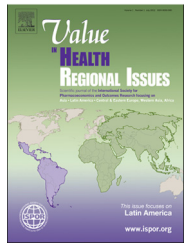
Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/vhri



Conducting and Disseminating Epidemiological Systematic Reviews in Latin America and the Caribbean: Pitfalls and Lessons Learned

Agustín Ciapponi, MD, MSc, Demián Glujovsky, MD, MSc, Sacha Alexis Virgilio, MSc, Ariel Esteban Bardach, MD, MSc, PhD*

Institute for Clinical Effectiveness and Health Policy, Center for Research in Epidemiology and Public Health, National Scientific and Technical Research Council Buenos Aires, Argentina

ABSTRACT

Objectives: To describe the experience, pitfalls, and lessons learned in conducting and disseminating epidemiological systematic reviews (SRs) in Latin America and the Caribbean between 2007 and 2016. **Methods:** We used a mixed-methods approach, including a descriptive cross-sectional study and a qualitative study of pitfalls and lessons learned. The following end points were analyzed: number of primary research studies included, country of origin, study design, risk of bias, citations in social media, number of researchers and experts involved, and time devoted by them to conduct SRs. Data for the qualitative study were collected through sessions with multiprofessional focus groups of the reviewers' core team held from February to March 2016. We performed a thematic analysis of the following domains: sources of information, evidence quantity and quality, statistical analysis, and dissemination of findings in both academic and social media. **Results:** A total of 19 SRs were produced, including 1016 primary research studies. Brazil (35%) and Argentina (19%) contributed the largest number of studies. The most frequent design was cross-sectional (35%). Only 27% of the studies included in the SRs were judged as having a low risk of bias. We identified key challenges at different stages of the process. We found substantial difficulties in all domains derived from the thematic analysis and proposed potential solutions for each of them. **Conclusions:** There are large gaps in epidemiological evidence from primary research, particularly from population-based studies. Special approaches are needed to identify, assess, synthesize, interpret, and disseminate epidemiological evidence from Latin America and the Caribbean.

Keywords: epidemiology, Latin America and the Caribbean, systematic reviews.

Introduction

Latin America and the Caribbean (LAC) is a large and cultural diverse region with 46 countries. The most commonly spoken languages are Spanish and Portuguese, but there are some English- and French-speaking countries as well. The population is estimated to be 642 million, which is projected to reach 673 million by 2020 [1].

Despite the progress made during the last several decades, LAC remains the most unequal region in the world [2]. The report published by the Economic Commission for Latin America and the Caribbean [2] in 2014 indicates that poverty remained stable, affecting 28% of the population, which corresponds to 167 million people living in poverty. Meanwhile, extreme poverty or indigence was 12% (2014).

During the last few decades, the region has experienced rapid and complex epidemiological changes. The rates of noncommunicable diseases and injuries have increased and there are many existing and emerging endemic diseases that are not completely controlled [3]. Most countries depend largely on external funding to sustain long-term research initiatives. This has limited the production of qualitative and quantitative research and has affected research priorities, which sometimes are not aligned with the region's most pressing social and health needs [4]. In spite of their limited resources, LAC researchers have made significant scientific contributions worthy of being analyzed and summarized through systematic reviews (SRs) to inform health and research decisions and to avoid future duplicate efforts.

There are many groups of researchers in the region that conduct SRs. A search of the Latin American and Caribbean Health Sciences Literature (LILACS database), performed in March 2011, identified 2241 studies potentially suitable to be classified as SRs, but only 15% fully met the criteria to be regarded as such and

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

*Address correspondence to: Agustín Ciapponi, Institute for Clinical Effectiveness and Health Policy, Center for Research in Epidemiology and Public Health, National Scientific and Technical Research Council, Dr Emilio Ravignani 2024, Ciudad Autónoma de Buenos Aires, Buenos Aires C1414CPV, Argentina.

E-mail: aciapponi@iecs.org.ar.

2212-1099$36.00 – see front matter © 2017 Published by Elsevier Inc. on behalf of International Society for Pharmacoeconomics and Outcomes Research (ISPOR).

http://dx.doi.org/10.1016/j.vhri.2017.07.011

a small percentage addressed epidemiological issues [5,6]. The Institute for Clinical Effectiveness and Health Policy (IECS) is a nongovernmental organization, affiliated with the University of Buenos Aires, founded by professionals from the medical and social sciences devoted to research, education, and technical cooperation with the goal of improving the efficiency, equity, quality, and sustainability of health care systems and policies in Argentina and Latin America. The institution has conducted many SRs focusing on evidence derived from LAC. The objective of this article was to describe our experience in conducting and disseminating epidemiological SRs of different diseases prevalent in LAC, focusing on the difficulties faced and the lessons learned.

Methods

We used a mixed-methods approach, including a descriptive cross-sectional study of completed SRs and a qualitative study focusing on pitfalls and lessons learned. The cross-sectional study described the epidemiological SRs conducted by the IECS between 2007 and 2016. The following end points were analyzed: number of studies included in the reviews; countries most represented; risk of bias; epidemiological design of studies; citations in literature and social media; number of participating researchers, experts, and librarians; and time devoted to conduct the SRs. In all cases, the risk of bias of the studies included in our SRs was assessed by an original tool containing the most important domains identified in methodological studies, including selection of participants, control of confounders, ascertainment of exposure and outcomes, and potential conflicts of interest [7–11].

The qualitative study summarized the main difficulties found and lessons learned during the completion and dissemination of the epidemiological SRs. Through a process of iterative group discussions held with all co-authors, we formulated a preliminary list of difficulties faced and lessons learned that was used to develop a semistructured questionnaire. Formal data collection was conducted through sessions with three multiprofessional focus groups held from February to March 2016, following standard methods [12]. During these three sessions involving SR researchers of the core IECS team, we included a total of seven physicians, a statistician, a librarian, and a journalist. The main domains discussed were sources and management of information, evidence quantity and quality, statistical analysis, and dissemination of findings in both academic and social media. One researcher led the discussion and an observer took notes. We performed a thematic analysis of the notes and the findings were organized in a matrix of domains, difficulties, and potential solutions to conduct and disseminate epidemiological SRs.

Results

Description of Analyzed SRs

We analyzed 19 SRs conducted by the institute to assess the field of epidemiology in LAC. These reviews included 1016 primary studies (median 34 studies, with a maximum of 168 and a minimum of 18). Fourteen of the SRs were already published [13–26].

Infectious diseases (n = 12) were the most frequent topics of study. The epidemiology of each condition was evaluated over the previous 10- to 15-year period, before the date of the search. Analyzed aspects included incidence, prevalence, fatality rate, morbidity, rate of hospitalization, and attributable direct and indirect costs. Five SRs focused on pediatric populations. The countries that contributed the most studies were Brazil (35%), Argentina (19%), and Mexico (9%) (see Table 1).

The most frequent epidemiological designs were cross-sectional studies (35%), surveillance reports (12%), and cohort studies (10%). Risk of bias was considered low only in 27% of the studies, and was moderate in 28% and high in 45%. Every SR searched MEDLINE, Embase, LILACS, and CENTRAL (Cochrane Library) with no language restrictions. To identify gray literature, we performed a generic and academic search on the Internet. Reports of the ministries of health of LAC countries, databases containing regional proceedings, annals of related specialties, books, and theses were searched. Authors of included studies were contacted for missing or additional information when necessary. In almost all SRs with meta-analysis we found I^2 to be greater than 90% for one or more outcomes.

All SRs concluded that further research was needed to fill the evidence gaps identified.

The mean impact factor of publications was 3.04 ± 1.51. In general terms, the number of references found in social media was very low, although we have to consider that some publications were very recent and had received more coverage in academic networks such as the Science Citation Index and ResearchGate (see Table 2).

On average, each SR required six researchers working for at least 5 hours per week over 8 months. The number of months required to complete each SR, however, varied significantly according to the number of hits that needed to be screened, the number of researchers allocated to the SR, and other context-related factors. The aggregate number of hours devoted to the SR process by researchers, experts, and librarians was 1049, 100, and 94 hours, respectively (see Table 3).

Qualitative Findings

The main qualitative findings are described in a matrix regarding difficulties and potential solutions to conduct epidemiological SRs in LAC for sources and management of information, evidence quantity and quality, statistical analysis, and dissemination of findings (see Table 4).

Discussion

The difficulties faced during the completion of SRs were caused by many factors. One is the information sources used. Health science research in LAC is not as developed as in the United States or Europe. Nevertheless, there is a considerable body of evidence that should be examined when conducting SRs [4]. Identifying LAC data in large databases such as MEDLINE, Embase, or Cochrane is very laborious and may be prone to bibliographic errors. Therefore, we had to design highly accurate filters to identify this information (see Annex 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2017.07.011).

LILACS is the most important database of scientific literature in the region. As of April 14, 2016, LILACS indexed 909 journals with 615,893 articles and 335,104 full texts, in addition to monographs and theses [1]. Checking this database to obtain data from LAC is essential. Nevertheless, using the LILACS database poses some obstacles. To perform an exhaustive search, the search must be conducted in the database's three languages—English, Spanish, and Portuguese. Even though the database has tutorials and descriptors for each language, developing a strategy to conduct an SR is very difficult without special training, especially for researchers from other regions [27–29].

In addition to the limitations of LILACS and other databases, the biggest challenge is finding the so-called gray literature, also

Table 1 – Main characteristics of epidemiological SRs included.

Condition	Studies (n)		Year of publication	Countries (n)	Brazil (n)	Argentina (n)	Mexico (n)	Others (n)	Risk of bias n (%)			More frequent designs*
	Retrieved	Included							Low	Moderate	High	
Rotavirus [15]	1655	168	1990–2009	168	49	16	15	86	60 (34)	6 (3)	111 (62)	C-S: 66; S: 16
Dengue [19]	2041	25	1995–2010	16	2	1	2	37	12 (48)	10 (40)	0	EE: 10; S: 9
Malaria [23]	3649	64	1990–2009	11	21	0	1	41	20 (31)	21 (33)	22 (34)	C-S: 24; S: 10
Influenza [18]	1080	31	1995–2008	10	9	5	2	15	8 (26)	1 (3)	22 (71)	Desc: 9; S: 6
Heart failure [26]	4792	145	1999–2014	13	93	33	9	15	22 (15)	85 (59)	35 (24)	C: 46; Desc: 39
Tuberculosis		68	2000–2010	10	28	0	7	14	13 (30)	7 (16)	24 (55)	C-S: 31; C: 12
Pneumococcal meningitis and bacteremia [22]	1257	39	2000–2010	11	13	5	0	24	11 (28)	23 (59)	5 (13)	S: 20; C-S: 11
Chronic disease due to arsenic [24]	430	47	2005–2014	1	0	47	0	0	4 (9)	16 (34)	16 (34)	C-S: 32; Eco: 10
COPD [20]	1185	26	2001–2010	10	12	3	10	14	9 (35)	6 (23)	11 (42)	C-S: 12; Desc: 6
Acute otitis media [13]	199	18	1988–2008	6	1	4	5	8	0	5 (28)	13 (72)	Desc: 8; C: 6
Pneumonia [17]	1220	69	1988–2008	15	17	11	4	36	29 (42)	6 (9)	34 (49)	Desc: 26; C-S: 21
Pneumococcal pneumonia [41]	704	23	2001–2010	9	7	5	1	13	5 (22)	7 (30)	11 (48)	S: 6; C: 5
Respiratory syncytial virus [21]	291	74	2000–2010	9	25	29	5	20	30 (45)	23 (34)	14 (21)	C-S: 26; C: 17
Varicella and herpes zoster [16]	484	26	2000–2010	9	6	6	0	14	7 (27)	1 (4)	12 (46)	S: 11; C-S: 6
Human papillomavirus [14]	990	79	1986–2009	18	21	15	16	31	0	19 (23)	65 (77)	C-S: 65; C-C: 13
Tobacco and income level [25]	1254	29	1989–2015	5	23	3	2	2	15 (54)	6 (21)	7 (25)	C-S: 28; Desc: 1
Inflammatory bowel disease	3444	25	2002–2015	9	12	1	4	8	2 (8)	14 (56)	9 (36)	S: 15; C-S: 7
Psoriasis [42]	1459	34	2001–2015	12	13	7	4	17	5 (15)	0	11 (32)	C-S: 22; Desc: 4
Primary immune thrombocytopenia	431	26	2000–2015	9	3	7	8	8	2 (8)	10 (38)	2 (8)	EE: 6; Desc: 9

COPD, chronic obstructive pulmonary disease; SR, systematic review.

* Labels: C, cohorts; C-C, case-control; C-S, cross-sectional; Desc, descriptive; Eco, ecologic; EE, economic evaluation; S, surveillance.

Table 2 – Dissemination of epidemiological SRs in academic and social media.

Condition	Date of publication	Journal	IF*	SNIP	SCI	Mentions				
						Twitter	Facebook	Google Scholar	ResearchGate	Mendeley
Rotavirus [21]	March 7, 2011	Rev Med Virol	5.574	ND	38	ND	ND	61	108	ND
Dengue [15]	December 1, 2013	Value Health Reg Issues	ND	0.285	8	ND	ND	11	70	ND
Malaria [12]	December 1, 2015	Value Health Reg Issues	ND	0.285	ND	1	1	1	48	6
Influenza [22]	December 5, 2012	Influenza Other Respir Viruses	2.201	ND	7	4	ND	11	30	14
Heart failure [16]	2016	Rev Esp Cardiol	3.792	ND	ND	ND	ND	ND	ND	ND
Tuberculosis	NA	–	ND	ND	ND	ND	ND	ND	ND	ND
Pneumococcal meningitis and bacteremia [18]	September 1, 2014	Pediatr Infect Dis J	2.723	ND	2	1	ND	7	46	11
Chronic disease due to arsenic [14]	December 15, 2015	Sci Total Environ	4.1	ND	3	1	1	5	121	6
COPD [19]	October 10, 2013	COPD	2.673	ND	5	ND	ND	11	159	ND
Acute otitis media [11]	June 10, 2011	Int J Pediatr Otorhinolaryngol	1.186	ND	14	1	1	31	35	17
Pneumonia [20]	January 1, 2012	Int J Infect Dis	1.859	0.984	17	1	ND	42	62	34
Pneumococcal pneumonia	NA	–	ND	ND	ND	ND	ND	ND	ND	ND
Respiratory syncytial virus [13]	April 24, 2014	Rev Med Virol	5.574	ND	2	ND	ND	3	142	ND
Varicella and herpes zoster [10]	December 1, 2012	Pediatr Infect Dis J	2.723	ND	3	2	1	6	37	9
Human papillomavirus [21]	October 4, 2011	PLoS One	3.234	ND	21	ND	ND	53	48	ND
Tobacco and income level [25]	2016	PAHO J	0.886	ND	ND	ND	ND	ND	ND	ND
Inflammatory bowel disease	NA	CRD42016035479	ND	ND	ND	ND	ND	ND	ND	ND
Psoriasis [42]	NA	CRD42016038325	ND	ND	ND	ND	ND	ND	ND	ND
Primary immune thrombocytopenia	NA	CRD42016039723	ND	ND	ND	ND	ND	ND	ND	ND

IF, impact factor (2014/2015); NA, not applicable; ND, not determined; SCI, Science Citation Index; SNIP, Source Normalized Impact per Paper; SR, systematic review.

Table 3 – Human resources needed to conduct SRs and initial number of bibliographical references identified.

Condition	References initially retrieved	Researchers involved (n)	Mean weekly hours	SR length (mo)	Total hours used in SR			
					Researcher	Expert	Librarian	Secretary
Rotavirus [21]	3110	10	4.4	7	2016	156	90	31
Dengue [15]	2401	11	5.8	11	2439	144	162	50
Malaria [12]	4616	10	4	10	1445	162	72	45
Influenza [22]	1092	7	5.8	8	1278	189	90	ND
Heart failure [16]	5145	5	5.2	7	783	0	68	31
Tuberculosis	61*	13	5.8	7	1566	184	81	32
Pneumococcal meningitis and bacteremia [18]	1218	5	4.5	5	423	45	45	23
Chronic disease due to arsenic [14]	471	5	4.5	7	513	135	135	45
COPD [19]	1860	6	4.5	10	1323	243	243	45
Acute otitis media [11]	195	4	4.5	8	837	72	72	36
Pneumonia [20]	1220	5	4.5	8	981	72	72	36
Pneumococcal pneumonia	704	5	4.5	5	423	45	45	23
Respiratory syncytial virus [13]	291	6	5.2	11	1566	144	162	50
Varicella and herpes zoster [10]	495	5	5.1	11	1269	144	162	50
Human papillomavirus [21]	1452	5	5.3	12	1053	162	108	54
Tobacco and income level	14327	4	6	6	648	0	45	23
Inflammatory bowel disease	4705	4	5	6	594	0	54	27
Psoriasis	2161	4	5	6	495	0	45	23
Primary immune thrombocytopenia	431	3	5	4	270	0	36	18
Average ± SD	2419 ± 3293	6.2 ± 3	5.0 ± 1	7.8 ± 2	1048.5 ± 587	99.8 ± 78	94.1 ± 55	35.7 ± 12

COPD, chronic obstructive pulmonary disease; SR, systematic review.
* One of the references is a report by the World Health Organization.

known as nonconventional, semipublished, or invisible literature. Although there are specialized sources for finding this literature, including GreyNet International, Open Grey, or the New York Academy of Medicine Grey Literature Report, they include very little evidence of LAC origin. This aspect of the search strategy is crucial to avoid publication bias [30]. Identifying gray literature is especially important because publishing an article in an indexed journal is more difficult for Latin American authors.

Accessibility and availability of data from official and non-official sources differ between the 46 LAC countries, and the volume of information can be substantial, thus making it virtually impossible to undertake an exhaustive search. Therefore, we complemented the search with strategies for generic Internet search engines that provide reasonably efficient ways to explore most sources of data, including ministries of health and non-governmental organization information. Nevertheless, a limitation of these strategies is that they are not entirely reproducible.

In addition to searching lists of references of important articles, we believe that contacting subject matter experts is essential to identify additional relevant studies and add value to the SR. Contacting key researchers or data holders can be difficult because of either their unresponsiveness or their lack of interest in sharing information.

In addition, lack of adequate search filters for different types of observational designs and the large quantity of references from additional sources resulted in a large number of references to screen in the first round. We therefore developed an online software to facilitate independent selection of articles by title/abstract and full text, allowing independent quality assessment and acquisition of basic quantitative outcomes [31]. This software, called the Early Review Organizing Software, has been very useful to us to manage and monitor processes more efficiently in the initial stages of the SRs.

Another aspect to consider is evidence quantity and quality. Because funding and opportunities are limited, wide gaps exist in the evidence obtained through primary research, and as a result secondary research, in the region. Therefore, as a region, we generally lack large epidemiological population-based studies from probabilistic samples that address the region's most relevant questions. Nevertheless, we must highlight the existence of important population-based registries of hospital events such as DataSUS (Brazil), DANE (Colombia), or Mexico's Health Secretariat, among others. In many cases, the absence of strong research networks results in a lack of standard practices, with the exception of some examples such as the microbiological laboratory database SIREVA, which contributes greatly to the

Table 4 – Difficulties and potential solutions to conduct epidemiological SRs.

Difficulties and lessons learned	Potential solutions
Sources and management of information	
• It is quite difficult to obtain epidemiological information from LAC. • LILACS, the core biomedical literature database of LAC, is not very intuitive and requires training for exhaustive searches. • The search in governmental and nongovernmental sources of the 46 countries of LAC is often inefficient because of their heterogeneity and the difficult access to many of them. • The contact with thematic experts, although difficult, is essential for a truly exhaustive search. • The use of software for SR management is key for the efficiency of the process.	• Sensitive strategies are required, preferably with the application of filters, for nonregional databases (see Annex 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2017.07.011). • The use of LILACS requires training for efficient and exhaustive searches using terms in English, Spanish, and Portuguese. • It is preferable to conduct the search in governmental and nongovernmental sources using strategies in generic Internet search engines. • No effort should be spared in contacting thematic experts to ensure an exhaustive search. • It is very worthwhile to use a software for SR management.
Quantity and quality of evidence	
• There are large gaps in evidence from epidemiological primary research in LAC. • Large population-based studies with adequate sampling are very infrequent. • There is a low proportion of epidemiological studies with low risk of bias. • There is a lack of universally accepted tools to assess the quality or risk of bias in observational studies used in epidemiology.	• Very sensitive and exhaustive searches should be conducted to identify the scarce relevant evidence available. • You can choose to use any of the validated tools to assess risk of bias but never use only summary measures of risk of bias. • We prefer to value the evidence using the most accepted domains in most risk-of-bias tools and report them separately to ensure transparency and adaptability to any of the validated tools.
Statistical analysis	
• The proportion meta-analysis is the proper approach to estimate summary prevalence or etiological fraction, requiring a previous transformation of the acrosine to stabilize the variance of the proportions. • There is a scarcity of prospective observational studies, and they frequently do not report incidence density that use person-time denominators required for the meta-analysis. • It is common to find very high levels of heterogeneity in meta-analyses of epidemiological studies in the LAC, even after applying methodological approaches to explain and reduce them.	• These types of analyses are less well known and statisticians are required to perform them. Nevertheless, there are statistical packages that allow performing the meta-analysis directly, without the need for previous transformations. • The control arm of clinical trials is an attractive source of appropriately measured incidence data. • The incidence density can be roughly estimated from the average follow-up of the patients. • All prespecified subgroup and sensitivity analyses, and eventually meta-regressions, should be performed to deal with the expected high levels of heterogeneity in these types of meta-analyses. • Given the still high statistical heterogeneity levels (and low or moderate clinical and methodological heterogeneity), we suggest performing meta-analysis using the random-effects model, which yields broader and therefore more conservative confidence intervals. • It is necessary to clearly report that the values to be considered in these cases are the extremes of the confidence intervals and not the central estimates, which can be misleading.
Dissemination of epidemiological SRs	
• Publications in peer-reviewed journals with a high impact factor do not guarantee adequate dissemination. • Even local journals with a lower impact factor could have more visibility for stakeholders. • Even when the reviews are widely disseminated, the epidemiology of diseases is ever-changing.	• Strategies that exceed mere publication or conference presentations are required to increase the dissemination of findings. • Social media and mass media could be key to the dissemination of the message. • It would be necessary to have repositories of SRs periodically updated to reflect the dynamic epidemiological situation of the region.

LAC, Latin America and the Caribbean; LILAC, Latin American and Caribbean Health Sciences Literature; SR, systematic review.

heterogeneity of clinical outcomes and methods. On the other side, in this "publish-or-perish world" many researchers are pushed to publish primary research with duplicate information or of very low quality (the so-called trash research) [32]. These limitations in primary research reduce the usefulness of SRs, regardless of the scientific rigor used to conduct the reviews.

Another difficulty—which is not specific to the region—is the lack of universally accepted tools to assess the quality or risk of bias of the observational/epidemiological studies (especially non-comparative studies) included in our SRs. In addition, many tools include quality of reporting elements that are not necessarily relevant to risk of bias. The identification of 86 specific risk-of-bias tools in an SR by Sanderson et al. [9] demonstrates this notable lack of consensus. Most tools included items for selection methods (92%), measurement of study variables (86%), design-specific sources of bias (86%), control of confounding (78%), and use of statistics (78%); only 4% addressed conflicts of interest [9]. For this reason, we designed our own tool on the basis of these elements, specifically those also highlighted in the Strengthening the Reporting of Observational Studies in Epidemiology checklist [10], to

report observational studies in epidemiology and in several methodological complementary articles [7–9,11]. We selected the fundamental items: selection of participants, control of confounding factors, measurement of exposure and outcomes, and conflicts of interest, with each item classified as low, moderate, or high risk of bias. For each study, we estimated a summary risk of bias using a classification algorithm (see Annex 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.vhri.2017.07.011). This summary risk is presented mainly for descriptive purposes, because it is a nonvalidated tool, but importantly for transparency, we always report the classification per criterion, which can then be used with any other grading tool. It is worth noting that the design assessed is relevant to our research question. As of note is our use of the control arms of clinical trials, used because of lack of incidence prospective studies, which we assess as noncomparative prospective observational studies.

Another aspect to consider is the statistical analysis. The methods used to conduct meta-analyses of epidemiological outcomes are less known than those used for intervention studies.

Proportion meta-analyses are suitable to estimate summary prevalence or etiological fractions. In these cases, we applied an arcsine transformation to stabilize the variance of proportions [33]. These analyses can be carried out directly with the statistical software package Stats-Direct (StatsDirect Ltd., England) or with STATA (StataCorp, College Station, TX), among others, after transformations.

To estimate incidence density, meta-analyses of incidence use a person-time denominator (e.g., number of cases per 100,000 person-year) [34]. Often, this information is not reported and it is therefore necessary to calculate this value by multiplying population size by mean follow-up. In addition to the aforementioned statistical packages, these calculations can be done with Comprehensive Meta-Analysis (Comprehensive Meta-Analysis (Version 2) [Computer software]. (2014). Englewood, NJ: Biostat. Available from http://www.comprehensive.com).

In addition to traditional methods, we calculate I^2 as a measure of the proportion of total variability attributable to between-study heterogeneity [35]. Whenever we found statistical, clinical, or methodological heterogeneity between studies but still considered meta-analysis appropriate, we used DerSimonian-Laird's random-effects model [36,37]. It is worth noting that before calculating summary measures it is necessary to conduct all prespecified analyses (and sometimes post hoc analyses) of subgroups and sensitivity (e.g., quality). These analyses allow the exploration of, and sometimes even the correction of, the causes of heterogeneity. In addition, if there are sufficient studies per outcome, meta-regression techniques can be used to identify the independent effect of each variable on the outcome. An I^2 of more than 75% is regarded as substantial heterogeneity and, therefore, performing a meta-analysis would be questionable [35]. Nevertheless, we believe that epidemiological studies deserve special consideration because of the frequency and severity of heterogeneity, as compared with experimental studies conducted under more controlled conditions, which usually cannot be rectified with the strategies described to explore heterogeneity. In these cases, we consider the following alternatives: 1) avoiding a meta-analysis and reporting data from individual studies only or just the maximum and minimum values, which is not very useful to inform decision-making processes; 2) providing a median and an interquartile range, which is more problematic than meta-analysis, because meta-analysis at least considers study weighting; or 3) conducting a meta-analysis under the random-effects model. We consider the option of using the random-effects model as the most useful because it considers variability across studies and generates wider confidence intervals, representing a more conservative approach. In instances of high levels of heterogeneity, however, the central estimate may be misleading and should be reported only for descriptive purposes. Here, the most significant value will be the confidence interval, which is more conservative (as previously explained, with the random-effects model the confidence interval will be wider but will be based on weighting studies). Because meta-analyses also report the results of individual studies graphically and numerically, we believe that this is the most informative of the three alternatives. Nevertheless, the potential limitations should be clearly explained to readers to prevent the central estimates from being regarded as the best estimates.

Regarding difficulties in the dissemination of SRs, a general publication issue is that LAC researchers prefer to send manuscripts to journals with higher impact factors. Because local journals usually have lower impact factors, authors often submit manuscripts previously rejected by international journals, and therefore the locally submitted/published articles may be of lower methodological quality. Frequently, international journals are not interested in LAC-specific issues or debates, and even if an article gets published in an international journal, dissemination to key stakeholders is limited by barriers such as the language of publication, lack of open access, or lack of awareness of the publication [38]. It would be very useful if local journals published articles in all three languages—Spanish, Portuguese, and English. For these reasons, several years ago we promoted an initiative called the Epidemiological Info Base of Latin America and the Caribbean [39,40], with the objective of presenting information (quantitative and geospatial) from SRs and meta-analyses about epidemiology, disease burden, and cost/use of resources for pathologies with high impact. We used an online, interactive, user-friendly interface that provided epidemiological information and performed meta-analyses to answer questions relevant to health decision makers, researchers, or professionals interested in the subject. Likewise, a database of SRs and economic evaluations published in the region was included, which provided useful bibliographic support. Unfortunately, lack of resources negatively impacted the sustainability of this initiative, just as it prevents the updating of SRs to reflect ever-changing epidemiological patterns. Fortunately, the Pan-American Health Organization hosts a geospatial Web page useful for many epidemiologically relevant diseases. Nevertheless, regardless of the relevance of the topic of study, not enough reports are available through social media to reach most stakeholders. The use of social media in LAC shows a secular incremental curve, which accounts for the low social media exposure garnered by our research. Regional research institutions are still getting acclimated to the use of social media. Perhaps to reach decision makers and researchers, more aggressive dissemination strategies aimed at mass media need to be developed.

Conclusions

Large gaps in epidemiological evidence from primary research exist, particularly in evidence from population-based studies with adequate sampling. The most frequent design was cross-sectional.

More sensitive strategies are needed, preferably strategies with filters, for nonregional databases. LILACS, the most important database in LAC, requires trained users to achieve exhaustive searches. Searches in official and nonofficial data sources of every LAC country are usually inefficient because of the heterogeneity of sources and access-related difficulties. Therefore, strategies involving generic Internet search engines are preferable. Contacting subject matter experts, although difficult, is essential to conduct truly exhaustive searches. The use of software to manage SRs is also key for an efficient process.

One of the difficulties identified is the lack of universally accepted tools to assess the risk of bias in observational studies. We prefer to assess separately the more widely accepted domains of the various published tools [9]. We found a low proportion of epidemiological studies with a low risk of bias.

With regard to the dissemination of SRs, publication in journals with high impact factors does not guarantee adequate communication and dissemination. Rather, local journals may offer more visibility to relevant stakeholders despite lower impact factors. Strategies should move beyond mere publication or presentation at congresses/conferences and should ideally include regular updates to repositories of SR data to reflect epidemiological changes in the region.

Acknowledgment

We thank Melissa Amyx for checking the English in the manuscript.

Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.vhri.2017.07.011 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

REFERENCES

[1] World Population Prospects: The 2015 Revision, DVD Edition. United Nations, Department of Economic and Social Affairs, Population Division (2015). 2016 http://esa.un.org/unpd/wpp/DVD/Files/1_Indicators%20(Standard)/EXCEL_FILES/1_Population/WPP2015_POP_F01_1_TOTAL_POPULATION_BOTH_SEXES.XLS. Accessed 14/4/2016.
[2] Economic Commission for Latin America and the Caribbean. Panorama Social de América Latina, 2014: http://repositorio.cepal.org/handle/11362/37626. Accessed 22/4/2016.
[3] Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095–128.
[4] Barreto SM, Miranda JJ, Figueroa JP, et al. Epidemiology in Latin America and the Caribbean: current situation and challenges. Int J Epidemiol 2012;41:557–71.
[5] Ciapponi A, Glujovsky D, Aleman A, et al. Identification of systematic reviews in LILACS. Auckland, New Zealand: Presented at: XX Cochrane Colloquium Scientific Evidence around the Globe, 2012.
[6] Rada G, Ciapponi A, Glujovsky D, et al. Using a collaborative online platform to identify systematic reviews in LILACS. Madrid, Spain: Presented at: XIX Cochrane Colloquium Scientific Evidence for Healthcare Quality and Patient Safety, 2011.
[7] Berra S, Elorza-Ricart JM, Estrada M-D, et al. Instrumento para la lectura crítica y la evaluación de estudios epidemiológicos transversales. Gac Sanit 2008;22:492–7.
[8] Fowkes FG, Fulton PM. Critical appraisal of published research: introductory guidelines. BMJ 1991;302:1136–40.
[9] Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. Int J Epidemiol 2007;36:666–76.
[10] von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007;370:1453–7.
[11] Wong WC, Cheung CS, Hart GJ. Development of a quality assessment tool for systematic reviews of observational studies (QATSO) of HIV prevalence in men having sex with men and associated risk behaviours. Emerg Themes Epidemiol 2008;5:23.
[12] Gill P, Stewart K, Treasure E, et al. Methods of data collection in qualitative research: interviews and focus groups. Br Dent J 2008;204:291–5.
[13] Bardach A, Ciapponi A, Garcia-Marti S, et al. Epidemiology of acute otitis media in children of Latin America and the Caribbean: a systematic review and meta-analysis. Int J Pediatr Otorhinolaryngol 2011;75:1062–70.
[14] Ciapponi A, Bardach A, Glujovsky D, et al. Type-specific HPV prevalence in cervical cancer and high-grade lesions in Latin America and the Caribbean: systematic review and meta-analysis. PLoS One 2011;6:e25493.
[15] Linhares AC, Stupka JA, Ciapponi A, et al. Burden and typing of rotavirus group A in Latin America and the Caribbean: systematic review and meta-analysis. Rev Med Virol 2011;21:89–109.
[16] Bardach A, Cafferata ML, Klein K, et al. Incidence and use of resources for chickenpox and herpes zoster in Latin America and the Caribbean—a systematic review and meta-analysis. Pediatr Infect Dis J 2012;31:1263–8.
[17] Gentile A, Bardach A, Ciapponi A, et al. Epidemiology of community-acquired pneumonia in children of Latin America and the Caribbean: a systematic review and meta-analysis. Int J Infect Dis 2012;16:e5–15.
[18] Savy V, Ciapponi A, Bardach A, et al. Burden of influenza in Latin America and the Caribbean: a systematic review and meta-analysis. Influenza Other Respir Viruses 2013;7:1017–32.
[19] Cafferata ML, Bardach A, Rey-Ares L, et al. Dengue epidemiology and burden of disease in Latin America and the Caribbean: a systematic review of the literature and meta-analysis. Value Health Reg Issues 2013;2:347–56.
[20] Ciapponi A, Lee A, Mazzoni A, et al. The epidemiology and burden of COPD in Latin America and the Caribbean: systematic review and meta-analysis. COPD 2014;11:339–50.
[21] Bardach A, Rey-Ares L, Cafferata ML, et al. Systematic review and meta-analysis of respiratory syncytial virus infection epidemiology in Latin America. Rev Med Virol 2014;24:76–89.
[22] Ciapponi A, Elorriaga N, Rojas JI, et al. Epidemiology of pediatric pneumococcal meningitis and bacteremia in Latin America and the Caribbean: a systematic review and meta-analysis. Pediatr Infect Dis J 2014;33:971–8.
[23] Bardach A, Ciapponi A, Rey-Ares L, et al. Epidemiology of malaria in Latin America and the Caribbean from 1990 to 2009: systematic review and meta-analysis. Value Health Reg Issues 2015;8:69–79.
[24] Bardach AE, Ciapponi A, Soto N, et al. Epidemiology of chronic disease related to arsenic in Argentina: a systematic review. Sci Total Environ 2015;538:802–16.
[25] Bardach A, García Perdomo HA, Ruano Gándara RA, et al. Niveles de ingreso y prevalencia de tabaquismo en América Latina: revisión sistemática y metaanálisis. Rev Panam Salud Publica 2016;40:263–71.
[26] Ciapponi A, Calderon M, Alcaraz A, et al. Burden of heart failure in Latin America: a systematic review and meta-analysis. Rev Esp Cardiol (Eng Ed) 2016;69:1051–60.
[27] Ciapponi A, Abdala V, Rada G, et al. Effective searching of LILACS database for systematic reviews (workshop). Hyderabad, India: Presented at: XXII Cochrane Colloquium Evidence-Informed Health: Opportunities and Challenges, 2014.
[28] Ciapponi A, Abdala V, Rada G, et al. Effective searching of LILACS database for systematic reviews (workshop). Presented at: XX Cochrane Colloquium Scientific Evidence around the Globe, Auckland, New Zealand, 2012.
[29] Abdala V, Rada G, Ciapponi A, et al. Effective searching of LILACS database for systematic reviews (workshop). Presented at: XIX Cochrane Colloquium Scientific Evidence for Healthcare Quality and Patient Safety, Madrid, Spain, 2011.
[30] Guyatt GH, Oxman AD, Montori V, et al. GRADE guidelines: 5. Rating the quality of evidence-publication bias. J Clin Epidemiol 2011;64:1277–82.
[31] Glujovsky D, Bardach A, García Martí S, et al. PRM2 EROS: a new software for early stage of systematic reviews. Value Health 2011;14:A564.
[32] Moher D, Glasziou P, Chalmers I, et al. Increasing value and reducing waste in biomedical research: Who's listening? Lancet 2016;387:1573–86.
[33] Freeman MF, Tukey JW. Transformations related to the angular and the square root. Ann Math Stat 1950;21:607–11.
[34] Rothman K, Greenland S. Modern Epidemiology. Philadelphia, PA: Lippincott-Raven, 1998.
[35] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
[36] Higgins J, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). London: The Cochrane Collaboration, 2011.
[37] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[38] Ciapponi A, Terrasa S. Necesitamos una publicación modelo de artículos originales en el campo de la Atención Primaria de la Salud? Arch Fam Gen Med 2004;1:6–10.

[39] Sguassero Y, Christensen C, Cuesta CB, et al. Evolución de pruebas parasitológicas y serológicas luego del tratamiento de la infección crónica por t. Cruzi: una revisión sistemática de estudios de seguimiento (en curso). Buenos Aires, Argentina: 4 Encuentro Internacional sobre Enfermedades Olvidadas y XVI Simposio sobre Control Epidemiológico de Enfermedades Transmitidas por Vectores, 2013.
[40] Ciapponi A, Glujovsky D, Bardach A, et al. Mapa Epidemiológico Latinoamericano. XI Reunión de la Red Cochrane Iberoamericana, XIII Congreso del LatinCLEN, I Jornada de Epidemiología Clínica. Lima, Perú: Universidad Peruana Cayetano Heredia, 2012.
[41] Bardach AE, Rey-Ares L, Calderon Cahua M, et al. Burden of Culture-Confirmed Pediatric Pneumococcal Pneumonia in Latin America and the Caribbean: A Systematic Review and Meta-Analysis. Value in Health Regional Issues. 2017;14:41–52.
[42] Hernandez-Vasquez A, Molinari L, Larrea N, Ciapponi A. Psoriasis in Latin America and the Caribbean: a systematic review. J Eur Acad Dermatol Venereol. 2017.