From:	Maria Cohn [mcohn@policyaction.com]
Sent:	20 March 2013 14:16
To:	MCAVAN Linda; ROMANO Emilia
Cc:	LERAILLEZ Anne; FLORENZ Karl-Heinz; RIES Frédérique; SCHLYTER Carl; CALLANAN Martin; ANDREASEN Marta; ROSSI Oreste
Subject:	Stakeholder meeting with the representatives of the electronic cigarette industry - follow up
Follow Up Flag:	Follow up
Flag Status:	Completed
Attachments:	NJoy - EP Leave behind-March meetings- FINAL.pdf; ASH Briefing on Electronic Cigarettes.pdf; NICE Draft Guideance.pdf

Dear MEP McAvan,

On behalf of NJOY Innovations Ltd., I would like to thank you and the ENVI Secretariat for organising yesterday the stakeholder meeting with the representatives of the electronic cigarette industry.

Attached you will find a copy of NJOY's position, as well as the briefings from Action on Smoking and Health (ASH) and the UK's National Institute for Health and Clinical Excellence (NICE) that Mr. Jeff Weiss referred to during the presentation. We hope that you find them useful for your work. Don't hesitate to let us know if you have any further questions or need additional information.

Best regards,

Maria Cohn
Consultant
M +32 489 334 317

Policy Action SPRL
Rue du Trône 60 | 1st floor | Brussels 1050 | Belgium
T +32 2 626 95 00 | F +32 2 626 95 01
www.policyaction.com

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NJOY[i] position on the draft TPD2 as it relates to electronic cigarettes

Committed smokers, previously unable or unwilling to entirely quit the act of smoking using traditional nicotine replacement therapy products, are finding electronic cigarettes a truly attractive alternative to cigarettes, and are switching in increasing numbers. Electronic cigarettes do not contain or combust tobacco, and instead deliver vaporised nicotine to adult smokers in a manner that replicates the hand-to-mouth and other rituals of smoking, without providing the toxic and carcinogenic products associated with tobacco cigarette smoking. NJOY's mission is nothing less than to make traditional tobacco cigarettes obsolete. To achieve this we must be able to promote and deliver products that are satisfying for our adult smoker customers.

We agree with certain of the concerns about the current unregulated state of the electronic cigarette industry, and the need to properly ensure adequate safety and quality standards across the EU. However, given the emerging scientific data that electronic cigarettes have enormous harm reduction potential and the increasing support of public health organizations like Action on Smoking and Health (ASH) and Britain's National Institute for Health and Clinical Excellence for the role that electronic cigarettes may be able to play in an effective harm reduction approach, we are concerned that the application of the full weight of pharmaceutical regulation could result in electronic cigarettes being withdrawn from the market. Article 18 risks removing tobacco's only real potential competitor from the market.

We do not believe that available research justifies the regulation proposed by the draft review of the Tobacco Products Directive**.** A more appropriate regulatory pathway is needed which recognises the specific characteristics of the product. The review of the EU Pharma Package expected in approximately 2 years time would, in our view, provide the appropriate platform for regulatory decisions regarding electronic cigarettes. On that basis we would respectfully request that you consider the following amendments to Article 18 and recitals 34 and 35 of the draft Directive:

TPD2 proposal	Suggested amendment
Article 18 - Nicotine-containing products 1. The following nicotine-containing products may only be placed on the market if they were authorised pursuant to Directive 2001/83/EC: (a) products with a nicotine level exceeding 2 mg per unit, or (b) products with a nicotine concentration exceeding 4 mg per ml or (c) products whose intended use results in a mean maximum peak plasma concentration exceeding 4 ng of nicotine per ml. 2. The Commission shall be empowered to adopt delegated acts in accordance with Article 22 to update the nicotine quantities set out in paragraph taking into account scientific developments and marketing authorisations granted to nicotine- containing products pursuant to Directive 2001/83/EC. 3. Each unit packet and any outside packaging of nicotine-containing products below the thresholds set out in paragraph 1 shall carry the following health warning: *This product contains nicotine and can damage your health.* 4. The health warning referred to in paragraph 3 shall comply with the requirements specified in Article 10(4). In addition, it shall: (a) be printed on the two largest surfaces of the unit packet and any outside packaging; (b) cover 30 % of the external area of the corresponding surface of the unit packet and any outside packaging. That proportion shall be increased to 32 % for Member States with two official languages and 35 % for Member States with three official languages. 5. The Commission shall be empowered to adopt delegated acts in accordance with Article 22 to adapt the requirements in paragraphs 3 and 4 taking into account scientific and market developments and to adopt and adapt the position, format, layout, design and rotation of the health warnings.	***Delete***

Justification: *Further analysis and a full impact assessment are needed before making electronic cigarettes subject to a regulation that has not been designed to regulate what are non-medicinal, smoking alternative products. Merely applying the pharmaceutical regulatory regime to electronic cigarettes, which are seen and used as smoking alternative products in the vast majority of EU Member States, would be inappropriate and does not necessarily provide the adequate framework to regulate this product. Moreover, applying these rules to electronic cigarettes without first assessing regulatory requirements could effectively restrict or remove the product from the market – despite the enormously helpful role they seem to be playing as part of an overall harm reduction strategy.*

TPD2 proposal	Suggested amendment
Recital 34 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use provides a legal framework to assess the quality, safety and efficacy of medicinal products including nicotine containing products. A significant number of nicotine-containing products were already authorised under this regulatory regime. The authorisation takes into account the nicotine content of the product in question. Subjecting all nicotine-containing products, whose nicotine content equals or exceeds the content of a nicotine containing product previously authorised under Directive 2001/83/EC, to the same legal framework clarifies the legal situation, levels out differences between national legislations, ensures equal treatment of all nicotine containing products usable for smoking cessation purposes and creates incentives for research and innovation in smoking cessation. This should be without prejudice to the application of Directive 2001/83/EC to other products covered by this Directive if the conditions set by Directive 2001/83/EC are fulfilled.	***Recital 34*** Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use provides a legal framework to assess the quality, safety and efficacy of medicinal products ~~including nicotine containing products~~. ***Considering that a*** significant number of nicotine-containing products ~~were~~ ***are*** already authorised under this regulatory regime, ***the European Commission shall as part of its upcoming review of the relevant pharmaceutical legislation conduct a study and a full impact assessment to determine the most appropriate regulation of electronic cigarettes on that basis.*** ~~The authorisation takes into account the nicotine content of the product in question. Subjecting all nicotine-containing products, whose nicotine content equals or exceeds the content of a nicotine containing product previously authorised under Directive 2001/83/EC, to the same legal framework clarifies the legal situation, levels out differences between national legislations, ensures equal treatment of all nicotine containing products usable for smoking cessation purposes and creates incentives for research and innovation in smoking cessation. This should be without prejudice to the application of Directive 2001/83/EC to other products covered by this Directive if the conditions set by Directive 2001/83/EC are fulfilled.~~

Justification: *The current pharmaceutical legislation was designed for medicinal products that are intended to be effective in the treatment of disease which, in this context, means the "curing" of a smoker's nicotine addiction through a progressive weaning from nicotine. Electronic cigarettes are not medicinal, and instead are an alternative smoking product. Subjecting all nicotine-containing products to a medicinal regime without first conducting a detailed impact assessment could effectively, yet unnecessarily, restrict or remove the product from the market. If these products are removed from the market at the same time that existing tobacco products are left on the market, committed adult smokers may return to the consumption of tobacco cigarettes, with all of the risks that entails. The proposed revision of the EU Pharma Package in two years' time would give legislators time to properly rectify this and determine an appropriate framework for the regulation of electronic cigarettes.*

TPD2 proposal	Suggested amendment
Recital 35 Labeling provisions should be introduced for nicotine containing products below the threshold set out in this Directive drawing the attention of consumers to potential health risks.	***Delete***

Justification: *Labeling requirements for electronic cigarettes should be examined as part of a full impact assessment done to determine appropriate regulation of electronic cigarettes on that basis, as part of the review of the EU Pharma Package and not as part of this current tobacco products regulation.*

[i] NJOY Innovations Ltd. is a UK-based electronic cigarette company established in 2012. Its parent company NJOY, Inc. is the market leader in electronic cigarettes in the US. NJOY produces electronic cigarettes, which are marketed exclusively to adult, committed smokers. NJOY Innovations Ltd. is registered in the European Transparency Register with ID. no. 829392410814-85.

January 2013

ash briefing
action on smoking and health

Electronic cigarettes

www.ash.org.uk

Summary

- E-cigarettes are evolving and there is increasing evidence to suggest that some if not all products provide effective nicotine delivery.
- There is little real-world evidence of harm from e-cigarettes to date, especially in comparison to smoking.
- E-cigarettes are used by both smokers and ex-smokers, but there is little evidence of use by those who have never smoked.
- ASH supports regulation to ensure the safety and reliability of e-cigarettes but, in the absence of harm to bystanders, does not consider it appropriate to include e-cigarettes under smokefree regulations.
- The Medicines and Healthcare products Regulatory Agency (MHRA) is currently reviewing options to regulate nicotine-containing products including e-cigarettes. Meanwhile, the National Institute for Health and Clinical Excellence (NICE) is developing guidance on harm reduction, which will include electronic cigarettes, for publication in May 2013.

Nicotine Substitution

Smoking is the largest, preventable cause of premature mortality in the UK. The goal of public health is to diminish the harm caused by tobacco products. While the ideal remains that people should stop using tobacco completely and permanently, consensus currently supports a properly regulated harm reduction approach[1,2,3]– a framework by which the harmful effects of smoking are reduced without requiring the elimination of a behaviour that is not necessarily condoned. Such strategies have proved successful in the past, for example within the contexts of needle exchange programmes for illicit drug use and the promotion of safer sex to prevent HIV infection.[4,5]

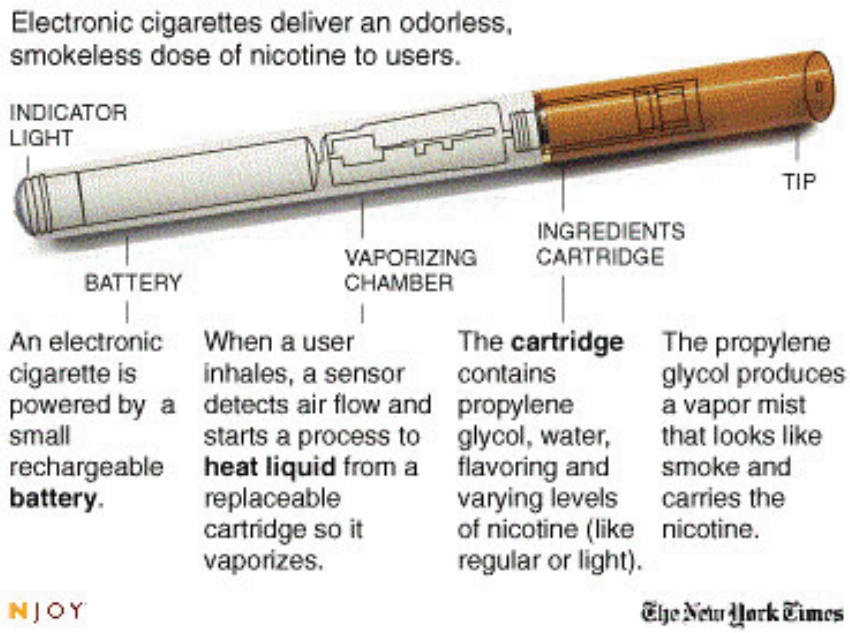
In 1976 Professor Michael Russell wrote: “People smoke for nicotine but they die from the tar.”[6] Indeed, the harm from smoking is caused almost exclusively by toxins present in tobacco released through combustion. By contrast, pure nicotine products, although addictive, are considerably less harmful. Electronic cigarettes consequently represent a safer alternative to cigarettes for smokers who are unable or unwilling to stop using nicotine.

The National Institute for Health and Clinical Excellence (NICE) is currently developing guidance on a harm reduction approach to smoking.[7] NICE’s recommendations, to be published in spring 2013, aim to inform on how best to reduce illness and deaths attributable to smoking through a harm reduction approach. As part of this guidance, NICE will include recommendations on electronic cigarettes.

What are e-cigarettes?

Electronic cigarettes, also known as electronic nicotine delivery systems (ENDS),[8] are designed to look and feel like cigarettes. They have been marketed as cheaper and healthier alternatives to cigarettes and for use in places where smoking is not permitted since they do not produce smoke.

A typical e-cigarette consists of three components: a battery, an atomiser and a cartridge containing nicotine. Most replaceable cartridges contain nicotine suspended in propylene glycol or glycerine and water. The level of nicotine in the cartridges may vary and some also contain flavourings.[9] Some e-cigarettes also have an indicator light at the end that glows when the user draws on the device to resemble a lit cigarette. When a user sucks on the device, a sensor detects air flow and heats the liquid in the cartridge so that it evaporates. The vapour delivers the nicotine to the user. There is no side-stream smoke but some nicotine vapour is released into the air as the smoker exhales.



Are e-cigarettes safe to use?

A draft review by the WHO's Tobacco Regulatory Group in 2009 notes that the extent of nicotine uptake and the safety of e-cigarettes have yet to be fully established.[8] Certainly, in the absence of thorough clinical evaluation and long term population level surveillance absolute safety of such products cannot be guaranteed. By comparison, the harm from tobacco smoking – the leading cause of preventable death in the UK – is well established.

Most of the safety concerns regarding electronic cigarettes relate to the absence of appropriate product regulation and inconsistencies in quality control. The current lack of any current authoritative oversight (although the MHRA is in the process of developing guidelines, see section on regulation) means that there is significant variability in device effectiveness, nicotine delivery and cartridge nicotine content both between and sometimes within product brands.[9] Furthermore, a recent study by the US Food and Drug Administration (FDA) has raised some safety concerns over the presence of toxins, released in low concentrations, from the vaporisation process of certain cartridges.[10] However, one study showed that after switching from tobacco to electronic cigarettes nicotine exposure was unchanged while exposure to selected toxicants was substantially reduced.[11]

There is little evidence of harmful effects from repeated exposure to propylene glycol, the chemical in which nicotine is suspended.[12,13] One study concludes that e-cigarettes have a low toxicity profile, are well tolerated, and are associated with only mild adverse effects.[14]

Is there a risk to non-users from e-cigarette vapour?

Although e-cigarettes do not produce smoke, users exhale a smoke-like vapour which consists largely of water. Any health risks of secondhand exposure to propylene glycol vapour

are likely to be limited to irritation of the throat. One study exposed animals to propylene glycol for 12 to 18 months at doses 50 to 700 times the level the animal could absorb through inhalation. Compared to animals living in normal room atmosphere, no localised or generalised irritation was found and kidney, liver, spleen and bone marrow were all found to be normal.[12]

The fact that e-cigarettes look similar to conventional cigarettes has been said to risk confusion as to their use in public places, such as on public transport.[15,16] However, given that the most distinctive feature of cigarette smoking is the smell of the smoke, which travels rapidly, and that this is absent from e-cigarette use, it is not clear how any such confusion would be sustained. Furthermore, the absence of risk from "secondhand" inhalation of vapour from e-cigarettes has been described as an "often unconsidered advantage" of e-cigarettes.[17] As an alternative to smoking, e-cigarettes are preferable in situations where secondhand smoke poses serious health risks to others, such as in vehicles or in the home.

Are e-cigarettes effective?

The degree of effectiveness depends on what effect is being measured. While public health professionals may be most concerned about their effectiveness in smoking cessation, the four benefits most widely perceived by smokers are the degree to which they satisfy the desire to smoke (60% of smokers), helping to cut down cigarettes (55%), help quit entirely (51%) and eradicating the smell of stale smoke (51%).[18,19] Effectiveness also varies between products and between users according to their experience in use.[20]

Currently in the UK, any nicotine-containing product which claims or implies that it can treat nicotine addiction is considered to be a medicinal product and is therefore subject to regulation by the MHRA. Consequently, e-cigarette manufacturers have avoided making such explicit claims. Furthermore, the WHO has stated that "the electronic cigarette is not a proven nicotine replacement therapy".[21]

Nevertheless, survey data suggests that about 4 in10[18] users do utilise them in an attempt to quit smoking and internet searches for the devices now exceed those for any other smoking cessation or nicotine replacement product.[22] There is some evidence to suggest that e-cigarette use leads to abstinence among some smokers who had not intended to quit.[23]

Empirical data on the effectiveness of e-cigarettes as a stop-smoking aid is limited and the risks and benefits are still being studied. Some reports from the published literature suggest that electronic cigarettes are inefficient nicotine delivery devices and result in only modest and unreliable increases in plasma nicotine levels.[24] Such findings appear to apply particularly to new users whereas studies using participants experienced in e-cigarette use have been found to derive more reliable nicotine intake levels.[14] Whether experienced users are able to use these devices in a way in which their nicotine intake is maximised, or the variability is down to such users preferring certain devices which might significantly differ from those used by inexperienced users, is yet to be determined.[25,26]

Nevertheless, growing evidence suggests that e-cigarettes are becoming more reliable in their nicotine delivery and that they have a beneficial impact in reducing subjective cravings and, in turn, number of cigarettes smoked.[14] Moreover, some studies have demonstrated an ability for certain brands of e-cigarettes to reduce subjective nicotine cravings despite delivering low plasma nicotine levels.[27]

Another feature of e-cigarettes that apparently lends to their effectiveness is an ability to satisfy the "hand to mouth" behavioural component that is not sufficiently addressed in more

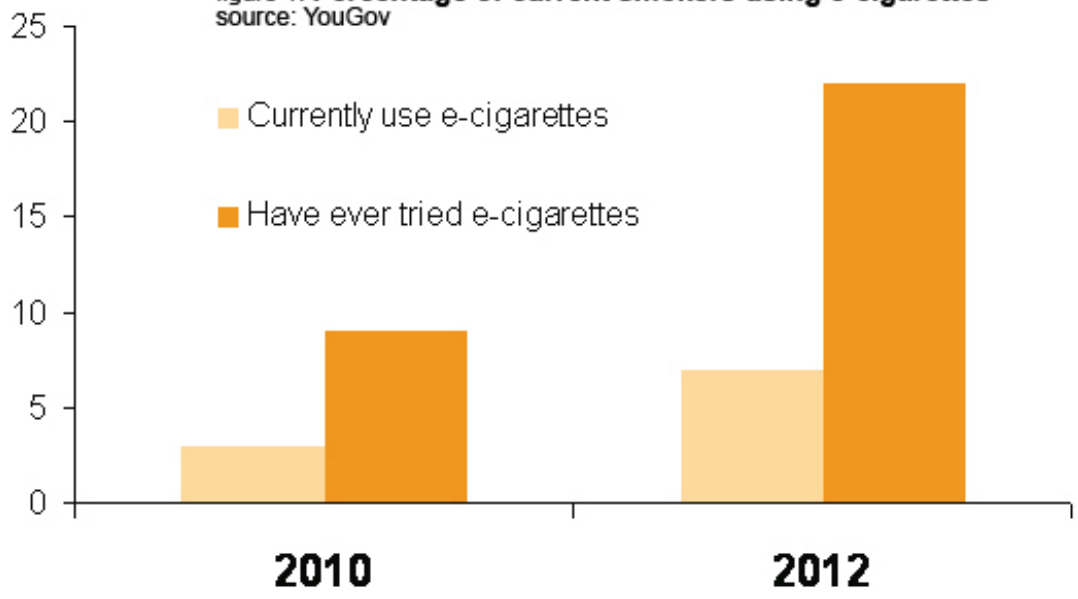
traditional nicotine replacement therapies. This has been demonstrated by users exhibiting reduced cravings, withdrawal symptoms and number of cigarettes smoked per day even when given a placebo e-cigarette.[14]

The potential value, and perceived effectiveness, of electronic cigarettes in aiding smoking cessation has been assessed in user surveys. Caution must be exercised with this data as the sample was recruited from e-cigarette users' websites. However, one such survey conducted internationally reported that 72% of users believed that e-cigarettes were beneficial in reducing cravings and withdrawal symptoms while 92% declared that the devices had reduced the number of conventional cigarettes they smoked. Indeed, in the same survey, 96% of former smokers claimed that e-cigarettes had helped them quit, and 79% reported a fear that if they stopped using them they would start smoking again.[9]

Who uses e-cigarettes in the UK?

Public awareness of e-cigarettes has grown substantially in recent years with online media playing an integral role in the growing popularity of the product. Between the years 2009 and 2011 searches via the search engine Google using the terms 'electronic cigarette' increased by fifty fold,[28] a fact the industry has attempted to capitalise on by funding various online adverts, web-pages and social networking site groups.[29] In addition to the influence of online media, there is also evidence to suggest that tighter tobacco control measures are also positively driving e-cigarette behaviour.[30]

figure 1: **Percentage of current smokers using e-cigarettes**
source: YouGov



According to an ASH YouGov survey awareness of electronic cigarettes has been increasing. For example, the percentage of smokers reporting in ASH YouGov surveys that they had never heard of e-cigarettes fell from 38% in 2010 to 21% in 2012.[31] Contemporaneous with this increased awareness has been an apparent doubling in the proportion of people reporting using the devices. According to a survey commissioned by ASH, 3% of smokers reported using e-cigarettes in 2010, a figure that increased to 7% in 2012. Similarly, the number of people reporting having tried e-cigarettes has increased significantly, more than doubling from 9% in 2010 to 22% in 2012 (see figure 1).

ASH estimates that there are 650,000 to 700,000 current users of e-cigarettes in the UK. This number is almost entirely made of current and ex-smokers; with perhaps as many as 125,000

people having replaced smoking with e-cigarette use. There is little evidence to suggest that anything more than a negligible number of non-smokers regularly use the product. [31,32]

Regulation

Currently, e-cigarettes are not regulated under smokefree law in the UK, and users are free to use them in public places such as bars, restaurants and on public transport.

An oft quoted advantage of smokefree legislation is that it de-normalises smoking, effectively distancing the behaviour from what is an accepted social norm. The ban on smoking in public places has reinforced in many people's minds that such behaviour has gone from a normal, widely accepted activity to one that is abnormal and unaccepted. There are concerns that e-cigarettes will undermine this process, threatening the now established practice of smokefree public places, such as at work or on public transport. However to date there is little evidence to suggest this is the case.

E-cigarettes are subject to general consumer protection law and it is the responsibility of trading standards officers to rule on their safety. In 2010, the Medicines and Healthcare Products Regulatory Agency (MHRA) held a public consultation on whether products containing nicotine such as e-cigarettes should be regulated.[33] Following this initial analysis a period of further research was commissioned, coordinated by the MHRA, and informed upon by an expert working group of the Commission on Human Medicines (CHM). This additional research will lead to a final decision being made in 2013. In the interim, the MHRA is working with e-cigarette manufacturers to develop a self-regulatory code of practice to foster high standards within the industry.

As well as the MHRA review, and following a referral from the Department of Health, NICE will publish its own guidance on e-cigarettes as part of a broader consultation on tobacco harm reduction, the results of which are expected to be published in May 2013. There is also a proposal to regulate nicotine- containing products as part of the revised EU Tobacco Products Directive.[34]

Conclusion

ASH believes that e-cigarettes, properly regulated to ensure safety and efficacy, should be made available as part of a harm reduction approach to tobacco. That is, we recognise that whilst efforts to help people stop smoking should remain a priority, many people either do not wish to stop smoking or find it very hard to do so. For this group, nicotine substitution products should be made available that deliver nicotine in a safe way, without the harmful components found in tobacco smoke. Most of the diseases associated with smoking are caused by inhaling smoke which contains thousands of toxic chemicals. By contrast, nicotine is relatively safe.

E-cigarettes, which deliver nicotine without the harmful toxins found in tobacco smoke, are likely to be a safer alternative to smoking. In addition, e-cigarettes reduce secondhand smoke exposure in places where smoking is allowed since they do not produce smoke. Nonetheless, nicotine is an addictive substance, e-cigarettes currently available are of highly variable safety and efficacy, and smokers are uncertain about the effectiveness of the product.

In the UK smokefree legislation exists to protect the public from the demonstrable harms of secondhand smoke. ASH does not consider it appropriate for electronic cigarettes to be subject to this legislation.

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NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

PUBLIC HEALTH DRAFT GUIDANCE

Tobacco: harm-reduction approaches to smoking

Introduction: scope and purpose of this draft guidance

What is this guidance about?

This guidance aims to reduce the illnesses and deaths caused by smoking tobacco among people who smoke and those around them. People who smoke can do this by:

- stopping smoking
- cutting down prior to quitting smoking
- smoking less
- abstaining from smoking temporarily.

These changes might involve substituting the nicotine in tobacco with nicotine from less harmful, **nicotine-containing products**. These include nicotine replacement therapy (NRT) products that are licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) as pharmaceutical treatments for smoking. They also include unregulated products such as 'electronic cigarettes'[1]. Nicotine-containing products might be used either temporarily or indefinitely and as a partial or complete **substitute for tobacco**.

The use of products containing tobacco as a means of 'harm reduction' is outside the scope of this guidance. This means that 'reduced exposure cigarettes' and 'smokeless tobacco' are excluded.

This guidance does not cover pregnant women and maternity services.

[1] These products may come under MHRA regulation in the future – an MHRA decision was pending when this draft guidance was finalised.

The recommendations cover:

- raising awareness of nicotine-containing products to reduce the harm from smoking
- self–help support
- people who want to quit smoking in one step
- people who are not prepared to quit smoking in one step
- behavioural support
- carbon monoxide breath testing
- prescribing NRT for harm reduction
- advising on the use of nicotine-containing products
- follow-up appointments
- temporary abstinence
- people living in closed institutions
- staff working in closed institutions
- commissioning stop smoking services
- education and training for practitioners
- **point-of-sale** promotion of licensed nicotine-containing products
- information on licensed nicotine-containing products.

For related NICE guidance that may be of relevance to tobacco harm reduction, see section 7.

Who is this guidance for?

The guidance is for: commissioners, managers and practitioners with public health as part of their remit. It is especially aimed at those involved in smoking cessation services within the NHS, local authorities and the wider public, private, voluntary and community sectors. The guidance may also be of interest to members of the public, especially people who want to stop or cut down the amount they smoke.

Why is this guidance being produced?

The Department of Health (DH) asked the National Institute for Health and Clinical Excellence (NICE) to produce this guidance.

The guidance should be implemented alongside other guidance and regulations (for more details see sections 4 and 7 on implementation and related NICE guidance respectively).

How was this guidance developed?

The recommendations are based on the best available evidence. They were developed by the Programme Development Group (PDG).

Members of the PDG are listed in appendix A.

The guidance was developed using the NICE public health programme process. See appendix B for details.

Supporting documents used to prepare this document are listed in appendix E.

What evidence is the guidance based on?

The evidence that the PDG considered included: reviews of the evidence, economic modelling and the testimony of expert witnesses. Further detail on the evidence is given in the considerations (section 3) and appendices B and C.

In some cases the evidence was insufficient and the PDG has made recommendations for future research.

More details of the evidence on which this guidance is based, and NICE's processes for developing public health guidance, are on the NICE website.

Status of this guidance

This is **draft** guidance.

This document does not include all sections that will appear in the final guidance. NICE is now inviting comments from stakeholders (listed on our website).

Note that this document is not NICE's formal guidance on tobacco harm reduction. The recommendations made in section 1 are provisional and may change after consultation with stakeholders.

The stages NICE will follow after consultation are summarised below.

- The Group will meet again to consider the comments, reports and any additional evidence that has been submitted.
- After that meeting, the Group will produce a second draft of the guidance.
- The draft guidance will be signed off by the NICE Guidance Executive.

For further details, see 'The NICE public health guidance development process: An overview for stakeholders including public health practitioners, policy makers and the public (second edition, 2009)'.

The key dates are:

Closing date for comments: 19 December 2012.

Next PDG meeting: 5–6 February 2013.

Contents

1 Draft recommendations

The evidence statements underpinning the recommendations are listed in appendix C.

The Programme Development Group (PDG) considers that the recommended approaches are cost effective.

For the research recommendations and gaps in research, see section 5 and appendix D respectively.

Context

Quitting smoking is the best way to improve the health of someone who smokes. **Quitting in one step** offers the best chance of being successful and is the least costly method. Investment in approaches to reduce the harm caused by tobacco should not detract from the provision of existing **stop smoking services,** which provide highly cost-effective interventions to help people quit in one step. Rather, the recommendations in this guidance are intended to support and extend the reach and impact of existing services.

Some people, particularly those who are highly dependent on smoking, may not be able (or do not want) to quit smoking in one step. Or they may not want to quit at all. Harm reduction approaches provide an alternative (see box 1).

Harm-reduction methods

Methods such as **cutting down to quit** may appeal to people who do not want to quit in one step. **Smoking less** is an option for those who are not currently interested in quitting smoking, although the health benefits are not clear. However, for some, this can be the start of a gradual change in behaviour that eventually leads them to quit smoking.

These strategies are also relevant to people who need to be abstinent, for example, because they are confined in an environment where smoking is prohibited, such as a prison or secure mental health unit.

In summary, offering a harm-reduction option may ultimately increase the number of people who quit smoking and can help reduce the harm to smokers and those around them.

Using nicotine without tobacco

A number of manufactured products contain nicotine without tobacco. Some are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) to ensure they are effective, deliver nicotine safely and are manufactured to a consistent quality standard.

Nicotine replacement therapy (NRT) products are licensed by the MHRA (that is, they have 'marketing authorisation') for use as a smoking cessation aid and for tobacco harm-reduction.

There is much less evidence on the effectiveness, **safety** and **quality** of other **nicotine-containing products,** such as electronic cigarettes, topical gels, and other products in development. However, these products may come under MHRA regulation in the future. (A decision from the MHRA on the regulation of such products was pending when this draft guidance was published.)

The recommendations use the phrase **licensed nicotine-containing products** to cover NRT products as well as other nicotine-containing products that might be licensed by the MHRA in the future.

Current evidence relates to NRT products. However, the process by which a drug is absorbed, distributed, metabolised and eliminated by the body suggests that other nicotine-containing products could be as effective, if they deliver a similar amount of nicotine. This includes, for example, electronic cigarettes.

Box 1 Harm reduction approaches to tobacco control

Harm reduction involves continued use of tobacco or nicotine, while reducing the harm caused by tobacco to the smoker and others. The options addressed in this guidance are:

- Quit smoking in one step with the help of 1 or more licensed nicotine-containing products and continue to use these products as a substitute for tobacco, possibly indefinitely.
- Cut down prior to quitting, by smoking fewer cigarettes or inhaling or smoking less of each cigarette, with or without the help of 1 or more licensed nicotine-containing products.
- Smoke less, by smoking fewer cigarettes, inhaling less or smoking less of each cigarette, with or without the help of 1 or more licensed nicotine-containing products.
- Temporarily abstain with or without the help of 1 or more licensed nicotine-containing products. This could be for a specific occasion (for example, while in hospital), for regular events (for example, when at work or in the home), or while confined in an environment where smoking is prohibited (for example, in a prison or secure mental health facility).

Recommendation 1 Raising awareness of nicotine-containing products to reduce the harm from smoking

Who should take action?

- National, regional and local organisations responsible for public health and tackling tobacco use. This includes:
  - professional bodies such as the British Medical Association and the royal medical and nursing colleges
  - regional tobacco control organisations
  - stop smoking services

  - statutory agencies, such as health and wellbeing boards, local authorities and their directors of public health
  - voluntary and community sector organisations.

What action should they take?

- Raise awareness among the public of the harm caused by smoking and secondhand smoke. Provide information on how people who smoke can reduce the risk of illness and death (to themselves and others) by using another source of nicotine, such as a licensed nicotine-containing product.

- Provide information in a range of formats and languages for different target groups.

- Ensure the information includes the following facts:
  - smoking causes a range of diseases and conditions including cancer, chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD)
  - most health problems are almost entirely caused by other components in cigarettes, not by the nicotine
  - smoking is highly addictive because it delivers nicotine very quickly to the brain and this makes quitting smoking difficult
  - nicotine replacement therapy (NRT) products are an effective way of reducing the harm from cigarettes
  - there are no circumstances when it is safer to smoke than to use NRT products and experts believe that lifetime use of NRT will be considerably less harmful than smoking
  - NRT products have been demonstrated to be safe to use for up to 5 years
  - little is known about the effectiveness, quality and safety of unregulated nicotine-containing products (such as electronic cigarettes) however, they are likely to be less harmful than cigarettes.

- Provide information on licensed nicotine-containing products:

  - what form they take
  - how to use them effectively when trying to quit or smoke less (either as a partial or complete substitute for smoking)
  - where to obtain them (including from GPs)
  - the cost compared with smoking.

Recommendation 2 Self-help support

Who should take action?

- National, regional and local organisations responsible for public health and tackling tobacco use. This includes:
  - professional bodies such as the British Medical Association and the royal medical and nursing colleges
  - regional tobacco control organisations
  - stop smoking services
  - statutory agencies, such as health and wellbeing boards, local authorities and their directors of public health
  - voluntary and community sector organisations.
- Organisations providing practitioners with training in reducing the harm caused by smoking, such as the National Centre for Smoking Cessation and Training (NCSCT).
- Telephone helplines and Internet support sites aimed at helping people to quit smoking.
- Manufacturers of licensed nicotine-containing products.
- Retailers.
- Social media websites.

What action should they take?

- Provide **self-help materials** in a range of formats and languages to meet the needs of different groups. People should be advised to:

  - try to stop smoking cigarettes altogether, either by quitting in one step or by cutting down first
  - smoke less, if they do not want to quit.

- Self-help materials should also include information on:
  - the benefits of using licensed nicotine-containing products
  - the type of products available
  - how to use them effectively to manage the cravings, mood swings and other effects of nicotine dependency
  - how to develop a schedule to cut down and gradually quit or smoke less (see recommendation 5)
  - where to obtain licensed nicotine-containing products, including from their GP
  - where to get further help and support.

Recommendation 3 People who want to quit smoking in one step

Who should take action?

- Frontline health and social care practitioners, in particular those working in:
  - primary and secondary healthcare (including GPs, practice nurses, pharmacists and health trainers)
  - residential and domiciliary care.

- Telephone helplines and Internet support sites aimed at helping people to quit smoking.

What action should they take?

- Identify people who smoke and advise them to quit smoking in one step as the best option[2].

[2] These actions are in line with NICE guidance on brief interventions and referral for smoking cessation, smoking cessation services and quitting smoking in pregnancy following childbirth, the DH's Stop smoking service delivery and monitoring guidance 2011/12 and the NICE menu of indicators.

- Offer support for quitting smoking in one step by[3]:
    - recommending **pharmacotherapy** and if able, offering to supply or prescribe it
    - either providing advice, discussion and targeted activities in a one-to-one or group session
    - or offering a referral to a stop smoking service for **pharmacotherapies** and more intensive **behavioural support**.

- Advise them that it may be possible to continue using licensed nicotine-containing products for as long as they need after they have stopped smoking.

- If someone declines the offer of support to quit smoking in one step, ask them if they would like to consider other options (see recommendation 4).

Recommendation 4 People who are not prepared to quit smoking in one step

Who should take action?

- Stop smoking advisers.

- Frontline health and social care practitioners, in particular those working in:
    - primary and secondary healthcare (including GPs, practice nurses, pharmacists and health trainers)
    - residential and domiciliary care.

- Telephone helplines and Internet support sites aimed at helping people to quit smoking.

[3] These actions are in line with NICE guidance on brief interventions and referral for smoking cessation, smoking cessation services and quitting smoking in pregnancy following childbirth, the DH's Stop smoking service delivery and monitoring guidance 2011/12 and the NICE menu of indicators.

What action should they take?

- Help people to identify why they smoke, the triggers for smoking and their smoking behaviour. Use this information to work through the harm-reduction options outlined in box 1.

- Use professional judgement to suggest which option(s) might be most suitable, based on the person's smoking behaviour, any quit attempt history and their health and social circumstances. Briefly discuss the merits of each option to help them choose.

- Ensure people know that it is easier to cut down to quit, or to smoke less, when using licensed nicotine-containing products (such as nicotine patches, gum, or spray). Tell them that their chances of success are greater when using such products.

- Recommend 1 or more NRT products to help them cut down to quit or smoke less. If possible, prescribe them or encourage people to ask their GP to do so (see recommendation 7).

- Advise that it may be possible to continue using licensed nicotine-containing products for as long as they need after they have stopped, or reduced, their smoking.

- If more intensive support is required, offer a referral to stop smoking services. These services provide pharmacotherapies and more comprehensive support and advice about harm reduction and quitting smoking in the longer term (see recommendations 5–8).

Recommendation 5 Behavioural support for harm reduction

Who should take action?

- Stop smoking advisers.

- Frontline health and social care practitioners who are trained to provide **behavioural support** to help people who smoke to quit.

- Telephone helplines and Internet support sites aimed at helping people to quit smoking.

What action should they take?

- Find out about the person's smoking behaviour and level of dependence by asking how many cigarettes they smoke – and how soon after waking. (See the 'Heaviness of smoking index' [HSI][4] a subset of 2 questions from the Fagerström test for nicotine dependence [FTND]. FTND is available in the Department of Health's Stop smoking service delivery and monitoring guidance 2011/12.)

- Use this information to help people set goals and discuss reduction strategies. This may include increasing the time interval between cigarettes, delaying the first cigarette of the day or choosing points during the day, or specific occasions, when they will not smoke.

- Help them develop a schedule that starts with the strategies they think they can most easily achieve. (See NICE guidance on behaviour change.)

- Help people who are cutting down to quit to set a specific quit date. Help them develop a schedule detailing how much they aim to cut down (and when) in the lead-up to that date. A quit date should normally be within 6 weeks from the start of receiving structured support.

- Help people who are aiming to smoke less (but not currently intending to quit smoking) to set a date when they will have achieved their reduction goal. Help them develop a schedule for this. Or identify specific times and events when they will not smoke.

- Where necessary, advise people how to use licensed nicotine-containing products effectively.

[4] Heatherton TF, Kozlowski LT, Frecker RC et al. (1989) Measuring the heaviness of smoking: using self-reported time to the first cigarette of the day and number of cigarettes smoked per day. British Journal of Addiction 84 (7): 791–9

- Follow them up to see whether they have achieved their goal/s. If those who set out to smoke less have been successful, assess their motivation to maintain that level, to further reduce the amount smoked or to quit smoking.

Recommendation 6 Carbon monoxide breath testing

Who should take action?

- Stop smoking advisers.
- Frontline health and social care practitioners, in particular those working in primary and secondary healthcare (including GPs, practice nurses, pharmacists and health trainers).

What action should they take?

- Use carbon monoxide (CO) breath testing to establish a baseline before someone starts to smoke less (whether they are intending to quit smoking or not). Conduct further tests to monitor progress. Provide positive feedback at appropriate intervals.
- Ensure staff carrying out carbon monoxide breath testing have been trained to do it correctly. Ensure they are able to interpret the results for people who are aiming to smoke less, as well as for people who are cutting down to quit.

Recommendation 7 Prescribing NRT for harm reduction

Who should take action?

- Stop smoking advisers.
- GPs and nurse prescribers.

What action should they take?

- Offer NRT products to people who smoke, as part of a harm-reduction strategy. All types of NRT should be on offer, either singly or in

combination, according to their preference and level of dependence. (For example, patches could be offered with gum or lozenges.)

- Advise people to replace each cigarette with an NRT product, for example, a lozenge or piece of gum. Ideally they should use this before the usual time they would have had the cigarette, to allow for the slower nicotine release from NRT products.

- Offer NRT products, as necessary, to help prevent a relapse among people who have quit smoking (whether in one step or by cutting down to quit) and those who have reduced the amount they smoke.

Recommendation 8 Advising on the use of nicotine-containing products

Who should take action?

- Stop smoking advisers.

- Frontline health and social care practitioners, in particular those working in:
  - primary and secondary healthcare (including GPs, practice nurses, pharmacists and health trainers)
  - local authorities
  - residential and domiciliary care.

- Telephone helplines and Internet support sites aimed at helping people to quit smoking.

What action should they take?

- Reassure people who smoke that licensed nicotine-containing products, are a safe and effective way of reducing the harm from cigarettes. Tell them that NRT products have been demonstrated to be safe to use for up to 5 years. Also tell them that experts believe that lifetime use of NRT will be considerably less harmful than smoking.

- Tell them they can use 1 product on its own or a combination of several different ones. Tell them that using more than 1 product is more likely to be successful, particularly for more dependent smokers. (For example, patches could be offered with gum, lozenges or a spray.)

- Reassure them that it is better to smoke less and use 1 or more of these products than to continue smoking at their current level. Give advice on how to use licensed nicotine-containing products correctly. This includes ensuring they use a sufficiently high dose to control cravings, prevent compensatory smoking and achieve quit, reduction or **temporary abstinence** goals.

- Advise people that licensed nicotine-containing products can be used for as long as they help reduce the desire to smoke – and indefinitely, if necessary.

- Tell people that some nicotine-containing products (for example, electronic cigarettes) are currently not regulated by the MHRA and therefore their safety and quality cannot be assured. However, tell them that these products are likely to be less harmful than cigarettes.

Recommendation 9 Follow-up appointments

Who should take action?

- Stop smoking advisers.

- Frontline health and social care practitioners who are trained to provide behavioural support to help people who smoke quit.

What action should they take?

- Offer follow-up appointments to review the progress of people who have adopted a harm-reduction approach to smoking.

- Encourage people who have not achieved or maintained their quit or smoking reduction goals to try again. Discuss whether they wish to change

their goals. Also discuss whether they would like to continue using the same licensed nicotine-containing product or would like to try a different one (or a different combination of products).

Recommendation 10 Temporary abstinence

Who should take action?

- Stop smoking advisers.
- Frontline health and social care practitioners who are trained to provide behavioural support to help people who smoke to quit.
- Telephone helplines and Internet support sites that help people to quit smoking.

What action should they take?

- Provide people who want (or need) to abstain temporarily on a short-, medium- or longer-term basis[5] with information about the different types of licensed nicotine-containing products and how to use them. Where possible, prescribe NRT (see recommendations 7 and 8).
- Provide people who want (or need) to abstain temporarily with behavioural support. This could include providing information on why it is important to reduce the harm caused by smoking and advice on how to do this via one-to-one or group sessions.
- For people who have successfully abstained from smoking on a temporary basis, assess their motivation to abstain again on other occasions (or for longer periods), smoke less or quit smoking (see recommendations 5–8).

For more recommendations for hospitals see NICE guidance on smoking cessation – acute and maternity services and smoking cessation – mental

[5] Short-term abstinence may involve taking fewer smoking breaks while at work. Medium-term abstinence may occur when admitted to hospital. Long-term abstinence might occur during a custodial sentence.

health services. See also hospitals and providers of long-term care in NICE's 'Smoking pathway'.

Recommendation 11 People living in closed institutions

Who should take action?

- Managers of services where smoking is not permitted, such as secure mental health units and custodial sites such as prisons and police stations.

What action should they take?

- Ensure those giving harm-reduction advice in situations where smoking is not permitted are trained to the same standard as NHS stop smoking advisers[6]. This includes people working in mental health and prison health services.

- Ensure staff recognise that smoking is an integral part of some people's lives and can, for example, be an aid to making friends and socialising. Also ensure staff recognise the issues arising from enforced smoking cessation, as opposed to voluntarily quitting.

- Ensure staff recognise how the environment may restrict the quitting techniques and coping mechanisms that people would normally use.

- Provide the support required for successful temporary abstinence from smoking (see recommendations 5–8). This includes prescribing or supplying NRT products.

- Ensure staff understand that, if someone reduces the amount they smoke (or quits completely), this can impact on their need for psychotropic medication. Ensure arrangements are in place to adjust their medication accordingly.

For other recommendations for mental health services see NICE guidance on smoking cessation – mental health services.

[6] The minimum standards for training are set by the National Centre for Smoking Cessation and Training (NCSCT).

Recommendation 12 Staff working in closed institutions

Who should take action?

- Managers of services where smoking is not permitted, such as secure mental health units and custodial sites such as prisons and police stations.
- Workplace managers (except where the premises are not enclosed).

What action should they take?

- Provide staff who smoke with advice and guidance on how to quit smoking in one step (see recommendation 3). If, after discussion, the person does not want (or does not feel able) to do this, ask them if they would like to consider a harm-reduction option, as outlined in box 1.
- Encourage staff to use stop smoking services to quit or reduce the amount they smoke.
- Encourage staff who do not want to quit smoking to use licensed nicotine-containing products to help them abstain immediately before and while on duty.
- Enforce temporary abstinence from smoking for the full period of duty for staff who have health and social care responsibilities in settings where people are not allowed to smoke.

Recommendation 13 Commissioning stop smoking services

Who should take action?

Commissioners of stop smoking services including:

- health and wellbeing boards, local authorities and their directors of public health
- clinical commissioning groups
- the NHS Commissioning Board.

What action should they take?

- Ensure investment in harm-reduction approaches to smoking does not detract from, but supports and extends the reach and impact of, existing **stop smoking services.** (The latter provide highly cost-effective interventions to help people quit smoking in one step.)

- Develop smoking cessation referral and treatment pathways to ensure a range of options and interventions are available to support people who wish to choose a harm-reduction approach (see box 1).

- Ensure the providers of stop smoking and other behaviour change services offer people who smoke the harm-reduction options outlined in box 1.

- Ensure services are available in the community, as part of primary and secondary healthcare and on offer from local authorities.

- Develop activity and outcome measures to help manage the performance of service providers that support people who want to cut down on their smoking before quitting, or who want to smoke less. These outcome measures could include:
    - specific indicators for particular target groups, for example, a 12-week as well as a 4-week quit rate for people setting a quit date
    - setting a quit date within 6 months of someone seeking help
    - having a 12-month post-quit date follow-up
    - a 50% reduction in cigarettes smoked within 6 weeks, for people who want to smoke less.

- Ensure service specifications include a requirement that providers of stop smoking services offer licensed nicotine-containing products on a long-term basis to help people maintain a quit attempt, or a reduced level of smoking.

- Ensure service specifications include a requirement that staff working in stop smoking services are trained to National Centre for Smoking Cessation and Training level 2, or the equivalent.

- Monitor service delivery and uptake to identify the points of contact when and where longer-term use of licensed nicotine-containing products is offered and its outcomes. Use this information to inform future commissioning.

Recommendation 14 Education and training for practitioners

Who should take action?

- Health Education England.
- Organisations providing training on the harm caused by smoking, such as the National Centre for Smoking Cessation and Training.
- Royal medical and nursing colleges, other professional bodies and universities.
- Commissioners, providers and managers of stop smoking services including health and wellbeing boards, local authorities and their directors of public health.

What action should they take?

- Include the principles and practice of tobacco harm reduction, as outlined in this guidance, within all relevant curricula.
- Ensure service specifications and service-level agreements state that staff are trained to National Centre for Smoking Cessation and Training level 2 (or the equivalent) and undertake regular continuing professional development. The aim is to ensure they are qualified to help people quit or cut down on their smoking.

Recommendation 15 Point-of-sale promotion of licensed nicotine-containing products

Who should take action?

- Tobacco retailers.

- Manufacturers of licensed nicotine-containing products.

What action should they take?

- Encourage people who smoke to consider the harm-reduction options outlined in box 1.
- Display licensed nicotine-containing products in shops and supermarkets, and on websites selling cigarettes and tobacco products.
- Ensure products are clearly priced.

Recommendation 16 Information on licensed nicotine-containing products

Who should take action?

Manufacturers of licensed nicotine-containing products.

What action should they take?

- Provide simple, clear instructions on how to use licensed nicotine-containing products to support the harm-reduction options outlined in box 1.
- Consider providing information on the outside packaging as well as on the inner leaflet.
- Package products in a way that makes it as easy as possible for people to take the recommended dose.
- Provide safety information, including details on long-term use.

2 Public health need and practice

Introduction

Tobacco smoking remains the single greatest cause of preventable illness and early death in England, accounting for 79,100 deaths among adults aged 35 and over in 2011 (NHS Information Centre 2012). Secondhand smoke causes an estimated 11,000 deaths a year in the UK from lung cancer, stroke and ischaemic heart disease (Jamrozik 2005).

Treating smoking-related illnesses cost the NHS in England an estimated £2.7 billion in 2006/07 (Callum et al. 2010). The overall financial burden to society has been estimated at £13.74 billion a year. This includes both NHS costs and loss of productivity due to illness and early death (Nash and Featherstone 2010).

Although smoking prevalence has declined sharply in the last 30 years, that decline now seems to be levelling off. In 2010, 1 in 5 adults in England (20%) smoked cigarettes, with prevalence highest among those aged 20–24 and 25–34 (28% and 26% respectively) (NHS Information Centre 2012).

People from routine and manual occupational backgrounds are almost twice as likely to smoke as those from managerial or professional backgrounds (27% versus 13%) (NHS Information Centre 2012). Smoking is responsible for at least half of the excess risk of premature death faced by middle-aged men in manual occupations, compared to those in professional groups (Jha et al. 2006).

Children and young people

Exposure to secondhand smoke in the home affects an estimated 5 million children under the age of 16 (British Medical Association 2007). Children's vulnerability to tobacco smoke has been well documented. A recent UK report estimated that passive smoking caused 22,600 new cases of wheeze and asthma, 121,400 new cases of middle ear infection and 40 sudden infant deaths (Royal College of Physicians 2010).

The health of babies born into lower income households is disproportionately affected by secondhand smoke. In addition, as they are growing up in an environment where smoking is the norm, they are more likely to start smoking in adolescence (British Medical Association 2007; Royal College of Physicians 2010).

Legislation requiring all large shops and supermarkets to remove cigarette displays at the point-of-sale came into force in April 2012. The aim is to reduce the impact of tobacco marketing on children and young people and so reduce the likelihood of them taking up smoking. Newsagents and small stores will be able to display cigarettes until 2015.

Quitting smoking

About 2 thirds (67%) of people who smoke say they would like to quit and 3 quarters (75%) of them say they have tried to stop in the past. In 2008, about a quarter (26%) had tried in the past year (Lader 2009). Most people attempt to quit without help. But only around 4% who quit without using behavioural or pharmacological therapy are successful for a year or longer (Hughes et al. 2004). This compares to about 15% of those who quit using the NHS Stop Smoking Service (Ferguson et al. 2005).

People often try many times to give up smoking before they eventually succeed. People who have recently tried and failed to quit are more likely to try again – but they are also more likely to relapse than those who have not tried to quit recently. Relapse is associated with:

- nicotine dependence
- exposure to smoking cues
- craving
- withdrawal symptoms
- lack of help to stop (the latter could include medication, behavioural support or support from family and friends)

(Zhou et al. 2009).

Reducing cigarette consumption

In 2009, 57% of smokers in England reported that they would find it difficult to go without smoking for a day. People in routine and manual occupational groups were more likely to say they would find this difficult than those in managerial and professional occupations (61% and 50% respectively). This difference was less in people who smoked 20 or more a day (83% and 78%) (NHS Information Centre 2011).

People from routine and manual groups are more likely to cut down first, rather than quit 'abruptly' (Siahpush et al. 2010). They inhale more nicotine from cigarettes and are more dependent than more affluent people. To take in more nicotine they inhale more deeply and smoke more of the cigarette which increases their exposure to the other toxins in tobacco smoke and, thus increases their risk of smoking-related disease. As people on a low income take in more nicotine they are likely to find it harder to quit and so may need additional support (Jarvis 2010).

The harm associated with cigarette smoking is almost entirely caused by the toxins and carcinogens found in tobacco smoke – not the nicotine (Royal College of Physicians 2007). Nicotine is the main addictive chemical that makes it difficult to quit smoking.

Medicinal products containing nicotine which aim to help people cut down, temporarily abstain or reduce the harm caused by smoking have been given marketing authorisation by the UK's Medicines and Healthcare Products Regulatory Agency (MHRA). These products are known as nicotine replacement therapy (NRT). A number of other, non-tobacco-based nicotine-containing products, including electronic cigarettes, are currently being considered by the MHRA. The results will be announced in Spring 2013. For further information, visit the MHRA website.

3 Considerations

The Programme Development Group (PDG) took account of a number of factors and issues when developing the recommendations.

Harm-reduction approaches

3.1 Stopping smoking leads to considerable health benefits – for smokers and those around them. These include: a reduction in the incidence and severity of chronic smoking-related conditions such as cardiovascular and peripheral vascular disease, stroke, certain cancers, chronic obstructive pulmonary disease and asthma. In addition, the need for medications (for example, neuroleptics, bronchodilators and antibiotics) is reduced, leading to subsequent cost savings (see NICE guidance on smoking cessation – acute and maternity services and smoking cessation – mental health services]. Using licensed nicotine-containing products as a substitute for cigarettes leads to the same benefits.

3.2 Harm-reduction strategies can be applied at both the individual and the population level. The PDG aimed to cover both. However it recognised that wider strategies not included here have a contribution to make. These include: regulation (for example, to restrict where smoking can take place); community-led strategies (such as making it the norm not to smoke); and pricing (so people quit or reduce the amount they smoke because it becomes too expensive).

3.3 People may temporarily abstain from smoking for a variety of reasons. It could be due to compliance with legislation banning smoking in the workplace and work vehicles, in public places and on public transport. For people in closed institutions, such as secure mental health units and prisons, temporary abstinence may be imposed for lengthy periods, even years. Some smokers temporarily abstain as a way of protecting the health of those

around them – and reducing the harm to themselves. Sometimes people use it as a way of working towards quitting smoking.

3.4 Most smokers adopt harm-reduction strategies on their own. However, the PDG considered that some people may benefit from advice about the different strategies and support available. The Group noted that providing this advice is an opportunity to start people thinking about longer-term harm-reduction strategies or quitting smoking altogether.

Stop smoking services

3.5 The PDG considered forthcoming changes to the commissioning of stop smoking services, as they move under local authority control. The Group noted that these services may require rebranding if they include harm-reduction strategies.

3.6 The PDG was aware that stop smoking services would need service provision guidance on the range of support to offer people trying to quit smoking, but who are unable (or unwilling) to give up nicotine. For example, decisions would be needed on:

- the length of time clients would be able to use the service
- how long nicotine replacement therapy (NRT) products could be prescribed – and paid for – from public funds
- the type of target-setting or performance measures that would be appropriate for harm-reduction strategies
- the way people who want to smoke less are supported.

3.7 Tariff-based funding of stop smoking services is a potential barrier to offering people harm-reduction options, as it is based on the number of people quitting smoking within a set time period.

3.8 People in closed institutions, such as prisons and secure mental health units, may experience enforced abstinence from smoking. The PDG made recommendations for the managers and staff

involved. They include offering to refer people to stop smoking services or having stop smoking services on-site. The recommendations also address the smoking behaviour of staff and carers in these settings. The PDG was mindful that advice on using NRT to help deal with enforced temporary abstinence may also help smokers in police custody.

NRT and other nicotine-containing products

3.9 Evidence is available from studies with up to 5 years follow-up which suggests that 'pure' nicotine, in the form available in NRT products, does not pose a significant health risk. This is the case whether it is used as a substitute for, or in combination with, cigarettes. Although there is a lack of data on using NRT products beyond 5 years, expert opinion is that lifetime use will be considerably less harmful than smoking.

3.10 Alternative nicotine devices, such as electronic cigarettes, are not currently regulated by the Medicines and Healthcare products Regulatory Agency (MHRA), although a decision is imminent. The guidance recommends the need for consistent information about their safety so people can make informed choices.

3.11 The PDG recognised that electronic cigarettes and similar products could be marketed in a way that ultimately promotes smoking.

3.12 The PDG was concerned that people might be put off by the cost of some nicotine-containing products. Of even more concern was the lower price of illicit tobacco. Some people may be at risk of a relapse after their prescriptions for NRT run out if they find cigarettes are cheaper.

3.13 In making a recommendation about NRT use, the PDG weighed the cost of prescriptions and health professionals' time against the risk of people not using it. The Group noted that prescribing NRT gave health professionals an opportunity for renewed contact with

people who smoke. This, in turn, could be used to support smokers' efforts to change their behaviour.

3.14 In practice, people trying to quit smoking often do not receive enough support and do not use sufficient NRT (or use it appropriately). This may also be a problem for people who are cutting down to quit or are reducing the amount they smoke.

3.15 The technology of nicotine delivery systems is likely to develop further in the near future. The PDG identified the need for ongoing evaluations of the efficacy and safety of both new nicotine-containing products and the delivery systems used.

3.16 Electronic cigarettes are becoming increasingly popular. As a result, the PDG advised that this guidance should be considered for a rapid update if electronic cigarettes become regulated by the MHRA.

Limitations of the evidence

3.17 There is a lack of (and limited) evidence on the effectiveness of harm-reduction strategies to tackle smoking (including evidence on any unintended consequences).

3.18 Most of the evidence came from clinical trials. There were few robust studies evaluating the impact of population-level harm-reduction strategies.

3.19 The PDG was aware of several costs and benefits that could result from quitting or reducing smoking. However, these are difficult to capture or quantify. They include: improved physical and mental wellbeing, improved productivity, and reduced harm to non-smokers through a reduction in their exposure to smoke. For those who are ill, stopping or reducing smoking can mean they have more time to participate in therapeutic activities.

3.20 The long-term health benefits of smoking less are uncertain.

3.21 There is mixed evidence on the effectiveness of behavioural support to support a harm-reduction approach (see recommendation 5). A range of interventions have been evaluated including brief advice, cognitive behavioural therapy, counselling and motivational interviewing. A limited number of studies evaluated interventions where the primary outcome was to help people cut down to quit smoking (mainly cognitive behavioural therapy and counselling). These studies showed a positive effect. There were more studies evaluating interventions where the primary outcome was smoking reduction (mainly motivational interviewing and counselling). The majority of these studies found no effect. The PDG therefore exercised caution when making recommendations about behavioural interventions.

3.22 Two cross-cutting themes were identified as a priority for future research: surveillance studies of harm-reduction strategies and the impact of these strategies on different subpopulations (see section 5).

Economics

3.23 An economic model was developed to assess a wide range of potential harm-reduction approaches. In general, the PDG noted that all 21 interventions in the model (apart from temporary abstinence with no support) were highly cost effective, compared with ‘no intervention’. This included 3 that were cost saving.

3.24 Many smokers may choose to substitute smoking with NCPs (for example, NRT gum) and may continue to use these products for very long periods of time. A 2-way sensitivity analysis was used to vary the effectiveness and duration of use of an NCP. The PDG noted that only when the NCP is provided for more than 5 or 10 years, and the quit rate is less than 6%, do the costs (to the NHS)

potentially outweigh the benefits. A supplementary analysis assumed there were no benefits from smoking less (in terms of QALYs and co-morbidities), other than an increased likelihood of quitting at 6 months. This showed that the costs potentially outweigh the benefits, when the reduction rate is 6% or less and someone uses licensed nicotine-containing products for 12 months or longer. When a reduction of 20% or more is achieved, the cost of extending NCP use to 2 years may be outweighed by the benefits.

3.25 People who use NRT to help quit smoking are more likely to use it again should they fail and try again. Modelling the cost effectiveness of using NRT for a single quit attempt, or treating subsequent quit attempts as independent may, therefore, underestimate its cost effectiveness.

3.26 When the impact of secondhand smoke was included in the model, the cost per quality-adjusted life year (QALY) was reduced for all the interventions modelled. The PDG noted that the other potential benefits associated with tobacco harm-reduction were not included. Examples include: increased productivity due to averted absenteeism from work; and a reduction in other smoking-related illnesses. The exclusion of these factors may, therefore, mean the benefits of reducing and quitting smoking are underestimated. If, for example, a smoker lost an average of 2 days productivity per year (relative to a former smoker), then this would amount to nearly £4000 in lost productivity over 30 years. (This estimate includes discounting at 3.5% per year.)

3.27 The PDG noted that smoking less as a harm-reduction approach could potentially attract people who would otherwise have carried on smoking as usual. Some of those who choose to smoke less may go on to quit smoking. Conversely, offering services to help people reduce their smoking may discourage others from quitting smoking. The main analysis showed that, for harm reduction

approaches to be cost effective, at least 2 more ‘reducers’ would be needed to offset each person who decided to smoke less instead of quitting. A supplementary analysis assumed there were no benefits from smoking less (in terms of QALYs and co-morbidities), other than an increased likelihood of quitting at 6 months. The analysis showed that for each potential ‘quitter’ lost, an additional 6 ‘reducers’ would be needed to offset the lost benefits.

3.28 As with any economic evaluation, the model has a number of limitations. These include a lack of data on how co-morbidities varied with recent or long-term abstinence, and the assumption that smokers use only 1 type of intervention in any 1 quit attempt.

This section will be completed in the final document.

4 Implementation

NICE guidance can help:

- Commissioners and providers in NHS organisations and local authorities meet national priorities and the requirements of the ‘Operating framework for the NHS in England 2012–13’ and the Department of Health’s ‘Commissioning outcomes framework'.
- National and local organisations improve quality and health outcomes and reduce health inequalities.
- Local authority health and wellbeing boards improve the health and wellbeing of people in their area.
- Local NHS organisations, local authorities and other local partners benefit from any identified cost savings, disinvestment opportunities or opportunities for re-directing resources.
- Provide a focus for integration and partnership working across social care, the NHS and public health organisations.

NICE will develop tools to help organisations put this guidance into practice. Details will be available on our website after the guidance has been issued.

5 Recommendations for research

The Programme Development Group (PDG) recommends that the following research questions should be addressed. It notes that 'effectiveness' in this context relates not only to the size of the effect, but also to cost effectiveness and duration of effect. It also takes into account any negative side effects.

More detail on the other gaps in the evidence identified during development of this guidance is provided in appendix D.

5.1 What are the health effects and efficacy of using licensed nicotine-containing products for more than 1 year? What is the impact of different doses and duration of use? What are smokers' views on long-term use? What is the impact of stopping smoking but continuing to use licensed nicotine-containing products for over a year on the onset and progression of smoking-related health conditions?

5.2 How great are the health benefits, of smoking less by substituting cigarettes with licensed nicotine-containing products?

5.3 How effective and cost effective are different behavioural strategies in helping people either to cut down in order to quit or to smoke less? This should include evaluations of specific components, such as scheduling and different types of behavioural support, delivered within a clearly defined harm-reduction intervention.

5.4 How effective and cost effective are self-help materials in helping people to cut down in order to quit or to smoke less? This could include leaflets, books, resource packs, web-based and electronic aids and strategies to promote their use.

5.5 How effective are population-level policies and interventions to support smoking harm-reduction strategies? For example, what impact do different marketing strategies have on the number of people who adopt a harm-reduction approach? Strategies to

compare could include ways of marketing the different types of licensed nicotine-containing product (prices, placements and promotions for licensed nicotine-containing product use and smoking).

Cross-cutting themes

5.6 Which harm-reduction approaches are smokers using and how do these affect smoking rates at population-level and among particular groups? How do these change over time? For example, how do young people respond to the wider adoption of harm-reduction strategies? Do these strategies contribute to a continued reduction in smoking prevalence among them, or does it make quitting smoking appear less important?

5.7 How effective are interventions to help people smoke less (without the intention of quitting)? Studies should focus on (and across) different subgroups including: those who are disadvantaged, people with mental health problems, prisoners and black and minority ethnic groups.

6 Updating the recommendations

This section will be completed in the final document.

7 Related NICE guidance

Published

Smokeless tobacco cessation: South Asians communities. NICE public health guidance 39 (2012)

Quitting smoking in pregnancy and following childbirth. NICE public health guidance 26 (2010)

School-based interventions to prevent smoking. NICE public health guidance 23 (2010)

Preventing the uptake of smoking by children and young people. NICE public health guidance 14 (2008)

Smoking cessation services. NICE public health guidance 10 (2008)

Workplace interventions to promote smoking cessation. NICE public health guidance 5 (2007)

Varenicline for smoking cessation. NICE technology appraisal 123 (2007)

Brief interventions and referral for smoking cessation. NICE public health guidance 1 (2006)

Under development

Smoking cessation: acute and maternity services. NICE public health guidance (publication expected November 2013)

Smoking cessation: mental health services. NICE public health guidance (publication expected November 2013)

8 Glossary

Behavioural support for tobacco harm reduction

Practical advice and discussion about goal-setting, self-monitoring and dealing with the barriers to reducing the amount someone smokes or quitting altogether.

Cutting down to quit

Someone gradually reduces the amount of tobacco they smoke with a view to stopping smoking within the next few months.

Licensed nicotine-containing products

Nicotine-containing products (see below) that are licensed have been given marketing authorisation by the Medicines and Healthcare products Regulatory Agency (MHRA). Currently, nicotine replacement therapy (NRT) products are the only type of licensed nicotine-containing product.

Nicotine-containing products

Products that contain nicotine but do not contain tobacco and so deliver nicotine without the harmful toxins found in tobacco. Some, such as nicotine replacement therapy (NRT), are regulated by the MHRA (see licensed nicotine-containing products). Others, such as electronic cigarettes and topical gels, were not covered by MHRA regulation at the time of publication of this draft guidance.

Nicotine replacement therapy (NRT) products

Nicotine replacement therapy products are licensed for use as a smoking cessation aid and for harm reduction, as outlined in the British National Formulary. They include: transdermal patches, gum, inhalation cartridges, sublingual tablets and a nasal spray.

Pharmacotherapies

This includes medication such as varenicline or bupropion, as well as nicotine replacement therapy (NRT) products.

Point-of-sale

Point-of-sale interventions take place at the point where tobacco could be sold. Primarily, they aim to deter shopkeepers from making illegal sales. In this guidance, they aim to raise smokers' awareness of licensed nicotine-containing products as a replacement for cigarettes.

Quality

In this guidance, the quality of nicotine replacement therapy (NRT) and other nicotine-containing products refers to the consistency of nicotine delivery, lack of defects and structural integrity of the product.

Quitting in one step

Quitting in one step is the standard approach to smoking cessation. The person makes a commitment to stop smoking on or before a particular date (the quit date). This may, or may not, involve the use of nicotine replacement therapy (NRT) products or medication (varenicline or bupropion) in the lead up to the quit date and for a limited period afterwards.

Safety

In this guidance, safety in relation to licensed nicotine-containing products refers to the incidence of minor and major side effects.

Self-help materials

Any manual or structured programme, in written or electronic format, that can be used to help someone try to quit smoking or smoke less without the help of health professionals, counsellors or group support. Materials can be aimed at anyone who smokes, particular populations (for example, certain age or ethnic groups), or they may be tailored to individual need.

Smoking less

Smoking less (or smoking reduction) generally involves smoking fewer cigarettes but it can involve smoking less of each cigarette.

Stop smoking services

Stop smoking services provide a combination of behavioural support and pharmacotherapy to aid smoking cessation. The behavioural support is free. The pharmacotherapy may incur a standard prescription charge. The evidence-based treatment is based on the National Centre for Smoking Cessation and Training (NCSCT) standard programme and involves practitioners trained to this standard.

Substitute for tobacco

Completely replacing cigarettes with one or more licensed nicotine-containing products for the medium or long term.

Temporary abstinence

Abstaining from smoking. This could be for a particular event or series of events, in a particular location, for specific time periods (for example, while at work, during long-haul flights or during a hospital stay), or even for the foreseeable future. (The latter might include, for example, abstinence while serving a prison sentence or while detained in a secure mental health unit.)

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Appendix A Membership of the Programme Development Group (PDG), the NICE project team and external contractors

Programme Development Group

PDG membership is multidisciplinary. The Group comprises academics, clinicians, representatives of the public, NHS commissioners and managers, public health practitioners and technical experts as follows.

Deborah Arnott Chief Executive, Action on Smoking and Health (ASH)

Paul Aveyard Professor (clinical) in Behavioural Medicine, Primary Care Clinical Sciences, University of Birmingham and UK Centre for Tobacco Control Studies

Gretel Baron Community member

Linda Bauld (Chair), Professor of Socio-management, University of Stirling and UK Centre for Tobacco Control Studies

John Britton Director, UK Centre for Tobacco Control Studies, University of Nottingham

Barrie Dwyer Community member

Ian Gray Principal Policy Officer, Chartered Institute of Environmental Health

Martin Jarvis Emeritus Professor of Health Psychology, Department of Epidemiology and Public Health, University College London

Shelley Mason Community member

Lisa McNally Public Health Principal, NHS Surrey

Ann McNeill Deputy Director, UK Centre for Tobacco Control Studies, Kings College London

Linda Mercy Consultant in Public Health, NHS Hertfordshire

Marcus Munafò Professor of Biological Psychology, University of Bristol and UK Centre for Tobacco Control Studies

Ruth Olding Tobacco Control Programme Manager, NHS Dudley

Janet Sinclair Lifestyle Coordinator, Stockport NHS Foundation Trust

Gerry Stimson Visiting Professor, London School of Hygiene and Tropical Medicine; Emeritus Professor, Imperial College London

Heather Thomson Associate Director, NHS Centre for Smoking Cessation and Training; Head of Health Improvement, NHS Leeds

Marjon Van Der Pol Reader in Health Economics, University of Aberdeen

Robert West Professor of Health Psychology, Cancer Research UK Health Behaviour Research Centre, Department of Epidemiology and Public Health, University College London

Martyn Willmore Performance Improvement Manager, Fresh – Smoke Free North East

NICE project team

Mike Kelly CPHE Director

Simon Ellis Associate Director

Hilary Chatterton Lead Analyst

Pete Shearn Analyst

Rachel Kettle Analyst

Patti White Analyst

Lesley Owen Technical Adviser, Health Economics

Victoria Axe Project Manager

Denise Jarrett Coordinator

Sue Jelley Senior Editor

Alison Lake Editor

External contractors

Evidence reviews

Review 1 was carried out by Cedar, Cardiff and Vale University Health Board. The principal authors were: Stephen Jones, Andrew Cleves, Fiona Morgan, Kathleen Withers, Judith White and Megan Dale.

Review 2 was carried out by the Support Unit for Research Evidence (SURE), Cardiff University. The principal authors were: Fiona Morgan, Alison Weightman, Sarah Whitehead, Helen Morgan, Ben Carter, Ellie Byrne, Ruth Turley and Andrew Cleves.

Review 3 was carried out by SURE. The principal authors were: Fiona Morgan, Alison Weightman, Sarah Whitehead, Helen Morgan, Ben Carter, Stephen Jones, Ellie Byrne and Ruth Turley.

Review 4 was carried out by SURE. The principal authors were: Ruth Turley, Helen Morgan, Jane Noyes, Alison Weightman, Fiona Morgan, Sarah Whitehead and Elizabeth Halstead.

Review 5 was carried out by SURE. The principal authors were: Helen Morgan, Fiona Morgan, Alison Weightman and Sarah Whitehead.

Cost effectiveness

The review of economic evaluations was carried out by Mapi Values and York Health Economics Consortium. The principal authors were: Paul Truman, Kristel Janssen, Margreet van Eerd, Evelien Bergrath and Catherine Mulvany.

The economic modelling was carried out by Mapi Values and York Health Economics Consortium. The principal authors were: Matthew Taylor, Paul Truman, Kristel Janssen, Margreet van Eerd, Evelien Bergrath and Catherine Mulvany.

See appendix E for the titles of the above reports.

Expert testimony

The views expressed in the expert papers below are the views of the authors and not those of NICE.

Expert paper 1 by Maciej L Goniewicz, Tobacco Dependence Research Unit, Queen Mary University of London

Expert paper 2 by Emma Beard, University College London

Expert paper 3 by Melanie McIlver, National Centre for Smoking Cessation and Training (NCSCT)

Expert paper 4 by Ann McNeill, UK Centre for Tobacco Control Studies

Expert paper 5 by Ian Gray, Chartered Institute of Environmental Health and Hilary Wareing, Co-Director, Tobacco Control Collaborating Centre

Expert paper 6 by Suzy Dymond-White, National Offender Management Service (NOMS)

Expert paper 7 by Gerard Hastings, Institute for Social Marketing and the Centre for Tobacco Control Research, University of Stirling

Expert paper 8 by Deborah Arnott, Action on Smoking and Health (ASH)

Chris Marriott, King's College London, provided verbal commentary on review 1.

Appendix B Summary of the methods used to develop this guidance

Introduction

The reviews and economic modelling report include full details of the methods used to select the evidence (including search strategies), assess its quality and summarise it.

The minutes of the Programme Development Group (PDG) meetings provide further detail about the Group's interpretation of the evidence and development of the recommendations.

All supporting documents are listed in appendix E and are available at the NICE website

Guidance development

The stages involved in developing this public health guidance are outlined in the box below.

1. Draft scope released for consultation

2. Stakeholder comments used to revise the scope

3. Final scope and responses to comments published on website

4. Evidence reviews and economic modelling undertaken and submitted to PDG

5. PDG produces draft recommendations

6. Draft guidance (and evidence) released for consultation and for field testing

7. PDG amends recommendations

8. Final guidance published on website

9. Responses to comments published on website

Key questions

The key questions were established as part of the scope. They formed the starting point for the reviews of evidence and were used by the PDG to help develop the recommendations. The overarching questions were:

Question 1: How effective and cost effective are pharmacotherapies in helping people to:

- cut down smoking before quitting
- cut down or abstain from smoking, temporarily or indefinitely?

How effective and cost effective are different combinations of NRT products?

Question 2: How effective and cost effective are ‘nicotine-containing products’ in helping people to:

- cut down smoking before quitting
- cut down or abstain from smoking, temporarily or indefinitely?

Question 3: Which kinds of behavioural support, counselling, advice or self-help (with or without pharmacotherapy) are effective and cost effective in helping people to:

- cut down smoking before quitting
- cut down or abstain from smoking, temporarily or indefinitely.

Question 4: Do some tobacco harm-reduction approaches have a differential impact on different groups (for example, people of different ages, gender, socioeconomic status or ethnicity)?

Question 5: Are there any unintended consequences from adopting a tobacco harm-reduction approach, for example, does it deter people from trying to stop smoking?

Question 6: How can practitioners deliver messages about tobacco harm reduction without weakening the impact of advice about the benefits of stopping smoking?

Question 7: What factors might act as barriers or facilitators to tobacco harm-reduction approaches?

Question 8: Does long-term use of pharmacotherapies or 'nicotine-containing products' have any ill-effects on health?

These questions were made more specific for each review (see reviews for further details).

Reviewing the evidence

Effectiveness reviews (Reviews 2, 3 and 5)

Three reviews of effectiveness were conducted. These covered:

- tobacco harm reduction approaches with the intention of quitting with or without help
- long-term tobacco harm-reduction approaches without intending to quit and with or without help
- long-term use of non-tobacco nicotine-containing products among people who have quit smoking abruptly.

See appendix E for details.

Identifying the evidence

A number of databases were searched in August 2011 for: systematic reviews, guidelines, randomised controlled trials (RCTs), controlled trials, controlled before-and-after studies, interrupted time series and uncontrolled before-and-after studies from January 1990. A number of national and international websites were also searched.

In addition, a range of databases were searched for information on studies in progress, unpublished research or research reported in the grey literature.

See each review for details of the databases and websites searched (and dates of any update searches). A call for evidence from registered stakeholders was made in August 2011.

Selection criteria

Studies were included in the effectiveness reviews if they covered the following people and at least one of the following interventions:

- people who want to quit smoking gradually, reduce their cigarette consumption or temporarily abstain from smoking
- people who have quit smoking abruptly and replaced cigarettes with nicotine replacement therapy or products containing nicotine.
- pharmacotherapies licensed for cutting down, temporary abstinence or harm reduction.

- other non-tobacco ‘nicotine-containing products’, such as ‘electronic cigarettes’ and topical gels.
- behavioural support, counselling or advice for individuals or groups.
- self-help.

Studies were excluded if they focused on pregnant women or were about:

- pharmacotherapies not licensed for cutting down, temporary abstinence or harm reduction
- products containing tobacco, including products that claim to deliver reduced levels of toxicity or that reduce exposure to tobacco smoke
- products that are smoked that do not contain tobacco
- smokeless tobacco products
- alternative or complementary therapies.

Review 1: Safety, risks and pharmacokinetics profiles of tobacco harm reduction technologies

Identifying the evidence

A range of databases and websites were searched in August 2011 for studies published from 1980 onwards. Included studies were RCTs, systematic reviews of RCTs of smoking harm reduction interventions that reported safety data, non-randomised trials with a strong focus on safety and risks of using NRT; randomised and non-randomised pharmacokinetic studies both particularly those with a high frequency of measurement of pharmacokinetic parameters over the study period, in order to inform the pharmacokinetic model; studies of any design that address special pharmacokinetic or safety considerations that arise, concerning use of NCPs as part of smoking harm reduction in the following groups:

- People with low socioeconomic status.

- People in black and minority ethnic groups.
- Subgroups based on age.
- People taking psychiatric medication.
- Breastfeeding mothers.

This was supplemented by grey literature searches and a call for evidence.

See the review for details.

Selection criteria

Studies were included in review 1 if they:

- reported on the safety, risks and pharmacokinetic profiles of tobacco harm-reduction strategies (principally the use of non-tobacco nicotine-containing products) both among people who continue to smoke and among smokers who have quit but continue to use NRT products indefinitely
- addressed special pharmacokinetic or safety considerations that arise when using nicotine-containing products to help reduce the harm from smoking among the following groups:
    - people with a low socioeconomic status
    - people from black and minority ethnic groups
    - subgroups based on age
    - people taking psychiatric medication
    - breastfeeding mothers.

In the absence of population-level data on the safety and risks of long-term nicotine use, the evidence on 'Swedish snus' was used as a proxy.

Studies were excluded if they focused on pregnant women.

Review 4: Barriers and facilitators to implementing tobacco harm reduction approaches, (including user and provider perspectives)

Identifying the evidence

A range of databases and websites were searched in August 2011 for: RCTs, systematic reviews of RCTs, non-randomised trials, qualitative and quantitative evidence of views and opinions, and process evaluations of intervention studies, from 1990 onwards.

This was supplemented by grey literature searches and two calls for evidence. Follow-up database searches were conducted in November 2011 and January 2012. See the review for details.

A call for evidence was also made.

Selection criteria

Studies were included in review 4 if they focused on the following people or services and at least one of the following interventions:

- people (or the families of people) who want to quit smoking gradually, reduce their cigarette consumption or temporarily abstain from smoking
- service providers, healthcare personnel and policy makers who may deliver/ commission/refer smokers to tobacco harm reduction interventions.
- pharmacotherapies licensed for cutting down, temporary abstinence or harm reduction (at the time of the reviews, only nicotine replacement therapy was licensed for these indications)
- other non-tobacco products containing nicotine (electronic cigarettes and topical gels).
- behavioural support, counselling, advice or self-help.

Studies were excluded if they focused on pregnant women.

Quality appraisal

Included papers were assessed for methodological rigour and quality using the NICE methodology checklist, as set out in the NICE technical manual 'Methods for the development of NICE public health guidance' (see appendix E). Each study was graded (++, +, –) to reflect the risk of potential bias arising from its design and execution.

Study quality

++ All or most of the checklist criteria have been fulfilled. Where they have not been fulfilled, the conclusions are very unlikely to alter.

+ Some of the checklist criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are unlikely to alter the conclusions.

– Few or no checklist criteria have been fulfilled. The conclusions of the study are likely or very likely to alter.

The main reasons for studies being assessed as (–) were:

- limited use of reliable outcomes
- lack of meaningful follow-up
- insufficient power or lack of evidence of power calculation
- failure to use intention to treat analyses.

The evidence was also assessed for its applicability to the areas (populations, settings, interventions) covered by the scope of the guidance. Each evidence statement concludes with a statement of applicability (directly applicable, partially applicable, not applicable).

Summarising the evidence and making evidence statements

The review data was summarised in evidence tables (see full reviews).

The findings from the reviews and studies were synthesised and used as the basis for a number of evidence statements relating to each key question. The

evidence statements were prepared by the external contractors (see appendix A).

The statements reflect their judgement of the strength (quality, quantity and consistency) of evidence and its applicability to the populations and settings in the scope.

Cost effectiveness

There was a review of economic evaluations and an economic modelling exercise.

Review of economic evaluations

The databases searched included most of NICE's core databases. The search strategies from the effectiveness reviews were used with a filter designed to identify economic and costs studies.

Studies were included if they reported on a full economic evaluation with the same populations and interventions as in the effectiveness reviews (see above).

Two studies were identified that met the inclusion criteria but only 1 was applicable. The results are reported in 'A rapid review of economic evidence on tobacco harm reduction strategies'. It is available on the NICE website.

Economic modelling

An economic model was constructed to incorporate data from the reviews of effectiveness and cost effectiveness. Its aim was to determine the cost-effectiveness of interventions to reduce the harm caused by smoking. The model covered quitting smoking using nicotine-containing products on a long-term basis. It also covered interventions to reduce smoking.

Following requests from the Programme Development Group, a supplementary analysis was undertaken to explore additional scenarios. The results are reported in: 'An economic evaluation of different interventions to promote tobacco harm reduction' and a supplementary analysis entitled, 'An

economic evaluation of different interventions to promote tobacco harm reduction: supplementary report'. They are available on NICE's website.

How the PDG formulated the recommendations

At its meetings between October 2011 and June 2012, the Programme Development Group (PDG) considered the evidence, expert testimony and cost effectiveness to determine:

- whether there was sufficient evidence (in terms of strength and applicability) to form a judgement
- where relevant, whether (on balance) the evidence demonstrates that the intervention or programme/activity can be effective or is inconclusive
- where relevant, the typical size of effect (where there is one)
- whether the evidence is applicable to the target groups and context covered by the guidance.

The PDG developed draft recommendations through informal consensus, based on the following criteria:

- Strength (type, quality, quantity and consistency) of the evidence.
- The applicability of the evidence to the populations/settings referred to in the scope.
- Effect size and potential impact on the target population's health.
- Impact on inequalities in health between different groups of the population.
- Equality and diversity legislation.
- Ethical issues and social value judgements.
- Cost effectiveness (for the NHS and other public sector organisations).
- Balance of harms and benefits.
- Ease of implementation and any anticipated changes in practice.

Where possible, recommendations were linked to an evidence statement(s) (see appendix C for details). Where a recommendation was inferred from the evidence, this was indicated by the reference ‘IDE’ (inference derived from the evidence).

Appendix C The evidence

This appendix lists the evidence statements from 5 reviews provided by external contractors (see appendix A and appendix E) and links them to the relevant recommendations. See appendix B for the meaning of the (++), (+) and (-) quality assessments referred to in the evidence statements.

Appendix C also lists 2 expert papers and their links to the recommendations and sets out a brief summary of findings from the economic analysis.

The evidence statements are short summaries of evidence, in a review, report or paper (provided by an expert in the topic area). Each statement has a short code indicating which document the evidence has come from. The letter(s) in the code refer to the type of document the statement is from, and the numbers refer to the document number, and the number of the evidence statement in the document.

Evidence statement 1.1a indicates that the linked statement is numbered 1a in review 1. **Evidence statement 2.4.1** indicates that the linked statement is numbered 4.1 in review 2. **Evidence statement 3.1.5** indicates that the linked statement is numbered 1.5 in review 3. **Evidence statement 4.1.37** indicates that the linked statement is numbered 1.37 in review 4. **Evidence statement 5.1** indicates that the linked statement is numbered 1 in review 5.

The 5 reviews of effectiveness are:

- Review 1: ‘Safety, risk and pharmacokinetics profiles of tobacco harm reduction technologies’
- Review 2: ‘The effectiveness of tobacco harm reduction approaches with the intention of quitting (that is, cutting down to quit or reduction to stop smoking), with and without assistance’
- Review 3: ‘The effectiveness of long-term harm reduction approaches without the prior intention of quitting’

- Review 4: ‘Barriers and facilitators to implementing tobacco harm reduction approaches, including user and provider perspectives’

- Review 5: ‘Long term use of non-tobacco nicotine containing products in individuals who have quit smoking abruptly’.

The reviews, expert papers and economic analysis are available online. Where a recommendation is not directly taken from the evidence statements, but is inferred from the evidence, this is indicated by **IDE** (inference derived from the evidence).

Where the Programme Development Group (PDG) has considered other evidence, it is linked to the appropriate recommendation below. It is also listed in the additional evidence section of this appendix.

Recommendation 1: evidence statements 1.1a, 1.1b, 1.1c, 1.2a, 1.2b, 1.3a, 1.3c, 1.4a, 1.4b, 1.4c, 1.5, 1.7, 1.8, 1.9, 2.3.1, 3.3.1, 3.8.3, 4.1.5, 4.1.17, 4.1.18, 4.1.37, 4.1.42, 5.4, 5.5, 5.6; additional evidence expert papers 1, 2, 8

Recommendation 2: evidence statements 4.1.4, 4.1.10, 4.1.11, 4.1.15, 4.1.17, 4.1.18

Recommendation 3: evidence statements 5.1, 5.2, 5.3

Recommendation 4: evidence statements 2.1, 2.1.1, 2.1.2, 3.1.1, 3.1.2, 3.1.3, 3.1.5; additional evidence expert paper 2

Recommendation 5: evidence statements 2.4, 2.4.1,.2.4.2, 2.4.3, 2.5, 2.5.1, 2.5.2, 2.6, 2.6.1, 2.6.2, 3.4, 3.4.1,.3.4.2, 3.4.3, 3.4.4, 3.4.5, 3.4.6, 3.4.7, 3.6.1, 3.6.2, 3.8.2, 4.1.15; IDE

Recommendation 6: IDE

Recommendation 7: evidence statements 2.1, 2.1.1, 2.1.2, 3.1.1, 3.1.2, 3.1.3, 3.1.5, 3.1.6, 3.8.1, 3.8.2

Recommendation 8: evidence statements 1.1a, 1.1b, 1.1c, 1.3a, 1.3c, 1.4b, 1.7, 2.1, 2.1.1, 2.1.2, 3.8.1, 3.8.2, 4.1.37, 4.1.42; additional evidence expert paper 2

Recommendation 9: IDE

Recommendation 10: evidence statement 3.4.8; additional evidence expert paper 2

Recommendation 11: evidence statement 4.1.7; additional evidence: expert papers 5, 6

Recommendation 12: evidence statements 4.1.7, 4.2.6; additional evidence: expert papers 5, 6

Recommendation 13: evidence statements 5.1, 5.2, 5.3, 5.4, 5.5

Recommendation 14: IDE

Recommendation 15: IDE

Recommendation 16: evidence statement 1.3c; IDE

Evidence statements

Please note that the wording of some evidence statements has been altered slightly from those in the evidence review(s) to make them more consistent with each other and NICE's standard house style. The superscript numbers refer to the studies cited beneath each statement. The full references for those studies can be found in the reviews.

Evidence statement 1.1a Risks and adverse events associated with nicotine replacement and nicotine containing products: primary studies

Evidence from 10 randomised controlled trials (4 [++][1–4] and 6 [+][5–10]) strongly suggests that adverse events are common when nicotine replacement therapy (NRT) is used for smoking harm reduction, but these tend to be mild or moderate and are rarely severe. No authors have attributed serious adverse events to NRT when used as part of smoking harm reduction. NRT is

generally well tolerated when used in this setting. Frequently reported adverse events depend on the route of administration but include throat irritation, coughing, nausea, vertigo/dizziness, vomiting or palpitations. One study[7] ([+]) reported no evidence of increased cardiac events in patients with existing cardiac disease treated with NRT for 18 months. The duration of use of NRT in these studies varied from 1–18 months. Follow up did not extend beyond 24 months, so the randomised trials do not provide safety data for longer-term use.

[1] Bolliger et al. 2000

[2] Carpenter et al. 2004

[3] Etter et al. 2002

[4] Rennard et al. 2006

[5] Batra et al. 2005

[6] Carpenter et al. 2003

[7] Haustein et al. 2004

[8] Joseph et al. 2008

[9] Kralikova et al. 2009

[10] Wennike et al. 2003

Evidence statement 1.1b Risks and adverse events associated with nicotine replacement and nicotine containing products: meta-analysis

Evidence from a meta-analysis[1] (++) of 2767 participants drawn from several of the randomised trials cited above plus 2 unpublished sources corroborates the findings shown above. The unpublished trials used NRT for 9 months and 12 months. The results suggest that there is no difference between NRT (used for between 6 and 18 months) and placebo in terms of mortality, serious adverse events or discontinuation of therapy due to adverse events. But nausea occurs more frequently with active NRT (odds ratio [OR] 1.69, 95% confidence interval [CI] 1.21–2.36). Use of the meta-analysis has 2 caveats:

- the meta-analysis re-iterates a substantial body of the same data from 6 randomised trials (3 [++][2–4] and 3 [+][5–7]) cited above
- there was substantial heterogeneity of results in the meta-analysis of serious adverse events.

[1] Moore 2011

[2] Batra et al. 2005

[3] Bolliger et al. 2000

[4] Etter et al. 2002

[5] Haustein et al. 2004

[6] Rennard et al. 2006

[7] Wennike et al. 2003

Evidence statement 1.1c Risks and adverse events associated with nicotine replacement and nicotine containing products: cardiovascular risk markers

Evidence from 5 randomised trials (2 [++][1,2] and 3 [+][3–5]) and 1 non-randomised, controlled study[6] (+) suggests that there are no substantial changes in risk markers for cardiac disease in people treated with NRT as part of smoking harm reduction. The randomised controlled trial evidence is cited from a Cochrane review [++][7]. Risk markers studied included white blood cell count, fibrinogen, C-reactive protein (CRP), lipids, F2-isoprostanes, 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), 1-hydroxypyrene (1-HOP). One (++) study[2] found favourable changes in both NRT and placebo groups. No study reported increases in risk markers for cardiovascular disease arising from NRT. Follow up did not extend beyond 24 months.

[1] Bolliger et al. 2000

[2] Rennard et al. 2006

[3] Batra et al. 2005

[4] Joseph et al. 2008

[5] Kralikova et al. 2009

[6] Haustein et al. 2004

[7] Stead and Lancaster 2007

Evidence statement 1.2a Safety of long-term use of nicotine replacement therapy and nicotine containing products

There are no studies available of the safety of NRT used in smoking harm reduction in the long term (maximum duration of NRT use is 5 years). The strongest evidence available for the long-term safety of NRT with concurrent smoking comes from a large subgroup of patients studied in the 5-year 'Lung health study'[1,2] (+) of NRT in smoking cessation, where a large patient group continued to smoke and continued to use NRT. The results of this multicentre randomised controlled trial suggest that long-term use of NRT is not associated with an increased incidence of harm, including cardiovascular events or cancer, with the latest analysis of outcome at 12.5 years from study outset.

[1] Murray et al. 1996

[2] Murray et al. 2009

Evidence statement 1.2b Safety of long-term use of nicotine replacement therapy and nicotine containing products: cardiac disease

Six studies (4 [+][1–4] and 1 [-][5]) evaluated the safety of NRT in patients with cardiac disease and did not find any increased incidence of cardiovascular events or any other adverse events.

[1] Mahmarian et al. 1997

[2] Leja et al. 2007

[3] Joseph et al. 2008

[4] Joseph et al. 1996

[5] Paciullo et al. 2009

[6]Tzivoni et al. 1998

Evidence statement 1.3a Risks associated with use of unlicensed nicotine containing products

All available evidence relates to electronic cigarettes (e-cigarettes). There is no evidence on the long-term safety of e-cigarettes, whether used alone or with concurrent cigarette smoking. There isn't a large volume of reliable evidence on the short-term safety of e-cigarettes. One (+) randomised crossover trial[1] found that the rate of acute adverse events arising from e-cigarette use (occurring on the first day of use) were intermediate between placebo e-cigarette and licensed nicotine inhalator. A non-randomised (+) study also found no acute effect on heart rate from the use of 2 models of e-cigarette[2].There are no firm cases of harm that are directly attributable to e-cigarette use. One news article in the British press[3] (-) reported a death from lipoid pneumonia where e- cigarette use was implicated by a treating clinician. The inquest to the death recorded an open verdict.

[1] Bullen et al. 2010

[2] Vansickel et al. 2010

[3] BBC, 2011

Evidence statement 1.3c Contents of e-cigarettes

There is evidence from 2 laboratory analyses (both [++])[1,2] that e-cigarettes can contain nicotine derived nitrosamine contaminants and diethylene glycol, a highly toxic substance. Most e-cigarettes include propylene glycol. This chemical is generally considered to be of low toxicity although there appears to be insufficient data concerning its inhalational toxicity. A physical evaluation of e-cigarettes (+)[3] found that e-cigarettes (including their constituent parts and instruction manuals) lack important information regarding contents, use and essential warnings. The same study[3] found that e-cigarettes frequently leak, presenting a hazard, and that there are currently no methods for proper disposal of e-cigarettes, including cartridges.

[1] Westenberger 2009

[2] [redacted]

[3] Trtchounian et al. 2011

Evidence statement 1.4a Impact of nicotine replacement therapies and nicotine containing products on the concentration of nicotine in the blood

Evidence from 6 (all [+])[1–6] controlled studies suggests that nicotine concentrations with smoking alone are typically in the range 22–30 ng/ml. When NRT use is accompanied by smoking, nicotine concentrations can rise to higher levels. The highest value observed was 63.4 ng/ml when a 44 mg patch was used with *ad libitum* smoking (+)[4]. Some authors suggest that smoking behaviour self-regulates to maintain a constant nicotine concentration but evidence (particularly for patches) suggests that this is imprecise.

Despite increased nicotine concentration with concomitant use, the evidence from two studies (+)[4,6] suggests there are no increases in the incidence of side effects or significant changes in physiological parameters such as blood pressure and heart rate.

[1] Ebert et al. 1984

[2] Fagerstrom et al. 2002

[3] Foulds et al. 1992

[4] Pickworth et al. 1994

[5] Russell et al. 1976

[6] Zevin et al. 1998

Evidence statement 1.4b Compensatory smoking

Compensatory smoking is a mechanism whereby smokers, who have reduced the number of cigarettes they smoke per day, modify their smoke intake, for example, by puffing more frequently or more intensely, and so titrate their nicotine intake[1] (+). Two studies[1,2] (1 [+] and 1 [-]) correlating reductions in expired carbon monoxide (CO) with reductions in the number of cigarettes per day have demonstrated that some compensation occurs, but that the

reduction in CO is significant. A narrative review of studies [-][3] suggests that for acute NRT forms (gum, lozenge, inhalator, nasal spray) a reduction in CO is accompanied by little change in plasma nicotine, suggesting close titration by subjects. In contrast, the same study found for nicotine patches, plasma nicotine increased, suggesting poor titration for the transdermal route.

Three studies[4,5,6] (all [+]) of snuff use and low yield cigarettes also indicate that users are able to manage their intake to achieve a plasma nicotine level of typically 35–37 ng/ml. One (+) study[6] showed that users of nasal snuff can generate similar plasma nicotine levels to those generated by smoking a cigarette, in approximately equal time (10 minutes).

[1] Hughes and Carpenter 2005

[2] Hughes 2000

[3] Fagerstrom and Hughes 2002

[4] Holm et al. 1992

[5] Jarvis et al. 2001

[6] Russell et al. 1981

Evidence statement 1.4c Nicotine absorption routes from NRT and e-cigarettes

The routes of absorption of medicinal nicotine are buccal (lozenge, gum, microtab, inhalator), dermal (patches) and nasal mucosa (nasal spray). Notably nicotine is mainly absorbed from the inhalator via the oral mucosa, with minimal absorption via the lungs. The degree of absorption of nicotine from e-cigarettes is uncertain, 2 studies (both [-])[1,2] suggest the delivery of nicotine by these devices is via buccal absorption.

[1] Russell et al. 1987

[2] Vansickel and Eissenberg 2012

Evidence statement 1.5 Pharmacokinetic data for each nicotine administration route

Cigarettes Evidence from a pharmacokinetic study (+) indicates that 10 minutes of cigarette smoking can generate an arterial blood Cmax of 38–40 ng/ml nicotine in Tmax 8 minutes and a venous blood Cmax of 17–19 ng/ml in a Tmax of 10–12 minutes[1].

Snus Absorption of nicotine from snus is primarily through the oral mucosa and can produce a venous blood Cmax of 14–15 ng/ml in a Tmax of 30–37 minutes (+)[2–4].

NRT lozenge/tablet These products dissolve in the mouth (and are not intended to be swallowed) and absorption of nicotine is primarily through the oral mucosa. A single dose of between 1 and 6 mg nicotine that is allowed to dissolve in the mouth can generate a Cmax of 2–9 ng/ml in Tmax of 10–90 minutes (+)[3,5–8]. Multiple, sequential doses do not appear to result in a Cmax higher than 30 ng/ml (+)[9–13].

NRT gum NRT gum is chewed in the mouth. Absorption of nicotine is primarily through the oral mucosa. When 2–4 mg nicotine or less is administered as gum and chewed for 20–30 minutes, a Cmax of 3–15 ng/ml is reached in Tmax of 20–56 minutes (+)[2,3,5,8,11,14]. Larger, sequential doses of 24–48 mg, chewed for 30 minutes each hour over 12 hours, result in a Cmax of 11–30 ng/ml in a Tmax of 28–30 minutes (+)[9,10,13].

NRT nasal spray The absorption route for nasal spray is primarily through the nasal mucosa. A dose of 0.5–2.5 mg nicotine, given via nasal spray over 5 minutes or less, can result in Cmax of 5–23 (mean 11) ng/ml in Tmax of 5–30 (mean 12) minutes (+)[15–19]. Nasal spray, therefore, appears to offer potentially rapid absorption of nicotine, compared to the other NRT routes.

NRT inhalator The pharmacokinetic data on the NRT inhalator appear to support buccal absorption as the primary nicotine absorption route. 20 minutes of use appears to generate a variable Cmax of mean 23 ng/ml (range 2–34) in Tmax of 27 minutes (range 20–32 minutes) (+)[20–21].

NRT patch The absorption route for nicotine patches is transdermal. Patches appear to offer slow, but sustained absorption of nicotine. Doses of 15–40 mg, given over 16–24 hours, can result in a Cmax of 19 ng/ml (range 14–26 ng/ml) in Tmax of mean 9 hours (range 6–12 hours) (+)[22–25].

e-cigarettes e-cigarettes are not licensed medicines in the UK and little is known about the extent to which they deliver nicotine to the circulation. A small volume of available data suggest that a 16 mg dose given over 5 minutes can result in a Cmax of 1.3 ng/ml in Tmax of 20 minutes (+)[21]. Data from one study (-)[26], suggest that 10 consecutive puffs at 30-second intervals, followed by 60 minutes of ab libitum use, can generate a Cmax of 16.3ng/ml in 75 minutes.

[1] Gourlay and Benowitz 1997

[2] Lunell and Curvall 2011

[3] Kotlyar et al. 2007

[4] Foulds 2003

[5] Dautzenberg 2007a

[6] Molander and Lunell 2000b

[7] Molander and Lunell 2000d

[8] Johnson and Johnson 2011a

[9] Dautzenberg 2007b

[10] Dautzenberg 2007c

[11] Molander and Lunell 2000a

[12] Molander and Lunell 2000c

[13] Johnson and Johnson 2011b

[14] Shiffman 2009

[15] Guthrie 1999

[16] Gourlay 1997b

[17] Perkins 1991

[18] Lunell 1995

[19] Sutherland 1992

[20] Molander 1996

[21] Bullen 2010

[22] Veaugh-Geiss 2010

[23] Gourlay 1997a

[24] Lewis 2007

[25] Vanakoski 1996

[26] Vansickel and Eissenberg 2012

Evidence statement 1.7 Snus and cancer risk[7]

The evidence suggests that there is a statistically significantly increased risk of some types of cancer (pancreatic, oesophageal and possibly squamous cell head and neck cancer) associated with using Swedish snus after taking account of the risk arising from concurrent smoking[1-5]. However, these risks from snus are substantially lower than those associated with smoking. Nicotine itself is not regarded as a carcinogen.

Compared to non-smokers, smokers are at increased risk of cancers of the lung, oesophagus, oropharyx, stomach, rectum and anus[5-10].

The risk of cancers (lung, pancreatic, oral, colon, rectum and anus) in dual smoker and snus users exceeds the risk of cancer attribute to using snus alone[6, 10-12].

[1] Boffetta et al. 2008

[2] Broadstock 2007

[3] Lee and Hamling 2009a

[4] SCENIHR 2008

[7] Although Swedish snus is excluded from the scope of this guidance, the evidence was used as a proxy measure of the effects of long-term nicotine use in the absence of long-term licensed nicotine-containing product data. For further details, see appendix 10 in evidence review 1.

[5] Lewin et al. 1998 (cited by Broadstock et al. 2007)

[6] Luo et al. 2007 (cited by Broadstock et al. 2007)

[7] Lagergren et al. 2000 (cited by Broadstock et al. 2007)

[8] Ye et al. 1999 (cited by Broadstock et al. 2007)

[9] Roosaar et al. 2008 (cited by Broadstock et al. 2007)

[10] Zendehdel et al. 2008 (cited by Broadstock et al. 2007)

[11] Boffetta et al. 2005 (cited by Broadstock et al. 2007)

[12] Nordenvall et al. 2011

Evidence statement 1.8 Snus and risk of myocardial infarction[7]

The evidence suggests that use of Swedish snus is associated with greater likelihood of fatal myocardial infarction[1-3]. Duration of exposure is not consistently reported but 1 study suggested that duration of exposure was 15 years[4]. The evidence suggests that lengthy exposure is not associated with a change in resting blood pressure but there is experimental evidence that nicotine may affect lipid metabolism[3].

Smokers are at substantially increased risk of myocardial infarction compared to non-smokers and also in comparison to non-smokers who use snus[5]. While former smokers currently using snus had an increased risk of acute myocardial infarction than never smokers[6], the risk in current smokers who also use snus was larger[5,6].

[1] Broadstock 2007

[2] Boffetta and Straif 2009

[3] SCENIHR 2008

[4] Bolinder et al. 1994 (cited by Broadstock et al. 2007)

[5] Huhtasaari et al. 1999 (cited by Broadstock 2007)

[6] Hergens et al. 2005 (cited by Broadstock 2007)

Evidence statement 1.9 Snus in the context of years of life lost due to tobacco

One systematic review [+][1] reports that the precise magnitude of health gain arising from choosing less harmful alternatives to smoking is difficult to quantify. It cites data from a modelling study[2] which estimates the extent of harm (in years of life lost) in 4 different exposure-based groups: smokers who continue to smoke, smokers who switch to snus, smokers who quit smoking and snus users who never smoked. The model suggests that the health benefit gained (that is, by reducing the number of life years lost) for a smoker who switches to snus, but who would not otherwise have quit smoking, is substantially greater than the life years lost by a snus user who never smoked. The model suggests that the life years lost by a smoker who switches to snus are only marginally greater than the life years lost by a smoker who quits tobacco altogether. The systematic review authors conclude that the overall population effect of snus is likely to be beneficial.

NRT should be an intuitively safer option than Swedish snus because it does not contain the numerous potentially harmful constituents of snus for example, nitrosamines. In terms of NRT, a safety issue to overcome is whether through smoking with concurrent NRT, any harm is likely to result from the maximum blood concentrations of nicotine achieved and also the potentially long-term exposure to nicotine. Data from Swedish studies presented in this report appear to be based on long-term exposure (decades). The same studies do not accurately estimate the volume of nicotine taken over time from cigarettes and snus combined. Studies of efficacy may inform the PDG whether NRT use with concurrent smoking leads to a reduced volume of smoking expressed as cigarettes per day.

[1] Scientific Committee on Emerging and Newly Identified Health Risks 2008

[2] Gartner et al. 2007 (cited by SCENIHR 2008)

Evidence statement 2.1 (including statements 2.1.1–2.1.2) How effective are pharmacotherapies in helping people cut down smoking before quitting?

2.1 Three RCTs examined the efficacy of NRT gum (1 [++][1] and 1 [+][2]) and lozenges (1 [++])[3]. In addition there was 1 (+) quasi-randomised controlled trial (quasi-RCT)[4] and 1 (-) uncontrolled before-and-after study (UBA)[5] with a combined intervention of behavioural therapy plus gum.

Two studies[1,3] were deemed to be studies at low risk of bias.

2.1.1 There is moderate evidence from 2 RCTs (1 [++][3] and 1 [+])[2] of no significant difference in long-term abstinence rates between gradual and abrupt cessation when using NRT (gum or lozenges) although the trend favours abrupt cessation. The CO and cotinine validated 4-week quit rate at 12 months was 16.5% for gradual compared to 24.0% for abrupt cessation, p=0.14[2]. The OR for CO validated abstinence at 6 months (gradual/abrupt) was 0.6 (95% CI 0.3, 1.2)[3].

2.1.2 There is moderate evidence from a large RCT ([++])[1] of a benefit from NRT versus placebo at 6 months; this was more marked in the 4 mg gum versus 2 mg dose rates with ORs of 6.0 (95%CI 2.9, 12.3) and 1.8 (95% CI 1.1, 2.9) respectively. Overall OR 2.86 (95% CI 1.93, 4.24).

The evidence from 2 much smaller studies, a quasi-RCT (+)[4] and an uncontrolled before-and-after study (–)[5], is inconsistent. In the quasi–RCT mean quit rates for standard treatment versus behavioural counselling with NRT respectively at 6months were 21% versus 27% (NS) and at 12 months 26% versus 27% (NS)[4]. In the UCBA study[5] 39% reported abstinence at 6 months and 68% reported a 50% or above reduction in cigarette consumption at the end of 8 weeks using a combination of gum and behavioural therapy. The difference in abstinence between participants who wanted to reduce to quit versus those who were refractory smokers was not significant (48% versus 32%, p=0.8)[5].

Applicability statement The evidence from the RCTs[1–3] is partially applicable to people in the UK because, although there were no UK-based trials, the

studies were community-based and are feasible within a UK setting. The Quasi -RCT relates specifically to recovering alcoholics[4]. The UBA was an intensive intervention which is unlikely to be feasible within the UK[5].

[1] Shiffman et al. 2009

[2] Etter et al. 2009

[3] Hughes et al. 2010

[4] Martin et al. 1997

[5] Jiménez-Ruiz et al. 2009

Evidence Statement 2.3.1 How effective are 'nicotine-containing products' in helping people cut down smoking before quitting?

For the purposes of this review 'nicotine containing products' were defined as 'electronic nicotine delivery systems' (sometimes known as 'electronic cigarettes' or 'e-cigarettes') and topical gels.

No studies were found that looked at the effectiveness of nicotine delivery systems (electronic cigarettes) for helping people to cut down before quitting.

Evidence Statement 2.4 (including statements 2.4.1–2.4.2) How effective are behavioural support, counselling, advice or self-help (with or without pharmacotherapy) in helping people cut down smoking before quitting?

2.4 Nine studies incorporated behavioural support, including 3 RCTs (1 [++][1], 1 [+][2],and 1 [-][3]), 4 quasi-RCTs (all [+])[4–7], 1 trial with partial randomisation (-)[8] and 2 uncontrolled before-and-after studies (both [–])[9,10].

Studies used behavioural intervention components in a variety of ways:

- Cognitive behavioural support (both [+])[4,7]
- Advice giving (+)[2]
- Investigating the feasibility of contingency management (providing tangible reinforcers contingent on abstinence or reduction of substance use to a target level". The tangible reinforcers in this study were gift certificates) (–)[8]
- Investigating the feasibility of computerised scheduled reduction (-)[10].

In the other studies, all participants received a behavioural component (2 [+], 1 [++][1], 2 [–][3,5,6,9]) and it is therefore not possible to infer the effectiveness of that component.

2.4.1 There is moderate evidence for the effectiveness of cognitive behavioural therapy versus standard therapy from 2 quasi-RCTs (both [+])[4,7] both in reducing the number of cigarettes per day prior to quitting, and in quitting itself. At 12 months, 41% of the Cognitive Behavioural Therapy (CBT) group and 6% of the control group were abstinent, p<0.01. Figures for 6 months were 53% and 6%, p<0.01[4]. At 12 months 19.8% (95% CI 13.0, 28.3) of the contactable CBT group were abstinent compared to 5.8 % (95% CI 2.1, 12.1, p<0.0001)[7]. At the same time point 11.5% (95% CI 6.4, 18.5, p<0.0001) had reduced their cigarettes per day (CPD) by 25% or more compared to 0% in the control group[7].

2.4.2 There is moderate evidence from 2 RCTs (1 [++][1] and 1 [-])[3] of a trend towards higher abstinence rates for abrupt cessation compared to gradual reduction when counselling is offered to both groups (in 1 study with nicotine[1]) but the findings are not significant. The OR for CO-verified abstinence at 6 months for gradual versus abrupt cessation, was 0.6 (95% CI 0.3, 1.2)[1]. At 12 months follow-up there was a non-significant difference in self-reported abstinence between sudden and gradual withdrawal groups: 51.85% versus 38.71%[3].

2.4.3 There is weak evidence from one quasi-randomised trial[5] (+) suggesting that cognitive behavioural therapy combined with advice to schedule and lengthen the time between cigarettes may enhance outcomes. Cotinine verified abstinence rates at 12 months were 44% (scheduled reduced), 18% (non-scheduled reduced), 32% (scheduled non-reduced) and 13% (non-scheduled non-reduced); p<0.05.

Applicability statement for evidence statements 2.4.1–2.4.7

This evidence is partially applicable to people in the UK. The use of rewards for response[8] is unlikely in this setting. However one study was based in the

UK[7] and one was a web-based intervention[2]. All the other studies were community- or high school-based and feasible within a UK setting.

[1] Hughes et al. 2010

[2] Etter 2011

[3] Gunther et al. 1992

[4] Cinciripini et al. 1994

[5] Cinciripini et al. 1995

[6] Martin et al. 1997

[7] Marks 2002

[8] O'Leary Tevyaw 2007

[9] Jiménez-Ruiz 2009

[10] Riley 2002

Evidence Statement 2.5 (including statements 2.5.1–2.5.2) Is there an optimal period for helping people cut down smoking with the aim of quitting?

2.5 Eleven studies reported reduction periods, including 5 RCTs (2 [++][1,2] and 3[+][3–5]), 3 quasi-RCTs (all [+])[6–8], 2 uncontrolled before-and-after studies (both [–])[9,10] and one secondary analysis of RCT data (-)[11].

Among the included studies, the reduction period varied from 7–10 days[8] through to 16 weeks[9]. Five studies employed reduction periods of between 2 and 5 weeks[2,3,4,6,7]. One[10] utilised a 7-week schedule and 2[1,5] an 8-week schedule.

One study[5] found no difference between 2 different reduction periods, although the interventions also differed. CO-verified quit rates at 12 months for the 3 groups (standard treatment with counselling over 4 weeks, counselling plus exercise and counselling plus NRT over 8 weeks) were 26%, 27% and 27% respectively.

None of the other included studies compared the effectiveness of different periods of cutting down prior to quitting. There was considerable variation in design between the studies and it is not possible to identify any relationship or trend between the length of the reduction period and the outcomes that is not subject to potential confounding by other aspects of the study designs.

However, 1 study[11] carried out a secondary analysis to examine whether delaying a quit attempt was associated with less success. This analysis was considered to be at high risk of bias.

2.5.1 There is weak evidence from a quasi-RCT[5] and a secondary analysis[11] to indicate that there is no relationship between time to planned or actual quit date and long-term abstinence rate among those cutting down prior to quitting.

2.5.2 There is no evidence concerning the optimum cutting-down period from 9 studies[1–4,6–10]. Reduction periods varied from 7 days to 16 weeks. None of the studies explored the effect of the reduction time on outcomes and, given the huge heterogeneity between studies, no relationship between reduction time and outcomes can be inferred.

Applicability statement for evidence statements 2.5.1 and 2.5.2

This evidence is partially applicable to people in the UK who smoke, one study was a large community based study[2] that may be feasible in the UK, although a secondary analysis is a methodologically weak study. One study looked specifically at recovering alcoholics[5].

[1] Shiffman 2009

[2] Hughes 2010

[3] Etter 2009

[4] Etter 2011

[5] Martin 1997

[6] Cinciripini 1994

[7] Cinciripini 1995

[8] Marks 2002

[9] Jiménez-Ruiz 2009

[10] Riley 2002

Evidence Statement 2.6 (including evidence statements 2.6.1–2.6.2) Is it more or less effective to draw up a schedule to help someone cut down smoking with the aim of quitting?

2.6 One (+) quasi-RCT[1] compared scheduled versus non-scheduled reduction. One (++) RCT[2] and 1 (+) quasi-RCT[3] compared different types of schedule.

2.6.1 There is weak evidence from 1 quasi-RCT[1]for scheduled versus non-scheduled reduction that cognitive behavioural therapy combined with advice to schedule and lengthen the time between cigarettes enhanced outcomes. Cotinine-verified abstinence rates at 12 months: 44% (scheduled reduced), 18% (non-scheduled reduced), 32% (scheduled non-reduced) and 22% (non-scheduled non-reduced); $p<0.05$.

2.6.2 There is weak evidence from 1 large RCT[2] and 1 quasi-RCT[3] that the type of smoking reduction schedule used does not make a difference. Reduction and abstinence rates did not appear to differ across the initially chosen methods (formal schedule, giving up 'easiest' cigarettes first, giving up 'hardest' cigarettes first) so the results were pooled across all the methods[2]. There was no difference between different intervention and scheduled reduction methods. CO-verified quit rates at 12 months for the 3 groups (standard treatment with counselling over 4 weeks, counselling plus exercise and counselling plus NRT over 8 weeks) were 26%, 27% and 27% respectively[3].

Applicability statement for evidence statements 2.6.1 and 2.6.2

This evidence is partially applicable to people in the UK since the studies are community-based and feasible in UK settings. One study however, was in a specific population (recovering alcoholics)[3].

[1] Cinciripini 1995

[2] Hughes 2010

[3] Martin 1997

Evidence statements 3.1.1–3.1.3, 3.1.5, 3.1.6 How effective are pharmacotherapies in helping people cut down or abstain from smoking temporarily or indefinitely without the aim of quitting?

3.1.1 There is strong to moderate evidence from 9 studies: 2 RCTs[1,2] (1 [++] and 1 [+]); 5 quasi-RCTs[3–7] (3 [+] and 2 [-]) and 2 UBAs[8,9] (both [-]) that NRT (gum or inhaler) versus placebo is effective in reducing cigarette consumption across multiple outcome measures and in eventual abstinence in smokers not looking to quit.

3.1.2 There is strong to moderate evidence from a meta-analysis of 3 RCTs[1,2,10] (2 [++] and [+]) and 1 (+) quasi-RCT[4] looking at 50% or more point prevalence reduction in CPD compared to baseline, that NRT, with or without a brief motivational interviewing (MI) component, is more effective than placebo with a relative risk (RR)=1.46 (95% CI 1.20, 1.78), with a number needed to treat (NNT) of 13 (95% CI 10, 20). A sensitivity analysis (excluding[10] which added a brief MI component to NRT) resulted in RR=1.35 (95% CI: 1.10, 1.65) and an NNT of 17 (95% CI 10, 50). Smoking reduction was verified by CO except in[2].

3.1.3 There is moderate evidence from a meta-analysis of 1 (++) RCT[1] and 2 quasi-RCTs (both [+])[3,7] that NRT is more effective than placebo in percentage reduction in cigarettes per day from baseline with a risk difference (RD) of −13.85 (95% CI: −25.5, −2.45).

3.1.5 There is strong evidence from a meta-analysis of 9 studies: 3 RCTs (2 [++][1,10] and 1 [+][2]) and 6 quasi RCTs[3,5,6,7,11,12] (all [+]) investigating cessation in populations not looking to quit that NRT with or without associated behavioural interventions has a statistically significant effect: RR=1.96 (95% CI 1.36, 2.80) with an NNT of 20 (95% CI 13, 34). A sensitivity analysis excluding studies with a behavioural component[10,11,12] found a similar result

for NRT alone: RR=1.93 (95%CI 1.26, 2.96) and an NNT of 20 (95% CI 13, 34).

3.1.6 There is moderate evidence from 1 (++) RCT[13] of patients undergoing elective surgery that nicotine patch versus placebo is effective in reducing post-operative smoking consumption, a statistically significant self-reported reduction was observed 30 days post-operation but this was not maintained at 6 months.

Applicability statement for evidence statements 3.1.1–3.1.6

The majority of the evidence is applicable to the UK as the studies are community based and feasible in UK settings, although one study[3] involved participants making several clinic visits, while another[14] was in a laboratory setting. One study was conducted within a specific population (patients undergoing elective surgery)[13].

[1] Bolliger 2000

[2] Etter 2007

[3] Batra 2005

[4] Hatsukami 2005

[5] Kralikova 2009

[6] Rennard 2006

[7] Wennike 2003

[8] Jiménez-Ruiz 2002

[9] Rennard 1990

[10] Chan

[11]Carpenter 2004

[12]Joseph 2008

[13] Warner 2005

[14]Foulds 1992

Evidence statement 3.3.1 How effective are 'nicotine-containing products' in helping people cut down or abstain from smoking, temporarily or indefinitely without the aim of quitting?

Very weak evidence from 1 (-) UBA[1] suggests that e-cigarette availability can help smokers reduce. This evidence may be applicable to the UK as it is community based and feasible in a UK setting.

[1] Polosa 2011

Evidence statements 3.4.1–3.4.8 How effective are behavioural support, counselling, advice or self-help (with or without pharmacotherapy) in helping people to cut down or abstain from smoking, temporarily or indefinitely, without the aim of quitting?

3.4.1 There is consistent evidence from 7 studies:2 RCTs[1,2] (both [+]), 4 quasi-RCTs[3,4,5,6] (all [+]) and 1 (-) CBA[7] that motivational interviewing – compared with other behavioural methods or with no support and whether provided in single or multiple sessions – is not effective in helping people to reduce smoking levels. This evidence applies to healthy adolescents and adults, with no statistically significant differences between groups reported across any of the studies reviewed. Weak evidence also exists for the lack of effectiveness of motivational interviewing for adolescent drug users[2,7] and military veterans with psychiatric problems[6], with these studies again finding no significant differences between groups for the outcomes reported.

3.4.2 There is strong evidence from a meta-analysis of 2 RCTs[1,2] (both [+]) and 3 quasi-RCTs[3,4,5] (all [+]) that motivational interviewing – compared with other behavioural methods or with no support and provided in single or multiple sessions – is not effective for smoking cessation in populations unable or unwilling to stop smoking: RR 1.34 (95% CI 0.75, 2.39; p=0.32). This is at variance with findings of a Cochrane systematic review of smoking cessation (Lai 2010). One (++) RCT[6] and 1 (+) quasi-RCT[7] suggest that the addition of NRT to a motivational component may improve the likelihood of abstinence: RR 3.09 (95% CI 1.06, 9.01; p=0.04).

3.4.3 There is moderate evidence from a large well-conducted (++) RCT[6] that NRT combined with a motivational component is effective, with a significant CO-validated 50% or more 7-day point prevalence reduction rate.

3.4.4 There is strong to moderate evidence from 4 studies:1(+) RCT[8], 1 (+) quasi-RCT[9], 1 (+) non-RCT[10] and 1 (-) CBA[11] designed to reduce the impact of environmental tobacco smoke on children – of no effect for a variety of behavioural methods versus standard care in reducing parental smoking. This evidence applies to parents of children with asthma[9,10] as well as to parents of healthy children[8,11].

3.4.5 There is moderate evidence from 2 RCTs[12,13] (both [+]) and 1 (-) UBA[14] that counselling combined with nicotine replacement therapy is not effective in helping adolescents[12] or adults[13,14] to reduce their cigarette consumption or to ultimately quit. There were no differences at follow-up between intervention and control groups for any smoking-related outcomes.

3.4.6 There is moderate evidence from 1 (++) RCT[15] that telephone counselling is an ineffective approach to reducing cigarette consumption. At the 12 month follow-up there were no significant differences between intervention and control groups in terms of numbers reducing their daily cigarette consumption by 50% or more or in carbon monoxide levels.

3.4.7 There is moderate evidence from 1 (+) quasi-RCT[16] that computer-aided and manual-aided approaches to assist with reduction had similar effect sizes. Twelve months after the start of the study there were no differences between groups in smoking reduction, and although more participants in the computer-aided group had made a quit attempt than in the manual-aided group, this difference was not statistically significant.

3.4.8 There is moderate evidence from 1 (+) systematic review of pre-operative smoking interventions[17] that counselling combined with NRT increases smoking cessation at the time of surgery for both brief and intensive interventions. However, only intensive interventions were effective at 12 month follow-up: RR 2.96 (95% CI 1.57, 5.55) for 2 trials.

Applicability statement for evidence statements 3.4.1–3.4.8

The majority of evidence is applicable to the UK as the studies are feasible in UK settings. However 3 studies[7,12,18] are noted to have issues regarding applicability. Studies of specific populations included adolescents[3,4,12,19]; adolescent drug users[2,7]; mental health[18.20,21];)patients undergoing elective surgery[17,22,23]; and parents[8,9,10,11].

[1] Horn 2007

[2] McCambridge 2005

[3] Kelly 2006

[4] Audrain-McGovern 2011

[5] Davis 2011

[6] Gulliver 2008

[7] Gray 2005

[6] Chan 2011

[7] Carpenter 2004

[8] Hovell 2000

[9] Irvine 1999

[10] Wakefield 2002

[11] Fossum 2004

[12] Hanson 2008

[13] Joseph 2008

[14] Hurt 2000

[15] Glasgow 2009

[16] Riley 2002

[17] Thomsen 2010

[18] Tidey 2002

[19] Horn 2007

[20] Griffiths 2010

[21]Schleicher 2010

[22] Munday 1993

[23] Walker 2009

Evidence statements 3.6.1–3.6.2 Is it more or less effective to draw up a schedule to help people cut down or abstain from smoking, temporarily or indefinitely, without the aim of quitting?

3.6.1 Weak evidence from 2 quasi-RCTs (1 [+][1] and 1 [-][2]) and 2 UBAs (both [−])[3,4] suggests using a schedule may assist in reducing smoking. Schedules included week-on-week reduction[3,4], increased inter-cigarette interval or selective elimination[1,2].

3.6.2 There is limited evidence from 2 quasi-RCTs (1 [+][1] and 1 [-][2]) of no difference in effect between different types of schedule (increasing inter-cigarette intervals or selective elimination).

Applicability statement for evidence statements 3.6.1 and 3.6.2

The evidence is partially applicable to people in the UK since all 4 studies were community-based (in the USA) and are feasible in UK settings.

[1] Riley 2002

[2] Riggs 2001

[3] Hatsukami 2005

[4] Hurt 2000

Evidence statements 3.8.1–3.8.3 Are there any unintended consequences from adopting a tobacco harm-reduction approach; for example, does it deter people from trying to cut down or abstain from smoking, temporarily or indefinitely?

3.8.1 There is strong evidence from 8 studies: 3 RCTs[1,2,3] (1[++][1] and 2 [+][2,3]), 3 quasi-RCTs[4,5,6] (all [+]) and 2 UBA(1 [+][7] and 1 [-][8]) reporting usage of NRT

for periods between 6 months and 5 years – to suggest that NRT is generally well-tolerated long term with severe side effects being relatively rare.

3.8.2 There is moderate evidence from 2 quasi-RCTs[6,9] (both [+]) that harm-reduction interventions do not deter smokers from wishing to quit.

3.8.3 There is weak evidence from a single (-) UBA[10] that frequent adverse events are reported by e-cigarette users. This finding supports the conclusions from review 1 that more evidence is required concerning the safety of e-cigarettes.

Applicability statement for evidence statements 3.8.1–3.8.3

Adverse event studies are likely to be applicable to the UK.

[1] Bollinger 2000

[2] Etter 2007

[3] Joseph 2008

[4] Batra 2005

[5] Kralikova 2009

[6] Wennike 2003

[7] Rennard 2006

[8] Jiménez-Ruiz 2002

[9] Carpenter 2004

[10] Polosa 2011

Evidence statement 4.1.4 Background environment factors described by smokers: social pressure to change smoking behaviour as a facilitator

Social pressure from friends, family or society in general to reduce, quit or implement smokefree homes and cars was described as a facilitator in 8 studies (1 [++][1], 6 [+][2–7],and 1 [-][8]). Smokers in 1 study were professionally supported to address their smoking behaviour[7].

[1] Bottorff 2009

[2] Bolliger 2000

[3] Richter 2002

[4] Stewart 2011

[5] Abdullah 2011

[6] Herbert 2011

[7] Phillips 2007

[8] Green 2005

Evidence statement 4.1.5 Background environment factors described by smokers: social support from friends, family and professionals as a facilitator

Social support from friends, family or professionals was perceived to be helpful in reducing smoking consumption in 3 (+) studies[1–3]. One study[1] involved surgery outpatients in receipt of a smoking telephone counselling intervention to reduce smoking consumption. Another study[2] involved low income women describing attitudes to smoking reduction or quitting and the third included adolescents describing ways in which they control smoking levels[3].

[1] Estabrooks 2010

[2] Stewart 2011

[3] Johnson 2004

Evidence statement 4.1.7 Background environment factors described by smokers: smoking restrictions promote smoking reduction

Eight studies (1 [++][1], 4 [+][2–5] and 3 [-][6–8]) included participants reporting that smoking restrictions helped them to reduce their smoking whether in: the home[1,2,6] at work[7] or in hospital[8].

[1] Jones 2003

[2] Abdullah 2011

[3] Herbert 2011

[4] Phillips 2007

[5] Robinson 2010

[6] Blackburn 2003

[7] Amos 1995

[8] Keizer 2009

Applicability statement for evidence statements 4.1.1–4.1.7

Just 7[-7] of the 21 studies on background environment factors described by smokers were based in the UK and two[8–9] from countries judged to have similar applicability to the UK.

[1] Amos 1995

[2] Beard 2011a

[3] Blackburn 2003

[4] Haddock 1997

[5] Jones 2011

[6] Phillips 2007

[7] Robinson 2010

[8] Hamilton 2000

[9] Thomsen 2009

Evidence statement 4.1.10 Smokers' attitudes, beliefs and experiences regarding THR efforts: smokers' perceived low ability in achieving smoking goals

A common theme across 3 studies (2 [+][1,2], 1 ungraded[3]) was that participants' lack of confidence in their ability to achieve their smoking goals was a barrier to changing smoking behaviour. These studies were conducted in potentially more vulnerable groups: pre-surgical patients[3]; low income women[1] and adolescents[2]. One study included smokers that were receiving professional support to address their smoking behaviour[3].

[1] Stewart 2011

[2] Johnson 2004

[3] Haddock 1997

Evidence statement 4.1.11 Smokers' attitudes, beliefs and experiences regarding THR efforts: perceived high nicotine dependence/smoking addiction

The addictive effect of smoking and the difficulty of resisting subsequent cravings were described as barriers to reducing smoking or implementing smokefree homes in 3 studies (1 [++][1], 1 [+][2] and 1 [-][3]). However, in a further (+) study[4], perceived dependence on smoking was not associated with quitting success among smokers who first cut down without professional support. The studies were conducted in general adult smokers[4], psychiatric inpatients[3] and parents and/or new fathers with children living at home[1,2]. One study included smokers that were professionally supported to address their smoking behaviour[2].

[1] Bottorff 2009

[2] Herbert 2011

[3] Keizer 2009

[4] Cheong 2007

Evidence statement 4.1.15 Smokers' attitudes, beliefs and experiences regarding THR efforts: smokers' own structuring and scheduling of smoking

Eight studies (1 [++][1] and 7 [+])[2–8] identified that smokers use structuring or scheduling smoking techniques to limit or reduce their cigarette consumption or temporarily abstain was a facilitator to change. These included: half-butting or smoking part of the cigarette[1–4]; inhaling less or not at all[2,4]; carrying only a set number of cigarettes[5]; borrowing cigarettes instead of buying[3]; cutting out unnecessary cigarettes for example, not chain smoking[2,3]; restricting the number of cigarettes smoked, where or when smoked[2,3,4,6] or delaying time

between cigarettes[1,2,3,7,8]. Three studies included smokers that were using NRT[2,4] or receiving behavioural interventions to achieve smoking goals[5].

[1] Bottorff 2009

[2] Beard 2011a

[3] Johnson 2004

[4] Okuyemi 2001

[5] Estabrooks 2010

[6] Nguyen 2009

[7] Poland 2009

[8] Robinson 2010

Evidence statement 4.1.17 Smokers' attitudes, beliefs and experiences regarding THR efforts: smokers' wish to protect children from smoke

Seven studies (2 [++][1,2] and 5 [+][3–7]) reported wishing to protect the health of their children as a facilitator to reducing their smoking[3] or in implementing smokefree homes[1,2,4–6] . Smokers in 1 study were receiving professional support to address their smoking behaviour[4].

[1] Bottorff 2009

[2]Jones 2011

[3] Nichter 2008

[4] Abdullah 2011

[5] Herbert 2011

[6] Phillips 2007

[7] Poland 2009

Evidence statement 4.1.18 Smokers' attitudes, beliefs and experiences regarding THR efforts: smokers' worries of harm to own health from smoking

Concern about the effect of tobacco on smokers' own health was a commonly reported facilitator across 13 studies (1 [++][1], 10 [+][2–11], 1 [-][12] and 1 ungraded[13]) looking at reducing smoking or implementing smokefree homes. Smokers described both worries of harm to their own health[2–7,13] and perceived benefits to health from reduction of smoking[1,8–10,12]. However 1 study found that worries about damage to health and quality of life from smoking or perceived benefits to health from quitting, were not associated with quitting success among smokers who first cut down[11]. Smokers' in 2 studies were receiving professional support to address their smoking behaviour[3,13].

[1] Bottorff 2009

[2] Bolliger 2000

[3] Estabrooks 2010

[4] Abdullah 2011

[5] Poland 2009

[6] Stewart 2011

[7] Hamilton 2000

[8] Beard 2011a

[9] Joseph 2005

[10] Shiffman 2007

[11]Cheong 2007

[12] Thomsen 2009

[13]Haddock 1997

Applicability statement for evidence statements 4.1.8–4.1.18

Of the 22 studies reporting smokers views regarding tobacco harm reduction, just 6 studies were solely conducted in the UK (1 [++][1], 4 [+][2–5],and 1 [-][6]), 1 (+) study in multiple countries including the UK[7] and 1 (+) study in a country deemed to have high applicability to the UK[8].

[1] Jones 2011

[2] Beard 2011a

[3] Haddock 1997

[4] Robinson 2010

[5] Phillips 2007

[6] Thomsen 2009

[7] Cheong 2007

[8] Hamilton 2000

Evidence statement 4.1.37 Smokers' attitudes, beliefs and experiences regarding e-cigarette use to assist THR: belief that e-cigarettes do not help with smoking craving

There was limited evidence from 1 cross-sectional survey (+)[1] that a small proportion of e-cigarette users (10%) believed that the product did not help with cravings in smokers aiming to cease or reduce smoking.

[1] Etter 2011

Evidence statement 4.1.42 Smokers' attitudes, beliefs and experiences regarding e-cigarette use to assist THR: e-cigarettes are perceived as less harmful than smoking

There was evidence from 2 cross-sectional surveys that a facilitator to change was the perception that e-cigarettes are less harmful to others or their own health than smoking by the majority of participants (1 [+][1] and 1 [-][2]) and perceived to help with withdrawal and craving symptoms of nicotine[2].

[1] Etter 2011

[2] Foulds 2011

Applicability statement for evidence statements 4.1.37–4.1.43

The evidence has limited applicability to the UK. One (+) study[1]included UK participants, although the majority were from USA and other countries. One (-) study[2] was conducted in a potentially biased sample of USA e-cigarette users attending an e-cigarette enthusiast meeting.

[1] Etter 2011

[2] Foulds 2011

Evidence statement 4.2.6

Five studies (2 [+][1,2], 3 [-][3-5]) examined barriers and facilitators encountered by mental health populations, from the perspective of patients and health workers. Common themes were boredom and a strong dependence on smoking[1,3,4] Many patients believed they were not offered adequate advice or assistance to address their smoking[1,4].This is supported in two studies by the relatively low proportion of mental health workers who considered smoking advice was an important part of their role[2,5].

Applicability statement for evidence statements 4.2.1–4.2.6 Three studies were based in the UK[1,2,6] and two studies were identified from Australia that is likely to have UK applicable evidence regarding adolescents[5] and psychiatric services[7].

[1] Ratschen 2010

[2] Ratschen 2009

[3] Keizer 2009

[4] Green 2005

[5] Ashton 2010

[6] Jones 2011

[7] Hamilton 2000

Evidence statement 5.1 Long-term NRT use

There is moderate evidence of long-term (12 months) NRT use in a small number of people who had quit smoking. The evidence is provided by 3 RCTs[1–3] (all [++]), 2 prospective cohort studies[4,5] (both [+]) and 1 (-) UBA[6]. This extended use is beyond the length of time that is recommended, treatment is usually between 8 and 12 weeks before the dose is reduced and eventually stopped. From the studies that provided 12-month follow-up data, 7% (range 3–11%) of individuals who had quit smoking were still using NRT. This evidence is for nasal spray[1,3,5] nicotine gum[2,6] and a range of NRT products[4].

[1] Blondal 1999

[2] Bjornson-Benson 1993; Murray 1996; Nides 1995

[3] Sutherland 1992

[4] Hajek 2007

[5] Schneider 2003

[6] Hatsukami 1993

Evidence statement 5.2 Long-term NRT use

There is moderate evidence that most long-term (12 months or over) use of nicotine gum or spray is within recommended dosage limits. The evidence is provided by 2 RCTs[1,2] (both [++]), 1 (+) prospective cohort study[3] and 2 cross-sectional surveys[4,5] (both [–]). For this dosage evidence participants in 3 studies[1,2,3] had quit smoking but the smoking status was not reported for participants in the other two studies[4,5].

[1] Blondal 1999

[2] Bjornson-Benson 1993; Murray 1996

[3] Schneider 2003

[4] Hughes 2004

[5] Johnson 1991

Evidence statement 5.3 Long-term NRT use

There is moderate evidence from 1 (++) RCT[1]and 1 (+) prospective cohort study[2] that nicotine dependence at baseline is a predictor of long-term NRT use at 12 months[1,2]. The data was from participants who had all quit smoking.

[1] Bjornson-Benson 1993

[2] Hajek 2007

Applicability statement for evidence statements 5.1–5.3

This evidence is directly applicable to people in the UK who attempt to quit smoking abruptly. Of the studies that reported NRT use at 12 months in former smokers, 2 studies were conducted in the UK (1 [++][1] and 1 [+][2]) and 3 were conducted in community settings (2 [++][3,4] and 1 [-][5]).

[1] Sutherland 1992

[2] Hajek 2007

[3] Blondal 1999

[4] Bjornson-Benson 1993; Murray 1996; Nides 1995

[5] Hatsukami 1993

Evidence statement 5.4 Long term e-cigarette use

There is no evidence of e-cigarette use for periods of 12 months or longer in individuals who quit smoking abruptly and insufficient evidence of the pattern of use.

Evidence statement 5.5 Long term e-cigarette use

There is weak evidence from 3 cross-sectional surveys (1 [+][1] and 2 [-][2,3]), possibly of e-cigarette enthusiasts, that e-cigarettes are used for 12 months or longer. Only 1 study[3] reports that some individuals have completely replaced cigarettes with e-cigarettes. There was no evidence related to the dosage used by long term e-cigarette users.

[1] Etter 2011

[2] Foulds 2011

[3] Heavner 2010

Evidence statement 5.6 Long term e-cigarette use

No evidence was identified on predictors or purchase patterns of e-cigarette use.

Applicability statement for evidence statements 5.4–5.6

The evidence is only partially applicable to people in the UK who quit smoking abruptly. This is because e-cigarettes are not licensed for smoking cessation. There is evidence from 3 cross-sectional surveys (1 [+][1], 2 [-][2,3]) in which participants were possibly e-cigarette enthusiasts[3]. However, the evidence does indicate that e-cigarettes are used in the UK[1,2] though it does not indicate if any of the e-cigarette users quit smoking abruptly.

[1] Etter 2011

[2] Heavner 2010

[3] Foulds 2011

Additional evidence

- Expert paper 1: 'Electronic cigarettes: nicotine delivery, efficacy in smoking cessation and potential for harm reduction'
- Expert paper 2: 'The prevalence and "effectiveness" of the use of NRT for smoking reduction and temporary abstinence among English smokers'
- Expert paper 5: 'Smokefree mental health review'.
- Expert paper 6: 'Prison service tobacco policy'.
- Expert paper 8: 'E-cigarettes: views from UK smoking cessation practitioners' and 'E-cigarette use in Great Britain: 2010 and 2012'.

Cost effectiveness review

The systematic search identified 2 studies that met the inclusion criteria. Only 1 study was of good quality and applicable for use in the development of

evidence statements. No evidence of the economic impact of cut-down to quit (CDTQ) was identified in this review and the authors developed their own cost-effectiveness model.

Economic modelling

Five co-morbidities (lung cancer, chronic obstructive pulmonary disease, stroke, myocardial infarction and coronary heart disease) were included in the model, as well as all-cause mortality.

The model was designed to assess a wide range of potential interventions and scenarios. Seven key quit or reduce scenarios, using various delivery routes, were assessed. A total of 21 scenarios (that is, individual or multi-component interventions) were modelled in the main analysis. The comparator in all cases was ‘no intervention’.

Of the scenarios which sought to help someone quit or reduce their consumption, 3 were cost saving and 12 were highly cost effective. The latter ranged from an estimate of £437 per quality-adjusted life year (QALY) to £8464 per QALY. Of the scenarios based around temporary abstinence, 5 were highly cost effective and 1 showed no benefit. The former ranged from an estimated £765 per QALY to £8,464 per QALY.

A sensitivity analysis was carried out of abrupt quitting supported by long-term nicotine-containing products. This estimated that the use of nicotine-containing products was cost effective for nearly all the scenarios. (Effectiveness of quit rate varied from 0–20%; duration of use of nicotine-containing products varied from 6 months to 10 years.) Only when nicotine-containing products were provided for more than 5 or 10 years and the quit rate was less than 6% did the costs potentially outweigh the benefits.

A supplementary analysis assumed there were no benefits from smoking less (in terms of QALYs and co-morbidities), other than an increased likelihood of quitting at 6 months. In such a case, the costs potentially outweigh the benefits when the reduction rate is 6% or less and someone uses a nicotine-containing product for 12 months or longer. The cost of extending NCP use to

2 years may be outweighed by the benefits, if a reduction of 20% or more is achieved.

It was anticipated that there may be some trade-off between the number of people quitting and the number who reduce the amount they smoke, according to the approach used. For example, by offering services to help people to reduce their smoking intake, it is plausible that some people who may otherwise have chosen (or attempted) to quit decide not to.

An analysis of the benefits associated with either quitting smoking or reducing smoking for a person aged 50 was undertaken. The model estimated that an intervention that achieves 1 additional ‘reducer’ will provide an additional 0.45 QALYs. It will also save the NHS approximately £767 over the person’s lifetime. An intervention that achieves 1 quitter, however, will gain 0.84 QALYs and will save the NHS £1,412 over the same period.

In other words, the benefits of reducing are approximately half those of quitting. So, for each ‘quitter’ drawn into reducing instead, any intervention would need to get at least 2 more people to reduce their smoking to offset that loss. The supplementary analysis (see above) showed that, for each potential quitter lost, 6 more ‘reducers’ would be needed to offset the lost benefits.

Clearly, it would be better to gain 1 quitter rather than 1 reducer. However, by offering services to help people to smoke less, a greater population may present for treatment, leading to additional benefits to society.

Appendix D Gaps in the evidence

The Programme Development Group (PDG) identified a number of gaps in the evidence related to the programmes under examination, based on an assessment of the evidence and expert comment. These gaps are set out below.

1. Data on the pharmacokinetics of new nicotine-containing products such as electronic cigarettes.
2. Data on the toxicity of nicotine replacement therapy (NRT) and nicotine-containing products, using smoking as a comparator, rather than a placebo.
3. Data on the safety of using licensed nicotine-containing products among different subgroups.
4. Data on the long-term psychological effects of nicotine use in relation to smoking status (smokers who have not cut down and people who have reduced the amount they smoke).
5. Data on the degree of misuse and accidental use of licensed nicotine-containing products (including NRT). For example, there is a lack of data on accidental ingestion of refill solutions by children.
6. Data on the extent to which compensatory smoking occurs when someone is trying to quit or cut down (such as deeper inhalation or smoking more of the cigarette). This includes data on whether the behaviour persists over time and whether the degree of compensation differs across groups (by degree of nicotine addiction or amount of cigarettes smoked).
7. Data on the effectiveness and cost effectiveness of the following in relation to helping people cut down in order to quit or smoke less:
    - behavioural support alone
    - different combinations of licensed nicotine-containing products
    - other nicotine delivery systems

- group support models as part of a ‘cut down to quit’ approach
- consumer-driven harm reduction, such as social norms and product demand
- different initiatives to prevent relapse.

8. Data on:
    - services offering harm-reduction strategies
    - level of compliance with different tobacco harm-reduction strategies
    - relapse rates and whether smoking increases following a relapse
    - tandem use of NRT and cigarettes
    - long-term health effects of harm-reduction strategies
    - behavioural effects of harm-reduction strategies
    - alcohol use and its association with the motivation to quit and someone’s motivators and behaviour while trying to quit or smoke less.
9. GPs’ and other prescribers’ attitudes towards, and views on, the barriers to and facilitators for using licensed nicotine-containing products.
10. Health professionals’ and service users’ views about the barriers to, and facilitators for, implementing tobacco harm-reduction strategies.
11. Service users’ and providers’ views on the impact of offering free NRT on the success of tobacco harm-reduction strategies.

Appendix E Supporting documents

Supporting documents include the following.

- Evidence reviews:
    - Review 1: ‘Safety, risk and pharmacokinetics profiles of tobacco harm reduction technologies’
    - Review 2: ‘The effectiveness of tobacco harm reduction approaches with the intention of quitting (that is, cutting down to quit or reduction to stop smoking), with and without assistance’
    - Review 3: ‘The effectiveness of long-term harm reduction approaches without the prior intention of quitting’
    - Review 4: ‘Barriers and facilitators to implementing tobacco harm reduction approaches, including user and provider perspectives’
    - Review 5: ‘Long term use of non-tobacco nicotine containing products in individuals who have quit smoking abruptly’.

- Review of economic evaluations: ’A rapid review of economic evidence on tobacco harm reduction strategies’.

- Economic modelling: ‘An economic evaluation of different interventions to promote tobacco harm reduction’ and a supplementary analysis entitled ’An economic evaluation of different interventions to promote tobacco harm reduction: supplementary report’.

- Expert papers:
    - Expert paper 1: ‘Electronic cigarettes: nicotine delivery, efficacy in smoking cessation and potential for harm reduction’
    - Expert paper 2: ‘The prevalence and ”effectiveness” of the use of NRT for smoking reduction and temporary abstinence among English smokers’

- Expert paper 3: ‘Routes to quit’
- Expert paper 4: ‘Harm reduction – views from a smokers' panel’
- Expert paper 5: ‘Smokefree mental health review’
- Expert paper 6: ‘Prison service tobacco policy’
- Expert paper 7: ‘Harm reduction: mapping the ripples’
- Expert paper 8: ‘E-cigarettes: views from UK smoking cessation practitioners’ and ‘E-cigarette use in Great Britain: 2010 and 2012’.

For information on how NICE public health guidance is developed, see:

- ‘Methods for development of NICE public health guidance (second edition, 2009)’
- ‘The NICE public health guidance development process: An overview for stakeholders including public health practitioners, policy makers and the public (second edition, 2009)’