Differences In Chronic Pain Prevalence Between Men And Women At Mid-Life: A Systematic Review Protocol

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Protocol

Keywords: chronic pain, persistent pain, prevalence, sex, sex inequalities, gender inequalities,

Posted Date: December 29th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1192864/v1

Abstract

Background: Epidemiological literature has revealed differences in chronic pain (CP) prevalence in men and women. Women have been found to be more likely to develop CP compared to men at different points of the life-course, such as childhood and old age. Less is known about differences in prevalence by sex during mid-life. While CP is most prevalent later in life, biological and physical changes in mid-life may predispose to an earlier differentiation in CP distribution – for example due to the menopause. The aim of this study is to describe the prevalence of CP at midlife in men and women, and to identify how these differences relate to results pertaining to other periods in the life-course.

Methods: This systematic review follows PRISMA guidelines. An electronic search will identify appropriate studies in the following databases: MEDLINE, to be accessed through Web of Science; and EMBASE, AMED and PSYCHinfo to be accessed through OVID. Two reviewers will independently screen each title and abstract and subsequently each full text following the inclusion criteria outlined in this protocol. The reference lists of eligible papers will also be screened to identify any further eligible studies. Any inconsistencies between reviewer decisions will be resolved through discussion. Studies eligible for data extraction will report estimates of CP prevalence, of prevalence for each sex, and difference in prevalence between sexes. Two reviewers will conduct data extraction using a standardised data extraction form. Quality assessment will be conducted using a risk of bias assessment tool for prevalence studies. The findings will be reported in a narrative synthesis and will comment on expected heterogeneity, following the Social Research Council Methods Programme guidelines. A random effects meta-analysis will be conducted where the reviewers can justify combining results.

Discussion: This review will summarise the prevalence of CP in men and women at mid-life, based on existing evidence. It is expected that the results will identify gaps in knowledge and areas for further research.

Systematic review registration: PROSPERO: CRD42021295895

Background

Rationale

Chronic pain (CP) – pain that lasts for longer than three months (1) – is becoming increasingly common (2–4), and threatens the physical, social and psychological wellbeing of those who suffer with it (5–11). While pain is a common experience, there is inequality in CP distribution between men and women, with women being more likely to experience CP at various stages of the life-course (12–19). There are different hypotheses around the rationale for this inequality: one is sex-linked factors, like hormones and reproductive factors (20–22), another is it related to discrepancies in the social and cultural experiences between genders (23–25), leading to forms of gendered stress. While systematic reviews have attested to the unequal distribution of CP in childhood and adolescence (26, 27) and older age (13, 17, 18, 28–32), the evidence is less clear about the prevalence of CP by sex at mid-life – a period with distinct social and physical challenges where growth is balanced with decline (33), related to heightened socioeconomic responsibilities and physiological changes, like the menopause. CP prevalence increases with age (19, 34), yet some evidence shows that the burden of pain is increasing for increasingly younger cohorts (35).The mid-life is a potentially sensitive period that may provide an arena for prevention and management interventions to decrease the burden of CP later in life.

Changes at mid-life may be associated with the emergence of CP, leading to significant impact on a person's ability to work (2, 36) and lead a fulfilling life (37–39). The mid-life –the period variously defined between ages of 40-65 (33, 40–44)- is a period in which both sex-linked and gender factors converge, and can be a period of stress (33, 45–50), at the same time as it is a time of social (33, 51) and physical (3, 33, 46) change. For example, there is epidemiological evidence suggesting that women experience more musculoskeletal pain around the perimenopause compared with pre-menopausal women, and that the pain persists into later life (31).

Previous systematic reviews have addressed the prevalence of CP by sex in the adult population spanning from 18 years to older age (16–19, 34). Mansfield *et al* (2016), for example, identified that prevalence of chronic widespread pain was higher in women over 40, while Fayaz et al (2016) reported an increase in prevalence of CP with age in the pooled sample. In summary, current systematic reviews of CP prevalence in adults either fail to differentiate between phases of adulthood (17, 18, 29, 34) or have not stratified results by sex at mid-life (15, 52, 53). By comparing CP prevalence at mid-life by sex, this review aims at addressing this gap in the literature.

Objectives

We will therefore carry out a systematic review to update the work of previous reviews to investigate CP prevalence by sex in midlife in the general population. It aims at answering the following questions:

- What is the prevalence of CP in men and women in the general population at mid-life?
- What is the difference in CP prevalence between men and women in the general population?

Heterogeneity in the results and variation across studies will be explored by geographic region, pain definition, and pain type. Geographic region has been shown to be related to differences in pain prevalence in other systematic reviews of CP incidence, with higher prevalence in lower-income countries (16, 34). Similarly, differences in pain definition (eg. the IASP definition of pain for 3 months or longer; pain duration for six months or longer; pain duration for 1 month or longer) have shown to have an effect on CP prevalence estimates (54). Lastly, the type of CP (eg. widespread chronic pain; fibromyalgia; chronic pelvic pain; chronic lower back pain) will represent further sources of heterogeneity since different conditions have different sex prevalence (55).

Study quality will be assessed using a tool developed for prevalence studies by Hoy et al (56), and previously used in reviews of pain prevalence literature (57).

Methods

This protocol is registered with the PROSPERO database and will be recorded using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) (58) (Additional file 1). PROSPERO will be updated with significant protocol amendments.

Eligibility criteria

Studies will be included if they:

- Are original studies published in peer reviewed journals.
- Examine the prevalence of CP in the 40-60 age group in men and women separately.
- Use samples selected from the general population.
- Use any clearly stated CP definition in line with the International Association for the Study of Pain (IASP) definition of pain lasting longer than three months (59), including both local and widespread CP.
- Clearly state the country in which data was collected.
- Use data from an observational study, such as prospective and retrospective cohorts, cross-sectional and case control studies.
- Are written in English.

Studies will be excluded if they:

- Do not meet inclusion criteria.
- Are reviews, conference proceedings, editorials and letters.
- Are samples of specific groups, eg. clinical samples, population minorities.
- Are specifically about neuropathic, diabetic or cancer pain.

Information sources and search strategy

An electronic search will identify appropriate studies. The selected databases are MEDLINE, to be accessed through Web of Science as an interface; and EMBASE, AMED and PSYCHinfo to be accessed through Ovid as an interface. These databases will be searched from earliest entries to 10 January 2022. The search strategy is based on CP terms, study terms, moderators, and limits. Different techniques will be followed to ensure the search terms identify all relevant articles, and the search strategy will be piloted to make sure it is selecting relevant articles. The search terms and various search tools used for the different databases are outlined in Table 1. The reference lists of fully eligible texts will also be screened to identify potential inclusions. (Table 1)

Study selection

Duplicate search results will be removed from the final search list, which will be stored in Rayyan QCRI – a free systematic review software. The review team will consist of three researchers and two of these [HR1] will independently screen each title and abstract for eligibility using a template (Table 2). The full text of the remaining articles will be retrieved using the UCL findit@UCL linking service. Inaccessible articles will be dealt with by contacting the authors directly. Each full text will be independently reviewed by two of the three researchers for final eligibility. Reasons for exclusion will be recorded and documented. At each stage of screening, any differences between researchers will be resolved through discussion. Figure 1 represents a flow diagram of the study selection process. (Table 2)

Data extraction and quality assessment

Data extraction will be conducted by the three reviewers for the following data items: citation details (including year of publication and title), study design, country, sample size, CP definition, CP type, CP measurement, age measurement, sex measurement, estimates of CP, estimates of sex difference, estimates of CP prevalence for each sex.

A data extraction form (Table 3) will be used and data will be extracted for each paper by two independent reviewers, who will resolve any discrepancies by discussion and supervision of an experienced member of the team (RH). (Table 3)

The primary estimates of interest are CP prevalence by sex and an estimate of the sex difference in pain (e.g. difference in prevalence or relative risk or odds ratio).

Quality assessment

Study quality will be addressed using a tool for risk of bias assessment for prevalence studies which explores internal and external validity and scores studies as low, moderate or high risk of bias (56). This tool has high interrater agreement, and it has previously been used in pain prevalence systematic reviews (57). For this review, two independent reviewers will use a checklist bases on this tool, which can be found in Table 3. (Table 3)

Synthesis

Narrative synthesis

A descriptive summary of studies will be provided using tables and addressing the following domains: primary outcomes, CP definition, CP type, sex/gender, age, geographic location (UN, WHO and HDI); and study quality assessment. It will comment on the similarity of the methods used by the different studies and on the possibility for meta-analysis.

Geographic region will be classified according to – the United Nations (UN) and World Health Organisation (WHO) region classification (60)(61), and the Human Development Index (HDI) for each country – a measures of population wealth (62), which has previously used in CP prevalence reviews (16,34).

The narrative synthesis will follow the Social Research Council Methods Programme guidelines (63), with a focus on identifying and exploring the prespecified sources of heterogeneity.

Meta-analysis

A meta-analysis will be conducted if enough studies provide the relevance prevalence information by sex for the defined age group, and where the reviewers can justify combining results.

A random effects meta-analysis will be used to combine estimates of CP prevalence by sex and a measure of difference in CP prevalence between sexes. These will be presented in a Forest plot. The I2 will be used to assess the extent of heterogeneity in estimates. If there are enough studies included, sub-group analysis or meta-regression will be performed to establish the extent of heterogeneity related to (i) geographic region (coded in three ways: UN, WHO and HDI), (ii) pain definition and (iii) pain type.

Publication bias will be assessed separately using a funnel plot. A sensitivity analysis excluding low quality studies will be carried out.

Reporting

The results of this systematic review will be shared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) 2020 guidelines (64).

[HR1]Key here is that two researchers independently screen each – this reads like 3 researchers are screening everything

Discussion

This study will review existing literature estimating CP prevalence and considers the differences by sex/gender at mid-life, contributing to the literature about sex differences in CP prevalence. Heterogeneity in results will be assessed according to geographic region, CP definition and type. The strengths and limitations will be considered, and measurements of sex (and gender) will be discussed in the context of similar reviews. The results of this review will provide a significant step towards identifying CP inequalities in mid-life between the sexes, and identify areas for further research. A better understanding of the relationship of CP emergence, sex and the middle years in the general population may inform better early-prevention-and-treatment strategies that tackle the distinct pathways for men and women.

Abbreviations

CP: Chronic Pain

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Availability of data and materials
Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding
Catherine Borra is supported by a PhD studentship funded by the Economic and Social Research Council (ESRC) and the Biotechnology and Biological Sciences Research Council (BBSRC) (award reference: ES/T00200X/1). Rebecca Hardy is Director of the CLOSER consortium, which is supported by the Economic and Social Research Council (ESRC) (award reference: ES/K000357/1).

Roles of funder: none.

Guarantor: Catherine Borra

Authors' contributions

CB is the main author of the draft of this manuscript. RH contributed with edits and methodological guidance, resulting in two further drafts. All authors read and approved the final manuscript.

Acknowledgements

Dr. Nazlin Bhimani provided search term guidance which was instrumental in developing the search strategy for this protocol.

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Tables

Table 1: Search strategy

From: Chronic pain prevalence in men and women in mid-life: a systematic review.

	MEDLINE (Web of Science)	*EMBASE + AMED + PSYCHinfo (Ovid)*
Pain terms	Chronic pain (MeSH Heading) OR fibromyalgia (MeSH Heading) NOT cancer OR diabetes OR neuropath* OR paed* OR child* OR adolescen*	Chronic pain OR persistent pain OR fibromyalgia (abstract) NOT cancer OR diabetes OR neuropath* OR paed* OR child* OR adolescen* (abstract)
Study terms	epidemiology OR cohort stud* OR cohort analys* OR cross sectional stud* OR cross sectional analys* OR observational analys* OR prevalence OR disease frequency	Epidemiolog* OR cohort stud* OR cohort analys* OR cross sectional stud* OR cross-sectional* OR cross sectional analys* OR observational analys* OR prevalence OR disease frequency NOT trial NOT clinical trial (abstract)
Moderators	Women OR female Men OR male	AND Male OR men (all fields) AND Female OR women (all fields)
Limits	Excluding RCTs and clinical studies/reviews English language only Journal articles only	English language only

Legend: MeSH terms are the Medical Subject Headings used for indexing articles in MEDLINE; The truncation command * is used to capture search terms which may have alternative endings; The Boolean logic operator AND combines results from the different search terms; The Boolean logic operator OR identifies results which include at least one of the search terms.

Table 2: Eligibility template
From: Chronic pain prevalence in men and women in mid-life: a systematic review.

Article reference	**Inclusion**														**Exclusion**							
	Original studies published in peer reviewed journals		Prevalence of CP in the 40-60 age group in men and women separately		Sample selected from the general population		CP definition in line with the International Association for the Study of Pain (IASP) definition		Clearly state the country in which data was collected		Observational studies		Written in English		Do not meet inclusion criteria		Reviews, conference proceedings, editorials and letters		Samples of specific groups, eg. clinical samples, population minorities		Ne dia ca
	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y

Table 3: Data extraction form
From: Chronic pain prevalence in men and women in mid-life: a systematic review

Screening form:

Bibliographic reference details:			
First author			
Title			
Journal			
Volume			
Year of publication			
Reviewer	CB	JP	RH
Date			
Inclusion	Yes	No	
Reasons for exclusion:			
Ineligible population	Yes	No	
Ineligible study design	Yes	No	
Ineligible outcome	Yes	No	
Ineligible publication type	Yes	No	
Not in English	Yes	No	
Duplicate	Yes	No	
Other			

Data extraction form:

Bibliographic reference details:			
First author			
Title			
Journal			
Volume			
Year of publication			
Reviewer	CB	JP	RH
Study characteristics:			
Study design	Cohort study	Cross-sectional study	Other:
Sample size			
Country			
Measurements:			
CP definition	IASP	Other:	
CP measurement			
Sex measurement	Self-reported sex	Self- reported gender	
Age measurement			
Outcomes:			
Outcome type	OR	%	Other:
Estimates of CP			
Estimates of sex difference			
Estimates of CP prevalence for each sex			
Risk of bias:			
External validity:			
Was the study's target population a close representation of the national population in relation to relevant variables?	Yes	No	
Was the sampling frame a true or close representation of the target population?	Yes	No	
Was some form of random selection used to select the sample, OR was a census undertaken?	Yes	No	
Was the likelihood of nonresponse bias minimal?	Yes	No	
Internal			
Were data collected directly from the subjects (as opposed to a proxy)?	Yes	No	
Was an acceptable case definition used in the study?	Yes	No	
Was the study instrument that measured the parameter of interest shown to have validity and reliability?	Yes	No	
Internal validity:			
Was the same mode of data collection used for all subjects?	Yes	No	
Was the length of the shortest prevalence period for the parameter of interest appropriate?	Yes	No	
Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	Yes	No	
Summary item on the overall risk of study bias	Low	Moderate	High

Figures

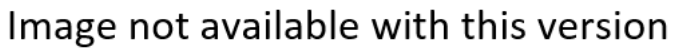

Figure 1

This image is not available with this version.

Supplementary Files

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- additionalfile1prismap.docx