–24.
38. Farren W, Goodacre L, Stigant M. Fatigue in ankylosing spondylitis: causes, consequences and self-management. *Musculoskeletal Care.* 2013;11:39–50.
39. Günaydin R, Göksel Karatepe A, Çeşmeli N, Kaya T. Fatigue in patients with ankylosing spondylitis: relationships with disease-specific variables, depression, and sleep disturbance. *Clin Rheumatol.* 2009;28:1045–51.
40. Eilertsen G, Ormstad H, Kirkevoid M, Mengschoel AM, Söderberg S, Olsson M. Similarities and differences in the experience of fatigue among people living with fibromyalgia, multiple sclerosis, ankylosing spondylitis and stroke. *J Clin Nurs.* 2015;24:2023–34.

**Ready to submit your research? Choose BMC and benefit from:**

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

**At BMC, research is always in progress.**

Learn more [biomedcentral.com/submissions](https://biomedcentral.com/submissions)

