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Inadequate critical appraisal of studies in systematic reviews of time to diagnosis

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Abstract

Objective: To analyze tools used to critically appraise primary studies included in systematic reviews (SRs) of time to diagnosis (TTD).

Study Design and Setting: We systematically searched MEDLINE via PubMed and Web of Science for SRs of TTD published up to the end of February 2015; we identified and characterized tools used for critical appraisal and classified their items.

Results: From 1,936 articles identified, we included 45 SRs that aimed to summarize the available information on the length (n = 16), determinants (n = 31), and/or consequences (n = 14) of TTD. For the 23 SRs (51%) reporting a critical appraisal process, 21 different tools were used, with 232 items assessing quality of reporting (64%), risk of bias or threats to generalizability (43%), statistical issues (5%), and/or an unclear domain (0.5%); 11% were specific to TTD issues. Overall, 36% of the 45 SRs assessed risk of bias and/or threats to generalizability.

Conclusion: Assessment of risk of bias and threats to generalizability in primary studies included in SRs of TTD is infrequent, nonstandardized and rarely concerns TTD study specificities. These findings highlight the need for guidance on critical appraisal of studies of TTD.

Keywords: Time to diagnosis; Early diagnosis; Systematic review; Risk of bias; Methodological quality; Critical appraisal

1. Introduction

Time to diagnosis (TTD) is defined as the interval from the first symptoms to the diagnosis of a disease [1,2]. TTD may be related to patient behaviors, physician skills, diagnostic test performance, and/or health care system organization, particularly health care accessibility [2]. Delayed diagnosis may have direct medical and psychological consequences for patients and their relatives and physicians and also medicolegal consequences: diagnosis delays are a major cause of lawsuits in health care [3,4]. All these reasons probably explain why TTD is a growing field of research with a marked increase of the number of related publications in the last 15 years (Appendix A at www.jclinepi.com, web-only supplementary material).

Studies of TTD have 3 main nonexclusive purposes: measuring length of TTD and its evolution over time, identifying the determinants of long TTD, and/or evaluating the relationship between short and long TTD and patient outcomes [1,2]. Long TTD is usually a priori considered associated with worse outcome. For example, the definition for "early diagnosis," the Medical Subject Heading term for TTD studies in PubMed, is "Generally, early diagnosis improves prognosis and treatment outcome" [5]. In most published studies of TTD, authors have concluded a high prevalence of diagnosis delay associated with worse outcome and the need for urgent corrective action [1]. Studies evaluating TTD are generally observational and

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What is new?

Key findings

- In this methodological systematic review, we evaluated the process of critical appraisal of primary studies included in systematic reviews of time to diagnosis and found that only 51% of the 45 included systematic reviews reported such process and only 36% reported an assessment of risk of bias and/or threats to generalizability.
- Among the 232 items composing the critical appraisal tools, 64% assessed the quality of reporting, whereas only 43% assessed risk of bias and/or threats to generalizability.

What this adds to what was known?

- The necessity of a critical appraisal of primary studies included in systematic reviews is generally well accepted, but its content is frequently found inadequate in systematic reviews of time to diagnosis included in our study, with important confusion between quality of reporting and assessment of risk of bias and threats to generalizability.

What is the implication and what should change now?

- Our findings highlight the need for a specific tool to assess risk of bias and threats to generalizability for studies of time to diagnosis.

retrospective and based on already diagnosed cases and then have specific design features exposing them to particular risk of bias and threats to generalizability. These risks include the participant selection process with the specific issue of undiagnosed cases. Such undiagnosed cases can be related to fulminant disease patterns or, in contrast, indolent or spontaneously favorable ones. Another specific feature of the design of studies of TTD is that the definition and measure of TTD can be exposed to risk of bias and threats to generalizability when time points are not obvious. The choice of these time points can be affected by knowledge of the health outcome, for a risk of overestimation of TTD with poor health outcomes [1]. Another important feature with inherent risk relates to the study of the associations between TTD and participant characteristics and health outcomes [1,2].

The internationally accepted reporting guideline for systematic reviews (SRs), the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), its ancestor Quality of Reporting of Meta-analyses (QUOROM), and the reporting guideline Meta-analysis Of Observational Studies in Epidemiology (MOOSE) require that articles specify and present the results of an assessment of risk of bias that may affect the cumulative evidence [6–8]. The measurement tool to assess the methodological quality of systematic reviews (AMSTAR) also recommends to assess and document the scientific quality of the included SRs [9]. Risk of bias tools were developed and validated to conduct SRs of randomized control trials and diagnosis test accuracy studies [10,11]; however, those available for observational studies are generic, mostly developed for studies of interventions [12,13], or are not fully validated [14,15]. As a first step to develop a specific critical appraisal tool for studies of TTD, we aimed to systematically identify and characterize tools used by authors of SRs to critically appraise the methodology of primary studies of TTD. The secondary objective was to identify determinants of an adequate critical appraisal defined as the assessment of risk of bias or threats to generalizability.

2. Methods

For the present SR, we defined critical appraisal of the methodology as the assessment of the risk of bias and threats to generalizability according to the definition used by the authors of the revised tool for the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-II), but we acknowledge that the scope of methodological quality is larger than this definition including ethical concerns, statistical issues, and even quality of reporting as defined in the Cochrane Handbook for Systematic Reviews of Interventions [10,11]. We conducted a methodological SR after the methodology proposed by the Centre for Reviews and Dissemination and reported it using PRISMA guidelines [6,16]. This SR was not registered in PROSPERO (international prospective register of SRs) because it does not cover SRs of exclusively methodological issues [17].

2.1. Search strategy and selection criteria

We systematically searched MEDLINE via PubMed and Web of Science for protocols for in-progress SRs or articles for completed SRs, with or without meta-analyses, of studies of TTD published in English or French up to the end of February 2015. The search strategy was developed from that used in previously published SRs of studies of TTD [1,2], including terms referring to time (delay, interval, time, early, earlier, timely, timeliness, late), health care accessibility (seeking, barrier), diagnosis (diagnosis, diagnoses, diagnostic), SR (systematic review, meta-analysis), and language (English, French). The search strategies were adapted to each database (Appendix B at www.jclinepi.com, web-only supplementary material). We also handsearched reference lists of included SRs and used Google Scholar to search for reports that cited included SRs. We excluded SRs evaluating the impact of an intervention to reduce TTD because a specific tool exists to evaluate risk