

REVIEW

Health outcomes of unpaid caregivers in low- and middle-income countries: A systematic review and meta-analysis

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Abstract

Aims and objectives: To explore differences in health outcomes between unpaid caregivers and noncaregivers living in low- and middle-income countries (LMICs).

Background: Previous meta-analyses found worse health outcomes for unpaid caregivers in high-income nations. However, no meta-analysis has considered unpaid caregivers from LMICs. A systematic integration of this topic may contribute to nursing care for unpaid caregivers in LMICs.

Design: Systematic review and meta-analysis of observational studies.

Methods: Following PRISMA statement, studies were searched for using the CINAHL, PubMed and SciELO databases, limited to publications until 31 December 2019. Random- and fixed-effects meta-analyses were used for data synthesis.

Results: Fourteen studies from Africa, Asia and South America were included. Unpaid caregivers of people with ill-health were more anxious and depressed than noncaregivers. Studies conducted in Asia and South America reported poorer health outcomes for unpaid caregivers than noncaregivers, whereas the trend for African studies was the opposite. Unpaid caregivers of healthy individuals may have better health status than noncaregivers, particularly those caring between 1–14 hr per week. Of the six studies which examined gender differences, two studies informed worse health outcomes for women, one presented the opposite effect, and three found no differences.

Conclusions: Individual, social, cultural and systemic factors play an important role in the health outcomes of unpaid caregivers in LMICs. More evidence is needed from LMICs. As unpaid caregivers are predominantly female, urgent attention to the health outcomes of female unpaid caregivers is required.

Relevance to clinical practice: The management of mental health problems, particularly anxiety and depression, should be an integral part of nursing care for unpaid caregivers living in LMICs. To further promote the health of unpaid caregivers in developing countries, stakeholders should consider launching educational campaigns that assist caregivers in finding ways to meet their cultural obligations while also reinforcing caregiver self-care.

KEYWORDS

gender, health outcomes, low- and middle-income countries, meta-analysis, systematic review, unpaid care

1 | INTRODUCTION

Caregiving, as defined by Ferrant, Pesando, and Nowacka (2014), is not exclusively associated with activities directly linked to health—for example caring for sick or disabled individuals—as it also involves all tasks and activities necessary for the maintenance, protection, and well-being of family members or the larger community. Observational studies and meta-analyses on the long-term consequences of these activities have confirmed that unpaid caregiving is associated with indicators of poorer physical health, higher prevalence of behavioural risk factors for chronic diseases, higher risk of mental health problems, increased use of health services and poorer living standards, compared to noncaregivers (Carmichael & Ercolani, 2016; Hirst, 2005; O'Reilly, Connolly, Rosato, & Patterson, 2008; Vitaliano, Scanlan, & Zhang, 2003).

The indivisible links between gender, health and sustainable development demand acknowledging and valuing unpaid care, which has become a challenge for public policy, and its consequences must be studied (United Nations General Assembly, 2015). In this line, it is particularly important to note that women spend between 2–10 times more time than men on unpaid care work (Ferrant et al., 2014), and their often-overlooked contributions to the health sector have been estimated to account for 3.1% of the global gross domestic product (Langer et al., 2015). Two meta-analyses have also reported that a greater caregiving burden and a lack of perceived social support make female unpaid caregivers more vulnerable to physical and mental health problems (Pinquart & Sörensen, 2006; Vitaliano et al., 2003). Likewise, gender inequality in unpaid caregiving has been demonstrated to be strongly related to social norms and institutions that are discriminatory towards women (for instance, restrictions and control over women's bodies, or biases that favour male children and devalue female children) and which restrict women's societal roles to reproductive and domestic functions (Ferrant et al., 2014).

Despite the heavier caregiver burden placed upon women living in low- and middle-income countries (LMICs) (Shahly et al., 2013), most studies are based in high-income nations. Caregiving activities may entail even higher costs to physical and/or mental health for female unpaid caregivers living in LMICs and may demand even greater time investments, compared to those affecting female caregivers in more developed economies. In Ghana, for example, the task of a physically demanding and time-consuming activity such as fetching water falls principally upon women (Ferrant et al., 2014). Moreover, when caring for sick individuals, men enjoy greater autonomy and social support than women in LMICs (Casale & Gibbs, 2015), an inequity further compounded by the lack of accessible, affordable and acceptable formal support services for caregivers (Fang et al., 2015; Hojman et al., 2017).

Although previous meta-analyses have compared the health of unpaid caregivers and noncaregivers (Pinquart & Sörensen, 2003; Vitaliano et al., 2003), most of the literature included in these studies came from high-income countries. Additionally, the only published narrative synthesis concerning the health of unpaid caregivers in developing nations did not include a comparison group of

What does this paper contribute to the wider global clinical community?

- The management of anxiety and depression in unpaid caregivers in low- and middle-income countries should be paramount in nursing practice.
- Reinforcing self-care behaviours in unpaid caregivers from developing nations should consider cultural obligations towards caregiving.
- More research on unpaid caregiving in low- and middle-income countries is needed, particularly regarding gender differences in health outcomes.

noncaregivers (Thrush & Hyder, 2014), so it is unclear whether unpaid caregivers living in these countries experience positive (or negative) health outcomes compared to noncaregivers. Furthermore, that literature review did not explore differences in the health outcomes of male and female caregivers, understating that unpaid caregivers are predominantly female.

Finally, interventions directed to unpaid caregivers should address not only psychological issues but also include physical health promotion and prevention (Pinquart & Sörensen, 2007). The multiple needs of this vulnerable group demand a holistic and bio-psycho-social approach to health, which might be well suited for the nursing profession, for example (All-Party Parliamentary Group on Global Health [APPG], 2016). Because nurses play a pivotal role in universal health coverage globally, especially in developing countries where in some settings nurses could be the only available health professionals, a systematic, meta-analytical examination of the health outcomes of unpaid caregivers in LMICs may inform nursing care in these settings.

2 | AIMS

The principal objective of this systematic review and meta-analysis was to explore differences in health outcomes between unpaid caregivers and noncaregivers living in low- and middle-income countries. Additionally, a secondary aim sought to explore gender differences in health outcomes among unpaid caregivers.

3 | METHODS

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses (File S1)) statement (Liberati et al., 2009) and recommendations adapted from the MOOSE group (Meta-analysis Of Observational Studies in Epidemiology) (Stroup et al., 2000) were used to structure this systematic review and meta-analysis.

As this study only involves data analysis of already published material, ethical approval was not required.

3.1 | Protocol and registration

The prospective registration of this systematic review was published in PROSPERO (International Prospective Register of Systematic Reviews) on 7 August 2017, under registration number CRD42017071785. Protocol amendments were made to include the use of meta-analytic techniques and to update the search criteria. The rationale for the incorporation of the meta-analysis component is explained in the data synthesis subsection of this article.

3.2 | Eligibility criteria

Briefly, nonrandomised observational studies conducted in LMICs were included. These studies must have compared unpaid caregivers and noncaregivers, in terms of their physical and/or mental health outcomes, health status, self-care behaviours and/or health services utilisation patterns. A detailed examination of eligibility criteria is described in Table 1.

3.3 | Information sources

The literature review was carried out using the CINAHL, PubMed and SciELO Citation Index databases. Additional studies were identified by checking the reference section of included articles.

3.4 | Search strategy

Search strategies are shown in the File S3. The basic search strategy combined the following free-text terms: unpaid care, health status, and low- and middle-income countries. Variations of free-text terms were specified to exclude the following study designs: experimental studies, qualitative studies and study protocols.

3.5 | Study selection and data collection process

The articles resulting from the search were managed using EndNote Web, and duplicates were removed, PM and MSL selected the articles and extracted data independently and in duplicate. Discrepancies were resolved by involving a third reviewer (IM).

3.6 | Data items

Each study was identified by the last name of the first author, the date of publication and the country of origin. Data were extracted according to PICOS criteria. Special attention was paid to how studies defined unpaid caregivers and noncaregivers (e.g., by specifying a certain number of hours, months or years of unpaid care to qualify as an unpaid caregiver).

TABLE 1 Study and report eligibility criteria

Study characteristic	Criteria
Participants	Individuals without distinction of age group, sex or ethnicity, living in LMICs (according to the World Bank income classification ^a) recruited from community or clinical samples.
Exposures	The exposed individuals were those who provided unpaid care in the home or in the community, to: (a) people affected by health problems or conditions of dependency, and (b) people who require no special care and have no obvious symptoms of disease, including activities that are related to and/or promote health, and are of potential interest to public health (e.g., cleaning or cooking) (Langer et al., 2015).
Comparators	The nonexposed individuals (non-CGs) were those who did not provide unpaid care to household or community members.
Outcomes	The main outcomes of interest for this systematic review were as follows: (a) physical diseases or manifestation (signs and symptoms) in the participants, registered either objectively (e.g., laboratory tests and physical examination) or by self-report, and (b) mental disorders or symptoms in the participants, registered by self-report (through the use of validated questionnaires), or through observer-rated or clinician-rated assessment (e.g., clinical interview). The following secondary outcome measures must have been assessed through valid self-report, observer-rated or clinician-rated assessments: (a) health status, quality of life or health-related quality of life; (b) self-care behaviours/skills; and (c) healthcare service utilisation. To be included, studies had to report any of these outcomes.
Study design	Nonrandomised observational studies to evaluate the effect of an exposure. Randomised and nonrandomised studies designed to evaluate the effect of an intervention were excluded.
Report characteristic	Criteria
Status	Published papers. Study protocols and grey literature were excluded.
Language	English or Spanish.
Date	From database inception to 31 December 2019.

^aThe full list of low- and middle-income countries by per capita gross national income is provided in the File S2.

3.7 | Risk of bias assessment

The Item Bank for Assessing Risk of Bias and Confounding for Observational Studies of Interventions or Exposures (RTI Item Bank) was used to evaluate the evaluated studies' risk of bias and confounding (Viswanathan, Berkman, Dryden, & Hartling, 2013). In this context, risk of bias is assessed by evaluating the probability that the true exposure effect was overestimated or underestimated in a given study (Higgins & Green, 2011). In particular, the following RTI Item Bank criteria were selected (with their respective number in parenthesis): "eligibility criteria" (no. 1), "recruitment strategies" (no. 2) and "comparison groups" (no. 3) for selection bias; "study measurements" (no. 6) for measurement bias; "selective outcomes reporting" (no. 9) and "selective harms reporting" (no. 10) for reporting bias; and "balanced allocation" (no. 12) and "confounding and adjustment" (no. 13) for confounding bias. Additionally, an assessment of the "overall study quality" (no. 11) was included (Viswanathan et al., 2013). Risk of bias was rated as "high," "low" or "unclear" for each criterion. PM and MSL, independently and in duplicate, were responsible for the assessment of risk of bias, with the assistance of IM.

3.8 | Data synthesis

The included studies' characteristic, findings and risk of bias assessments were synthesised and accompanied by comparative tables and a forest plot (i.e., the graphical display of the estimated effect and confidence interval for each study) to facilitate interpretation of the results.

Meta-analytic techniques were incorporated into this systematic review—which required updating the original protocol—because the statistical synthesis of outcomes permitted the objective evaluation of conflicting results found in primary studies (Higgins & Green, 2011).

To proceed with the statistical synthesis, data were converted into a suitable format (e.g., computation of standard deviations based on *p*-values). If a study reported multiple groups of unpaid caregivers of individuals with closely related diseases (e.g., type 1 and type 2 diabetes), they were treated as a single group of unpaid caregivers. Similarly, if studies reported missing data without disaggregation by study group, it was assumed that missing values were equally divided between unpaid caregivers and noncaregivers. Standardised mean differences (Cohen's *d*) were calculated to measure effect size for studies reporting continuous outcomes, to facilitate inter-study comparisons. Based on Cohen's threshold levels, the magnitude of the effect size may be interpreted, as small ($d = 0.2$), medium ($d = 0.5$) and large ($d = 0.8$) (Cohen, 1988). As for studies reporting dichotomous outcomes, odds ratio (OR) was chosen to measure effect size, and it can be interpreted as small ($OR = >1.5$), medium ($OR = >3.0$) and large ($OR > 5.0$), according to Chen, Cohen and Chen (2010).

To control for sources of clinical and methodological diversity, statistical syntheses only considered studies that included unpaid caregivers of individuals with health problems in cross-sectional studies (by far, the most used study design). For the rest of studies, a narrative synthesis was conducted, and their respective effect size measures (and confidence intervals) were presented. Heterogeneity was evaluated with I^2 (i.e., "the percentage of total variation across studies that is due to heterogeneity rather than chance"; Higgins, Thompson, Deeks, & Altman, 2003, p. 558), setting a $\geq 75\%$ cut-off for considerable heterogeneity (Higgins & Green, 2011), for which case sensitivity analyses were conducted. If unexplained and considerable statistical variations were detected, a narrative synthesis was undertaken.

In accordance with the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2011), the statistical synthesis prioritised the inclusion of adjusted estimates, which is how the results were presented in the primary studies examined. Nevertheless, studies that only reported crude estimates (or those with a "high" risk of bias) were not excluded from these analyses, though these scenarios were explored through sensitivity analyses. Fixed-effects, inverse-variance-weighted meta-analyses were conducted within a study if the study reported various indicators for the same type of outcome. Random-effects meta-analysis were conducted using the inverse-variance weighting method to combine effect size measures across studies and reporting Cohen's *d* (for continuous data) or odds ratios (for dichotomous data) with their respective confidence intervals set at 95% (95% CI) (Higgins & Green, 2011). The use of the inverse-variance approach allowed for the adjustment of study weights accounting for between-study heterogeneity (Higgins & Green, 2011). Exploration of the forest plot was carried out to identify possible sources of heterogeneity (e.g., geographical location of the studies), by performing further subgroup analyses. Statistical analyses were conducted using RevMan v5.3 (2014).

4 | RESULTS

4.1 | Study selection

As shown in Figure 1, after reviewing 1,538 unique studies on the basis of the selection criteria, 14 studies were included in the systematic review (Arango-Lasprilla et al., 2010; Awadalla, Ohaeri, Al-Awadi, & Tawfiq, 2006; Awadalla, Ohaeri, Salih, & Tawfiq, 2005; Chen & Liu, 2012; de Lima, Santos, Sawada, & de Lima, 2014; Koyagani et al., 2018; Laks, Goren, Dueñas, Novick, & Kahle-Wroblecki, 2016; Mugisha et al., 2013; Ohaeri, Awadalla, & Farah, 2009; Posner et al., 2015; Rej, Tennyson, Lee, & Eisenberg, 2019; Zhang, Xiong, Huijken, Zhang, & Zhang, 2013; Zhang, Yao, Yang, & Zhou, 2014; Zhou, Mao, Lee, & Chi, 2016) and 11 studies in the meta-analysis (Arango-Lasprilla et al., 2010; Awadalla et al., 2006; Awadalla et al., 2005; de Lima et al., 2014; Koyagani et al., 2018; Laks et al., 2016; Mugisha et al., 2013; Ohaeri et al., 2009; Posner et al., 2015; Zhang et al., 2013; Zhang et al., 2014).

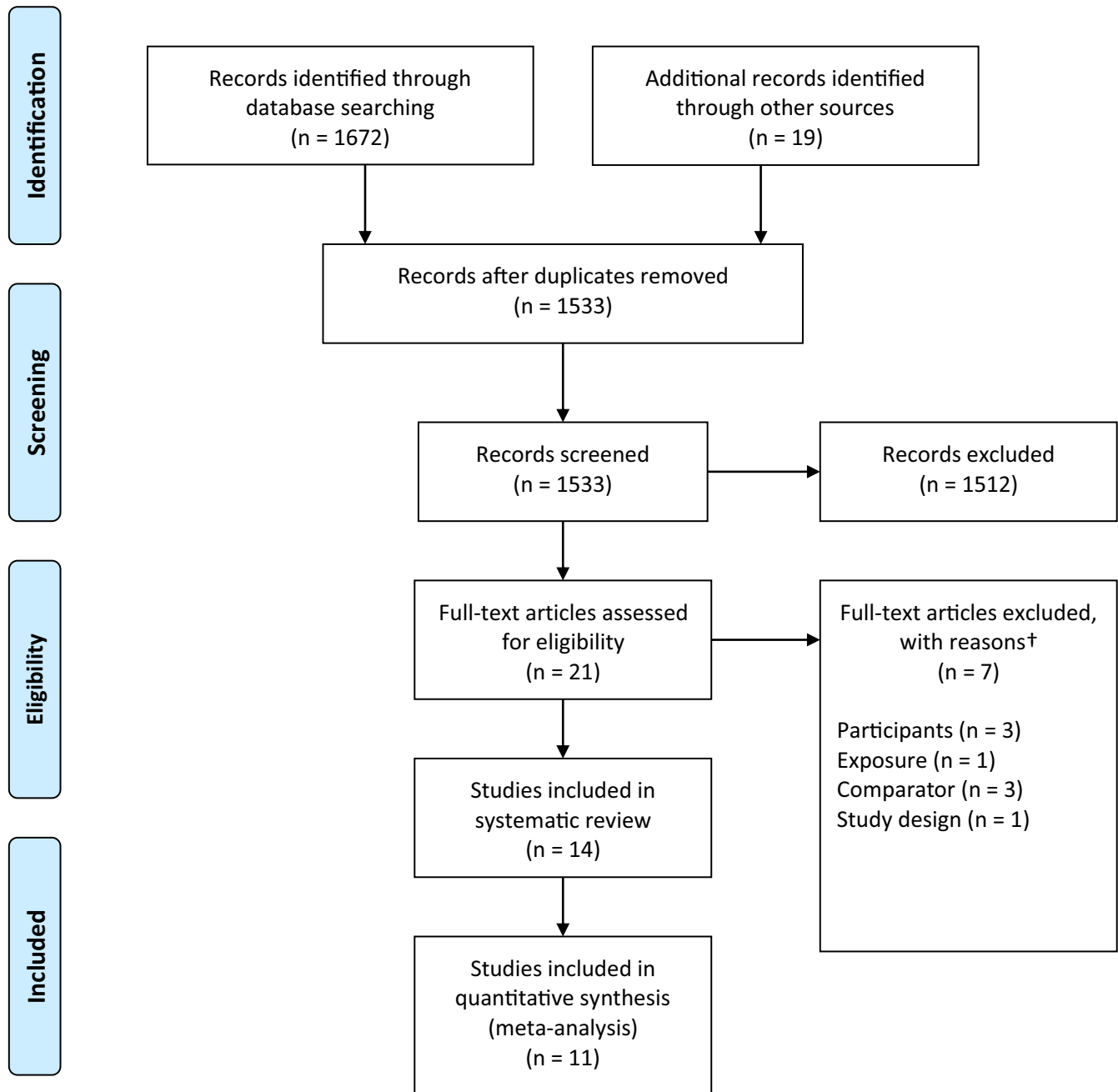


FIGURE 1 PRISMA flow diagram. †There may be more than one reason for excluding an article [Colour figure can be viewed at wileyonlinelibrary.com]

4.2 | Study characteristics

The characteristics of the included studies are presented in Table 2. The studies came from Africa (Awadalla et al., 2006; Awadalla et al., 2005; Koyagani et al., 2018; Mugisha et al., 2013; Ohaeri et al., 2009), Asia (Chen & Liu, 2012; Koyagani et al., 2018; Rej et al., 2019; Zhang et al., 2013, 2014; Zhou et al., 2016) and South America (Arango-Lasprilla et al., 2010; de Lima et al., 2014; Laks et al., 2016; Posner et al., 2015). Because Koyagani et al. (2018) classified as middle-income countries some nations that are classified as high-income countries according to the country classification

criteria used in this systematic review (e.g., Czech Republic), only data from low-income countries were considered for this specific study.

Eleven studies were cross-sectional in design (Arango-Lasprilla et al., 2010; Awadalla et al., 2006; Awadalla et al., 2005; de Lima et al., 2014; Koyagani et al., 2018; Laks et al., 2016; Mugisha et al., 2013; Ohaeri et al., 2009; Posner et al., 2015; Zhang et al., 2013, 2014), and three were cohort studies (Chen & Liu, 2012; Rej et al., 2019; Zhou et al., 2016).

The studies included in this systematic review represented a total of 124,268 individuals, with a mean weighted (according to

TABLE 2 Characteristics of included studies

Study, year (country)	Gender (% of women)	Exposed	Comparators	Outcomes ^a (instruments)	Study design
Arango-Lasprilla et al., 2010 (COL)	81.8% in exposed, 41.0% in comparators	99 family caregivers responsible for daily care (for at least 6 months) for individuals with dementia, with no history of neuro-psychiatric disorders	95 healthy noncaregivers of the general population	HRQoL (SF-36)	Cross-sectional
Awadalla, 2005 (SUD)	50.0% in exposed, 42.2% in comparators	300 family caregivers who provide more hours of daily care for psychiatric outpatients (diagnosed 1 or more years ago)	211 noncaregivers of the general population	QoL (WHOQOL-Bref)	Cross-sectional
Awadalla, 2006 (SUD)	61.0% in exposed, 37.4% in comparators	240 family caregivers who assist diabetes mellitus outpatients (diagnosed at least 1 year ago) with ADLs and treatment adherence	139 healthy noncaregivers of the general population, living in the same areas as the caregivers	QoL (WHOQOL-Bref)	Cross-sectional
Chen, 2012 (CHN)	53.0% in the whole sample	1,196 older adults (55+ years) living with and caring for grandchildren who are 6 years or younger ^b	1,645 older adults (55+ years) living with and not caring for grandchildren who are 6 years or younger	HS (CHNS-SRHM)	Cohort
de Lima, 2014 (BRA)	70.0% in exposed, not reported in comparators	44 unpaid caregivers of primary care patients affected by stroke for at least 3 months	83 noncaregivers, primary care patients, without stroke or severe comorbidities, living in the same areas as the caregivers	QoL (WHOQOL-Bref)	Cross-sectional
Koyanagi, 2018 (LICs) ^c	48.3% in exposed, 49.7% in comparators	19,440 friend/family caregivers (18+ years) of a person with a long-term condition or disability, or frailty	85,845 noncaregivers (18+ years) of the general population	Depression (DSM-IV), sleep problems (WHS), perceived stress (PSS)	Cross-sectional
Laks, 2015 (BRA)	53.1% in exposed, 49.7% in comparators	209 family caregivers (18+ years) of patients with Alzheimer's disease or dementia	10,644 noncaregivers (18+ years) of the general population	Comorbidities (CCI), depression (PHQ-9), PI (WPAI), HRQoL (SF-36), health service utilisation	Cross-sectional
Mugisha, 2013 (UGA)	65.8% in exposed, 47.7% in comparators	380 community/family caregivers (50+ years), with or without HIV (with or without antiretroviral therapy)	130 noncaregivers (50+ years), with or without HIV (with or without antiretroviral therapy), living in the same areas as the caregivers	HS (SAGE), grip strength, BMI, and caregiver burden ^d	Cross-sectional
Ohaeri, 2009 (SUD)	53.7% in exposed, 52.8% in comparators	257 family caregivers responsible for daily care for individuals with epilepsy in outpatient care (diagnosed at least 1 year ago)	248 noncaregivers of the general population	QoL (WHOQOL-Bref)	Cross-sectional
Posner, 2015 (COL)	64.4% in exposed, 58.8% in comparators	90 family caregivers responsible for daily care (for at least 3 months) for individuals with dementia in outpatient care, with no history of neuro-psychiatric disorders	51 healthy noncaregivers, with no history of neuro-psychiatric disorders, living in the same areas as the caregivers	Depression (PHQ-9), and HRQoL (SF-36)	Cross-sectional
Rej, 2019 (PHL)	58.2% in exposed, 47.3% in comparators	182 primary caregivers (for at least 1 year) of any household member with chronic illness/disability	1,051 noncaregivers living in the same metropolitan area as the caregivers	Telomere length	Cohort

(Continues)

TABLE 2 (Continued)

Study, year (country)	Gender (% of women)	Exposed	Comparators	Outcomes ^a (instruments)	Study design
Zhang, 2013 (CHN)	72.4% in exposed, 75.8% in comparators	58 family caregivers for inpatients with Alzheimer's disease and vascular dementia	58 noncaregivers	Psychological distress (SCL-90)	Cross-sectional
Zhang, 2014 (CHN)	51.8% in exposed, 50.0% in comparators	300 spousal caregivers of cancer inpatients, with no history of mental illness or chronic disease	600 healthy noncaregivers of the general population, with no history of mental illness, living in the same areas as the caregivers	Psychological distress (SCL-90), fatigue (FS-14)	Cross-sectional
Zhou, 2016 (CHN)	62.8% in exposed, 61.1% in comparators	465 older adults (60+ years) caring for their grandchildren younger than 16 years of age ^e	334 older adults (60+ years), noncaregivers, living in the same areas as the caregivers	HS (CHNS-SRHM), ADLs and IADLs	Cohort

Abbreviations: COL, Colombia; SUD, Sudan; CHN, China; BRA, Brazil; LICs, low-income countries; UGA, Uganda; PHL, Philippines; ADLs, Activities of daily living; HIV, human immunodeficiency virus; HRQoL, Health-related quality of life; SF-36, Short Form 36 Health Survey; QoL, quality of life; CHNS-SRHM, China Health and Nutrition Survey self-reported health measure; WHOQOL-Bref, World Health Organization 26-item Quality of Life Instrument; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; WHS, World Health Survey; PSS, Perceived Stress Scale; CCI, Charlson comorbidity index; PHQ-9, Patient Health Questionnaire 9 item; PI, productivity impairment; WPAL, Work Productivity and Activity Impairment questionnaire; SAGE, adapted version of 16 questions of a module of the SAGE (Study on global ageing and adult health questionnaire), SCL-90, The Symptom Checklist-90; BMI: Body Mass Index; FS-14:14-item Fatigue Scale; IADLs: Instrumental Activities of Daily Living.

^aOutcomes of interest for this systematic review, as reported in each study.

^bCaregiving load for exposed group was operationalised as: (a) high intensity (15 or more caregiving hours per week) and (b) low intensity (1–14 caregiving hours per week). Total sample size reported for the study (N = 14,954), noting that caregiving status was assessed in older adults living in households with the presence of children aged 0–6 (about 19% of the total sample), with approximately 8% being exposed to caregiving, and 11% being nonexposed.

^cOnly data for low-income countries were considered.

^dAssessed caregiver burden as a composite measure, including difficulties related to own self-care.

^eOlder adults in exposed group were categorised into two groups: (a) repeated caregivers (n = 226), who were current caregivers at baseline (year 2009) and follow-up (year 2012) time points; and (b) previous caregivers (n = 239), who took care of their grandchildren at baseline but not at follow-up.

study size) age of 38.0 years and a mean age which ranged from 35.0–70.9 years old. The completion rates of secondary education varied from 26.8%–88.0%. Unpaid caregivers were mostly women recruited from communities or hospitals in urban areas, who provided daily care and in-home assistance to individuals with mostly mental, behavioural or neurodevelopmental disorders. Three studies included senior adult participants (Chen & Liu, 2012; Mugisha et al., 2013; Zhou et al., 2016), with two of them focusing on the unpaid care of minors (Chen & Liu, 2012; Zhou et al., 2016). Only one study defined a minimum criterion of weekly hours of care to qualify as an unpaid caregiver (1 hr) (Chen & Liu, 2012), and four studies stated a minimum number of months of care to be considered an unpaid caregiver (3–12 months) (Arango-Lasprilla et al., 2010; Laks et al., 2016; Posner et al., 2015; Zhou et al., 2016).

4.3 | Risk of bias assessment

The risk of bias summary is displayed in Figure 2. Four studies did not provide enough information to ensure comparability across the study groups, nor did they clearly describe their recruitment strategies, so their risk of bias was evaluated as “unclear” (Arango-Lasprilla et al., 2010; Awadalla et al., 2006; Awadalla et al., 2005; Zhang et al., 2013). The majority of included studies implemented consistently valid and reliable measures and were thus assigned a “low” risk of bias. “High” risk of bias was detected in one study due to selective outcome reporting of health-related quality of life data (i.e., insufficient detail for results to be included in meta-analysis) (Posner et al., 2015). Confounding risk of bias was “unclear” in one study, because the techniques used to balance the distribution of confounding variables were not specified (de Lima et al., 2014), and this risk was deemed to be “high” in two other studies, whose design or analysis did not consider any confounding variables (Zhang et al., 2013) or which failed to match a relevant variable that ended up unbalanced (Zhang et al., 2014). The rest of the studies reported adjusted estimates by gender, age, educational level, marital status, occupation, income and/or area of residence, among other variables. Additionally, one study demonstrated the balance between the selected groups by quota sampling (Ohaeri et al., 2009), while another used propensity score weighting (Chen & Liu, 2012). Finally, one longitudinal study controlled for baseline values of a set of nonspecified sociodemographic, health-related and social support variables (Zhou et al., 2016).

4.4 | Syntheses of results

In line with the aims of this systematic review, syntheses of study results are grouped in two broad categories: (a) comparisons of health outcomes of unpaid caregivers and noncaregivers living in LMICs and (b) gender differences in the health outcomes of unpaid caregivers.

4.4.1 | Health outcomes of unpaid caregivers versus noncaregivers

Eleven of the 14 studies included in this systematic review made cross-sectional comparisons between unpaid caregivers of individuals with health problems (e.g., HIV, cancer or diabetes mellitus) and noncaregivers (Arango-Lasprilla et al., 2010; Awadalla et al., 2006; Awadalla et al., 2005; de Lima et al., 2014; Koyagani et al., 2018; Laks et al., 2016; Mugisha et al., 2013; Ohaeri et al., 2009; Posner et al., 2015; Zhang et al., 2013, 2014). This first subgroup of studies was synthesised together. The three remaining studies were cohort studies, of which two included unpaid caregivers of individuals without any apparent medical condition (Chen & Liu, 2012; Zhou et al., 2016), and another compared health outcomes of unpaid caregivers of chronically ill and disabled family members versus noncaregivers (Rej et al., 2019); their findings are presented in a narrative fashion under the heading health outcomes of unpaid caregiving in cohort studies.

Health outcomes of unpaid caregivers of individuals with health problems

These studies included unpaid caregivers of individuals with cancer, dementia, diabetes mellitus, epilepsy, HIV, mental disorders (e.g., schizophrenia) and stroke, as well as unpaid caregivers of individuals with long-term conditions, disabilities or frailty. These studies assessed mental health (i.e., anxiety and depression), physical health (physical diseases, such as diabetes mellitus, or signs of physical diseases, such as poor nutritional status), health-related quality of life (i.e., measures that mainly included subjective well-being in physical and mental health domains), quality of life (measures that included broader domains, not strictly related to health; for instance, spiritual well-being), health status and healthcare services utilisation in unpaid caregivers. Thus, the presentation of study results has been grouped by the types of health outcomes assessed. Additionally, as subgroup analyses revealed that the geographical location of the studies was a source of substantial heterogeneity, geographical trends are presented at the end of this first subsection.

Mental health. The synthesis of two studies that compared symptoms of anxiety between unpaid caregivers of hospitalised patients with dementia or cancer and noncaregivers (Zhang et al., 2013, 2014) found statistically significant differences between the two groups, with a small effect size indicating greater symptoms of anxiety in unpaid caregivers ($d = 0.33$, $p < .001$, $I^2 = 0\%$) (Figure 3). This estimation included studies with a “high” risk of bias in the “overall study quality” dimension.

Unpaid caregivers of patients hospitalised with cancer and individuals with dementia had greater depressive symptoms than noncaregivers (Laks et al., 2016; Posner et al., 2015; Zhang et al., 2013, 2014). These differences were statistically significant, with a small-to-medium effect size ($d = 0.39$, $p < .001$, $I^2 = 0\%$) (Figure 3). The exclusion of studies with a “high” risk of confounding bias did not substantially modify the effect size.

	Eligibility criteria (n°1)	Recruitment strategies (n°2)	Comparison groups (n°3)	Study measurement (n°6)	Selective outcomes reporting (n°9)	Selective harms reporting (n°10)	Balanced allocation (n°12)	Confounding and adjustment (n°13)	Overall study quality (n°11)
Arango-Lasprilla, 2010	?	?	?	+	+	+	+	+	?
Awadalla, 2005	?	?	?	+	+	+	+	+	?
Awadalla, 2006	?	+	?	+	+	+	+	+	?
Chen, 2012	+	+	+	+	+	+	+	+	+
de Lima, 2014	+	+	+	+	+	+	?	?	?
Koyanagi, 2018	+	+	+	+	+	+	+	+	+
Laks, 2015	+	+	+	+	+	+	+	+	+
Mugisha, 2013	+	+	+	+	+	+	+	+	+
Ohaeri, 2009	?	+	+	+	+	+	+	+	+
Posner, 2015	+	+	+	+	-	+	+	+	+
Rej, 2019	+	+	+	+	+	+	+	+	+
Zhang, 2013	?	?	?	+	+	+	-	-	-
Zhang, 2014	+	+	+	+	+	+	+	-	-
Zhou, 2016	+	+	+	+	+	+	+	+	+

FIGURE 2 Risk of bias summary. Notes. In each dimension, the number in brackets identifies the relevant item from the Item Bank for Assessing Risk of bias and confounding for Observational Studies of Interventions or Exposures; ●: "low" risk of bias; ●: "high" risk of bias; ?: "unclear" risk of bias [Colour figure can be viewed at wileyonlinelibrary.com]

In addition, a meta-analysis of two studies with a "low" risk of bias reported that unpaid caregivers of individuals with dementia or a disability present greater odds of being diagnosed with depression compared with noncaregivers (OR = 1.52, $p < .001$, $I^2 = 0\%$) (Figure 4).

Health-related quality of life. The considerable clinical variety of the studies assessing physical and mental health-related quality of life led to considerable heterogeneity ($I^2 = 93\%$ in both cases). Nonetheless, the interpretation of the pooled study results was greatly clarified after the studies were grouped according to the type of health condition of the care recipients. This analysis demonstrated that the unpaid caregivers

of patients with dementia, diabetes mellitus, and stroke reported worse physical ($d = -0.26$, $p < .001$, $I^2 = 44\%$) and mental ($d = -0.33$, $p = .006$, $I^2 = 76\%$) health-related quality of life than noncaregivers (Arango-Lasprilla et al., 2010; Awadalla et al., 2006; de Lima et al., 2014; Laks et al., 2016). On the other hand, the unpaid caregivers of patients with mental disorders and epilepsy showed better physical ($d = 0.44$, $p < .001$, $I^2 = 63\%$) and mental ($d = 0.37$, $p < .001$, $I^2 = 0\%$) health-related quality of life than noncaregivers (Awadalla et al., 2005; Ohaeri et al., 2009) (Figures 5 and 6). These estimates exhibited statistically significant differences, with small-to-mid effect sizes and heterogeneity within acceptable limits, and they included studies with "unclear" selection bias and confounding bias risk.

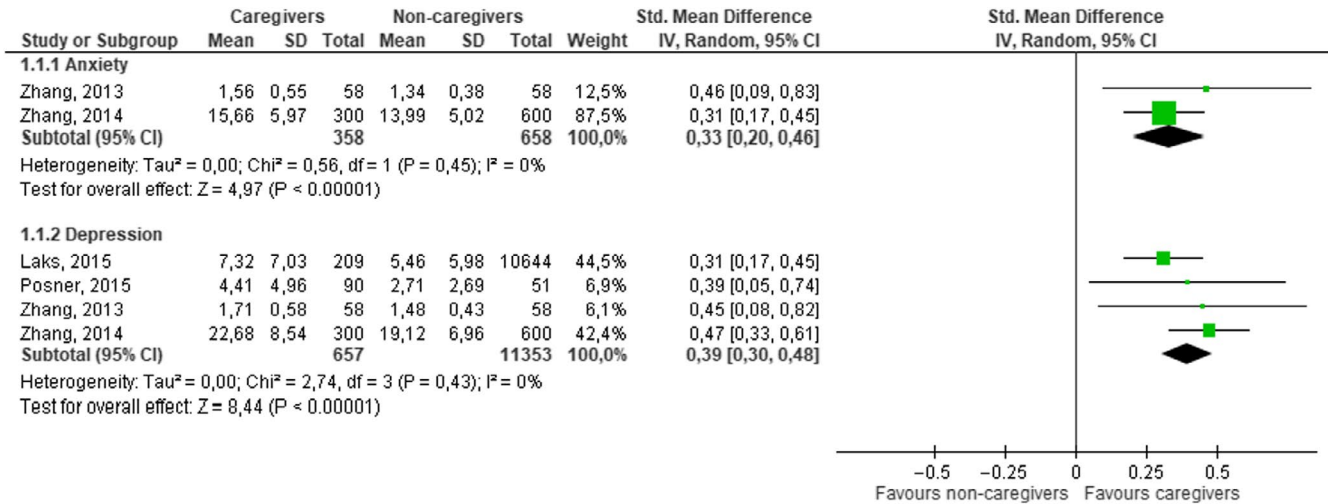


FIGURE 3 Forest plot for mental health outcomes in unpaid caregivers of individuals with health problems versus noncaregivers. Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation; Std., standardised [Colour figure can be viewed at wileyonlinelibrary.com]

Quality of life. As with the health-related quality of life analysis, grouping the studies by the type of health problem affecting the care recipients facilitated the synthesis of results in two studies that evaluated quality of life (Mugisha et al., 2013; Ohaeri et al., 2009). A significantly better quality of life was observed among unpaid caregivers of individuals with epilepsy or HIV receiving community-based treatment, in comparison to noncaregivers ($d = 0.42$, $p < .001$, $I^2 = 27\%$). However, the statistical synthesis of quality of life of unpaid caregivers of individuals with diabetes or stroke resulted in substantial statistical heterogeneity, which is why a narrative synthesis was carried out. The narrative synthesis determined that while unpaid caregivers of individuals affected by a stroke had a worse quality of life than noncaregivers ($d = -0.48$, $p = .01$) (de Lima et al., 2014), there were no statistically significant differences in quality of life of unpaid caregivers of individuals with diabetes compared to their counterparts ($d = -0.04$, $p = .73$) (Awadalla et al., 2006).

Health status. Health status was assessed in a single study on unpaid caregivers of people with HIV living in the community (Mugisha et al., 2013). The group of noncaregivers had statistically significant greater odds of being in the lowest health status quartile than unpaid caregivers (OR = 2.02, $p = .006$).

Healthcare services utilisation. The study by Laks et al. (2016) used different indicators to assess healthcare services utilisation (i.e., emergency room visits, hospitalisations and healthcare visits) in unpaid caregivers of people with dementia versus noncaregivers. A within-study meta-analysis found statistically significant differences, meaning that unpaid caregivers used health services more than noncaregivers ($d = 0.23$, $p < .001$) (Figure 7).

Geographical comparisons. There was a statistically significant subgroup effect ($p < .001$) for geographical areas (Africa, Asia and South America), meaning that the region where the studies were conducted statistically significantly modified the effect of unpaid caregiving. Studies conducted in Africa displayed statistically significant differences in favour of unpaid caregiving (i.e., unpaid caregivers had “better” health outcomes), though the effect size was small, and there was substantial heterogeneity ($d = 0.23$, $p = .010$, nine comparisons, $I^2 = 87\%$) (Awadalla et al., 2006; Awadalla et al., 2005; Mugisha et al., 2013; Ohaeri et al., 2009). The sole inclusion of studies with “low” risk of bias in the “overall study quality” dimension yielded a small-to-medium effect size, in the absence of heterogeneity ($d = 0.40$, $p < .001$, four comparisons, $I^2 = 0\%$) (Mugisha et al., 2013; Ohaeri et al., 2009). In the case of Asia, a small statistically significant effect size, which indicated poorer health outcomes for unpaid

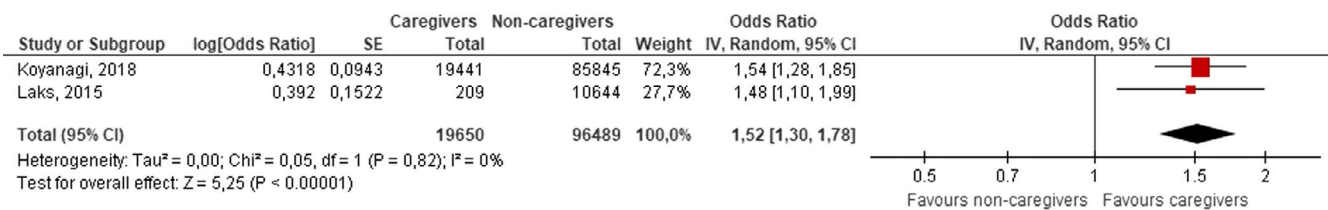


FIGURE 4 Forest plot of the association between unpaid caregiving for individuals with health problems and depression. Abbreviations: CI, confidence interval; IV, inverse variance; SE, standard error [Colour figure can be viewed at wileyonlinelibrary.com]

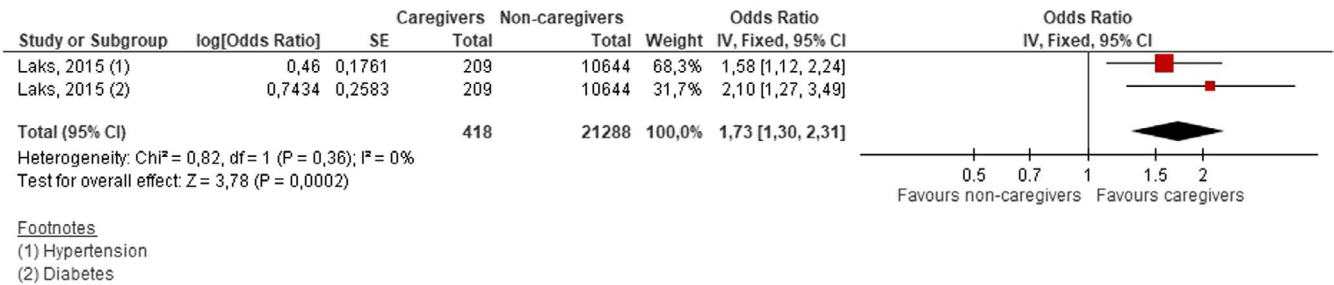


FIGURE 5 Forest plot of the association between unpaid caregiving for individuals with health problems and physical diseases. Abbreviations: CI, confidence interval; IV, inverse variance; SE, standard error [Colour figure can be viewed at wileyonlinelibrary.com]

caregivers, was found ($d = -0,37$, $p < .001$, five comparisons, $I^2 = 7\%$) (Zhang et al., 2013, 2014); although this estimate displayed a degree of heterogeneity within acceptable limits, only studies with an “overall study quality” suggesting a “high” risk of bias could be included. The same poorer results for unpaid caregivers were found in the South American studies ($d = -0,30$, $p < .001$, 12 comparisons, $I^2 = 50\%$) (Arango-Lasprilla et al., 2010; de Lima et al., 2014; Laks et al., 2016; Posner et al., 2015), and sensitivity analysis did not change the results.

Health outcomes of unpaid caregiving in cohort studies

In this subsection, three cohort studies were included (Chen & Liu, 2012; Rej et al., 2019; Zhou et al., 2016), all of which displayed

“low” selection or confounding risk of bias, and which assessed health status (Chen & Liu, 2012; Zhou et al., 2016), activities of daily living (Zhou et al., 2016) and telomere length (i.e., a marker of disease susceptibility) (Rej et al., 2019), in unpaid caregivers of individuals without any apparent medical condition (Chen & Liu, 2012; Zhou et al., 2016), and unpaid caregivers of chronically ill and disabled family members (Rej et al., 2019). The results of all studies are presented as a narrative synthesis.

Health status. Grandparents with high-intensity caregiving displayed poorer health status than noncaregivers ($\beta = -0,05$, standard error [SE] = 0.03, $p < .05$), whereas low-intensity unpaid

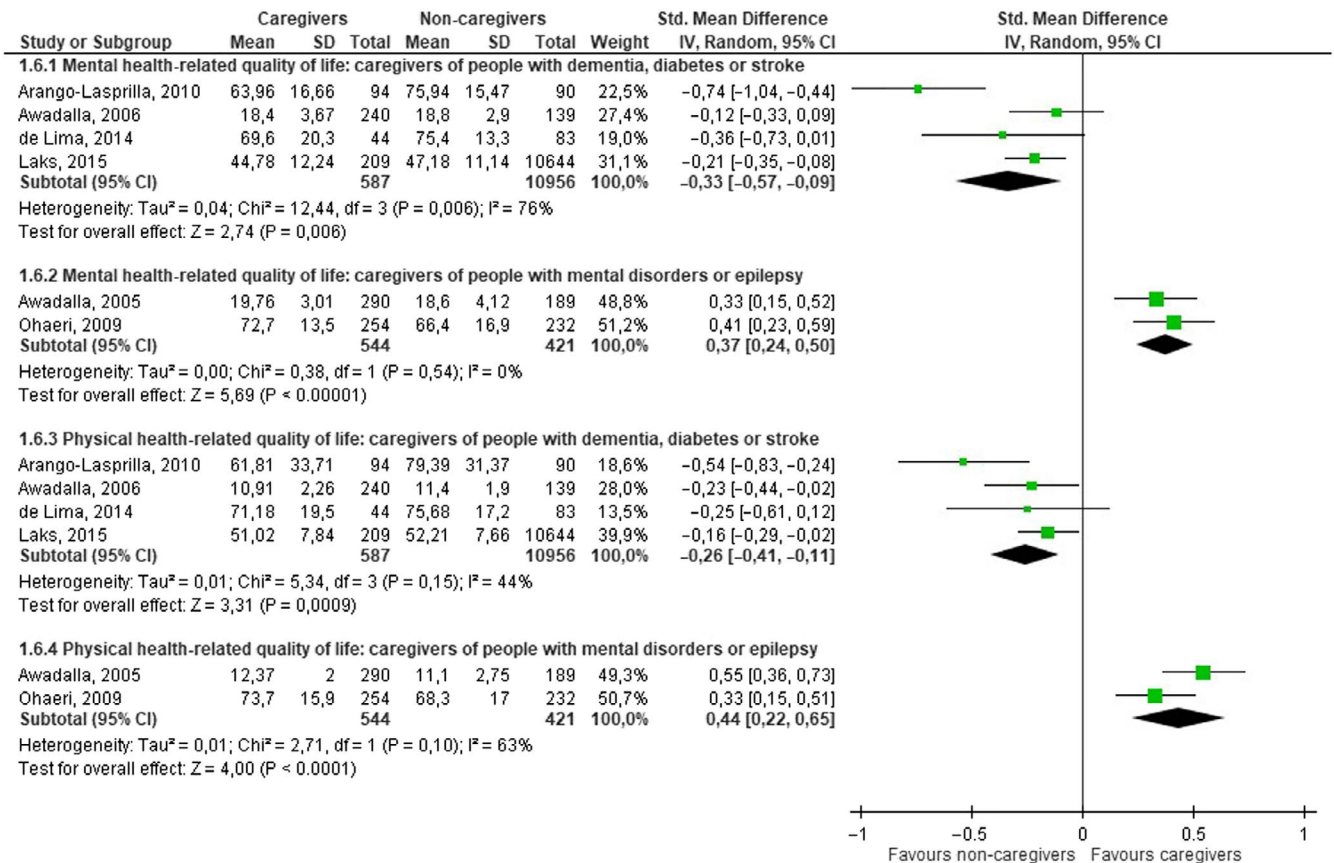
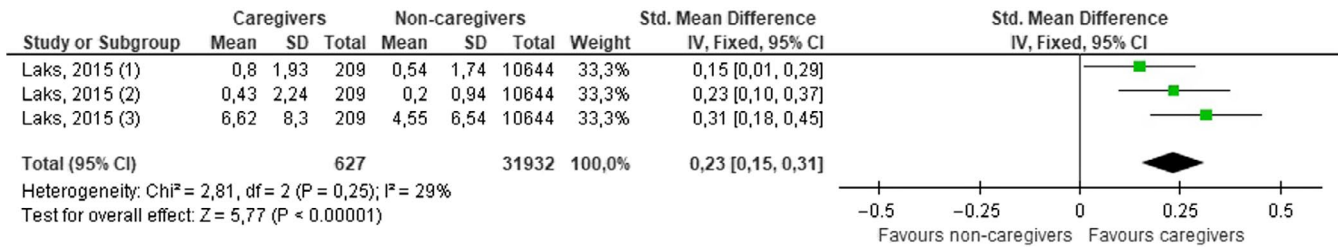


FIGURE 6 Forest plot for health-related quality of life in unpaid caregivers of individuals with health problems versus noncaregivers. Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation; Std., standardised [Colour figure can be viewed at wileyonlinelibrary.com]



Footnotes

- (1) Emergency room visits
 (2) Hospitalizations
 (3) Healthcare visits

FIGURE 7 Forest plot for healthcare services utilisation in unpaid caregivers of individuals with health problems versus noncaregivers. Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation; Std., standardised [Colour figure can be viewed at wileyonlinelibrary.com]

caregivers perceived a lower decrease in their health status compared to noncaregivers (β for age = -0.30 , $SE = 0.02$, $p < .001$; β for age \times low-intensity caregiving = 0.16 , $SE = 0.06$, $p < .01$) (Chen & Liu, 2012). In Zhou et al. (2016), grandparents' unpaid caregivers who were reassessed at follow-up displayed a better health status than noncaregivers (standardised $\beta = 0.13$, $SE = 0.14$, $p = .041$), just like grandparents who did not continue providing services as unpaid caregivers (standardised $\beta = 0.01$, $SE = 0.11$, $p = .049$).

Activities of daily living. Zhou et al. (2016) reported that grandparents who were repeated and prior unpaid caregivers, compared to noncaregivers, displayed no significant alterations in their ability to perform basic (standardised $\beta = -0.06$, $SE = 0.21$, $p > .10$, $N = 558$; standardised $\beta = -0.04$, $SE = 0.16$, $p > .10$, $N = 570$) and instrumental daily living activities (standardised $\beta = -0.03$, $SE = 0.17$, $p > .10$, $N = 558$; standardised $\beta = 0.04$, $SE = 0.14$, $p > .10$, $N = 570$), respectively.

Telomere length. Chronicity of unpaid care (total caregiving years) for chronically ill and disabled family members did not predict telomere length in either minimally (adjusted by age, sex and age by sex interaction: $\beta = -0.003$, $SE = 0.002$, $p = .274$) or maximally controlled model ($\beta = -0.003$, $SE = 0.002$, $p = .215$).

4.4.2 | Health outcomes of male and female unpaid caregivers

Finally, further comparisons and analyses of the health outcomes of male and female unpaid caregivers were restricted by the small number of studies assessing or reporting gender differences in caregiving. Chen and Liu's study (2012) included unpaid caregivers of individuals without any apparent medical condition, and the gender difference data from studies of unpaid caregivers of individuals with health problems were insufficiently detailed to use in a meta-analysis (Awadalla et al., 2005, 2006; Mugisha et al., 2013; Ohaeri et al., 2009; Rej et al., 2019); thus, a narrative synthesis is presented herein.

Female unpaid caregivers of patients with mental disorders and epilepsy had a poorer quality of life than their male counterparts ($p < .001$) (Awadalla et al., 2005; Mugisha et al., 2013; Ohaeri et al., 2009). In contrast, no statistically significant differences were found regarding the health outcomes of female and male unpaid caregivers of diabetic patients (Awadalla et al., 2006). Likewise, no differences were found between women and men caring for people with HIV in the community in terms of their perceived burden ($\beta = 1.25$, $p > .05$, $N = 352$) (Mugisha et al., 2013). Rej et al. (2019) found no evidence for an interaction between chronicity of care and sex ($\beta = -0.004$, $p = .373$) in their cohort study. Finally, a longitudinal study showed that among older adults with high-intensity caregiving, men displayed a poorer health status than women ($\beta = -0.23$, $SE = 0.05$, $p < .001$), and no statistically significant differences were found in association with the gender of low-intensity unpaid caregivers ($\beta = 0.02$, $SE = 0.05$, $p > .05$) (Chen & Liu, 2012).

5 | DISCUSSION

5.1 | Summary of evidence

This systematic review included fourteen studies conducted in Africa, Asia and South America. Unpaid caregivers were found to have higher anxiety and depressive symptoms than noncaregivers, whereas the medical condition affecting the care recipients was an important contributing factor in the health and quality of life outcomes of their caregivers. In general, the worst health and quality of life outcomes were observed in dementia and stroke caregivers. Results from one study found a higher likelihood of having chronic diseases and increased use of health services among dementia unpaid caregivers compared to noncaregivers. Subgroup analyses of all of the studies revealed statistically significant geographical differences, with studies conducted in Asia and South America reporting poorer health outcomes for unpaid caregivers than noncaregivers, whereas the opposite trend (i.e., worse health outcomes for non-caregivers) was found in the African studies. The narrative synthesis of cohort studies about caregiving for individuals with no apparent

medical conditional also suggests an important variation in the caregivers' health outcomes; although there may be health benefits of caregiving, its effect is significantly determined by the intensity of caregiving. On the other hand, a cohort study found no evidence for an association between years of unpaid caregiving for chronically ill and disabled family members and telomere length. Finally, of the six studies that assessed or reported gender differences in unpaid caregiving, three found significant gender differences, with two of them reporting poorer quality of life among female unpaid caregivers.

5.2 | Possible explanations for findings

Given that, in the presence of substantial heterogeneity, subgroup analysis by geographical areas revealed important differences in the health outcomes, the following section dives into the geographic differences that may explain these differential health outcomes of unpaid caregivers, as well as gender differences within this group. In Asia and South America, the poorer health outcomes observed in unpaid caregivers of patients with chronic diseases replicate the findings of developed countries (Bremer et al., 2015; Goren, Gilloteau, Lees, & DiBonaventura, 2014) and previous meta-analyses (Pinquart & Sörensen, 2003, 2007). The scarcity and/or unequal distribution of health services (by geographic area or due to social status) for treating these conditions (especially dementia) (Fang et al., 2015; Hojman et al., 2017) in these regions may render them inaccessible to potential patients, thus imposing a higher caregiving load in these LMICs, while, at the same time, strong feelings of filial obligation, typical of these cultures, can be a source of psychological stress for unpaid caregivers and an obstacle to the acceptability of formal support services for caregivers (Zhang, Clarke, & Rhynas, 2019). In Africa, in contrast, unpaid caregivers from a heterogeneous sample of sick individuals in the community—half of whom had HIV/AIDS—may have been assisted by active family and social support, as suggested by a review of ageing and HIV-related caregiving (Small, Aldwin, Kowal, & Chatterji, 2019), the stability of the clinical status of the recipients of care (Pinquart & Sörensen, 2007) and religious coping strategies (Awadalla et al., 2005; Ohaeri et al., 2009). Some of the health benefits experienced by the low-intensity caregiving group in Chen & Liu, (2012), and in repeated and prior unpaid caregivers studied by Zhou et al. (2016), can be attributed to an active lifestyle in older adults, the financial and emotional support provided by families, and the assurance of reciprocity at more advanced ages (Chen & Liu, 2012; Zhou et al., 2016). Similarly, as noted by Rej et al. (2019), since caregiving for family members is a highly valued cultural practice in the Philippines, caregiving stress may not be perceived as strong as in the case of Western cultures, which might be a plausible explanation for the lack of association between chronicity of caregiving and telomere length in the study by Rej et al. (2019)

Even though gender differences in health care are relevant in Asia and cultural norms privilege men's use of family resources,

affecting women's access to health care (Song & Bian, 2014), only two studies conducted in Asia sought to detect gender-related differences in unpaid caregivers (Chen & Liu, 2012; Rej et al., 2019), and the one study that found statistically significant gender differences, in favour of women, hypothesised that the poorer health outcomes observed in men are due to the societal notion of caregiving as a female activity and, thus, the lack of male referents (Chen & Liu, 2012). In contrast, all African studies conducted gender comparisons of the unpaid caregivers, finding a poorer quality of life among the women, which may be associated with factors such as the marked economic subordination of African women, the societal expectation that they become the main providers of child-care and social support, and poor living arrangements and conditions, whereas male caregivers enjoy more autonomy and social support to deal with their caregiving load (Casale & Gibbs, 2015; Namasivayam, Osuorah, Syed, & Antai, 2012). Lastly, even though traditional gender roles are prevalent in South America, which poses an important obstacle to the redistribution of care between men and women (Campaña, Gímez-Nadal, & Molina, 2018), and despite regional efforts to include gender equity in public policies (Bárcena, Prado, Rico, & Pérez, 2017), none of the South American studies examined differences in health outcomes in connection with the gender of unpaid caregivers; therefore, it is necessary to generate more scientific evidence to clearly delineate the specific focus of public policies and to more effectively promote equality between men and women unpaid caregivers.

In the only literature review available on the topic (Thrush & Hyder, 2014), it was found that unpaid caregivers experienced physical and mental burdens; however, these results were limited by methodological decisions, such as the inclusion of evidence that is very difficult to compare (both quantitative and qualitative studies), and because many of the reviewed studies lacked nonexposed individuals. In contrast, the present systematic review and meta-analysis found an association between unpaid caregiver status and depression.

5.3 | Limitations

The cross-sectional design of most of the included studies prevented drawing any conclusion about the causal effects of caregiving, an issue that may be reflected by the studies having an "unclear" selection risk of bias or "unclear" or "high" confounding risk of bias. Moreover, the study findings proved to be highly heterogeneous, with the exception of the meta-analysis for anxiety and depression. Additionally, more research is needed to represent the cultural and structural specificities of LMICs. On the other hand, the scope of this review was limited to articles published in English or Spanish, which may have biased the selection of studies from Latin America. The exclusion of databases and/or grey literature meant that some relevant studies may have been excluded. Finally, as highlighted by the Cochrane Handbook for Systematic Reviews of Interventions regarding the identification of nonrandomised studies

(e.g., observational studies) (Higgins & Green, 2011), the absence of a reliable standard filter or search strategy for observational studies evaluating the effects of exposures, and the incomplete or inconsistent reporting of these types of studies, may have precipitated the exclusion of additional studies.

5.4 | Implications for research and public policy

The rapid social and economic changes experienced by LMICs (Shetty, 2012), and the growing ageing population requiring home care (Lancet, 2014), will certainly have consequences for the health of unpaid caregivers, and further empirical longitudinal explorations is needed. Since societal attitudes towards caregiving are pivotal in determining the life trajectories of unpaid caregivers (Carmichael & Ercolani, 2016), the role that cultural obligations have on the burden and health of unpaid caregivers and on their access to formal support services should be studied in greater depth to inform public policy in these countries. In the same vein, as cultural obligations are not gender neutral (Bárcena et al., 2017), the gendered health effects of caregiving should be researched and further considered by policymakers to facilitate and encourage the integration of women in the formal labour market across LMICs.

Most of the studies included in this systematic review and meta-analysis were cross-sectional, yet carefully-designed longitudinal studies, addressing selection and/or confounding biases, are required in order to draw solid causal inferences regarding health outcomes of unpaid caregivers. Additionally, an important proportion of the studies focused on the provision of caregiving for others due to illness or disability, thus ignoring the intersections between gender, life course, and caregiving (Corna, 2013), and how the lack of support with childcare may have a negative impact on the trajectories of female caregivers living in LMICs. Finally, the extent to which the unpaid caregivers' burden was concentrated in a single person was not measured in the studies included, which may have had a major effect on the health outcomes of unpaid caregivers, especially for those with poor living conditions and arrangements.

6 | CONCLUSION

While unpaid caregivers of individuals with health problems seemed to have worse mental health than noncaregivers, low-intensity caregiving for healthy individuals may be potentially beneficial to the health status of unpaid caregivers living in LMICs. Significant geographical differences were found for the health outcomes of unpaid caregivers of individuals with medical problems, suggesting the interplay of social, cultural and systemic factors. Although more evidence is needed from LMICs to clearly disentangle the role of caregiving on the health outcomes of unpaid caregivers, urgent attention to the study of gender differences in the health outcomes of caregivers is required to adequately tailor support for those responsible for

caregiving, an activity which demands major time investments for women in LMICs.

7 | RELEVANCE TO CLINICAL PRACTICE

The health status of unpaid caregivers will be one of the most relevant issues in the near future worldwide, particularly in LMICs, as the global health trends, characterised by ageing-related illnesses, will increase the demand for family caregiving. Notwithstanding the limitations of this systematic review and meta-analysis (i.e., the scarcity and heterogeneity of the literature), the results appear to suggest, in line with studies carried out in developed countries, that the prevention and/or treatment of mental health problems, particularly anxiety and depression, should be an integral part of nursing care for unpaid caregivers. In light of the characteristics of caregiving in LMICs, health promotion for unpaid caregivers in these countries should consider the development of formal care support services and educational campaigns aimed at assisting caregivers in finding ways to meet cultural obligations while also emphasising the importance of caregiver self-care. Although very few studies explored gender differences in the health outcomes of unpaid caregivers, which might be a potential indicators of gender bias, caregiving in LMICs is an eminently feminine activity, and this variable should be considered, in clinical practice, to promote the health of unpaid female caregivers and to prevent mental health problems in this vulnerable population.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTION

IM was the guarantor of this systematic review and meta-analysis, and provided her expert opinion during the reviewing process. PM and M-SL gave valuable input to the study design, and were in charge of data extraction and risk of bias assessment under the supervision of IM. All authors contributed equally to the narrative synthesis. PM was in charge of the statistical synthesis. All authors edited, modified and approved the final version of this manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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