Integration of patient characteristics and the results of Chlamydia antibody testing and hysterosalpingography in the diagnosis of tubal pathology: an individual patient data meta-analysis


CRD summary
This individual patient data meta-analysis found that a combination of patient characteristics, with Chlamydia antibody testing and hysterosalpingography, was best for diagnosing bilateral tubal pathology in subfertile women. This conclusion follows from the data presented and is likely to be reliable.

Authors' objectives
To use individual patient data meta-analysis to determine whether combining a patient's medical history and physical examination results, with those of tubal patency tests, could improve the prediction of tubal pathology. Also, to create a clinical tool for calculating the probabilities of tubal pathology and of bilateral tubal pathology.

Searching
MEDLINE and EMBASE were searched, without language restrictions, to January 2010 and search terms were reported. The bibliographies of relevant studies were screened for additional articles, and study authors were contacted to identify further studies.

Study selection
Studies were eligible for inclusion if they reported diagnostic data on both the Chlamydia antibody test and hysterosalpingography or hystero-contrast-sonography, and if they used laparoscopy as a reference test to verify tubal pathology.

All the included studies were of women who were referred for subfertility work-up. For all included patients, other causes of subfertility, such as anovulation or low semen quality, were excluded. Studies excluded women with various categories of previous surgery (abdominal, pelvic, or tubal). The mean age of study participants was 31 to 32 years, and the median duration of subfertility was 1.4 to three years. The studies used enzyme-linked immunosorbent assay, immunofluorescence or micro-immunofluorescence techniques for Chlamydia antibody testing. The percentage of patients with primary subfertility ranged from 11 to 75.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality
The methodological quality of the included studies was assessed using the QUADAS criteria. Additional items were added for the description of selection criteria, execution of diagnostic tests, and the diagnostic strategy that was used.

The number of reviewers who assessed quality was not reported.

Data extraction
The authors of all eligible studies were invited to collaborate. Those who were willing to participate were provided with a detailed study proposal, and asked to provide their original data. If variables and categories were not adequately labelled, a separate data dictionary was requested.

The data sets had to include: anonymous patient identifiers, patient characteristics (age, type of subfertility, body mass index, etc.), Chlamydia antibody test results, tubal patency test results, and the results of the diagnostic laparoscopy. For hysterosalpingography or hystero-contrast-sonography (tubal patency tests), tubal pathology was defined as impaired or absent flow of contrast medium in the fallopian tubes. For laparoscopy, tubal pathology was defined as the occlusion of the fallopian tubes, with or without hydrosalpinges or peritubal adhesions. Any and bilateral tubal pathologies were recorded separately.
The completeness of the data sets was assessed, based on the availability of data on patient identifiers, diagnostic test results, and target disease. Data from the study authors were compared with the published results, for consistency. Participating authors were contacted to confirm missing data or to discuss any major discrepancies. A collaborators meeting was held, for further discussion and clarification of data.

The number of reviewers who extracted the data was not reported.

**Methods of synthesis**

The prevalences of any and bilateral tubal pathologies were calculated separately, for individual studies and for all the data. Estimates of the sensitivity and specificity of the Chlamydia antibody test, hysterosalpingography, and hystero-contrast-sonography, for the detection of tubular pathology were calculated, for individual studies and overall. A missing value analysis was performed and missing patient characteristic and diagnostic data were imputed, using a 10-round imputation procedure.

Univariate and multivariate logistic regression models were developed for any and for bilateral tubal pathology. Odds ratios and 95% confidence intervals, as well as probabilities, were calculated for all candidate variables. Variables with a probability of less than 0.30 were considered as candidate predictors in the multivariate logistic regression, and a significance of 0.20 was used to retain predictors in the model. Random intercepts were used in both models to account for between-study heterogeneity in the prevalence of tubal pathology. Four models were constructed: a patient characteristics model; a patient characteristics model, with the addition of the Chlamydia antibody test; a patient characteristics model, with the addition of hysterosalpingography or hystero-contrast-sonograph; and a patient characteristics model, with the addition of the antibody test and hysterosalpingography or hystero-contrast-sonography.

The diagnostic performance of the four models was assessed using receiver operating characteristic analyses. The individual diagnostic performances of the Chlamydia antibody test, hysterosalpingography and hystero-contrast-sonography were plotted. Women were classified by their predicted probability of tubal pathology, based on each model, and the percentage of patients who were correctly reclassified following the addition of hysterosalpingography or hystero-contrast-sonography was calculated.

A clinical diagnostic tool was derived from the model. This included medical history, physical examination, the Chlamydia antibody test, and hysterosalpingography or hystero-contrast-sonography. The tool calculated a summary score to indicate the probability of any or bilateral tubal pathology.

**Results of the review**

Ten eligible studies were found; the authors of one study could not be traced, two authors did not respond to initial contact, and a further three reported that their data were lost. Four studies, with 4,883 participants, were included in the analysis. There were no major differences in participant selection, prevalence of tubal pathology, and other participant characteristics, between the included and excluded studies. The quality of the data was considered sufficient for all included studies; there were minimal differences between the received data and published results. The QUADAS assessment indicated that the main methodological concerns were partial verification bias and no blinding for interpretation of the reference standard.

The overall pooled prevalence of any tubal pathology was 25% (range 18 to 27) and of bilateral tubal pathology was 12% (range nine to 16).

**Any tubal pathology:** The pooled sensitivity of Chlamydia antibody test alone was 53% (95% CI 48 to 58), with a specificity of 72% (95% CI 69 to 74). The pooled sensitivity of hysterosalpingography alone was 75% (95% CI 69 to 81), with a specificity of 74% (95% CI 71 to 77). The patient characteristics model included duration and type of subfertility, previous pelvic inflammatory disease, previous pelvic surgery, and previous Chlamydia infection. The area under the curve was 0.63 (95% CI 0.61 to 0.65). The addition of the Chlamydia antibody test increased the predictive value (AUC 0.67). The addition of hysterosalpingography, to the patient characteristics model, increased the predictive value (AUC 0.76). The addition of both the antibody test and hysterosalpingography did not increase prediction beyond that for the patient characteristics model with hysterosalpingography.

**Bilateral tubal pathology:** The pooled sensitivity of the Chlamydia antibody test was 66% (95% CI 59 to 72), with a specificity of 70% (95% CI 68 to 73). The pooled sensitivity of hysterosalpingography was 62% (95% CI 50 to 71),
with a specificity of 91% (95% CI 89 to 93). The patient characteristics model included duration of subfertility, previous pelvic inflammatory disease, and previous Chlamydia infection. It gave an area under the curve of 0.63 (95% CI 0.60 to 0.66). Combining this model with either the Chlamydia antibody test or hysterosalpingography increased the predictive value (AUC 0.72), and addition of both tests further increased the predictive value (AUC 0.76).

Details of the clinical diagnostic tool were reported.

**Authors' conclusions**
The combination of patient characteristics with Chlamydia antibody testing and hysterosalpingography was best for diagnosing bilateral tubal pathology in subfertile women.

**CRD commentary**
The review addressed a clearly stated objective. Appropriate inclusion criteria were defined and relevant studies were sought, without language restrictions. Attempts to contact the study authors were reported. The methodological quality of the included studies, and their ability to represent the overall data, were assessed. Methods for cross-checking the data provided by study authors were reported. The meta-analysis methods were reported in detail and appear to have been appropriate.

Overall, the authors' conclusions follow from the data presented and are likely to be reliable.

**Implications of the review for practice and research**
The authors did not specify any recommendations for clinical practice and future research.

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