Utility of direct measurement of low-density lipoprotein cholesterol in dyslipidemic pediatric patients


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
Direct measurement of low-density lipoprotein cholesterol (DLDL-C) in dyslipidemic pediatric patients (children and adolescents).

Type of intervention
Screening and primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Hyperlipidemic children and adolescents younger than 21 years fasting for a minimum of 12 hours and with triglyceride levels less than 4.52 mmol

Setting
Hospital. The economic setting was Boston, USA.

Dates to which data relate
The main effectiveness data were obtained from a single study conducted in 1997. Resource and cost data were derived from 1997 sources. The price year was not stated.

Source of effectiveness data
The estimates of accuracy in classifying patients into treatment groups, as established by the NCEP, and the positive and negative predictive values for each method were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness analysis, but whether it was undertaken retrospectively or prospectively is unclear.

Study sample
Overall 92 fasting hyperlipidemic pediatric patients were included in the analysis. The mean age of patients was 11.6 (+/- 3.8) years (range: 4 - 20). More than 70% had a history of premature heart disease and nearly all patients had a family history of hyperlipidemia. Power calculations to determine the sample size were not undertaken.
Study design
This was a case series conforming to an approved protocol. Data were collected, based on samples, over a six month period.

Analysis of effectiveness
The basis for the analysis of effectiveness can most accurately be described as intention to treat. The primary health outcome was the accuracy in classifying patients into treatment groups as established by the NCEP and positive and negative predictive values for each method compared with the reference procedure.

Effectiveness results
At the LDL-C concentration cut-offs commonly used for making therapeutic decisions, with the DLDL-C method compared with beta-quantification LDL, the percentage of patients correctly classified into each group were:

83% of patients in group <3.37 mmol/L;
55% of patients in group 3.37-4.13 mmol/L;
43% of patients in group 4.14-4.91 mmol/L;
81% of patients in group 4.92 mmol/L.

The corresponding percentages with the Friedewald LDL were 67%, 82%, 79% and 91%. The percentage positive predictive value for the DLDL-C method was higher than that for the Friedewald at cut-off levels of 3.37 mmol/L and 4.14 mmol/L, (p=0.24). The percentage negative predictive value for the DLDL-C was lower than that for the Friedewald at cut-off levels below 3.37 mmol/L and below 4.14 mmol/L, (p=0.10). (The values were graphically represented).

Clinical conclusions
The DLDL-C method had a significant negative bias and misclassified patients into incorrect treatment groups more often than the Friedewald method. The negative predictive value for the DLDL-C method was lower than that for the Friedewald method.

Measure of benefits used in the economic analysis
The benefit measure was the number of patients appropriately classified into treatment groups.

Direct costs
Labour, instrument and reagents costs were included in the analysis. Resource and cost data were reported separately. The quantity/cost boundary adopted was the hospital. Discounting was not undertaken because of the short study period. The price year was not stated.

Statistical analysis of costs
Not undertaken.

Indirect Costs
Not considered.

Currency
US dollars ($).
Sensitivity analysis
Not undertaken.

Estimated benefits used in the economic analysis
See Effectiveness Results above.

Cost results
The total cost for measuring LDL-C by the Friedewald calculation was $3.40 per assay compared with $10.20 per assay for the DLDL-C method.

Synthesis of costs and benefits
Costs and benefits were not combined.

Authors’ conclusions
In hyperlipidemic children the DLDL-C method has significant negative bias at LDL levels greater than 3.37 mmol/L. The negative predictive value of the DLDL-C method is less than that of the Friedewald method. In addition, the cost of the DLDL-C assay is three times greater than that of the Friedewald method. The question arises whether the convenience of not fasting is worth the significantly greater cost of performing the non-fasting method.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear. Levels of LDL-C are commonly monitored by the Friedewald equation involving an indirect calculation that requires an overnight fast. You, as a user of this database, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The data do not appear to have been used selectively. However, as no sensitivity analysis was conducted, the results need to be treated with some caution. As noted by the authors, the validity of the results is questionable on the grounds that it is possible that a small population of lipoprotein, likely to be intermediate-density lipoprotein, is removed from the LDL fraction in the DLDL-C assay during precipitation but not from the beta-quantification method.

Validity of estimate of measure of benefit
No summary benefit measure was used in the study and, as such, the authors conducted a costs and outcomes analysis.

Validity of estimate of costs
Resource and cost data were reported separately. The costing methodology lacked some details, in particular, the price year was not stated. As no statistical analysis was conducted, the costs need to be treated with a degree of caution. However, important cost items do not appear to have been omitted.

Other issues
The authors’ conclusions are likely to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. However, appropriate comparisons were made with other studies in terms of accuracy in classifying patients into treatment groups as established by the NCEP. Results do not appear to have been presented selectively.

Implications of the study
The authors postulated that on the basis of the negative bias of the DLDL-C assay at lower LDL-C concentrations a small population of lipoprotein, probably intermediate-density lipoprotein, is removed from the LDL fraction in the DLDL-C assay during precipitation but not from the beta-quantification method. This is a topic for further research.
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