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REVIEW

Population-based prevalence surveys during the Covid-19 pandemic: A systematic review

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Summary

Population-based prevalence surveys of Covid-19 contribute to establish the burden of infection, the role of asymptomatic and mild infections in transmission, and allow more precise decisions about reopen policies. We performed a systematic review to evaluate qualitative aspects of these studies, assessing their reliability and compiling practices that can influence the methodological quality. We searched MEDLINE, EMBASE, bioRxiv and medRxiv, and included cross-sectional studies using molecular and/or serological tests to estimate the prevalence of Covid-19 in the general population. Survey quality was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies. A correspondence analysis correlated methodological parameters of each study to identify patterns related to higher, intermediate and lower risks of bias. The available data described 37 surveys from 19 countries. The majority were from Europe and America, used antibody testing, and reached highly heterogeneous sample sizes and prevalence estimates. Minority communities were disproportionately affected by Covid-19. Important risk

Abbreviations: BioS, biological sample; JBI, Joanna Briggs Institute; N/A, not applicable; NPS, nasopharyngeal swabs; MERS, Middle East respiratory syndrome; P, prevalence; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RT-PCR, reverse-transcriptase polymerase chain reaction; S, sensitivity; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

of bias was detected in four domains: sample size, data analysis with sufficient coverage, measurements in standard way and response rate. The correspondence analysis showed few consistent patterns for high risk of bias. Intermediate risk of bias was related to American and European studies, municipal and regional initiatives, blood samples and prevalence >1%. Low risk of bias was related to Asian studies, nationwide initiatives, reverse-transcriptase polymerase chain reaction tests and prevalence <1%. We identified methodological standards applied worldwide in Covid-19 prevalence surveys, which may assist researchers with the planning, execution and reporting of future population-based surveys.

KEYWORDS

Covid-19, cross-sectional studies, epidemiology, infectious diseases, prevalence, SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

1 | INTRODUCTION

In December 2019, the third most important coronavirus in the twenty-first century (severe acute respiratory syndrome coronavirus 2 – SARS-CoV-2) was identified as the causative agent of SARS outbreak in Wuhan, Hubei province, China.^{1,2} SARS-CoV-2 has spread rapidly around the world leading the disease (Covid-19) to acquire pandemic status on 11 March 2020.³ As of 14 October 2020, there are ~38 million confirmed cases and ~1.1 million reported deaths in 216 countries, areas or territories. More than 50% of these cases were reported in the United States, India and Brazil, the worsthit countries.^{4,5}

According to the current evidence, the main form of SARS-CoV-2 spreading is through human-to-human transmission via respiratory droplets and contact routes.⁶ The standard diagnostic testing method is the reverse-transcriptase polymerase chain reaction (RT-PCR) test,^{7,8} which is able to detect current infections, and it is recommended for people with Covid-19 symptoms and for all close contacts of the confirmed cases. A complementary approach is to use antibody tests (e.g., point-of-care test or enzyme-linked immuno-sorbent assay) to detect a past infection and the production of antibodies (IgM and/or IgG) against SARS-CoV-2.⁸

Covid-19 causes diverse degrees of illness, ranging from asymptomatic infection to severe pneumonia.⁹ However, surveillance is only based on the confirmed cases, which can represent an underestimation of total cases due to non-testing in mildly affected or asymptomatic individuals. Population-based prevalence surveys can help to establish the disease epidemiology, the burden of infection, the role that asymptomatic and mild infections play in the transmission, and to enable precise evidence-based decisions about control and reopen policies, while no pharmacological intervention is available.¹⁰ Moreover, accurate estimates of the basic reproduction number, of exposed and susceptible populations, and the fatality rates can be obtained.^{11,12}

Statistical extrapolations will only be reliable for the population if (i) the sample of individuals is sufficient, random and representative

of the general population; (ii) if the measurements are standardized and (iii) if the tests used have adequate sensitivity and specificity, among other factors.¹³ For example, a recent systematic review and meta-analysis evaluated the diagnostic accuracy of serological tests in 40 studies. The conclusion indicated that the use of existing pointof-care serological tests is not supported by available evidence due to low performance.¹⁴ Thus, a critical evaluation of these parameters is necessary to verify the reliability of the population-based surveys of Covid-19.

We performed a systematic review to evaluate and summarize the main results regarding the Covid-19 prevalence obtained through population-based surveys, their reliability and biases. Our main aims were to evaluate the qualitative aspects of these studies and to compile practices that can influence positively or negatively the methodological quality.

2 | METHODS

2.1 | Registration and reporting

The protocol for this systematic review was registered on PROS-PERO (ID: CRD42020202186). Reporting was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Supplementary Checklist).

2.2 | Search strategy

Systematic literature searches for published and unpublished (preprint) articles were conducted from 15 July to 05 September 2020. MEDLINE (accessed via PubMed), EMBASE, bioRxiv and medRxiv databases were searched using the following controlled vocabulary heading and terms: 'seroprevalence', 'prevalence', 'serology', 'immunoassay', 'enzyme linked immunosorbent assay', 'real time polymerase chain reaction', 'cross-sectional study', 'population screening',

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TABLE 1 Characteristics of 37 population-based prevalence surveys during the Covid-19 pandemic until September 2020

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TABLE 1 (Con	itinued)											
Continent and region	Coverage	No. rounds	Period (2020)	Sample selection method	No. of tests	Biological samples	Test(s) used	Test validation ^a	Sensitivity (95% CI) ^b	Specificity (95% CI) ^b	Prevalence (95% CI)	Ref
Neustadt- am-Rennsteig/ Germany	Munici pality	1	May 12-22	All households from the community were invited	620	Pharyngeal washes Blood drawn	RT-PCR, 2 ELISAs, 2 CLIAs for IgG, 1 CMIA for IeG	Uninformed			RT-PCR: 0% Antibody: 8.4%	¥ ¥ I L ଞ୍
Hungary	Country	7	May 1-16	Random selection based on settlements using two-stage stratified strategy, and stratification by age from the nonulation resitry	10,575	Blood	RT-PCR Automated antibody test	Uninformed			68/10.000 (50-86)	_E Y
Iceland	Country	1	April 1-4	Random selection (not detailed)	2283	NPS	RT-PCR	NA	6 genome copies per reaction	No cross- reactivity observed	0.6% (0.3-0.9)	(27)
Castiglione d'Adda/ Lombardy/Italy	Munici pality	7	May 18-June 7	Random selection stratifying by sex and age classes from the municipal regitry list	509	NPS Serum blood drawn	CLIA for IgG	Uninformed			22.6% (17.2-29.1%)	(28)
Vó/Vêneto/Italy	Munici pality	7	Beginning of lockdown: February 21- 29,	Sampling from the majority of the municipality population	Beginning of lockdown: 2812	SdN	RT-PCR	٩	E gene: 5 genome copies per reaction		Beginning of lockdown: 2.6% (2.1–3.3)	(29)
			End of lockdown: March 7		End of lockdown: 2343ª				RdRp gene: 50 genome copies per reaction		End of lockdown: 1.2% (0.8–1.8)	
Luxembourg	Country	с	April 15-May 5	Random selection defined by the crossing of the 3 stratification variables through a deterministic random bit generator within strata	RT-PCR: 1842 IgA and IgG: 1820	NPS Blood drawn	RT-PCR CE-labelled ELISA for IgA/IgG	Yes, cohort of hospitalized patients	Combined (IgA/ IgG): 85.7%	Combined (IgA/ IgG) 99.5%	RT-PCR: 0.3% IgA: 11.0% IgG: 1.9% Both IgA and IgG: 1.6%	(30)
Slovenia	Country	L	April 20-May 1	Random selection of a representative sample using central population register data	1366	SdN	Two-target PCR- based assay	Yes	100%	100%	0.15% (posterior mean 0.18%, 95% Bayesian CI: 0.03-0.47; 95% highest density region 0.01-0.41)	(31)
Spain	Country	H	April 27-May 11	Random selection of households based on census tracts using stratified two- stage strategy and performed by national institute of statistics	61,075	Finger-prick blood Blood drawn	LFIA for IgG/IgM CLIA for IgG	Yes, RT-PCR -positive individuals for both tests	lgG: 82.1% IgM: 69.6%	lg G: 100% Ig M: 99%	Point-of-care test: 5.0% (4.7–5.4) Immunoassay: 4.6% (4.3– 5.0)	(32)
Barcelona/Spain	Munici pality	-	April 21-24	Random selection from individuals registered at a primary health care facility	311	Capillary blood	LFIA for IgG/IgM	Uninformed			5.47% (3.44-8.58)	(88)

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Ref	(34)	(35)	(36)		(37)	(38)	(39)	(40)	(41) nues)
Prevalence (95% CI)	Norra djurgårdsstaden: 4.1% (±3.5%) Tensta: 30% (±9.7%)	Set 1: 10.11% (7.31-12.92) Set 2: 10.84% (7.94-13.73)	R1: 4.8% (2.4–8.0) R2: 8.5% (5.9–11.4) R3: 10.9% (7.9–14.4) R4: 6.6% (4.3–9.4) R5: 10.8% (8.2–13.9)		4.06% (exact binomial: 2.84–5.60)	Raw: 1.5% (exact binomial: 1.1-2.0) Test adjusted: 1.2% (0.7-1.8) Census weighted: 2.8% (1.3-4.7)	3.1% (90% CI: 1.4-4.8)	2.5% (1.4-4.5)	22.7% (20.1-25.5) (Conti
Specificity (95% CI) ^b	100%-95.5%	96%-100% (depending on the antigen used)	100%		99.5% (99.2- 99.7)	4) 99.5% (99.2- 99.7)		%66	er 99.6%-100%
Sensitivity (95% CI) ^b	≥100%	100%	93% Ve		82.7% (76–88.4) s	82.8% (76.0–88.	94% (81–99)	93.2%	92.9%-100% (14 days aft symptom onset)
Test validation ^a	Yes, serum from negative and RT-PCR-positive individuals	Yes, compared to ELISA assays (Eurolmmun AG) against the S1 and N proteins	Yes, sera from pre-pandemic negative controls and RT-PCR-positi individuals		Yes, RT-PCR- positive individual	Yes, RT-PCR- positive individuals	Yes, RT-PCR- positive individuals	No, by CDC testing 1laboratory	No, by other studies
Test(s) used	LFIA for IgG/IgM	Multiplexed serology assay (developed in this paper)	Automated (ELISA)		LFIA	LFIA	Automated immunodiagnostic system	Automated immunodiagnostic system	CLIA for IgG
Biological samples	Uninformed	Finger-prick blood	Peripheral venous blood		Uninformed	Capillary blood	Serum	Plasma	Plasma
No. of tests	213 Norra djurgårdsstader 123 Tensta: 90	878 Set 1: 435 Set 2: 443	2766		863	3330	505	696	917
Sample selection method	Random selection (not detailed)	Random selection of adults in households and mail distribution of home-sampling kits	Random selection based on an already existing representative sample of the general population (bus santé study)		Random selection with stratification in subgroups based on age, sex, race, and ethnicity distribution	Facebook ads targeting a sample of individuals living within the county by demographic geographic characteristics and stratification	Random selection from landline and cell phone numbers and re-stratification by census designations	Random selection of households based on two-stage cluster strategy	Random selection of volunteers after stratification by ZIP code, age and gender within ZIP code
Period (2020)	June 17–18	April 01- May 31	April 6-May 9 (once every week for 5 weeks)		April 10–14	April 3-4	June 10-July 6	April 28-May 3	May 4-19
No. rounds	-	2	2		4	-	4	4	-
Coverage	Munici pality	Municipality	Municipality		County	County	State	County	County
Continent and region	Stockholm/ Sweden	Stockholm/ Sweden	Geneva/ Switzerland	North America	Los Angeles/ California/ USA	Santa Clara/ California/USA	Connecticut/ USA	DeKalb and Fulton counties/ Georgia/USA	Blaine/Idaho/ USA

TABLE 1 (Continued)

TABLE 1 (Co	ntinued)											
Continent and region	Coverage	No. rounds	Period (2020)	Sample selection method	No. of tests	Biological samples	Test(s) used	Test validation ^a	Sensitivity (95% CI) ^b	Specificity (95% CI) ^b	Prevalence (95% CI)	Ref
Indiana/USA	State	-	April 25-29	Random selection based on a list of residents derived from tax r eturns, and stratification using public health preparedness districts as sampling strata	3658	NPS Peripheral venous blood	RT-PCR CLIA for IgG	No, by manufacturer	100% (14 days after symptom onset)	99.6% (14 days after symptom onset)	RT-PCR raw: 1.74% (1.10-2.54) Antibody raw: 1.01% (0.76-1.45) Overall estimate: 2.79% (2.02- 3.70)	(4.2)
Baton Rouge/ Louisiana/ USA	Region	,	July 15-31	Random selection using a method developed by public democracy, choosing between residents with digital ads for recruitment, and re- stratification of volurteers by census designations	2138	NPS Blood drawn	RT-PCR Automated (qualitative immunoglobulin for IgG)	Uninformed			6.6%	(4.3)
Orleans and Jeferson Parishes/ Louisiana/USA	County	r.	May 9-15	Random selection based on a novel 2-step system developed by public democracy considering >50 characteristics, i ncluding social determinants of health and census population data	2640	NPS Blood drawn	RT-PCR Automated (qualitative immunoglobulin for IgG)	No. by CDC and other studies	100% (95.1–100) (17 days after symptom onset) (Bryan et al., 2020)	99.90% (Bryan et al., 2020)	Raw: 6,9% (6,0%0%) Census-weighted: 7,8% (7,8%-7,9%)	(44)
South America												
Barrio Mugica/ Buenos Aires city/ Argentina	Municipalit	× 1	June 10-July 1	Random selection using two-stage strategy using geographical areas determined by the department of statistic and census	873	Finger-prick blood	Automated (ELISA)	Yes, RT-PCR confirmed cases	95% (after 21 days of symptom onset)	100%	Weighted IgG: 53.4% (52.8-54.1)	(45)
Brazil	Country	H	May 14–21	Random selection of households based on census tracts from sentinel cities in all Brazilian states	24,995	Finger-prick blood	LFIA for IgG/IgM	No, pooled estimate based on four validation studies	84.8% (95% CI: 81.4-87.8)	99% (95% Cl: 97.8-99.7)	1.4% (1.3–1.6)	(46)
Espírito santo/Brazil	State	-	May 13-15	Random selection based on census tracts using most populous municipalities in the state and lesser populous municipalities	5775 Prevalence step: 4612 Extension step: 116:	Finger-prick blood 3	LFIA for IgG/IgM	No, by manufacturer	86.4%	97.63%	Prevalence step: 2.1% (1.67-2.52) Extension step: 0.26% (0.05-0.75)	(4)

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TABLE 1 (Con	tinued)											
Continent and region	Coverage	No. rounds	Period (2020)	Sample selection method	No. of tests	Biological samples	Test(s) used	Test validation ^a	Sensitivity (95% CI) ^b	Specificity (95% CI) ^b	Prevalence (95% Cl)	Ref
Maranhão/ Brazil	State	T	27 July- 8 August	Aandom selection of households based on census tracts in three stratified stages in four regions	3156	Serum	Automated CLIA for IgG/IgM	No, by other studies		99.7%	40.4% (35.6-45.3)	(48)
Teresina/ Piaul/Brazil	Munici pality	~	April 19- May 31 (1- week interval)	Aandom selection of households based on the registry of 78 basic health units and stratification by sex, age, and geographical distribution	6300	Uninformed	LFIA for IgG/IgM	No, by manufacturer	86%	866	R1: 0.56% (0.18–1.3) R2: 0.89% (0.39–1.75) R3: 1.44% (0.77–2.45) R4: 2% (1.19–3.14) R5: 3.78% (2.63–5.24) R6: 5.78% (4.3–7.3) R7: 8.33% (6.61–10.33)	(4.9)
Rio Grande do Sul/ Brazil	State	ო	April 11- May 11 (2- week interval)	Aandom selection of households based on census tracts using multi-stage sampling strategy in sentinel cities	13,111 R1: 4151 R2: 4460 R3: 4500	Finger-prick blood	LFIA for IgG/IgM	Yes, RT-PCR confirmed cases	84.8% (81.4- 87.8%) - pooled	99.0% (97.8- 99.7%) - pooled	R1: 0.048% (0.006-0.174) R2: 0.135% (0.049-0.293) R3: 0.222% (0.107-0.408)	(50)
São Paulo/Brazil	Munici pality	-	May 4-12	Random selection of households in six districts	517 Randomly-selected: 299 Cohabitants: 218	Serum blood drawn	CLIA for IgG/IgM	No, by other studies	IgM: 100% IgG: 100% (20 days after symptom onset)	IgM: 94.1% IgG: 99.5% (20 days after symptoms onset)	Census-weighted: 4.7% (3.0-6.6)	(51)
Baixada Santista/são Paulo/Brazil	Region	H	Uninformed	Aandom selection of households based on census tracts and stratification by age, gender and living conditions	2342	Uninformed	LFIA for IgG/IgM	Yes, RT-PCR confirmed cases after more than 14 days of symptoms			1.4% (0.93-1.93)	(2)
Abbreviations: 95% nasopharyngeal and "Repeated people b ^b lf test validation w ^c Sensitivity and spec	Cl, 95% co l oropharyr etween the 'as perform cificity repo	nfidence igeal sw: first an ed interi	interval; CLIA, chabs; R, Round. d second rounds. nally by the study the study or the	emiluminescent micropa or in a publication perfi reference cited, accordir	rticle immunoasse ormed by the sam ig to the Test val	ay; ELISA, enzym, e authors. N/A v idation' column.	e-linked immunoso vas considered whe	rbent assay; LFIA, latt en the RT-PCR metho	eral flow immuno d (gold standarc	aassay; NHS, N; aasaay; NHS, N;	ttional Health Service	NPS,

'severe acute respiratory syndrome coronavirus 2' and 'Covid-19'. These terms and their synonyms were combined using logical operators and adapted according to the searched database. Only articles published in English were retrieved. The complete search strategy for each database is on Table S1.

2.3 | Inclusion and exclusion criteria

The review included cross-sectional or repeated cross-sectional studies using molecular or serological tests to estimate the prevalence of Covid-19 in municipalities, regions, states or countries around the world. Studies were excluded based on the following criteria: (i) non-cross-sectional studies, (ii) studies with correlation between Covid-19 and other diseases or health determinants, (iii) non-random selection of participants (e.g., convenience sampling), (iv) inclusion of a specific group of participants only (e.g., with comorbidities, pregnant, elderly, healthcare workers, pediatric patients), and (v) non-human samples.

2.4 | Article screening and data extraction

Four pairs of authors (AMM and CLML, ABG and JGK, ASS and VBF, and GDC and JCP) independently reviewed the titles and abstracts, in parallel, and included publications identified by either author for full-text review. These authors also reviewed full texts to determine which publications met the inclusion criteria and then re-analysed the texts and supplemental materials to extract the following relevant information, when available: (i) authors, (ii) study location, (iii) coverage, (iv) study type, (v) random sampling method, (vi) period of testing, (vii) number of tests, (viii) biological samples, (ix) type of test used, (x) if test validation was performed, (xi) the test sensitivity and specificity, (xii) prevalence and (xiii) statistical methods (Table 1). Disagreements in the screening and data extraction were discussed among the reviewers and, if consensus cannot be reached, a third reviewer (ATW) made the ultimate decision.

2.5 | Survey quality

We assessed each survey quality by using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies.¹³ This tool evaluates nine domains: (D1) sample frame adequacy, (D2) recruitment method, (D3) sample size, (D4) study subjects and the setting, (D5) coverage, (D6) diagnostic methods, (D7) the reliability and standardization of measurements, (D8) statistical analysis, and (D9) the response rate. For each study, 'yes', 'no' and 'unclear' options were selected, meaning 'low', 'high' and 'unclear' risk of bias, respectively. The number of 'yes' answers to these nine domains was counted, with a higher number of yes representing less risk of bias. Graphs considering each risk of bias domain across all studies were prepared using the robvis R package v. 0.3.0.900.¹⁵

2.6 | Definitions

Additional objective criteria were adopted for the survey quality assessment. For D4, the prevalence estimates should be stratified by conventional sex and age classes minimally. For D5, 'no' was chosen when there was a lack of a subgroup representativity. If the response rate >70% or <70% with adequate sample size, 'yes' was chosen. The option 'unclear' was selected only if there was no information about the response rate in the article. For D6, a method was considered valid if the sensitivity >70%. For D7, self-sampling was considered as a practice of high risk of bias. In the case of a collection described by health professionals or trained individuals and using standardized methods, we assumed a low risk of bias. For D8, a minimum description of statistical methods was sufficient to classify the study as low risk of bias. For D9, if the response rate <70% without stratification or statistical management, the study was considered to have a high risk of bias. Response rate >70% or appropriate management of low response rate was related to a low risk of bias, while missing information about the proportion of tested in relation to the recruited individuals was associated with unclear.

2.7 | Data analysis

A correspondence analysis was performed to visualize the relationships among categories of the row and column variables in a lowdimensional graphic. The row variables (respective categories) were (i) study continent (Africa, Asia, Europe, North America and South America); (ii) coverage (country, region and municipality); (iii) biological samples (BioS) (uninformed, blood only, both swab and blood, serum/plasma, and swab only); (iv) test validation (external, uninformed, yes [internal] and RT-PCR [N/A (not applicable): goldstandard]); (v) test sensitivity (S) (<80%, 80%-90%, 90%-100%, unavailable and RT-PCR [N/A: gold-standard]). The column variables (respective categories) were (vi) prevalence (<1%, 1%-3%, 3%-5%, 5%–20% and >20%) and (vii) risk of bias (low [≤ 1 high risk], intermediate $[1 < high risk \le 3]$, and high [>3 high risk] (see Survey Quality). Two studies^{18,34} were split due to widely divergent prevalences reported in each part of the municipalities investigated. Therefore, despite the 37 studies included, 39 records were considered in this analysis. The PROC CORRESP from SAS Studio (Release 3.8, Enterprise Edition) available on the SAS OnDemand for Academics platform was used to perform the correspondence analysis.

3 | RESULTS

Of 49 full-text articles screened, we excluded 12 (Table S2), and identified 37 eligible for extensive review (Figure 1, Table 1). Of these, 23 (62.2%) were preprint, while 14 (37.8%) were peer reviewed and published. Fifteen articles (40.5%) were from Europe, 8 (21.6%) from North America, 8 (21.6%) from South America, 5 (13.5%) from Asia and 1 (2.7%) from Africa. The countries with the

vast majority of population-based prevalence study initiatives were the United States (n = 8; 21.6%), Brazil (n = 7; 18.9%) and the United Kingdom (n = 3; 8.1%). Importantly, 15 of the 16 studies in the Americas were conducted in the United States or Brazil, which are included in the TOP three of confirmed cases and deaths worldwide. In total, 19 countries had studies included in this analysis (Figure 2). Considering the coverage of these studies, 16 (43.2%) had regional (state/province/county) scope, 13 (35.1%) were restricted to municipalities and 8 (21.6%) were nationwide studies.

The vast majority of studies (n = 25; 67.6%) reported only antibody testing, while the exclusive use of RT-PCR was presented in 5 (13.5%), and both tests were conducted in 7 (18.9%) studies. The authors of 15 (46.9%) of the 32 studies that used serological tests reported their own validation test performance, while in 13 (40.6%), the validation performed by other studies or by the manufacturer was described. Excluding Wuhan's (China) screening programme¹⁷ that tested 9,899,828, at least 394,090 individuals were tested in the other 36 studies that reported the number of tests. However, this number was highly variable among studies (mean: 10,946.94, median: 1990, standard deviation (SD): 27,382.34). Considering the periods of these surveys, most of them were conducted between April and July 2020 (Figure 3).

Most studies (n = 35; 94.6%) presented low risk of bias overall, but only one had low risk of bias in all nine domains.³² Two studies showed overall unclear risk of bias.^{34,49} Apart from these, another three studies had a sum of high and unclear risk of bias higher than the low risk of bias^{16,20,27} (Figure S1). Considering the nine domains established and three possible answers (low, unclear and high), on average, 6.35, 1.43 and 1.19 of each option were chosen, respectively. The median values were 6.0, 1.0 and 1.0, while the SDs were 1.44, 1.26 and 1.08. Considering the sum of the results with some risk of bias (unclear and high), the mean, median and SD were 2.62, 3.0 and 1.46, respectively. Considering each domain in all studies, >75% low risk of bias across the studies was observed in five domains. On the other hand, three criteria (data analysis with sufficient coverage, measurements in standard way, and response rate adequacy) were adequate in <50% of the studies. The remaining domain (sample size) was adequate in \sim 70% of the studies (Figure 4).

Considering the analysis of correspondence performed (Figures 5 and S2) among seven main variables (continent, coverage, biological samples, test validation, sensitivity, prevalence and risk of bias), we found some important correlations. European, North- and South-American studies presented, in general, an intermediate risk of bias, while Asian studies tended to a low risk of bias. Regarding the coverage of the studies, regional and municipal studies presented an association with intermediate risk of bias, while nationwide studies were related to low risk of bias.

Studies that performed molecular tests on nasopharyngeal swabs (NPS) tended to have a low risk of bias, while those with blood samples were related to intermediate risk. Regarding prevalence, the majority of the studies with swab samples (RT-PCR) showed prevalence (P) < 1%, while studies using only blood, or swab and blood, exhibited P > 1%. Validation in serological tests had no significant

impact on the quality of studies, since both external and internal validation were related to intermediate risk of bias. On the other hand, the use of the gold standard (RT-PCR) was associated with low risk of bias. P < 1% was more frequent in studies with low risk of bias, while P > 1% was associated with intermediate risk of bias. Some categories presented in Figure 5 have not been reported here after manual examination due to their low frequency (e.g., Africa, BioS: Uninformed, S: <80%).

4 | DISCUSSION

We observed that important limitations of the studies were the low sample size and the low response rate (Figure 4). These factors influence heavily on reliable prevalence estimates.⁵³ Moreover, the recruitment by letter, by mail or online may play a significant role in reducing the response rate and inadequately address the target population.^{54,55}

For example, in the Icelandic study,²⁷ the authors discussed the small variation in the prevalence estimates between open invitation and random selection recruitments. However, the random selection methods were not detailed and the sample size to detect the estimated prevalence was not adequate (<2529 individuals).⁵⁶ In the Slovenian study,³¹ despite being considered nationwide, the sample size was 1366, which represented $\sim 7 \times$ less than necessary (10,179),⁵⁶ and there was no management of the low response rate (<50%). Some authors seem to have not been concerned with managing this issue because even though the response rate was low, there was still an adequate sample.^{23,35,36,40,42} Repeated crosssectional studies featured a widely distinct prevalence estimate on each round.^{29,36,49,50} This trend might be caused by the ascending curve of infected people, following the epidemic's natural course. Therefore, there was a need for different sample sizes for each period. Unfortunately, some studies did not yield adequate sample size in all rounds.49,50

The same proportion of studies validated their methods internally to report accuracy^{16,21,23,24,30,32,34-39,45,50,52} or used sensitivity and specificity given by manufacturers or other external studies.^{18-20,22,36,40-42,44-51} We also noticed that it is quite unclear if the field teams followed standardized protocols for the data collection and testing. The absence of complete information resulted in a loss of quality in the methodological analysis,¹³ and we speculate that one rationale would be the editing process of these articles, which were published as letters or comments. In some studies,^{23,24,35} the samples were collected by the participants themselves, which causes an increase in the number of discarded samples and can reduce the sensitivity, especially of RT-PCR, highly influenced by a well done sample collection procedure.⁵⁷

However, the studies presented several strengths to highlight. Valid methods consistently stated the identification of the condition and the manufacturer indicated this accuracy. The majority of the sampling methods was conducted appropriately regarding randomness, and the participants were well described and stratified, thus



FIGURE 1 PRISMA flowchart of the literature search

mitigating possible selection bias.^{18,19,24,26,28,30,33,37,39,43,44,46,48-51} A strong trend was observed in relation to the sampling procedures used in Brazil. All studies used a standardized household sampling method based on census tracts^{46–48,50–52} or healthcare units.⁴⁹

An interesting method of sample selection was the use of social network ads targeting individuals by demographic and geographic characteristics and stratification, which despite being convenient inserts the biases of technology usage and the participation of people most likely to be infected. However, in these cases, statistical management seems to have been adequate to accommodate the sampling issues in the prevalence estimates.^{38,43} Biases were also introduced when volunteers were recruited, but data analysis was conducted properly in these cases.^{41,43} Nevertheless, these practices cover up important methodological issues despite minimizing the biases of studies and they should be avoided.

Covid-19 has an extensive spectrum of manifestation, including asymptomatic infection, mild disease, severe pneumonia and death.^{2,9} Asymptomatic individuals may play an important role in viral transmission.¹⁰ The prevalence of asymptomatic infection in the community is still unclear, but essential to estimate the true Covid-19

prevalence. Generally, infection rates are calculated based on tests in symptomatic patients, and it may cause serious underestimations in prevalence.¹⁰⁻¹² This issue can be circumvented by surveying randomly recruited populations.¹¹

In fact, the asymptomatic rate of infection is quite hard to estimate. Nevertheless, we can consider some relevant observations. The proportion of symptom-free patients with Covid-19 in most studies is higher than SARS⁵⁸ and Middle East respiratory syndrome (MERS)⁵⁹ coronavirus epidemics, which was reported to lay between 0% and 7.5%. However, in the case of Covid-19, these rates were widely variable among PCR-positive and/or seropositive, ranging from 19.6%⁴⁷ to 69%.²³ The burden of the disease among symptomatic individuals was higher in older age groups,^{28,29} and there was no statistical difference in the viral load of symptomatic versus asymptomatic.²⁹ On the other hand, RT-PCR- and antibody-negative participants also reported symptoms,^{25,27} raising the possibility of infection by other respiratory aetiological agents. However, the comparability of asymptomatic rate estimates is hindered by different approaches applied, since the period of symptoms screening before the sampling ranged from 1 week²³ to several months.²⁶



FIGURE 2 Map of countries and specific regions with prevalence surveys. Red dots represent regions and cities where the initiatives were performed. In nationwide studies, the point was placed in the centre of the country



FIGURE 3 Timeline of population-based Covid-19 prevalence surveys conducted worldwide, with the duration of each survey and an overview of the most represented periods. Black dots on the left represent the date of the first confirmed case in the country of each survey

Some studies demonstrated a disproportionate seroprevalence in black communities,^{24,40,42–44,46,47,51} multiracial, Hispanic, Indigenous, and Asian persons,^{24,34,38,39,44,46} as well as in public-facing workers^{17,24,43} and slums population.^{18,45} These data show the disparities that minority communities face to access healthcare systems, arisen from a complex relationship of social, environmental, economic and structural inequities.^{60,61} Therefore, a priori knowledge of these trends in seroprevalence is essential for the sample design and for the instruction of field teams regarding protective measures in these surveys.

Sample frame appropriate Study participants sampled appropriately Sample size adequate Study subjects and setting described in detail Data analysis with sufficient coverage Valid methods for identification of condition Condition measured in standard reliable way Appropriate statistical analysis Response rate adequate or managed appropriately 0% 25% 75% 50% 100% Unclear Not applicable Low High

FIGURE 4 Risk of bias assessment summary table across all studies. *No weights were applied for different studies. †Not applicable was selected in 'sample size adequate' because the study had zero prevalence (impossible to calculate the sample size required)



FIGURE 5 Correspondence analysis of seven important variables of population-based Covid-19 prevalence surveys. The categories of row (continent, coverage, biological samples, test validation and sensitivity) and column (risk of bias and prevalence) variables are represented in blue and red, respectively. Light red, yellow and green ellipses represent high, intermediate and low risk of bias, respectively. BioS, biological sample; S, sensitivity; P, prevalence; VaIT: test validation

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In the study from Stockholm,³⁴ it was observed a significant difference in seroprevalence between the two areas (4.1% in middleto high-income suburb and 30% in lower income suburb). The authors related this high prevalence with cramped accommodation, which enhances cluster transmission, and with a majority of public-facing workers in the suburb. In Mumbai,¹⁸ the authors found a higher seroprevalence in the slums (54.1%) compared with non-slums (16.1%). Thus, it is discussed that the epidemic may be in advanced stages in slums due to higher population density.

The data from Brazilian studies^{46–52} suggest that Covid-19 pandemic was highly heterogeneous in the country, with rapid growth in North and Northeast regions, and slow progression in the South and Centre-West regions. These data demonstrate the impact of differences in demographics, urban infrastructure and income on the viral transmission and seroprevalence, emphasizing health inequality.^{62,63}

It is important to note that the data presented here are based on the articles until 5 September 2020. Therefore, more recent articles are not included in the analysis and a future investigation may identify whether or not these patterns will continue to be observed. In addition, previous preprint articles can be currently published. In general, we believe that the peer review process should contribute to increase the quality of these unpublished articles with a higher risk of bias.

We have decided not to conduct a meta-analysis because of the prevalence heterogeneity among studies and the different stages of pandemic faced in the countries and continents at the time of each survey. Thus, a summary measure of meta-analysis would not be able to generalize overall findings sufficiently. In contrast, we found that a correspondence analysis was more able to detect the correlation among variables.

In this analysis, few consistent patterns were observed for studies with a high risk of bias, indicating that particular methodological choices of each study may affect its quality, not choices that are being made in many studies worldwide. The high number of 'unclear' reported (n = 53; 15.9%) may be related to the accelerated speed of publication, the forgetfulness of these items in the writing process of the manuscript or the lack of knowledge of checklists like

the one used in this work.¹³ Therefore, we recommend the use of standardized checklists for the planning, execution and reporting of prevalence studies. Intermediate risk of bias was associated with American and European studies, municipal and regional initiatives, blood samples, P > 1%, and internal/external validation. Low risk of bias was associated with Asian studies, nationwide initiatives, P < 1%, NPS samples and RT-PCR tests. As correspondence analysis is a descriptive statistical analysis, we carefully examined the patterns observed and their frequency to detect only patterns that are effectively consistent.

5 | CONCLUSION

To our knowledge, this is the first systematic review to summarize Covid-19 prevalence surveys in the general population by correlating practices that can influence positively or negatively the methodological quality. Although the number of studies included were relatively low (n = 37) and the correspondence analysis presents some outliers due to the low representativeness of some categories, our findings allowed the identification of practices applied worldwide in Covid-19 prevalence studies associated with the methodological quality. These data may assist researchers in the planning, execution and reporting of future population-based surveys with high methodological quality.

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CONFLICT OF INTEREST

The authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Conceptualization: Claudia Elizabeth Thompson, Liane Nanci Rotta, Vinícius Bonetti Franceschi. *Methodology*: All authors. *Formal analysis*: Alvaro Vigo, Claudia Elizabeth Thompson, Liane Nanci Rotta, Vinícius Bonetti Franceschi. *Investigation*: Andressa Barreto Glaeser, Amanda de Menezes Mayer, Andressa Schneiders Santos, Ana Trindade Winck, Carem Luana Machado Lessa, Gabriel Dickin Caldana, Julia Gonçalves Küchle, Julia Gonçalves Küchle, Vinícius Bonetti Franceschi. *Data curation*: Vinícius Bonetti Franceschi. *Writing – original draft*: All authors. *Writing – review and editing*: Andressa Schneiders Santos, Ana Trindade Winck, Alvaro Vigo, Claudia Elizabeth Thompson, Liane Nanci Rotta, Paulo Ricardo Gazzola Zen, Vinícius Bonetti Franceschi. *Visualization*: Alvaro Vigo, Vinícius Bonetti Franceschi. *Supervision*: Ana Trindade Winck, Alvaro Vigo, Claudia Elizabeth Thompson, Liane Nanci Rotta, Paulo Ricardo Gazzola Zen.

DATA AVAILABILITY STATEMENT

The authors affirm that the processed data supporting our findings are available within the article and its supplementary materials. Raw data are accessible upon request to the corresponding author (Claudia Elizabeth Thompson).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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