*P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: the PRISMA Statement[1].

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Abstract

Systematic reviews and meta-analyses constitute the most reliable evidence for determining the effects of healthcare interventions. However, surveys of the quality of their reporting suggest there is considerable room for improvement. The QUOROM (*QU*ality *O*f *R*eporting *O*f *M*eta-analysis) Statement, a reporting guideline published in 1999, was developed to help improve the quality of reporting meta-analysis of randomized trials. Since its development the evidence base about how best to conduct and report systematic reviews and meta-analyses has increased substantially. Several conceptual, methodological and practical developments have also emerged. Accordingly, we have revised the QUOROM Statement substantially.

Twenty-nine systematic review authors, methodologists, clinicians, medical editors and a consumer participated in a 3-day meeting in 2005 and extensive post meeting electronic correspondence. A survey was used to help develop the update for the QUOROM Statement, PRISMA (*P*referred *R*eporting *I*tems for *S*ystematic reviews and *M*eta-*A*nalyses). PRISMA aims to improve the reporting of systematic reviews and meta-analyses of healthcare interventions. The decisions made during and after the meeting were informed by evidence, whenever possible. Conceptual and structural changes resulted in a 27-item checklist and four-phase flow diagram. Only items deemed essential

were included in the new checklist. The flow diagram was modified to show numbers of identified records, excluded articles, and included studies.

To improve the dissemination and uptake of PRISMA, an accompanying explanation and elaboration document has been developed, that provides explanation of the checklist items and summarises the underpinning evidence.

Introduction

Systematic reviews and meta-analyses have become increasingly important in healthcare. Clinicians read them to keep up to date with their field (1, 2) and they are often used as a starting point for developing clinical practice guidelines. Granting agencies may require a systematic review to ensure there is justification for further research (3) and some healthcare journals are moving in this direction (4). As with all research, the value of a systematic review depends on what was done, what was found, and the clarity of reporting. As with other publications, the reporting quality of systematic reviews varies, limiting readers' ability to assess the strengths and weaknesses of those reviews.

Several studies have evaluated the quality of review reports. In 1987, Mulrow examined 50 review articles published in four leading medical journals in 1985 and 1986 and found that none met all eight explicit scientific criteria, such as a quality assessment of included studies (5). In 1987, Sacks and colleagues (6) evaluated the adequacy of reporting of 83 meta-analyses on 23 characteristics in six domains. Reporting was generally poor; between 1 and 14 characteristics were adequately reported (mean = 7.7; SD = 2.7). A 1996 update of this study found little improvement (7).

To address the suboptimal reporting of meta-analyses, an international group developed a guidance called the QUOROM Statement (*QU*ality *O*f *R*eporting *O*f *M*eta-analyses), which focused on

the reporting of meta-analyses of randomized controlled trials (RCTs). In this article, we summarize a revision of these guidelines, renamed PRISMA (*P*referred *R*eporting *I*tems for *S*ystematic reviews and *M*eta-*A*nalyses).

History of QUOROM

Following the procedures used to develop the CONSORT Statement for reporting randomized trials (8), 30 individuals were invited to participate in a 2-day conference in Chicago, in 1996. The objective was to develop evidence-based guidance for improving the quality of reporting of meta-analyses of RCTs. That conference resulted in the QUOROM Statement (9): 21 checklist items that document the process of completing a meta-analysis, and a diagram that details the number and status of included articles at each stage of the meta-analysis process.

Since the QUOROM publication in 1999, the evidence base underlying the conduct of systematic reviews has matured. When *The Cochrane Library's* Methodology Register (which includes reports of studies relevant to the methods for systematic reviews and health and social care evaluations) was first developed in 1999, it contained approximately 1000 entries; the second issue in 2008 contains 10648 entries. Recent reviews have shown, however, improvements in the quality of conducting or reporting systematic reviews have not been

realized (10-14). It remains unclear whether using QUOROM is associated with more complete reporting of reviews (15).

Other reasons for updating QUOROM included a more comprehensive understanding of some conceptual issues, methodological advances, practical innovations in the conduct and reporting of systematic reviews, and changes in terminology.

Terminology

The terminology used to describe a systematic review and meta-analysis has evolved over time. One reason for changing the name from QUOROM to PRISMA was the desire to encompass both systematic reviews and meta-analyses. We have adopted the definitions used by the Cochrane Collaboration (16). A systematic review is a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Meta-analysis is the use of statistical techniques in a systematic review to integrate the results of included studies. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies in a systematic review. A more detailed discussion can be found in the accompanying PRISMA explanatory and elaboration paper (18)

Conceptual issues in the changes from QUOROM to PRISMA

Four conceptual issues have informed the development of the PRISMA Statement. These are discussed briefly below and more fully in the accompanying explanatory and elaboration document (18). First, we recognize that completing a systematic review is an appropriately iterative process. The conduct of a systematic review depends heavily on the scope and quality of included studies and thus systematic reviewers may need to modify their original review protocol while it is being conducted. Any systematic review reporting guide should recommend that such changes can be reported and explained without suggesting that they are inappropriate. Awareness of the iterative nature of reviews is an important feature of the PRISMA Statement (items 5, 11, 16, and 23). Aside from Cochrane reviews, all of which should have a protocol, only about 10% of systematic reviews report working from a protocol (19). Without a protocol that is publicly accessible, it is difficult to judge appropriate from inappropriate modifications.

Second, we distinguish between conduct and reporting research. That distinction is less straightforward for systematic reviews than when assessing the reporting of an individual study, because the reporting and conduct of systematic reviews are, by nature, closely intertwined. For example, the failure of a systematic review to report the assessment of the risk of bias in included studies may be seen as a marker of poor conduct, given the importance of this activity in the systematic review process (20).

Third, we acknowledge increasing awareness that for studies included in a systematic review a thorough assessment of the risk of bias requires both a "study-level" assessment (e.g., adequacy of allocation concealment) and, a newer approach, called "outcome-level" assessment. An outcome-level assessment involves evaluating the reliability and validity of the data for each important outcome by determining the methods used to assess them in each individual study (21). The quality of evidence may differ across outcomes, even within a study, such as between a primary efficacy outcome, which is likely to be very carefully and systematically measured, and the assessment of serious harms (22), which may rely on spontaneous reports by investigators; this information should be reported to allow an explicit assessment of the extent to which an estimate of effect is correct (21). For example, evidence from several trials indicated that administering a combination of topical and systemic antibiotic prophylaxis to intensive care unit

patients decreases infections and mortality (23). The outcome "emergence of bacterial antibiotic resistance", however, has not been reliably assessed in existing studies (23). Authors should report any assessment of the risk of bias for all important outcomes, if done.

Fourth, we recognize the important role selective reporting bias has among studies (e.g., publication bias) in the conduct and interpretation of systematic reviews (24). In addition, outcome reporting bias within individual studies has recently been empirically demonstrated (25,26). In light of this evidence, systematic reviewers need to consider how they will investigate possible selective reporting when conducting a systematic review and to report such results. Beyond possible selective reporting within individual studies, the implication of this bias on the conduct and reporting of systematic reviews themselves is unclear; some previous research has identified selective outcome reporting in the context of systematic reviews (27).

Developing the PRISMA Statement

A 3-day meeting was held in Ottawa, Canada, in June 2005 with 29 participants, including review authors, methodologists, clinicians, medical editors and a consumer. The objective of the Ottawa meeting was to revise and expand the QUOROM checklist and flow diagram, as needed.

The executive committee completed the following tasks, prior to the meeting: a systematic review of studies examining the quality of reporting of systematic reviews; a comprehensive literature search to identify methodological and other articles that might inform the meeting, especially in relation to modifying checklist items; and an international survey of review authors, consumers, and groups commissioning or using systematic reviews and meta-analyses, including the International Network of Agencies of Health Technology Assessment (INAHTA) and the Guidelines International Network (GIN). The survey aimed to ascertain views of QUOROM, including the merits of the existing checklist items. The results of these activities were presented during the meeting and are summarized on the PRISMA web site (www.prisma-statement.org).

Only items deemed essential were retained or added to the checklist. Some additional items are nevertheless desirable and review authors should include these, if relevant (28). For example, it is useful to indicate whether the systematic review is an update (29) of a previous review, and to describe any changes in procedures from those described in the original protocol.

Shortly after the meeting a draft of the PRISMA Statement was circulated to the group, including those invited to the meeting but unable to attend. A disposition file was created containing comments and revisions from each respondent, and the Statement was subsequently

revised several times. After 11 revisions the group approved the checklist, flow diagram and this summary paper.

Although no direct evidence was found to support retaining or adding some items, evidence from other domains was believed to be relevant. For example, Item 5 asks authors to provide registration information about the systematic review, including a registration number, if available. Although systematic review registration is not yet widely available (30,31), the participating journals of the International Committee of Medical Journal Editors (ICMJE) (32) now require all clinical trials to be registered in an effort to increase transparency and accountability (33). Those aspects are also likely to benefit systematic reviewers, possibly reducing the risk of an excessive number of reviews addressing the same question (11; 34) and providing greater transparency when updating systematic reviews.

The PRISMA Statement

The PRISMA Statement consists of a 27-item checklist (Table 1) and a four-phase flow diagram (Figure). The aim of the PRISMA Statement is to help authors improve the reporting of systematic reviews and meta-analyses. We have focused on trials but PRISMA can also be used as a basis for reporting systematic reviews of other types of research, particularly those evaluating interventions. PRISMA may also be useful for critical appraisal of published systematic reviews. However, the

PRISMA checklist should not be considered a quality assessment instrument to gauge the quality of a systematic review.

From QUOROM to PRISMA

The new PRISMA checklist differs in several respects from the QUOROM checklist and the substantive specific changes are highlighted in Table 2. Generally, the PRISMA checklist 'decouples' several items present in the QUOROM checklist, and where applicable, several checklist items are linked to improve consistency across the systematic review report.

The flow diagram has also been modified. Before including studies and providing reasons for excluding others, the review team must first search the literature. This search results in records. Once these records have been screened and eligibility criteria applied, a smaller number of articles will remain. The number of included articles might be smaller (or larger) than the number of studies, because articles may report on multiple studies and because results from a particular study may be published in several articles. To capture this information the PRISMA flow diagram now requests information on these phases of the review process.

The PRISMA explanatory and elaboration paper

In addition to the PRISMA Statement, a supporting explanation and elaboration document has been produced (18) following the style used for other reporting guidelines (35-37). The process of completing this document included developing a large database of exemplars to highlight how best to report each checklist item, and identifying a comprehensive evidence base to support the inclusion of each checklist item. The explanation and elaboration document was completed after several face-to-face meetings and numerous iterations among several meeting participants after which it was shared with the whole group for additional revisions and final approval (18). Finally, the group formed a dissemination subcommittee to help disseminate and implement PRISMA.

Discussion

The quality of reporting of systematic reviews is still not optimal (10-14, 19). In a review of 300 systematic reviews few authors reported assessing for publication bias (19) even though there is overwhelming evidence both for its existence (24) and its impact on the results of systematic reviews (38). Even when publication bias is assessed, there is no guarantee that systematic reviewers have assessed or interpreted it appropriately (39). Although the absence of reporting such an

assessment does not necessarily indicate that it was not done, reporting an assessment of publication bias is likely to be a marker of the thoroughness of the conduct of the systematic review.

Several approaches have been developed to conduct systematic reviews on a broader array of questions. For example, systematic reviews are now conducted to investigate cost-effectiveness (40), diagnostic (41,42) or prognostic questions (43), genetic associations (44) and policy making (45-47). The general concepts and topics covered by PRISMA are all relevant to any systematic review, not just those whose objective is to summarize the benefits and harms of a healthcare intervention. However, some modifications of the checklist items or flow diagram will be necessary in particular circumstances. For example, assessing the risk of bias is a key concept but the items used to assess this in a diagnostic review are likely to focus on issues such as the spectrum of patients and the verification of disease status, which differ from reviews of interventions. The flow diagram will need adjustments when reporting individual patient data meta-analysis (48).

The PRISMA Statement should replace the QUOROM Statement for those journals that have endorsed QUOROM. We hope that other journals will support PRISMA; they can do so by registering on the PRISMA web site. To underscore to authors, and others, the importance of transparent reporting of systematic reviews, we encourage supporting journals to reference the PRISMA Statement and include the PRISMA

web address in their Instructions to Authors. We also invite editorial organizations to consider endorsing PRISMA and encourage authors to adhere to its principles.

We have developed an explanatory document (18) to increase usefulness of PRISMA. For each checklist item, this document contains an example of good reporting, a rationale for its inclusion, and supporting evidence, including references. We believe this document will also serve as a useful resource for those teaching systematic reviews. We encourage journals to include reference to the explanatory document in their Instructions to Authors.

Like any evidence-based endeavour, PRISMA is a living document. To this end we invite readers to comment on the revised version, particularly the new checklist and flow diagram, through the PRISMA web site. We will use such information to inform PRISMA's continued development.

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491 Table 1 - Checklist of items to include when reporting a systematic
492 review or meta-analysis
493

Section/topic	#	Checklist item
TITLE		
Title	**1**	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	**2**	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions; and implications of key findings; funding for the systematic review; systematic review registration number.
INTRODUCTION		
Rationale	**3**	Describe the rationale for the review in the context of what is already known.
Objectives	**4**	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS).
METHODS		
Protocol and registration	**5**	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address) and, if available, provide registration information including the registration number.
Eligibility criteria	**6**	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility giving rationale.
Information sources	**7**	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.
Search	**8**	Present full electronic search strategy for at least one major database, including any limits used, such that it could be repeated.
Study selection	**9**	State the process for selecting studies (i.e., screening, eligibility, included in the systematic review and, if applicable, included in the meta-analysis).

Section/topic	#	Checklist item
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	20	For all outcomes considered (benefits and harms) present, for each study: (a) simple summary data for each intervention group, (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include, for each, confidence intervals and measures of consistency.
Risk of bias	22	Present results of any assessment of risk of bias across studies (see item

Section/topic	#	Checklist item
across studies	2	15).
Additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression).
DISCUSSION		
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	25	Discuss limitations at study and outcome-level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	27	Describe sources of funding and other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.

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499Table 2 – Substantive specific changes between the QUOROM checklist
500and the PRISMA checklist (a tick indicates the presence of the topic in
501QUOROM or PRISMA).

Section/Topic	Item	QUOROM	PRISMA	Comment
Abstract		√	√	QUOROM and PRISMA ask authors to report an abstract. However, PRISMA is not specific about format.
Introduction	objective		√	This new item (4) addresses the explicit question the review addresses using the PICO reporting system (which describes the Participants, Interventions, Comparisons, Outcome(s) of the systematic review), together with the specification of the type of study design (PICOS); the item is linked to items 6,11 and 18 of the checklist.
Methods and Results	protocol		√	This new item (5) asks authors to report whether the review has a protocol and if so how it can be accessed.
	Search	√	√	Although reporting the search is present in both QUOROM and PRISMA checklists, PRISMA asks authors to provide a full description of at least one electronic search strategy (item 8). Without such information it is impossible to repeat the authors' search.
	Assessment of risk of bias in included studies	√	√	Renamed from "quality assessment" in QUOROM. This item (12) is linked with reporting this information in the results (item 19). The new concept "outcome-level" assessment has been introduced.

	Assessment of bias across studies		√	This new item (15) asks authors to describe any assessments of bias in the review, such as selective reporting within the included studies. This item is linked with reporting this information in the results (item 22).
Discussion		√	√	Although both QUOROM and PRISMA checklists address the discussion section, PRISMA devotes 3 items (24-26) to the discussion. In PRISMA the main types of limitations are explicitly stated and their discussion required.
Funding			√	This new item (27) asks authors to provide information on any sources of funding for the systematic review.

Figure - Flow of information through the different phases of a systematic review

Identification

Screening

Eligibility

Included