

# Developing a Framework for Assessing the Applicability of the Target Condition in Diagnostic Research

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**KEYWORDS:** Applicability, Systematic review, QUADAS-2, Reference standard, Target condition

## INTRODUCTION

Assessment of the applicability of primary studies to the review questions is an essential but often challenging aspect of systematic reviews of diagnostic test accuracy studies (DTA reviews).

## OBJECTIVES

To explore review authors' applicability assessments for the QUADAS-2 reference standard domain within Cochrane DTA reviews, by highlighting applicability concerns, identifying potential issues with assessments. Using the findings to develop a framework for assessing the applicability of the target condition as defined by the reference standard.

## METHODS

Methodological review. DTA reviews in the Cochrane Library that used QUADAS-2 and judged applicability for the reference standard domain as "high concern" for at least one study, were eligible. One reviewer extracted the rationale for the "high concern", this was checked by a second reviewer. Two reviewers categorized the rationale inductively into themes, a third reviewer verified these. Discussions in the QUADAS development group (steering group and expert panel) regarding the extracted information informed framework development.

## RESULTS

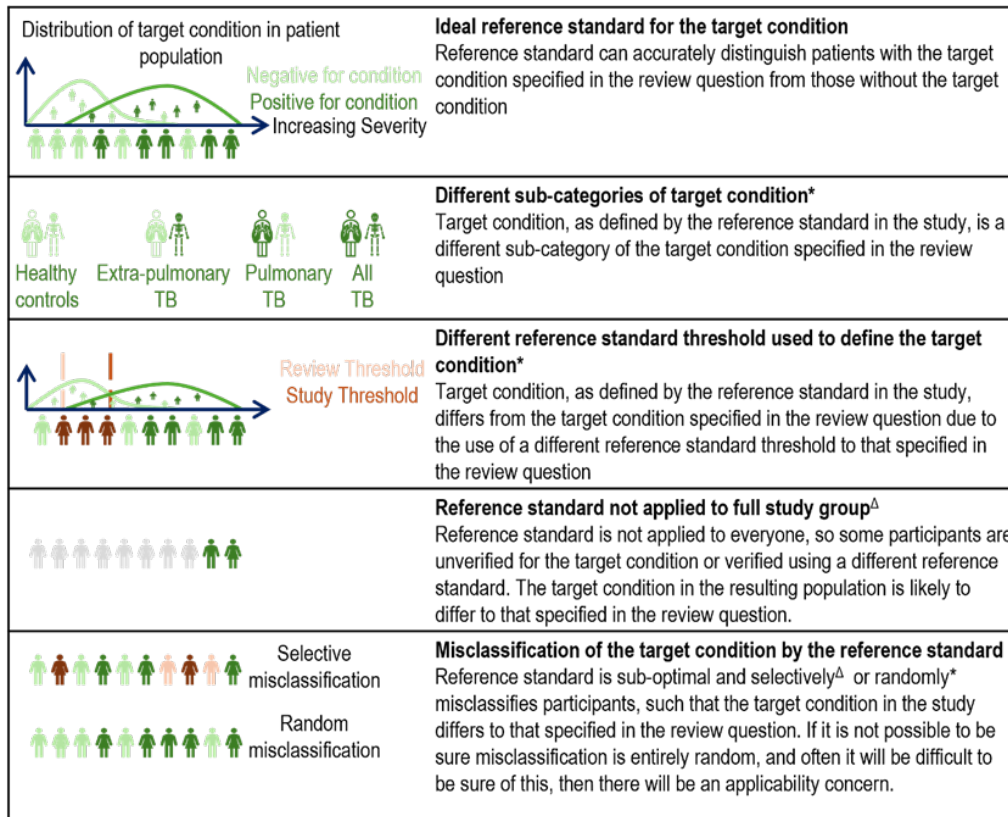
We identified 50 eligible reviews. We identified potential issues over half (n=28) of the included reviews. In 7, applicability assessments deviated from QUADAS-2 definitions and in 21 applicability concerns were insufficiently described. Five themes emerged in the remainder: study uses different reference standard threshold to define the target condition (6 reviews), misclassification by the reference standard in the study such that the target condition in the study does not match the review question (11 reviews), reference standard could not be applied to all participants resulting in a different target condition (5 reviews), misunderstanding QUADAS-2 applicability (7 reviews), and insufficient information (21 reviews).

The Figure shows the framework that was informed by our findings and discussions. Our framework outlines four potential applicability concerns for the assessment of the target condition as defined by the reference standard: different sub-categories of the target condition, different threshold used to define the target condition, reference standard not applied to full study group, and misclassification of the target condition by the reference standard (Figure).

## CONCLUSION

Clear sources of applicability concerns are identifiable, but several Cochrane review authors struggle to adequately identify and report them. We have developed the first applicability framework to guide review authors in their assessment

of applicability concerns for the QUADAS reference standard domain. The development of a framework for the QUADAS-2 domains Patient selection and Index Test are ongoing.



<sup>Δ</sup>Applicability issue linked to risk of bias (RoB) judgement (if high applicability concerns applicability, then high RoB); \*Applicability issue separate from RoB judgement

Figure 1. Framework for assessing the applicability of the target condition in diagnostic research