Systematic survey of randomized trials evaluating the impact of alternative diagnostic strategies on patient-important outcomes

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Abstract

Objectives: To provide a perspective on the current practice of randomized clinical trials (RCTs) of diagnostic strategies focusing on patient-important outcomes.

Study Design and Setting: We conducted a comprehensive search of MEDLINE and included RCTs published in full-text reports that evaluated alternative diagnostic strategies.

Results: Of 56,912 unique citations, we sampled 7,500 and included 103 eligible RCTs, therefore suggesting that MEDLINE includes approximately 781 diagnostic RCTs. The 103 eligible trials reported on: mortality ($n = 41$; 39.8%); morbidities ($n = 63$; 61.2%); symptoms/quality of life/functional status ($n = 14$; 13.6%); and on composite end points ($n = 10$; 9.7%). Of the studies that reported statistically significant results ($n = 12$; 11.6%), we judged 7 (58.3%) as at low risk of bias with respect to missing outcome data and 4 (33.3%) as at low risk of bias regarding blinding. Of the 41 RCTs that reported on mortality, only one (2.4%) reported statistically significant results. Of 63 RCTs addressing morbidity outcomes, 11 (17.5%) reported statistically significant results, all of which reported relative effects of greater than 20%.

Conclusion: RCTs of diagnostic tests are not uncommon, and sometimes suggest benefits on patient-important outcomes but often suffer from limitations in sample size and conduct. © 2017 Elsevier Inc. All rights reserved.

Keywords: Clinical trials; Diagnostic techniques and procedures; Accuracy; Alternative diagnostic strategies; Patient outcome; Evidence-based medicine

1. Introduction

Laboratory tests and medical imaging [1,2] are necessary for accurate diagnosis and constitute an essential component of patient management [3–5]. Clinicians often adopt tests for routine clinical use on the basis of diagnostic accuracy alone, implicitly assuming that use of accurate tests will improve outcomes: patients will live longer or live better. Even when tests are accurate, however, this may not be the case. A test may not provide incremental diagnostic information over and above inferences based on prior available information; even if a test provides incremental information, results may not change patient management or management may change, but the change may not improve outcome.

Thus, one can conceptualize a hierarchy of diagnostic evidence from that which addresses the capability to capture an image or quantify a laboratory finding; addresses diagnostic accuracy; evaluates test impact on patient management; and informs effects on patient-important outcomes [6–8]. This hierarchy implies that smaller subsets of patients will benefit from a test as researchers advance from simply measuring diagnostic accuracy to evaluating improvements in outcomes (Appendix Fig. 1 on the journal's Web site at www.elsevier.com) [9].

When, despite demonstration of test accuracy, patient benefit remains in doubt, randomized clinical trials (RCTs) that address the impact of alternative diagnostic strategies on patient-important outcomes are required [6–8,10–12]. This principle is well established for screening tests, and investigators have conducted many trials of screening tests. RCTs of test-and-treatment strategies are not, however, routinely performed, recognition of the importance of RCTs of diagnostic tests remains limited [10], and the RCTs thus far conducted remain poorly characterized.

We therefore conducted a systematic survey of diagnostic strategy RCTs to characterize their topic areas, population, setting, intervention and control groups, patient-important outcomes, risk of bias, and results.

2. Methods

2.1. Eligibility criteria

We included studies that met the following criteria:

i)   Randomized control trial.
ii)   Published in full-text report with no language restrictions.
iii) Assessed alternative diagnostic tests or strategies (for instance, test A vs. test B or test A vs. no test). We defined "diagnostic studies" as those that evaluate tests used for diagnosis in patients presenting to any medical setting with symptoms or problems suggesting they may have a target condition. Test results in such situations either aim to decrease or increase the probability the target condition exists.
iv)   Examined the impact of the diagnostic strategies being evaluated on at least one patient-important outcome.

We excluded studies meeting the following criteria:

v)   Crossover studies.
vi)   Studies in which the only patient-important outcome measured was cost.
vii) Studies in which the only patient-important outcomes measured were adverse effects of the testing procedure.
viii) Screening studies (i.e., evaluating tests undertaken when patients have no symptoms or problems suggesting they may have a target condition).
ix)   Monitoring studies (patients already have the diagnosis of the condition of interest, and tests are being used to assess degree of improvement or deterioration).
x)   Studies focused exclusively on diagnostic test accuracy that did not report impact on patient-important outcomes.

2.2. Search strategy

An experienced research librarian searched in MEDLINE via OVID (1946 to December 1, 2013) using a comprehensive search strategy including both subject