

Bivariate meta-analysis of predictive values of diagnostic tests can be an alternative to bivariate meta-analysis of sensitivity and specificity

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Abstract

Objective: Meta-analysis of predictive values is usually discouraged because these values are directly affected by disease prevalence, but sensitivity and specificity sometimes show substantial heterogeneity as well. We propose a bivariate random-effects logitnormal model for the meta-analysis of the positive predictive value (PPV) and negative predictive value (NPV) of diagnostic tests.

Study Design and Setting: Twenty-three meta-analyses of diagnostic accuracy were reanalyzed. With separate models, we calculated summary estimates of the PPV and NPV and summary estimates of sensitivity and specificity. We compared these summary estimates, the goodness of fit of the two models, and the amount of heterogeneity of both approaches.

Results: There were no substantial differences in the goodness of fit or amount of heterogeneity between both models. The median absolute difference between the projected PPV and NPV from the summary estimates of sensitivity and specificity and the summary estimates of PPV and NPV was 1% point (interquartile range, 0–2% points).

Conclusion: A model for the meta-analysis of predictive values fitted the data from a range of systematic reviews equally well as meta-analysis of sensitivity and specificity. The choice for either model could be guided by considerations of the design used in the primary studies and sources of heterogeneity. © 2012 Elsevier Inc. All rights reserved.

Keywords: Systematic reviews; Meta-analyses; Diagnostic test accuracy; Sensitivity and specificity; Positive predictive value; Negative predictive value

1. Background

Current guidance for meta-analyses of diagnostic test accuracy advocates the use of hierarchical methods to summarize estimates of sensitivity and specificity or the diagnostic odds ratio [1,2]. Sensitivity and specificity are not always the most intuitive measures for clinicians, as they express at the group level how many diseased and nondiseased were correctly identified as such by the test. Clinicians may be more familiar with predictive values [3,4]. The positive predictive value (PPV), for example, expresses the probability of disease in those testing positive. Similarly, the negative

predictive value (NPV) expresses the probability of the absence of disease in those testing negative.

For clinicians interested in predictive values, meta-analyses of these statistics may be easier to understand and to apply in practice. In addition, predictive values may suffer less from work-up bias and problems associated with partial and differential verification bias than sensitivity and specificity [5]. In many studies, test positives are verified by a different clinical reference standard than test negatives. Examples are accuracy studies where biopsy is the reference standard; if no lesion is found, biopsy cannot be done. In these studies, test negatives are either not verified at all or clinically followed-up for verification of the negative test result. Different reference standards may also be applied for ethical reasons, where one hesitates to use the preferred but invasive reference standard in test negatives,

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What is new?

- Current guidance for meta-analyses of diagnostic test accuracy advocates the use of hierarchical methods to summarize estimates of sensitivity and specificity or the diagnostic odds ratio.
- We propose a model for direct meta-analysis of predictive values, using similar hierarchical methods.
- A model for the meta-analysis of predictive values fitted the data from a range of systematic reviews equally well as meta-analysis of sensitivity and specificity.
- The choice for either model could be guided by considerations about the designs used in the primary studies and likely sources of heterogeneity.

who have a lower probability of disease. Under these circumstances, summarizing predictive values may be more meaningful than meta-analysis of sensitivity and specificity.

Meta-analysis of predictive values in systematic reviews of test accuracy studies has been discouraged for several reasons. Predictive values are expected to be more heterogeneous than other accuracy measures because they would vary more directly with changes in disease prevalence. Sensitivity and specificity, in contrast, are assumed to be more stable characteristics of tests, which would make summary estimates of sensitivity and specificity more meaningful. The sources of variation and bias for sensitivity and specificity are better understood than those for predictive values. Yet, one could successfully argue that these arguments are too simple. Sensitivity and specificity are not fixed test properties either. They describe the behavior of a test under specific conditions, and they typically change across different segments of the disease spectrum and with varying disease prevalence [6–8].

We propose a model for the meta-analysis of predictive values, based on a previously published bivariate logitnormal random-effects model for the meta-analysis of sensitivity and specificity.

If it is true that predictive values are more heterogeneous than sensitivity and specificity, one can expect a lower goodness of fit with a model for meta-analysis based on predictive values. We therefore compared, across a range of published systematic reviews, to what extent a model for meta-analysis based on predictive values provides a better—or worse—summary of the data than an equivalent model based on sensitivity and specificity [9]. We also compared the summary estimates from the model for predictive values with projected estimates from a meta-analysis of sensitivity and specificity, using the median prevalence and Bayes' rule.

2. Methods**2.1. Study set**

We used a set of 31 meta-analyses, selected and analyzed for a previously published report on bias and variation in diagnostic accuracy studies. The meta-analyses cover a wide range of clinical topics and diagnostic tests, such as imaging tests, laboratory tests, physical examination, and questionnaires. For more details on the search process, selection and data-extraction, we refer to the original report [10]. In short, a number of electronic databases were searched for systematic reviews published between January 1999 and April 2002 and fulfilling the following criteria: 1) assessment of diagnostic test accuracy; 2) including at least 10 original studies on the same diagnostic test; 3) no exclusion of primary studies based on design features; and 4) the ability to reproduce the 2×2 tables from the original studies. We excluded case–control studies to allow for realistic estimates of prevalence and predictive values.

2.2. Definitions

For every study, in each systematic review, we calculated the PPV and NPV, and the sensitivity and specificity from the reported numbers. The PPV was defined as the proportion of patients with the target condition in those testing positive on the test under evaluation. Similarly, the NPV was defined as the proportion of patients without the target condition in those testing negative on the test under evaluation. Conventionally, sensitivity was defined as the proportion of patients testing positive in those with the target condition. Specificity was defined as the proportion of patients testing negative in those without the target condition.

2.3. Descriptive statistics

We calculated the median, interquartile range (IQR), and minimum and maximum predictive values, sensitivity, and specificity of the studies in each review. We plotted these descriptive statistics for PPV and NPV side by side to those for sensitivity and specificity.

2.4. Meta-analysis

We developed a bivariate logitnormal random-effects model for meta-analysis of predictive values. This model has the same form as the previously proposed bivariate logitnormal model for meta-analysis of sensitivity and specificity [9]. That model was in itself based on an approach to meta-analysis introduced by Van Houwelingen et al. [11,12].

The original bivariate model was used to obtain summary estimates of sensitivity and specificity for each test in a review. In this model, pairs of sensitivity and specificity are jointly analyzed, incorporating any correlation that is to be expected between these two measures using a random-effects approach. The correlation between sensitivity and specificity will be mainly driven by threshold effects:

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