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Health outcomes of unpaid care workers in low- and middle-income countries: a protocol for a systematic review.

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TITLE

Health outcomes of unpaid care workers in low- and middle-income countries: a protocol for a systematic review.

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WORD COUNT

2,387

ABSTRACT

INTRODUCTION
The literature on health outcomes of unpaid care work have included studies coming from high-income countries, and have reported gender inequalities that make caregiving women more vulnerable to physical and mental health problems. It is unknown the impact of unpaid care work on the health of those living in low- and middle-income countries, where women's autonomy is more limited.

METHODS AND ANALYSIS
We will conduct a systematic review and meta-analysis of observational studies on health outcomes according to unpaid caregiving status and sex of people living in low- and middle-income countries. CINAHL, PubMed, and SciELO Citation Index will be searched for reports in English or Spanish with published results from inception until June 1 2017. Studies must have included persons 18 years and older living in low- and middle-income countries, recruiting participants who do or do not provide unpaid care to their household or community members, reporting either physical and/or mental health problems, self-reported health-related quality of life, self-care skills/behaviors, or use of any healthcare services in the participants. Data extraction, the assessment of risk of bias and confounding, and qualitative synthesis will be carried out by two independent reviewers with the assistance of a third party.

DISSEMINATION
Results are expected to be published in peer-reviewed journals from the field of Health and Gender, or Health and Inequality.

REGISTRATION
The protocol for systematic review and meta-analysis was submitted to the International Prospective Register of Systematic Reviews (PROSPERO) on July 11 2017, a record number has not been assigned yet.

STRENGTHS AND LIMITATIONS OF THIS STUDY
- The PRISMA-P checklist and recommendations from the MOOSE group were used for the publication of this protocol.
- Evidence coming from low- and middle-income countries will be searched.
- Sex differences among unpaid caregivers will be reviewed.
- Recommendations from the Cochrane Collaboration and the Agency for Healthcare Research and Quality were used to design this systematic review.

AMENDMENTS
This section will include any changes introduced to the protocol after its publication.

INTRODUCTION

Inequalities in people's opportunity to participate in decision making processes, exercising power, and accessing healthcare resources, differentially expose people to health risks.[1-2] These stratified social relations occur along lines of social class, gender, ethnicity, and sexuality, among others, introducing undesirable inequalities in health, and violating the right to health.[1-2] Acting on these social determinants of health implies a redistribution of power for the benefit of disadvantaged groups.[2] Relations of social inequality between the sexes configure the status of political, economic, and social subordination of women,[3] affecting their autonomy –i.e. the capacity and conditions to freely make decisions impacting their lives-,[4] leading to inequitable health outcomes, worse economic and social consequences of illness, and unresponsive healthcare systems.[5] Being one of the most influential social determinants of health, the achievement of gender equality has been recognized as a development goal.[6]

Unpaid care work, defined as unpaid services providing what is necessary for the health, well-being, maintenance, and protection of household or community members,[7] is a gendered activity, with women spending more time on it than men.[8] Notwithstanding the enormous contribution of unpaid care work to health production and sustainable development of communities, the lack of recognition, value, and support to unpaid caregivers, has rendered women more vulnerable to physical and mental health problems.[5]

Complementarily, systematic reviews and meta-analyses have confirmed that unpaid caregivers exhibited much higher stress hormone levels and lower antibody response than non-caregivers, increased prevalence of behavioral risk factors for chronic diseases, such as unhealthy diets and sedentary lifestyle, and reported more use of healthcare services.[9-10] Moreover, a longitudinal study has demonstrated that unpaid caregivers end up poorer, have lower wellbeing and health, than their counterparts.[11]

Unpaid care work is costly. According to the Global Valuing the Invaluable analysis which measured the economic contribution of paid and unpaid work that women make to the health sector, the unpaid care work of women, after accounting for gender wage differentials and social security benefits, could be valued at 3.09% of global gross domestic product.[12] Invisibly subsidizing the healthcare sector, as this is not considered in national accounts.[12]

Although women's autonomy is more limited in low- and middle-income countries (LMICs),[13] with women from these backgrounds dedicating more hours to unpaid care work as men are less engaged in these activities,[8,12] the literature syntheses on health outcomes of unpaid care work have included studies coming from high-income countries, making sex comparisons.[9-10] It is unknown the impact of unpaid care work on the health of those living in LMICs, and accounting for sex differences might further enhance with high-income countries.

OBJECTIVES

The objective of this systematic review is to evaluate the health outcomes associated with unpaid care work in LMICs, taking into account sex differences. This systematic review will aim to answer the following question:

1. What are the health outcomes of unpaid care workers, in comparison with those

who do not perform unpaid care activities in LMICs?

2. Do health outcomes of unpaid care workers from LMICs differ by sex?

METHODS AND ANALYSIS

The protocol of this systematic review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRIMSA-P) checklist,[14] and some of the recommendation of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group, which were adapted.[15]

STUDY ELEGIBILITY CRITERIA

Participants

Persons 18 years and older, without distinction of sex or ethnicity, who do or do not provide unpaid care services to their household or community members, in LMICs.

Exposure

Subjects who do provide unpaid care services to their household or community members, whose care recipients may be those in permanent care or dependency, children aged 0 to 14 years, healthy people 15 to 64 years who do not require special health care, and older adults aged 65 years and over. Assistance with activities of daily living and instrumental activities of daily living will be taken into consideration.

Comparators

Subjects who do not provide unpaid care services. This may include also those subjects who do not qualify for inclusion as caregivers based on a threshold of hours of unpaid care work. Or exposed subjects who acted as their own controls in a longitudinal study.

Outcomes

Studies must have included at least one of the following outcomes: physical and/or mental health problems, self-reported health-related quality of life, self-care skills/behaviors, and use of any healthcare services.

Study design

Observational studies (e.g., case series, cross-sectional study, case control study, cohort studies). Additionally, systematic reviews and meta-analyses of observational studies will be included. Controlled trials will be excluded.

Context

General population or clinical samples LMICs, according to the World Bank income classification.[16]

REPORT ELIGIBILITY CRITERIA

Completed studies with published results, in English or Spanish, from their inception until June 1, 2017, will be included. Study protocols will be excluded.

INFORMATION SOURCES

The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and

Scientific Electronic Library Online (SciELO) Citation Index will be searched. Additionally, Reference lists of included studies will be screened for relevant papers.

SEARCH STRATEGY
The search strategy is detailed as follow:

Cumulative Index to Nursing and Allied Health Literature (CINAHL)
1. ((MH "Caregivers") OR ((TI Care*) AND (TI Informal)) OR ((TI Care*) AND (TI Unpaid)))
2. ((MH "Caregiver Role Strain (NANDA)") OR (MH "Caregiver Well-Being (Iowa NOC)") OR (MH "Caregiver Stressors (Iowa NOC)") OR (MH "Caregiver Physical Health (Iowa NOC)") OR (MH "Caregiver Lifestyle Disruption (Iowa NOC)") OR (MH "Health Status+") OR (MH "Stress+") OR (MH "Psychological Well-Being") OR (MH "Perceived Health (Iowa NOC)+") OR (MH "Quality of Life+") OR (MH "Self Care+") (MH "Health Resource Utilization") OR (MH "Health Services Needs and Demand+") OR (MH "Behavioral and Mental Disorders+"))
3. ((MH "Experimental Studies+") OR (MH "Random Assignment") OR (MH "Placebos") OR (TI Time Series Analysis) OR (AB Time Series Analysis) OR (TI Time Trend) OR (AB Time Trend) OR (TI Trend Analysis) OR (AB Trend Analysis) OR (TI Before After Stud*) OR (AB Before After Stud*) OR (TI Pretest Posttest) OR (AB Pretest Posttest) OR (TI Pre Test Post Test) OR (AB Pre Test Post Test) OR (TI Pre/Post Test) OR (AB Pre/Post Test) OR (MH "Quasi-Experimental Studies+"))
4. ((MH "Research Protocols") OR (TI Clinical Protocol) OR (AB Clinical Protocol) OR (TI Study Protocol) OR (AB Study Protocol))
5. ((MH "Qualitative Studies+") OR (MH "Focus Groups") OR (TI Key Informant) OR (AB Key Informant))
6. ((TI Semi Structured) OR (AB Semi Structured) OR (TI Semistructured) OR (AB Semistructured) OR (TI Unstructured) OR (AB Unstructured) OR (TI Informal) OR (AB Informal) OR (TI In-Depth) OR (AB In-Depth) OR (TI Face-to-Face) OR (AB Face-to-Face) OR (TI Structured) OR (AB Structured) OR (TI Guide) OR (AB Guide))
7. ((MH "Interviews+") OR (TI Discussion) OR (AB Discussion))
8. ((MH "Low and Middle Income Countries") OR (MH "Central America+") OR (MH "Latin America") OR (MH "South America+") OR (MH "West Indies+") OR (MH "Asia, Central+") OR (MH "Asia, Southeastern+") OR (MH "Asia, Western+") OR (MH "China+") OR (MH "Macao") OR (MH "Mongolia") OR (MH "North Korea") OR (MH "Europe, Eastern") OR (MH "Indian Ocean Islands+") OR (MH "Melanesia+") OR (MH "Micronesia+") OR (MH "Polynesia+") OR (MH "Developing Countries") OR (TI low income countr*) OR (AB low income countr*) OR (TI middle income countr*) OR (AB middle income countr*) OR (TI low N3 middle N3 countr*) OR (AB low N3 middle N3 countr*) OR (TI lmic) OR (AB lmic) OR (TI lamic) OR (AB lamic) OR (TI lami) OR (AB lami) OR (TI lmi) OR (AB lmi))
9. S1 AND S2
10. S3 OR S4 OR S5
11. S6 AND S7

12. S10 OR S11
13. S9 NOT S12
14. Limiters – Has Abstract
15. ((LA English) OR (LA Spanish))
16. S8 AND S13 AND S14 AND S15

PubMed
1. (Caregivers[Mesh] OR (Informal[Title/Abstract] n3 Care*) OR (Unpaid[Title/Abstract] n3 Care*))
2. (Stress, Psychological[Mesh] OR Stress, Physiological[Mesh] OR Health Status[Mesh] OR Health Lifestyle[Mesh] OR Self Care[Mesh] OR Quality of Life[Mesh] OR Health Resources/utilization[Mesh] OR Health Services/utilization[Mesh] OR Mental Disorders[Mesh] OR "Physical Health"[Title/Abstract] OR Well-Being[Title/Abstract])
3. (Clinical Trial[Publication Type] OR Clinical Trials as Topic[Mesh] OR Random Allocation[Mesh] OR Placebos[Mesh] OR Control Groups[Mesh] OR Meta-Analysis[Publication Type] OR Systematic Review[Title/Abstract] OR Quasi-Random*[Title/Abstract] OR Interrupted Time Series Analysis[Mesh] OR Time Series[Title/Abstract] OR Time Trend[Title/Abstract] OR Trend Analysis[Title/Abstract]) OR Controlled Before-After Studies[Mesh] OR Before After Study[Title/Abstract] OR pretest posttest[Title/Abstract] OR pre test post test[Title/Abstract] OR pre/post-test[Title/Abstract] OR Quasi-experiment*[Title/Abstract])
4. (Clinical Protocol[Mesh] OR Study Protocol[Title])
5. (Qualitative Research[Mesh] OR Focus Groups[Mesh] OR Ethnograph*[Title/Abstract] OR Key Informant[Title/Abstract])
6. (Semi-Structured[Title/Abstract] OR Semistructured[Title/Abstract] OR Unstructured[Title/Abstract] OR Informal[Title/Abstract] OR In-Depth[Title/Abstract] OR Face-to-Face[Title/Abstract] OR Structured[Title/Abstract] OR Guide[Title/Abstract])
7. (Interview*[Title/Abstract] OR Discussion*[Title/Abstract])
8. (Developing Countries[Mesh] OR Africa[Mesh] OR Caribbean Region[Mesh] OR Central America[Mesh] OR Latin America[Mesh] OR South America[Mesh] OR Asia, Central[Mesh] OR Asia, Northern[Mesh] OR Asia, Southeastern[Mesh] OR Asia, Western[Mesh] OR China[Mesh] OR Democratic People's Republic of Korea[Mesh] OR Mongolia[Mesh] OR Europe, Eastern[Mesh] OR Melanesia[Mesh] OR Micronesia[Mesh] OR Polynesia[Mesh] OR Low Income Countr*[Title/Abstract] OR Middle Income Countr*[Title/Abstract] OR (Low Middle Income) OR LMIC[Title/Abstract] OR LAMIC[Title/Abstract] OR LAMI[Title/Abstract] OR LMI[Title/Abstract])
9. #1 AND #2
10. #3 OR #4 OR #5
11. #6 AND #7
12. #10 OR #11
13. #9 NOT #12
14. (hasabstract[text])

15. (English[lang] OR Spanish[lang])
16. #8 AND #13 AND #14 AND #15

Scientific Electronic Library Online (SciELO) Citation Index

1. TS=("caregiver*")
2. TS=("care*") AND TS=("unpaid")
3. TS=("care*") AND TS=("unpaid")
4. #1 OR #2 OR #3
5. TS=("stress*") OR TS=("strain") OR TS=("health status") OR TS=("quality of life") OR TS=("lifestyle") OR TS=("self care") OR TS=("well-being") OR TS=("mental health") OR TS=(mental NEAR/1 disorder)
6. TS=("health*") AND TS=("service*") AND TS=("use")
7. TS=("health*") AND TS=("service*") AND TS=("utilization")
8. #5 OR #6 OR #7
9. TS=(intervention NEAR/0 stud*) OR TS=(experiment*) OR TS=("clinical trial*") OR TS=("controlled trial") OR TS=(random*) OR TS=(allocat*) OR TS=(placebo*) OR TS=("control group*") OR TS=(metaanalysis) OR TS=("meta analysis") OR TS=(systematic NEAR/0 review*) OR TS=(quasi NEAR/0 random*) OR TS=("time series") OR TS=("time trend") OR TS=("trend analysis") OR TS=("before after") OR TS=("before and after") OR TS=("pretest posttest") OR TS=("pre test post test") OR TS=("pre post test") OR TS=(quasi NEAR/0 experiment*)
10. TS=("clinical protocol") OR TI=("study protocol")
11. TS=(qualitative NEAR/2 (research* OR method* OR technique* OR inquir*)) OR TS=("focus group*") OR TS=(hermeneutic*) OR TS=(ethnograph*) OR TS=("key informant*")
12. TS=("semi structured") OR TS=(unstructured) OR TS=(unpaid) OR TS=("in depth") OR TS=("face to face") OR TS=(structured) OR TS=(guide)
13. TS=(interview*) OR TS=(discussion*)
14. TS=("Developing Countries") OR TS=("Africa") OR TS=("Caribbean Region") OR TS=("Central America") OR TS=("Latin America") OR TS=("South America") OR TS=("Asia, Central") OR TS=("Asia, Northern") OR TS=("Asia, Southeastern") OR TS=("Asia, Western") OR TS=("China") OR TS=("Eastern Europe") OR TS=("Mongolia") OR TS=("Democratic People's Republic of Korea") OR TS=("Melanesia") OR TS=("Micronesia") OR TS=("Polynesia") OR TS=((low OR middle) NEAR/3 income NEAR/2 countr*) OR TS=("low income") OR TS=("middle income") OR TS=(lmic OR lamic OR lami OR lmi)
15. #4 AND #8
16. #9 OR #10 OR #11
17. #12 AND #13
18. #16 OR #17
19. #15 NOT #18
20. #19 AND LANGUAGE:(English OR Spanish)
21. #14 AND #20

STUDY RECORS

All study records will be imported into EndNote Web and duplicates will be removed. The study selection process will be carried out in two stages (screening of title/abstract, and full-text assessment of articles), with two reviewers independently, and in duplicate, determining inclusion/exclusion of study records based on previously specified criteria. If discrepancies arose during any stage, these will be solved by discussion and confirmed by a third reviewer. Finally, data from multiple records of the same study will be pieced together.

Data extraction will be carried out using a standardized sheet recommended by the Cochrane Handbook of Systematic Reviews of Interventions,[17] following the same reviewing process described above, with regular meetings held to verify the quality of the extracted data. The following data will be extracted from each study included in this review: (1) First author, year of publication, and country of origin; (2) Participants inclusion/exclusion criteria (age, sex, ethnicity, socio-economic status, and/or urban/rural residence) and setting (e.g. general population or clinical sample); (3) Exposure/comparison characteristics, including criteria for classification as unpaid care worker (e.g., number of hours), and type of care tasks provided; (4) Type of outcomes reported (i.e. clinical, patient-reported, or use of healthcare services), instruments, follow-up periods (in case of longitudinal studies), and main findings (with effect size, confidence intervals, and statistical significance); (5) Type of study design.

OUTCOMES AND PRIORITISATION

Included studies must report any outcome of interest, and, in the case of longitudinal studies, baseline levels of these outcomes must be reported. Due to the inclusion of cross-sectional and longitudinal studies, no distinction based on follow-up periods will be made. The primary outcome will be mental and/or physical health problems of participants measured either objectively or by self-report of symptoms or illnesses. Secondary outcomes will be: (1) self-reported health-related quality of life; (2) self-care skills/behaviors; and (3) use of any healthcare services.

RISK OF BIAS - INDIVIDUAL STUDIES

To assess the risk of bias and confounding in the included studies, we will use the "Item Bank for Assessing Risk of Bias and Confounding for Observational Studies of Interventions or Exposure" developed by the Agency for Healthcare Research and Quality (AHRQ).[18]

This tool includes an assessment of thirteen sources of bias and confounding: variations across groups of the study in the inclusion/exclusion criteria, the recruitment strategies or the length of follow-up, inappropriate selection of the comparison group, failing to account for important variations in the execution of the study, outcome assessor not blinded to exposure status of participants, study measures of dubious validity and reliability or implemented inconsistently, impact of high or differential loss to follow-up not assessed, important outcomes or harms/adverse events not reported, study limitations hampers the credibility of the study, no documented attempts to balance the allocation between the groups, and important confounding variables not taken into account.[18]

The same procedure described above for the study selection and the data extraction will be employed to assess the risk of bias of the included studies.

DATA SYNTHESIS

A qualitative synthesis of the included studies will be conducted to provide an overview of the differences in health outcomes among participants coming from LMICs, taking into account the study characteristics and risk of bias/confounding. Sex differences in health outcomes among unpaid caregivers living in these countries will also be explored. These results will be summarized using comparative tables recommended in the Cochrane Handbook for Systematic Reviews of Interventions.[17]

DISSEMINATION

The results of this systematic review will be published in peer-reviewed journals covering topics such as: Gender and Health, and Health Inequalities.

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AUTHORS' CONTRIBUTIONS

IM is the guarantor of this systematic review and provides her expert opinion during the reviewing process; PM and ML made valuable input to the design of this systematic review, and will be in charge of the data extraction and risk of bias assessment under the supervision of IM. IM, PM, and ML will contribute equally to data synthesis. All authors edited, modified, and approved the final version of this manuscript.

FINANCIAL SUPPORT

ROLE OF FUNDERS

The funding institution is not involved in any part of this study.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form. The authors have no competing interests to disclose.

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KEYWORDS
Unpaid Care Work; Health Outcomes; Systematic Review

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ABSTRACT

INTRODUCTION
The literature on health outcomes of unpaid care work has included studies coming from high-income countries, and has reported gender inequalities that make caregiving women more vulnerable to physical and mental health problems. The impact of unpaid care work on the health of those living in low- and middle-income countries, where women's autonomy is more limited is unknown.

METHODS AND ANALYSIS
We will conduct a systematic review of observational studies on health outcomes according to unpaid caregiving status and sex of people living in low- and middle-income countries. CINAHL, PubMed, and SciELO Citation Index will be searched for reports in English or Spanish with published results from inception until June 1 2017. We expect the studies to have recruited individuals in low- and middle-income countries, including exposed and non-exposed groups to participation in unpaid care to members if their households or community, reporting either physical and/or mental health problems, self-reported health-related quality of life, self-care skills/behaviours, or use of any health care services in the participants. Data extraction, the assessment of risk of bias and confounding, and qualitative synthesis will be carried out by two independent reviewers with the assistance of a third party.

DISSEMINATION
Results are expected to be published in peer-reviewed journals from the field of Health and Gender, or Health and Inequality.

REGISTRATION
The protocol for systematic review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) on August 7 2017, under record number CRD42017071785.

STRENGTHS AND LIMITATIONS OF THIS STUDY
- The PRISMA-P checklist and recommendations from the MOOSE group were used for the publication of this protocol.
- There have been no recent syntheses of the evidence on the state of health of unpaid caregivers in low- and middle-income countries.
- There are no recent systematic reviews on gender differences in the health status of caregivers who come from these countries.
- Recommendations from the Cochrane Collaboration and the Agency for Healthcare Research and Quality were used to design this systematic review.

AMENDMENTS
This section will include any changes introduced to the protocol after its publication.
A set of amendments to the protocol that were carried out are listed below:
1. The lower age limit (18 years and over) was eliminated to include all participants

regardless of age.

2. The reference to the fact that participants may or may not carry out unpaid care work was eliminated. These conditions apply and were duly developed in the description of the exposure and comparator.

INTRODUCTION

The inequality of opportunities for participating in decision-making processes, exercise of power and access to health resources differentially exposes people to health risks [1-2]. This social stratification occurs throughout categories such as social class, gender, ethnicity and sexuality, among others, introducing undesirable inequalities in health, constituting a violation of the right to health [1-2]. Acting on these social determinants of health involves redistributing power for the benefit of the most vulnerable groups [2]. Unequal social relations between sexes shapes the status of political, economic and social subordination of women, [3] affecting their autonomy--which is made up of capabilities and conditions to freely make decisions that have an impact on their lives-- [4] and that cause disparities in health results, worse economic and social consequences of poor health, and health systems with ineffective resolving power [5]. As one of the most influential social determinants of health, attaining gender equity has been recognized as a development goal [6].

Unpaid care work, defined as the service of health maintenance, well-being and the protection of family and community members, [7] is an activity that is determined by gender, with more women devoting time to it than men [8]. In spite of the huge contribution to unpaid care work to producing health and sustainable development of communities, the lack of recognition, valuation and support to those who are devoted to these tasks, it has made women more vulnerable to physical and mental health problems [5] .

Additionally, systematic reviews and meta-analyses have confirmed that the unpaid care is related to higher levels of stress hormones and worse response of antibodies, greater prevalence of behavioural risk factors for chronic diseases, such as unhealthy diets and sedentary lifestyles and greater use of health services compared to subjects that do not provide these services [9-10]. Moreover, a longitudinal study showed that unpaid caregivers end up being poorer and less happy and healthy than their counterparts [11].

Unpaid care work is costly. According to the Global Valuing the Invaluable Analysis, which measured the economic contribution of paid and unpaid work that women make to the health sector, unpaid care by women, after accounting for gender wage differentials and social security benefits, could be valued at 3.09% of the global gross domestic product [12], invisibly subsidizing the health sector because it is considered in national accounts [12].

Women's autonomy is more limited in low- and middle-income countries (LMICs) [13], devoting more hours to unpaid work than women in high income countries (HICs). This is due to the lower participation of men in LMICs in these tasks [8,12]. Additionally, it has been reported that the objective and subjective burden due to unpaid care work is greater in LMICs than in HICs, representing a decline for family economy, and being greater for female caregiver than for male caregivers.[14]

In spite of this scenario, literature syntheses on health outcomes of unpaid care work have included participants who come from HICs,[9-10] and have made comparisons between the sexes, confirming the worst outcomes for women. The only review carried out in developing countries focused on recipients of care for the chronically ill or disabled, and did not focus on the comparison between unpaid care workers and those who do not participate in these tasks [15].

Therefore, the specific contribution of unpaid care work in health in LMICs cannot be

elucidated by the current status of the synthesis of evidence. Furthermore, considering the differences in health as a result of the sex of the caregiver may facilitate the comparison with the HICs and help define future intervention strategies in countries in which the limited autonomy of women could considerably affect their state of health.

OBJECTIVES

The objective of this systematic review is to evaluate the health outcomes associated with unpaid care work in LMICs, taking into account sex differences. This systematic review will aim to answer the following question:

1. What are the health outcomes of unpaid care workers compared to those who do not perform unpaid care activities in LMICs?
2. Do health outcomes of unpaid care workers from LMICs differ by sex?

METHODS AND ANALYSIS

The protocol of this systematic review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRIMSA-P) checklist [16] and some of the recommendation of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group, which were adapted [17].

STUDY ELEGIBILITY CRITERIA

Participants

Individuals without distinction of age, sex, or ethnicity, living in LMICs.

Exposure

Provision of unpaid care to household or community members. For the purposes of this systematic review, unpaid care work was defined as the set of activities carried out for the development and well-being of the everyday life of members of the home or the community, involving the care of people affected by permanent health problems or condition of dependency, care of children aged between 0 to 14, healthy people aged between 15 to 65 (healthy, who do not require special care or have symptoms clinically identifiable diseases), and the care of adults over 65 years of age. This conceptualization has been used in time-use surveys in Chile[18].

Comparators

Unpaid care to household or community members not provided. This may include subjects that do not qualify as unpaid caregivers according to a certain threshold of hours of care. Also, in the case of the longitudinal studies without a control group, it can refer to the subjects who acted as their own control, based on the change of the status of unpaid care provider.

Outcomes

The studies must include at least one of the following outcomes: physical and/or mental health problems, health-related quality of life, self-care behaviour or skills, and use of health services. These outcomes must use objective or self-reported measures.

Study design

Observational studies (e.g., case series, cross-sectional study, case control study, cohort studies). Additionally, systematic reviews and meta-analyses of observational studies will be included. Controlled trials will be excluded.

Context
General population or clinical samples LMICs, according to the World Bank income classification [19].

REPORT ELIGIBILITY CRITERIA
Completed studies with published results, in English or Spanish, from their inception until June 1, 2017, will be included. Study protocols will be excluded.

INFORMATION SOURCES
The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and Scientific Electronic Library Online (SciELO) Citation Index will be searched. Additionally, reference lists of included studies will be screened for relevant papers.

SEARCH STRATEGY
The search strategy is presented in a supplementary file. Terms related to exposure (e.g., "caregivers" and "unpaid"), outcomes (e.g. "State of health" and "self-care"), and contexts (e.g., "low and middle income countries") will be used. In addition, a series of terms will be used to exclude reports of studies according to their design (i.e., studies that assessed the effectiveness of interventions, or qualitative studies).

STUDY RECORDS
All study records will be imported into EndNote Web and duplicates will be removed. The study selection process will be carried out in two stages (screening of title/abstract, and full-text assessment of articles), with two reviewers independently, and in duplicate, determining inclusion/exclusion of study records based on previously specified criteria. If discrepancies arise during any stage, these will be solved by discussion and confirmed by a third reviewer. Finally, data from multiple records of the same study will be pieced together.
Data extraction will be carried out using a standardized sheet recommended by the Cochrane Handbook of Systematic Reviews of Interventions,[20] following the same reviewing process described above, with regular meetings held to verify the quality of the extracted data. The following data will be extracted from each study included in this review: (1) First author, year of publication, and country of origin; (2) Participants inclusion/exclusion criteria (age, sex, ethnicity, socio-economic status, and/or urban/rural residence) and setting (e.g. general population or clinical sample); (3) Exposure/comparison characteristics, including criteria for classification as unpaid care worker (e.g., number of hours), and type of care tasks provided; (4) Type of outcomes reported (i.e. clinical, patient-reported, or use of healthcare services), instruments, follow-up periods (in case of longitudinal studies), and main findings (with effect size, confidence intervals, and statistical significance); (5) Type of study design.

OUTCOMES AND PRIORITISATION

Included studies must report any outcome of interest, and, in the case of longitudinal studies, baseline levels of these outcomes must be reported. Due to the inclusion of cross-sectional and longitudinal studies, no distinction based on follow-up periods will be made. The primary outcome will be mental and/or physical health problems of participants measured either objectively or by self-report of symptoms or illnesses. Secondary outcomes will be: (1) self-reported health-related quality of life; (2) self-care skills/behaviours; and (3) use of any healthcare services.

RISK OF BIAS - INDIVIDUAL STUDIES

To assess the risk of bias and confounding in the included studies, we will use the "Item Bank for Assessing Risk of Bias and Confounding for Observational Studies of Interventions or Exposure" developed by the Agency for Healthcare Research and Quality (AHRQ).[21]

This tool includes an assessment of thirteen sources of bias and confounding: variations across groups of the study in the inclusion/exclusion criteria, the recruitment strategies or the length of follow-up, inappropriate selection of the comparison group, failing to account for important variations in the execution of the study, outcome assessor not blinded to exposure status of participants, study measures of dubious validity and reliability or implemented inconsistently, impact of high or differential loss to follow-up not assessed, important outcomes or harms/adverse events not reported, study limitations hampers the credibility of the study, no documented attempts to balance the allocation between the groups, and important confounding variables not taken into account.[21]

The same procedure described above for the study selection and the data extraction will be employed to assess the risk of bias of the included studies.

DATA SYNTHESIS

A qualitative synthesis of the included studies will be conducted to provide an overview of the differences in health outcomes among participants coming from LMICs, taking into account the study characteristics and risk of bias/confounding. Sex differences in health outcomes among unpaid caregivers living in these countries will also be explored. These results will be summarized using comparative tables recommended in the Cochrane Handbook for Systematic Reviews of Interventions.[20]

DISCUSSION

For over two decades, the United Nations have called on member states to include unpaid work in economic and vital statistics.[22-23] Today, in the Region of Latin America, a small number of countries have national time-use surveys, and very few have implemented a nation-wide system of care. This scenario is replicated in other regions of the developing world.[24] The protocol of a systematic review reported here echoes this reality and aims to contribute to the acknowledgment and valuation of unpaid care work in LMICs.

It is expected that the political and economic obstacles to overcome the unequal division of unpaid work, particularly in LMICs, will be expressed in a small number of studies that compare caregivers and non-caregivers, being these publications rather recent. Additionally, the socio-economic and geographical variety among the LMICs will

help to understand how the exercise of care is related to other socio-cultural variables. The authors of this systematic review anticipate limitations due to the eligibility criteria and the sources of information used. By limiting publications to the English or Spanish languages, and the scope of studies published in other languages (for example, Chinese or Arabic), a geographical bias in favour of evidence from Latin America may have been introduced. This decision has been made considering the financial resources and the time set for this systematic review.

Again, for reasons of economy of resources for this systematic review, we have opted for the design of a search strategy that excludes terms related to experimental studies. In this regard, Cochrane Collaboration recognizes that the process of identifying non-random studies (NRS) in searches and their subsequent selection may be prone to biases due to lack of a predefined search strategy and to report highly heterogeneous characteristics of the study design, compared to the randomized clinical trials.[20]

Finally, this systematic review was limited to the review of the evidence published in the databases mentioned in the subsection "Sources of Information." This will hinder the detection of selection biases because grey literature search will not be conducted, nor will the authors and authorities be contacted on the subject to identify additional sources, due to the previously mentioned reasons.

DISSEMINATION

The results of this systematic review will be published in peer-reviewed journals covering topics such as: Gender and Health, and Health Inequalities.

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AUTHORS' CONTRIBUTIONS

IM is the guarantor of this systematic review and provides her expert opinion during the reviewing process; PM and ML made valuable input to the design of this systematic review, and will be in charge of the data extraction and risk of bias assessment under the supervision of IM. IM, PM, and ML will contribute equally to data synthesis. All authors edited, modified, and approved the final version of this manuscript.

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ROLE OF FUNDERS

The funding institution is not involved in any part of this study.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form. The authors have no competing interests to disclose.

APPENDIX

The search strategy is detailed as follow:

Cumulative Index to Nursing and Allied Health Literature (CINAHL)

1. ((MH "Caregivers") OR ((TI Care*) AND (TI Informal)) OR ((TI Care*) AND (TI Unpaid)))
2. ((MH "Caregiver Role Strain (NANDA)") OR (MH "Caregiver Well-Being (Iowa NOC)") OR (MH "Caregiver Stressors (Iowa NOC)") OR (MH "Caregiver Physical Health (Iowa NOC)") OR (MH "Caregiver Lifestyle Disruption (Iowa NOC)") OR (MH "Health Status+") OR (MH "Stress+") OR (MH "Psychological Well-Being") OR (MH "Perceived Health (Iowa NOC)+") OR (MH "Quality of Life+") OR (MH "Self Care+") (MH "Health Resource Utilization") OR (MH "Health Services Needs and Demand+") OR (MH "Behavioral and Mental Disorders+")
3. ((MH "Experimental Studies+") OR (MH "Random Assignment") OR (MH "Placebos") OR (TI Time Series Analysis) OR (AB Time Series Analysis) OR (TI Time Trend) OR (AB Time Trend) OR (TI Trend Analysis) OR (AB Trend Analysis) OR (TI Before After Stud*) OR (AB Before After Stud*) OR (TI Pretest Posttest) OR (AB Pretest Posttest) OR (TI Pre Test Post Test) OR (AB Pre Test Post Test) OR (TI Pre/Post Test) OR (AB Pre/Post Test) OR (MH "Quasi-Experimental Studies+"))
4. ((MH "Research Protocols") OR (TI Clinical Protocol) OR (AB Clinical Protocol) OR (TI Study Protocol) OR (AB Study Protocol))
5. ((MH "Qualitative Studies+") OR MH "Focus Groups") OR (TI Key Informant) OR (AB Key Informant))
6. ((TI Semi Structured) OR (AB Semi Structured) OR (TI Semistructured) OR (AB Semistructured) OR (TI Unstructured) OR (AB Unstructured) OR (TI Informal) OR (AB Informal) OR (TI In-Depth) OR (AB In-Depth) OR (TI Face-to-Face) OR (AB Face-to-Face) OR (TI Structured) OR (AB Structured) OR (TI Guide) OR (AB Guide))
7. ((MH "Interviews+") OR (TI Discussion) OR (AB Discussion))
8. ((MH "Low and Middle Income Countries") OR (MH "Central America+") OR (MH "Latin America") OR (MH "South America+") OR (MH "West Indies+") OR (MH "Asia, Central+") OR (MH "Asia, Southeastern+") OR (MH "Asia, Western+") OR (MH "China+") OR (MH "Macao") OR (MH "Mongolia") OR (MH "North Korea") OR (MH "Europe, Eastern") OR (MH "Indian Ocean Islands+") OR (MH "Melanesia+") OR (MH "Micronesia+") OR (MH "Polynesia+") OR (MH "Developing Countries") OR (TI low income countr*) OR (AB low income countr*) OR (TI middle income countr*) OR (AB middle income countr*) OR (TI low N3 middle N3 countr*) OR (AB low N3 middle N3 countr*) OR (TI lmic) OR (AB lmic) OR (TI lamic) OR (AB lamic) OR (TI lami) OR (AB lami) OR (TI lmi) OR (AB lmi))
9. S1 AND S2
10. S3 OR S4 OR S5
11. S6 AND S7
12. S10 OR S11

13. S9 NOT S12
14. Limiters – Has Abstract
15. ((LA English) OR (LA Spanish))
16. S8 AND S13 AND S14 AND S15

PubMed

1. (Caregivers[Mesh] OR (Informal[Title/Abstract] n3 Care*) OR (Unpaid[Title/Abstract] n3 Care*))
2. (Stress, Psychological[Mesh] OR Stress, Physiological[Mesh] OR Health Status[Mesh] OR Health Lifestyle[Mesh] OR Self Care[Mesh] OR Quality of Life[Mesh] OR Health Resources/utilization[Mesh] OR Health Services/utilization[Mesh] OR Mental Disorders[Mesh] OR "Physical Health"[Title/Abstract] OR Well-Being[Title/Abstract])
3. (Clinical Trial[Publication Type] OR Clinical Trials as Topic[Mesh] OR Random Allocation[Mesh] OR Placebos[Mesh] OR Control Groups[Mesh] OR Meta-Analysis[Publication Type] OR Systematic Review[Title/Abstract] OR Quasi-Random*[Title/Abstract] OR Interrupted Time Series Analysis[Mesh] OR Time Series[Title/Abstract] OR Time Trend[Title/Abstract] OR Trend Analysis[Title/Abstract]) OR Controlled Before-After Studies[Mesh] OR Before After Study[Title/Abstract] OR pretest posttest[Title/Abstract] OR pre test post test[Title/Abstract] OR pre/post-test[Title/Abstract] OR Quasi-experiment*[Title/Abstract])
4. (Clinical Protocol[Mesh] OR Study Protocol[Title])
5. (Qualitative Research[Mesh] OR Focus Groups[Mesh] OR Ethnograph*[Title/Abstract] OR Key Informant[Title/Abstract])
6. (Semi-Structured[Title/Abstract] OR Semistructured[Title/Abstract] OR Unstructured[Title/Abstract] OR Informal[Title/Abstract] OR In-Depth[Title/Abstract] OR Face-to-Face[Title/Abstract] OR Structured[Title/Abstract] OR Guide[Title/Abstract])
7. (Interview*[Title/Abstract] OR Discussion*[Title/Abstract])
8. (Developing Countries[Mesh] OR Africa[Mesh] OR Caribbean Region[Mesh] OR Central America[Mesh] OR Latin America[Mesh] OR South America[Mesh] OR Asia, Central[Mesh] OR Asia, Northern[Mesh] OR Asia, Southeastern[Mesh] OR Asia, Western[Mesh] OR China[Mesh] OR Democratic People's Republic of Korea[Mesh] OR Mongolia[Mesh] OR Europe, Eastern[Mesh] OR Melanesia[Mesh] OR Micronesia[Mesh] OR Polynesia[Mesh] OR Low Income Countr*[Title/Abstract] OR Middle Income Countr*[Title/Abstract] OR (Low Middle Income) OR LMIC[Title/Abstract] OR LAMIC[Title/Abstract] OR LAMI[Title/Abstract] OR LMI[Title/Abstract])
9. #1 AND #2
10. #3 OR #4 OR #5
11. #6 AND #7
12. #10 OR #11
13. #9 NOT #12
14. (hasabstract[text])
15. (English[lang] OR Spanish[lang])
16. #8 AND #13 AND #14 AND #15

Scientific Electronic Library Online (SciELO) Citation Index

1. TS=("caregiver*")
2. TS=("care*") AND TS=("unpaid")
3. TS=("care*") AND TS=("unpaid")
4. #1 OR #2 OR #3
5. TS=("stress*") OR TS=("strain") OR TS=("health status") OR TS=("quality of life") OR TS=("lifestyle") OR TS=("self care") OR TS=("well-being") OR TS=("mental health") OR TS=(mental NEAR/1 disorder)
6. TS=("health*") AND TS=("service*") AND TS=("use")
7. TS=("health*") AND TS=("service*") AND TS=("utilization")
8. #5 OR #6 OR #7
9. TS=(intervention NEAR/0 stud*) OR TS=(experiment*) OR TS=("clinical trial*") OR TS=("controlled trial") OR TS=(random*) OR TS=(allocat*) OR TS=(placebo*) OR TS=("control group*") OR TS=(metaanalysis) OR TS=("meta analysis") OR TS=(systematic NEAR/0 review*) OR TS=(quasi NEAR/0 random*) OR TS=("time series") OR TS=("time trend") OR TS=("trend analysis") OR TS=("before after") OR TS=("before and after") OR TS=("pretest posttest") OR TS=("pre test post test") OR TS=("pre post test") OR TS=(quasi NEAR/0 experiment*)
10. TS=("clinical protocol") OR TI=("study protocol")
11. TS=(qualitative NEAR/2 (research* OR method* OR technique* OR inquir*)) OR TS=("focus group*") OR TS=(hermeneutic*) OR TS=(ethnograph*) OR TS=("key informant*")
12. TS=("semi structured") OR TS=(unstructured) OR TS=(unpaid) OR TS=("in depth") OR TS=("face to face") OR TS=(structured) OR TS=(guide)
13. TS=(interview*) OR TS=(discussion*)
14. TS=("Developing Countries") OR TS=("Africa") OR TS=("Caribbean Region") OR TS=("Central America") OR TS=("Latin America") OR TS=("South America") OR TS=("Asia, Central") OR TS=("Asia, Northern") OR TS=("Asia, Southeastern") OR TS=("Asia, Western") OR TS=("China") OR TS=("Eastern Europe") OR TS=("Mongolia") OR TS=("Democratic People's Republic of Korea") OR TS=("Melanesia") OR TS=("Micronesia") OR TS=("Polynesia") OR TS=((low OR middle) NEAR/3 income NEAR/2 countr*) OR TS=("low income") OR TS=("middle income") OR TS=(lmic OR lamic OR lami OR lmi)
15. #4 AND #8
16. #9 OR #10 OR #11
17. #12 AND #13
18. #16 OR #17
19. #15 NOT #18
20. #19 AND LANGUAGE:(English OR Spanish)
21. #14 AND #20

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	2-3
Support:			
Sources	5a	Indicate sources of financial or other support for the review	10
Sponsor	5b	Provide name for the review funder and/or sponsor	10
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	10
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6 & Supplementary File
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	n/a
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	n/a
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

BMJ Open

Health outcomes of unpaid care workers in low- and middle-income countries: a protocol for a systematic review.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-018643.R2
Article Type:	Protocol
Date Submitted by the Author:	13-Dec-2017
Complete List of Authors:	Magaña, Irene; Universidad de Santiago de Chile, Escuela de Psicología, Facultad de Humanidades; Universidad de Santiago de Chile, Centro de Estudios Migratorios (CEM) Martínez, Pablo; Universidad de Santiago de Chile, Escuela de Psicología, Facultad de Humanidades; Universidad de Santiago de Chile, CITIAPS Loyola, María-Soledad; Universidad de Santiago de Chile, Escuela de Psicología, Facultad de Humanidades; Universidad de Santiago de Chile, Centro de Estudios Migratorios (CEM)
Primary Subject Heading:	Public health
Secondary Subject Heading:	Sociology, Epidemiology, Global health
Keywords:	Unpaid Care Work, Health Outcomes, Low- and Middle-Income Countries, Systematic Review

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TITLE
Health outcomes of unpaid care workers in low- and middle-income countries: a protocol for a systematic review.

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WORD COUNT

2,387

ABSTRACT

INTRODUCTION
The literature on health outcomes of unpaid care work has included studies coming from high-income countries, and has reported gender inequalities that make caregiving women more vulnerable to physical and mental health problems. The impact of unpaid care work on the health of those living in low- and middle-income countries, where women's autonomy is more limited is unknown.

METHODS AND ANALYSIS
We will conduct a systematic review of observational studies on health outcomes according to unpaid caregiving status and sex of people living in low- and middle-income countries. CINAHL, PubMed, and SciELO Citation Index will be searched for reports in English or Spanish with published results from inception until June 1 2017. We expect the studies to have recruited individuals in low- and middle-income countries, including exposed and non-exposed groups to participation in unpaid care to members if their households or community, reporting either physical and/or mental health problems, self-reported health-related quality of life, self-care skills/behaviours, or use of any health care services in the participants. Data extraction, the assessment of risk of bias and confounding, and qualitative synthesis will be carried out by two independent reviewers with the assistance of a third party.

DISSEMINATION
Results are expected to be published in peer-reviewed journals from the field of Health and Gender, or Health and Inequality.

REGISTRATION
The protocol for systematic review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) on August 7 2017, under record number CRD42017071785.

STRENGTHS AND LIMITATIONS OF THIS STUDY
- The PRISMA-P checklist and recommendations from the MOOSE group were used to strengthen the publication of this protocol.
- There have been no recent syntheses of the evidence on the state of health of unpaid caregivers in low- and middle-income countries, nor on the gender differences in the health status of caregivers who come from these countries.
- Recommendations from the Cochrane Collaboration and the Agency for Healthcare Research and Quality were used to design this systematic review.
- This systematic review will be limited to published articles; no grey literature will be searched.
- Searches will be limited to studies published in English and Spanish languages.

AMENDMENTS
This section will include any changes introduced to the protocol after its publication.

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A set of amendments to the protocol that were carried out are listed below:

1. The lower age limit (18 years and over) was eliminated to include all participants regardless of age.
2. The reference to the fact that participants may or may not carry out unpaid care work was eliminated. These conditions apply and were duly developed in the description of the exposure and comparator.

INTRODUCTION

The inequality of opportunities for participating in decision-making processes, exercise of power and access to health resources differentially exposes people to health risks [1-2]. This social stratification occurs throughout categories such as social class, gender, ethnicity and sexuality, among others, introducing undesirable inequalities in health, constituting a violation of the right to health [1-2]. Acting on these social determinants of health involves redistributing power for the benefit of the most vulnerable groups [2]. Unequal social relations between sexes shapes the status of political, economic and social subordination of women, [3] affecting their autonomy--which is made up of capabilities and conditions to freely make decisions that have an impact on their lives-- [4] and that cause disparities in health results, worse economic and social consequences of poor health, and health systems with ineffective resolving power [5]. As one of the most influential social determinants of health, attaining gender equity has been recognized as a development goal [6].

Unpaid care work, defined as the service of health maintenance, well-being and the protection of family and community members, [7] is an activity that is determined by gender, with more women devoting time to it than men [8]. In spite of the huge contribution to unpaid care work to producing health and sustainable development of communities, the lack of recognition, valuation and support to those who are devoted to these tasks, has made women more vulnerable to physical and mental health problems [5] .

Additionally, systematic reviews and meta-analyses have confirmed that the unpaid care is related to higher levels of stress hormones and worse response of antibodies, greater prevalence of behavioural risk factors for chronic diseases, such as unhealthy diets and sedentary lifestyles and greater use of health services compared to subjects that do not provide these services [9-10]. Moreover, a longitudinal study showed that unpaid caregivers end up being poorer and less happy and healthy than their non-caregiving counterparts [11].

Unpaid care work is costly. According to the Global Valuing the Invaluable Analysis, which measured the economic contribution of paid and unpaid work that women make to the health sector, unpaid care by women, after accounting for gender wage differentials and social security benefits, could be valued at 3.09% of the global gross domestic product [12], invisibly subsidizing the health sector because it is considered in national accounts [12].

Women's autonomy is more limited in low- and middle-income countries (LMICs) [13], devoting more hours to unpaid work than women in high income countries (HICs). This is due to the lower participation of men in LMICs in these tasks [8,12]. Additionally, it has been reported that the objective and subjective burden due to unpaid care work is greater in LMICs than in HICs, representing a decline for family economy, and being greater for female caregiver than for male caregivers.[14]

In spite of this scenario, literature syntheses on health outcomes of unpaid care work have included participants who come from HICs,[9-10] and have made comparisons between the sexes, confirming the worst outcomes for women. The only review carried out in developing countries focused on recipients of care for the chronically ill or disabled, and did not focus on the comparison between unpaid care workers and those who do not participate in these tasks [15].

Therefore, the specific contribution of unpaid care work in health in LMICs cannot be elucidated by the current status of the synthesis of evidence. Furthermore, considering the differences in health as a result of the sex of the caregiver may facilitate the comparison with the HICs and help define future intervention strategies in countries in which the limited autonomy of women could considerably affect their state of health.

OBJECTIVES
The objective of this systematic review is to evaluate the health outcomes associated with unpaid care work in LMICs, taking into account sex differences. This systematic review will aim to answer the following question:
  1. What are the health outcomes of unpaid care workers compared to those who do not perform unpaid care activities in LMICs?
  2. Do health outcomes of unpaid care workers from LMICs differ by sex?

METHODS AND ANALYSIS
The protocol of this systematic review followed the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRIMSA-P) checklist [16] and some of the recommendation of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group, which were adapted [17].

STUDY ELEGIBILITY CRITERIA
Participants
Individuals without distinction of age, sex, or ethnicity, living in LMICs.

Exposure
Provision of unpaid care to household or community members. For the purposes of this systematic review, unpaid care work was defined as the set of activities carried out for the development and well-being of the everyday life of members of the home or the community. Unpaid care work may involve the care of people who are: 1) affected by permanent health problems or condition of dependency; 2) children aged between 0 to 14; 3) healthy people aged between 15 to 65, who do not require special care or have symptoms clinically identifiable diseases; and, 4) adults over 65 years of age. This conceptualization has been used in time-use surveys in Chile[18].

Comparators
Individuals who do not provide unpaid care to household or community members. This may include subjects that do not qualify as unpaid caregivers according to a certain threshold of hours of unpaid care work provided, according to the study definition. Also, in the case of the longitudinal studies without a control group, it can refer to the subjects who acted as their own control, based on the change of the status of unpaid care provider.

Outcomes
The studies must include at least one of the following outcomes: physical and/or mental health problems, health-related quality of life, self-care behaviour or skills, and use of health services. These outcomes must use objective or self-reported measures.

Study design
Observational studies (e.g., case series, cross-sectional study, case control study, cohort studies). Additionally, systematic reviews and meta-analyses of observational studies will be included. Controlled trials will be excluded.

Context
General population or clinical samples LMICs, according to the World Bank income classification [19].

REPORT ELIGIBILITY CRITERIA
Completed studies with published results, in English or Spanish, from their inception until June 1, 2017, will be included. Study protocols will be excluded.

INFORMATION SOURCES
The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and Scientific Electronic Library Online (SciELO) Citation Index will be searched. Additionally, reference lists of included studies will be screened for relevant papers.

SEARCH STRATEGY
The search strategy is presented in a supplementary file. Terms related to exposure (e.g., "caregivers" and "unpaid"), outcomes (e.g. "State of health" and "self-care"), and contexts (e.g., "low and middle income countries") will be used. In addition, a series of terms will be used to exclude reports of studies according to their design (i.e., studies that assessed the effectiveness of interventions, or qualitative studies).

STUDY RECORDS
All study records will be imported into EndNote Web and duplicates will be removed. The study selection process will be carried out in two stages (screening of title/abstract, and full-text assessment of articles), with two reviewers independently, and in duplicate, determining inclusion/exclusion of study records based on previously specified criteria. If discrepancies arise during any stage, these will be solved by discussion and confirmed by a third reviewer. Finally, data from multiple records of the same study will be pieced together.
Data extraction will be carried out using a standardized sheet recommended by the Cochrane Handbook of Systematic Reviews of Interventions,[20] following the same reviewing process described above (two independent reviewers and a third to resolve any disagreements), with regular meetings held to verify the quality of the extracted data. The following data will be extracted from each study included in this review: (1) First author, year of publication, and country of origin; (2) Participants inclusion/exclusion criteria (age, sex, ethnicity, socio-economic status, and/or urban/rural residence) and setting (e.g. general population or clinical sample); (3) Exposure/comparison characteristics, including criteria for classification as unpaid care worker (e.g., number of hours), and type of care tasks provided; (4) Type of outcomes reported (i.e. clinical, patient-reported, or use of healthcare services), instruments, follow-up periods (in case of longitudinal studies), and main findings (with effect size,

confidence intervals, and statistical significance); (5) Type of study design.

OUTCOMES AND PRIORITISATION

Included studies must report any outcome of interest, and, in the case of longitudinal studies, baseline levels of these outcomes must be reported. Due to the inclusion of cross-sectional and longitudinal studies, no distinction based on follow-up periods will be made. The primary outcome will be mental and/or physical health problems of participants measured either objectively or by self-report of symptoms or illnesses. Secondary outcomes will be: (1) self-reported health-related quality of life; (2) self-care skills/behaviours; and (3) use of any healthcare services.

RISK OF BIAS - INDIVIDUAL STUDIES

To assess the risk of bias and confounding in the included studies, we will use the "Item Bank for Assessing Risk of Bias and Confounding for Observational Studies of Interventions or Exposure" developed by the Agency for Healthcare Research and Quality (AHRQ).[21]

This tool includes an assessment of thirteen sources of bias and confounding: variations across groups of the study in the inclusion/exclusion criteria, the recruitment strategies or the length of follow-up, inappropriate selection of the comparison group, failing to account for important variations in the execution of the study, outcome assessor not blinded to exposure status of participants, study measures of dubious validity and reliability or implemented inconsistently, impact of high or differential loss to follow-up not assessed, important outcomes or harms/adverse events not reported, study limitations hampers the credibility of the study, no documented attempts to balance the allocation between the groups, and important confounding variables not taken into account.[21]

The same procedure described above for the study selection and the data extraction will be employed to assess the risk of bias of the included studies, with two independent reviewers and a third to resolve any disagreements.

DATA SYNTHESIS

A qualitative synthesis of the included studies will be conducted to provide an overview of the differences in health outcomes among participants coming from LMICs, taking into account the study characteristics and risk of bias/confounding. Sex differences in health outcomes among unpaid caregivers living in these countries will also be explored. These results will be summarized using comparative tables recommended in the Cochrane Handbook for Systematic Reviews of Interventions.[20]

DISCUSSION

For over two decades, the United Nations have called on member states to include unpaid work in economic and vital statistics.[22-23] Today, in the Region of Latin America, a small number of countries have national time-use surveys, and very few have implemented a nation-wide system of care. This scenario is replicated in other regions of the developing world.[24] The protocol of a systematic review reported here echoes this reality and aims to contribute to the acknowledgment and valuation of unpaid care work in LMICs.

It is expected that the political and economic obstacles to overcome the unequal division of unpaid work, particularly in LMICs, will be expressed in a small number of studies that compare caregivers and non-caregivers, being these publications rather recent. Additionally, the socio-economic and geographical variety among the LMICs will help to understand how the exercise of care is related to other socio-cultural variables. The authors of this systematic review anticipate limitations due to the eligibility criteria and the sources of information used. By limiting publications to the English or Spanish languages, and the scope of studies published in other languages (for example, Chinese or Arabic), a geographical bias in favour of evidence from Latin America may have been introduced. This decision has been made considering the financial resources and the time set for this systematic review.

Again, for reasons of economy of resources for this systematic review, we have opted for the design of a search strategy that excludes terms related to experimental studies. In this regard, Cochrane Collaboration recognizes that the process of identifying non-random studies (NRS) in searches and their subsequent selection may be prone to biases due to lack of a predefined search strategy and to report highly heterogeneous characteristics of the study design, compared to the randomized clinical trials.[20] Finally, this systematic review was limited to the review of the evidence published in the databases mentioned in the subsection "Sources of Information." This will hinder the detection of selection biases because grey literature search will not be conducted, nor will the authors and authorities be contacted on the subject to identify additional sources, due to the previously mentioned reasons.

ETHICAL CONSIDERATIONS

As this study is a systematic review, there is no requirement for ethical review and approval.

DISSEMINATION

The results of this systematic review will be published in peer-reviewed journals covering topics such as: Gender and Health, and Health Inequalities.

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AUTHORS' CONTRIBUTIONS

IM is the guarantor of this systematic review and provides her expert opinion during the reviewing process; PM and ML made valuable input to the design of this systematic review, and will be in charge of the data extraction and risk of bias assessment under the supervision of IM. IM, PM, and ML will contribute equally to data synthesis. All authors edited, modified, and approved the final version of this manuscript.

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ROLE OF FUNDERS

The funding institution is not involved in any part of this study.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form. The authors have no competing interests to disclose.

APPENDIX

The search strategy is detailed as follow:

Cumulative Index to Nursing and Allied Health Literature (CINAHL)

1. ((MH "Caregivers") OR ((TI Care*) AND (TI Informal)) OR ((TI Care*) AND (TI Unpaid)))

2. ((MH "Caregiver Role Strain (NANDA)") OR (MH "Caregiver Well-Being (Iowa NOC)") OR (MH "Caregiver Stressors (Iowa NOC)") OR (MH "Caregiver Physical Health (Iowa NOC)") OR (MH "Caregiver Lifestyle Disruption (Iowa NOC)") OR (MH "Health Status+") OR (MH "Stress+") OR (MH "Psychological Well-Being") OR (MH "Perceived Health (Iowa NOC)+") OR (MH "Quality of Life+") OR (MH "Self Care+") (MH "Health Resource Utilization") OR (MH "Health Services Needs and Demand+") OR (MH "Behavioral and Mental Disorders+")

3. ((MH "Experimental Studies+") OR (MH "Random Assignment") OR (MH "Placebos") OR (TI Time Series Analysis) OR (AB Time Series Analysis) OR (TI Time Trend) OR (AB Time Trend) OR (TI Trend Analysis) OR (AB Trend Analysis) OR (TI Before After Stud*) OR (AB Before After Stud*) OR (TI Pretest Posttest) OR (AB Pretest Posttest) OR (TI Pre Test Post Test) OR (AB Pre Test Post Test) OR (TI Pre/Post Test) OR (AB Pre/Post Test) OR (MH "Quasi-Experimental Studies+"))

4. ((MH "Research Protocols") OR (TI Clinical Protocol) OR (AB Clinical Protocol) OR (TI Study Protocol) OR (AB Study Protocol))

5. ((MH "Qualitative Studies+") OR MH "Focus Groups") OR (TI Key Informant) OR (AB Key Informant))

6. ((TI Semi Structured) OR (AB Semi Structured) OR (TI Semistructured) OR (AB Semistructured) OR (TI Unstructured) OR (AB Unstructured) OR (TI Informal) OR (AB Informal) OR (TI In-Depth) OR (AB In-Depth) OR (TI Face-to-Face) OR (AB Face-to-Face) OR (TI Structured) OR (AB Structured) OR (TI Guide) OR (AB Guide))

7. ((MH "Interviews+") OR (TI Discussion) OR (AB Discussion))

8. ((MH "Low and Middle Income Countries") OR (MH "Central America+") OR (MH "Latin America") OR (MH "South America+") OR (MH "West Indies+") OR (MH "Asia, Central+") OR (MH "Asia, Southeastern+") OR (MH "Asia, Western+") OR (MH "China+") OR (MH "Macao") OR (MH "Mongolia") OR (MH "North Korea") OR (MH "Europe, Eastern") OR (MH "Indian Ocean Islands+") OR (MH "Melanesia+") OR (MH "Micronesia+") OR (MH "Polynesia+") OR (MH "Developing Countries") OR (TI low income countr*) OR (AB low income countr*) OR (TI middle income countr*) OR (AB middle income countr*) OR (TI low N3 middle N3 countr*) OR (AB low N3 middle N3 countr*) OR (TI lmic) OR (AB lmic) OR (TI lamic) OR (AB lamic) OR (TI lami) OR (AB lami) OR (TI lmi) OR (AB lmi))

9. S1 AND S2

10. S3 OR S4 OR S5

11. S6 AND S7

12. S10 OR S11

13. S9 NOT S12
14. Limiters – Has Abstract
15. ((LA English) OR (LA Spanish))
16. S8 AND S13 AND S14 AND S15

PubMed

1. (Caregivers[Mesh] OR (Informal[Title/Abstract] n3 Care*) OR (Unpaid[Title/Abstract] n3 Care*))
2. (Stress, Psychological[Mesh] OR Stress, Physiological[Mesh] OR Health Status[Mesh] OR Health Lifestyle[Mesh] OR Self Care[Mesh] OR Quality of Life[Mesh] OR Health Resources/utilization[Mesh] OR Health Services/utilization[Mesh] OR Mental Disorders[Mesh] OR "Physical Health"[Title/Abstract] OR Well-Being[Title/Abstract])
3. (Clinical Trial[Publication Type] OR Clinical Trials as Topic[Mesh] OR Random Allocation[Mesh] OR Placebos[Mesh] OR Control Groups[Mesh] OR Meta-Analysis[Publication Type] OR Systematic Review[Title/Abstract] OR Quasi-Random*[Title/Abstract] OR Interrupted Time Series Analysis[Mesh] OR Time Series[Title/Abstract] OR Time Trend[Title/Abstract] OR Trend Analysis[Title/Abstract]) OR Controlled Before-After Studies[Mesh] OR Before After Study[Title/Abstract] OR pretest posttest[Title/Abstract] OR pre test post test[Title/Abstract] OR pre/post-test[Title/Abstract] OR Quasi-experiment*[Title/Abstract])
4. (Clinical Protocol[Mesh] OR Study Protocol[Title])
5. (Qualitative Research[Mesh] OR Focus Groups[Mesh] OR Ethnograph*[Title/Abstract] OR Key Informant[Title/Abstract])
6. (Semi-Structured[Title/Abstract] OR Semistructured[Title/Abstract] OR Unstructured[Title/Abstract] OR Informal[Title/Abstract] OR In-Depth[Title/Abstract] OR Face-to-Face[Title/Abstract] OR Structured[Title/Abstract] OR Guide[Title/Abstract])
7. (Interview*[Title/Abstract] OR Discussion*[Title/Abstract])
8. (Developing Countries[Mesh] OR Africa[Mesh] OR Caribbean Region[Mesh] OR Central America[Mesh] OR Latin America[Mesh] OR South America[Mesh] OR Asia, Central[Mesh] OR Asia, Northern[Mesh] OR Asia, Southeastern[Mesh] OR Asia, Western[Mesh] OR China[Mesh] OR Democratic People's Republic of Korea[Mesh] OR Mongolia[Mesh] OR Europe, Eastern[Mesh] OR Melanesia[Mesh] OR Micronesia[Mesh] OR Polynesia[Mesh] OR Low Income Countr*[Title/Abstract] OR Middle Income Countr*[Title/Abstract] OR (Low Middle Income) OR LMIC[Title/Abstract] OR LAMIC[Title/Abstract] OR LAMI[Title/Abstract] OR LMI[Title/Abstract])
9. #1 AND #2
10. #3 OR #4 OR #5
11. #6 AND #7
12. #10 OR #11
13. #9 NOT #12
14. (hasabstract[text])
15. (English[lang] OR Spanish[lang])
16. #8 AND #13 AND #14 AND #15

Scientific Electronic Library Online (SciELO) Citation Index

1. TS=("caregiver*")
2. TS=("care*") AND TS=("unpaid")
3. TS=("care*") AND TS=("unpaid")
4. #1 OR #2 OR #3
5. TS=("stress*") OR TS=("strain") OR TS=("health status") OR TS=("quality of life") OR TS=("lifestyle") OR TS=("self care") OR TS=("well-being") OR TS=("mental health") OR TS=(mental NEAR/1 disorder)
6. TS=("health*") AND TS=("service*") AND TS=("use")
7. TS=("health*") AND TS=("service*") AND TS=("utilization")
8. #5 OR #6 OR #7
9. TS=(intervention NEAR/0 stud*) OR TS=(experiment*) OR TS=("clinical trial*") OR TS=("controlled trial") OR TS=(random*) OR TS=(allocat*) OR TS=(placebo*) OR TS=("control group*") OR TS=(metaanalysis) OR TS=("meta analysis") OR TS=(systematic NEAR/0 review*) OR TS=(quasi NEAR/0 random*) OR TS=("time series") OR TS=("time trend") OR TS=("trend analysis") OR TS=("before after") OR TS=("before and after") OR TS=("pretest posttest") OR TS=("pre test post test") OR TS=("pre post test") OR TS=(quasi NEAR/0 experiment*)
10. TS=("clinical protocol") OR TI=("study protocol")
11. TS=(qualitative NEAR/2 (research* OR method* OR technique* OR inquir*)) OR TS=("focus group*") OR TS=(hermeneutic*) OR TS=(ethnograph*) OR TS=("key informant*")
12. TS=("semi structured") OR TS=(unstructured) OR TS=(unpaid) OR TS=("in depth") OR TS=("face to face") OR TS=(structured) OR TS=(guide)
13. TS=(interview*) OR TS=(discussion*)
14. TS=("Developing Countries") OR TS=("Africa") OR TS=("Caribbean Region") OR TS=("Central America") OR TS=("Latin America") OR TS=("South America") OR TS=("Asia, Central") OR TS=("Asia, Northern") OR TS=("Asia, Southeastern") OR TS=("Asia, Western") OR TS=("China") OR TS=("Eastern Europe") OR TS=("Mongolia") OR TS=("Democratic People's Republic of Korea") OR TS=("Melanesia") OR TS=("Micronesia") OR TS=("Polynesia") OR TS=((low OR middle) NEAR/3 income NEAR/2 countr*) OR TS=("low income") OR TS=("middle income") OR TS=(lmic OR lamic OR lami OR lmi)
15. #4 AND #8
16. #9 OR #10 OR #11
17. #12 AND #13
18. #16 OR #17
19. #15 NOT #18
20. #19 AND LANGUAGE:(English OR Spanish)
21. #14 AND #20

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	2-3
Support:			
Sources	5a	Indicate sources of financial or other support for the review	10
Sponsor	5b	Provide name for the review funder and/or sponsor	10
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	10
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6

Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6 & Supplementary File
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	n/a
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	n/a
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	n/a
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.