The asthma control test and asthma control questionnaire for assessing asthma control: systematic review and meta-analysis


CRD summary
The authors concluded that the Asthma Control Test and Asthma Control Questionnaire (versions 6 and 7) performed well when assessing "controlled" and "not well-controlled" asthma at prespecified cut-off points but not for "uncontrolled" asthma. The findings may have been overstated. The usefulness of the findings is limited by differences between the included studies and because the comparisons were indirect.

Authors' objectives
To assess the diagnostic accuracy of the Asthma Control Test and Asthma Control Questionnaire for asthma control.

Searching
PubMed, EMBASE and Web of Science were searched between 1998 and December 2011 for relevant articles. Search terms were reported. No language or publication restrictions were applied. Cochrane Central Register of Controlled Trials (CENTRAL) was searched in 2012. Reference lists of review articles were searched manually.

Study selection
Eligible trials were studies that assessed the diagnostic accuracy of the Asthma Control Test and Asthma Control Questionnaire (not the children's versions) and reported adequate data to enable calculation of sensitivity and specificity. Studies that applied multiple assessments using the same instrument in one patient were excluded from the review.

Reference standards for asthma control were those defined by the Global Initiative for Asthma (GINA), National Asthma Education and Prevention Programme (NAEPP) and Brazilian guidelines. Prespecified cutoff points for "controlled", "not well-controlled" and "uncontrolled" asthma and definitions for non-prespecified cutoff points for asthma control levels were defined in the review.

Included studies were conducted in USA, the Asia-Pacific region and Europe between 2004 and 2012. Included patients were seen in primary, secondary and tertiary care settings. Where reported, the mean age of patients ranged from 34.9 to 49.9 years. Where reported, asthma severity varied between studies. Most patients in most studies had mild or moderate asthma; in some studies most patients had moderate or severe asthma. Most studies also included patients with intermittent asthma. Three different versions (five, six and seven) of the Asthma Control Questionnaire were used in the different studies. The two diagnostic tools included up to seven domains to assess asthma control levels, including day and nighttime symptoms, activity limitation and use of short-acting beta2-agonists.

Two reviewers screened studies for inclusion.

Assessment of study quality
Studies were assessed using the revised quality assessment tool for diagnostic accuracy studies (QUADAS-2). Studies were assessed for risk of bias and applicability on four domains: patient selection, index test, reference standard and flow and timing. Studies assessed as low on all four domains related to bias or applicability were judged to have overall low risk of bias or low concern regarding applicability. Studies assessed as high or unclear in one or more domains were judged overall to be at risk of bias or to have concerns regarding applicability. Various study design characteristics were assessed (as reported in the review).

Two reviewers independently assessed study quality. Disagreements were resolved through consensus or referral to a third reviewer.

Data extraction
True and false positive results and true and false negative results were extracted to construct 2x2 tables for studies based
on prespecified cutoff points and studies based on non-prespecified cutoff points.

Two reviewers independently extracted data and any discrepancies were resolved through consensus or referral to a third reviewer. Primary authors were contacted for further information where necessary.

**Methods of synthesis**

A bivariate random-effects model was used to pool data to calculate sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratios (DOR), along with their 95% confidence intervals (CI). Data were pooled where at least four studies reported results. Where fewer than four studies reported data, results were presented as medians and ranges (minimum and maximum). Data were presented separately for studies based on prespecified and non-prespecified cutoff points and separately by level of asthma control and diagnostic tool used.

Hierarchical summary receiver operating characteristic (HSROC) curve analysis was undertaken and the HSROC area under the curve (AUC) was used to assess the degree of accuracy of the tests according to established guidelines (excellent, very good, good and poor; as defined in the review).

Statistical heterogeneity was assessed using Cochran’s Q and the I² statistic (I²>50% indicated significant heterogeneity). Subgroup analysis and meta-regression were performed to investigate the effects of the different tools for assessing asthma control levels and study and patient characteristics (as reported in the review).

Publication bias was assessed using funnel plots.

**Results of the review**

Twenty-one cross-sectional diagnostic accuracy studies (23,624 patients) were included in the review. Twelve studies assessed the Asthma Control Test, six studies assessed the Asthma Control Questionnaire and three studies assessed both tools. Only three studies were considered to have overall low risk of bias. All studies had low concern regarding applicability.

Prespecified cut-off studies assessing the Asthma Control Test showed good diagnostic accuracy in "controlled" asthma patients (sensitivity 0.77, 95% CI 0.68 to 0.84, specificity 0.84, 95% CI 0.74 to 0.91; nine studies) and "not well-controlled" patients (sensitivity 0.75, 95% CI 0.63 to 0.83, specificity 0.82, 95% CI 0.76 to 0.87; 11 studies) but not for "uncontrolled" asthma patients (sensitivity 0.49, 95% CI 0.42 to 0.56, specificity 0.92, 95% CI 0.86 to 0.96; seven studies). Statistical heterogeneity was reported for pooled estimates.

All three versions of the Asthma Control Questionnaire had higher sensitivity compared to the Asthma Control Test but lower specificity in "controlled" asthma patients (median results were reported as fewer than four studies assessed this outcome). The Asthma Control Questionnaire showed good diagnostic accuracy in "not well-controlled patients" using version 7 (sensitivity 0.74, 95% CI 0.61 to 0.83, specificity 0.81, 95% CI 0.72 to 0.88; five studies) and version 6 (sensitivity 0.65, 95% CI 0.52 to 0.76, specificity 0.90, 95% CI 0.86 to 0.92; four studies) but there was some evidence of statistical heterogeneity. Version 5 of the Asthma Control Questionnaire showed slightly higher specificity compared to the Asthma Control Test but lower sensitivity (three studies) in "not well-controlled" patients (median results were reported as fewer than four studies assessed this outcome).

Sensitivity and specificity values significantly increased for both the Asthma Control Test and Asthma Control Questionnaire when non-prespecified cut-off value studies were assessed and compared to prespecified studies.

Pooled results for likelihood ratios and diagnostic ratios were reported in the review. Results for subgroup analyses and meta-regression were reported in the review. Funnel plots suggested that potentially relevant unpublished data may have been missed.

**Authors' conclusions**

The Asthma Control Test and Asthma Control Questionnaire (versions 6 and 7) performed well when used to assess "controlled" and "not well-controlled" asthma at the prespecified cut-off points but were not useful for assessing "uncontrolled" asthma.

**CRD commentary**
The review question and supporting inclusion criteria were stated clearly. There was satisfactory search of the literature with no language and publication restrictions. However, funnel plots suggested that potentially relevant unpublished data may have been missed. Each stage of the review process was conducted in duplicate which reduced potential for reviewer error and bias. Study quality was assessed. Most studies were at some risk of bias. The authors acknowledged that sensitivity and specificity can be overestimated in studies at high risk of bias.

It was unclear whether suitable methods were used to calculate diagnostic odds ratios and there was evidence of statistical heterogeneity for some pooled results. The authors investigated heterogeneity extensively but it was unclear whether pooling of such varied studies was appropriate. The authors acknowledged that no clear definitions of asthma control were available and neither the Global Initiative for Asthma nor the National Asthma Education and Prevention Programme are gold standards for the assessment of asthma control. They acknowledged that the comparisons between the Asthma Control Test and Asthma Control Questionnaire were indirect.

The authors’ conclusions reflect the evidence but the studies were heterogeneous and it was unclear whether the findings were overstated. It was not possible to comment on the comparative performance of the two diagnostic tools as they were not compared directly and this limits the usefulness of the findings.

**Implications of the review for practice and research**

**Practice:** The authors stated that the Asthma Control Test was suitable for use in clinical practice but the Asthma Control Questionnaire needed further cross-validation.

**Research:** The authors stated that additional long-term randomised controlled trials were needed to compare the Asthma Control Test to a sham test (adjusting for asthma interventions) to assess future risk of asthma outcomes.

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