

# Questionnaires used to assess barriers of clinical guideline use among physicians are not comprehensive, reliable, or valid: a scoping review

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## Abstract

**Objective:** This study described the number and characteristics of questionnaires used to assess barriers of guideline use among physicians.

**Study Design and Setting:** A scoping review was conducted. MEDLINE and EMBASE were searched from 2005 to June 2016. English-language studies that administered a questionnaire to assess barriers of guideline use among practicing physicians were eligible. Summary statistics were used to report study and questionnaire characteristics. Questionnaire content was assessed with a checklist of 57 known barriers.

**Results:** Each of the 178 included studies administered a unique questionnaire. The number of questionnaires increased yearly from 2005 to 2015. Few were pilot-tested (50, 28.1%) or tested for psychometric properties (3, 1.7%). Two were based on theory. None probed for the full range of known barriers. Ten included a free-text option. The majority assessed professional barriers (177, 99.4%) but few of the 14 factors within this domain. Questionnaire characteristics did not change over time.

**Conclusion:** Organizations administered questionnaires that were not reliable or valid and did not comprehensively assess barriers and may have selected interventions unlikely to promote guideline use. Research is needed to construct a questionnaire that is practical, adaptable, and robust and leads to the selection of interventions that support guideline use. © 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Clinical practice guidelines; Barriers; Implementation; Questionnaires; Questionnaire design; Scoping review

## 1. Introduction

Clinical practice guidelines offer recommendations for the organization and delivery of care according to best available evidence combined with professional judgment, and patient and family values and preferences [1]. Indeed, guidelines are viewed as a fundamental resource by which to plan, deliver, evaluate, and improve the quality of health care services [1]. Unfortunately, interventions commonly used to implement guidelines have a small and inconsistent impact [2] and reports of underuse and overuse of

guidelines abound [3–5]. Hence, there is a need to improve the implementation and use of guidelines. This would enhance the quality of care and capitalize on the considerable investment in guideline development by health care organizations worldwide.

Various determinants can either facilitate or function as barriers of guideline use [6–8]. These determinants include guideline characteristics and other factors at the individual (patient, provider), organizational, or system level. A Cochrane systematic review by Baker et al. found that interventions that had been selected and tailored to address identified barriers were more likely to improve professional practice compared with either no intervention or simple dissemination of guidelines [9]. Baker et al. found that studies used different single and multiple methods for identifying barriers, most often interviews, focus groups, and questionnaires, and advocated for ongoing research on how to choose and use

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### What is new?

#### Key findings

This study found that the use of questionnaires to assess barriers of guideline use among physicians increased yearly from 2005 to 2015, but the quality and capacity of questionnaires to thoroughly and accurately assess the full range of known potential barriers did not.

#### What this adds to what was known?

A cochrane systematic review first published in 2005 showed that clinical guideline implementation was more successful when interventions were based on advance identification of barriers. The Tailored Implementation for Chronic Diseases Checklist includes 57 unique potential barriers of guideline use organized in seven domains. Questionnaires used to assess barriers of guideline use did not probe for these known barriers.

#### What is the implication and what should change now?

Numerous organizations may be duplicating effort and misusing resources by administering questionnaires that are not comprehensive, reliable, or valid; and by then selecting interventions based on incomplete and inaccurate information that may be unlikely to promote guideline use. Research is needed to develop and promote broad use of a standardized, yet adaptable questionnaire that would ultimately generate more complete and accurate findings on which to base guideline implementation planning.

barrier assessment methods specific to a guideline and/or setting. Krause et al. described the methods used for identifying barriers of guideline use in five European countries [10]. A variety of methods generated 601 unique barriers so, similar to Baker et al., Krause et al. concluded that there was no best way to identify barriers.

Questionnaires are frequently used to identify barriers of guideline use [9,10]. For example, the BARRIERS scale is a 29-item questionnaire to identify barriers of practice change that has been widely used in nursing [11]. Questionnaires can reach a large and diverse audience of guideline users, and given that questionnaires can now be administered online, they represent an inexpensive means of gathering information about barriers. Research by Baker et al. [9] and Krause et al. [10] suggests that physicians are most often the target of barrier questionnaires. It is currently not known if there is a standard or validated questionnaire that is commonly used to assess barriers of guideline use among physicians, or the number, type, and content of

questionnaires used for this purpose. The primary aim of this study was to describe the characteristics of questionnaires used to assess barriers of clinical guideline use among physicians. A secondary aim was to explore trends in questionnaire characteristics over time given awareness of the need to tailor guideline implementation based on identified barriers after publication of the Baker et al. review [9]. This knowledge is needed to understand if one or more questionnaires are fully and accurately assessing barriers of guideline implementation, information needed to select interventions that are likely to lead to guideline use.

## 2. Methods

### 2.1. Approach

The overall aim of this research was to describe the characteristics of questionnaires used to assess barriers of clinical guideline use among physicians, rather than evaluating or summarizing the survey outcomes or barriers identified; therefore, a scoping review approach was used. A scoping review can be used to describe the quantity and quality of research in a given area and identify gaps that can be addressed through ongoing research [12]. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria guided reporting of the methods and findings [13]. Data were publicly available so institutional review board approval was not necessary. A protocol for this review was not registered.

### 2.2. Searching

MEDLINE and EMBASE were searched in March 2015 for studies published from January 1, 2005 to December 31, 2014 that reported the results of a questionnaire administered to assess barriers of guideline use among physicians. The search was updated in July 2016 to include studies published from January 1, 2015 to that date. These databases were chosen because they are the most extensive sources of peer-reviewed medical literature. The chosen time span coincided with the publication of the Baker et al. systematic review on tailoring, first published in 2005, then updated in 2010 and 2015 with similar findings [9]. The search strategy was purposefully broad to enhance sensitivity (Additional File 1 at [www.jclinepi.com](http://www.jclinepi.com)). The search strategy was comprised of Medical Subject Headings only that matched the concepts of guideline use and barriers. Searches were limited to English language to avoid the cost of translation as this study was conducted on a volunteer basis by an international working group.

### 2.3. Screening

Titles and abstracts of search results were reviewed independently by A.R.G. and two research assistants. All items

selected by at least one of these reviewers were retrieved for further assessment. If more than one publication described a single study and each presented the same data, the most recent was included. The eligibility criteria used to screen search results were based on the population, intervention, comparisons, outcomes framework. The population of interest was practicing physicians or multidisciplinary groups of which more than half were physicians. The clinical topic on which the questionnaire was based was classified as overall management (ie, two or more clinical interventions), prevention, diagnosis, treatment, follow-up care, or palliative care. The intervention of interest was self-report questionnaires that could be administered by regular mail, electronic mail, online, or as an in-person interview in the setting of a professional office or conference. Questionnaires pertained to specific guidelines for any condition or disease, or related procedures or settings of care that were explicitly identified in the publication (not about use of guidelines in general). Questionnaires could be applied to a given group of physicians in one or more locations such as family practices or hospitals, or to individuals of one or more physician specialties in many locations or countries. Eligible study designs included cross-sectional surveys (baseline or following one or more interventions), or before and after individuals were exposed to the same intervention. Studies were eligible if the questionnaire was fully available, meaning the questionnaire was either included in the article, or available as an online journal supplement or on an Internet site. Outcomes of interest were the determinants/barriers of guideline use addressed by the questionnaire (not the results of the survey). As search results were reviewed, selection criteria were expanded to specify studies that were not eligible. Studies were not eligible if they focused on barriers of guideline use in general; guidelines focused on logistical procedures (eg, informed consent, sign-out, referral); were directed at patients, health professionals other than practicing physicians, or single respondents representing organizations; the study design was based on qualitative interviews rather than a questionnaire; or if they were publications in the form of guidelines, conference proceedings or abstracts, protocols, letters, editorials, or commentaries.

A data extraction form was developed to collect information on author, publication year, country, clinical topic, clinical intervention, setting of respondents, specialty of respondents, mode of questionnaire administration, type of response options, any underlying theory explicitly named in the methods that informed questions, validation of the questionnaire (pilot-testing, psychometric testing), and barriers addressed by the questionnaire. To categorize barriers, we considered using domains from existing taxonomies of barriers but found that most were not up-to-date or comprehensive, or they were focused on the adoption of innovations in general including technology, clinical interventions, or quality improvement

interventions [7,14–16]. One framework emerged that was current, comprehensive, and relevant to the adoption of guidelines. Based on a systematic review and international consensus process, Flottorp et al. compiled 57 determinants grouped in seven domains: guideline factors; individual health professional factors; patient factors; professional interactions; incentives and resources; capacity for organizational change; and social, political, and legal factors [8]. A.R.G. and two research assistants pilot-tested the form on three articles through four iterations of extraction and discussion until data extraction was consistent. Data from all eligible studies were double-extracted by two research assistants. Data extracted from a subset of studies were independently checked by A.R.G. and M.W. who discussed and resolved discrepancies through two rounds. Then M.W. independently verified all extracted data, including the classification of barriers with the Flottorp et al. framework [8].

#### 2.4. Data analysis

Clinical topic or intervention addressed by each questionnaire was coded as a disease category using the International Classification of Diseases-10 (ICD-10), version 2015 ([apps.who.int/classifications/icd10/](http://apps.who.int/classifications/icd10/)). Summary statistics were used to describe the number of studies by year published, country, clinical topic and intervention, disease category, setting and type of respondents, mode of questionnaire administration, response options, underlying theory, validation, and barrier domains based on the Flottorp et al. framework [8]. The quality of individual studies was not assessed because that is not customary for a scoping review.

#### 2.5. Patient involvement

Patients were not involved in this research.

### 3. Results

#### 3.1. Search results

A total of 2,265 unique articles were identified of which 1,671 were excluded based on screening of titles and abstracts, leaving 594 full-text articles to be screened. Of these, most were excluded (322) because the questionnaire was not available. Others were excluded because they did not specify a guideline on which the questionnaire was applied (29), were targeted at an organizational representative (3), respondents were not primarily practicing physicians (31), were based on a procedural rather than a clinical guideline (9), were studies involving qualitative interviews (5), not published in the English language (4), ineligible publication type (12), or the methods lacked sufficient detail (1). Ultimately, 178 studies were eligible for analysis (Fig. 1, PRISMA diagram). Data extracted from included studies are available in [Additional File 2](#) at

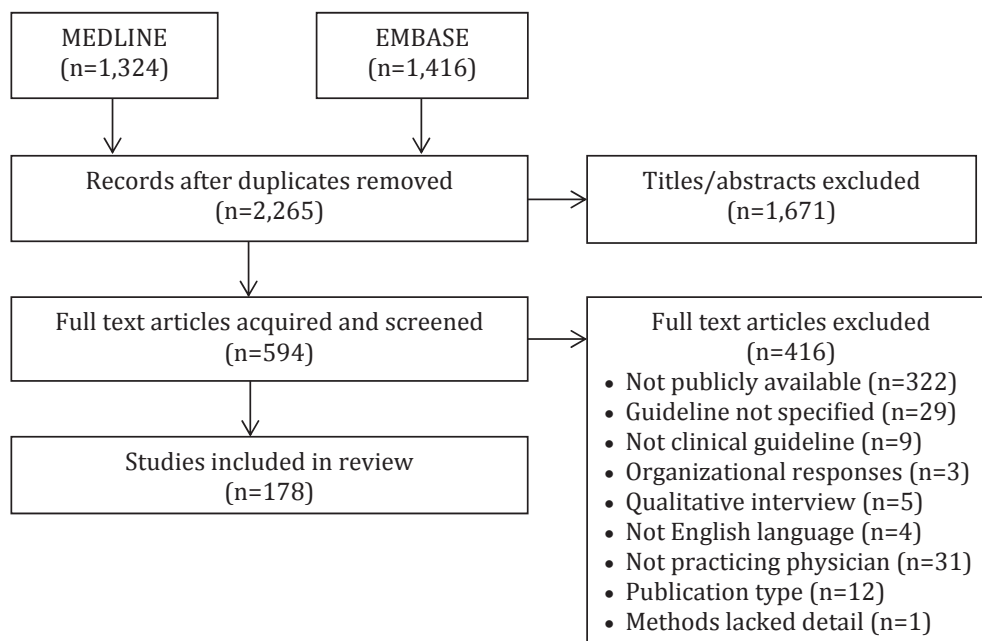


Fig. 1. PRISMA diagram of search results. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

[www.jclinepi.com](http://www.jclinepi.com) [17–50] [51–90] [91–128] [129–163] [164–194].

### 3.2. Study characteristics

Studies were published from 2005 to 2015. The number published per year increased from 2005 to a peak in 2013 of 34 studies (Fig. 2). Studies were conducted in 30 countries, most often in the United States (49, 27.5%) followed by the United Kingdom (27, 15.2%) and Italy (10, 5.6%). More than a third of the studies targeted respondents from multiple clinical settings (64, 40.0%). Other clinical settings included general practice (50, 28.1%), primary care (21, 11.8%), acute care (22, 12.4%), and teaching hospitals (18, 10.1%) with one each in home-based, long-term, and palliative care. Questionnaires were aimed at a large variety of physician specialties, and many were directed at multiple types of physicians (66, 37.1%). Over the years, use of

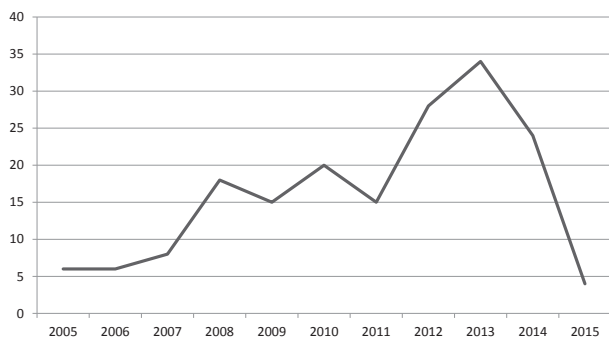


Fig. 2. Number of included studies published per year.

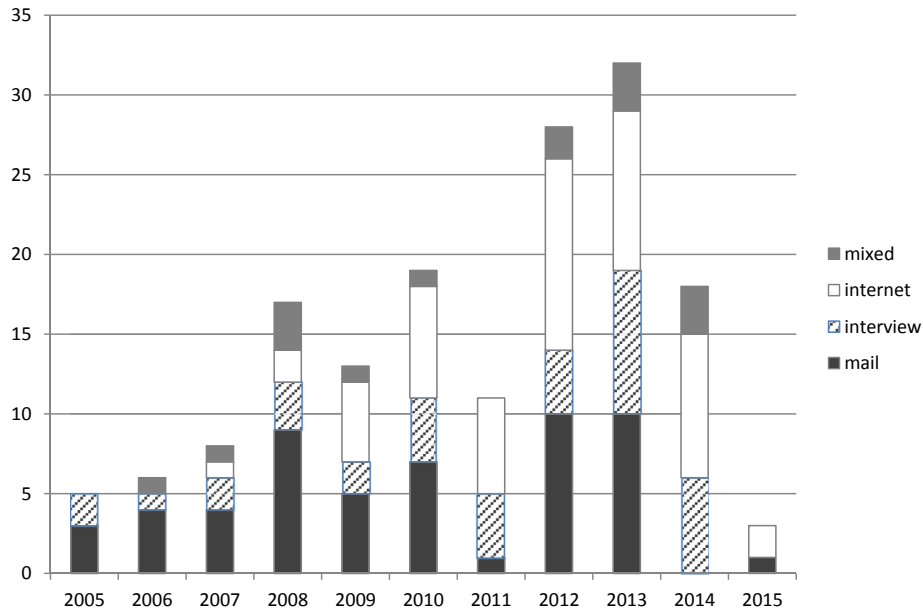
online questionnaires steadily increased although the use of regular mail remained common up to and including 2015 (Fig. 3).

### 3.3. Guideline topics on which questionnaires were based

Half of the guidelines on which questionnaires were based addressed overall management of a disease or condition (91, 51.1%). Other guidelines addressed treatment (38, 21.3%), screening (23, 12.9%), prevention (19, 10.7%), diagnosis (5, 2.8%), and follow-up care (2, 1.1%). Guideline topics were mapped to 22 ICD-10 disease categories. The disease categories most commonly addressed were cancer (35, 19.7%), cardiovascular disease (33, 18.5%), respiratory conditions (17, 9.6%), and digestive system disorders (15, 8.4%). These conditions comprised 56.2% of eligible studies (Table 1).

### 3.4. Questionnaire characteristics

Most questionnaires included multiple types of response options including multiple choice, open-ended questions and rating scales (115, 64.6%). Two of the 178 studies reported having used a theory to inform the content of the questionnaire (Theory of Planned Behaviour, RE-AIM framework). Most studies did not validate the questionnaire before use (112, 62.9%). Few studies based their questionnaire on a previously administered questionnaire (13, 7.3%), pilot-tested their questionnaire among a sample of guideline users (50, 28.1%), or assessed its psychometric properties (3, 1.7%).



The following number of studies per year did not report how the questionnaire was administered (n=13): 2014 – 3, 2013 – 2, 2011 – 4, 2010 – 1, 2009 – 2, 2008 – 1

Fig. 3. Mode of questionnaire administration by publication year.

### 3.5. Questionnaire barrier domains

All but one questionnaire (177, 99.4%) focused on individual health professional barriers (Table 2). Most other

Table 1. Disease category of guidelines addressed in questionnaires

Disease category <sup>a</sup>	Studies	
	n	%
Cancer	35	19.7
Cardiovascular disease	33	18.5
Respiratory conditions	17	9.6
Digestive system disorders	15	8.4
Surgery and anesthesia	11	6.2
Mental health	9	5.1
Infectious diseases	8	4.5
Genitourinary disorders	7	3.9
Musculoskeletal disorders	6	3.4
Patient safety	5	2.8
Metabolic diseases	4	2.2
Pregnancy and childbirth	4	2.2
Child health	3	1.7
Eye diseases	3	1.7
Vascular disorders	3	1.7
Immunologic conditions	3	1.7
Ear, nose, and throat conditions	2	1.1
HIV-AIDS	2	1.1
Congenital disorders	2	1.1
Health promotion	2	1.1
Cerebrovascular disease	2	1.1
Preventive medicine	1	0.6
Multiple	1	0.6

<sup>a</sup> Based on International Classification of Diseases–10 version 2015 ([apps.who.int/classifications/icd10/browse/2015/en](https://apps.who.int/classifications/icd10/browse/2015/en)).

barrier domains were included in few questionnaires; for example, guideline factors (8, 4.5%); patient factors (7, 3.9%); professional interaction (4, 2.2%); incentives and resources (8, 4.4%); or social, political or legal factors (5, 2.8%). No questionnaires addressed organization-level factors. Few questionnaires included a free-text option in which respondents could specify barriers (10, 5.6%). None of the questionnaires addressed all domains. Most questionnaires addressed one domain (161, 90.4%); two, three, and four domains were addressed by eight (4.5%), four (2.2%), and five (2.8%) questionnaires, respectively. Questionnaires that addressed two or more domains were largely published in 2010 or later (17, 9.6%) as were questionnaires that included a free-text response option (10, 5.6%), however, the number is small, and many questionnaires that included one domain only (108, 60.7%) were also published in 2010 or later so there did not appear to be an increasing trend over time in the administration of questionnaires that probed for multiple potential barriers of guideline use.

Table 2. Domains of determinants addressed in questionnaires

Domain	Addressed (n, %)	
	No	Yes
Guideline	170, 95.5	8, 4.5
Individual health professional	1, 0.6	177, 99.4
Patient	171, 96.1	7, 3.9
Professional interaction	174, 97.8	4, 2.2
Incentives and resources	170, 95.5	8, 4.4
Capacity for organizational change	178, 100.0	0, 0.0
Social, political, and legal	173, 97.2	5, 2.8
Free-text response option	168, 94.4	10, 5.6



**Table 3.** Determinants addressed in questionnaires

Flottorp domain [9] ( <i>n</i> subdomains)	Addressed in questionnaires ( <i>n</i> )	
	Yes	No
Guideline (13)	Quality of evidence for the recommendation (2) Clarity (3) Cultural appropriateness (2) Accessibility of the recommendation (4) Source of the recommendation (2) Consistency with other guidelines (1) Compatibility (2)	Strength of the recommendation Feasibility Accessibility of the intervention Effort Triability Observability
Individual health professional (14)	Domain knowledge (75) Awareness/familiarity with recommendation (95) Knowledge about own practice (28) Skills needed to adhere (2) Agreement with recommendation (28) Attitudes toward guidelines in general (14) Expected outcome (9) Intention and motivation (4) Self-efficacy (2) Nature of the behavior (138) Capacity to plan change (2)	Learning style Emotions Self-monitoring or feedback
Patient (5)	Patient needs (1) Patient preferences (2) Patient motivation (3) Patient behavior (1)	Patient beliefs and knowledge
Professional interaction (3)	Communication and influence (4)	Team processes Referral processes
Incentives and resources (7)	Availability of necessary resources (7) Financial incentives/disincentives (1)	Nonfinancial incentives/disincentives Information systems Quality assurance/patient safety systems Continuing education Assistance for clinicians
Capacity for organizational change (7)	—	Mandate, authority, accountability Capable leadership Strength of supporters/opponents Regulations, rules, policies Priority of necessary change Monitoring and feedback Assistance for organizational change
Social, political, and legal (5)	Payer or funder policies (2) Malpractice liability (3)	Economic constraints Contracts Legislation

Many subdomains within each of the seven barrier domains were not addressed at all, or addressed in few questionnaires (Table 3). In the individual health professional domain, the most frequently addressed subdomains were as follows: nature of the behavior, referring to what the respondent would do in a given case scenario (138, 77.5%), awareness or familiarity with the recommendations (95, 53.4%), knowledge of the clinical domain (75, 42.1%), agreement with the recommendations (28, 15.7%) and knowledge of one's own practice (28, 15.7%).

#### 4. Discussion

The assessment of potential barriers of guideline use was shown to be essential for guideline implementation planning by the Baker et al. Cochrane review in 2005 [9]. This scoping review found that the number of studies in which

questionnaires were used to assess barriers of the use of specific clinical guidelines on many diseases among physicians of numerous specialties increased almost yearly since 2005. However, no standard or commonly used questionnaire emerged—each of the 178 included studies developed and administered a unique questionnaire, few were pilot-tested, and none were fully evaluated for psychometric properties. Furthermore, no questionnaires probed for the full range of barrier domains and subdomains that are known to be potential barriers of guideline use, and only 10 included a free-text response option to probe for barriers in an open-ended fashion. Even among the most frequently reported domain of individual health professional barriers, the majority of questionnaires reported few of the 14 subdomains. These characteristics did not appear to change over time. Thus, although the need to assess barriers of guideline use may be widely recognized, numerous organizations may be misusing resources by administering questionnaires that are not

comprehensive, reliable, or valid; and then by selecting interventions based on incomplete and inaccurate information that may be unlikely to promote guideline use.

The strengths of this research include use of rigorous systematic review methods and description of barriers with the Flottorp et al. framework [8] of known determinants of guideline use. It offered detailed definitions and helpful examples of questions for each subdomain, was easy to apply, and resulted in a thorough analysis of the content of the questionnaires administered in the included studies. However, the Flottorp et al. framework may not necessarily be ideal because it relied on published studies and was not based on an overall theoretical standpoint. Several additional issues may limit the interpretation and use of these findings. Although we searched the two most relevant databases of medical literature pertaining to physicians and used rigorous searching and screening processes, our search strategy may not have identified all relevant studies. We did not search the gray literature, assuming that most empirical research on guideline implementation would be found in indexed databases. Publication bias, or the tendency for journals to publish positive results or surveys with high response rates, may have influenced the number and type of studies that were retrieved. We purposefully did not include questionnaires that elicited views about guidelines in general because we were interested in the process of identifying barriers of disease-specific guideline use. Studies were eligible if the questionnaire was available in the article itself, online as a journal supplement, or on a web site. It was beyond the resources available to this project to contact 322 authors requesting their questionnaire. Hence, the findings reported here may be biased because 36% (178/500) of questionnaires were included in the review. Although this represented 322 excluded studies, a large number of studies remained eligible for analysis ( $n = 178$ ). Conversely, questionnaires used in studies that did not include the questionnaire or at least specify the questions in Section 2 may have been low quality, in which case our results are positively overestimated. We did not extract data on the questionnaire findings reported in eligible studies or assess the methodological quality of eligible studies because that is typically not done in a scoping review.

This study aimed to describe whether and how barriers of the use of specific guidelines were being assessed by questionnaires targeted to physicians. It is therefore distinct from systematic reviews that reviewed other types of instruments. For example, Lewis et al. identified 104 instruments for measuring implementation outcomes of particular relevance to mental health such as cost, feasibility, fidelity, penetration, and sustainability [195]. Brennan et al. identified 84 instruments for assessing determinants of continuous quality improvement outcomes in primary care such as climate for quality improvement, perceived team effectiveness, and quality of care among others [196]. Chaudoir et al. identified 62 instruments for measuring determinants

of the implementation of health innovations, where health innovations were referred to in Section 1 as interventions, practices, and guidelines, and were not further defined in the Section 2 or search strategy [197]. The Chaudoir et al. review resulted in a heterogeneous list of instruments of relevance to different stakeholders and a wide range of implementation issues that were not specifically linked to type of innovation, for example, critical thinking, coping style, satisfaction with electronic health records, intention to leave place of employment scale, healthy heart kit for patients, and various team- and organizational-level climate instruments. Thus, as far as we have found, this represents the first attempt to describe questionnaires that assess barriers of the use of specific clinical guidelines among physicians.

Questionnaires may not be the ideal way to collect information about barriers and enablers of guideline implementation and use. In part, this may explain why many studies included in this review largely addressed self-reported behavior based on sample patient scenarios, rather than the range of barriers included in the Flottorp et al. framework [8]. Interviews or focus groups may be preferred approaches because they are able to collect detailed information about the interplay and impact of multiple factors that influence whether and how guidelines are used [198]. Both Baker et al. and Krause et al. noted that qualitative methods were commonly used to collect information about barriers and facilitators [9,10]. However, questionnaires, which were increasingly administered online, remain a feasible option for efficiently collecting such information from a large number of guideline users and, with some improvement, could be optimized for this task.

First, some reflection is needed on why the surveys used in included studies focused largely on individual physician factors. Were the authors not aware of the need to select and tailor guideline implementation based on an assessment of barriers; or were they not aware of determinant frameworks such as that published relatively recently by Flottorp et al. [8]. If so, then guideline developers or implementers should be encouraged to partner with implementation scientists to investigate barriers of guideline use. Alternatively, did they choose to probe mainly for individual health professional factors because they thought these were the issues most relevant to the guidelines in question, or that physicians would not be able to respond to questions about other types of barriers such as patient, organizational, or system-level factors? Even if the latter issue was true, none of the questionnaires fully probed for the physician-specific factors known to be potential barriers of guideline use. How the questionnaire findings were used for guideline implementation planning is also not known.

These reflections suggest several avenues of further research to understand how to optimize barrier assessment questionnaires. One, despite recommendations to use theories when planning behavior change interventions [199], this study found that two of the 178 questionnaires were

reported to have been designed based on an explicit theory or theoretical framework. The use of “home grown” rather than theory-based, validated instruments has been identified by others as a limitation in implementation science [200]. In future research, theories of behavior change [16,201,202], and existing taxonomies of determinants of practice such as the Flottorp et al. framework [8], could be used to develop and then validate questionnaires.

Second, physicians may not be able to identify all barriers or the most important ones. Research is needed to assess if physicians alone can provide valid responses to a questionnaire that is based on multiple barrier domains. If not, then questionnaires should be targeted at a greater diversity of health care professionals to collect a broader range of perspectives. Also, the research reported here could be repeated to investigate questionnaires that have been used to survey patients or consumers, clinicians other than physicians, and health system managers or policy makers who may have different views of, and experiences with barriers of guideline use.

Third, guideline developers have few resources with which to develop and implement guidelines, including the assessment of barriers on which to base implementation planning. Therefore, it may be ideal to develop and validate a single questionnaire that could be adapted and widely used, saving individuals or groups from duplicating effort, and using resources to generate their own questionnaires. Ideally, such a questionnaire could be tailored to suit the needs of different clinical contexts or health care settings. Wide use of such a standardized questionnaire would ultimately generate more complete and accurate findings on which to base guideline implementation planning. However, as Flottorp et al. made clear [8], the number of potential barriers of guideline use is considerable. A comprehensive questionnaire could be very lengthy, leading to low response rates by physicians. Further research must investigate how to construct a questionnaire that is practical to administer yet generates information leading to the selection and implementation of interventions that support guideline use.

In conclusion, this review identified several limitations of questionnaires that have been used to assess barriers of guideline use among physicians and identified several issues that warrant further examination by the members of the Guidelines International Network Implementation Working Group toward the potential development of a standardized, more robust questionnaire.

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## Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.jclinepi.2016.12.012>.

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