Evaluating national guidelines for prevention of cardiovascular disease in primary care

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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 study examined national guidelines for the prevention of cardiovascular disease (CVD) in primary care. The guidelines for the USA, Canada, UK, New Zealand (NZ) and Australia were analysed. Each guideline identified three principal drug intervention areas. These were the lowering of blood pressure with antihypertensive drugs, aspirin, and the lowering of cholesterol with drugs.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients at risk of developing CVD. This included sudden cardiac death, myocardial infarction, new onset angina, stroke, transient ischaemic attack or peripheral vascular disease.

Setting
The setting was primary care. The economic study was multi-national since it referred to the USA, Canada, UK, NZ and Australia.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2003. No dates for resource consumption were reported. The price year might have been 2004.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the characteristics of the five national guidelines;

the reference population; and

the effectiveness of aspirin, antihypertensive treatment, and cholesterol-lowering treatment.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify primary studies. The primary studies might have been identified selectively. Evidence on guidelines came mainly from official publications. The effectiveness data were estimated from several studies, including systematic reviews and meta-analyses of clinical trials.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
The use of systematic reviews and meta-analyses of clinical trials enforces the internal validity of the data obtained for treatment effectiveness.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
A total of 14 primary studies provided evidence. Information on the five national guidelines was derived from 9 studies, characteristics of the reference population were obtained from 1 study, and clinical data on the efficacy of the treatments were derived from 4 studies.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The main characteristics of the five national guidelines (screening of patients, eligibility for treatment, and treatment goals) were reported in detail.

In particular, Australian and NZ guidelines recommend aspirin if the 5-year CVD risk exceeds 15%. US and Canadian guidelines recommend aspirin if the 5-year coronary heart disease (CHD) risk exceeds 6%. UK guidelines recommend aspirin in patients over 50 years if the 5-year CHD risk exceeds 15%.

For antihypertensive treatment, the blood pressure threshold at which treatment is recommended varies widely, from 170/100 mmHg in NZ to 140/90 mmHg in the US and Canadian guidelines.

For statins, US and Canadian guidelines use low-density lipoprotein levels in combination with a series of categorical risk factors to determine eligibility. UK guidelines use total cholesterol in combination with CHD risk. Australian and NZ guidelines use the ratio of total cholesterol to high-density lipoprotein cholesterol in combination with CVD risk.

The reference population comprised 2,000 persons aged 16 years and over. These were randomly selected from the 9,965 persons included in a survey of 1999 - 2000 data to reflect the age-gender structure of the US population in 2001.

The relative risk of CHD, which includes sudden cardiac death, myocardial infarction and new onset angina, was 0.72 (95% confidence interval, CI: 0.60 - 0.87) for individuals on aspirin. The relative risk of cerebrovascular disease (CVA), which includes stroke or transient ischaemic attack, was 1.02 (95% CI: 0.85 - 1.23). However, the absolute reduction in cardiovascular risk was offset by 0.3%, owing to an absolute increase in the incidence of major bleeding of 0.3% (95% CI: 0.2 - 0.4) per 5 years of treatment.
Compared with placebo, for individuals on antihypertensive treatment, the relative risk of CHD was 0.83 (95% CI: 0.72 - 0.91) and the relative risk of CVA was 0.64 (95% CI: 0.57 - 0.75).

Compared with initial antihypertensive treatment, when on more intensive antihypertensive treatment, the relative risk of CVA was 0.77 (95% CI: 0.63 - 0.95) and the relative risk of CHD was 0.95 (95% CI: 0.81 - 1.11).

When on statins, the relative risk of CHD was 0.69 (95% CI: 0.64 - 0.74) and the relative risk of CVA was 0.70 (95% CI: 0.57 - 0.86).

**Measure of benefits used in the economic analysis**
The summary benefit measure was the total number of cardiovascular events prevented over a 5-year time period under the five national guidelines. An annual discount rate of 3% was applied.

**Direct costs**
The perspective adopted in the study was not stated clearly, but only direct medical costs were included in the economic evaluation. In particular, the health services considered were drugs (aspirin 81 mg, hydrochlorothiazide 25 mg, atenolol 50 mg, enalapril 20 mg and atorvastatin 20 mg), staff, and laboratory services. The follow-up costs associated with each treatment were also considered (assuming a 6-month follow-up). The unit costs were presented but the resource use data were unclear. The estimation of the costs was based on US costs obtained from the Red Book and average wholesale prices. Resource consumption appears to have reflected standard treatment patterns. Discounting was relevant since the costs were incurred during a 5-year time horizon, and an annual rate of 3% was applied. The price year might have been 2004.

**Statistical analysis of costs**
Statistical analyses of the costs were not carried out.

**Indirect Costs**
The indirect costs were not taken into consideration.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not performed.

**Estimated benefits used in the economic analysis**
As expected, the proportion of individuals eligible for treatment increased with age with all guidelines. Canadian guidelines identified the highest proportion as eligible for treatment, while NZ guidelines identified the fewest.

The discounted total number of cardiovascular events prevented over a 5-year time period for all ages was:

32.4 in the USA (0.0 for ages 16 - 24, 0.2 for ages 25 - 34, 1.1 for ages 35 - 44, 4.0 for ages 45 - 54, 6.2 for ages 55 - 64, 8.1 for ages 65 - 74, 8.5 for ages 75 - 84, and 4.3 for ages 85+);

38.1 in Canada (0.0 for ages 16 - 24, 0.3 for ages 25 - 34, 1.4 for ages 35 - 44, 5.2 for ages 45 - 54, 7.8 for ages 55 - 64, 9.6 for ages 65 - 74, 9.6 for ages 75 - 84, and 4.1 for ages 85+);

30.1 in the UK (0.0 for ages 16 - 24, 0.0 for ages 25 - 34, 0.2 for ages 35 - 44, 2.4 for ages 45 - 54, 5.6 for ages 55 - 64, 9.3 for ages 65 - 74, 8.5 for ages 75 - 84, and 4.1 for ages 85+);
30.0 in NZ (0.0 for ages 16 - 24, 0.0 for ages 25 - 34, 0.1 for ages 35 - 44, 1.3 for ages 45 - 54, 4.4 for ages 55 - 64, 8.4 for ages 65 - 74, 10.8 for ages 75 - 84, and 4.9 for ages 85+); and

35.4 in Australia (0.0 for ages 16 - 24, 0.1 for ages 25 - 34, 0.7 for ages 35 - 44, 2.9 for ages 45 - 54, 6.2 for ages 55 - 64, 9.8 for ages 65 - 74, 10.7 for ages 75 - 84, and 4.9 for ages 85+).

Thus, Canadian guidelines were associated with the highest number of CVD events prevented. Australian guidelines caused net harm in the younger patients since the benefits of aspirin were outweighed by the risk of major bleeding in young adults at low risk of CVD.

Cost results
The total costs incurred over a 5-year time period for all ages were:

$3,073,697 in the USA ($108,002 for ages 16 - 24, $259,597 for ages 25 - 34, $430,936 for ages 35 - 44, $556,390 for ages 45 - 54, $539,828 for ages 55 - 64, $543,248 for ages 65 - 74, $436,708 for ages 75 - 84, and $198,988 for ages 85+);

$4,124,756 in Canada ($107,483 for ages 16 - 24, $386,482 for ages 25 - 34, $631,357 for ages 35 - 44, $854,816 for ages 45 - 54, $765,561 for ages 55 - 64, $684,170 for ages 65 - 74, $506,333 for ages 75 - 84, and $188,553 for ages 85+);

$2,990,313 in the UK ($60,861 for ages 16 - 24, $232,285 for ages 25 - 34, $317,023 for ages 35 - 44, $500,426 for ages 45 - 54, $541,749 for ages 55 - 64, $666,499 for ages 65 - 74, $468,417 for ages 75 - 84, and $203,053 for ages 85+);

$1,843,754 in NZ ($0 for ages 16 - 24, $0 for ages 25 - 34, $23,154 for ages 35 - 44, $171,994 for ages 45 - 54, $366,084 for ages 55 - 64, $513,906 for ages 65 - 74, $436,708 for ages 75 - 84, and $198,988 for ages 85+); and

$3,798,226 in Australia ($155,204 for ages 16 - 24, $299,047 for ages 25 - 34, $458,234 for ages 35 - 44, $616,207 for ages 45 - 54, $688,846 for ages 55 - 64, $723,658 for ages 65-74, $610,564 for ages 75 - 84, and $246,466 for ages 85+).

Thus, NZ guidelines were associated with the lowest 5-year total costs.

Synthesis of costs and benefits
Average cost-effectiveness ratios (ACERs; i.e. the cost per CVD event prevented) were calculated to combine the costs and benefits of the alternative guidelines.

The ACER was:

$94,800 in the USA ($12,661,400 for ages 16 - 24, $1,522,500 for ages 25 - 34, $404,000 for ages 35 - 44, $138,600 for ages 45 - 54, $86,600 for ages 55 - 64, $67,200 for ages 65 - 74, $51,100 for ages 75 - 84, and $46,200 for ages 85+);

$108,300 in Canada ($7,474,300 for ages 16 - 24, $1,324,100 for ages 25 - 34, $440,100 for ages 35 - 44, $162,900 for ages 45 - 54, $97,800 for ages 55 - 64, $71,000 for ages 65 - 74, $52,800 for ages 75 - 84, and $46,400 for ages 85+);

$99,200 in the UK ($0 for ages 16 - 24, $5,933,100 for ages 25 - 34, $1,269,500 for ages 35 - 44, $208,400 for ages 45 - 54, $97,600 for ages 55 - 64, $71,900 for ages 65 - 74, $55,200 for ages 75 - 84, and $49,000 for ages 85+);

$61,500 in NZ ($0 for ages 16 - 24, $0 for ages 25 - 34, $187,700 for ages 35 - 44, $129,500 for ages 45 - 54, $82,600 for ages 55 - 64, $60,900 for ages 65 - 74, $50,700 for ages 75 - 84, and $45,600 for ages 85+); and

$107,400 in Australia (-$22,311,300 for ages 16 - 24, $2,639,900 for ages 25 - 34, $624,600 for ages 35 - 44, $213,000
for ages 45 - 54, $111,400 for ages 55 - 64, $73,800 for ages 65 - 74, $57,000 for ages 75 - 84, and $49,900 for ages 85+).

A striking result was that the NZ guidelines offered significant cost and cost-effectiveness advantages over other guidelines, but they also prevented the fewest cardiovascular events due to the low number of patients treated with aspirin. If the NZ guidelines used US Preventive Services Task Force recommendations on the use of aspirin, the total cardiovascular events prevented would rise to 35.9, but the guidelines would remain the most cost-effective.

Authors' conclusions
Cardiovascular disease (CVD) prevention was useless in young adults. Further, guidelines that used risk as the principal determinant of treatment (New Zealand) were more efficient than those that continued to deal with individual risk factors separately (Canada and the USA). Aspirin and initial antihypertensive treatment were the most cost-effective preventive interventions.

CRD COMMENTARY - Selection of comparators
No explicit justification for the choice of the five national guidelines was provided. A description of each guideline and its relevant source was provided. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence appears to have been derived from selectively identified studies. A systematic review of the literature was not performed to identify primary studies. There was limited information on the studies used to estimate clinical inputs. However, the use of meta-analyses of clinical trials and systematic reviews ensures a high internal validity of the primary studies. The methods used to extract and combine the primary estimates were not described, and the issue of heterogeneity across the primary studies was not addressed. The robustness of the clinical estimates was not investigated in sensitivity analyses.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It is not comparable with the benefits of other health care interventions. However, the number of CVD events avoided represents an intermediate measure commonly used in the evaluation of primary prevention strategies. The impact of the interventions on mortality or quality of life was not investigated, although it would have been helpful.

Validity of estimate of costs
The perspective adopted in the study was unclear. Only the direct medical costs were considered in the analysis. The source of the data was reported for all items. A breakdown of the costs was provided and most unit costs were presented. However, the source of the data on quantities of resources used was not clear. No statistical analyses of the costs were carried out, and US data were used to derive the costs. These costs were specific to the US setting and the impact of alternative estimates was not investigated. The price year was implicitly reported, which aids reflation exercises in other time periods.

Other issues
The author did not compare the actual findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed. The results of the analysis were presented in detail (i.e. for age classes). The author noted that the analysis made several assumptions that might not reflect real-world situations. For example, clinicians might not follow national guidelines and patients might not comply with treatment. However, since these assumptions apply to all guidelines, they should not alter the comparative results of the study.

Implications of the study
The study results had three main implications. First, CVD prevention should be focused on the old rather than the young. Second, guidelines should consider risk rather than individual risk factors, thus risk equations are better predictors of benefit than risk factors. Third, guidelines should be liberal in recommending aspirin and initial antihypertensive treatment, but conservative in insisting on the use of third-line antihypertensive drugs. This latter point contrasts the recommended strategy of prescribing medications to reach blood pressure targets for the primary prevention of CVD.

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None stated.

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**Other publications of related interest**


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