Application of the Sherlock Mycobacteria Identification System using high-performance liquid chromatography in a clinical laboratory

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The Sherlock Mycobacteria Identification System (SMIS; MIDI Inc.) was examined. This uses computerised software and a high-performance liquid chromatograph (HPLC; Hewlett Packard series 1100) to identify mycobacteria to the species level.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised fresh clinical isolates and stock cultures of clinical isolates.

Setting
The setting was a clinical microbiology laboratory. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from April 1998 to April 2000. The price year was not provided.

Source of effectiveness data
The effectiveness evidence was derived from a single study and authors' assumptions.

Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of specimens as that used in the effectiveness study.

Study sample
No justification for the choice of the sample size was provided. A total of 370 isolates was included in the analysis. There were 126 fresh cultures and 244 stock cultures. A single group of specimens was considered.

Study design
The effectiveness evidence on the SMIS results was derived from a case series study, which appears to have been conducted prospectively in a single centre, the clinical microbiology laboratory at the York Hospital in York (PA), USA. The length of follow-up was not reported.
**Analysis of effectiveness**

The outcome measure used in the analysis was the accuracy of the SMIS in comparison with the reference methods. The SMIS result was considered correct if the correct species name of an isolate was listed on the software report as the first choice, regardless of the magnitude of the similarity index value accompanying that species' name. If the SMIS and the reference method identifications differed, or the SMIS was unable to identify an isolate, a fresh extract of a new subculture of the isolate on the Middlebrook 7H10 agar was analysed in the SMIS a second time. If an isolate was misidentified by the SMIS when first tested, it was counted as a misidentification, regardless of whether it was correctly or incorrectly identified when it was reanalysed. If it was unidentified by the SMIS when first tested, and then correctly or incorrectly identified when the chromatography was repeated, it was counted as either a correct or incorrect identification. The predictive values for the accuracy of SMIS software assignments of unknown mycobacterial isolates to each of the mycobacterial species or group was determined. More specifically, the number of correct SMIS calls for a given species was divided by the total number of times that isolates were correctly or incorrectly assigned by the SMIS to that species.

**Effectiveness results**

Of the 370 isolates, 327 (88%) were named by the SMIS software and 43 (12%) were unidentified.

The SMIS correctly named 279 isolates (75% of the total number of mycobacterial isolates and 85% of the isolates given a name by the system).

The number of isolates misidentified was 48 (13% of the total isolates studied and 15% of the isolates named by the system).

The correct identification ranged from 4 to 100% depending on the species of the isolates.

Only 4 isolates (M. lentiflavum, M. phlei, M. smegmatis and M. vaccae) for which the SMIS software library had no data were tested. All 4 isolates were correctly called "no match" (unidentified) by the system.

The predictive value of the SMIS for species identification was 85% overall, but it ranged from 27 to 100%.

Of the 370 isolates studied, 115 (31%) had to be analysed a second time because the initial results were either incorrect (38 isolates), or the isolates were unidentified (77 isolates). For these 115 retested isolates, the SMIS identification for 33 (29%) changed from incorrect or unidentified to correct. Results from another 28 (24%) remained incorrect, results for 43 (37%) remained unidentified, results for only 1 (1%) changed from incorrect to unidentified, and results of 10 (9%) changed from unidentified to incorrect.

In many cases, a mycobacterial isolate that had been misidentified could be easily identified correctly by calculating the relative peak height ratios (RPHRs) of mycolic acids and comparing these figures with known values for species with similar chromatographic profiles of mycolic acids. By using RPHRs and relative retention times, all 48 SMIS-misidentified isolates and 39 (91%) of the 43 SMIS-unidentified isolates could be correctly identified without additional tests.

**Clinical conclusions**

The effectiveness study showed that the SMIS, combined with a knowledge of RPHRs, relative retention times and phenotypic characteristics, represented a rapid and accurate diagnostic strategy.

**Methods used to derive estimates of effectiveness**

Some assumptions on the efficacy of the comparators were made.

**Estimates of effectiveness and key assumptions**

The authors assumed that all the reference tests had 100% accuracy in detecting mycobacteria.
Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used in the economic study. In effect, a cost-consequences analysis was carried out.

Direct costs
Discounting was not relevant since the costs were incurred during a short time. The unit costs were not reported separately from the quantities of resources used. The health services included in the economic evaluation were materials and labour. Further details of the cost analysis were not provided. The cost/resource boundary of the study, the source of the data and the price year were not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The total costs associated with the test of each isolate and control were:

- $10.94 ($4.46 for material and $6.48 for labour) with SMIS-HPLC,
- $26.58 ($14 for material and $12.58 for labour) with nucleic acid probes, and
- $42.31 ($14.48 for material and $27.83 for labour) with the biochemical test.

The initial software and hardware costs of the SMIS were just over $50,000 and an annual service contract was about $4,000.

Synthesis of costs and benefits
The costs and benefits were not combined because a cost-consequences analysis was performed.

Authors' conclusions
The use of the Sherlock Mycobacteria Identification System (SMIS) for the identification of clinical isolates represented a rapid, accurate and efficient approach in comparison with traditional reference methods (i.e. biochemical tests and nucleic acid probes).
CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, which were considered to be reference methods. Therefore, their selection appears to have been appropriate. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The basis of the analysis of effectiveness was a review of case series for the intervention strategy, while the reference methods were assumed to have 100% accuracy. The source of the evidence therefore appears to have been somewhat weak, as the alternative strategies were not directly compared. The use of a more robust design would have assisted in drawing firmer conclusions about the accuracy of the SMIS.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted.

Validity of estimate of costs
The cost analysis was strictly limited to the costs of the tests, including labour and materials. The initial acquisition costs of the SMIS equipment were also reported. However, in general, little information on the cost analysis was provided since the study mainly focused on the study of efficacy of the interventions, the cost analysis representing a secondary aim of the study. The analysis considered the costs associated with performing the tests and repeating them due to initial uncertain results. The authors noted that the cost analysis of the SMIS should consider the purchase price of the system, the cost of an annual service contract, and the number of isolates recovered and analysed (by HPLC) each month.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Consequently, the external validity of the study was low. Sensitivity analyses were not conducted. The study referred to clinical isolates that needed to be investigated for the identification of mycobacteria, and this was reflected in the conclusions of the analysis.

Implications of the study
The authors suggested that, in a very experienced mycobacteriology laboratory familiar with HPLC, the introduction of the SMIS might not be as useful as it could be in less experienced, general clinic microbiology laboratories that isolate a large variety of mycobacterial species. The authors also noted that the cost-advantages of the SMIS could be reduced if a large proportion of isolates have to be reprocessed. Further studies should include strains of additional species or subspecies, and should investigate the ability of the system to identify mycobacteria directly from broth cultures.

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