REVIEW



Burden of Disease of Gonorrhoea in Latin America: Systematic Review and Meta-analysis

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ABSTRACT

Introduction: *Neisseria gonorrhoeae* causes gonorrhoea, a globally neglected but increasing disease. This systematic review and meta-analysis reviewed the epidemiology and economic burden of gonorrhoea in Latin America and the Caribbean (LAC).

Methods: We searched PubMed, EMBase, Cochrane Library, EconLIT, CINAHL, CRD, LILACS, Global Health, Global Dissertations and Theses, SciELO, Web of Science databases, countries' ministries of health, and the IHME's Global Burden of Disease databases. Studies

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C. Palermo e-mail: mariacarolinapalermo@yahoo.com.ar published in the last 10 years (20 years for economic studies) were included if conducted in any LAC country, without language restrictions. The main outcome measures were incidence/ prevalence, proportion of co-infections, case fatality rates, specific mortality/hospitalisation rates, direct/indirect costs, and impact of gonorrhoea on quality of life. To assess evidence quality, we used a checklist developed by the US National Heart, Lung, and Blood Institute for observational studies and trial control arms, the Cochrane Effective Practice Organization of Care Group tool for randomised controlled trials, and the CICERO checklist for economic studies.

Results: We identified 1290 articles; 115 included epidemiological studies and one included an economic study. Ministry of health data

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T. Pinto GSK, Panama City, Panama e-mail: thatiana.x.pinto@gsk.com from Argentina, Brazil, Chile, Colombia, Mexico, and Uruguay were identified. Gonorrhoea prevalence was 1.46% (95% confidence interval [CI] 1.00–2.00%) from 48 studies and 5.68% (95% CI 4.23–7.32%) from 58 studies for nonhigh-risk and high-risk populations, respectively. Cumulative incidence for the high-risk population was 2.05 cases per 100 persons/year. Few published studies were rated as "good" in the risk of bias assessments. Variations in the methodology of the sources and limited information found in the countries' surveillance systems hinder the comparison of data.

Conclusion: The burden of gonorrhoea in LAC is not negligible. Our results provide public health and clinical decision support to assess potential interventions to prevent gonorrhoea. *Trial Registration*: The protocol is registered on PROSPERO (CRD42021253342). The study was funded by GlaxoSmithKline Biologicals SA (GSK study identifier VEO-000025).

Keywords: Caribbean; Economics; Epidemiology; Gonorrhoea; Latin America; Systematic review

Key Summary Points

Why carry out the study?

Gonorrhoea is a sexually transmitted disease that can cause serious complications.

Rates of gonorrhoea are increasing in many countries, and some population groups are at a disproportionately high risk of gonorrhoea.

To our knowledge, this systematic review is the first to estimate the disease burden of gonorrhoea in Latin America and the Caribbean including information from scientific literature, GBD, and ministries of health databases.

What was learned from the study?

Gonorrhoea prevalence was high (1.46%) in Latin America and the Caribbean and higher (5.68%) in high-risk populations, including men who have sex with men, sex workers, transgender people, and vulnerable groups comprising ethnic minorities, low educational level, or low socioeconomic status; rates of gonorrhoea were higher in men than in women; coinfections with other pathogens were frequent.

Our results will be valuable to decisionmakers considering potential health policies to control gonorrhoea.

INTRODUCTION

Gonorrhoea is a sexually transmitted disease (STD) caused by infection with the bacterium *Neisseria gonorrhoeae*, transmitted by either sexual or perinatal contact. Many gonorrhoea infections are asymptomatic, and therefore reported cases underestimate the true burden of disease [1]. Untreated gonorrhoea can cause serious complications such as pelvic inflammatory disease (which in turn may result in chronic pain, infertility, and increased risk of ectopic pregnancy) and may also increase the risk of acquiring or transmitting human immunodeficiency virus (HIV) [1].

Global incidence rates for gonorrhoea in people aged 15–49 years were estimated by the World Health Organisation (WHO) at 20 per 1000 women and 26 per 1000 men, with approximately 87 million new infections in 2016 [2]. Estimated prevalence was 0.9% in women and 0.7% in men, or 30.6 million cases worldwide [2]. Prevalence was highest in the WHO Africa region (1.9% in women, 1.6% in men) [2]. Rates of gonorrhoea are increasing in many countries, and the disease is an expanding public health concern [3].

Some population groups bear a disproportionately high burden of gonorrhoea compared with the general population. These risk groups include gay, bisexual, and other men who have sex with men (MSM) [3], transgender women [4], sex workers [5], racial and ethnic minorities [6], indigenous populations [6] and international travellers [3, 7].

Detailed data on the epidemiology and economic burden of gonorrhoea in individual countries in Latin America and the Caribbean (LAC) will be valuable to decision-makers considering potential health policies to control the disease. The primary objective of this systematic review and meta-analysis was to estimate the disease burden (incidence, prevalence, direct and indirect cost, and impacts on health-related quality of life) of gonorrhoea in LAC. Secondary objectives included identifying information on disease burden in pregnant women and highrisk population groups, co-infections and trends in disease burden over time.

METHODS

This systematic review and meta-analysis were part of a broader systematic literature review that also considered studies on antimicrobial resistance in gonorrhoea. This article presents the epidemiological and economic studies identified.

This review included published and unpublished local, regional and international data following Cochrane methods [8]. A meta-analysis of data from observational studies conducted in LAC (including the control arms of clinical trials) was conducted, following MOOSE [9] guidelines for meta-analyses of observational studies and PRISMA guidelines for reporting systematic reviews and meta-analyses [10, 11]. The protocol followed the PRISMA-P declaration [12] and was registered in PROSPERO, an international prospective registry of systematic reviews, under the registration number CRD42021253342.

Eligibility Criteria

Eligibility criteria are summarised in Table 1. Systematic reviews and meta-analyses were considered only as a source of primary studies. When data or subsets of data were reported in more than one publication, we selected the one with the largest sample size. We planned to use international dollars adjusted for inflation.

Data Sources and Search Strategy

The following electronic databases were searched for eligible articles up to 13 February 2021: PubMed, EMBase, Cochrane Library (CEN-TRAL). EconLIT. Cumulative Index of Nursing and Allied Health Literature (CINAHL). Centre for Reviews and Dissemination (CRD) York, Latin American and Caribbean Literature in Health Sciences (LILACS), Global Health (OVID), Global Dissertations and Theses (Pro-Quest), SciELO and Web of Science. Detailed search terms are presented in Supplementary Material Table S1. The reference lists of identified studies and systematic reviews/meta-analvses were hand-searched for additional information. In addition, we searched databases of proceedings of regional and international congresses and doctoral theses (e.g. ICID Abstracts, British Association of Sexual Health and HIV, XI Encuentro Nacional de Enfermedades Infecciosas 2018, Congreso Latinoamericano de Infectología Pediátrica). Websites of major regional medical societies, experts and associations such as the Pan-American Infectious Diseases Association, the Argentine Society of Infectious Diseases and the Latin American Society of Pediatric Infectious Diseases were consulted.

We also analysed the databases of regional ministries of health in which relevant information was available and searched for grey literature in Pan-American Health Organization (PAHO) and hospital reports by using generic internet search engines (Google) and through the Global Burden of Disease (GBD) model [13].

Article Selection

Publications were screened by two reviewers using title and abstract according to the eligibility criteria. Discrepancies were solved by agreement of the entire team. Potentially eligible articles were retrieved in full text for further analysis. All screening phases of the study used

	Criteria
Geographic scope	All LAC countries
Participants	All LAC patients, regardless of age, sex or population type
Epidemiological trial types	Randomised controlled trials (RCTs) or quasi-RCTs
	Controlled and uncontrolled before-after studies
	Interrupted time series (ITS) and controlled ITS (STIC)
	Cohort studies
	Case-control studies
	Cross-sectional studies
	Epidemiological surveillance reports
	Case series
Economic trial types	Cost-effectiveness studies or economic evaluations
	Budget impact analyses
	Cost of illness studies
Outcomes (at least one of)	Incidence
	Prevalence
	Proportion of co-infections
	Case fatality rates
	Specific mortality and hospitalisation rates
	Direct and indirect costs of gonorrhoea
	Impact of gonorrhoea on health-related quality of life
Date range for epidemiological studies	Published since January 1, 2011 (past 10 years)
Date range for economic studies	Published since January 1, 2001 (past 20 years)
Study size	Case series: at least 20 cases
	Remaining study types: at least 100 participants
	For studies in newborns there was no study sample size limit
Language	No language restrictions

Table 1 Eligibility criteria

LAC Latin America and the Caribbean

COVIDENCE [14, 15], a web-based platform designed to process systematic reviews.

Data Extraction

From eligible articles, the research team extracted data using previously piloted pre-designed data extraction forms. Data extracted were: publication and study characteristics (type of publication, year published, authors, geographic location, study design including domains for risk of bias assessment); study population characteristics (age, sex, sample size, risk evaluation for *N. gonorrhoeae*, inclusion/exclusion criteria); and outcomes (incidence rate, prevalence, co-infections, specific *N. gonorrhoeae* mortality, case fatality rate, hospitalisation rate, length and recurrence of an acute episode, indirect and direct costs, and resource use). The original authors were contacted if necessary to obtain any missing information or clarification.

Risk of Bias Assessment

Published epidemiological studies were assessed for risk of bias by two independent reviewers, with discrepancies resolved by consensus with the whole team. For observational studies and the control arm of trials we used a checklist developed by the US National Heart, Lung, and Blood Institute [16] that classifies studies as high (poor), moderate (fair) and low risk of bias (good). For evaluation of cohort studies and cross-sectional studies the tool comprises 14 items, and for case series there are 9 items. For randomised controlled trials (RCTs) and quasi-RCTs the Cochrane Effective Practice Organization of Care (EPOC) Group [17] tool was used, and for before-after studies. ITS and STIC we used the relevant items from the Cochrane EPOC criteria [17]. Each criterion was scored as low, high or uncertain risk. For those rated as uncertain we attempted to obtain more information from the study authors.

For economic studies quality assessment was conducted using the Criteria for Cost-Effectiveness Review Outcomes (CiCERO) checklist [18].

Statistical Analysis of Epidemiological Studies

The primary meta-analyses were conducted using meta-proportion analysis, applying arcsine transformation to stabilise the variance of proportions (Freeman-Tukey variant of the square root arc-sine method of transformed proportions), where $y = \arcsin[\sqrt{r}]$

 $(n + 1))] + \arcsin[\sqrt{(r/(n + 1)/(n + 1))}]$, with a variance of 1/(n + 1), and where *n* is the size of the population [19]. The pooled ratio was calculated as the subsequent transformation of the weighted mean of the transformed proportions, using weights of variance of arc-sine inverse for the fixed and random effects model. Statistic I^2 was calculated as a measure of the proportion of the overall variation attributable to heterogeneity between studies [20]. A value of $I^2 > 60-70\%$ was considered as substantial heterogeneity and below 30% as low heterogeneity. We applied DerSimonian-Laird weights for the random effects model [21] where heterogeneity was found between studies [22]. Stats Direct and STATA 14.0 were used for all analyses.

There was considerable variation in followup period, so incidence rates were calculated in person-years by dividing the number of new cases in the follow-up period by the total person-years in the group at risk, expressed as number of cases per 100,000 person-years. This incidence density rate is an appropriate measure of incidence when follow-up times are uneven [23].

Publication bias between studies was explored using funnel graphs where there were at least ten studies. Selective reporting within studies was evaluated by comparing available protocols with the published studies.

Subgroup analyses were conducted for three groups, defined according to their risk of having gonorrhoea (high-risk, non-high-risk or unreported risk). The high-risk population included MSM, sex workers, transgender people and vulnerable groups comprising ethnic minorities, low educational level or low socioeconomic status. Non-high risk was defined as those not at high risk. Further subgroup analyses were conducted on the different categories defining high risk. Further subgroup analyses were performed according to: the type of study sampling (representative sampling, health system convenience sampling and community convenience sampling); the symptoms compatible with gonorrhoea (yes, no, not reported); the population HIV status (positive, negative); pregnancy (yes, no); biological sex (male, female); the type of sample for females (urine,

endocervical/vaginal); and age group (15–29 years, 30–50 years, 18–50 years).

Sensitivity analyses were performed by restricting the analyses to studies with a low risk of bias.

Compliance with Ethics Guidelines

Ethics approval was not required as this study was based on published data and therefore did not involve human participants.

RESULTS

Literature Search

After removing duplicates, the literature searches identified 1290 articles to be screened using title and abstract, of which 279 were retrieved for full-text assessment. Of these, 115 epidemiological studies [24–138] (three of which also reported data on antimicrobial resistance) [47, 122, 138] and one economic study [139] were eligible for inclusion in the review (Fig. 1). There were 91 full papers, 22 abstracts and 3 epidemiological bulletins. Studies excluded at full-text review are listed in Supplementary Material Table S2.

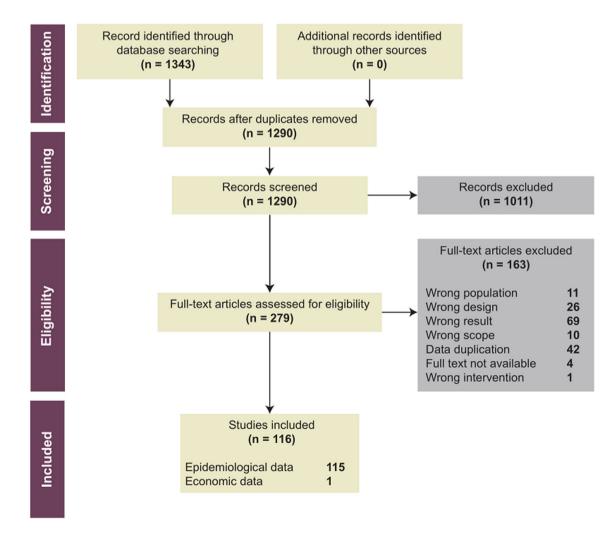


Fig. 1 Flow chart

	General	population		Non-high-risk population			High-risk population			
	Central estimate	95% CI, lower limit	95% CI, upper limit	Central estimate	95% CI, lower limit	95% CI, upper limit	Central estimate	95% CI, lower limit	95% CI, upper limit	
Risk level										
Non-high	1.46%	1.00%	2.00%							
High	5.68%	4.23%	7.32%							
Not reported	5.97%	2.47%	10.86%							
Sampling										
Random representative sampling				0.40%	0.11%	0.88%	1.66%	1.32%	2.04%	
Convenience (health system)				1.82%	1.24%	2.51%	6.16%	3.94%	8.85%	
Convenience (community)				0.19%	0.01%	0.90%	4.46%	3.24%	5.88%	
Symptoms										
Yes				7.26%	0.96%	18.73%	12.82%	3.07%	27.89%	
No				1.10%	0.07%	1.54%	5.37%	3.81%	7.17%	
HIV-positive	2.02%	1.14%	3.15%							
Pregnant women				1.16%	0.37%	2.39%	2.98%	1.67%	4.65%	
Biological sex										
Male				2.68%	0.02%	9.59%	6.57%	4.56%	8.93%	
Female				1.61%	0.98%	2.39%	3.73%	2.26%	5.54%	
Risk category										
Sex worker	3.77%	1.99%	6.09%							
MSM	6.01%	4.14%	8.20%							
Transgender	7.90%	6.08%	9.93%							
Vulnerable group	5.86%	0.89%	14.8%							
Type of sample in females										
Urine				1.26%	0.69%	2.00%	3.69%	1.76%	6.28%	
Endocervical/ vaginal				1.95%	0.12%	2.84%	3.84%	2.00%	6.24%	
Age										
15–29 years	1.39%	0.44%	2.86%							

Table 2 Results of the meta-analysis of proportions of gonorrhoea

	General	population		Non-higl	n-risk popu	lation	High-risk population			
	Central estimate	95% CI, lower limit	95% CI, upper limit	Central estimate	95% CI, lower limit	95% CI, upper limit	Central estimate	95% CI, lower limit	95% CI, upper limit	
30–50 years	0.98%	0.15%	2.53%							
18-50 years	2.13%	1.08%	3.52%							
Incidence rate (cases per 100 people/year	2.05	0.42	3.69							
Proportion of positive sites ^a										
Cervicitis	10.96%	3.46%	21.96%							
Cervical swab positive	6.80%	3.90%	10.42%							
Urethritis	42.03%	17.22%	69.22%							
Urethral swab/ urine positive	13.14%	0.15%	41.83%							
Rectitis	45.98%	21.19%	71.89%							
Rectal swab positive	18.92%	5.99%	36.89%							
Pharyngitis	32.62%	11.02%	59.15%							
Pharyngeal swab positive	33.23%	8.29%	64.90%							
Conjunctivitis	1.58%	0.06%	5.13%							
Asymptomatic carrier	72.86%	39.73%	95.77%							
5-year period										
2010-2014				2.73%	0.98%	5.32%	6.18%	3.00%	10.40%	
2015-2019				1.50%	0.94%	2.20%	7.42%	4.20%	11.46%	
Studies with low risk of bias				0.47%	0.11%	1.06%	1.66%	1.32%	2.04%	

 Table 2 continued

CI confidence interval; HIV human immunodeficiency virus; MSM men who have sex with men; + positive ^aIn studies reporting more than one site of infection

Population	Range of gonorrhoea prevalence reported					
High-risk populations	0% [29, 54, 59, 91] to 42.8% [57]					
Non-high-risk populations	0% [25, 51, 70, 72, 79, 99–101, 111, 134] to 11.8% [47]					
Studies in which the population risk could not be determined	0.2% [138] to 31.5% [138]					
Symptomatic patients	1% [37] to 42.8% [57] (in the latter study the symptom was puruler urethral discharge)					
Asymptomatic population	0-32.5% [138]					
Hospitalised patients and pregnant women	0% [25] to 3.4% [25]					
Males	0% to 42.8% [57]					
Females	0% [25, 29, 79, 91, 99–101] to 21.5% [43]					
Sex workers	0% [29] to 15.6% [36]					
Men who have sex with men	0.7% [132] to 16.2% [83]					
Transgender women	3.8-12.3% [77]					
Vulnerable populations	0-42.8% [57]					

Table 3 Range of gonorrhoea prevalence reported

Characteristics of Included Studies and Participants

Supplementary Material Table S3 summarises the characteristics of the included studies. The studies included 103,965 participants, of whom 36,304 were males and 55,674 females (4898 pregnant). Age ranged from 0 years (< 3 month) [50] to 93 years [59], with mean age between 8.5 years [115] and 54 years [59] and median age between 7.9 years [113] and 45 years [95]. The reported female-to-male ratio was 1.5.

Of the included studies, 51 (n = 50,926 participants; 49%) assessed a population at increased risk of gonorrhoea (sex workers, MSM, transgender people, vulnerable groups), and 49 studies (n = 47,086 participants; 45%) assessed a population at non-high risk for gonorrhoea. In two studies (n = 1997 participants; 2%) the included participants belonged to high-risk and non-high-risk groups in similar proportions, and the population risk was not reported in 14 studies (n = 3956 participants; 4%). The most frequently reported risk categories were sex workers (n = 34,931, 34% of total) and MSM (n = 14,988, 14% of total).

Risk of Bias Assessment

Most of the cross-sectional/cohort studies (n = 71) (Supplementary Material Table S4) and the only case series (Supplementary Material Table S5) were categorised as 'fair'. Six studies were categorised as 'good' (Supplementary Material Table S4).

Epidemiological Results

Prevalence

Table 2 summarises the results of meta-analyses of proportions of patients with gonorrhoea conducted (for details of each analysis, see Supplementary Material Figures S1 to S48). In the general population the prevalence for individuals at non-high risk was 1.46% (95% confidence interval [CI] 1.00%, 2.00%) from 48 studies, and for people at high risk the prevalence was 5.68% (95% CI 4.23%, 7.32%) from 58 studies. Prevalence in the HIV + population

			-		0			. 0					
Year	Age < 1	Age 1–4	Age 5–9	Age 10–14	Age 15–19	Age 20–29	Age 30–39	Age 40–49	Age 50–59	Age 60–69	Age 70–79	Age 80 +	Total
2009	0	0	0	0	0	0	0	0	0	1	0	0	1
2010	9	3	0	2	4	4	4	1	1	1	0	2	31
2011	15	2	0	1	2	12	8	5	1	0	0	1	47
2012	25	3	1	1	12	15	4	2	4	1	0	1	69
2013	17	2	1	1	7	14	13	6	5	2	1	1	70
2014	24	4	0	1	6	19	13	8	7	2	4	0	88
2015	26	0	1	1	12	16	14	8	5	4	0	2	89
2016	26	1	1	2	11	19	12	9	7	3	4	1	96
2017	35	6	2	5	10	20	21	13	11	7	8	5	143
2018	26	4	4	3	6	26	18	7	7	2	6	3	112
2019	24	2	2	4	15	19	22	10	7	4	6	3	118
2020	17	2	1	3	5	16	17	8	6	1	2	2	80

Table 4 Number of hospitalisations due to gonococcal infections by gender in Brazil, 2009–2020 [143]

Table 5 Total cost and mean cost of hospital days due togonococcal infection in Brazil between 2008 and 2020[143]

Year	Total cost (Brazilian real R\$)	Average cost (Brazilian real R\$)
2008	18,173	454
2009	59,818	1129
2010	15,277	477
2011	25,917	632
2012	49,523	718
2013	33,442	492
2014	57,799	688
2015	48,342	483
2016	41,464	451
2017	67,395	492
2018	71,237	614
2019	62,037	526
2020	42,903	442

Brazilian real prices were adjusted for inflation based on the Brazilian consumer price index and are reported as Brazilian real in 2021 [143] was 2.02% (95% CI 1.14%, 3.15%) from 17 studies, and in pregnant women it was 1.16% (95% CI 0.37%, 2.39%) for those at non-high risk and 2.98% (95% CI 1.67%, 4.65%) for those at high risk (Table 2). The range of gonorrhoea prevalence reported in various populations is shown in Table 3.

One study reported 802,162 for gonococcal infection in Brazil between 2009 and 2019 [31], and another reported two hospitalisations for gonococcal meningitis in children aged < 3 months [50] in Mexico (2012–2017). In the city of Medellin, 700 outpatient consultations for gonorrhoea were reported between 2002 and 2006 (76.4% men), equivalent to 2.8% of the consultations for STDs registered in the city in that period [46].

Incidence

Six studies reported incidence data for high-risk populations [27, 32, 49, 58, 68, 93]. Two [32, 68] provided CI information, which enabled a meta-analysis, resulting in an estimate of 2.05 cases per 100 people/year (95% CI 0.42 to 3.69; I^2 66.7%) (Table 2). In the other four [27, 49, 58, 93], although no variability was

reported, a median value corresponding to 24 cases per 100 people/year with an interquartile range of 10.1 to 36.4 per 100 people/year was estimated. In the non-high-risk population, no studies reported incidence density. In the studies in which population risk could not be determined, the reported incidence was 8.3/ 100 000 inhabitants [40, 41] and 31.6/100 000 inhabitants [119], and in another study the incidence range in males and females was 14–57 and 3–12 cases per 100 000 inhabitants, respectively [75].

Deaths and Complications

No deaths from gonorrhoea were reported. One study [63] reported two cases of infertility as the only complication of gonococcal disease. No cases of disseminated disease or obstetric complications were reported. Two cases of meningitis as a manifestation of neonatal disease were reported [50] and 13 cases of neonatal gonococcal ophthalmia (0.1% of gonorrhoea cases reported in the study; 13/9613 cases) [41].

Co-infections

Co-infections were common: 42.9% with herpes simplex virus (HSV) [48], 0.8% [103] to 100% [63, 82, 103] with *Chlamydia trachomatis*, 5.6% [140] to 100% [117] with human papillomavirus (HPV), 7.1% [48] to 20% [73, 117] with syphilis, 15.7% [115] to 50% [38] with *Trichomonas vaginalis*, 10.5% with concomitant bacterial

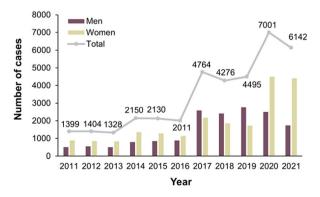


Fig. 2 Number of cases of gonococcal infection in the genitourinary tract in Mexico, 2011–2021 [146]

vaginosis [115], 11.1% [118] to 21.4% [48] with *Mycoplasma genitalium*, 100% with *Mycoplasma hominis* [98], 75.3% with *Ureaplasma urealyticum/parvum* and 2.8% with hepatitis C virus [140]. One study reported 81.5% of co-infections with more than one microorganism (*M. genitalium, M. hominis, Gardnerella vaginalis* and *T. vaginalis*) [43]. In the 14 studies that included 100% of people living with HIV, between 0% [54, 72] and 13.3% [93] were associated with *N. gonorrhoeae*.

Sensitivity Analysis

In the sensitivity analysis restricted to studies with a low risk of bias, the combined prevalence was 0.47% (95% CI 0.11%, 1.06%) in the general population at non-high risk and 1.66% (95% CI 1.32%, 2.04%) in the general population at high risk (Table 2).

Health-Related Quality of Life

No studies were found reporting information on health-related quality of life.

Economic Studies

Only one economic study meeting our criteria was identified [139], a cost-effectiveness study using a Markov model to compare usual care with a strategy for reducing the incidence of sexually transmitted infections (including gonorrhoea) in female sex workers located on the northern border of Mexico. The CiCERO checklist categorised the study as having a low risk of bias. The study provided information on some unit costs for gonorrhoea management in Mexico: diagnostic test for gonorrhoea, US\$22; azithromycin 100 mg, US\$14; ceftriaxone 125 mg, US\$7.70; benzathine penicillin, US\$5 [139]. No other health resources or costs for gonorrhoea were identified.

Ministry of Health Databases

In Argentina, 30,348 cases of genital gonococcal infection were registered between 2011 and

2018, and in 2018, 53% of the total registered cases were verified (n = 16 150). A new version of the National Health Surveillance System (SNVS), SNVS 2.0, was implemented in 2018, which may have led to the increase seen in the number of cases registered. In all years with data available by biological sex, gonorrhoea cases predominated in males, triple the number in females (Supplementary Material Table S6). Between 2011 and 2018 just one death attributable to gonococcal infection was registered in Argentina (in 2018), in a male aged 70–74 years [141, 142].

In Brazil, 43 deaths associated with gonococcal infection were recorded between 2009 and 2020. The peak was reported in 2017, when ten deaths occurred (70% male). Hospitalisations due to gonococcal infections increased from 1 in 2009 to 80 in 2020, with the highest number in people aged < 1 year and 20---39 years (Table 4) [143]. The cost of hospital days due to gonococcal infection reached 42,903 Brazilian reals in 2020 (Table 5).

In Chile, hospital days due to gonococcal infection totalled 306 in 2018, with females having more total days than males (229 compared with 77) but with no statistically significant difference between the averages (p > 0.798) (Supplementary Material Table S7) [144]. The number of new cases was 2768 in 2017 (Supplementary Material Table S8).

In Colombia, six deaths due to gonorrhoea as defined by International Classification of Diseases (ICD)-10 codes were registered between 2011 and 2020, all male and most (4/6) aged > 65 years (Supplementary Material Table S9) [145].

In Mexico, the number of gonococcal infections registered has shown an increasing trend in recent years, peaking at 7001 cases in 2020. In 2017–2019, cases in males exceeded those in females, while in 2011–2016, 2020 and 2021 there were more cases in females than in males (Fig. 2, Supplementary Material Table S10) [146].

In Uruguay, there were 53 hospital discharges for gonorrhoea between 2015 and 2019, according to a Department of Health Surveillance (DEVISA) report (Supplementary Material Table S11). We could not find any detailed information about the burden of disease due to gonorrhoea for the Central American countries.

Global Burden of Disease (GBD)

From GBD, we obtained modelled information on incidence rates, prevalence, mortality and disability-adjusted life-years (DALYs) for different age groups (0-14, 15-19, 20-24, 25-49, 50–69 and > 70 years) between 2011 and 2019 from most LAC countries. Incidence and prevalence rates, expressed as new and prevalent cases per 100 000 person-years, respectively, remained stable over this period in most of the countries included. In all countries, in both sexes, the highest incidence and prevalence rates both occurred between 20 and 24 years of age and decreased towards the extreme ages of life. The mortality rate, expressed as deaths per 100,000 person-years, also remained stable in the period evaluated in most of the countries.

DISCUSSION

This systematic review and meta-analysis summarised available evidence from the scientific literature on the epidemiological burden of gonorrhoeal disease in LAC over the past 10 years. Almost half the population in the identified epidemiological studies was from groups at increased risk for gonorrhoea, such as sex workers, MSM, transgender people and vulnerable groups. Prevalence in the non-highrisk population was 1.46%, lower than that in the high-risk population, which was 5.68%. The estimated incidence was 2.05 cases per 100 people/year in the high-risk population. Our review indicates a higher rate of gonorrhoea in men than in women, mainly in the high-risk population.

To our knowledge, this is the first comprehensive review of the burden of gonorrhoea across the countries of the LAC region that includes information from ministries of health databases and GBD as well as the scientific literature. However, this review has some limitations arising from variations in the methodology of the sources, particularly regarding the ministries of health surveillance systems. Furthermore, most of the published studies identified were rated as "fair" in the risk of bias assessments and few (n = 6) were rated as "good". Five of the six studies with randomised sampling were conducted in specific population subgroups and may not be generalisable to wider populations. The limited information found in the countries' surveillance systems hinders the comparability with data obtained from GBD [147].

Our results are consistent with previous publications. In a systematic review covering the global general adult (aged 15-49 years) population excluding risk groups, the prevalence of gonorrhoea in 2016 was found to be 0.9% (95% uncertainty interval [UI] 0.7-1.1%) in females and 0.7% (95% UI: 0.5-1.1%) in males [2]. In South Africa, the prevalence of gonorrhoea in the general adult population in 2017 was 6.6% in females and 3.5% in males [148]. Two reviews involving populations of female sex workers, one in China (2000-2011) and one in Africa (1999-2019), reported a gonorrhoea prevalence of 6% and 5.46% respectively [149, 150], similar to our results in the high-risk population. A systematic review of the prevalence of four STDs in young people aged 10-25 years in LAC was published in 2022, after the cut-off date for our search [151]. This review identified 15 population-based studies, of which eight reported data on the prevalence of N. gonorrhoeae. Prevalence in women ranged from 0 to 2.9% (8 studies, 4845 participants), prevalence in pregnant women was 1% (1 study, 2071 participants), prevalence and in men aged < 20 years was 0% (2 studies, 666 participants) [151]. The results from this review are specific to populations aged 10-25 years [151] and therefore cannot be compared directly with the results from our study which included subjects of all ages.

Our study also included relevant epidemiological information obtained through the ministries of health. The scarcity or absence of data on mortality or hospitalisations is striking, possibly reflecting the low lethality of gonorrhoea and/or probable under-reporting of data. For example, in Argentina, registered rates were 6.68–8.09 cases per 100,000 inhabitants, while in Canada in 2011–2014 a rate of 34.8–45.7 cases per 100,000 inhabitants was reported [152], with the disease predominating among males in both countries.

The higher prevalence of gonorrhoea in high-risk populations reported in this study underscores the need for targeted interventions and prevention strategies for these populations, such as improved access to testing, treatment and prevention methods such as condoms and pre-exposure prophylaxis. The study's finding that gonorrhoea is more prevalent in men than women can serve as a basis for screening and treatment guidelines, particularly in symptomatic patients. The fact that no serious complications or deaths from gonorrhoea were reported in the included studies suggests that the disease has a low lethality, but the limited information found in country surveillance systems limits comparison with data from other regions.

The methodological limitations in data sources and the lack of economic studies of the burden of gonorrhoea in the LAC region noted in the study highlight the need for further research to improve understanding of the disease's epidemiology and economic burden in this region. This could help to inform resource allocation and policy decisions regarding gonorrhoea prevention, screening and treatment. Overall, the study findings underscore the importance of monitoring and addressing the global burden of gonorrhoea, particularly in high-risk populations, and improving the availability of quality data for informed decision-making.

CONCLUSION

Although we identified many published studies in this review, population-based epidemiological studies were scarce, and only one economic study was identified from the LAC region. This indicates a need for more evidence on costs and resource utilisation associated with gonorrhoea, together with epidemiological studies representative of the general population, to form a more comprehensive view of the epidemiological and economic burden of gonorrhoea in LAC countries. Our findings will be useful to decision-makers considering potential health interventions to control gonorrhoea.

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Compliance with Ethics Guidelines. Ethics approval was not required as this study was based on published data and therefore did not involve human participants.

Data Availability. All data generated or analysed during this study are included in this published article/as Supplementary Material files.

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