A guide to smoking cessation in Scotland 2010

Addendum on tobacco harm reduction (2014)

This addendum is intended to be used in conjunction with *A guide to smoking cessation in Scotland 2010*. It contains recommendations on tobacco harm-reduction approaches while emphasising the principle of the preferred outcome of quitting smoking and nicotine use entirely, and the delivery of support for smoking cessation to achieve this. Note that these recommendations only refer to the general population and do not apply to pregnant women or those planning a pregnancy, and there are others for whom abrupt smoking cessation is particularly important (for example, pre-operative smoking cessation in high-risk groups). It also contains advice on practical issues around the use of unlicensed nicotine-containing products (such as electronic cigarettes) for clients accessing smoking cessation services.

Recommendations:

Organisations/bodies responsible for public health, tobacco control and smoking cessation services should:

- ensure that investment in harm-reduction approaches does not detract from, but supports, enhances, and extends the reach and impact of, smoking cessation services in line with existing recommendations in *A guide to smoking cessation in Scotland 2010*

- advise **all smokers** that stopping abruptly in one step, in line with the existing recommendations in *A guide to smoking cessation in Scotland 2010*, gives the best chance of successful long-term abstinence from smoking, and the greatest health benefits

- offer or advocate harm-reduction approaches for smokers who are highly dependent on nicotine and who currently do not feel ready/able/willing to quit abruptly in one step, as follows:

  - **for smokers who want to stop smoking entirely but who do not want to, or feel unable to, give up nicotine:** advocate ongoing use of licensed nicotine-containing products[1], consider offering and advise on use of one or more licensed nicotine-containing product(s) to be used for as long as needed

1. 'Licensed nicotine-containing products' refers to products containing nicotine that have received marketing authorisation as a smoking cessation or smoking harm-reduction product by the UK medicines regulator, the Medicines and Healthcare products Regulatory Agency (MHRA) – Nicotine Replacement Therapy (NRT) products. This process ensures these products meet particular standards of consistent manufacture and quality, are effective, and deliver nicotine safely.

after cessation to prevent relapse to smoking, providing such products for a reasonable time-limited duration where applicable and subject to good clinical judgement (taking into account factors like the client's history of quit attempts and record of engagement with cessation services)

- **for smokers who want to stop smoking entirely but who do not want to do it abruptly in one step:** offer a 'cut down to quit' approach in a range of settings, with behavioural support, with or without the use of licensed nicotine-containing products (but preferably with them to maximise chances of success), develop appropriate referral and treatment pathways, and offer follow-up appointments to review progress and provide support

- **for smokers who want or need to abstain from smoking temporarily, but who do not want to stop smoking entirely:** advocate a temporary abstinence approach, offering it and providing licensed nicotine-containing products for temporary abstinence in some settings/circumstances such as situations where abstinence is involuntary e.g. admission to hospital or to closed institutions such as prisons (for a reasonable, time-limited duration). Consider offering and providing it for temporary abstinence in other settings where abstinence from smoking is required (e.g. to avoid exposing others to second-hand smoke) but smoking outside may be impractical/impossible. In cases where licensed nicotine-containing products are not provided to the smoker, signpost them to pharmacies that sell (and provide advice on how to use) licensed nicotine-containing products approved for this purpose

- **for smokers who want to make reductions in tobacco consumption but who do not want to stop smoking entirely at present:** explain about smoking reduction (see below) and signpost to pharmacies that provide advice on the use of, and who sell, licensed nicotine-containing products approved for this purpose

- **for all the above harm-reduction approaches for highly nicotine-dependent smokers who do not want to or feel unable to quit abruptly in one step:** discuss with smokers the differing health benefits and merits of each approach. This includes clarifying that 'cutting down' on cigarette consumption alone has unclear health benefits (although smokers who cut down are more likely to stop smoking eventually); clarifying that smoking cessation improves health far more than continuing smoking at a reduced rate; and informing them of the different licensed nicotine-containing products available that will improve their chances of success and of how pharmacies can advise on their use in these ways

- **for pregnant smokers, smokers planning a pregnancy, and others for whom abrupt smoking cessation is particularly important (for example, pre-operative smoking cessation in high-risk groups):** advise smoking cessation abruptly in one step in line with the guidance given in *A guide to smoking cessation in Scotland 2010*, encouraging them to quit completely rather than delay their quit attempt or attempt to reduce smoking

- raise awareness of the safety of licensed nicotine-containing products (those regulated by the UK Medicines and Healthcare products Regulatory Agency). Explain how the use of one or more licensed nicotine-containing products as a harm-reduction measure can reduce the risk of illness and death (to smokers themselves, and to others by reducing or eliminating second-hand smoke by reduction or cessation respectively), and how their long-term use as a complete substitute for tobacco is always safer than continued smoking

- advise users of, or those enquiring about, unlicensed nicotine-containing products such as electronic cigarettes that, in contrast to licensed pharmacotherapies, there is little direct evidence available on their quality, effectiveness and safety, but that current expert opinion on the limited evidence available is that they are expected to be considerably less hazardous than smoking

- use clinical judgement regarding unlicensed nicotine-containing products in a manner that:
  - does not dissuade or prevent the users of such products from receiving and benefiting from evidence-based smoking cessation support
  - emphasises that, while the use of licensed nicotine-containing products over unlicensed ones is strongly preferable, the priority should be to prevent relapse to smoking; therefore users of unlicensed products should not be advised to discontinue use of such products if it risks relapse to smoking

Overview of tobacco harm-reduction approaches

The following key messages from existing guidelines[2] still stand:

- Smoking cessation is the best way to reduce tobacco-related illness and death.
- Smoking cessation abruptly in one step is the best option, where possible, as it:
  - is the best way to improve the health of a smoker and of those around them
  - offers the best chance of smoking cessation long-term
  - is least costly to provide.
- Group or 1:1 behavioural support from smoking cessation services (SCSs) plus pharmacotherapy (nicotine replacement therapy (NRT), bupropion, or varenicline) is the best way of achieving long-term success in smoking cessation.

This approach has the strongest supporting evidence, will provide the greatest health benefits and so is the 'gold standard' for smoking cessation. Health Boards should continue to provide smoking cessation abruptly in one step through SCSs with behavioural support and pharmacotherapy.

Rationale and context for harm reduction

For highly nicotine-dependent smokers who currently do not feel ready/able/willing to stop smoking or nicotine use completely (or to quit abruptly in one step), or who need to be abstinent from tobacco temporarily, there are other ways of reducing tobacco-related harm:

- **Smoking cessation, using one or more licensed nicotine-containing products for as long as necessary to prevent relapse**
  Health Boards should provide this, for a reasonable duration, to clients who set a quit date and attend support through the SCS and who are feel they are unable or are unwilling to give up nicotine entirely. Health Boards should consider subject to clinical judgement (e.g. based on quitting history or whether client has attended SCSs) whether to provide licensed nicotine-containing products for long-term use for others (e.g. as relapse prevention for ex-smokers who have quit outside of SCSs).
- **Cutting down prior to quitting smoking***
  Health Boards should provide this through SCSs (i.e. with behavioural support), along with appropriate referral and treatment pathways.
- **Smoking reduction with no intention to quit***
  Health Boards should signpost to pharmacies that provide advice on using licensed nicotine-containing products for this approach and who sell licensed nicotine-containing products approved for this purpose. If a smoker subsequently becomes ready to set a quit date, then they should be advised to join services in line with national smoking cessation guideline recommendations.
- **Temporary abstinence***
  Health Boards should supply and fund licensed nicotine-containing products for temporary abstinence in some situations; e.g. where abstinence is involuntary such as admission to hospital or to closed institutions such as prisons (for a reasonable,

2. NHS Health Scotland and ASH Scotland (2010). *A Guide to smoking cessation in Scotland 2010*. Edinburgh: NHS Health Scotland.

time-limited duration). They should consider offering and providing licensed nicotine-containing products for temporary abstinence in other settings (e.g. in the home to avoid exposing others to second-hand smoke, particularly where there may be difficulties in getting outside to smoke). When it is not possible to fund provision of licensed nicotine-containing products to the smoker for this purpose, the concept of temporary abstinence should be explained to them and they should be signposted to pharmacies for purchase of, and advice on, using licensed nicotine-containing products for this purpose. If a smoker subsequently becomes ready to set a quit date, then they should be advised to join services in line with national smoking cessation guideline recommendations.

* with or without the use of one or more licensed nicotine-containing products

Such approaches are consistent with Scottish Government tobacco prevalence and performance targets[3] and thus where publicly funded support should focus. These approaches may help to reach the 38% and 29% of smokers in the two most deprived quintiles who continue to smoke (compared to 23% in the general population). They offer additional options to those for whom traditional smoking cessation services and approaches (smoking cessation abruptly in one step – the preferred approach) have not engaged or succeeded. This widening of options could potentially make a valuable contribution to narrowing the gap in health inequalities.

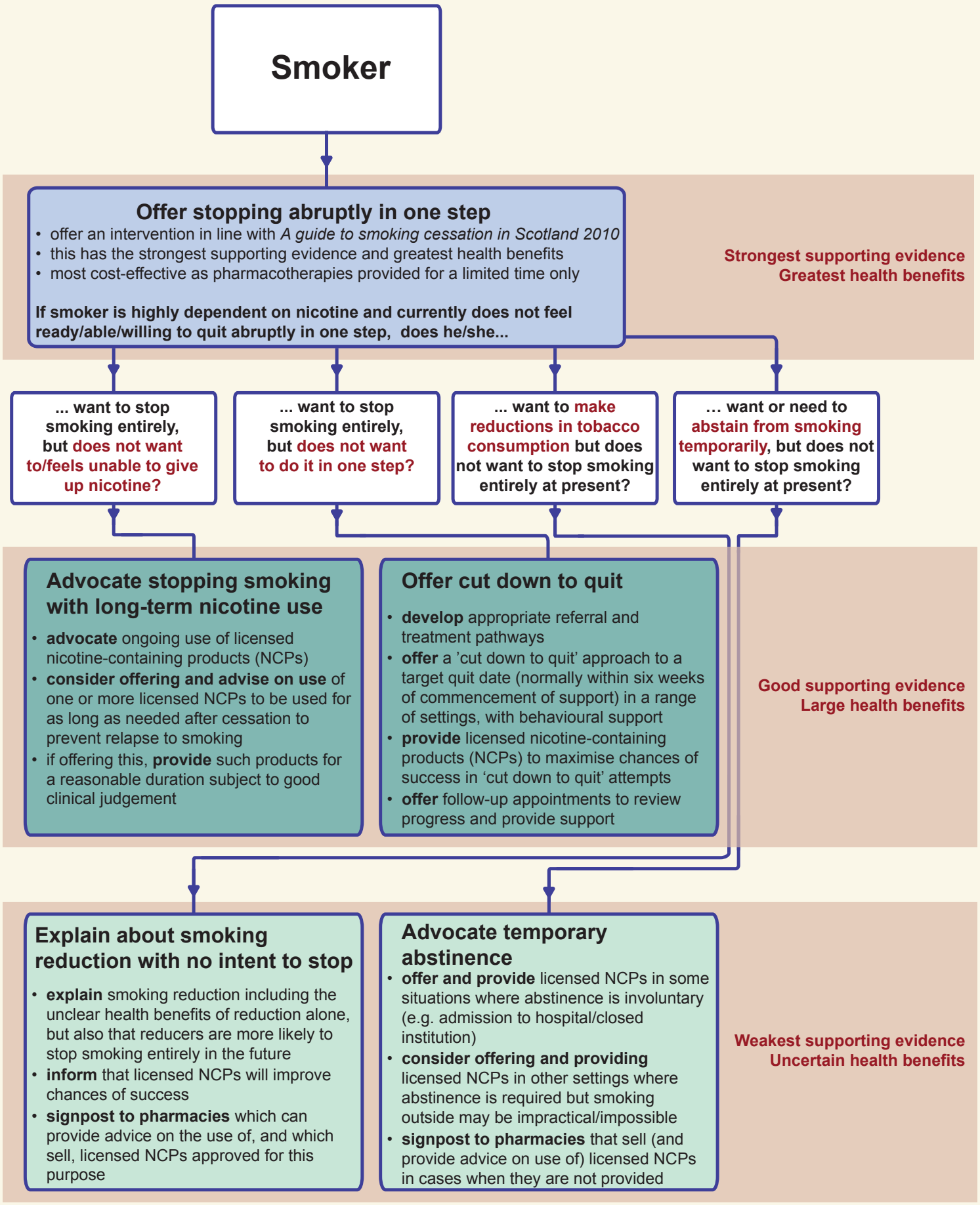
The four harm-reduction approaches are not equivalent in terms of the health benefits they provide. They differ in their effectiveness, in terms of success in achieving reduction or cessation, and cost-effectiveness. The recommendations above reflect the priority that smoking cessation services in Scotland are expected to place on each, informed by evidence. Health Boards should take the following issues into account, and identify with their smoking cessation service and prescribing colleagues whether and how they wish to consider and/or fund those approaches with less supporting evidence (i.e. smoking reduction with no intention to quit, temporary abstinence).

Services should prioritise the delivery of approaches with the strongest evidence of health benefits, effectiveness and cost-effectiveness. They should offer harm-reduction approaches to smokers by determining what the most health-improving intervention is that is achievable for them, providing the intervention and support where appropriate, or raising awareness of these approaches and signposting to sources of advice (i.e. pharmacies where support such as advice on the use of licensed nicotine-containing products can be obtained and these products can be purchased).

The pathway figure, on the next page, provides a graphic representation of the four harm-reduction approaches, based on the strength of evidence for health improvement, safety and effectiveness evidence of each.

3. Scottish Government (2013). *Creating a Tobacco-Free Generation: A Tobacco Control Strategy for Scotland.* Edinburgh: Scottish Government.

Figure: Recommended pathway for offering tobacco harm-reduction approaches in Scotland, and strength of evidence for different approaches



Note: 'Licensed nicotine-containing products' (NCPs) refers to products containing nicotine that have been authorised by the UK medicines regulator, the Medicines and Healthcare products Regulatory Agency (MHRA). For guidance on unlicensed nicotine products such as electronic cigarettes, see page 13.

Details on tobacco harm-reduction approaches

These methods of reducing tobacco-related harm can provide an alternative for those highly nicotine-dependent smokers who are unable or unwilling to quit smoking in one step, or to be completely abstinent from nicotine. While the importance of complete abstinence from smoking as the ultimate aim needs to be retained, these approaches may be particularly suitable for highly dependent smokers, those who are unlikely to engage with, or use, SCSs that focus on abrupt smoking cessation, or those who need to be abstinent from smoking temporarily such as in prisons or secure mental health units, smoke-free NHS or local authority settings or enclosed workplaces.

These methods may involve the continued use of nicotine as either a partial or complete, temporary or long-term substitute for smoking. In some instances (cutting down to quit), there is evidence for the effectiveness of behavioural support in conjunction with continued use of nicotine, while in other instances there is a lack of evidence for the effectiveness of behavioural support in conjunction with nicotine use. However, engaging people who are attempting smoking reduction or temporary abstinence with the future offer of behavioural support if/when they become ready to set a quit date may potentially lead to their consideration of setting a quit date and ultimately quitting.

It is safer to use licensed nicotine-containing products than to continue smoking, even with long-term use of such products. The harm caused by smoking (morbidity and mortality) is caused almost exclusively by the other components in tobacco smoke which are toxic and carcinogenic such as carbon monoxide and tar, rather than by the addictive ingredient nicotine[4]. As licensed nicotine-containing products deliver nicotine more slowly than cigarettes and have fewer other potentially addictive chemicals, current licensed nicotine-containing products are less likely to maintain dependence than smoking. Their quality, safety and efficacy profile is assured, and they are an effective and safe way of reducing the harm from tobacco for the smoker and for those around them through reduction or elimination of second-hand smoke (for smoking reduction and cessation respectively).

Smoking cessation with long-term use of licensed nicotine products

Use of licensed nicotine-containing products long-term to prevent relapse to smoking (in smokers who do not want or feel unable to give up nicotine) is strongly preferable to risking relapse and, if successful, could potentially bring large health benefits.

As licensed nicotine-containing products are considered very safe in comparison to continued smoking, their long-term use as an exclusive substitute for tobacco use is safer than continued smoking or risking relapse. Research studies have directly tracked the health outcomes of long-term (up to five years) use of licensed nicotine-containing products, and found that they are safe to use for these extended durations of treatment. Direct evidence for their use beyond five years is lacking; however, expert opinion is that lifetime use will be considerably safer than smoking.

4. Royal College of Physicians (2007). *Harm reduction in nicotine addiction: helping people who can't quit*. A report by the Tobacco Advisory Group of the Royal College of Physicians. London: RCP.

Therefore, longer-term provision of licensed nicotine-containing products within reason – and only for those who feel unable or do not want to be completely abstinent from nicotine – should be considered for the purposes of minimising relapse.

There is, however, mixed evidence and gaps in the evidence regarding the effectiveness of harm-reduction methods such as the long-term use of NRT. Studies of extended treatment with NRT (that is, providing extended treatment to **all** smokers for harm-reduction purposes) are limited and inconclusive – more studies are needed (with oral NRT, two small trials had no effect albeit low compliance whereas two other trials found a significant effect[5]; other studies found no benefit for using patches beyond eight weeks[6]).

As the evidence on the general effectiveness of extended treatment with NRT is limited and longer-term provision of NRT has cost implications, longer-term provision should not be provided routinely as a matter of course to **all** smokers who have recently quit or are going through a quit attempt, either within or outside of smoking cessation services.

Clinical judgement should be exercised with regard to whether to provide NRT for longer-term use based on factors such as:

- whether the client reports that, or it appears likely that, they would be at high risk of relapse if NRT provision were discontinued following normal treatment duration and they perceive the continued use of the products to be helpful
- the degree of engagement the client has had with the service
- how recent the quit attempt was and whether they have been using NRT for this purpose already
- the duration of extended treatment and associated prescribing costs.

Summary:

- **Health:** Using licensed NCPs to prevent relapse to smoking, if effective, could potentially bring large health benefits.
- **Effectiveness:** Studies of long-term use of licensed NCPs (based on studies of NRT) in the general population are limited and inconclusive.
- **Safety:** Long-term use of licensed NCPs (based on studies of NRT) is safe for up to five years although evidence beyond this is lacking; however, expert opinion from NICE guidance is that lifetime use will be considerably safer than smoking.

Cutting down prior to quitting smoking

There is evidence that:

- NRT is effective in helping people reduce cigarette consumption in the short term, and cease all cigarette use
- smokers who reduce cigarette consumption prior to quitting through use of NRT or behavioural support (as opposed to stopping abruptly on a set date) have similar cessation outcomes with cutting down to quit as with abrupt cessation.

5. Hajek P, Stead LF, West R et al. (2013). Relapse prevention interventions for smoking cessation. *Cochrane Database of Systematic Reviews*, Issue 8. Art. No.: CD003999. DOI: 10.1002/14651858.CD003999.pub4.
6. Stead LF, Perera R, Bullen C et al (2012). Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews*, Issue 11. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub4.

Given the similar success rates to smoking cessation abruptly in one step, this approach can be expected to provide large health benefits.

There is insufficient evidence to provide more precise details on which smokers would benefit from this approach, the optimal components of behavioural support or specific details of schedules for cutting down to quit. However, expert opinion from recent NICE harm-reduction guidance suggests that when helping people who are cutting down prior to stopping smoking, the quit date should normally be within six weeks of the start of initiation of support.

This may be an option for a 'shared care' approach e.g. behavioural support provision from SCSs supplemented with advice on NRT use in this way when collecting prescription supplies of the licensed nicotine-containing products from pharmacies.

Summary:
Health: Large health benefits once smoking cessation has occurred.
Effectiveness: Cutting down prior to quitting has similar success rates to stopping smoking abruptly; licensed NCPs (based on studies of NRT) are effective for reduction (short-term albeit not sustained) and for cessation. Insufficient evidence regarding specific components of behavioural support and optimal schedules for cutting down.
Safety: Despite mixed/gaps in the evidence around combined use of NRT and cigarettes, likely to be safe so long as concurrent NRT use and cigarette use is of short duration.

Smoking reduction with no intention to stop smoking

There is uncertainty over whether reducing smoking alone (without complete cessation) has any health benefits. Smokers often compensate for reduced cigarette consumption by taking more or deeper puffs of each remaining cigarette smoked, reflected in cigarette reduction not being matched by proportionate biochemical reductions. Additionally, reductions do not result in any clear health benefits, suggesting that health improvement does not correspond directly with reduction – for some diseases caused by smoking (such as some cardiovascular diseases), the relationship between cigarette consumption and disease is not linear; e.g. a small amount of smoking increases risk of heart disease by a substantial amount.

Reductions are generally not long-term; i.e. as measured at six-month follow-up or beyond. There is no evidence to recommend behavioural support (e.g. motivational interviewing, counselling, telephone support) to support smoking reduction. There is also mixed evidence and gaps in the evidence around the combined use of NRT and cigarettes and mild/moderate adverse effects when NRT is used for smoking reduction.

However, there is some preliminary evidence that those who reduce the amount they smoke – even if they were not originally planning to quit – are actually more likely to go on to quit, particularly if they use a licensed nicotine-containing product while they

reduce and which may also help reduce compensatory smoking.

Therefore, if an individual is unable or unwilling to engage in other more beneficial forms of behavioural change regarding their smoking (cutting down with the intent of quitting or complete cessation with long-term use of a licensed nicotine-containing product), it is preferable for them to reduce smoking, rather than continue to smoke at their current level, in light of the increased likelihood that they may go on to quit. For such smokers, there may be merit in offering time-limited support to promote the likelihood that an individual will eventually achieve abstinence from tobacco use.

Summary:
Health: Unclear evidence of whether there are health benefits for reduction alone without cessation.
Effectiveness: Reductions tend to be short-term only rather than sustained. No evidence to recommend behavioural support for this purpose.
Safety: Mixed evidence and gaps in the evidence around the combined use of NRT and cigarettes, and mild/moderate adverse effects when NRT is used for smoking reduction.
Other: Reducers may be more likely to quit ultimately, so some behaviour change is preferable to none.

Temporary abstinence

In contrast to the other harm-reduction approaches, the purpose of temporary abstinence is not to seek to make lasting changes in behaviour, but instead to manage smoking withdrawal symptoms in situations where abstinence is required either involuntarily (e.g. upon admission to hospital or a closed institution) or voluntarily (e.g. to reduce smoking in the home environment and thereby avoid smoking around children or other household members). Given its temporary nature, this approach would not be expected to offer lasting health benefits on its own, although it may provide the opportunity of engagement with the individual around a more lasting cessation or reduction attempt. As with smoking reduction with no intent to quit, there is mixed evidence and gaps in the evidence regarding this harm-reduction method (e.g. safety and effectiveness of the combined use of NRT and cigarettes).

However, as it is considered safer to use licensed nicotine-containing products instead of smoking, those who need to be temporarily abstinent from smoking can be advised that they should use licensed nicotine-containing products to manage their abstinence and relieve withdrawal symptoms.

Unless it triggers a more sustained behaviour change, there may be little health benefit to the smoker themselves in being only temporarily abstinent (although there may be benefits to others through, for example, second-hand smoke reduction, positive role-modelling). However, engagement with services and/or pharmacies (for purchase/supply of licensed nicotine-containing products) around temporary abstinence could provide an opportunity to engage in more sustained behaviour change around cessation or reduction at a later date. Time-limited support of this type may help to eventually

achieve abstinence from smoking, especially if the smoker is confined to places covered by the smoke-free legislation.

Summary:
Health: Unlikely to have lasting health benefits for the individual concerned; however, it is better to use licensed nicotine-containing products rather than continue to smoke. There are potential health benefits to others through second-hand smoke reduction.
Effectiveness: Evidence for the effectiveness of NRT even without behavioural support.
Safety: Mixed evidence and gaps in the evidence around the combined use of NRT and cigarettes, long-term use of NRT, and mild/moderate adverse effects when NRT is used for smoking reduction, albeit these may not be applicable depending on the extent of cigarette use and NRT use.
Other: May provide opportunities of engagement for smoking cessation/reduction in the future.

Pregnant smokers, smokers planning a pregnancy, and other high-risk population sub-groups

The evidence on harm-reduction approaches for smoking does not include specific sub-populations such as pregnant women and only applies to the general population. Pregnant women should be encouraged to quit completely rather than delay their quit attempt. In addition, in light of some mixed evidence around NRT use by pregnant women and some mixed evidence around NRT use for harm reduction for the general population, pregnant women should receive interventions in line with those given in *A guide to smoking cessation in Scotland 2010*. This may also apply to other groups at high risk and for whom complete abstinence from smoking is particularly important – for example, pre-operative smoking cessation and those suffering from smoking-related (induced or exacerbated) diseases.

Role of pharmacies in tobacco harm reduction

The national community pharmacy smoking cessation scheme offers evidence-based smoking cessation support in line with the definition of specialist/intensive smoking cessation support[7] and as per national specification. Pharmacies also sell licensed nicotine-containing products that can be used for the harm-reduction approaches described in this addendum. Pharmacies should advise all smokers enquiring about pharmacy smoking cessation services or purchasing licensed nicotine-containing products that quitting smoking in one step gives the best chance of long-term abstinence from smoking. For smokers following the harm-reduction approaches in this addendum, pharmacies should provide information to smokers about how to use licensed nicotine-containing products effectively to achieve their harm-reduction goals, and then if a smoker subsequently becomes ready to set a quit date, they should be advised to join services in line with national smoking cessation guideline recommendations, either non-pharmacy specialist services or pharmacy services as per national pharmacy scheme specification.

7. NHS Health Scotland (2012). Definition of specialist/intensive smoking cessation support, revised by database project board. Available from: www.healthscotland.com/documents/4661.aspx

Cost-effectiveness of tobacco harm-reduction approaches

Economic modelling conducted as part of the NICE process indicates that, of a wide range of harm-reduction approaches examined, most were highly cost-effective compared to 'no intervention' (the one exception being temporary abstinence with no support). This also included three interventions aimed at quitting or reducing tobacco consumption that were actually cost-saving. However, harm-reduction approaches are less cost-effective than abrupt smoking cessation in one step.

A consideration in NICE's analysis was that offering a smoking reduction approach could potentially discourage smokers who would otherwise have stopped entirely, to reduce instead (conferring less health benefits, possibly none). As there are uncertainties in whether smoking reduction alone confers health benefits, economic modelling was run for two different scenarios. Assuming reduction confers some health benefit (in addition to increasing the likelihood of ultimate smoking abstinence), two 'reducers' would be required for each person who decides to reduce the amount they smoke, instead of stopping outright; results indicated that smoking reduction was only half as cost-effective as smoking cessation. Assuming reduction alone confers zero health benefit (the only benefit being increased likelihood of subsequent complete abstinence), six 'reducers' would be required to offset the lost benefits of one quitter; results also indicated reductions of 20% or more in tobacco consumption would be required for the benefits to outweigh the costs of providing licensed nicotine-containing products for two years. Assuming a lower reduction rate of 6% or less, costs could outweigh benefits if licensed nicotine-containing products were provided for 12 months or longer. The full details of the NICE economic modelling are available at: http://guidance.nice.org.uk/PH45/SupportingEvidence

Addressing the gaps in the evidence on harm-reduction approaches

Further gaps in the evidence identified by NICE that could be assisted by research and practice in Scotland – for example, through the development of pilot projects or 'action research' approaches that have a suitably robust evaluation component – are available on the NICE website, at: http://publications.nice.org.uk/tobacco-harm-reduction-approaches-to-smoking-ph45/gaps-in-the-evidence

Key source material for this addendum

Unless otherwise indicated, all recommendations above have been drawn from one or more of the following:

- NHS Health Scotland and ASH Scotland (2010). *A guide to smoking cessation in Scotland*. NHS Health Scotland, Edinburgh.
- National Institute for Health and Care Excellence (NICE) (2013). Public Health Guidance 45 - *Tobacco harm-reduction approaches to smoking.*
- Stead, L.F., Lancaster, T., (2010). Interventions to reduce harm from continued tobacco use, in: The Cochrane Collaboration, Stead, L.F. (Eds.), *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd, Chichester, UK.
- Lindson-Hawley, N., Aveyard, P., Hughes, J.R., (2012). Reduction versus abrupt cessation in smokers who want to quit, in: The Cochrane Collaboration, Lindson-Hawley, N. (Eds.), *Cochrane Database of Systematic Reviews.* John Wiley & Sons, Ltd, Chichester, UK.

Unlicensed nicotine-containing products/ Electronic cigarettes (e-cigarettes)

Guidance in this area, as distinct from the preceding section and other areas of public health guidance, is based on limited research. This research focuses primarily on electronic cigarettes that are one alternative source of nicotine to cigarettes besides nicotine replacement therapy, although some electronic cigarette products claim to be nicotine-free[8]. However, new products and brands with differing ingredients and mechanisms of action are becoming increasingly available, and the field requires a range of issues to be considered, including forthcoming changes to the regulations that will apply to currently unlicensed products – see below for details. Forthcoming changes to the regulatory structures applying to e-cigarettes will mean that some e-cigarette products may seek to be regulated by the UK medicines regulatory agency (the MHRA) and become licensed nicotine products, while others will instead be on general sale as is the case at present, but subject to new controls on product quality and consumer protection. All these factors will need to be considered in due course; this guidance can only take into account the evidence currently available, and research inevitably cannot keep pace with this rapidly evolving arena.

Context

Abstinence from all nicotine products through abrupt quitting with traditional duration of pharmacotherapy provision will provide the best health outcomes; however, the use of harm-reduction approaches such as 'cutting down to quit' and/or the use of nicotine-containing products as an exclusive substitute for tobacco for those highly nicotine-dependent smokers who currently do not feel ready/able/willing to cease nicotine product use entirely will still provide health benefits compared to continued smoking, and may increase the number of people who reduce the health risks of tobacco, quit smoking in the longer run, and reduce the harm to those around them.

The worst scenario is that smokers continue to smoke cigarettes with all the associated morbidity and mortality. While nicotine is highly addictive, using nicotine-containing products without these toxins and carcinogens is preferable to using forms of nicotine with them. This applies to both licensed and unlicensed nicotine products, although we have considerably more confidence in the quality, safety and effectiveness of existing licensed products.

Unlicensed products

Unlike licensed nicotine-containing products regulated by the MHRA (e.g. patch, gum, nasal and mouth sprays, sublingual tablet, lozenges, and inhalator; other products are in development) for harm reduction, there is very little evidence on the quality (e.g. pharmacokinetics or consistency of contents), safety, or effectiveness of electronic cigarettes or other unlicensed nicotine-containing products. However, current expert opinion on the limited evidence available suggests that they are likely to be considerably

8. de Andrade M, Hastings G, Angus K et al (2013). *The marketing of electronic cigarettes in the UK*. Cancer Research UK. Available from: www.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@pol/documents/generalcontent/cr_115991.pdf

less hazardous than tobacco smoking. Furthermore, this is a rapidly evolving area with a wide range of unlicensed products being sold and used, each with currently unknown but potentially different safety and effectiveness profiles. This limited evidence is for the general population and there are no studies of their effectiveness or safety in sub-populations.

There is growing popularity of these products and they appear to be taking market share from existing licensed NRT products[9]. In addition, there are concerns and unanswered questions about electronic cigarettes that have been raised by researchers, policymakers and practitioners. These include: the motives and intentions of manufacturers and their increasingly diverse marketing strategies; the increased involvement of the tobacco industry in this domain in relation to the Framework Convention for Tobacco Control's Article 5.3 (the protection of health policy from the vested interests of the tobacco industry); the potential for use of these products to lead into resuming or taking up smoking; to undermine the enforcement of smoke-free legislation or the 'denormalisation' of smoking[10].

In light of these issues, it seems sensible and practical to consider each smoker on a case-by-case basis, applying clinical judgement around each individual smoker's circumstances, based on underlying principles and recommendations focussed on minimising the potential of relapse to smoked tobacco.

It is also important, in the context of the increasing prevalence of unlicensed products like electronic cigarettes – with the possibility that increasing availability of e-cigarettes will result in lower uptake and engagement with cessation services – that smokers using these devices are not denied access to evidence-based smoking cessation support that they would otherwise benefit from. As the benefits of traditional smoking cessation pharmacotherapies and behavioural support are generally additive (they both independently improve a smoker's chances of successfully quitting), it would not be helpful, and could be harmful, to deny access to other aspects of cessation support for the increasing numbers of users of unlicensed nicotine products.

Key practical considerations for those using, or enquiring about the use of, unlicensed nicotine-containing products such as electronic cigarettes:

What nicotine products should be recommended for use in the tobacco harm-reduction approaches outlined in this guidance addendum?

- It is much preferable to use licensed nicotine-containing products that have robust assurances on product safety, quality and effectiveness, and these are the products which should be recommended by smoking cessation professionals.

9. Smoking Toolkit Study. The Smoking Toolkit Study is a monthly survey of a nationally representative sample of adults in England, designed to provide information about smoking prevalence and behaviour. University College London/Cancer Research UK/Department of Health. Available from: www.smokinginengland.info/latest-statistics/
10. de Andrade M, Hastings G, Angus K et al (2013). *The marketing of electronic cigarettes in the UK*. Cancer Research UK. Available from: www.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@pol/documents/generalcontent/cr_115991.pdf

How harmful are unlicensed nicotine-containing products like electronic cigarettes in comparison with smoking standard cigarettes?

- The limited evidence available suggests that they are likely to be less hazardous than tobacco smoking. However, the limited research conducted to date shows that there can be significant variance in nicotine levels[11] in these devices and contaminants of potential concern[12] in some products. In addition, their pharmacokinetics (mechanisms of action) are largely undocumented and unknown. Finally, new products are becoming regularly available with similarly unknown but potentially different constituents and mechanisms of action.

What advice should be given if the smoker uses unlicensed nicotine-containing products already or is intent on using unlicensed products instead of licensed ones?

- Users of unlicensed nicotine-containing products should be advised of the points above (e.g. that it is strongly preferable to use a licensed nicotine-containing product such as an inhalator or combination NRT products, and that it is only appropriate to continue using unlicensed products if advice and encouragement to use licensed products is refused by the smoker).
- However, if the smoker continues to express a strong/clear preference for the use of an unlicensed nicotine product over a licensed one as their choice:
  - encourage access to evidence-based aspects of smoking cessation support that they would otherwise benefit from (e.g. attendance at behavioural support sessions for a smoking cessation attempt)
  - adopt an approach that places minimising the risk of relapse to smoking above discontinuing use of an unlicensed nicotine product – use clinical judgement, taking into account their quitting history. In addition, consider their past experience of, and willingness to switch to, a licensed nicotine-containing product, and whether the smoker reports they are finding their e-cigarette use helpful in dealing with cravings and they feel they might relapse to smoking if they discontinued its use or used a licensed product.
- Be aware that a number of Health Boards and a range of other locations (e.g. workplaces, public transport) have prohibited the use of products like e-cigarettes on their premises, and advise accordingly.

Can a smoker who is insistent on continuing using an unlicensed nicotine-containing product (e.g. an electronic cigarette) combine it with a licensed NRT product?

This is possible but the following considerations should be taken into account:

- This addendum already advocates the use of a licensed NCP to continuing cigarette smokers as a harm-reduction approach.
- Survey evidence in England (Scotland is expected to be broadly similar) shows that licensed NCPs are often used alongside tobacco cigarettes in continuing smokers, and the same is increasingly true for e-cigarettes.
- Current expert opinion is that e-cigarette use is likely to be considerably less hazardous than smoking.

11. Goniewicz ML, Kuma T, Gawron M, Knysak J, Kosmider L. Nicotine levels in electronic cigarettes. *Nicotine Tob Res*. 2013 Jan;15(1):158-66.
12. Goniewicz ML, Knysak J, Gawron M et al. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control*. 2014 Mar;23(2):133-9.

- The limited evidence that exists on the nicotine delivery of these products suggests that they deliver nicotine more slowly than cigarettes and are more similar to faster-acting NRT products[13,14] albeit with greater uncertainty over safety and reliability of nicotine delivery and dosing. Newer 'second generation' devices appear to deliver nicotine faster than earlier cigarette-like models; however, nicotine delivery from newer devices still appears to be substantially slower than smoking[14].
- Some brands of e-cigarettes are unreliable or have batteries which do not last sufficiently long for heavy smokers – in the event of device failure, a readily available 'back-up' product in the form of fast-acting NRT could help manage withdrawal and potentially avoid relapse to smoking.
- Providing a slow-acting licensed product such as a patch for those intent on continuing use of e-cigarettes during a quit attempt would be consistent with the principles of NRT 'combination therapy' and may be useful for smokers who are very dependent upon nicotine.

Is there a risk of overdosing on nicotine, or any other safety considerations that clients intent on using electronic cigarettes alongside another licensed nicotine product should know about?

- E-cigarette use is thought likely to be less harmful than standard cigarette use (although there is limited direct evidence, current expert opinion is that they are likely to be considerably less harmful than standard cigarettes) and, from the limited evidence that currently exists, their nicotine delivery appears to be more similar to faster acting NRT than to tobacco cigarettes.
- Limited direct evidence on the devices themselves[15], and close analogy with well-established tobacco cigarette smoking behaviour, suggests that users of e-cigarettes appear to self-determine ('titrate') their dose of nicotine through their puffing behaviour in a similar manner to tobacco cigarettes.
- As nicotine dosage from e-cigarettes has a component of user control, serious self-overdosing of nicotine among e-cigarette users has not been identified as a major concern in monitoring of e-cigarette use to date.
- However, it should be noted that these products may deliver nicotine inconsistently or unreliably, as previously described, so the possibility of such adverse events cannot be entirely ruled out in those intent on continuing use of e-cigarettes.
- While, as above, there are some circumstances under which it may be appropriate to provide a licensed nicotine-containing product for use in the cessation attempt of a client who also intends to continue use of an e-cigarette, the simultaneous use of tobacco cigarettes and e-cigarettes and licensed nicotine-containing products (NRT) should be avoided given the unknown effects and potential safety issues this might bring.
- For safety, users of e-cigarettes, especially those who are also considering supplementing their e-cigarette use with another licensed nicotine product, should be advised to carefully monitor their dosing, especially when using slower-acting nicotine products which take longer to deliver peak nicotine levels and could surprise the user with a delayed, unexpected, nicotine peak.
- Symptoms of acute nicotine overdose include: nausea, vomiting, abdominal pain,

13. Vansickel AR, Eissenberg T. Electronic cigarettes: effective nicotine delivery after acute administration. *Nicotine Tob Res*. 2013 Jan;15(1):267-70.
14. Farsalinos KE, Spyrou A, Tsimopoulou K, Stefopoulos C, Romagna G, Voudris V. Nicotine absorption from electronic cigarette use: comparison between first and new-generation devices. *Sci Rep*. 2014 Feb 26;4:4133.
15. Dawkins L, Corcoran O. Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. *Psychopharmacology (Berl)*. 2014 Jan;231(2):401-7.

salivation, sweating, a rapid pulse, headaches, and dizziness – if symptoms of overdose are observed, all nicotine intake should be immediately stopped and medical assistance should be sought.
- Bupropion and varenicline should not currently be supplied to a smoker using an unlicensed nicotine-containing product (similarly to the way bupropion and varenicline are not indicated for use along with licensed nicotine-containing products).

Tobacco industry involvement in harm reduction

Tobacco manufacturers are increasingly investing in alternative nicotine products (both licensed and unlicensed) with at least one manufacturer in the process of bringing a novel nicotine product to the UK market as a licensed medicine through the MHRA authorisation process. Scotland is bound by the World Health Organization's *Framework Convention on Tobacco Control* (FCTC). Article 5.3 of the convention states that: 'In setting and implementing their public health policies with respect to tobacco control, parties shall act to protect these policies from commercial and other vested interests of the tobacco industry in accordance with national law.'

Public bodies should act in accordance with Scotland's obligations under the FCTC in the event that tobacco companies, in their role as manufacturers of alternative nicotine products, attempt to influence matters of public health policy at the local level. A series of detailed guiding principles and recommendations on the implementation of Article 5.3, is available at: www.who.int/fctc/guidelines/article_5_3.pdf

Regulatory developments

In June 2013, the UK medicines regulator, the MHRA, announced that it intended to regulate all nicotine-containing products (including electronic cigarettes) as medicines. However, this was conditional on a piece of European legislation – the European Tobacco Products Directive – completing its passage through the European legislative process. In October 2013, during the passage of the Tobacco Products Directive, the European Parliament rejected mandatory medicinal regulation for e-cigarettes, and an alternative 'two-track' system was proposed. Under this system e-cigarettes that make a therapeutic claim to treat or prevent disease (which includes claims of being effective smoking cessation aids) will be subject to regulation as medicines. E-cigarettes that do not make therapeutic claims will instead be subject to consumer regulation under a range of new controls on maximum nicotine content and concentration, advertising and marketing regulations, and ingredient and emissions quality control. The revised Directive was formally agreed by the European Parliament plenary during February 2014. The legal changes to the regulations surrounding e-cigarettes required by the Directive are expected to come into effect in the UK in 2016.

Updates and contact details

This guidance addendum will be updated in light of any significant new developments in the evidence-base around tobacco harm-reduction approaches, or unlicensed nicotine-containing products.

For any questions regarding the content of this document, please contact:

Fiona Moore
Public Health Adviser
Evidence for Action
Public Health Science
NHS Health Scotland
fiona.moore2@nhs.net

Rory Morrison
Senior Policy & Research Officer
Action on Smoking and Health Scotland
rmorrison@ashscotland.org.uk