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REVIEW ARTICLE

A scoping review finds that guides to authors of protocols for observational epidemiological studies varied highly in format and content

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Abstract

Objective: To identify, characterize, and explore author guides on the role, format, and content of protocols for observational epidemiological studies, particularly cohort and case-control studies.

Study Design and Setting: Scoping review. We searched for guides in Medline, Embase, Google Scholar, 10 general medical and epidemiological/public health journals, and 10 major funders' websites. Two review authors extracted data. We classified guides as ''main'' based on word count and number of protocol items, described such guides more comprehensively and analyzed number of citations as an indicator of uptake.

Results: Thirty-nine protocol guides were included intended for cohort studies ($n = 3$), case-control studies ($n = 1$), or epidemiological studies in general ($n = 35$). Content and format were highly variable. Several guides had a broader focus than protocol development, e.g., also including study conduct and reporting. The guideline developmental process was often reported sparsely. One guide, intended for interventional studies, combined a systematic preparatory process with a primary focus on protocol development. We categorized seven guides as 'main'. In general the guides were cited infrequently, indicating limited uptake.

Conclusion: Guides for authors of protocols for observational epidemiological studies varied highly in format and content. We suggest that such guides should routinely be based on a systematic preparatory process.

Keywords: Observational epidemiological study protocol; Publicly available protocols; Study registration; Analysis plan; Observational epidemiological study; Scoping review

1. Introduction

The protocol for a research study is important as it is the core document for the scientific and practical planning of a study, as well as a foundation for its conduct, analysis, and reporting. When publicly available the study protocol can be used for appraisal, allowing others to evaluate the relevance and reliability of the planned study [1].

Public availability of a study protocol is especially important in the context of risk of selective reporting of outcomes, also known as p-hacking, data mining, cherry picking, or data dredging [2]. Selective reporting of ''positive results'' and selective nonreporting of ''negative results'' poses a major threat to the reliability of research results [3−5], increases research waste [6], and undermines the credibility of the scientific process. Public availability of a study protocol and its analysis plan provides an incentive for researchers to adhere to the plan and provides interested parties with the opportunity to directly compare the

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What is new?

Key findings

- We identified 39 guides for authors of protocols for observational epidemiological studies.
- The content and format of the guides varied considerably. Most guides addressed general epidemiological studies, and most did not focus exclusively on protocol development. Only one guide was highly cited, and this was a book on case-control studies, where the role of the protocol was a tangential aspect.
- The reporting of the guideline's development process was often absent or sparse.

What this adds to what was known?

- There exist several guides for authors of protocols for observational epidemiological studies, but they vary in content and format, are generally not cited often, and the development process is rarely described in detail.

What is the implication and what should change?

- We suggest that guides of protocols for observational epidemiological studies should be based on a systematic preparatory process.

published results of a study with its planned analyses, either informally or as part of a formal assessment of risk of bias in studies included in a systematic review [7−9].

Selective outcome reporting within a study is closely related to selective publication of entire studies (i.e., publication bias), often combined in the overarching concept of reporting bias [10]. Trial registries, e.g., ClinicalTrials.gov, provide an incentive for publication of registered "negative" studies, and provide interested parties with an opportunity to identify (e.g., in the context of a systematic review) registered but unpublished studies. The information on outcomes and analysis provided in trial registries overlaps to some degree with the full analysis plan of a protocol but will typically be incomplete [11].

Study protocols, and selective outcome reporting, have not been investigated much within observational epidemiology [12]. There has been little tradition for publishing protocols, though that may slowly be changing. Historically, there has been little consensus on whether publicly available protocols and study registration should be encouraged [12]. Some have argued that public availability of the analysis plan will reduce risk of selective outcome reporting [13], and that study registration will mitigate risk of publication bias [12−16]. Others have argued that public availability of protocols and study registration will create a new layer of bureaucracy, which would needlessly take up resources, and that researchers will lack flexibility in their analysis due to the fear of being labeled data dredgers [17]. There is also a case for emphasizing the difference between randomized trials, where data can be collected in a structured way and fitted to a predefined analysis framework, and observational epidemiological studies, where data often are collected in a less structured way, and data analysis may need to be more interactive [17,18].

It seems important to reduce risk of selective outcome reporting also in observational epidemiological studies, while keeping in mind the uniqueness of such studies. A relevant basis for this quest is to explore the role, format, and content of protocols in observational epidemiology, including any guidance provided to protocol authors. We have found no review of such guidance.

We therefore thought it interesting to identify, characterize, and explore author guides on the role, format, and content of protocols for observational epidemiological studies−particularly cohort and case-control studies. Further, we also wanted to describe in more detail the specific guidance on analysis plan, registration, and public availability of protocols.

2. Methods

2.1. Type of review

A scoping review [19].

2.2. Definition

Following "A Dictionary of Epidemiology" [20] we defined observational epidemiological studies as those that involve: "the use of epidemiological reasoning, knowledge, and methods in studies that are nonexperimental. Epidemiological studies and programs (e.g., surveillance) in which main conditions (e.g., exposure) are not under the direct control of the researcher." Such studies include, e.g., cohort, case-control, or cross-sectional studies, as well as interrupted time series or controlled before after studies. According to this definition observational epidemiological studies can investigate effects of exposure as well as interventions. Randomized trials fall outside this definition, because they are experimental in nature (though they may be regarded epidemiological in a broad sense).

2.3. Eligibility criteria

We included guides that made suggestions on the role, format, or content of observational epidemiological study protocols. We included guides in any format, e.g., guidelines, sections in textbooks, journal articles, or sections on journal websites or funder websites. Guides in any lan-

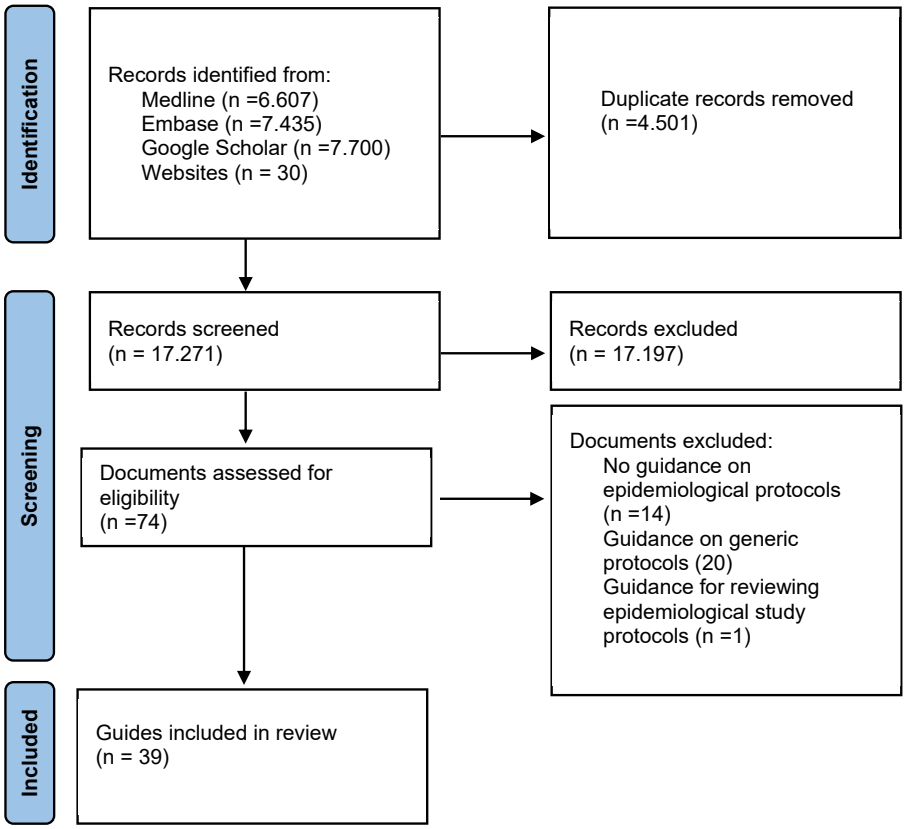

Fig. 1. Flowchart of records, documents, and included guides.

guage and with any publication year were eligible.

If a guide solely contained short remarks (i.e., one or two lines) it was excluded. We also excluded guides that provided guidance for randomized controlled trials or simply were not specified for epidemiological studies, i.e., generic protocol guidance.

2.4. Search strategy and information sources

We searched Medline, Embase, and Google Scholar. We also searched websites of the top 10 funders of health research based on their annual budget [21], and the top 10 general medical journals and the top 10 epidemiology/public health journals ranked according to 2020 Web of Science Journal Impact Factor (see Appendix A). All journals and funders were contacted by e-mail.

In a full-text search (i.e., Google Scholar) the first 100 hits were systematically screened. Additionally, a snowball search—a search of the references, of forward citation (meaning a search of the articles that have cited the included document), and similar articles—of all included guides were performed. One reviewer (D.M.) screened title and abstract for eligibility, followed by a full-text review of eligibility. The citations were managed with Endnote X9 and screened through Covidence.

2.5. Data extraction

We extracted basic descriptive information from each guide: title, authors, publication year, country, journal, document type (e.g., book or article), study type (cohort or case-control, other study types were labeled general epidemiological studies), aim, context of guidance, funding/conflict of interest. We extracted data on whether the primary focus of the guide was protocols or whether some other focus was primary, e.g., general epidemiological guidance; whether the guidance was for reporting of the protocol or guidance on the content of the protocol; and any information on development process.

We extracted ad verbatim quotes from author guides on the role, format, and content of protocols, with special emphasis on analysis plan, registration, and public availability of protocols. The extraction was done independently by two authors (D.M. and A.F.) with a third (A.H.) serving as an arbiter.

2.6. Categorization and analysis

Based on the extracted information, we categorized the guides into recommendation, checklist, or template. A guide was categorized as recommendation if it used regular prose, as checklist if it provided a list of items to include in the protocol, and as template if it provided blank spaces to

Table 1. Characterization of guides

Guides[a]	Type[b]	Format	Focus[c]	Guidance[d]	Words[e]	Citation[f]	Protocol items[g]
Main guides							
GE[h]							
MCRI 2019 [26]	Temp.	Website	Protocol	Content	11,540	n/a	26 (100)
Andrews 2016 [27]	Recom.	Article	Other	Content	1821	118 (24)	23 (88)
Philadelphia 2020 [28]	Temp.	Website	Protocol	Content	7426	n/a	22 (85)
WHO 2021 [29]	Temp.	Website	Protocol	Content	4529	11 (11)	22 (85)
Wang 2022 [30]	Temp.	Article	Protocol	Content	5963	0 (0)	21 (81)
Fronteira 2013 [31]	Recom.	Article	Protocol	Content	2291	3 (1)	18 (69)
UCLH 2010 [32]	Recom.	Website	Protocol	Content	1753	n/a	18 (69)
Not main guides							
Cohorts							
Berger 2009 [33]	Recom.	Article	Other	Content	338	375 (31)	14 (54)
Berger 2012 [34]	Recom.	Article	Other	Content	345	217 (24)	16 (62)
Velentgas 2013 [35]	Recom.	Book	Protocol	Content	2433	261 (33)	10 (38)
Case-control studies							
Schlesselman 1982 [36]	Check.	Book	Other	Content	1206	5803 (149)	14 (54)
GE							
Alba 2020 [37]	Recom.	Article	Other	Content	1710	13 (7)	17 (65)
Alberta 2009 [38]	Temp.	Website	Protocol	Content	1387	n/a	15 (58)
Ali 2013 [39]	Temp.	Website	Protocol	Content	1432	0 (0)	16 (62)
Altpeter 2005 [40]	Recom.	Article	Other	Content	509	25 (2)	19 (73)
Andrews 1996 [41]	Recom.	Article	Other	Content	850	35 (1)	20 (77)
Bailey 1991 [42]	Recom.	Article	Other	Content	778	22 (1)	20 (77)
Bassel 2019 [43]	Recom.	Website	Protocol	Content	928	0 (0)	18 (69)
Botha & Yach 1987 [44]	Recom.	Article	Protocol	Content	952	3 (1)	8 (31)
Cafri & Paxton 2018 [45]	Recom.	Article	Other	Content	594	3 (1)	4 (15)
Cook 1991 [46]	Recom.	Article	Other	Content	1141	10 (3)	14 (54)
ECDC 2014 [47]	Check.	Website	Protocol	Content	445	n/a	14 (54)
EMA 2012 [48]	Recom.	Website	Protocol	Content	934	5 (1)	20 (77)
EMA 2017 [49]	Recom.	Website	Other	Content	1259	n/a	19 (73)
ENCePP 2018 [50]	Check.	Website	Protocol	Content	986	27 (3)	18 (69)
ENCePP 2020 [51]	Recom.	Website	Protocol	Content	737	n/a	17 (65)
FDA 2005 [52]	Recom.	Website	Other	Content	191	15 (1)	7 (26)
FDA 2013 [53]	Recom.	Website	Other	Content	325	1 (1)	13 (50)
Goldberg 2007 [54]	Recom.	Article	Other	Content	1385	2 (1)	18 (69)
Goldin & Sayre 1996 [55]	Recom.	Article	Other	Content	527	10 (1)	12 (46)
Goodman 2020 [56]	Recom.	Article	Other	Content	116	4 (2)	8 (31)
Hoffmann 2019 [57]	Recom.	Article	Other	Content	1639	71 (36)	15 (58)
Rosenthal 2014 [58]	Recom.	Article	Protocol	Content	1425	15 (2)	20 (77)
Schnetzler 2012 [59]	Recom.	Article	Other	Content	155	1 (1)	13 (50)
Swaen 2018 [60]	Recom.	Article	Other	Content	369	18 (6)	13 (50)
Sydney 2021 [61]	Temp.	Website	Protocol	Content	1478	n/a	21 (81)
Vray 2000 [62]	Recom.	Article	Other	Content	185	0 (0)	7 (27)
Wang 2021 [63]	Temp.	Article	Other	Reporting	4161	55 (55)	16 (62)
Yang 2010 [64]	Recom.	Article	Other	Content	178	173 (16)	9 (35)

[a] Status as main guides was based on word count (≥1500) and protocol items addressed (≥18).
[b] Type of guidance provided by the guides: recommendation (recom.), template (temp.), or checklist (check.).
[c] Primary focus of the publication could be protocol (only) or general epidemiological research practices (including the protocol).
[d] Does the guide address the content or reporting of the observational epidemiological study protocol.
[e] Only words used in guidance on observational epidemiological protocol was counted.
[f] Total number of citations to the publication with yearly citation in parathesis. n/a: not applicable, e.g., websites not included in Google Scholar.
[g] Number of protocol items addressed by the document and percent (%) in parathesis (the protocol items were developed based on the SPIRIT guidelines for clinical trials protocols and the STROBE guideline for epidemiological studies).
[h] GE: General epidemiological consist of guides that are on epidemiology in general or guides for other study types than cohort and case-control studies.

Table 2. Protocol items

Protocol items[a]	*n* (%)[b]
Title	17 (44)
Study registration	17 (44)
Funding	15 (38)
Roles and responsibilities	20 (51)
Background and rationale	35 (90)
Specific objectives	38 (97)
Study design	39 (100)
Study setting	18 (46)
Eligibility criteria	31 (79)
Outcomes	29 (74)
Participant timeline	28 (72)
Sample size	33 (85)
Recruitment	16 (41)
Data collection	31 (79)
Data management	29 (74)
Analyses plan	39 (100)
Bias and confounding	31 (79)
Harms	14 (36)
Ethical considerations	20 (51)
Protocol amendments	23 (59)
Informed consent	20 (51)
Confidentiality	17 (44)
Declaration of interests	10 (26)
Access to data	6 (15)
Limitations	19 (49)
Dissemination and communication	21 (54)

[a] Protocol items for observational epidemiological protocols were developed partly from SPIRIT guidelines for protocol items in randomized controlled trials and, for items unique to epidemiological studies, from the STROBE guideline.

[b] n was the absolute number of documents which addressed each item.

be filled in, accompanied by some guidance. We analyzed citations (both total and per year) using Google Scholar (dated November 2022) and checked whether protocol format and content in guides were based on a systematic preparatory development process following a defined methodology that included, e.g., synthesis of previous guides (search procedures, findings, and synthesis process); a Delphi process (or other broad consultation with stakeholders); and a face-to-face meeting (in person or online).

We categorized the guides according to a standardized system of protocol items. These protocol items were derived from the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist [22] and from the Strengthening the Reporting of Observational studies in Epidemiology reporting guideline [23] for items unique to observational epidemiological studies.

We sorted the guides into two groups—main and not-main—based on length (≥1500 words) and protocol items (i.e., number of protocol items ≥18). Then we characterized the main guides in more detail.

Finally, we noted if guide characteristics differed according to publication platform (e.g., book, website, or articles).

2.7. Reporting, conduct, and protocol

The reporting of this review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for scoping reviews [24] and the conduct adheres to the Joanna Briggs Institute's guide for scoping reviews [25]. The study protocol can be found in Appendix H.

3. Results

3.1. Search

The search in Medline, Embase, and Google Scholar resulted in 30 included guides. The websites of top 10 medical journals, top 10 epidemiological journals, and top 10 funders resulted in two inclusions; 22 of 30 responded to our e-mail without providing any new inclusions. Lastly, a snowball search of all the included guides resulted in another seven guides included, resulting in a final inclusion of 39 guides (Fig. 1). The Google Scholar search identified all websites, all books, and some articles; the Medline, Embase, website, and snowball search identified only articles.

3.2. Basic characterization of included guides

The author guides were published from 1982 to 2022 (median publication year 2013), and eight (21%) guides were published from 2018 to 2022. The guides were categorized as recommendations ($n = 28$), templates ($n = 8$), and checklists ($n = 3$) (Table 1). The guides focused on different study types: cohort studies ($n = 3$), case-control studies ($n = 1$), and general epidemiological studies ($n = 35$). The general epidemiological studies were subdivided into generic epidemiological studies ($n = 22$), "pharmacoepidemiologic" studies ($n = 7$), "nonintervention" studies ($n = 2$), "cohort event monitoring" studies ($n = 1$) (i.e., a standard method of surveillance of newly approved drugs), and "observational intervention" studies ($n = 3$). Seventeen of the guides in the generic epidemiological category only specified that the guides were for "epidemiological" or "observational" studies; five guides, however, specified that cohort, case-control, and cross-sectional studies were examples of "observational" or "epidemiological" studies.

Thirty-eight guides provided guidance on content while one provided guidance on reporting of protocols.

Four guides had zero citations, eight guides were not citable (not included in Google Scholar), 18 guides were cited less than 10 times per year, nine guides were cited more than 10 times per year, and the most cited (and oldest)

guide (Schlesselman 1982) [36] was cited 149 times per year. The median number of total citations was 11 (interquartile range 2−35), and the median number of citations per year was 2 (interquartile range 1−16) (dated November 2022).

3.3. Guides on role of study protocol

Nineteen guides addressed the methodological role of protocols for observational epidemiological studies (see Appendix B). Several quotes indicated that the role of the protocol was ''fundamental'' to research, as a ''road map'' or ''guide'' for the researchers, and as designating an a priori hypothesis to prevent ''data mining.'' Though mostly the documents differed on which aspects of the role of the protocol they emphasized.

3.4. Guides on format of study protocol

Thirty-one guides addressed the order of items, being largely in agreement, though with some differences, mainly whether title, abstract, references, appendix, and registration should be included (see Appendix C). None provided guidance on the total length and only sporadically on the length of specific segments of the protocol.

3.5. Guides on content of study protocol

We developed 26 protocol items (Table 2). There was a high degree of variation on items between guides. The median of items per guide was 16 (interquartile range 13−20). The guide that addressed most protocol items was Murdoch Children's Research Institute (MCRI) 2019 (n = 26; 100%) and the guide that addressed fewest items was Cafri & Paxton 2018 (n = 4; 15%) (Table 1). Both ''study design'' and ''analyses plan'' were addressed in all guides (n = 39; 100%), and ''access to data'' was the least addressed protocol item (n = 6; 15%).

3.6. Guides on analysis plan in study protocols

We found some variation on the level of detail from a single sentence to more than 1000 words (see Appendix D). The rationale behind the text was similar: planned statistical analysis, power calculation, statistical software used, analysis of primary and secondary outcomes, strategy for confounders and effect modifiers, and how to deal with missing data.

3.7. Guides on registration and public availability of study protocols

We found quotes on study registration and public availability of protocols in thirteen guides (see Appendix E). Four of these explicitly endorsed public availability of protocols, whereas eleven mentioned and endorsed study registration. None of the documents advised against public availability of protocols or study registration. The reasons given were to enhance ''transparency'' and limiting ''reporting bias'' and ''publication bias.''

3.8. Characterization of main guides

We characterized seven author guides as main: MCRI 2019 [26], Andrews 2016 [27], Philadelphia 2020 [65], World Health Organization 2021 [29], Wang 2022 [30], Fronteira 2013 [31], University College London Hospitals 2010 [32] (Table 3).

3.9. Systematic preparatory process

The developmental process behind the guides was often reported sparsely and varied from some guides that were based on a full systematic preparatory process, e.g., Wang 2022, to guides that included some elements, e.g., Berger 2009 [33], to guides that reported nothing on how they were developed (see Appendix F).

3.10. Analysis of publication platform

Guides published as articles, websites, and books had an average word count of 1247, 2357, and 1820, respectively, and an average number of protocol items of 15, 18, and 12, respectively.

4. Discussion

We identified 39 author guides on the role, format, and content of protocols for observational epidemiological studies. There was considerable variation between guides on format and which items they addressed, though with convergence on two items: study design and statistical methods. The reporting of the developmental process was often sparse. Only Wang 2022 [30] combined a systematic preparatory process with a primary focus on protocol guidance. Most guides agreed that the protocol minimized the risk of selective outcome reporting, and four guides recommended public availability of protocols. We categorized seven guides as main.

To our knowledge there are no previous published reviews of guides to authors of observational epidemiological study protocols. Halm et al. [66] developed a checklist from a literature search in PubMed and on various websites. However, this checklist has not been peer-reviewed and the aim was to help reviewing epidemiological study protocols not authoring them.

Tetzlaff et al. [67] conducted a systematic review of guidelines for randomized clinical trial protocol content. They found 40 eligible guidelines with a high degree of variation on items (called ''concepts'' in their review) with no guideline containing all items and very little consensus on items such as primary outcome, allocation concealment, conflicts of interest, and trial registration. This corresponds

Table 3. Characteristics of main guides[a]

Guides	MCRI 2019	Andrews 2016	Philadelphia 2020
Guide type	Template	Recommendation	Template
Format	Website	Article	Website
Guide for study type[b]	''Observational study''	''Pharmaco-epidemiological studies''	''Observational study''
Examples of study sub-types[c]	Cohort	Cohort	Cohort
	Case-control	Case-control	Case-control
	Cross-sectional	Cross-sectional	Cross-sectional
Clinical area	Pediatrics	General	Pediatrics
Primary focus of publication[d]	Protocol	Good research practice	Protocol
No. of protocol items[e]	26 (100)	23 (88)	22 (85)
No. of words[f]	11.540	1.821	7.426
No. of citations[g]	n/a	90 (18)	n/a
Country of origin	Australia	International	USA
Language	English	English	English
Initiated by	Murdoch Children's Research Institute	International Society for Pharmaceutical Engineering	Institutional Review Board at CHP

CHP, children's hospital of philadelphia; ISPE, international society for pharmaceutical engineering; ISPOR, professional society for health economics and outcomes research; MCRI, murdoch children's research institute; UCLH, university college london hospitals; WHO, World Health Organization.

[a] Status as main guides was based on word count (≥1500) and protocol items addressed (≥18).

[b] Description of overall study type from the guide.

[c] Examples of observational epidemiological study subtypes explicitly mentioned in the guide.

[d] Primary focus of the publication could be protocol (only) or general epidemiological research practices (including the protocol).

[e] Number of protocol items addressed by the document and percent (%) in parathesis (the protocol items were developed based on the SPIRIT guidelines for clinical trials protocols and the STROBE guideline for epidemiological studies).

[f] The word count is based only on the part of the documents that contained guidance on the epidemiological study protocol.

[g] Total number of citations to the publication with yearly citation in parathesis. n/a: not applicable, e.g., websites not included in Google Scholar citations.

with our findings of variation between the author guides for observational epidemiological studies.

There is an ongoing project, the Standardized Protocol Items Recommendations for Observational Studies, which aims to create a checklist for protocol reporting of cohort, case-control, and cross-section studies [68]. Besides the protocol no part of this project had been published as of November 2022.

We performed a broad and sensitive search, and two authors performed the data extraction with a third serving as an arbiter. One author performed the search and screening, which may miss some relevant abstracts [69], though the bulk of our included studies came through a full-text search. There is no consensus on how to search websites of journals and funders', but since these guides need to be available for authors, a too complicated and prolonged website search would find guides that most authors probably would not.

If an author to a protocol for an observational epidemiological study were to ask us for advice, we would recommend Wang 2022 [30] for observational intervention studies, while emphasizing the subjective nature of such advice. We await publication of further guides based on a systematic preparatory development process aimed specifically for other subtypes of studies.

We planned and categorized our review as a ''scoping review'', as this is a term often used for reviews with a broad scope, and a descriptive and explorative nature. Alternative terms could have been ''mapping review'', focusing more on the descriptive aspect [66], or a ''methodological'' review, focusing on the methodological topic [67]. However, the terminology is fluid and seems to be still evolving.

Moher et al. [70] has published methods for developers of health research reporting guidelines (e.g., protocol reporting guidelines). The methods may be considered relevant, also for the development of protocol guides, and involved eight main steps: literature review, stakeholder identification, Delphi exercise, face-to-face meeting, consultation with stakeholders, developing guidance statement, dealing with feedback and criticism, and keeping the guideline up-to-date. Only Wang 2022 [30] followed these or similar steps and had a primary focus on protocol development. There were, however, several useful guides with a comprehensive preparatory process, that we did not classify as 'main' guides, e.g., Wang 2021 [71] and Alba 2020 [37]. Their focus was broader than guiding

WHO 2021	Wang 2022	Fronteira 2013	UCLH 2010
Template	Template	Recommendation	Recommendation
Website	Article	Article	Website
"Cohort event monitoring study"	Observational intervention studies ("Real-World Evidence")	"Epidemiological observational study"	"Observational study"
No subtype mentioned	Cohort	Cohort	Cohort
	Case-control	Case-control	Case-control
		Cross-sectional	Cross-sectional
COVID-19	General	General	General
Protocol	Protocol	Protocol	Protocol
22 (85)	21 (81)	18 (69)	18 (69)
4.529	5963	2.291	1.753
0 (0)	0 (0)	3 (1)	n/a
International	International	Portugal	UK
English	English	English and Portuguese	English
World Health Organization	ISPE & ISPOR	Single author	Biostatistics group at University College London

specifically on protocols, e.g., Alba 2020 wanted "to develop good epidemiological practice guidelines specifically for global health epidemiology," and only a minor part of this endeavor concerned the protocol.

As of November 2022, the most frequently cited guide was Schlesselman 1982 [36], which was a book that primarily focused on case-control study design, conduct, and analysis, and contained a brief checklist for protocols. Only one of the main guides was cited 10 times per year or more, Andrews 2016 [27] (24 citations per year), though two of the other main guides were published in 2021 [29] or 2022 [30], with little time to accrue citations, and eight other guides were published on websites not included in Google Scholar's counts of citations [26,32,38,61,65,72–74]. In contrast the reporting guideline for randomized controlled trials protocols (SPIRIT 2013) has 4.446 citations with 556 citations per year [1] and the reporting guideline for systematic reviews and meta-analyses protocols (PRISMA-P) has 9.125 citations with 1.621 citations per year [75], indicating that these reporting guidelines are being used by authors. An important distinction, though, is that SPIRIT 2013 and PRISMA-P are protocol reporting guidelines, and not protocol content guidelines (only one of the included guides addressed reporting).

The restricted general uptake of the guides, assessed by a low number of citations, calls for reflection. One reason could be the absence of a strong tradition within observational epidemiology to publish formal study protocols, in part reflected in the fact that observational epidemiological studies do not need to follow as strict standards and regulations as randomized trials [76–78]. Still, the number of published observational epidemiological study protocols has increased over time (a simple search in PubMed for "cohort OR case-control AND protocol" in title indicated a rise from 21 in 2010 to 314 in 2020). Also the number of observational studies registered at ClinicalTrials.gov has increased considerably (searches by study type and a specific year indicated 100% increase over 10 years from 3967 entries in 2010 to 8884 in 2020). Other possible factors are lack of awareness of the guides, a perception that such guides are not needed, or that they are not of the necessary quality. Interestingly, a substantial proportion (20%) of the guides we identified had been published recently (2018–2022), which could indicate an increased interest in the issue.

One of the two protocol items that all guides included was analyses plan. This reflects the importance of the analyses in planning the study and in mitigating outcome reporting bias. Outcome reporting bias has been empirically demonstrated in randomized trials [3], and there is little reason to believe that it is not prevalent in other types of epidemiological research. The regulatory constraints for randomized trials are stricter than for observational epidemiological studies, so the risk of outcome reporting bias in observational epidemiological studies could be higher, enhancing the need for publicly available protocols with detailed data analysis plans.

One of the more puzzling yet recurring arguments against public availability of protocols and study registration has been that neither is necessary if there is an open access to data, where investigators share epidemiological data, study sample, data elements, and methods for data collection in a post publication registry [17]. However, it seems more implementable for editors and peer-reviewers to enforce a call for registration of studies, which is transparent to all stakeholders, as compared to enforcing post hoc data access, which comes with considerable logistical challenges as well as ethical concerns about patient data. Interestingly, ''access to data'' was the least used of all protocol items ($n = 6$). There has been a parallel debate in the psychological literature with similar arguments [79].

5. Conclusion

We identified 39 guides to authors of protocols of observational epidemiological studies, of which seven were categorized as main guides. There was considerable variation between the guides on format and content. Only one author guide, intended for protocols for observational studies of interventions, combined a systematic preparatory process with a primary focus on protocol development. We suggest that guides for authors of protocols for observational epidemiological studies should routinely be based on a systematic preparatory process.

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Supplementary data

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