Prevention of cardiovascular disease

Evidence Update January 2014


Evidence Update 50
Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline, available from the NICE Evidence Services topic page for [cardiovascular disease – prevention](#).

**Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.**

NICE Evidence Services are a suite of services that provide online access to high quality, authoritative evidence and best practice.

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Introduction

This Evidence Update identifies new evidence that is relevant to, and may have a potential impact on, the following reference guidance:


   A search was conducted for new evidence from 1 January 2008 to 1 June 2013. A total of 28,835 pieces of evidence were initially identified. Following removal of duplicates and a series of automated and manual sifts, 23 items were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprising topic experts, reviewed the prioritised evidence and provided a commentary.

Other relevant NICE guidance

The focus of the Evidence Update is on the guidance stated above. However, overlap with other guidance has been outlined as part of the Evidence Update process. Where relevant, this Evidence Update therefore makes reference to the following guidance:


NICE Pathways

NICE pathways bring together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. The following NICE Pathways cover advice and recommendations related to the reference guidance for this Evidence Update:

- **Diet**, NICE Pathway
- **Physical activity**, NICE Pathway

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

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1 NICE-accredited guidance is denoted by the Accreditation Mark  

Evidence Update 50 – Prevention of cardiovascular disease (January 2014)
**Key points**

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG’s opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

<table>
<thead>
<tr>
<th>Potential impact on guidance</th>
<th>Key point</th>
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### Policy: a national framework for action

- Modest population-wide reductions in major cardiovascular disease (CVD) risk factors in England and Wales could result in cost savings to the NHS, as well as health improvements.

- Food policies setting stricter targets to bring about greater improvements in UK dietary intake of industrially-produced trans fatty acids (IPTFAs), saturated fats, salt and fruit and vegetables, resembling those achieved in other countries, could further reduce deaths from CVD.

### Salt

- A population-wide campaign by the UK Food Standards Agency, involving both the promotion of the health risks of too much salt and working with industry to reduce salt in the food supply, appears to have reduced salt intake. However, reductions in intake may not be equal across gender, age and socioeconomic groups.

- Reducing UK salt intake by 3 g/day might prevent approximately 10,000 deaths and 10,000 non-fatal cardiovascular events each year. This would exceed benefits from smoking cessation programmes, weight loss interventions in individuals, and statins. Reduction in salt intake by as little as 1 g/day may be more cost-effective than blood pressure-lowering drugs.

- Local policies to reduce intake of salt from foods provided by the public sector might result in fewer cases of hypertension, and corresponding decreases in direct healthcare costs.

- Mandatory limits on salt in processed foods could be a cost-effective and even cost-saving means of tackling CVD, whereas lifestyle counselling does not appear to be cost-effective.

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### Saturated fats
- Consuming polyunsaturated fat in place of saturated fat could substantially reduce coronary heart disease (CHD) events. Yes
- A Mediterranean-style diet reduces risk of CHD, and olive oil intake is associated with reduced risk of mortality. Yes
- Increasing the price of foods such as take-away pizza and high-sugar soft drinks may reduce total daily energy intake, weight and insulin levels among young adults. Yes

### Trans fats
- Policies to reduce IPTFAs in food appear to be effective. National and local bans (such as banning IPTFA use in food processing or in restaurants) seem to be most effective at eliminating IPTFAs from the food supply. Yes

### Common agricultural policy
- Reducing the amount of saturated fat consumption that may be attributable to common agricultural policy subsidies could lead to reductions in cardiovascular mortality. Yes

### Practice
#### Regional CVD prevention programmes – programme development
- A low-risk lifestyle (not smoking, normal BMI, moderate daily activity, modest alcohol consumption, and healthy diet) may substantially reduce risk of stroke. Yes
- A community health promotion intervention may lead to favourable changes in energy and fat intake and physical activity level, particularly among women and people with low educational levels. Yes
- Population-based lifestyle counselling and education, to reduce CVD risk through behaviour change, has limited use in general populations. Further research is needed to assess effectiveness in high-risk populations. Yes
- Additional evidence is now available about the types of people who do and do not attend general health checks, and whether health checks may or may not be beneficial. Yes

### Children and young people
- Limited evidence suggests that child obesity-prevention programmes might have a small effect on BMI in children aged 6 to 12 years. Yes

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### Potential impact on guidance

<table>
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<tr>
<th>Key point</th>
<th>Yes</th>
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<tr>
<td><strong>Areas not currently covered by NICE PH25</strong></td>
<td></td>
<td><img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /> <img src="https://example.com/yes.png" alt="Yes" /></td>
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<tr>
<td>Sugar-sweetened drinks may be associated with an increased risk of incident hypertension, though causality is uncertain. Evidence that artificially sweetened drinks might also be associated with hypertension is conflicting.</td>
<td><img src="https://example.com/yes.png" alt="Yes" /></td>
<td><img src="https://example.com/yes.png" alt="Yes" /></td>
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<td>Approval of plant sterol-enriched foods for sale in Canada could result in savings to the healthcare system from a reduced incidence of CHD through lower blood cholesterol levels. Evidence is lacking for a long-term direct effect of plant sterols on heart disease, for compliance with consuming sterols at appropriate levels, and for effects on inequalities.</td>
<td><img src="https://example.com/yes.png" alt="Yes" /></td>
<td><img src="https://example.com/yes.png" alt="Yes" /></td>
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<td>E-learning to promote dietary behaviour change may not produce clinically significant or cost-effective changes in dietary behaviour. However, evidence testing the latest technology, or the efficacy of e-learning as part of a wider education programme, is lacking.</td>
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1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update. The commentaries focus on the ‘key references’ (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from the guidance.

Policy: a national framework for action

Economic basis of the guidance

NICE public health guidance 25 ([NICE PH25](#)) states that changes in cardiovascular disease (CVD) risk factors brought about by intervening at the population level could lead to substantial benefits. The policy goals identified in the guidance are likely to be the most effective and cost-effective way of reducing CVD at population level.

To inform the development of the guidance, Barton et al. (2011) developed an economic model to estimate the cost effectiveness of a population-wide risk factor reduction programme aimed at preventing CVD in England and Wales. A generic spreadsheet model was developed in 4 stages:

- Determining NHS costs and quality-adjusted life years (QALYs) lost for 1 case of CVD.
- Assessing cases of CVD prevented or postponed for intervention of known effectiveness.
- Combining results from the first 2 stages to estimate potential outcomes for a single combination of age, sex, and risk.
- Aggregating results to estimate NHS costs and QALYs gained for the whole population of England and Wales.

The model was then applied to 2 general scenarios (small decreases in blood pressure and in cholesterol) and to 2 specific legislative interventions (reducing dietary intake of salt and of industrially-produced trans fatty acids [IPTFAs]). The main outcome measures were cardiovascular events avoided, QALYs gained, and healthcare cost savings. Outcomes were based on a 10-year time period.

A programme reducing cardiovascular events by 1% could result in a gain of 98,000 QALYs and NHS savings of at least £30 million a year compared with no intervention. Reducing mean cholesterol or blood pressure levels by 5% could result in annual savings of at least £80 million and a gain of at least 260,000 QALYs. Reducing dietary salt intake by 3 g/day could see a gain of 131,000 QALYs, with savings of £40 million a year. Reducing intake of IPTFAs by 0.5% of total energy could save £235 million a year and gain 754,000 QALYs.

Limitations of the evidence included that:

- The model considered a 10-year time frame (as opposed to lifetime) and included only people aged 40–79 years. Additionally, only CVD outcomes and NHS costs were considered, whereas interventions may also benefit other chronic diseases and other sectors of the economy such as employment. Results may therefore be underestimates.
- The model assumed that without intervention, population risk of CVD would remain constant. Any changes to this risk might affect future costs and QALYs.
- The model lacked a full probabilistic sensitivity analysis, because some data inputs (such as risk factor distribution in the population) were available only as point estimates.

The evidence suggests that modest population-wide reductions in major CVD risk factors in England and Wales could result in cost savings to the NHS, as well as health improvements.
These results are consistent with the overall aims of NICE PH25. Any further modelling could potentially consider wider health and economic outcomes.

Additional information about the study by Barton et al. (2011) is also available from an independent critical appraisal report produced for the Centre for Reviews and Dissemination's NHS Economic Evaluation Database.

**Key reference**

**National food policies**

NICE PH25 states that changes in CVD risk factors can be brought about by intervening at the population and individual level, but national or regional policy and legislation are particularly powerful levers. The guidance also includes specific recommendations on food policies, for example, reducing dietary salt, saturated fats and IPTFAs. Recommendations within these specific areas are discussed in detail in later sections. The following article discusses food policy across several areas.

A modelling study set in the UK by O’Flaherty et al. (2012) estimated potential reductions in CVD mortality if stricter nutritional policy targets for salt, fat, and fruit and vegetable intake were implemented. Mortality reductions were estimated between 2006 and 2015 using a spreadsheet model synthesising data on population, diet and mortality among adults aged 25–84 years. Diet and mortality data were obtained from national surveys and official statistics, and effects of dietary changes on CVD mortality were based on recent meta-analyses. Reduction in CVD mortality was estimated for 2 scenarios: conservative (based on continuation of recent trends) and aggressive (based on more substantial changes in dietary intake). The assumptions for changes in dietary intake for each scenario were:

- Fraction of total energy from IPTFAs: conservative=−0.5%, aggressive=−1%.
- Fraction of total energy from saturated fat: conservative=−1%, aggressive=−3%.
- Daily salt intake: conservative=−1 g, aggressive=−3 g.
- Daily fruit and vegetable intake: conservative=+1 portion, aggressive=+3 portions.

From the model, it was estimated that the conservative scenario could result in a total of 12,500 fewer deaths per year from CVD (8300 from coronary heart disease [CHD] and 4200 from stroke). In the aggressive scenario, deaths per year from CVD could be reduced by 29,900 (19,000 from CHD and 10,900 from stroke).

Limitations of the evidence included that:

- Estimations for the aggressive scenario assumed food policies in other countries would have a similar effect in the UK, without considering political or cultural differences.
- Death was the only outcome measure; non-fatal conditions may also have benefited.
- The effect of increasing intake of nuts, grains, sugars, fish or omega-3 fatty acids was not modelled for.

The evidence suggests that food policies setting stricter targets to bring about greater improvements in UK dietary intake of IPTFAs, saturated fats, salt and fruit and vegetables, resembling those achieved in other countries, could further reduce deaths from CVD. This is consistent with recommendations in NICE PH25 that national policies can have beneficial effects on CVD.

A further modelling study by Scarborough et al. (2012) found that achieving UK targets for intake of fruit and vegetables, salt and saturated fats could have substantial health benefits.
1.1 Salt

UK Food Standards Agency salt campaign

NICE PH25 recommends supporting the Food Standards Agency so that it can continue to promote – and take the lead on – the development of EU-wide salt targets for processed foods.

A before-and-after study by Shankar et al. (2013) assessed the impact of a campaign by the Food Standards Agency to reduce salt intake among the UK population. The campaign (part of a wider programme of work on salt intake reduction) began in 2004 with both a public awareness campaign about the health risks of too much salt, and work with the food industry on product reformulation. The present study assessed the impact of the campaign, using spot urinary sodium data and socio-demographic information from the Health Survey for England over 2003–7 (average sample size per year=4453). Individual data were then aggregated into group-level data within 3 categories: birth cohort (5 cohorts based on year of birth), area of residence (North, South, Midlands), and gender. The average number of people in each subgroup was 121. Fixed-effects models were then used to examine trends in salt intake before and after the campaign’s implementation, and any differing effects on salt intake between socio-demographic groups.

A two-way fixed effects model showed that the campaign appeared to reduce urinary sodium levels across almost all groups, with an average reduction of approximately 10%. The average reduction in urinary sodium was greater among women (11–23% reduction across all age cohorts) than among men (5–16% reduction). Greater effects were seen among younger than older women, but in men it was the reverse with the largest effects seen in older cohorts. Among men, a greater reduction was seen in urinary sodium in the South (16%) than in the Midlands and North (8% and 9% respectively). Location did not have a major influence among women. From a one-way fixed effects model, it was found that neither a high level of education nor the relative price of salty food significantly affected urinary sodium levels. However, compared with a high income, a low income was associated with a significantly greater risk of higher salt intake (coefficient=0.33, 5% significance level).

Limitations of the evidence included that:

- Spot urinary sodium measurement may less accurately predict salt intake than 24-hour samples because urinary sodium levels vary over a day (however the authors suggested that spot urinary sodium levels correlate with 24-hour measurements).
- Spot urinary sodium data were available for only a limited number of years.
- The grouping of data meant that samples were small.
- The salt campaign was national and therefore control groups were not possible. The absence of control groups may reduce the certainty of any causality between the campaign and effects on salt intake.

The evidence suggests that a population-wide campaign by the UK Food Standards Agency, involving both the promotion of the health risks of too much salt and working with industry to reduce salt in the food supply, appears to have reduced salt intake. However, reductions in intake may not be equal across gender, age and socioeconomic groups. This evidence is
consistent with recommendations in \textit{NICE PH25} to support the work of the Food Standards Agency and to work with industry to reduce salt content of foods. It also provides useful information about sub-groups that may be at greater risk from salt intake.

\textbf{Millett et al. (2012)} also analysed spot urinary sodium data from the Health Survey for England between 2003 and 2007. Similar general trends for declining salt intake were found, along with some socioeconomic variation.

Further analysis of the effects of the Food Standards Agency campaign was done by \textit{Sutherland et al. (2013)}. It was found that since 1997, salt use at the table in the UK has steadily declined, and that reduction in salt use was significantly greater after the campaign. Socioeconomic and geographical variation in salt use was also observed.

Further examination of variation in salt intake across Britain was conducted in a study by \textit{Ji et al. (2013)}. A significant north–south pattern of salt intake was found, and measures of low socioeconomic status appeared to be associated with higher levels of salt intake.

Additional information about continuing plans to reduce salt intake in the UK, including new targets, is available in the government’s Food Network salt strategy \textit{(part of the Public Health Responsibility Deal)}, which was published in March 2013.

\textbf{Key reference}

\textbf{Supporting references}
Ji C, Kandala NB, Cappuccio FP (2013) \textit{Spatial variation of salt intake in Britain and association with socioeconomic status}. BMJ Open 3: e002246


\textbf{Effect of population-wide dietary salt reduction on CVD}
\textit{NICE PH25} recommends accelerating the reduction in salt intake among the population, aiming for a maximum intake of 6 g per day per adult by 2015 and 3 g by 2025.

A modelling study set in the USA by \textit{Bibbins-Domingo et al. (2010)} assessed the potential effect of population-wide reductions in dietary salt on population health and compared it with other public health and clinical interventions. Potential impacts of salt reduction were examined using the Coronary Heart Disease Policy Model – a computer simulation of heart disease in adults aged 35–84 years, with an extension of the model to assess stroke. The data in the model were derived from national data sets and calibrated to national event-rate estimates. Estimates were made of the effect of reducing salt intake on reducing systolic blood pressure (based on results of a large meta-analysis, and data from 2 clinical trials) and fed into the model. Effects of reduced dietary salt were then also compared with smoking cessation, weight loss, statin treatment, and treatment of hypertension.

It was estimated that a 3 g/day reduction in salt could lead to annual reductions in the number of new cases of: CHD by 60,000 to 120,000; stroke by 32,000 to 66,000; and myocardial infarction by 54,000 to 99,000. The annual number of deaths from any cause could also be reduced by 44,000 to 92,000.

The reduction in new cases of CHD by 60,000 after lowering salt intake by 3 g/day was more than might be achieved with:

- a 50% reduction in smoking and tobacco exposure (41,000)
- a 5% reduction in body-mass index among obese adults (59,000)
- statin therapy (52,000).

Reducing salt intake by 3 g/day was calculated to save 194,000 to 392,000 QALYs and $10 to 24 billion in healthcare costs annually. The authors concluded that interventions to reduce salt (even at a more modest reduction of 1 g/day achieved gradually over a 10-year period) would be more cost-effective than drug treatments to lower blood pressure in all people with hypertension.

Limitations of the evidence included that:

- The model assumed that health benefits of salt reduction were mediated through effects on blood pressure, and effects unrelated to blood pressure were not fully accounted for.
- The model assumed a linear relationship between salt intake and blood pressure, but the authors noted that this may not necessarily be the case.
- The assumptions, healthcare delivery systems and costs used in the model were specific to the USA, so data may not be directly transferable to the UK.

If similar effects of reducing dietary salt intake by 3 g/day were observed in the UK (having a population approximately one fifth the size of the USA), then there might be 10,000 fewer deaths and 10,000 fewer non-fatal events each year. This is in line with results from 2 recent UK studies. A modelling study set in the UK by O’Flaherty et al. (2012) estimated that a 3 g reduction in daily salt intake (from 8.6 to 5.6 g) might result in 6600 fewer CVD deaths (range 1700–26,000). Additionally, the England and Wales modelling study by Barton et al. (2011) estimated that reducing salt intake by 3 g/day (from a current mean intake of approximately 8.5 g/day) might prevent approximately 4450 deaths and 30,000 cardiovascular events.

Taken together, the evidence suggests that reducing UK salt intake by 3 g/day might prevent approximately 10,000 deaths and 10,000 non-fatal cardiovascular events each year. This would exceed benefits from smoking cessation programmes, weight loss interventions in individuals, and statins. Reduction in salt intake by as little as 1 g/day may be more cost-effective than blood pressure-lowering drugs.

These data add substantial weight to the evidence base available during the development of NICE PH25. Although consistent with current recommendations to accelerate reduction in salt intake among the population, there may now be a case for strengthening the recommendations, which could have a potential impact on guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

Another modelling study set in the USA by Smith-Spangler et al. (2010) also found that population strategies to reduce salt intake (including collaboration with food manufacturers, and a sodium tax) could substantially reduce stroke and myocardial infarction incidence, with considerable associated healthcare cost savings.

**Key reference**

**Supporting reference**
Health impact of local policies to reduce salt intake in public services

NICE PH25 recommends ensuring all food procured by, and provided for, people working in the public sector and all food provided for people who use public services, is low in salt.

A modelling study set in the USA by Gase et al. (2011) performed a health impact analysis of the effect of local policies for reducing salt content in foods to reduce salt intake. Two hypothetical policies were devised and modelled across 6 settings serving food to the public (24,000 children and 15,113 adults served daily), all of which were operated or contracted out by the County of Los Angeles government. One approach (modelled for child care, meals for older people, buffet cafeterias and mobile trucks) was a 30% reduction in sodium content of all foods served. The second approach (modelled for hospital cafeterias and county government cafeterias) was labelling, promoting, subsidising and providing low-salt foods.

Using data for the average number of meals eaten per year in each setting, and the expected level of salt reduction per meal, reduction in average daily consumption of sodium was calculated. Data from a meta-analysis were then used to convert reduction in sodium intake into reduction in average systolic blood pressure. Reductions in direct healthcare costs were also assessed, as were the costs of implementing the salt-reduction policies.

The study estimated that among adults, consumption of sodium would decrease by an average of 0.23 g/day (salt equivalent=0.59 g). Across all settings, the average daily reductions ranged from 0.22 g (salt equivalent=0.56 g) in both the mobile trucks and meals for older people settings, to 0.77 g (salt equivalent=1.97 g) in hospital cafeterias. An average reduction in daily salt intake of 0.23 g/day could lead to a decrease in systolic blood pressure among adults with hypertension of 0.71 mmHg. This would equate to 388 fewer cases of uncontrolled hypertension in the adult study population, and an annual decrease of $629,724 in direct healthcare costs. Estimated year 1 start-up costs for the County of Los Angeles ranged from $227,753 to $1,723,539 (the authors noted that the wide range in values was mainly due to uncertainty over the potential changes in food costs).

Limitations of the evidence included that:

- It was assumed that the day-to-day customer base in each setting was stable; greater variability in customers may have reduced the impact of the intervention.
- Analyses did not examine socioeconomic factors.
- As a modelling study set in the USA, and based on effects of salt intake on blood pressure, it is subject to the same limitations described for Bibbins-Domingo et al. (2010) in the above section ‘Effect of population-wide dietary salt reduction on CVD’.

The evidence suggests that local policies to reduce intake of salt from foods provided by the public sector might result in fewer cases of hypertension, and corresponding decreases in direct healthcare costs. These data are consistent with recommendations in NICE PH25 to ensure that food available in the public sector is low in salt, and adds to the evidence base for the effect of local salt reduction policies.

Key reference
Mandatory limits on salt in processed foods alongside other interventions

NICE PH25 recommends:

- Ensuring food producers and caterers continue to reduce the salt content of commonly consumed foods (including bread, meat products, cheese, soups and breakfast cereals).
- Introducing national legislation if necessary.

A modelling study set in Australia by Cobiac et al. (2012) assessed the cost effectiveness of interventions (including mandatory salt limits) for primary prevention of CVD in all people aged 35–84 years who had never had heart disease or stroke. The interventions were:

- Whole population interventions – mandatory reduction of salt in bread, margarine and cereal, and a community heart health programme.
- Behaviour interventions for people at increased risk of CVD – dietary advice (including to switch to phytosterol-enriched margarine), and an intensive lifestyle programme with specialised counselling.
- Drug treatments for people at increased risk of disease – including aspirin, and drugs to lower blood pressure and cholesterol.
- Current practice – dietary advice, drugs to lower blood pressure and cholesterol, and voluntary reduction of salt in bread, margarine and cereal.

Estimates of the efficacy of voluntary and mandatory salt reduction were based on a study of sodium reduction in New Zealand and data for consumption of bread, margarine and cereal in Australia. Other estimates of intervention efficacy were from meta-analyses of relevant randomised controlled trials (RCTs). A discrete time Markov model was used to simulate ischaemic heart disease, stroke, and costs of intervention over lifetime to calculate cost per health gain in disability-adjusted life years (DALYs). All costs were adjusted to 2008 Australian dollars.

The study found that mandatory salt limits in bread, margarine and cereal could lead to a population gain of 80,000 DALYs. This intervention also seemed to be the most cost-effective – and was in fact cost saving. The authors suggested that packaging the mandatory salt limit intervention with risk-based prescribing of preventive drugs could reduce current lifetime healthcare expenditure by AUS$3.7 billion. It was further observed that lifestyle interventions to improve diet and exercise seemed to offer poor value for money (cost effectiveness ranging from AUS$1 million to $2.1 million/DALY) with little health benefit for the population.

Limitations of the evidence included that:

- Additional benefits from reduced smoking, increased physical activity, or other possible lifestyle changes were not captured so effects may have been underestimated.
- It was assumed that intervention effects were sustained with their continuing delivery. This assumption appears reasonable when the environment is permanently changed, for instance food reformulation. However, lifestyle interventions may often only achieve short-term behaviour changes. Further evidence is needed to clarify sustainability of different interventions.
- The model used Australian cost data that may not be directly transferable to the UK.

The evidence suggests that mandatory limits on salt in processed foods could be a cost-effective and even cost-saving means of tackling CVD, whereas lifestyle counselling does not appear to be cost-effective. Although broadly consistent with recommendations in NICE PH25 for manufacturers to reduce salt in common foods, there now appears to be evidence that mandatory limits on salt in processed foods may be substantially more effective than voluntary reformulation, and may even be cost saving. This approach is consistent with wider literature on effectiveness of mandatory versus voluntary approaches in public health policies and interventions aimed at, for example, tobacco control (Joosens and Raw 2006).
As recommendations currently state only that national legislation should be introduced ‘if necessary’, there may now be a case for strengthening the recommendations and this evidence could have a potential impact on guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

**Key reference**

**Supporting reference**

1.2 Saturated fats

**Consuming polyunsaturated fat in place of saturated fat**

*NICE PH25* recommends:

- Encouraging manufacturers, caterers and producers to reduce substantially the amount of saturated fat in all food products, considering supportive legislation if necessary.
- Creating favourable conditions for industry and agriculture to produce dairy products for human consumption that are low in saturated fat.

However, no recommendations are made specifically about consumption of unsaturated fats.

A systematic review and meta-analysis by *Mozaffarian et al. (2010)* investigated whether replacing saturated fat with polyunsaturated fat (PUFA) can affect CHD outcomes. RCTs of adults in which total or omega-6 PUFA consumption was increased for at least 1 year (through meal provision or dietary advice), without any other major interventions (such as blood pressure control), were eligible. Only trials that had a control group without a PUFA intervention, and that reported relevant outcomes including myocardial infarction, CHD death, or sudden death, were included. A total of 8 trials (n=13,614; outcome events=1042) were included. The median trial duration was 4.25 years. The average weighted proportion of energy intake consumed as PUFA in intervention groups was 14.9% (range 8.0–20.7%) and 5.0% (range 4.0–6.4%) in control groups.

Each 5% increase in energy from PUFA was associated with a pooled reduction in risk of myocardial infarction or death from CHD of 19% (risk reduction [RR]=0.81, 95% confidence interval [CI] 0.70 to 0.95, p=0.008), and a reduced CHD risk of 10% (RR=0.90, 95% CI 0.83–0.97, p value not stated). Meta-regression analysis showed that study duration independently determined risk reduction (p=0.017), with greater benefits seen in longer studies.

Limitations of the evidence included that:

- The results could not fully distinguish between benefits of increasing PUFA versus decreasing saturated fat.
- The trials are relatively old, having been published between 1968 and 1992 (although it is unlikely that the biological effects of PUFA have changed over time).
- Many of the RCTs included in the meta-analysis had design limitations, for example:
  - Some trials provided all or most meals, which may increase compliance but limit generalisability.
  - Some trials provided only dietary advice, which may increase non-compliance but increase generalisability.
  - Several trials were not double blind.
Methods for estimating and reporting PUFA and saturated fat consumption in each trial varied.

Some trials provided foods that contained omega-3 PUFA, which may be a confounding factor.

Evidence suggests that consuming PUFA in place of saturated fat could substantially reduce CHD events. This is partly consistent with recommendations in NICE PH25, for example that the food industry should reduce saturated fat in their products. However, there now appears to be evidence that saturated fat should not only be reduced, but be replaced with PUFA, which may have a potential impact on current guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

Additional information about the study by Mozaffarian et al. (2010) is also available from an independent critical appraisal report produced for the Centre for Reviews and Dissemination’s Database of Abstracts of Reviews of Effects.

Key reference

Mediterranean-style diet

One of the considerations during development of the recommendations for NICE PH25 was that vegetarian and Mediterranean-style diets are consistently associated with lower CVD mortality. However, the guidance does not specifically recommend a Mediterranean-style diet.

A prospective cohort study in Spain (n=41,078) by Buckland et al. (2009) examined the effect of a Mediterranean diet on risk of CHD. Healthy volunteers aged 29–69 years from the 5 Spanish centres of the European Prospective Investigation into Cancer and Nutrition (EPIC) study were followed up between 1992 and 2004 for an average of 10.4 years. Questionnaires were used to ask about food intake over the previous year, and socio-demographic and lifestyle characteristics including smoking, physical activity and medical history. Adherence to a Mediterranean diet was scored out of 18, based on intake of fruit, vegetables, olive oil and fish (with points also awarded for low meat and dairy intake, and moderate alcohol intake). Non-fatal coronary events identified by questionnaire were validated against medical records. Fatal events were based on Spanish mortality registry data. Multivariable Cox proportional hazards regression models (stratified by centre and age, and adjusted for several a priori confounding risk factors) were used to assess CHD risk in relation to Mediterranean diet adherence.

Fatal or non-fatal acute myocardial infarction was confirmed in 468 participants and 141 people had unstable angina needing revascularisation. After stratification and adjustment, a higher Mediterranean diet score was associated with a significantly lower risk of CHD (hazard ratio [HR]=0.60, 95% CI 0.47 to 0.77, p<0.001). A 1-unit increase in Mediterranean diet score was associated with a 6% reduced risk of CHD (HR=0.94, 95% CI 0.91 to 0.97, p<0.001).

Limitations of the evidence included that:

- The Mediterranean diet score gave similar weight to each component, but the relative contribution of some components (for example, olive oil) may be greater.
- Some people may have altered their diet because of a preclinical or clinical stage of a chronic disease at recruitment (however sensitivity analyses excluding the first 2 years of follow-up, and participants with chronic diseases at baseline, did not alter effects).
• People with diabetes, hypertension, and hyperlipidaemia had a higher Mediterranean diet score, which may be due to medical advice (although these disorders were adjusted for).

• Cultural and lifestyle differences in Spain, along with potential greater expense of a Mediterranean diet outside Mediterranean countries, may limit generalisability to the UK.

A further analysis by Buckland et al. (2012) of the Spanish cohort of the EPIC study (n=40,662) evaluated the association between olive oil intake and mortality. Follow-up was between 1992 and 2009, with an average duration of 13.4 years. Lifestyle, dietary information and mortality data were obtained as for Buckland et al. 2009 discussed above. Cox proportional hazards regression models, adjusted for several potential confounders, were used to test the association between olive oil intake and mortality. Olive oil intake values included adjustment for total energy intake (standardised to 2000 kcal/day).

A total of 1915 deaths occurred: 416 caused by CVD, 956 by cancer, 417 by other causes, and 126 by an undefined cause. In comparison with people who consumed no olive oil, those in the highest quartile of consumption (≥29.4 g oil/2000 kcal/day) had a reduced risk of both overall mortality (HR=0.74, 95% CI 0.64 to 0.87, p<0.001) and CVD mortality (HR=0.56, 95% CI 0.40 to 0.79, p=0.001). For each increase in olive oil of 10 g/2000 kcal/day, risk of overall mortality decreased by 7% (HR=0.93, 95% CI 0.90 to 0.97) and risk of CVD mortality decreased by 13% (HR=0.87, 95% CI 0.80 to 0.94). It is possible that the use of questionnaires may have led to reporting bias about dietary intake, however the association between olive oil and mortality did not change after excluding people with implausible energy intakes (according to cut offs defined in a previous study of energy intake data).

Taken together, the evidence suggests that a Mediterranean-style diet reduces risk of CHD, and olive oil intake is associated with reduced risk of mortality.

NICE PH25 does not specifically recommend a Mediterranean-style diet, therefore this evidence may have a potential impact on the guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods. Additional issues that may also need to be assessed include the cost of the diet in the UK and the risk of widening inequalities. The development and analysis of a diet more relevant to the UK, reflecting the same principles as the Mediterranean diet, might be useful.

Additionally, a multicentre RCT (n=7447) in Spain by Estruch et al. (2013) assessed a Mediterranean diet for primary prevention of cardiovascular events in people at high cardiovascular risk. Participants were randomised to: Mediterranean diet plus extra-virgin olive oil; Mediterranean diet plus mixed nuts; or a control low-fat diet. Risk of a composite endpoint of myocardial infarction, stroke, and death from cardiovascular causes was reduced by approximately 30% with both Mediterranean diet plus olive oil (HR=0.70, 95% CI 0.54 to 0.92, p=0.01) and Mediterranean diet plus nuts (HR=0.72, 95% CI 0.54 to 0.96, p=0.03). The 30% reduction in risk appears to be greater than the reduction achieved by statins (Taylor et al. 2013).

A Cochrane review of RCTs by Rees et al. (2013) also recently assessed Mediterranean diet for primary prevention of CVD. From 11 trials (n=52,044), some evidence of benefit on cardiovascular risk factors, such as reduction in total cholesterol, was seen. Clinical end points were not widely reported, and the RCT by Estruch et al. (2013) discussed above was not included in the review because it did not meet the inclusion criteria of a minimal comparison group.

Key references

**Supporting references**


Taylor F, Huffman MD, Macedo AF et al. (2013) Statins for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews issue 1: CD004816

**Effect of fast-food prices on consumption and health outcomes**

NICE PH25 recommends creating conditions whereby products containing lower levels of salt and saturated fat are sold more cheaply than high salt and saturated fat products, considering legislation and fiscal levers if necessary.

An analysis of 20-year cohort data (n=5115) from the USA by Duffey et al. (2010) investigated the effect of food and drink prices on consumption, energy intake, and weight. Data were taken from the Coronary Artery Risk Development in Young Adults (CARDIA) longitudinal study. Recruits were aged 18–30 years from 4 US cities, and were representative of age, sex, ethnicity, and education level at each location. Dietary data were collected at baseline (1985–6), year 7 (1992–3), and year 20 (2005–06). Food price data were compiled for a list of standard items: cola, whole milk, take-away hamburger, and take-away pizza. The consumer price index 2006 was used as the baseline to adjust values to 2006 dollars. Questionnaires were used to assess usual dietary intake, age, education, income, family structure, and physical activity. Height and weight were measured by technicians. Fasting insulin and glucose were obtained by blood sampling. Statistical models, adjusted for the cost of living, were used to estimate effect of price on consumption.

Over the 20 years of the study, the inflation-adjusted real price of cola and pizza decreased, whereas whole milk and hamburgers increased slightly in price. From the model, a 10% increase in the price of cola and pizza was associated with a reduced energy intake from both these foods (cola: −7.12%, standard error=1.83, p<0.001; pizza: −11.5%, standard error=3.06, p<0.001). Increasing the price of both cola and pizza by $1 was associated with reductions in total daily energy intake (−181 kcal, standard error=34, p<0.001), weight (−3.7 pounds, 95% CI −5.2 to −2.1 pounds, p<0.05), and insulin resistance score (−0.45, 95% CI −0.59 to −0.31, p<0.05). Increasing the price of both cola and pizza had an additively greater effect than increasing price of one of these foods.

Limitations of the evidence included that:

- A small number of foods and drinks were analysed, so the impact on diet more generally was not clear. For example, fruit and vegetable consumption was not assessed.
- The relationship between price and consumption may not necessarily be causal and could be affected other factors not accounted for by the study.
- Results may not be generalisable outside the USA or to those outside the 18–30 years age range of the study.

Evidence suggests that increasing the price of foods such as take-away pizza and high-sugar soft drinks may reduce total daily energy intake, weight and insulin levels among young adults. Current recommendations in NICE PH25 state only to ‘create conditions’ whereby products containing lower levels of salt and saturated fat are sold more cheaply than high salt and saturated fat products. However, data may now suggest that health benefits could be obtained by stronger intervention in markets, for example by specifically increasing the price of these foods.
of less healthy foods, which may be a potential impact on guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

Further information on the potential role of food duties for unhealthier foods is available from the National Heart Forum ("What is the role of health-related food duties?") and Sustain ("How food duties could provide the money to protect children’s health and the world they grow up in.")

Key reference

1.3 Trans fats

Effect of policies to reduce IPTFAs in foods

NICE PH25 recommends:

- Eliminating the use of IPTFAs for human consumption.
- Introducing legislation to ensure that IPTFA levels do not exceed 2% in the fats and oils used in food manufacturing and cooking.
- Creating and sustaining local and national conditions which support a reduction in the amount of IPTFAs in foods, while ensuring levels of saturated fat are not increased.
- Developing UK-validated guidelines and information for the food service sector and local government on removing IPTFAs from the food preparation process.

However, no recommendations are made specifically about legislation to ban IPTFAs.

A cross-sectional before-and-after study in the USA by Angell et al. (2012) assessed the effect on IPTFAs in fast foods of regulations introduced in 2008 to ban IPTFA use in restaurants in New York City. In 2007, customers exiting a sample of 275 outlets of national fast-food chains between noon and 2:00pm were surveyed about their purchase (n=6969 purchases) and asked to provide their receipt for verification. A survey at the same 275 outlets was then carried out in 2009 (n=7885 purchases); any outlets that had closed were replaced by another from the same chain in the same or a neighbouring area. Food items on receipts were matched against nutritional information on company web sites. The distribution of customers across types of food chain was similar in 2007 and 2009 (average distribution from both years: 53% hamburger chains, 28% sandwich chains, 12% fried chicken chains, and approximately 4% each from pizza and Mexican food chains).

Overall, between 2007 and 2009, decreases were seen in:

- Mean IPTFA content per purchase from 2.9 g to 0.5 g (mean difference [MD]=−2.4 g; 95% CI −2.8 to −2.0, p<0.001).
- Mean IPTFA plus saturated fat content from 13.8 g to 11.9 g (MD=−1.9 g; 95% CI −2.5 to −1.2, p<0.001).
- Mean IPTFA content per 1000 kcal from 3.2 g to 0.5 g (MD=−2.7 g; 95% CI −3.1 to −2.3, p<0.001).

Saturated fat content increased slightly by 0.55 g (95% CI 0.1 to 1.0, p=0.011). The proportion of purchases with 0 g IPTFA increased from 32% to 59%, and the maximum IPTFA content of a single purchase decreased from 28 g to 5 g. To consider potential differences in exposure to IPTFAs based on neighbourhood income, a multivariate analysis (controlling for total calories purchased, sex of customer, restaurant chain and poverty rate of the restaurant location) was performed. No significant difference in the change in IPTFA content of purchases was seen between areas with high and low rates of poverty.
Limitations of the evidence included that:

- Only chain restaurants were included, which may not be representative of all outlets.
- The cross-sectional study design, and the absence of a control group, meant that changes in IPTFA content could not be definitively attributed to changes in legislation.
- There may be other reasons for the changes seen than outlets reducing IPTFA content of their products, such as customers selecting lower fat items (although the authors noted multiple examples of reformulated or new products with lower or no IPTFA content).

A systematic review by Downs et al. (2013) also assessed policies, including self-regulation, for reducing IPTFAs in food. Peer-reviewed studies were included if they:

- Were empirical and performed in a ‘real-world’ setting (modelling studies of hypothetical policies were excluded).
- Examined an IPTFA policy involving, for example, labelling, voluntary limits or bans.
- Examined a policy’s effect on IPTFA levels in, for example, food, diet, blood or breast milk.

A total of 26 studies were included, involving: labelling alone (8 studies); voluntary self-regulation (5 studies); local bans (5 studies); national bans (4 studies); and labelling and voluntary limits (4 studies). In 20 studies a post-test or pre-test–post-test design was used, 3 studies were interrupted case series, 2 were cross-sectional, and only 1 study had a formal case-control design. Heterogeneity of the studies prevented meta-analysis.

Overall, IPTFA content of food decreased with all types of policy. Most effective were national bans (IPTFAs eliminated from almost 100% of all foods) and local bans (95–99.5% of fried foods and 92–97% of other restaurant foods free of IPTFAs). Mandatory IPTFA labelling and voluntary limits had a more variable effect depending on food type. In 10 studies looking at formulation of foods, saturated fat levels after the introduction of IPTFA policies did not increase as IPTFA levels decreased (except in specific foods, such as bakery products and popcorn).

Biochemical and health outcomes were examined by 2 studies identified by the review. A case-control study (n=1797 pairs) examined effects of voluntary self-regulation on risk of myocardial infarction. A significant association between myocardial infarction risk and level of IPTFAs in subcutaneous fat was seen before but not after the intervention (it was also noted that median quintiles of IPTFA levels were higher before the intervention than after). The second study was by Vesper et al. (2012) examining data on plasma levels of trans fatty acids taken from the National Health and Nutrition Examination Survey (a cross-sectional survey of the US population weighted to be nationally representative). Between 2000 and 2009, plasma levels of trans fatty acids decreased by 58% from 93.1 micromol/litre to 39.0 micromol/litre. This suggests that IPTFA consumption may be decreasing across the whole of the USA, not just in areas that have introduced IPTFA legislation.

Limitations of the review included that:

- Studies in ‘real-world’ settings may have overestimated reduction in IPTFAs because of sampling limitations (for example, considering only a small number of foods).
- Studies were not directly comparable, for example, regulations for labelling foods as IPTFA-free, and the nature of IPTFA bans, varied between countries.

Taken together, evidence suggests that policies to reduce IPTFAs in food appear to be effective. National and local bans (such as banning IPTFA use in food processing or in restaurants) seem to be most effective at eliminating IPTFAs from the food supply. This is consistent with some aspects of NICE PH25, for example eliminating the use of IPTFAs for human consumption, introducing legislation for maximum levels of IPTFAs in fats and oils used in food manufacture, and creating and sustaining local and national conditions which
support a reduction in IPTFAs in foods. However, evidence that the greatest effects may be achieved through legislation specifically banning IPTFAs may have a potential impact on the guidance. The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

**Key references**


**Supporting reference**


1.4 Marketing and promotions aimed at children and young people

No new key evidence was found for this section.

1.5 Commercial interests

No new key evidence was found for this section.

1.6 Product labelling

No new key evidence was found for this section.

1.7 Health impact assessment

No new key evidence was found for this section.

1.8 Common agricultural policy

**Effect of the common agricultural policy on dietary saturated fats and CVD**

NICE PH25 recommends that negotiation should ensure that at European Union and national level, the common agricultural policy (CAP) takes account of public health issues and that health benefits should be an explicit, legitimate outcome of CAP spending. The principle should also be encouraged that funds should reward or encourage the production of highly nutritious foods such as fruit, vegetables, whole grains and leaner meats.

A study by Lloyd-Williams et al. (2008) estimated the level of CVD within 15 European Union countries (before the 2004 enlargement) that could be a result of excess dietary saturated fats attributable to the CAP. The original aims of the CAP were to ensure an adequate supply of food, and to prevent rural poverty. But current subsidies (for example to the dairy industry in production of butter and full-fat milk) may now be a cause of increasing consumption of foods high in saturated fats. From a spreadsheet model, data were synthesised on population, diet, cholesterol levels and mortality rates. A conservative estimate was made that without CAP subsidies, saturated fat consumption could be reduced by 1% (2.2 g). It was then assumed that the 1% reduction in saturated fat was replaced with 0.5% monounsaturated and 0.5% polyunsaturated fats. Using data from meta-analyses, the expected reductions in serum cholesterol concentration, and consequential reductions in cardiovascular and stroke deaths, were then estimated.
Reducing saturated fat consumption by 1% and replacing it with monounsaturated and polyunsaturated fat was estimated to reduce blood cholesterol by 0.06 mmol/litre. This could result in 9800 fewer CHD deaths and 3000 fewer stroke deaths per year.

Limitations of the evidence included that:

- The quality and availability of recent CHD mortality data varied within countries.
- Factors other than CAP subsidies may have had an effect, such as food advertising.
- The model was relatively simple and did not consider socioeconomic variables.

Based on conservative estimates, the evidence suggests that reducing the amount of saturated fat consumption that may be attributable to CAP subsidies could lead to reductions in cardiovascular mortality. This provides additional data consistent with recommendations in NICE PH25 that health benefits should be an outcome of CAP spending.

**Key reference**

1.9 Physically active travel

No new key evidence was found for this section.

1.10 Public sector catering guidelines

See Gase et al. (2011) in ‘Health impact of local policies to reduce salt intake in public services’ in section 1.1 ‘Salt’.

1.11 Take-aways and other food outlets

No new key evidence was found for this section.

1.12 Monitoring

See Shankar et al. (2013) in ‘UK Food Standards Agency salt campaign’ in section 1.1 ‘Salt’.

**Practice**

1.13 Regional CVD prevention programmes – good practice principles

No new key evidence was found for this section.

1.14 Regional CVD prevention programmes – preparation

No new key evidence was found for this section.

1.15 Regional CVD prevention programmes – programme development

**Lifestyle factors**
NICE PH25 recommends:

- Developing a population-based approach.
• Ensuring a 'programme theory' is developed and used to underpin the programme.
• Linking the programme with existing strategies for targeting people at particularly high risk of CVD.
• Working closely with regional and local authorities and other organisations to promote policies which are likely to encourage healthier eating, tobacco control and increased physical activity. Policies may cover spatial planning, transport, food retailing and procurement.

_Effect of healthy lifestyle on stroke_

A prospective cohort study by Chiuve et al. (2008) in the USA (n=43,685 men from the Health Professionals Follow-up Study, and 71,243 women from the Nurses' Health Study) examined the effect of multiple lifestyle factors on stroke risk. All participants were free of CVD and cancer. Information was obtained via survey on smoking status, weight, hypertension, hypercholesterolaemia, diabetes, height, parental history of myocardial infarction, physical activity, diet, alcohol consumption, and drug treatments (including aspirin and vitamin E supplements; and in women, postmenopausal hormones). Diet was assessed via a scoring system based on intake of vegetables, fruit, nuts, soy, cereal fibre, meat, fat, and multivitamins. A low-risk lifestyle was defined as not smoking, a BMI less than 25 kg/m², 30 minutes/day of moderate activity, modest alcohol consumption (in men 5 to 30 g/day; in women 5 to 15 g/day), and being within the top 40% of a healthy diet score.

Follow-up began in 1984 for women and 1986 for men, and continued until occurrence of stroke, cancer, death or study end in 2004. Multivariable relative risks were estimated with Cox proportional-hazards models adjusted for parental history of myocardial infarction before age 60, regular aspirin use, and vitamin E supplementation (plus use of hormone therapy for women).

During follow-up, among women there were 1559 strokes (853 ischaemic, 278 haemorrhagic) and among men 994 strokes (600 ischaemic, 161 haemorrhagic). Compared with women who had no low-risk lifestyle factors, women with all 5 low-risk factors were at less risk of any stroke (relative risk [RR]=0.21, 95% CI 0.12 to 0.36) and of ischemic stroke (RR=0.19, 95% CI 0.09 to 0.40). The same comparison among men indicated a similarly reduced risk of both any stroke (RR=0.31, 95% CI 0.19 to 0.53) and ischemic stroke (RR=0.20, 95% CI 0.10 to 0.42). The proportion of total stroke cases that may have been attributable to lack of adherence to a low-risk lifestyle was 47% among women and 35% in men.

Limitations of the evidence included that data were self-reported and may be prone to bias, and were gathered from health professionals and nurses whose demographics may limit generalisability. Also, the study did not assess interventions for stroke reduction, only factors that may be associated with reduced risk of stroke.

The evidence suggests that a low-risk lifestyle (not smoking, normal BMI, moderate daily activity, modest alcohol consumption, and healthy diet) may substantially reduce risk of stroke. This evidence is consistent with recommendations in NICE PH25 to promote policies to encourage healthier eating, tobacco control and increased physical activity.

**Key reference**


**Community-based health promotion**

A cohort study in the Netherlands by Wendel-Vos et al. (2009) investigated the effect of a community health promotion intervention on lifestyle factors among men and women aged 31–70 years. The intervention was performed in Maastricht from which a cohort (n=2356) was recruited and compared with a control cohort (n=758) from Doetinchem. The intervention was aimed at decreasing CVD prevalence by increasing physical activity and reducing fat intake.
and smoking. Although population-based, the intervention specifically targeted people of low socioeconomic status, and people with (or at high risk of) CVD. Examples of the interventions used were nutrition parties, advice on cooking cheap and healthy meals, printed guides of walking and cycling routes, daily aerobics programmes on television, and anti-smoking campaigns. Data were collected over a 5-year period via physical examination, a general questionnaire and a food-frequency questionnaire. Adjustments to analyses were made for age, sex and educational level as appropriate, and also to help prevent effects caused by regression to the mean.

No significant differences between groups were seen among men or those with moderate or high educational level. However, significant differences (all $p \leq 0.05$) in adjusted mean change in lifestyle factors between groups were seen for:

- Energy intake in women ($-0.2$ megajoule [~50 kcal]/day) and in those with a low educational level ($-0.2$ megajoule [~50 kcal]/day).
- Fat intake in women ($-2.5$ g/day) and in those with a low educational level ($-3$ g/day).
- Time spent walking among women ($+2.2$ hours/week) and among those with a low educational level ($+2.3$ hours/week).
- Time spent on total physical activity in leisure time among women ($+2.1$ hours/week).
- Time spent cycling among those with a low educational level ($+0.6$ hours/week).

Limitations of the evidence included that:

- The intervention was delivered to the whole community and not specifically to the cohort recruited for the study, which may weaken causality between outcomes and intervention.
- Much of the data were self-reported and may be prone to bias.
- Both cohorts were previously involved in monitoring studies and may be more health conscious than the general population.
- The study was based in the Netherlands and may not be fully generalisable to the UK.

Evidence suggests that a community health promotion intervention may lead to favourable changes in energy and fat intake and physical activity level, particularly among women and people with low educational levels. Although NICE PH25 does not specifically discuss community-based health promotion, the data are consistent with recommendations to promote policies to encourage healthier eating, tobacco control and increased physical activity.

Other relevant guidance from NICE in this area can be found in ‘Behaviour change: the principles for effective interventions’ (NICE PH6) and ‘Community engagement’ (NICE PH9).

**Key reference**

**Lifestyle counselling and education**
An RCT in Denmark by Toft et al. (2008) compared the effect of multifactorial lifestyle counselling ($n=6,091$) with non-intervention control ($n=3,324$) on dietary habits in a sample of all individuals living in western Copenhagen County. Participants in the intervention group were screened to assess risk of ischaemic heart disease, and then offered a relevant lifestyle counselling talk about smoking, physical activity, diet or alcohol. Those in the highest quintile of risk, or with high-risk factors (daily smoking, diabetes, glucose intolerance, overweight, or high blood pressure or cholesterol level) were also offered relevant group counselling on diet, physical activity or smoking. For the group counselling, 6 sessions of 2 hours were scheduled over 4–6 months. At 1 and 3 years, people at high risk were invited back for a further health examination and risk assessment. Group sessions were again offered to those still at high risk, whereas participants at low risk and in the control group were followed by questionnaire.
At 5 years, a health examination and brief final lifestyle counselling was provided to all participants. Dietary intake was measured on a validated, self-administered 48-item food frequency questionnaire.

At 5 years, compared with the control group, vegetable intake had significantly increased in the intervention group for both men (net change 23 g/week, p=0.04) and women (net change 27 g/week, p=0.01). Intake of highly saturated fats had decreased significantly in the intervention versus control group for both men (OR=0.59, 95% CI 0.41 to 0.86, p=0.01) and women (OR=0.42, 95% CI 0.30 to 0.59, p<0.0001). Fruit and fish intake were significantly greater in the intervention group at 3 years but not at 5 years.

Limitations of the evidence included that the questionnaire was self-reported and may have introduced bias. The authors also reported a ‘high degree’ of loss to follow-up.

A Cochrane review (n=163,471) by Ebrahim et al. (2011) assessed multiple risk factor interventions for primary prevention of CHD. RCTs were included that used counselling or education for longer than 6 months to modify more than 1 cardiovascular risk factor. Adults aged 35 years or over, with no evidence of CHD, who were from general populations or occupational groups, or had specific risk factors (such as diabetes) were eligible. A total of 55 trials were identified, mostly targeting a combination of factors including diet, exercise, weight, salt, alcohol, stress, smoking, and adherence to drug treatment. Interventions were generally quite individualised and included workshops, lectures, individual sessions and counselling, written material, assignments, shopping tours and cooking sessions. Primary outcomes were total mortality, fatal CHD and fatal stroke.

In trials reporting clinical event end points, there was no effect on total mortality (OR=1.00, 95% CI 0.96 to 1.05, p=0.84; 14 trials, n=132,564) or on CHD mortality (OR=0.99, 95% CI 0.92 to 1.07, p=0.81; 11 trials, n=132,564). However, risk of total mortality and combined fatal and non-fatal cardiovascular events was reduced in high risk individuals such as those with hypertension (OR=0.78, 95% CI 0.68 to 0.89, p=0.00026; 6 trials, n=17,852) or diabetes (OR=0.71, 95% CI 0.61 to 0.83, p=0.000015; 4 trials, n=12,307).

Limitations of the evidence included that:

- Heterogeneity was considerable (I²>85%) for all risk factor analyses, and was not explained by comorbidities, allocation concealment, use of drugs to lower blood pressure or cholesterol, or age of the trial. This may reduce the validity of the meta-analyses.
- The authors allowed up to 25% of participants in each trial to have had prior CVD events, which may bias findings because these participants may benefit more from interventions.
- The median trial duration was 12 months, limiting the conclusions that can be drawn about long-term effects.

The evidence suggests that population-based lifestyle counselling and education, to reduce CVD risk through behaviour change, has limited use in general populations. Further research is needed to assess effectiveness in high-risk populations. This is consistent with recommendations in NICE PH25 that initiatives aimed at the whole population should include local policy and regulatory initiatives rather than individualised health promotion interventions.

Key references
General health checks

NICE PH25 recommends that CVD prevention programmes should be linked with existing strategies for targeting people at particularly high risk of CVD and take account of ongoing, accredited screening activities by GPs and other healthcare professionals. This includes the NHS Health Checks programme.

Two reviews recently examined general health checks.

A systematic review of quantitative and qualitative studies by Dryden et al. (2012) investigated demographic factors affecting whether people engaged with health checks. Studies of general or preventive health checks in developed countries assessing risk factors for CVD were included. Only studies in adults at high risk of CVD or in hard-to-reach groups were eligible. The review included 39 studies, of which 17 were from the UK.

The studies suggested that people who were least likely to attend health checks tended to:

• Be male, older, single and white.
• Have low incomes, low socioeconomic status, and be unemployed or less well educated.
• To have more cardiovascular risk factors, including smoking.
• Value health and health checks less strongly, have low self-efficacy, and feel less in control of their health.

Limitations of the evidence included that:

• The search method was defined as ‘an exploratory scoping study approach’ and formal statistical meta-analysis was deemed inappropriate.
• Health checks in older people were excluded, and only general or preventive health checks for the risk factors of CVD were included, so results may not be fully generalisable.

A Cochrane review (n=182,880) by Krogsbøll et al. (2012) also examined health checks with the aim of quantifying their benefits and harms with an emphasis on patient-relevant outcomes. RCTs comparing health checks with no health checks in adults unselected for disease or risk factors were included. Trials among older people were excluded. Health checks were defined as screening general populations for more than 1 disease or risk factor in more than 1 organ system. A total of 16 trials were identified, of which 14 had available outcome data. Primary outcomes were all-cause mortality and disease-specific mortality. For mortality outcomes, meta-analysis using a random-effects model was performed, whereas other outcomes were analysed qualitatively.

In trials reporting total mortality, no difference was seen for health checks compared with no health checks (risk ratio [RR]=0.99, 95% CI 0.95 to 1.03, p=0.49; 9 trials, n=155,899). Similar results were seen in trials reporting cardiovascular mortality (RR=1.03, 95% CI 0.91 to 1.17, p=0.62; 8 trials, n=152,435) and cancer mortality (RR=1.01, 95% CI 0.92 to 1.12, p=0.81; 8 trials, n=139,290). No effects were seen for clinical events or other measures of morbidity. General health checks seemed to have no impact on hospital admissions, disability, worry, specialist referrals, additional visits to doctors or time off work, but most of these outcomes were rarely reported.

Limitations of the evidence included that

• Important harmful outcomes such as the number of follow-up diagnostic tests or short-term psychological effects were often not studied.
• Many of the studies date back to the 1960s and may not represent current practice. For example, the nature of health checks and any actions taken as a result of checks, are likely to change over time.
Taken together, these reviews provide additional evidence about the types of people who do and do not attend general health checks, and whether health checks may or may not be beneficial. These data add to the evidence base available when NICE PH25 was developed, and will need to be considered in any future review of the guidance. The evidence for general health checks should be considered in the context of broader population-based approaches for prevention of CVD. The availability of new evidence since publication of NICE PH25 may have a potential impact on guidance.

The details of any impact are outside the scope of the Evidence Update. Decisions on how the new evidence may impact guidance will not be possible until the guidance is reviewed by NICE following its published processes and methods.

**Key references**


**1.16 Regional CVD prevention programmes – resources**

No new key evidence was found for this section.

**1.17 Regional CVD prevention programmes – leadership**

No new key evidence was found for this section.

**1.18 Regional CVD prevention programmes – evaluation**

No new key evidence was found for this section.

**1.19 Children and young people**

**Interventions for preventing obesity in children**

NICE PH25 recommends that children and young people should be helped to have a healthy diet and lifestyle. This includes helping them to develop positive, life-long habits in relation to food. This can be achieved by ensuring the messages conveyed about food, the food and drink available – and where it is consumed – is conducive to a healthy diet.

A Cochrane review by Waters et al. (2011) assessed interventions to prevent obesity in children. Controlled trials (with or without randomisation) of childhood obesity prevention interventions, policies or programmes in place for 12 or more weeks were included. Of the 55 studies identified, 50 were from high-income countries, and 39 involved children aged 6–12 years. A broad range of programme components were used in the studies. Primary outcomes were: weight and height, per cent fat content, BMI, ponderal index (a measure of leanness), skin-fold thickness, and prevalence of overweight and obesity.

From the meta-analysis it appeared that programmes were effective at reducing adiposity, but not all interventions were effective. The authors noted several promising policies and strategies, including: a school curriculum promoting healthy diet and lifestyle; more opportunities for physical activity in the school week; improving food in schools; environments and practices to support healthy eating and activity; and support for teachers and parents in encouraging children to adopt healthier lifestyles. Overall, children in the intervention groups had a standardised mean difference in BMI or zBMI (a standardised form of BMI) of −0.15 kg/m² (95% CI −0.21 to −0.09 kg/m²; p<0.00001; 37 studies, n=27,946).
Results for age subgroups were:

- 0 to 5 years: $-0.26 \text{kg/m}^2$ (95% CI $-0.53$ to $0.00 \text{kg/m}^2$, $p=0.052$; 8 studies, $n=1815$)
- 6 to 12 years: $-0.15 \text{kg/m}^2$ (95% CI $-0.23$ to $-0.08 \text{kg/m}^2$, $p=0.000019$; 31 studies, $n=18,983$)
- 13 to 18 years: $-0.09 \text{kg/m}^2$ (95% CI $-0.20$ to $0.03 \text{kg/m}^2$, $p=0.14$; 10 studies, $n=7148$)

From 8 studies reporting adverse effects, there was no evidence of unhealthy dieting, increased levels of underweight, or body image issues. Interventions did not appear to increase health inequalities.

Limitations of the evidence included the unexplained high level of heterogeneity that was apparent in all age groups and could not be explained by randomisation status, or type, duration or setting of the intervention. Additionally, a broad range of programme components were used in the studies, meaning it was not possible to distinguish which were most effective. The authors also noted of the included studies that designs needed to be strengthened, and longer term outcomes measuring equity, potential harms and costs were needed.

The authors concluded that child obesity-prevention programmes might have a small effect on BMI in children aged 6 to 12 years, but further studies are needed. This evidence is consistent with recommendations in NICE PH25 that children and young people should be helped to have a healthy diet and lifestyle. Further guidance from NICE in this area can be found in ‘Managing overweight and obesity among children and young people’ (NICE PH47).

**Key reference**


1.20 Public sector food provision

See Gase et al. (2011) in ‘Health impact of local policies to reduce salt intake in public services’ in section 1.1 ‘Salt’.

1.21 Physical activity

See Chiuve et al. (2008), Wendel-Vos et al. (2009), Toft et al. (2008), and Ebrahim et al. (2011) in ‘Lifestyle factors’ in section 1.15 ‘Regional CVD prevention programmes – programme development’.

1.22 Health impact assessments of regional and local plans and policies

No new key evidence was found for this section.

1.23 Take-aways and other food outlets

See Angell et al. (2012) in ‘Effect of policies to reduce IPTFAs in foods’ in section 1.3 ‘Trans fats’.

1.24 Nutrition training

See Gase et al. (2011) in ‘Health impact of local policies to reduce salt intake in public services’ in section 1.1 ‘Salt’.
Areas not currently covered by NICE PH25

Effect of sweetened drinks on blood pressure

Although NICE PH25 includes some recommendations about high-sugar foods (such as labelling, and restrictions on marketing to children), no recommendations are made specifically about sweetened drinks, either with sugar or artificially.

An analysis of prospective cohort studies (n=223,891) by Cohen et al. (2012) examined the association between incident hypertension and both sugar-sweetened drinks and artificially sweetened drinks. The study analysed data from 3 large cohorts: the Nurses' Health Studies I (n=88,540 women) and II (n=97,991 women) and the Health Professionals' Follow-Up Study (n=37,360 men). Participants were grouped according to number of sweetened drinks consumed: less than 1 per month; 1–4 per month; 2–6 per week; 1 or more per day. Multivariable Cox proportional hazards regression models (adjusted for confounding factors such as intake of alcohol, vitamins, minerals, trans fats and fibre) were used to calculate hazard ratios for incident clinically diagnosed hypertension.

In a pooled analysis of all 3 cohorts, risk of incident hypertension was increased among people who had at least 1 sugar-sweetened drink daily versus those who had fewer than 1 of these drinks per month (adjusted HR=1.13, 95% CI 1.09 to 1.17, p value not stated). The same pattern was also seen for artificially sweetened drinks, with hypertension risk increased for those who had at least 1 artificially sweetened drink daily versus those who had less than 1 of these drinks per month (adjusted HR=1.14, 95% CI 1.09 to 1.18, p value not stated).

Limitations of the evidence included that:

- Outcomes may have been affected by confounding factors, such as:
  - sodium intake, which was not well measured by the study
  - items consumed in place of sweetened drinks among those who had fewer of these drinks
  - differing lifestyle factors between those consuming many and those consuming few sweetened drinks.
- Both intake of drinks and hypertension were self-reported and may be prone to bias.
- Serving sizes of drinks may have varied between participants.
- Data were gathered from health professionals and nurses whose demographics may limit generalisability. Soft drink composition (for example, use of high-fructose corn syrup) and consumption in the USA may also be different from the UK.
- A definitive mechanism for increased hypertension risk in consumers of both sugar-sweetened drinks and artificially sweetened drinks was not established.

A cross-sectional analysis (n=2696) of population samples in the USA and the UK by Brown et al. (2011) found similar associations between sugar-sweetened drinks and increased blood pressure. However, intake of artificially sweetened drinks appeared to be inversely associated with blood pressure.

Evidence suggests that sugar-sweetened drinks may be associated with an increased risk of incident hypertension. Evidence that artificially sweetened drinks might also be associated with hypertension is conflicting. Although there are no specific recommendations about sweetened drinks in NICE PH25, limitations of the evidence (particularly potential confounders that hinder conclusions around causality) mean that this evidence is unlikely to have an impact on current guidance.

Key reference
Foods enriched with plant sterols

NICE PH25 does not make any recommendations specifically about the consumption of plant sterols. However, one of the considerations during development of the recommendations was that daily consumption of products containing plant sterols and stanols may reduce blood cholesterol by about 10% – and so may reduce CVD mortality substantially. However, it was not clear how a recommendation on their use might impact on inequalities in health. The Programme Development Group believed this issue deserved further attention. Additionally, ‘Lipid modification’ (NICE CG67) states that people should not routinely be recommended to take plant sterols and stanols for the primary prevention of CVD.

A modelling study in Canada by Gyles et al. (2010) estimated savings to the healthcare system through impact on CHD if plant sterols were approved for consumption\(^2\). The study employed a variation of a ‘cost-of-illness analysis’ (measuring costs of a specific disease, in this case CHD) to model savings associated with preventing or avoiding CHD.

The model comprised several assumptions, based on a review of peer-reviewed scientific literature, each of which was assigned a value for 4 scenarios (ranging from ‘ideal’ to ‘very pessimistic’):

- ‘Success rate’ – the proportion consuming sterols at the necessary rate (ideal=47.0%, very pessimistic=5.0%).
- Cholesterol reduction due to plant sterol consumption (ideal=10.8%, very pessimistic=5.0%).
- CHD reduction due to 1% reduction in serum low-density lipoprotein-cholesterol (ideal=3.0%, very pessimistic=1.0%)
- CHD reduction due to plant sterol consumption (ideal=32.4%, very pessimistic=5.0%).

The estimated cost reductions used in the model (corresponding to a 1% decrease in overall incidence of CHD) for the different cost categories were: physician care, mortality, long-term and short-term disability=1.00% each; drugs=0.50%; hospital costs=0.16%; other direct costs=0.23%.

Results from the model suggested that if plant sterol-enriched foods were made available for sale in Canada, annual savings to the healthcare system could be between CAN$38 million (very pessimistic scenario) and CAN$2.45 billion (ideal scenario).

Limitations of the evidence included that:

- The authors noted that no long-term studies have examined direct effects of plant sterols on heart disease, so the model is based on assumed effects mediated by cholesterol.
- It was not possible to estimate the cost premium of foods enriched with sterols in Canada, because a market for these goods is not established. As a result, a cost-effectiveness or cost-benefit analysis could not be performed. The authors noted that an excessive price premium would result in a lower economic benefit of plant sterol-enriched foods.
- The price premium of sterol-containing products may have implications for health inequalities but this was not examined by the study.
- Cost data may not be directly applicable to the UK.

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\(^2\) In May 2010, Health Canada’s Food Directorate approved the addition of plant sterols to a limited range of foods.
The evidence suggests that approval of plant sterol-enriched foods for sale in Canada could result in savings to the healthcare system from a reduced incidence of CHD through lower blood cholesterol levels. However, the lack of long-term evidence for a direct effect of plant sterols on heart disease, and uncertainties around effects on inequalities, mean that the results are unlikely to have an impact on NICE PH25. Further research is needed in line with the existing NICE research recommendation ‘What effect would a regular daily intake of 2.5 g of stanols or sterols have on the incidence of cardiac and stroke events? How can we best evaluate stanols in terms of their acceptability, affordability, effectiveness, cost effectiveness and impact on health inequalities?’

An update to the lipid modification guideline (NICE CG67) is currently underway. The draft scope states that issues that will be covered include a cardioprotective diet including stanols and sterols.

**Key reference**


**Adaptive e-learning for dietary behaviour change**

NICE PH25 does not make any recommendations specifically about the use of e-learning.

A health technology assessment by Harris et al. (2011) examined adaptive e-learning interventions for dietary behaviour change. RCTs of people aged 13 years or over assessing interactive software programs for improving dietary behaviour were eligible. A total of 43 studies (n=21,811), all in high-income countries, were identified. Most interventions were aimed at reducing fat intake (28 studies) or increasing fruit and vegetable intake (21 studies). The most common delivery method was via the internet (22 studies) followed by CD-ROM (8 studies) and computer kiosks (6 studies). The most frequently used techniques were: goal setting; feedback on performance; information on consequences of behaviour; barrier identification or problem solving; self-monitoring of behaviour; and instruction on performing the behaviour. Primary outcomes were measures of dietary intake. Cost effectiveness was assessed by a model comparing e-learning with advice from a healthcare professional.

E-learning had a significant effect on weighted mean differences in daily intake of fruit and vegetables (+0.24 servings, 95% CI 0.04 to 0.44 servings, p=0.019; 12 studies, n=6657) and total energy consumed from fat (–1.4%, 95% CI –2.5 to –0.3%, p=0.012; 10 studies, n=3518). Effects on intake of total fats, saturated fat, dietary fibre and energy were non-significant. The economic evaluation model suggested that the incremental cost-effectiveness ratio with e-learning was £102,112 per QALY. For values up to about £200,000 per QALY gained, dietary advice alone was the preferred option. The authors stated that e-learning was not cost-effective at conventional levels of £20,000–30,000 per QALY gained.

Limitations of the evidence included that:

- Of the 43 studies, 30 were rated as weak and 13 as moderate; none were from the UK.
- E-learning is a fast-moving area. The most recent study in the review was from 2010, so technologies such as the latest developments in social media were not covered.
- E-learning may be better suited to delivery as part of a programme, whereas this review appeared to assess its efficacy in isolation.
- Many studies did not report the intended intensity or frequency of the intervention, and those that did showed considerable variation (ranging from 1 hour, to weekly interaction over a year). Not all studies reported actual time spent using the intervention.
- No published economic evaluations were identified, and it was difficult to determine costs associated with e-learning because most studies did not report cost data.
Evidence suggests that e-learning to promote dietary behaviour change may not produce clinically significant or cost-effective changes in dietary behaviour. However, the latest technology was not assessed, nor was the efficacy of e-learning as part of a wider education programme. Limitations of the evidence mean that these data are unlikely to have an impact on NICE PH25. Further research to address the limitations stated above is needed. The authors noted that further study should not be undertaken until theoretically informed work, addressing which aspects of the target population, target behaviour, content and delivery of the intervention are likely to lead to positive results, is completed.

**Key reference**
2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Regional CVD prevention programmes – programme development

- General health checks in adults for reducing morbidity and mortality from disease.

Further evidence uncertainties for prevention of CVD can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.
Appendix A: Methodology

Scope
The scope of this Evidence Update is taken from the scope of the reference guidance:


Following expert advice, it was agreed that the scope of the Evidence Update should focus primarily on nutritional and dietary aspects of CVD prevention as these are the areas most likely to have changed. Smoking and alcohol topics are covered extensively by other NICE guidance.

Searches
The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 1 January 2008 (the end of the search period of NICE public health guidance 25) to 1 June 2013:

- ASSIA (Applied Social Science Index and Abstracts)
- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- EconLit (American Economic Association electronic bibliography)
- EMBASE (Excerpta Medica database)
- HMIC (Health Management Information Consortium) database
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)
- PsycINFO

The Evidence Update search strategy replicates the strategy used by the original guidance (for key words, index terms and combining concepts) as far as possible. If this is not practical, then the search replicates the basic PICO (population, intervention, comparison, outcome) structure of the original searches. Where necessary, the strategy is adapted to take account of changes in search platforms and updated indexing language.

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The following search terms, used in the original search strategy for NICE PH25, were removed for the Evidence Update search: smoking, tobacco, stress, alcohol, drinking.

Some additional terms were added relating to fats, oils, salt, sugar, food policy, food labelling, and physical activity. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews.

Additionally, 3 studies (Downs et al 2013, Krogsbøll et al. 2012, Waters et al. 2011) were identified outside of the literature search. Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

There is more information about how NICE Evidence Updates are developed on the NICE Evidence Services website.
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Figure 1 Flow chart of the evidence selection process

28,835 records identified through search

8763 duplicates from searching

20,072 records after duplicates removed

14,643 records excluded at first sift

5429 records included after first sift

5008 records excluded at second sift

421 records included after second sift

384 records excluded at critical appraisal and evidence prioritisation

40 records discussed by EUAG

3 additional records identified by EUAG outside original search

23 records included by EUAG in published Evidence Update

17 records excluded by EUAG

EUAG – Evidence Update Advisory Group
Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

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Visiting Professor of Public Health Epidemiology, Nuffield Department of Obstetrics and Gynaecology, and Emeritus Fellow of New College, University of Oxford

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