Comparative effectiveness of guidelines for the management of hyperlipidemia and hypertension for type 2 diabetes patients
Shah ND, Mason J, Kurt M, Denton BT, Schaefer AJ, Montori VM, Smith SA

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 international contemporary guidelines for the management of hypertension and hyperlipidaemia in patients aged 40 to 80 years, with type 2 diabetes. The authors concluded that all the guidelines were similarly effective, but their costs varied and a more risk-targeted approach could reduce costs. The clinical sources were reliable, but some methodological limitations might affect the validity of the authors’ conclusions. Further investigation is needed to corroborate these findings.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of international contemporary guidelines for the management of hypertension and hyperlipidaemia, in patients aged 40 to 80 years, with type 2 diabetes.

Interventions
Ten strategies were considered: treatment for all; four US guidelines; Canadian, European, British, and Australian guidelines; and no treatment.

Treatment was the initiation of statin and angiotensin-converting enzyme (ACE) inhibitor treatment at diagnosis of diabetes with no further measurement and no dose increases.

US guideline one was statin treatment for patients with a low-density lipoprotein (LDL) level of 130mg/dL or more, and ACE inhibitor for those with a systolic blood pressure (SBP) over 130mmHg or a diastolic blood pressure (DBP) over 85mmHg.

US guideline two was statin treatment for patients with LDL of 100mg/dL or more, and ACE inhibitor for a SBP over 130mmHg or a DBP over 80mmHg.

US guideline three was statin treatment for patients with a high-risk and LDL of 100mg/dL or more, a moderate-risk and LDL of 130mg/dL or more, or a low-risk and LDL of 190mg/dL or more, and ACE inhibitor for a SBP over 140mmHg or a DBP over 90mmHg.

US guideline four was statin treatment at diagnosis of diabetes, increasing according to Adult Treatment Panel (ATP) III guidelines, and ACE inhibitor at diagnosis, increasing treatment according to Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 7 guidelines.

The Canadian guideline was statin treatment for patients with LDL of 2.5mmol/L or more, or a total cholesterol to high-density lipoprotein (HDL) ratio of four or more, and ACE inhibitor for a SBP over 130mmHg or a DBP over 80mmHg.

The European guideline was statin treatment for patients with LDL of 2.5mmol/L or more, or total cholesterol of 4.5mmol/L or more, and ACE inhibitor for a SBP over 130mmHg or a DBP over 80mmHg.

The British guideline was statin for LDL of 2.0mmol/L or more, or total cholesterol of 4mmol/L or more, and ACE inhibitor for a SBP over 130mmHg or a DBP over 80mmHg.
The Australian guideline was statin for LDL of 2.5mmol/L or more, or HDL of less than 1mmol/L, and ACE inhibitor for a SBP over 130mmHg or a DBP over 80mmHg.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model of type 2 diabetes patients, that estimated primary prevention measures and considered three modifiable risk factors (blood glucose level, blood pressure, and lipid levels) for stroke or cardiovascular events. A 40-year time horizon was considered. The authors stated that the analysis took the perspective of the third-party payer.

Effectiveness data:
The clinical data were from a selection of relevant sources. The key data for metabolic factors and transition probabilities between metabolic states were from the Mayo Clinic’s Diabetes Electronic Management System (DEMS), which included data from 663 patients. This provided the data for the effect of medication on the metabolic factors, which was the key input for the analysis. Other data, such as the probabilities of initial coronary heart disease (CHD) and stroke events, were from the UK Prospective Diabetes Study (PDS).

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The summary benefit measure was the probability of CHD or a stroke event. The number-needed-to-treat (NNT) to avoid an event was reported.

Cost data:
The economic analysis considered the additional drug costs that were directly associated with the management of hypertension and hyperlipidaemia. These drug costs were derived from the Red Book average wholesale prices. The lowest price was used in the base case. Dosages were based on the guidelines and real-world data from the DEMS. The costs were presented in US dollars ($).

Analysis of uncertainty:
Various ranges of medication costs were considered.

Results
In men, the NNT was 7.0 with US guideline one, 6.7 with US guideline two, 7.6 with US guideline three, 6.6 with US guideline four and with the Canadian guideline, 6.5 with the European, British, and Australian guidelines, and 14.4 with treatment on diagnosis. The events avoided per 1,000 treated were 142.6 with US one, 150.4 with US two, 132.3 with US three, 151.4 with US four, 152.8 with Canadian, 153.3 with European, 153.8 with British, 153.9 with Australian, and 81.0 with treatment on diagnosis.

The medication costs per event avoided were $129,428 with US one, $139,204 with US two, $117,269 with US three, $141,185 with US four, $147,705 with Canadian, $152,385 with European, $156,817 with British, $157,186 with Australian, and $63,708 with treatment on diagnosis.

In women, the NNT was 6.9 with US one, 6.6 with US two, 7.5 with US three, 6.6 with US four, 6.5 with Canadian, European, British, and Australian, and 11.7 with treatment without guidelines. The events avoided per 1,000 treated were 145.6 with US one, 151.8 with US two, 133.0 with US three, 152.5 with US four, 153.6 with Canadian, 153.9 with European, 154.1 with British, 154.3 with Australian, and 70.7 with treatment without guidelines.

The medication costs per event avoided were $134,655 with US one, $144,773 with US two, $115,999 with US three, $147,011 with US four, $153,952 with Canadian, $158,784 with European, $163,488 with British, $163,775 with
Australian, and $75,886 with treatment without guidelines.

The clinical guidelines had similar effectiveness, but their costs varied, being higher with the Australian guideline and lower with US ones. Changes in the medication prices did not alter the base-case conclusions.

**Authors’ conclusions**
The authors concluded that all guidelines were similarly effective, but their costs varied and a more risk-targeted approach could reduce costs.

**CRD commentary**

**Interventions:**
A justification for the selection of the comparators was given. The authors included the existing international guidelines and previous guidelines from the USA to demonstrate the impact of changes in recommendations. All the guidelines were clearly described.

**Effectiveness/benefits:**
The clinical data were from two sources that were key publications for diabetes patients. The effect of medication on metabolic factors and the patients’ characteristics were from DEMS, which was a valid source for the USA, as it collected real-world clinical data over a relatively long period. The UK PDS is a well-known source of data for diabetes patients and it is often used for long-term decision models. The impact of variations in the clinical inputs on the cost-effectiveness estimates was not evaluated. Event rates are disease-specific, but the NNT is a more generalisable measure.

**Costs:**
The economic analysis was restricted to a limited perspective as only the medication costs were considered. The authors did not justify their exclusion of the costs associated with medications for glycaemic control. The unit costs and resource quantities were not presented separately, and only the annual medication costs were reported. The price year was not stated, making it impossible to conduct reflation exercises. The economic analysis was not fully presented.

**Analysis and results:**
The results were extensively presented. Average cost-effectiveness ratios were reported. An incremental analysis would have been more appropriate for identifying the best guideline. The uncertainty was partly investigated by varying the drug costs. The findings, if confirmed, have important policy implications as the use of the latest US guidelines could substantially reduce the budget impact of the medical costs for patients with diabetes, with a minimal impact on effectiveness. The authors acknowledged that a limitation of their analysis was the exclusion of items, such as adverse events, the discontinuation rate, and non-adherence.

**Concluding remarks:**
The clinical sources were reliable, but some methodological limitations might affect the validity of the authors’ conclusions. More studies are needed to corroborate these findings.

**Funding**
Funding received from the Agency for Healthcare Research and Quality, and the National Science Foundation, USA.

**Bibliographic details**

**PubMedID**
21283569

**DOI**
10.1371/journal.pone.0016170