The tale of two serologic tests to screen for syphilis: treponemal and nontreponemal - does the order matter?

Owusu-Edusei K, Koski KA, Ballard RC

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.

CRD summary
This study examined the cost-effectiveness of algorithms to screen for syphilis, considering the order of testing, in high- and low-prevalence settings. One-step algorithms had high unnecessary treatment rates, making two-step algorithms preferred. A nontreponemal test followed by a treponemal test was more cost-effective than treponemal first, in the low-prevalence setting, and cost-saving in the high-prevalence setting. The cost-effectiveness framework was appropriate, but there were some methodological limitations and limited reporting, which might affect the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of four algorithms to screen for syphilis, using treponemal or nontreponemal tests or both, considering the order of testing, in high- and low-prevalence settings. The low-prevalence setting considered the general US population, while the high-prevalence setting considered pregnant women in sub-Saharan Africa.

Interventions
The four algorithms were nontreponemal only (on-site), treponemal only, nontreponemal first, and treponemal first. In the first two algorithms, positive cases were treated. In the second two, patients with positive results were given the other type of test, and those with positive results on both tests were treated.

The treponemal tests were *Treponema pallidum* passive particle agglutination assay, enzyme immunoassays, and the fluorescent treponemal antibody absorption test. The nontreponemal tests were the rapid plasma reagin test, and the venereal disease research laboratory test.

Location/setting
USA and sub-Saharan Africa/laboratory and hospital.

Methods
Analytical approach:
The analysis was based on a cohort decision model that focused on the treatment of patients who did not need it. A lifetime horizon was considered for the low-prevalence setting, and the length of the gestation period in pregnant women was considered for the high-prevalence setting. The authors stated that the perspective of the health care system was adopted.

Effectiveness data:
The clinical data were from a selection of relevant sources and authors’ opinions. Where available, the epidemiological data were from US sources for low prevalence, and sub-Saharan Africa for high prevalence. A key input was the rate of unnecessary treatment. Some assumptions were needed.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The number of treated cases was the summary benefit measure. In the high-prevalence setting, birth outcomes were also considered.

Cost data:
The economic analysis included the costs of treponemal and nontreponemal tests, follow-up, and the treatment of syphilis. The costs of having a low birth weight, congenital syphilis, and neonatal deaths were included for the high-prevalence setting. The unit costs were presented for the screening tests, while the treatment costs were reported as category totals. Some costs were based on Medicare tariffs, while most of the data were from published studies. All costs were in US dollars ($) and the price year was 2008.

Analysis of uncertainty:
The uncertainty was investigated in threshold analyses, which determined the critical value for an input at which the cost-effectiveness decision switched from one algorithm to another. Two-way sensitivity analyses were carried out. The ranges of values were based on the literature or authors’ opinions.

Results
Low prevalence: In the hypothetical cohort of 10,000 individuals, there were 34 actual cases treated with nontreponemal first, 34 with treponemal first, 40 with treponemal only, and 43 with nontreponemal only. The unnecessary treatment rate was 0.88% with nontreponemal first, 0.88% with treponemal first, 16.45% with treponemal only, and 9.37 with nontreponemal only. The total net costs were $48,000 with nontreponemal first, $51,000 with treponemal first, $89,000 with treponemal only, and $58,000 with nontreponemal only.

Nontreponemal first was the reference strategy. Both treponemal first and treponemal only were dominated as they were less effective and more expensive than another strategy. The incremental cost per additional case treated was $1,100 with nontreponemal only.

High prevalence: In the hypothetical cohort of 10,000 pregnant women, the number of actual cases treated was 350 with nontreponemal first, 350 with treponemal first, 603 treponemal only, and 580 with nontreponemal only. The unnecessary treatment rate was 0.13% with nontreponemal first, 0.13% with treponemal first, 1.60% with treponemal only, and 0.39% with nontreponemal only. Cost savings were associated with each strategy.

Non-treponemal first was more cost saving than treponemal first, but nontreponemal only saved the most costs. Both treponemal first and nontreponemal first prevented fewer adverse birth outcomes than treponemal only or nontreponemal only.

The sensitivity analysis showed that the cost of the treponemal test should be below $5.8 in the low-prevalence setting and $1.8 in the high-prevalence setting, to make the treponemal first algorithm more cost-effective than the nontreponemal first algorithm. Other variables had less impact on the study results.

Authors’ conclusions
The authors concluded that one-step algorithms had high unnecessary treatment rates, making two-step algorithms preferred, although the one-step algorithms prevented more adverse health outcomes. The nontreponemal first strategy was the more cost-effective than treponemal first, in the low-prevalence setting, and cost-saving in the high-prevalence setting, due to fewer confirmatory tests.

CRD commentary
Interventions:
The authors justified their selection of the comparators, as international organisations recommended using two serologic tests; a nontreponemal screening test, with a confirmatory treponemal test, to reduce the risk of a false-positive diagnosis. They assessed the most commonly used treponemal and nontreponemal tests.
Effectiveness/benefits:
The authors made appropriate distinctions between the high- and low-incidence settings, but the approach used to identify the data for these two settings was not clear. No literature search was reported. The authors did not provide any information on the methods, such as the design, patient population, and type of interventions, of these source studies, limiting the possibility of judging the validity of these data. Authors’ opinions were needed to estimate other inputs. To address these limitations, the authors considered wide ranges of values for these inputs in the sensitivity analyses. The benefit measure was the immediate outcome of the screening programmes, which was disease specific and might not be comparable with the health benefits of other interventions.

Costs:
The categories of costs appear to have been relevant to the perspective of the health care system, but the costs were not reported in detail. The data sources were not clearly described and a breakdown of cost items was not given. Some total categories of costs were reported. Discounting was not reported and would have been relevant for the lifetime horizon of the analysis. In general, the economic data were not presented transparently. The costs were varied in the sensitivity analysis.

Analysis and results:
The results were extensively presented and various model outcomes were reported. The costs and benefits of the screening programmes were combined in an incremental analysis. The uncertainty was extensively investigated, using deterministic techniques, and the findings were clearly reported. The authors noted some limitations to their analysis, mainly relating to the use of modelling and parameters from various sources. The analysis appears to have been specific to the USA and might not be transferable to other settings.

Concluding remarks:
The cost-effectiveness framework was appropriate, but there were some methodological limitations and the limited reporting of the data sources might affect the validity of the authors’ conclusions.

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