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Smoking harm reduction approaches:

A rapid review of the literature

Version 1.0

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Details of Evidence Review Report

Title: Smoking harm reduction approaches: A rapid review of the literature

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Date: January 2026

Version: 1.0

Publication/Distribution: This document will be published on the Public Health Wales website

Review date: February 2029

Protocol details: The protocol is available on request.

Contents

1. Executive summary

- Smoking is the single greatest preventable cause of disease and mortality in Wales. *Help Me Quit,* in line with National Institute for Health Care Excellence (NICE) recommendations and its Minimum Service Standards, currently provides support based around an 'abrupt quit', where the client agrees a 'quit date' after which they will no longer smoke (sometimes described as the 'not one puff' rule)

- There is increasing interest in whether harm reduction pathways, like cutting down smoking before quitting, maybe more effective at reducing harms from smoking among people not yet ready to quit and thus unable to accept support within an abrupt quit service model.

- The aim of this rapid review was to build on two Cochrane reviews (Lindson Hawley *et al.*, 2016; Lindson *et al.*, 2019) by searching for evidence published since 2015 in order to understand 'What is the evidence for different approaches to 'harm reduction' in smoking cessation services (as opposed to the current standard 'abrupt quit' model) in terms of reducing and/or quitting smoking in the general adult population not yet ready to quit?

- Nine randomised trials reported in 11 studies met our inclusion criteria. Two trials were conducted in the UK. Evidence was narratively synthesised based on the type of intervention reported in the trials: behavioural-only interventions (n=3); varenicline plus behavioural interventions (n=2); and nicotine replacement therapy plus behavioural interventions (n=4).

- Evidence from a diverse set of behavioural-only interventions did not support a sustained effect on smoking reduction or improved smoking cessation and abstinence.

- Evidence on varenicline plus behavioural support from two studies were varied in quality, one high-quality multinational trial supported this intervention for greater smoking reduction and cessation.

- Evidence from four poor quality studies combining NRT with behavioural support for reduction, cessation or a combination of the two found no evidence of effectiveness on verified smoking reduction or cessation outcomes.

- Most studies reported interventions were applicable to Wales but only two studies reported the harms and cost-effectiveness of their intervention leaving the balance of benefits, costs and harms unknown.

- Self-reported smoking reduction or abstinence were as much as ten times larger than estimates verified by carbon monoxide. This highlights a strength of our review to focus on verified outcomes.

- In combination with existing Cochrane reviews on harm reduction and smoking reduction interventions our review shows no substantial development to depart from existing NICE guidelines and minimum standards for *Help Me Quit*.

2. Background and purpose

Smoking is the single greatest preventable cause of disease and mortality in Wales with over one in ten of all deaths between 2020 and 2022, amongst adults aged 35 and over, attributable to smoking (Emmerson *et al*, 2024). Smoking harms are socially patterned, with smoking-related mortality rates in the most deprived areas in Wales triple the rates in the least deprived (Emmerson *et al*, 2024). Smoking prevalence in Wales fell between 2013 to 2022 from 20% to 13% among adults but recently quit rates among treated smokers have declined from 53.6 % to 50.4% between 2021 and 2024 (Public Health Wales, 2025). Crucially, the population of smokers that remain is changing, with higher proportions not ready to commit to a quit date, or coming from more deprived and marginalised populations, who may be less able to benefit from an abrupt quit intervention. An estimated 330,000 Welsh adults continue to smoke (Public Health Wales, 2025a), highlighting that despite achieving good quit-rates (NCSCT, 2005), a major challenge remains. A high proportion of smokers supported to quit don't succeed and may benefit from a different intervention that is more likely to help them.

Help Me Quit is a service that helps people in Wales to stop smoking. Run in partnership with Public Health Wales and Health Boards, the service follows minimum standards and NICE guidelines including NG209 (NICE, 2021). *Help me Quit* is an abrupt stop smoking service that aims to:

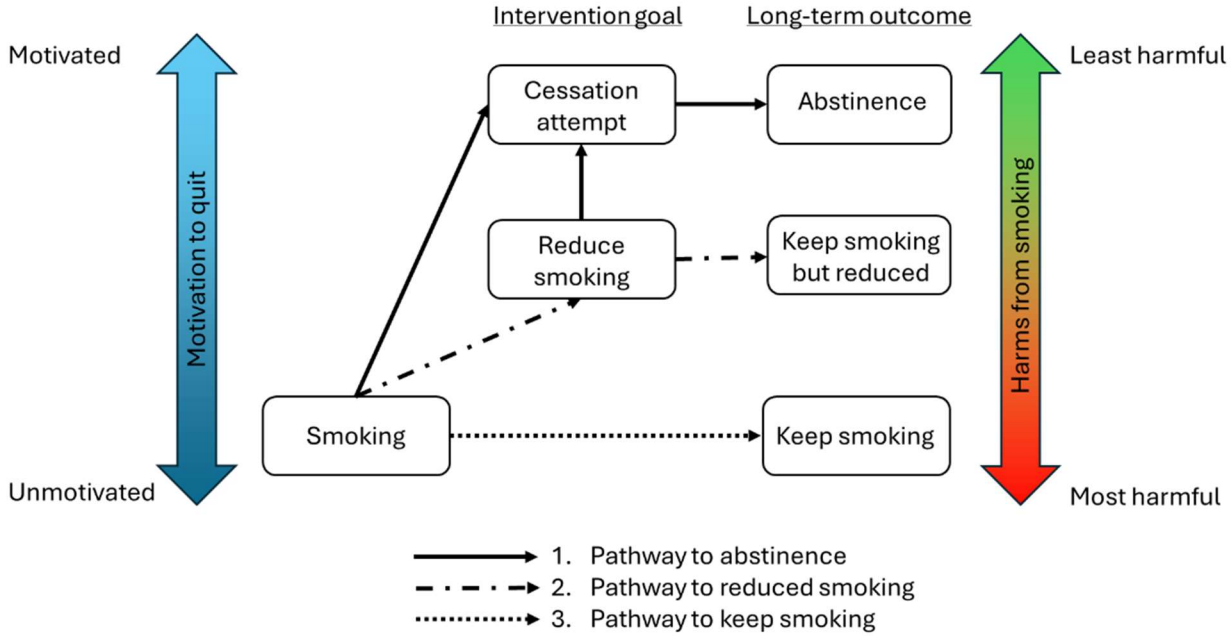
- maximise reach and engagement with smokers who are motivated to quit;
- provide 7 support sessions over 12 weeks;
- support smokers to set a target quit date within the first two support sessions; and
- monitor success via exhaled carbon monoxide measures 4 weeks after the target quit date.

Whilst *Help Me Quit* successfully supports half of treated smokers (those attending a session and setting a quit date) to quit, those left untreated continue to smoke. Untreated smokers have very different needs and preferences for models of support (Public Health Wales, 2025). A recent service review identified a need to evolve the service to better cater for untreated smokers. Current advice from *Help Me Quit* for smokers that are not ready to commit to a quit date (Public Health Wales, 2025b) focuses on the benefits of quitting and aims to increase motivation to quit to enable uptake of cessation support. A longstanding question is whether smoking harm reduction can be achieved more gradually by encouraging people not ready to commit to a quit date to reduce smoking instead. Figure 1 (adapted from Fucito *et al.*, 2024) is theoretical outline of gradual smoking harm reduction by illustrating distinct pathways targeted at people based on their motivation to quit that vary in intervention goals, long-term outcomes and theoretical reduction in harm to health. The improvement in smoking harms represented in the figure is based on observational associations between reductions in smoking and long-term health outcomes (Chang *et al.*, 2021). No trials estimating similar health effects of reduced smoking have been found (Lindson-Hawley *et al.*, 2016). The theoretical outline (Figure 1) includes three pathways:

1. Pathway to abstinence – Includes direct support for a cessation attempt when smokers are ready to commit to a quit date, as well as indirect cessation support via reduction i.e. smokers not willing to set a quit date are supported to reduce smoking as an intermediate goal before making a cessation attempt. Thus, abstinence is the long-term outcome but it

occurs more slowly than an abrupt quit
2. Pathway to reduced smoking - Smokers not yet ready to commit to a quit are supported to reduce smoking without a goal of stopping completely, with the long-term outcome of continued smoking but at a reduced level.
3. Pathway to keep smoking - Smokers unmotivated to reduce or quit smoking receive no support, set no goals and keep smoking with no change in harms.

Figure 1: Theoretical change in harm from reduction versus (vs.) cessation (adapted from Fucito *et al.*, 2024)



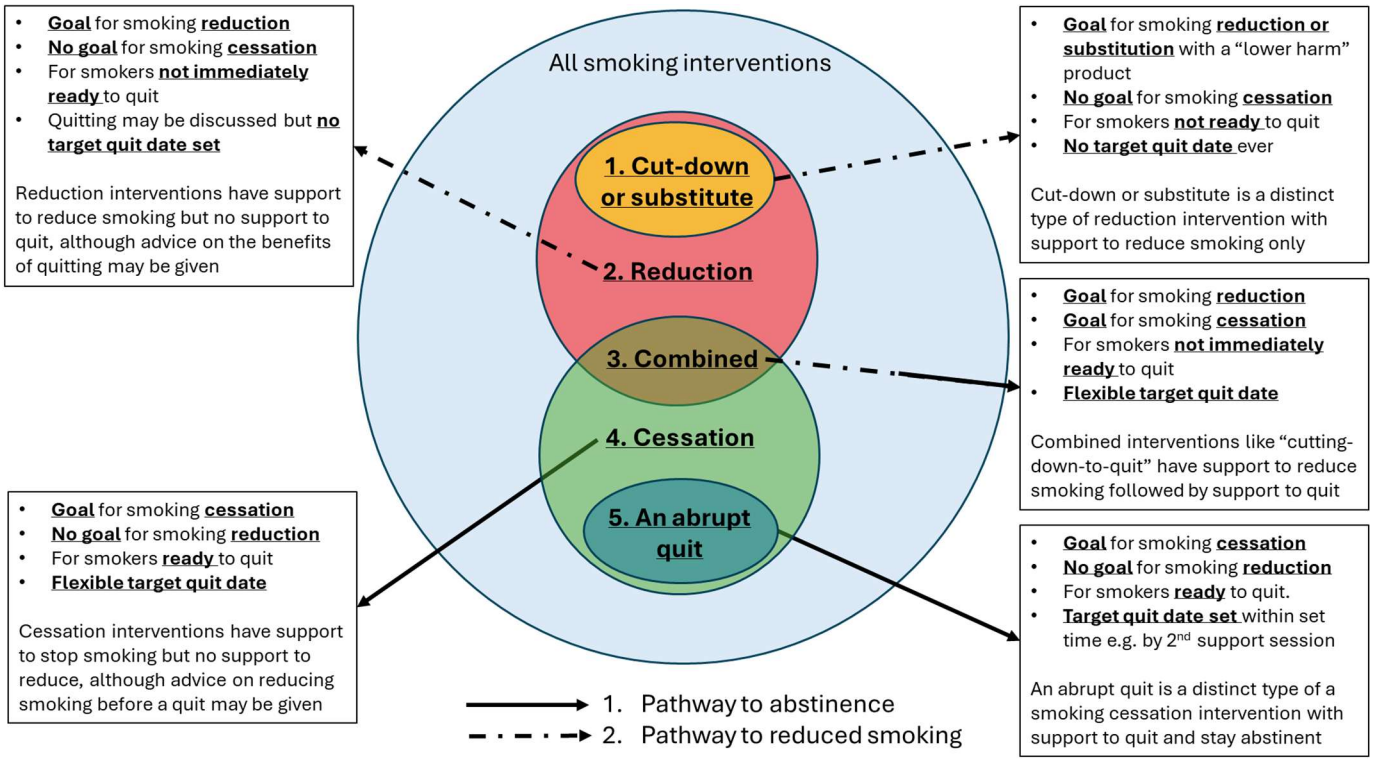
There is no single definition of tobacco harm reduction, but generically harm reduction can be defined as "a method designed to reduce the risk of harm associated with a certain behaviour without necessarily reducing the frequency of that behaviour" (National Library of Medicine, 2003). The concept of harm reduction has been used by the tobacco industry to produce products marketed at reducing the health harms of tobacco smoking, for example, low tar cigarettes or heated tobacco products. However, there is currently no independent evidence that such products are less harmful than cigarettes, in terms of reduced disease or mortality (Tobacco Tactics, 2022). The *Help Me Quit* service review highlighted that several Health Boards are using a 'harm reduction' approach with examples of innovative and evidence-based practice, but inconsistencies exist in the conceptualisation, design and implementation of these approaches (Public Health Wales, 2025). NICE suggests harm can be reduced by measures or products that support smoking less or temporarily abstaining from smoking tobacco. Such smoking harm reduction approaches for people who do not want, or are not ready, to stop smoking in one go, include (Lindson-Hawley *et al.*, 2016; NICE 2021):

- A longer-term pathway to abstinence using established methods to support cessation and adhere to tobacco abstinence without an agreed quit date.
- Reducing smoking by substituting cigarettes, partially or fully, for other nicotine containing products that are less harmful than cigarettes e.g. nicotine replacement therapy.
- Prescribed medicinal products to reduce smoking by easing cravings for smoking like

varenicline, Cytisine or Bupropion.
- Behavioural support to reduce the frequency of smoking behaviours

As behavioural support, nicotine replacement therapy (NRT) or prescription medication are also key components of cessation interventions. There is overlap in the evidence for approaches for harm reduction and smoking cessation. Figure 2 combines the theoretical pathways to reduced smoking or abstinence (illustrated in Figure 1) with types of smoking interventions to show that reduction and cessation are sometimes exclusive, but can also be combined. Types of smoking interventions can be distinguished by their goals, motivations and flexibility into five categories, as illustrated in Figure 2. Compared with continued smoking, all of the categories in figure 2 could be viewed as harm reduction. *Help Me Quit* minimum service standards recognise that some smokers will need flexibility in agreeing a future quit date or will only engage with a reduction programme initially but there are no national standards for harm reduction meaning interventions can vary from one health board to another. One approach that has been used is 'cutting down to stop', which falls into *category 3 Combined*.

Figure 2: Conceptual illustration of overlapping and distinct features of smoking reduction and cessation interventions.



There is strong evidence that a combination of face-to-face behavioural support and NRT or prescription only medication can aid smoking reduction and indirectly lead to subsequent quitting (Public Health Wales, 2025). But uncertainty in the evidence base remains in relation to whether harm reduction approaches 1) increase long-term abstinence; 2) reduces harm from smoking given there is harm at any level of smoking; 3) involving substituting with other products affects motivation to quit or makes re-lapse more likely. As part of the of the *Help Me Quit* service review being undertaken by Public Health Wales, which has identified the need to expand smoking cessation services within Wales and standardise harm reduction approaches across health boards,

the Evidence Service were asked to identify evidence to help inform this work.

There are over 70 Cochrane reviews on smoking cessation interventions collating more than 2,500 randomised controlled trials (representing categories 4 and 5 in Figure 2) (Lu *et al.* 2024). Our scoping searches identified just two Cochrane reviews relevant to harm reduction. In 2016, Lindson-Hawley *et al.* collated 24 trials in *category 1. Cut down or substitute*, Figure 2. Most studies excluded people currently interested in quitting smoking, but the assessments and cut-off points used to establish eligibility varied. Over half of the trials tested nicotine replacement therapy either on its own or combined with behavioural support. Six interventions investigated a mixture of products aimed at substituting normal cigarette smoking with alternatives proposed to reduce exposure to harmful components including tobacco-based products (snus, low-tar cigarettes, electronically heated cigarettes) and non-tobacco, nicotine-containing e-cigarettes or vapes. Two trials tested behavioural support on its own. Prescribed medication as a harm reduction aid was looked at in just two trials, one for bupropion and another for varenicline (standard titration of 0.5mg for 3 days, 1 mg for 4 days, then 2 mg going forwards). Based on eight trials in a pooled analysis nicotine replacement therapy (two trials gave a choice of products, fours trials gave 2mg or 4mg gum, two trials gave an inhaler) increased the likelihood of reducing cigarettes per day by 50% from baseline (Risk ratio 1.75, 95% Confidence Interval [CI]=1.44 to 2.13) and quitting smoking (RR=1.87, 95% CI=1.43 to 2.44). Evidence for cessation outcomes was graded as low, meaning that further research could improve confidence in the estimated effect. The evidence for all other interventions indicated a possible benefit to reduction or cessation, but was unclear owing to imprecision. When objective measures like carbon monoxide (CO) and cotinine were used they generally showed smaller reductions than self-reported measures, making verification of outcomes necessary. Importantly, none of the trials directly measured harms to health caused by smoking leaving the theory presented in Figure 1 untested in trials. However, the review highlights that people who do not wish to quit can be helped to cut down the number of cigarettes they smoke and to quit smoking in the long term, using nicotine replacement therapy, despite original intentions not to do so. (Lindson-Hawley *et al.,* 2016).

In 2019, Lindson *et al.,* collated 51 trials falling to categories *2 Reduction* (12 trials) and *3 Combined* (29 trials) in Figure 2. Reduction approaches varied greatly encompassing behavioural advice and support as well as pharmacotherapy. Common approaches included:

- Replacing cigarettes with nicotine replacement therapy
- Behavioural support for reduction with prescribed medication
- Setting a goal number of cigarettes per day to work toward
- Setting smoke-free time periods or locations such as at home or work
- Gradually increasing the time between cigarettes
- Eliminating routine or least preferred cigarettes smoked at specific times
- Gradually increasing the time between waking and first cigarette

Studies often combined multiple approaches making it difficult to isolate the effectiveness of any single method (Supplementary table 1). Interventions were mostly delivered face to face (38 trials) with extra contact via telephone, text messages, self-help materials or computerised support. Contact time varied from 6 minutes to 16 hours, delivered over one to 28 sessions. Most trials (n=27) compared reduction approaches to an abrupt quit. Compared with an abrupt quit, reduction-to-quit interventions resulted in fewer quit attempts (RR=0.92, 95% CI=0.85,0.99; 13 studies; 5389 participants), but were equally effective in terms of abstinence at 6 months (RR=1.01, 95% CI=0.87 to 1.17; 22 studies, 9219 participants). Overall suggesting that cutting

down may be a helpful approach to stop smoking for people not ready to commit to quitting. Behavioural support for reduction aided by pharmacotherapy (nicotine replacement therapy or prescribed medication) compared with behavioural support for reduction alone resulted in higher quit rates (RR=1. 68, 95% CI=1.09 to 2.58; 11 studies, 8636 participants) (Lindson *et al.,* 2019). Trials in general populations of smokers were eligible for inclusion and only 3 studies reported baseline motivation to quit among their participants, therefore it remains unknown whether a reduction intervention is superior to an abrupt quit specifically for people less motivated to quit.

Despite not setting a quit date during the intervention in 36 of the 75 trials included in Cochrane reviews to date (Lindson Hawley *et al.,* 2016; Lindson *et al.,* 2019), interventions supporting smoking reduction can lead participants to a quit and achieve long-term abstinence. Behavioural support for reduction combined with nicotine replacement therapy is likely to be the best approach for improving long-term abstinence in general populations of smokers. Our work aims to build on these two reviews by examining the evidence base for smoking harm reduction approaches, published since 2015 (the date of the last search conducted by Lindson-Hawley *et al.* 2016). We focussed on identifying the latest evidence on interventions designed to achieve reduction (pathway 2, figure 1) or abstinence via reduction (pathway 1, figure 1). We also aimed to find interventions delivered to smokers not yet ready to quit, that fall into categories 1, 2, 3 and 4 (figure 2), where advice or goals for reduced smoking may or may not be combined with goals for cessation. This rapid review will specifically answer the question:

> What is the evidence for different approaches to 'harm reduction' in smoking cessation services (*as opposed to the current standard 'abrupt quit' model*) in terms of reducing and/or quitting smoking in the general adult population not yet ready to quit?

3 Methods

3.1 Eligibility criteria

Table 1 outlines the eligibility criteria that identified primary studies were screened against for inclusion into this rapid review. For detail inclusion and exclusion criteria see Appendix 1, supplementary table 2. For cessation outcomes we have defined a timescale longer than 4 months to distinguish trials we include from current practice in Help Me Quit. The current abrupt quit model is delivered over 12 weeks with a quit date set in session 2 for some point within 12 weeks. Successful cessation is then measured 4 weeks after the quit date, so a conservative estimate of the latest time-point after baseline that current service users might have abstinence measured is 16 weeks (or 4 months). While Cochrane reviews set their outcome measurement timepoint as 6 months, we have varied from this to keep the inclusion criteria as broad as possible. We included interventions testing advice/support on using e-cigarettes for smoking reduction, but only if the e-cigarettes were not provided by investigators, because current Public Health Wales policy does not support e-cigarette provision. We also excluded interventions involving alternative tobacco-based products as provision of these as part of stop smoking services are also not supported.

Table 1: Eligibility criteria for studies to be included in the rapid review

Population	Intervention / Exposure	Comparison / Control	Outcomes
Adult smokers in the general population who are not willing or able to commit to a quit date	Smoking harm reduction: interventions aiming to reduce exposure to tobacco smoking without a commitment to quit abruptly. May or may not be alongside a longer-term or more flexible smoking cessation intervention (but not an abrupt quit). May include behavioural support, nicotine replacement therapy, or pharmacotherapy including varenicline, cytisine (aka cytisinicline), Bupropion). But excluding tobacco-based products (e.g. snus or heated cigarettes) or the provision of free vapes. Includes categories 1, 2, 3 and 4 in Figure 2	No intervention or Waitlist control or Smoking cessation interventions without smoking reduction prior to a quit attempt (i.e. an abrupt quit). May include behavioural support, nicotine replacement therapy, or pharmacotherapy including varenicline, cytisine (aka cytisinicline), Bupropion).	Tobacco exposure reduction – measurements of a longer pathway to abstinence via reduced smoking. Intermediate markers like reduced smoking amount, temporary abstinence, quit attempts or cessation over a timescale longer than 4 months

3.2 Search methods

3.2.1 Scoping searches

Scoping searches were conducted by two reviewers (LJ and AFM) in repositories of secondary evidence, and relevant topic websites between 13th and 22nd August 2025. These included:

- JBI (Joanna Briggs Institute)
- WHO (World Health Organization)
- NICE (National Institute for Health and Care Excellence)
- UK & Welsh Government websites
- PROSPERO
- ASH (Action on Smoking and Health)
- NIHR (National Institute for Health and Care Research)
- EPPI Centre
- What Works for Wellbeing
- Campbell Collaboration
- Cancer Research UK
- Health Technology Wales
- SIGN (Scotland Intercollegiate Guidelines Network)
- AHRQ (Agency for Healthcare Research and Quality)
- CDA (Canada's Drug Agency)
- Google Scholar

The results of these scoping searches informed discussions with stakeholders and the

development of the protocol.

3.2.2 Literature search

A search of databases and resources was conducted to identify published primary studies. All searches were conducted on 25th September 2025. The following databases were searched:

- MEDLINE
- EMBASE (now including clinicaltrials.gov)
- CINAHL
- PsycINFO

Search concepts and keywords included:

- 'smoking reduction'
- 'smoking cessation'
- 'harm reduction'
- 'risk reduction'
- 'controlled smoking'
- 'scheduled smoking'
- fading
- tapering
- reducing
- swapping
- cutting down or back
- substituting and
- phasing out smoking

Searches were limited to records published after 2015 based on the last search date in Lindson-Hawley, *et al.,* 2016. Searches were limited to studies published in the English language. An initial search strategy was drafted in Ovid MEDLINE by an Information Specialist (AFM) and then translated to the other databases by the same Information Specialist. The search strategy used for MEDLINE can be found in Appendix 1.

Four key systematic reviews (Lindson-Hawley *et al.*, 2016; Lindson *et al.*, 2019; Lopes *et al.*, 2022; Klemperer *et al.*, 2023), identified during preliminary scoping searches, were hand-search to identify any additional studies that may have been missed by our database searches. Any other systematic reviews meeting our eligibility criteria identified from our searches were included for the purpose of hand-searching. A topic expert was consulted to inquire if updated but unpublished results existed from relevant Cochrane reviews (Lindson-Hawley *et al.*, 2016; Lindson *et al.*, 2019) and additional literature from this inquiry was added into our results for screening.

3.3 Study record management and selection process

3.3.1 Study record management

Preliminary scoping search results were recorded in an Excel spreadsheet and assessed for eligibility by two reviewers (AFM or LJ). The records identified from database and initial supplementary searches were imported into an EndNote library (version 20, Philadelphia, PA, Clarivate) where duplicates were removed. The remaining records were imported into Rayyan (AI-Powered Systematic Review Management Platform (Ouzzani, *et al.,* 2016) for screening, where

further duplicates were identified and removed. Records from supplementary searches of inclusions in systematic reviews meeting our eligibility criteria for primary studies were managed separately using an Excel spreadsheet.

3.3.2 Study Selection process

Titles and abstracts were screened once by two reviewers (KS & LJ) in Rayyan, with 20% of the records screened in duplicate by a third reviewer (AFM) to ensure consistency and to minimise bias. Inter-rater reliability for title and abstract screening was calculated as 98.5%. Any uncertainty was discussed within the review team and clarifications in understanding of the eligibility criteria were documented. All studies included after title and abstract screening had their full texts reviewed by one reviewer (LJ) and 50% each were screened by two second reviewers (KS or AFM) so that 100% of the full texts were screened in duplicate. Any decision conflicts were discussed within the team, and a consensus for inclusion was reached. During screening, several papers were identified reporting a non-randomised analysis of a potentially eligible trial. These were citation tracked to identify the primary trial paper, which was then screened to establish whether it had already been included and if not then if it met our inclusion criteria. These supplementary searches did not result in any additional inclusions as the primary trial papers were either out of date; previously screened and excluded, or new but excluded as they didn't meet our inclusion criteria. Records included at each stage of the process and reasons for exclusion were recorded in a PRISMA flow diagram (figure 3).

3.4 Critical appraisal

Critical appraisal was undertaken using the Critical Appraisal Skills Programme (CASP) checklist for randomised controlled trials (CASP, 2025). A single reviewer (KS) undertook critical appraisals for all studies included in the rapid review, and a second reviewer (LJ) checked 20% for consistency. Any additional points or disagreements were resolved between the two reviewers. Findings were incorporated into the data extraction table and the potential implications of the quality of the included studies have been discussed in the findings section of this rapid review.

3.5 Data extraction

Data from the included primary studies were extracted into a Word document table by a single reviewer (KS or HS). A second reviewer (LJ) then checked the data for consistency. The following information was extracted:

- Study reference (Author and year of publication)
- Country
- Aim of study
- Study design

- Participant characteristics including number of, age, sex, eligibility criteria (previous smoking habit if reported; motivation/willingness/readiness to stop or reduce smoking) and the use of incentives for research or as part of the intervention
- Brief description of intervention and control conditions
- Data collection and methods relevant to intervention delivery or outcome measurement
- Outcomes assessed (if relevant to our inclusion criteria) including self-reported reduction in cigarettes per day; quit attempts, or abstinence alongside verification method like exhaled carbon monoxide or other blood-based or salivary biomarkers. Abstinence measures could include 7 day point-prevalence (not smoking for the last 7 days, verified by a single exhaled carbon monoxide measure), sustained abstinence (not smoking for a defined period where multiple verifications are made throughout the period), floating sustained abstinence (where the timing of a quit varies and so the sustained abstinence period is anchored to the timing of the quit for an individual participant rather than a fixed time since baseline for all participants)
- Findings, including all relevant measures of the effect of the intervention on tobacco use, reduction, cessation, abstinence and cost-effectiveness estimates.

In addition to the above data, further detail on the intervention design and delivery and conditions were extracted including:

- Setting
- Context
- Mode of delivery
- Duration
- Reduction aims
- Cessation aims
- Description of intervention
- Description of control
- Behaviour change techniques / underlying theory

3.6 Behavioural Change Technique Analysis

To explore whether there were any common behavioural change techniques used across the smoking reduction and cessation interventions, we conducted an analysis with the Behavioural Change Technique Taxonomy (Michie *et al.*, 2013), using the information provided in the intervention descriptions from the papers and protocols, where available.

3.7 Synthesis

Evidence has been narratively synthesised based on the type of intervention in a trial, which was classified based on the primary approaches used as 1) Behavioural only interventions; 2)

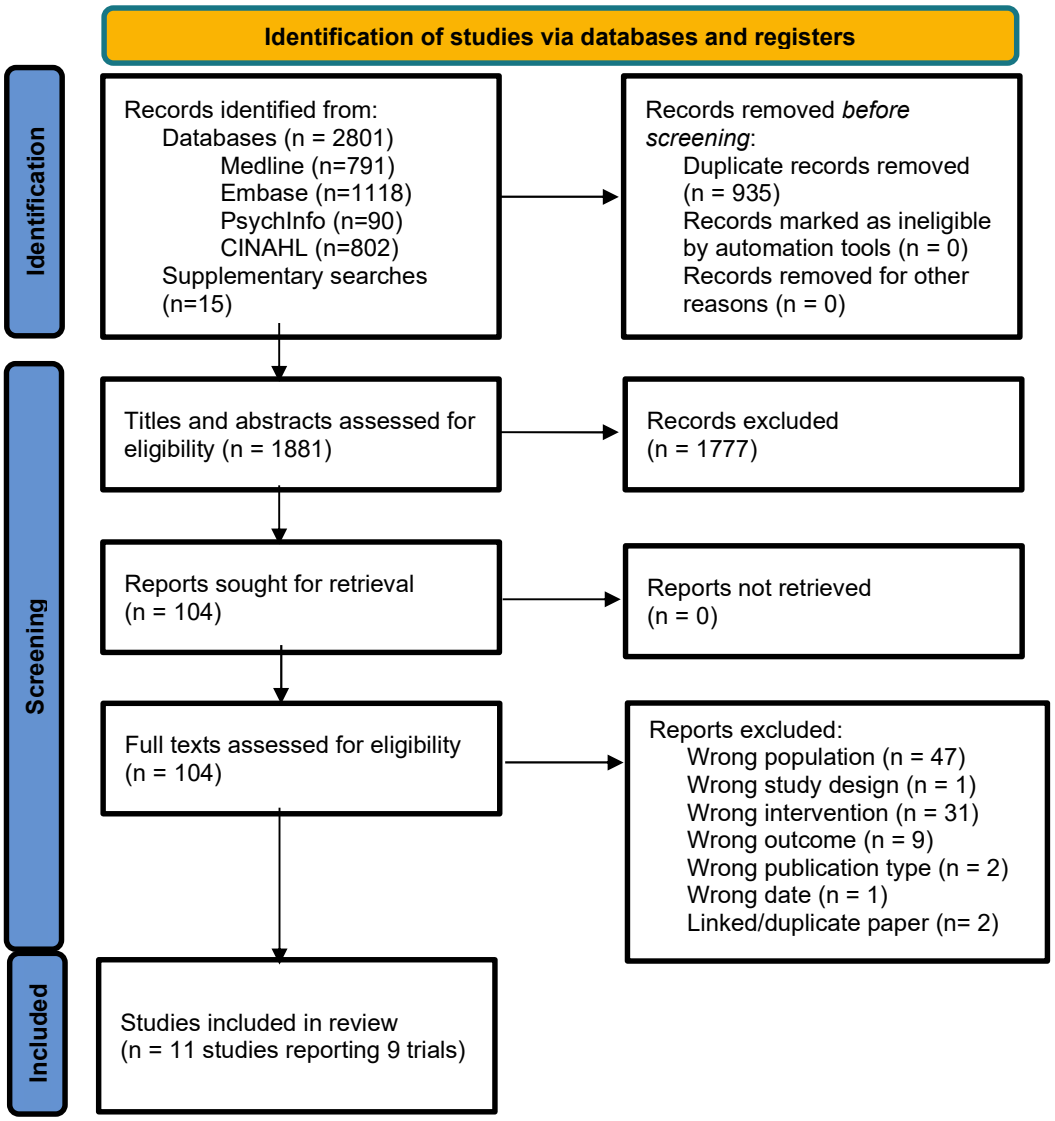
Behavioural & Pharmacological (Varenicline); and 3) Behavioural & Pharmacological (Nicotine replacement therapy). Interventions were also classified and synthesised based on their goals for reduction or cessation, in line with Figure 2, as 1) Cut down or Substitute; 2) Reduction; 3) Combined; or 4) Cessation. Meta-analysis was not performed, owing to heterogeneity between studies in terms of intervention delivery, and outcome measurement definition and timing.

4. Results

4.1 Study Selection

The results of searches and screening for inclusion are displayed in Figure 3. Searches yielded a total of 2,816 records, of which 935 were duplicates, leaving 1,881 records to be screened. After title and abstract screening, 104 records had their full texts reviewed. Records were primarily excluded for being in the wrong population (n=47), usually because populations were smokers already motivated to quit, or the wrong intervention (n=31). Excluded interventions fell into figure 2 category 4. Cessation, that included no reduction advice or goals, or category 5. Abrupt quit and were no different from the existing *Help Me Quit* model.

Figure 3: PRISMA flow diagram of the search results and selection of studies in screening.



4.2 Study characteristics

After screening, nine trials reported in 11 studies were eligible for inclusion in the final synthesis (Ebbert *et al.*, 2015; Farley *et al.*, 2017; Guo *et al.*, 2023; Hatsukami *et al.,* 2020; Machulska *et al.*, 2021; Steinberg *et al.*, 2018; Taylor *et al.*, 2023; Weng *et al.*, 2020; Zhao *et al.*, 2021). Details on individual study characteristics can be found in the supplementary table 3 (Appendix 2). In brief, all studies used a randomised controlled trial design with either two-, three-, or four-arms. One study was a feasibility study (Farley *et al.*, 2017), one was a pilot study (Zhao *et al.*, 2021), and one was a proof-of-concept study (Steinberg *et al.*, 2018).

Three studies were conducted in Hong Kong (Guo *et al.*, 2023; Weng *et al.*, 2020; Zhao *et al.*, 2021) two in the UK (Farley *et al.*, 2017; Taylor *et al.*, 2023); two in the USA (Hatsukami 2020; Steinberg *et al.*, 2018); and one in Germany (Machulska *et al.*, 2021). The study by Ebbert *et al.* (2015) was conducted internationally across ten countries, which included the UK. Seven studies offered incentives (cash or vouchers) to participants, including incentives following participation in the trial (Taylor *et al.*, 2023), incentives if all assessments were completed (Steinberg *et al.*, 2018), and incentives for either attending study sites for verification or 'passing' each verification of abstinence in the trial (Farley *et al.*, 2017; Guo *et al.* 2023; Weng *et al.*, 2020; Zhao *et al.*, 2021). Hatsukami *et al.* (2020) offered compensation for research participation and adherence to protocol. Smokers in the complete substitution of smoking by nicotine replacement therapy group were awarded a bonus payment if they had a carbon monoxide (CO) test result of ≤4 ppm at verification, while the comparator group only had to attend for a CO test.

Detail on the characteristics of the interventions can be found in supplementary table 4 (Appendix 2). We identified three trials of behavioural only interventions (Machulska *et al.*, 2021; Taylor *et al.*, 2023; Weng *et al.*, 2020); two trials of varenicline and behavioural interventions (Ebbert *et al.*, 2015; Steinberg *et al.*, 2018); and four trials of NRT and behavioural interventions (Farley *et al.*, 2017; Guo *et al.*, 2023; Hatsukami *et al.*, 2020; Zhao *et al.*, 2021). Two studies (Hatsukami *et al.*, 2020; Steinberg 2018) had the primary aim for participants to reduce smoking (with no specific target for cessation), four studies (Guo *et al.*, 2023; Weng *et al.*, 2020; Zhao *et al.*, 2021; Machulska *et al.*, 2021) had the primary aim of cessation (with no specific target for reduction) and three studies (Ebbert *et al.*, 2015; Taylor *et al.*, 2023; Farley *et al.*, 2017) combined cessation and reduction targets explicitly aiming for cessation via reduction. The overlap between the two ways of classifying interventions in presented in the table 2:

Table 2: Classification of trials included in the review by category and components of intervention

	Components of intervention		
Category figure 2	Behavioural support only	Behavioural support + Varenicline	Behavioural support + NRT
2. Reduction		Steinberg *et al.*, 2018	Hatsukami *et al.*, 2020
3. Combined	Taylor *et al.*, 2023	Ebbert *et al.*, 2015	Farley *et al.*, 2017
4. Cessation	Machulska *et al.*, 2021; Weng *et al.*, 2020		Guo *et al.*, 2023; Zhao *et al.*, 2021

Two studies had no eligibility criteria regarding participants' motivation or willingness to reduce or quit smoking (Guo *et al.*, 2023; Zhao *et al.*, 2021). Weng *et al.* (2020) stated that participants should be willing to reduce or quit smoking with no timeframe. Five studies recruited participants willing to reduce smoking but not willing or planning to quit either immediately (Taylor *et al.*, 2023); within one month (Ebbert *et al.*, 2015; Farley *et al.*, 2017; Steinberg *et al.*, 2018) or within three months (Hatsukami *et al.*, 2020). Although participants were not required to be willing to quit immediately, Ebbert *et al.* (2015) did require participants to make a quit attempt within three months, and Machulska *et al.* (2021) recruited participants *motivated* to quit but only within the next six months, not immediately.

Trial outcomes for smoking reduction were primarily self-reported but were presented alongside changes in exhaled carbon monoxide (or other biomarkers) and included: change in cigarettes per day; reduced smoking by ≥50% or ≥75% at 1 week to 18 months from baseline. Outcomes for smoking cessation were primarily verified and included: continuous abstinence rates at 4 weeks to 18 months from baseline; floating sustained abstinence; quit attempts; 7-day point prevalence at various timepoints from baseline. Verification of self-reported abstinence was most often by exhaled carbon monoxide (CO), but also salivary cotinine or by urinary biomarkers (Hatsukami *et al.*, 2020).

4.3 Critical appraisal

Critical appraisal results are presented in Table 3. All studies addressed clear research questions, but some studies were of higher methodological quality than others. Randomisation of participants was generally carried out, although in Farley *et al.* (2017) participant randomisation was not respected by pharmacists. With the exception of two studies (Farley *et al.*, 2017; Hatsukami *et al.*, 2020), all study participants were accounted for at the conclusion of the trials.

Participant blinding was carried out in the two trials where Varenicline was the intervention (Ebbert *et al.*, 2015; Steinberg *et al.*, 2018). However, it was not possible in the other trials where differences in approach to behavioural support are easy to perceive or provision of nicotine replacement therapy was not compared with a placebo therapy. Likewise, it was not always possible for investigators to be blinded to the intervention they were delivering. Investigators assessing the outcomes were blinded, although in two studies, this was not described (Hatsukami *et al.*, 2020; Machulska *et al.*, 2021). Except for Hatsukami *et al.*, 2020, results of the studies were mostly reported comprehensively, with precision of the estimate provided. Only one study (Taylor *et al.*, 2023) provided evidence on cost-effectiveness. Results from six studies were thought to be applicable to the Welsh population (Ebbert *et al.*, 2015; Hatsukami *et al.*, 2020; Steinberg *et al.*, 2018; Taylor *et al.*, 2023; Weng *et al.*, 2020; Zhao *et al.*, 2021).

Table 3: Critical appraisal findings (based on the CASP critical appraisal tool for randomised controlled trials)

Question	Ebbert *et al.*, 2015	Steinberg *et al.*, 2018	Taylor *et al.*, 2023	Weng *et al.*, 2020	Guo *et al.*, 2023	Zhao *et al.*, 2021	Machulska, *et al.*, 2021	Farley *et al.*, 2017	Hatsukami *et al.*, 2020
Section A – Is the basic study design valid for a randomised controlled trial?									
1. Did the study address a clearly formulated research question?	+	+	+	+	+	+	+	+	+
2. Was the assignment of participants to interventions randomised?	+	+	+	+	+	+	+	-	CT
3. Were all participants who entered the study accounted for at its conclusion?	+	+	+	+	+	+	+	-	-
Section B – Was the study methodologically sound?									
4. (a) Were the participants 'blind' to intervention they were given?	+	+	-	-	-	-	CT	-	-
5. (b) Were the investigators 'blind' to the intervention they were giving?	+	+	-	-	-	-	CT	+	-
4. (c) Were the people assessing/analysing outcome/s 'blinded'?	+	+	+	+	+	+	CT	+	CT
5. Were the study groups similar at the start of the trial?	+	+	+	+	+	-	+	-	+
6. Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?	+	+	+	+	+	+	+	-	-
Section C – What are the results?									
7. Were the effects of intervention reported comprehensively?	+	+	+	+	+	+	+	+	-
8. Was the precision of the estimate of the intervention effect reported?	+	+	+	+	+	+	+	+	-
9. Do the benefits of the intervention outweigh the harms and costs?	CT	CT	-	CT	CT	CT	CT	CT	CT
Section D – Will the results help locally?									
10. Can the results be applied to your local population/in your context?	+	+	+	+	CT	CT	-	CT	+

+=Yes; - = No; CT=Can't tell

4.4 Behavioural Change Technique Analysis

Table 4 displays a summary of behavioural change techniques used in the interventions. Twenty-two behavioural change techniques were identified. Individual interventions included between five and fifteen behavioural change techniques. The most commonly included techniques were 'instruction on how to perform the behaviour' (n=9 studies) and 'feedback on outcomes of behaviour' (n=9 studies). 'Goal setting- behaviour' (n=7), 'pharmacological support' (n=6), 'Information about health consequences' (n=5) and 'reward (outcome)' (n=5) were also commonly used.

Table 4: Summary of behaviour change techniques used in interventions in the review

	Ebbert *et al.*	Farley *et al.*	Guo *et al.*	Hatsukami *et al.*	Machulska *et al.*	Steinberg *et al.*	Taylor *et al.*	Weng *et al.*	Zhao *et al.*	**TOTAL**
1.1 Goal setting (behaviour)	■	■	■			■	■	■	■	7
1.2 Problem solving	■		■				■			3
1.3 Goal setting (outcome)	■	■	■			■				4
1.7 Review outcome (goal)	■	■	■							3
2.3 Self-monitoring of behaviour				■	■		■			3
2.7 Feedback on outcomes of behaviour	■	■	■	■	■	■	■	■	■	9
3.2 Social support (practical)							■	■	■	3
3.3 Social support (emotional)							■	■	■	3
4.1 Instruction on how to perform the behaviour	■	■	■	■	■	■	■	■	■	9
5.1 Information about health consequences			■		■	■		■	■	5
5.2 Salience of consequences			■							1
6.2 Social comparison			■							1
8.4 Habit reversal		■	■	■	■					4
8.7 Graded tasks	■	■								2
10.8 Incentive (outcome)				■				■		2
10.10 Reward (outcome)		■	■	■				■	■	5
11.1 Pharmacological support	■	■	■	■		■			■	6
12.2 Restructuring the social environment			■				■			2
12.3 Avoidance/reduce exposure to cures	■		■							2
13.5 Identity associated with changed behaviour							■			1
15.1 Verbal persuasion about capability			■				■	■	■	4
15.3 Focus on past success	■									1
TOTAL	10	9	15	7	5	6	10	9	9	

4.5 Results of syntheses

Results on the effectiveness of interventions from the nine included studies are narratively summarised below according to the type of intervention delivered to participants. These have been categorised as: behavioural-only interventions; nicotine replacement therapy *plus* behavioural interventions; and pharmacological *plus* behavioural interventions.

4.5.1 Behavioural-only interventions

Three studies investigated the effectiveness of behavioural-only interventions (Machulska *et al.*, 2021; Taylor *et al.*, 2023; Weng *et al.*, 2020). These included Virtual Reality training using Approach Bias Modification plus short behavioural counselling (Machulska *et al.*, 2021); behavioural support to reduce smoking and increase physical activity (Taylor *et al.*, 2023); and modified approaches to referrals to cessation services (Weng *et al.*, 2020).

Machulska et al. (2021) conducted a two-arm randomised controlled trial in Germany, which used Approach Bias Modification embedded into a Virtual Reality task. The authors aimed to explore whether this approach would modify existing cognitive biases for smoking and subsequently alter smoking behaviour, although no specific target for reducing or quitting was described. Participants were included in the study if they self-reported motivation to quit smoking within the next 6 months. In the intervention group, participants were asked to put red bordered items in the trash and blue-bordered items in a box. Items with a red-border were smoking-related, and items with a blue-border were non-smoking related items. Participants in the control group carried out a similar task in virtual reality, putting red bordered items in a right-hand-side box and blue-bordered items in a left-hand-side box. However, there was no link between smoking-related items and border colour. Both groups took part in 6 sessions over 2 weeks. All participants were also provided with behavioural counselling for smoking cessation and had access to an app where they could record and track how many cigarettes they had smoked. Outcomes were self-reported and CO-verified at baseline, post-test (2 weeks) and follow-up (7-8 weeks).

For the outcome *smoking reduction*, there was no statistically significant evidence of an intervention effect as both groups self-reported a decrease in cigarettes smoked per day across time by 8 to 10 cigarettes over 8 weeks. The intervention group initially reduced smoking faster (-1.36 SE 0.43 cigarettes per day; p=0.001) than the control group. However, the rate of decline in smoking reduced over time, meaning that between 4 and 8 weeks, the count of daily smoked cigarettes started to rise again especially in the experimental group, so that at 8 weeks smoking rates had reduced by the same amount in both groups.

For the outcome *smoking cessation,* there was also no statistically significant evidence of an intervention effect at either 3 or 7 weeks. At 3 weeks, 27% of smokers in the intervention group vs. 16% of smokers in the control group self-reported they had ceased smoking (p=0.674). By 7 weeks, 22% of smokers in the intervention group vs. 23% of smokers in the control group had ceased smoking (p=0.754). Analysis of changes in exhaled carbon monoxide confirmed that while both groups reduced smoking, there were no differences in the magnitude of smoking reduction

between groups (12.3 (SD 11.2) ppm and 13.6 (SD 7.4) ppm in the intervention and control groups at 9 weeks, (p=0.807)).

In summary, there was no statistically significant evidence of any effect on self-reported reduction or cessation outcomes at 8 weeks, which was supported by verified, carbon monoxide measurements. This study was considered to be of higher quality, although it was unclear whether participants and investigators analysing results were blinded to group allocation (intervention or control).

Taylor et al. (2023) carried out a two-arm randomised controlled trial in the UK to explore whether behavioural support to reduce smoking and increase physical activity was effective at both reducing smoking and prolonging abstinence. Participants were included if they wanted to reduce smoking but not quit immediately. The intervention group received eight weekly sessions of in-person or telephone behavioural support lasting 10 to 60 minutes to reduce smoking and increase physical activity, with an additional 6-weeks support available on request for those wishing to quit. The control group received brief written advice on smoking cessation only with signposting to local services. Smoking was self-reported and those reporting a quit attempt at 3 and 9 months provided exhaled CO data. Those verified as abstinent at nine months provided exhaled CO at 15 months.

For the outcome *smoking reduction*, there was evidence of an intervention effect on self-reported reduction in smoking of ≥50% from baseline with 18.9% of the intervention group vs. 10.5% of the control group meeting that goal at three months (OR=1.98; 95% CI=1.35 to2.90; p<0.0004). The effect was smaller at 9 months with 14.4% vs. 10.0% of intervention and control participants reducing baseline smoking amount by at least 50% (OR=1.52; 95% CI=1.01 to 2.29; p=0.043). In absolute terms, the adjusted mean difference (AMD) in cigarettes smoked per day at three months was lower by 5.6 cigarettes in the intervention group (AMD= −5.62; 95% CI=−9.80 to −1.44; p=0.009), but by nine months the difference was much smaller by just 1 cigarette per day and no longer statistically significant (AMD=−0.95; 95% CI=−5.37 to 3.46; p=0.67).

For the outcome *smoking cessation,* slightly more of the intervention vs. control group made a quit attempt (17% vs. 15%) and were verified as abstinent (9% vs. 4%) at 6 months, but neither outcome equated to a statistically significant difference (OR= 1.15 ,95% CI= 0.8 to 1.64 for quit attempts, and OR=2.30, 95% CI=0.70 to 7.56 for abstinence). Even fewer participants were verified as abstinent at twelve months (6% of the intervention and 1% of the control group, OR= 6.33, 95% CI=0.76 to 53.10), which again was not a statistically significant difference.

For the outcome *cost effectiveness,* the estimated direct intervention cost was £239.18 (with sensitivity analyses ranging from £204 to £292) per person. The intervention was estimated to lead to a non-statistically significant increase in costs of £173.50 (95% CI= −£353.82 to £513.77) and a non-statistically significant decrease in QALYs of -0.006 (95% CI= −0.033 to 0.021), compared with the control. Therefore there was no evidence of cost-effectiveness.

There was evidence that, compared with brief advice, the intervention nearly doubled the odds of participants halving their baseline smoking habit at 3 months, equating to an average extra reduction of 5.6 cigarettes per day in the intervention group. However, by 9 months the average

extra reduction was just 1 cigarette per day in the intervention vs. the control group. Early reductions in smoking at 3 months were not sustained at 9 months and did not translate into more abstinence at 6 or 12 months. This study was well designed and considered to be higher quality, but the intervention showed no evidence of cost-effectiveness.

Weng et al. (2020) was a three-arm randomised trial comparing a 12-page self-help smoking cessation booklet alone (control group) and two different 12-week approaches to supported referrals to smoking cessation services for smokers at community hot-spots in Hong Kong. These approaches were described as 1) on-site referral (OSR): where counsellors helped willing participants make appointments with a smoking cessation service. Participants also received a reminder tailored to their appointment date and daily text messages for 1 month; 2) text messaging referral (TMR): participants were not referred on site but received sixteen fixed schedule text messages over 2 months. Both intervention groups also received the same self-help booklet as the control group; an additional smoking harms health warning leaflet; a referral card to utilise smoking cessation services; and prompts to use smoking cessation services during telephone follow-up at 1, 2 and 3 months. The intervention was designed to include participants who were either willing to quit or reduce smoking. No specific target for reduction or cessation was described. Outcomes were self-reported via questionnaire at baseline and telephone at 1, 2, 3, 6, and 18 months. Verification was determined by exhaled CO data, which was recorded in-person from all at baseline, but only those self-reporting a quit for 7+ days at 3, 6, and 18 months were verified.

For the outcome *smoking reduction,* at 3 months there was no statistically significant evidence of an intervention effect on the odds of reducing baseline smoking by 50% for either on-site referral (18.7%) or text-message referral (16.9%) compared with the control group (16.2%) with an OSR group adjusted odds ratio (aOR) of 1.21(95% CI= 0.79 to 1.85) and a TMR group aOR of 1.29 (95%CI= 0.85 to 1.97). Similarly, at 6 months, the percentage of participants that had halved their baseline smoking habit was not statistically different between the OSR group (20.3%), the TMR group (16.1%), and the control group (19.3%), with the OSR group aOR of 0.90, (95% CI= 0.60 to 1.33); and the TMR group aOR of 0.84(95%CI=0.56 to 1.26). At 18 months, there was evidence that more participants in the OSR group (14.2%) reduced their smoking by 50% compared with the control group (10.4%), aOR= 1.74, (95% CI= 1.05 to 2.91). However, there was no difference between the TMR group vs. control group, with the TMR group also having 10.4% of participants achieving a 50% reduction from baseline at 18 months (aOR= 1.33, 95% CI=0.79 to 2.26).

For the outcome *smoking cessation,* participants receiving an on-site referral were more likely to use smoking cessation services (OR= 6.99, 95% CI=1.09 to 11.94). According to self-reported abstinence, more of the OSR group and TMR group were abstinent than the control group at 3 months (14.4%, 95% CI=13.0%, 8.6% respectively) and 6 months (17.7%, 17.1%, 12.0% respectively). But there was no strong statistical evidence of a difference in self-reported abstinence between groups at any time (3 months OSR aOR= 1.54 95% CI=0.96 to 2.49; TMR aOR= 1.32 95% CI=0.81 to 2.15; 6 months OSR group aOR= 1.56, 95% CI=1.00 to 2.42, TMR group aOR= 1.40, 95% CI=0.90 to 2.19). The verified estimates for abstinence were approximately half the size of self-reported estimates with only 7.6% of the OSR group, 7.8% of the TMR group and 3.9% of the control group confirmed as abstinent at 6 months. There was no evidence of an intervention

effect on verified abstinence from smoking at 6 months (OSR group aOR= 1.83 95% CI=0.95 to 3.53; TMR group aOR= 1.82, 95% CI=0.94 to 3.52).

For the outcome *cost effectiveness,* the estimated cost per participant reporting abstinence at 6 months was similar for the OSR (US$124.8) and TMR (US$131.9) groups, which were both approximately 30% lower than that of the control group (US$180.7). The precision of these cost estimates is not estimated but considering there was limited evidence of effectiveness of this intervention it is unlikely to be cost-effective despite the lower costs.

In summary, there was no evidence of effect on self-reported halving baseline smoking at 1, 2, 3, or 6 months for on-site or text-message referral vs. control. In contrast, there was evidence of an effect on self-reported halving baseline smoking at 18 months for on-site, but not text-message, referral vs. control. Weak evidence suggested self-reported abstinence was higher at 6 months for on-site referral vs. control, but there was no evidence supporting an effect at 3, or 18 months. There was no evidence of effect of either on-site referral or text-message reminders compared with brief advice on verified smoking abstinence at 6 months. This study was considered to be high quality, with the only issue with blinding of intervention.

In this diverse selection of behavioural interventions, we found no evidence that any approach altered the likelihood of verified abstinence at 8 weeks (Machulska *et al.* 2021), 6 months (Taylor *et al.* 2023; Weng *et al.* 2020) or 12 months (Taylor *et al.* 2023). While Weng *et al.* (2020) reported some evidence of effect of either onsite-referral or text-message referral vs. brief advice on self-reported abstinence at 6 months, evidence was inconsistent at other time-points and not supported by verified outcomes. There was some evidence from Taylor *et al.* (2023) and Weng *et al.* (2020) that baseline smoking could be reduced by 50% more often by those receiving a behavioural intervention. But evidence of effects at an early timepoint (4 weeks or 3 months) got weaker at later time points (8 weeks or 9 months). Therefore, evidence from these behavioural interventions does not support a sustained effect on smoking reduction or improved smoking cessation and abstinence.

4.5.2 Pharmacological (varenicline) plus behavioural interventions

Two studies measured the effectiveness of Varenicline delivered alongside a behavioural intervention (Ebbert *et al.*, 2015; Steinberg *et al.*, 2018). Participants in the study by Ebbert *et al.* (2015) received a smoking cessation booklet and tailored behavioural counselling in addition to Varenicline. Participants in the study by Steinberg *et al.* (2018) received strategies for smoking reduction and counselling, including one motivational interviewing session alongside Varenicline.

Ebbert et al. (2015) was a combined intervention comparing the effectiveness of Varenicline titrated to 1mg twice daily for 24 weeks vs. placebo on smoking reduction and cessation. Individuals could join the trial if they were not ready to quit smoking within 1 month, but willing to reduce and try quitting within 3 months. Participants were set targets for reduction of cigarettes by ≥ 50% from baseline to 4 weeks and ≥ 75% from baseline to 8 weeks. They were asked to make a quit attempt by 12 weeks. The trial took place across ten countries, including the UK. The first 12 weeks of treatment in the trial were the reduction phase and the next 12 weeks were the abstinence phase. All participants received tailored smoking cessation counselling and a *Clearing*

the Air: Quit Smoking Today booklet. Counselling was consistent with recommendations of the "Treating Tobacco Use and Dependence" clinical practice guidelines. Counsellors were urged to be consistent and brief, to focus on problem solving (e.g. what triggers the urge to smoke) and skills training (e.g. practical actions to avoid smoking), and to highlight successes not failures. Reduction advice included increasing time between cigarettes; and rank-ordering cigarettes from easiest to hardest to give up. Tobacco use was self-reported and exhaled carbon monoxide (CO) measurements were obtained at all clinic visits.

For the outcome *smoking reduction,* there was statistically significant evidence of intervention effect on self-reports of reduced smoking by ≥50% at 4 weeks from baseline for 47.1% of participants receiving Varenicline, and 31.1% receiving placebo (RR=1.5, 95% CI=1.3 to 1.7), and reducing smoking by ≥75% at 8 weeks from baseline for 26.3% of participants receiving Varenicline, and 15.1% receiving placebo (RR=1.8, 95% CI=1.4 to 2.2).

For the outcome *smoking cessation,* there was also evidence of intervention effect on verified continuous abstinence between 15-24 weeks (32.1% of the Varenicline group vs. 6.9% of the placebo group, RR=4.6, 95% CI=3.5 to 6.1). Among participants abstinent from 15-24 weeks, the median time to becoming abstinent was 50 days (7 weeks) for Varenicline vs. 85 days (12 weeks) for placebo ($p < 0.0001$).

In summary, providing 1 mg of Varenicline twice daily alongside behavioural support to reduce smoking for 12 weeks, followed by 12 weeks of behavioural support for cessation, increased the percentage of participants reducing their baseline smoking by 50% at 4 weeks and by 75% at 8 weeks. Greater reductions in smoking also translated to earlier cessation by 5 weeks and higher maintenance of continuous abstinence between 15 and 24 weeks. This was a high-quality study.

Steinberg et al. (2018) conducted a small 4-week proof of concept trial in the USA exploring the effectiveness of Varenicline titrated to 1mg twice daily on smoking reduction and cessation. Individuals were eligible to participate if they were Interested in cutting down, but not quitting within 30 days. All participants were provided information regarding medication use and strategies for reducing the amount they smoked. This was a reduction intervention with 4 weekly counselling sessions lasting 20 or 35-minutes where participants were encouraged to *reduce* smoking. At visit four, they received an intervention adapted from motivational interviewing, followed by advice to *quit*, although no target quit date was set as part of the intervention. Outcomes were self-reported and verified with exhaled CO measures.

For the outcome *smoking reduction,* 38% of participants receiving Varenicline vs. 20% of participants in the placebo group self-reported reducing their baseline smoking by 50% at 6 months. This was not statistically significant (OR=2.45; 95% CI= 0.53 to 11.38; p=0.2553). In absolute terms the difference at 6 months in smoking between groups was just 1 cigarette (p=0.363). The Varenicline and control groups had reduced by a similar amount (4 to 5 cigarettes per day) from a mean of 14 to 10 cigarettes per day, whilst the placebo group had reduced from 16 to 11 cigarettes per day.

For the outcome *smoking cessation,* there was also no statistically significant evidence of intervention effect on quit attempts or carbon monoxide concentrations. Thirty two percent of

the Varenicline group made a quit attempt by 6 months, vs. 14% in the placebo group, although this was not a statistically significant difference (OR= 2.44, 95% CI=0.65 to 9.12). Both groups had lower carbon monoxide (CO) at the end-of-treatment ($p < 0.001$), at 1 month ($p=0.035$), and 6 months ($p=0.045$) follow-up, verifying the reduction observed in self-reported smoking for both groups. However, there was no evidence of an intervention effect as the amount that carbon monoxide reduced was not statistically significantly different between groups at 6 months (ratio=1.04; 95% CI: 0.78 to 1.38; $p=0.812$).

In summary, providing 1 mg of Varenicline twice daily alongside behavioural support to reduce smoking for 28 days without setting any cessation goals did not improve verified reduction or cessation outcomes more than a placebo by 6 months follow-up. This was a higher quality study, but low confidence in effects could be a result of the relatively small sample size and much shorter intervention period.

There is strong evidence of effectiveness for greater smoking reduction and cessation from one large higher quality multinational study of Varenicline plus behavioural support (Ebbert *et al.* 2015). This is consistent with the effect estimates but not statistical significance for smoking reduction from another higher quality but smaller study with a shorter intervention supporting reduction but not cessation (Steinberg *et al.* 2018). Ebbert *et al.* (2015) found evidence that in the context of a combined intervention with 12 weeks of behavioural support to reduce smoking followed by 12 weeks of behavioural support to quit smoking, participants receiving 1mg Varenicline twice daily were four times more likely to have maintained continuous abstinence (verified by carbon monoxide) at 6 months than those receiving placebo. Whereas Steinberg *et al.* (2018) found no differences in carbon monoxide at 6 months after providing 4 weeks of behavioural support for reducing (but not quitting) smoking alongside Varenicline 1 mg twice daily or placebo. Overall, supporting behavioural interventions with Varenicline could be a powerful method for smoking reduction and cessation. Further research could confirm the importance of the duration of an intervention and the need for combined reduction and cessation goals as used by Ebbert *et al.* (2015) rather than a reduction only approach as used by Steinberg *et al.* (2018).

4.5.3 Nicotine replacement therapy plus behavioural interventions

Four lower quality studies examined the effectiveness of nicotine replacement therapy (NRT) delivered alongside a behavioural intervention (Farley *et al.*, 2017; Guo *et al.*, 2023; Hatsukami *et al.*, 2020; Zhao *et al.*, 2021). The behavioural element in these studies included a community pharmacy programme offering NRT combined with behavioural support to reduce and then quit smoking for 1 month or 4 months (Farley *et al.*, 2017), personalised behavioural support to quit smoking via instant messaging and a chatbot for 3 months (Guo *et al.*, 2023), brief counselling on reducing smoking for 2 months (Hatsukami *et al.*, 2020), and personalised behavioural support to quit smoking via instant messaging for 2 months (Zhao *et al.*, 2021).

Farley et al. (2021) conducted a feasibility study of a 2x2 factorial trial to investigate the effectiveness of shorter (4 weeks) vs. standard (16 weeks) length programme of behavioural

support vs. self-help for smoking reduction and cessation in community pharmacies in inner-city Birmingham, UK. Individuals were eligible if they were not planning to quit smoking within 1 month but were wanting to reduce. Participants were assigned to either behavioural support for 16 weeks (group 1) or 4 weeks (group 2), or self-help materials for 16 weeks (group 3) or 4 weeks (group 4). Regardless of group, all participants received NRT for 9 months, were given advice on reducing smoking in four steps, were regularly asked if they felt ready to quit and if so, they were then offered a referral to a smoking cessation programme. Outcomes included 'floating sustained abstinence', defined as self-reported abstinence (or up to a total of 5 cigarettes smoked) over 4 weeks, starting at any point from day 15 after the quit date. The four steps to smoking reduction involved reducing the amount of cigarettes smoked: Step 1: by 25% of baseline; Step 2: by 50% of baseline; Step 3: by 75% of baseline; Step 4: by 100% of baseline. They were also asked to make a quit attempt at step 4. Outcomes were self-reported and verified by exhaled CO at 4 weeks and 6 months post quit for those that declared abstinence.

For the outcome *smoking reduction,* there was no statistically significant evidence of effect on sustaining a 50% reduction in baseline smoking from 9 to 12 months for either factor (1. intervention delivery mode, behavioural support vs. self-help; or 2. intervention duration, 4 weeks vs. 16 weeks). While 8.8% of participants in the 4-week programmes and 2.9% of participants in the 16-week programmes sustained a reduction, the difference was not statistically significant (RR= 3.00; 95% CI=0.45 to 20.44). A total of 8.3% of participants who received behavioural support compared with 3.1% of participants in the self-help groups sustained a reduction but the difference was not statistically significant (RR=2.67; 95% CI=0.40 to 18.19). In absolute terms over 12 months, the number of cigarettes smoked per day reduced by a pooled mean of 2.29 (SD=7.9) in the 4-week, 2.26 (SD=5.4) in the 16-week, 1.58 (SD=7.2) in the behavioural support, and 3.36 (SD=6.1) in the self-help groups respectively, none of which were statistically different.

For the outcome *smoking cessation,* intervention length had no effect, with 8.8% of participants in both the 4- and 16-week programmes achieving floating sustained abstinence 4 weeks after quitting (RR=1.00; 95 % CI= 0.24 to 4.10). Fewer participants receiving behavioural support set a quit date than those receiving self-help (9% vs. 21%), similarly floating sustained abstinence 4 weeks after quitting was less prevalent among those getting behavioural support compared with participants getting self-help (5.5% vs. 12.5%), but none of the differences between groups was statistically significant (relative risk 0.44; 95% CI= 0.10 to 1.95).

In summary, there was no evidence of effect on smoking reduction or cessation based on the length of or delivery mode of a behavioural support intervention supported with NRT. This was a lower quality study. The feasibility study identified issues with pharmacists adhering to the randomised allocations, in the belief that behavioural support was too important not to give people allocated to the self-help arms. It was decided not to conduct a full trial as the intervention was not feasible owing to difficulty in recruitment, randomisation as intended leading to imbalances in participants characteristics at baseline, participant drop out and engagement among pharmacists delivering the intervention. Pharmacists were uncomfortable randomising participants and saw abrupt cessation as a preferrable goal, which highlights the challenge of researching alternative approaches in real-world settings.

Guo et al. (2023) aimed to evaluate the effect of NRT sampling (whereby participants were provided with a limited supply of NRT) plus personalised real-time behavioural support via instant

messaging and a chatbot compared with SMS messages containing general health advice over 3 months on smoking cessation in Hong Kong. No eligibility criteria relating to participants' motivation to reduce or quit smoking were described. Intervention and control groups both received brief advice initially, which included advice to quit promptly using NRT or smoking cessation services. The intervention included 1 week of free NRT plus instant messages personalised by baseline readiness to quit and target quit date, covering topics such as knowledge and skills of quitting, benefits of quitting, strategies to manage urges to smoke for self-efficacy, and smoking cessation services. Message schedules were personalised by baseline readiness to quit and target quit date (if one was made). A total of 6 reminders from the chatbot were sent every 2 weeks over 12-weeks. The chatbot answered common queries related to cessation-like quitting methods, craving management, self-efficacy to quit, and novel tobacco products. Control group participants received regular SMS messages regarding healthy lifestyles at a similar frequency to the intervention group. Participants were asked to make a quit attempt by 12 weeks. Abstinence was verified at 6 and 12 months after baseline using exhaled CO measurements.

For the outcome *smoking reduction,* there was no statistically significant evidence of effect at 6 or 12 months. A total of 19.7% of participants in the intervention group reduced the number of cigarettes smoked per day by 50% of their baseline amount at six months compared with 17.8% of participants in the control group (OR= 1.13; 95% CI: 0.75 to 1.71). A total of 26.9% of participants in the intervention group had reduced the number of cigarettes smoked per day by 50% of their baseline amount at 12 months, compared with 22.3% of the control group (OR= 1.28; 95% CI: 0.88 to1.85).

For the outcome *smoking cessation,* at 6 months, 47.0% vs. 38.0% had made a self-reported quit attempt in the intervention and control group, which was statistically significant (OR=1.45; 95% CI=1.06 to 1.97; p=0.019). However, there was also no statistically significant evidence of an effect on verified abstinence through exhaled CO measures at 6 or 12 months. Only 3.9% and 5.4% of participants in the intervention group were declared abstinent by verified measures at 6 and 12 months, which was similar to the control group with 3.0% and 4.5% at 6 and 12 months (6 months OR= 1.31; 95% CI= 0.57 to 3.04; 12 months OR= 1.21; 95% CI= 0.60 to 2.45).,

In summary, there was evidence that combining NRT sampling and personalised messages vs. general health messages increased the odds of a quit attempt within 6 months. But this did not translate into greater reductions or verified abstinence at 6 or 12 months. This study was considered to be of reasonable quality, limited by a lack of blinding and the combination of personalised messaging with a 1 week sample of NRT, which prevents measuring the effectiveness (or lack) of individual intervention components.

Hatsukami et al. (2020) compared usual smoking to a reduction intervention where smokers were not asked to quit but instead instructed and financially incentivised to completely substitute smoking cigarettes with a fast-acting NRT (4mg nicotine gum or lozenge of their choice and titrated down to 2mg if adverse side effects were experienced). Participants in the NRT group also received brief counselling on how to avoid smoking cigarettes. Individuals were eligible for inclusion if they had not made a serious quit attempt in the past 3 months and were not planning to quit smoking within the next 3 months. Outcomes were measured using various biomarkers, used to validate tobacco exposure, including exhaled CO which was collected at each visit.

For the outcome *smoking reduction,* there was some descriptive evidence that complete substitution of smoking with NRT (CS-NRT) reduced self-reported cigarettes per day more over 8 weeks (Median (min/max) 9.6 (0.9 to 40.7) compared with usual smoking (Median (min/max) 0.7 [-3.6 to 12.0]), although a direct comparison of the group medians is not reported. Verification of reduction in smoking by exhaled CO each week was measured for both groups. No direct statistical comparison of groups is reported, but the verified CO measures were significantly different at 8 weeks compared to baseline for the NRT group, but not the control group. Differences displayed between groups for change in CO were smaller than the effect observed for self-reported data.

For the outcome *smoking cessation,* 17% of participants in the NRT achieved 7-day abstinence as verified by exhaled CO at 8 weeks. Similar figures were not reported for the usual smoking groups, leaving the comparison of this outcome unknown.

In summary, there is descriptive evidence supporting that complete substitution of smoking with NRT had larger reductions in self-reported smoking and to a lesser extent in verified exhaled CO at week 8 compared with the control group. Abstinence rates were 17% at 8 weeks for the intervention group (complete substitution by NRT) but were not reported for the control group. Smaller differences for carbon monoxide measures suggest that complete substitution was difficult to achieve and that differences between the groups, based on self-reported cigarettes per day, are exaggerated.

This paper had the most quality issues of all studies included in the review. Information was not provided on the method of participant randomisation. There was differential dropout between groups that was not accounted for in analyses. Precision (95% confidence intervals) were not provided for our outcomes of interest. There was incomplete outcome reporting and pairwise comparison for all outcomes for the NRT vs. usual smoking groups were not conducted. Therefore, it was not possible to determine the certainty of any observed differences between the two groups.

Zhao et al. (2021) assessed the feasibility of a mobile chat-based intervention combined with nicotine replacement therapy sampling on abstinence amongst smokers residing in Hong Kong over 2 months. No eligibility criteria relating to participants' motivation to reduce or quit smoking were described. All participants received nicotine replacement therapy, brief smoking cessation advice, and active referral to smoking cessation services. Participants in the intervention group also received personalised text messages and chat-based support via instant messaging. Each message was personalised according to the participant's sex, age, and smoking pattern. Message content and conversation initiation and facilitation was similar to Guo *et al.* (2023). They also received booster telephone calls at 4 and 8 weeks. The control group received general smoking cessation text messages at similar frequency to the intervention group. However, counsellors did not respond to any messages from participants and no telephone booster was given at follow-up. No specific target for reduction or cessation was described. Outcomes were self-reported and verified using exhaled CO at 3 and 6 months.

For the outcome *smoking reduction,* there was no evidence of difference in self-reported halving of baseline smoking at 3 months, with 24.2% of intervention compared with 24.6% of control

group participants achieving a ≥50% reduction of their baseline smoking amount (aOR=0.80; 95% CI=0.32 to 2.01; p=0.64). At 6 months, 32.3% of intervention participants and 19.3% of control group participants achieving a ≥50% reduction of their baseline smoking amount, which was not statistically significant different after adjustment (aOR=1.74; 95% CI=0.71 to 4.26; p=0.22).

For the outcome *smoking cessation*, there were no statistically significant differences in quit attempts, self-reported abstinence or verified abstinence at any time-point. Verified abstinence rates at 3 months were 3.2% in the intervention compared to 1.8% in the control group (OR= 1.07; 95% CI=0.08 to 13.65; p=0.960) and at 6 months, with1.6% in the intervention compared to 0% in the control group (OR not estimable). Self-reported abstinence was slightly higher, but not statistically significantly different at 3 months (12.9% intervention vs. 10.5% control, aOR=1.12; 95% CI=0.34 to 3.71, p=0.856) and 6 months (16.0% intervention vs. 5.3% control, aOR=2.82; 95% CI=0.70 to 11.30, p=0.144). At 6 months, 90.3% of intervention participants compared to 77.2% of participants in the control group had made a quit attempt, which was not a statistically significant different (aOR=2.61; 95% CI= 0.88 to 7.82; p=0.085).

In summary, there was no evidence that NRT alongside personalised text message and chat-based support compared with general text messages about smoking cessation affected smoking reduction, cessation or quit attempts. Study quality was limited by imbalanced baseline characteristics including a higher perceived importance of quitting in the intervention group and lack of blinding of the intervention.

Overall, four poorer quality studies combining NRT with behavioural support for reduction (Hatsukami *et al.* 2020), cessation (Guo *et al.* 2023; Zhao *et al.* 2021) or a combination of the two (Farley *et al.* 2021) demonstrate there is little evidence of an effect on verified smoking reduction or cessation outcomes. However, Guo *et al.* (2023) did find that participants receiving NRT plus personalised real-time behavioural support through mobile phone interventions had 45% higher odds of a self-reported quit attempt compared with the control group. Hatsukami *et al.* (2020) described larger reductions in self-reported smoking, and to a lesser extent carbon monoxide concentrations for participants completely substituting smoking with fast-action NRT, suggesting again that differences in self-reported data are likely to be exaggerated.

5. Discussion

5.1 Summary of evidence

This review collated the evidence of effectiveness for approaches to smoking harm reduction among smokers not yet ready to commit to a quit date. We included nine interventions aiming for reduced smoking or reduction prior to cessation compared with the current standard 'abrupt quit' model where smokers do not reduce smoking before their quit date. Included interventions used various behavioural support aproaches alone or in combination with prescribed medication (Varenicline) or NRT. The best evidence of effectiveness for reducing and quitting smoking came from one higher quality large multicentre trial of Varenicline compared with placebo, which was prescribed alongside 12 weeks behavioural support to reduce smoking, followed by 12 weeks of behavioural support to stop smoking (Ebbert *et al.*, 2015). Participants receiving Varenicline were

four times more likely than placebo to have maintained verified continuous abstinence at 6 months. Other included trials, which varied in quality and approaches to the intervention, showed inconsistent evidence for reducing smoking and no evidence of effectiveness for verified smoking cessation outcomes. Verification of smoking reduction or abstinence is well-known to be important to avoid inflated effect estimates commonly seen in self-reported outcome measures. Indeed, seven studies included in our rapid review showed larger effect estimates based on self-reported data compared with estimates verified with exhaled CO, reinforcing the importance of using biomarkers to confirm the effectiveness of these types of interventions. (Farley *et al.*, 2017, Hatsukami *et al.*, 2020, Machulska *et al.*, 2017, Steinberg *et al.*, 2018, Taylor *et al.*, 2023, Weng *et al.*, 2020, Zhao *et al.*, 2021). Lastly, all trials were in general populations of smokers not ready to quit, therefore the evidence for targeted or tailored smoking harm reduction interventions among specific populations defined by age, socio-economic position or health, remains an important area for future reviews.

The three studies using solely behavioural support approaches described very different interventions focused on either a combination of reduction and cessation goals (Taylor *et al.*, 2023) or cessation goals alone (Machulska *et al.*, 2021, Weng *et al.*, 2020). Collectively, included evidence for behavioural support interventions did not support a sustained effect on smoking reduction or improved smoking cessation and abstinence. Both Machulska *et al.*, (2021) and Taylor *et al.*, (2023) reported greater reductions in their intervention groups at earlier follow-up timepoints, but the differences got smaller over time and neither study saw improved cessation rates in the intervention groups when compared with control groups. Weng *et al.*, (2020) saw evidence of a higher rates of self-reported reduced smoking by 18 months, but not at earlier time-points. As reduction measures in Weng *et al.*, (2020) were unverified, this may explain the anomalous finding. For example, verified abstinence rates at 18 months were just 4% to 6% across groups compared with 15% to 18% estimated for self-reported abstinence, thus the difference in self-reported reduction estimates at 18 months is likely to be unreliable (Weng *et al.*, 2020). The evidence of effectiveness of behavioural approaches to smoking reduction in our review contrasts with an existing Cochrane review, which found a high certainty evidence of effectiveness of behavioural approaches (specifically counselling) to smoking cessation (Hartman-Boyce *et al.*, 2021). In 194 trials verified abstinence rates improved by 44% (95% credible interval 22% to 70%) in behavioural smoking cessation trials (Hartman Boyce *et al.*, 2021). However, our findings do align with behaviour-only smoking reduction trials, of which there were just 2 out of 51 trials synthesised in Lindson *et al.*, (2019). Like our findings, imprecise evidence of effectiveness was observed (RR=1.49, 95% CI=0.59 to 3.76). The difference in effectiveness may be related to the small number of trials, the diversity of behavioural approaches used for reduction to date or could suggest that achieving smoking abstinence via behavioural only interventions to reduce smoking is harder.

Four poorer quality studies combining NRT with behavioural support for reduction (Hatsukami *et al.*, 2020), cessation (Guo *et al.*, 2023; Zhao *et al.*, 2021) or a combination of the two (Farley *et al.*, 2021) provided limited evidence of an effect on verified smoking reduction or cessation outcomes. This contrasts evidence synthesised by Lindson-Hawley *et al.*, 2016 from reduction only interventions that estimated from 8 trials that NRT was effective for reducing baseline smoking by 50% (RR=1.75, 95% CI= 1.44 to 2.13); and quitting smoking (10% intervention vs. 5% control, RR=1.87, 95% CI=1.43 to 2.44) (Lindson-Hawley *et al.*, 2016). Additionally, 7 interventions combining reduction and cessation goals estimated fast-acting NRT more than doubled the likelihood of verified abstinence at 6 months (RR=2.56 95% CI=1.93 to 3.39) (Lindson *et al.*, 2019).

Furthermore, NRT is well-established as an effective approach to smoking cessation (RR=1.55, 95% CI=1.49 to 1.61) (Hartman-Boyce *et al.*, 2018). Although the effectiveness of NRT in reduction trials is similar in magnitude to cessation trials the absolute prevalence of abstinence in reduction trials with NRT is lower at just 2 to 6%, compared with 10 to 16% in cessation trials (Lindson-Hawley, *et al.*, 2016, Lindson *et al.*, 2019, Hartman-Boyce *et al.*, 2018). Participants in reduction trials typically have a lower motivation to quit, which may explain the lower abstinence rates achieved using NRT compared with cessation trials. While reduction interventions involving NRT may be effective for increasing abstinence the absolute % of smokers achieving abstinence is lower than for comparable cessation interventions, which may mean that smoking harms are reduced to a lesser extent.

Supporting behavioural interventions with Varenicline could be a powerful method for smoking harm reduction. Trials in our rapid review reporting the effect of Varenicline plus behavioural support were collectively consistent in supporting larger reductions and cessation smoking rates in the intervention compared with the control groups, but inconsistent in the precision of effects. Both trials combined Varenicline 1mg twice daily plus counselling and reported verified outcomes. Ebbert *et al.*, (2015) was a large multi-centre trial of a 24-week combined reduction and cessation intervention among participants willing to set a quit date within 3 months, which reported a nearly doubled rate of smoking reduction (26 vs. 15%, RR= 1.8, 95% CI= 1.4 to 2.2) and a quadrupled rate of abstinence (32 vs. 7%, RR= 4.6, 95% CI= 3.5 to, 6.1) for those taking Varenicline. While Steinberg *et al.*, (2018), was a small trial of a 4-week reduction only intervention among participants willing to reduce smoking but not quit, it reported a similar doubled rate of reduction (38 vs. 20%, OR= 2.45, 95% CI= 0.53 to 11.38) for those taking Varenicline, although not statistically significant. Ebbert *et al.*, (2015) included participants that were more willing to commit to a quit, provided behavioural support for cessation, and delivered a longer intervention than Steinberg *et al.*, (2018). Such differences in motivation to quit, intervention duration, or intervention goals may explain the difference the precision of effects observed. A systematic review of trials of Varenicline among smokers not ready to discontinue tobacco use included five trials (Lopes *et al.*, 2022), three of which were not included in our review as they were published prior to 2015. Lopes *et al.,* (2022), found that combining Ebbert *et al.*, (2015) with two earlier trials, produced high certainty evidence that smokers taking Varenicline vs. placebo doubled the rate of verified abstinence at 6 months (RR=2.00 95% CI=1.70, 2.35). The estimated effect on abstinence of Varenicline when used in reduction trials is similar in both relative and absolute terms to the pooled effect from 41 cessation trials (23 vs. 10%, RR= 2.32, 95% CI= 2.15, 2.51) (Livingstone-Banks *et al.*, 2023). Further research could provide clarity on outstanding uncertainty, but Varenicline offers the potential to achieve similar rates of abstinence in interventions combining reduction and cessation goals among smokers not willing to commit immediately, as that achieved in cessation trials involving smokers more motivated to quit. The observed increases in abstinence are an important contribution to reducing smoking harms.

Our secondary outcome of interest was cost effectiveness. We found only two studies reporting on the cost effectiveness of their smoking harm reduction interventions (Taylor *et al.*, 2023; Weng *et al.*, 2020), neither of which reported evidence that their interventions were effective therefore there was no evidence of cost-effectiveness either.

5.2 Strengths and limitations of the available evidence

Our rapid review included nine randomised controlled trials, most of which were considered good quality, although there was variation. Trials were well designed with random assignment, blinding of assessors to treatment, balanced group characteristics, equal treatment across groups other than the intervention, comprehensive reporting of effect estimates and precision. Studies of lower quality (Farley *et al.*, 2017; Hatsukami *et al.*, 2020, Machulska *et al.*, 2021) were all at risk of performance bias owing to a lack of blinding of participants and investigators to treatment allocation, which is an inherent problem common to all behavioural interventions. Only one study (Taylor *et al.*, 2023) provided evidence on both cost-effectiveness and harms, which means it has not been possible to judge the balance of benefits, costs and harms. Results from six studies were thought to be applicable to the Welsh population because they tested interventions that could be implemented by Public Health Wales (Ebbert *et al.*, 2015; Hatsukami *et al.*, 2020; Steinberg *et al.*, 2018; Taylor *et al.*, 2023; Weng *et al.*, 2020). Although Farley *et al.* (2017) was based in the UK, issues with participant randomisation and intervention delivery mean the research process was not reliable and thus the findings are not generalisable. Guo *et al.*, 2023; Machulska *et al.*, 2017; and Zhao *et al.*, 2021, tested technology-based interventions involving virtual reality, instant messaging with a chatbot and personalised messaging developed in non-English or Welsh language so were considered unlikely to be easily applicable for implementation in Wales.

Across all of the interventions we included in our rapid review, seven studies incorporated both self-reported and verified outcomes based on expired CO levels (Farley *et al.*, 2017, Hatsukami *et al.*, 2020, Machulska *et al.*, 2017, Steinberg *et al.*, 2018, Taylor *et al.*, 2023, Weng *et al.*, 2020, Zhao *et al.*, 2021). In three trials (Hatsukami *et al.*, 2020, Machulska *et al.*, 2017, Steinberg *et al.*, 2018) comparing changes in self-reported cigarettes per day alongside changes in carbon monoxide, estimated group differences were larger for the subjectively compared to the objectively collected data. In four trials, with self-reported and verified abstinence, estimates of abstinence were always smaller when verified by at least half (Weng *et al.*, 2020, Farley *et al.*, 2017), but sometimes by as much as six or ten times smaller (Taylor *et al.*, 2023, Zhao *et al.* 2021). This limitation of self-reported data highlights the strength of our work, by excluding studies with no verified outcome measurements.

5.3 Strengths and limitations of this rapid review

Our rapid review was based on established guidelines for conducting rapid reviews to capture all relevant publications with minimal risk of bias in a timely manner. In terms of the strengths, we combined systematic searches of four electronic databases with supplementary searches of relevant systematic reviews and contact with an expert in the field. To shorten the timeframe for the review, most titles and abstracts were screened by a single reviewer. Twenty percent of titles and abstract were reviewed in duplicate and showed 98.5% inter-rater reliability, providing reassurance that few studies of relevance are likely to have been missed. All full-texts were screened in duplicate. Differences in inclusion decisions were discussed and resolved among the team. Reviewers conducting the current rapid review were not authors of any included studies (in contrast to relevant Cochrane reviews) and no reviewers have any involvement in tobacco industry, which reduces potential bias in design, conduct or interpretation of the review related to competing interests. In terms of limitations, data extraction was done by a single reviewer and consistency checked by another, rather than being extracted entirely in duplicate. Synthesis was limited to narrative rather than undertaking a meta-analysis, which would have taken more time

but may not have provided greater insight owing to the small number of studies that were included.

Our rapid review included nine trials, which appears low compared with the most recent relevant systematic reviews (Lindson-Hawley *et al.*, 2016, Lindson *et al.*, 2019, Lindson *et al.*, 2025) and could be considered a limitation. However, the small number of trials is explained by our strict inclusion criteria, which were designed to find studies most relevant to the Public Health Wales smoking service review. For example, we specified that participants in trials should be unwilling or unable to commit to a quit date at recruitment to best represent smokers not currently served by *Help Me Quit*. In addition, we specified included interventions could test advice/support on using e-cigarettes for smoking reduction, but only if the e-cigarettes were not provided by investigators, because current Public Health Wales policy does not support e-cigarette provision.

Overall, the most common reasons for exclusion of studies from our review were because the type of participants (n=47) or interventions (n=31) involved didn't meet our inclusion criteria. When excluded based on participants this was most often a selected non-general population, such as those recruited from health care settings, those with specific health conditions like anxiety, heart disease, etc.; or smokers that were already willing to quit. When excluded based on the intervention this was most often because both trial arms involved an abrupt quit where all participants had to set a quit date within 4 months. We can compare our inclusions with two overlapping Cochrane systematic reviews that had some differences in their inclusion criteria (Lindson *et al.*, 2019, Lindson *et al.*, 2025). Lindson *et al.* (2019) included 13 studies published after 2015, four of which appeared in our database searches with the rest screened against our inclusion criteria as part of supplementary searching. Ultimately two of the 13 studies were included (Ebbert *et al.*, 2015, Farley *et al.*, 2017). Similarly, studies included in Lindson *et al.*, (2019) but not in our rapid review didn't match our inclusion criteria for participants (those ready to quit (n=4); or recruited from healthcare settings, not general populations (n=3)) and the wrong intervention type (an abrupt quit in both the intervention and control groups (n=2)). One other study was excluded for only having self-reported outcomes. From our searches, we did not include any trials of e-cigarettes for smoking reduction. We found all e-cigarette trials that we screened provided e-cigarettes to participants. Similarly, Lindson *et al.*, (2025) found almost all (100 of 104) trials of e-cigarette advice provided e-cigarettes as part of the intervention. All of the four e-cigarette advice trials identified in Lindson *et al.*, (2025) appeared in our searches but did not meet our inclusion criteria because they were a selected (not general) population of dual users of e-cigarettes and tobacco (Czoli *et al.*, 2019, Martinez *et al.*, 2021, Vickerman *et al.*, 2022) or only included self-reported abstinence without verification (Elling *et al.*, 2023). The agreement between inclusions in our review and relevant Cochrane reviews supports the sensitivity of our search strategy. We have also identified a gap in evidence for approaches to harm reduction involving advice on, but not provision of, e-cigarettes for general populations of smokers.

5.4 Implications for practice and policy

We undertook this rapid review as part of the *Help Me Quit* service review to establish whether the evidence base for the effectiveness of specific harm reduction interventions at an individual level had developed since 2019. Our findings show no substantial development beyond studies synthesised in the 2016 and 2019 Cochrane reviews on smoking reduction and reducing harms from smoking (Lindson-Hawley et al., 2016, Lindson et al., 2019), which form the basis of existing NICE guidelines and minimum standards for *Help Me Quit*. Existing evidence, outlined in the aforementioned NICE guidance, supports the use of behavioural support alongside NRT and

prescribed medication for smoking harm reduction. We identified a gap in evidence for advice, but not provision of, e-cigarettes as a tool for smoking harm reduction for general populations of smokers who are not ready to commit to quitting.

Our rapid review identified Varenicline as an effective medication, alongside behavioural support, as part of an intervention combining goals to reduce and then quit smoking for smokers not immediately ready to commit to a quit date. Varenicline, manufactured by Pfizer, was withdrawn from the global market in 2021, however, a generic version was made available in autumn 2024 and Champix has been available since June 2025 (NCSCT, 2025). During its withdrawal, between 2021 and 2024, varenicline was not available to HMQ clients in Wales, and its uptake may have been uneven following renewed availability in 2024. The *Help Me Quit* service review highlighted that the proportion of smokers supported by HMQ who are using varenicline or other prescribed medication remains low by historic standards, suggesting potential for expansion of the service to support harm reduction among those not initially willing to commit to a quit date.

NICE guidance (NICE, 2021) on harm reduction within stop-smoking support recommends that investment in harm-reduction approaches does not detract from, but supports and extends the reach and impact of, existing stop-smoking support. NICE also recommends stop-smoking referral and treatment pathways include a range of approaches that is available to support people who opt for a harm-reduction approach. In line with the best evidence on reducing smoking (Lindson-Hawley et al., 2016, Lindson et al., 2019), NICE recommend providers of stop-smoking support offer NRT on a long-term basis to help people maintain a lower level of smoking. Our review does not offer any more recent evidence to challenge or extend NICE guidance as the studies we included involving NRT were poorer quality.

More flexibility in current service requirements around committing to a quit date within two sessions has been a suggested improvement by frontline staff delivering *Help Me Quit* (Public Health Wales, 2025). Lindson *et al.*, (2019) show similar rates of abstinence as in an abrupt quit can be achieved through reduction interventions incorporating more flexibility around target quit dates. In our rapid review, the best evidence for harm reduction came from Ebbert *et al.*, (2015), which involved prescribing Varenicline alongside a two-stage intervention combining behavioural support for achieving reduction goals with a later focus on achieving cessation goals. An alternative pathway for people not willing to commit to a quit date by session two in *Help Me Quit* could involve a reduction pathway for supporting goals for reducing smoking followed by referral back to cessation support to allow later quit attempts when service users are ready.

The extent to which smoking reduction, in the absence of subsequent smoking cessation, reduces harms from smoking is a matter of debate. Combined with previous Cochrane reviews, our rapid review found that smoking reduction interventions resulted in people smoking less but estimates of how much varied from 0 to 15 fewer cigarettes per day. Neither Lindson-Hawley *et al.*, (2016) or our rapid review found evidence on the direct benefits to health of smoking reduction interventions. In the absence of direct evidence, the potential for health benefits of smoking less must be inferred from observational evidence. Jackson, *et al.*, 2024, estimate that on average, smokers in Britain who do not quit lose approximately 20 minutes of life expectancy for each cigarette they smoke. Therefore, a reduction of 15 cigarettes per day might translate to 5 hours extra lifespan for each day smokers maintain that reduction. However, as the association between cigarette smoking and health is not linear , with the largest fall in risk of cancers or cardiovascular diseases occurring between 0 and 10 cigarettes per day (Dai *et al.*, 2022), the biggest benefits are

likely to be gained by quitting completely rather than reducing from say 20 to 10 cigarettes per day. The major benefit of smoking reduction interventions, therefore, is probably the effect it has on increasing the likelihood of quitting longer-term.

5.5 Implications for future research

Our review explored the behaviour change techniques used in smoking reduction interventions and found between 5 and 15 techniques were identifiable. Lindson *et al.*, (2019), previously described the complex multicomponent nature of these interventions makes it tricky to isolate the evidence for any particular technique. Future research is needed to investigate the most effective features of reduction-to-quit interventions to maximise cessation rates (Lindson *et al.*, 2019). Smoking cessation services could also benefit from collating evidence on more distal outcomes from smoking cessation, like motivation to quit or quit attempts, which could form the basis of an introductory pathway for smokers not yet ready to commit to a quit. As our rapid review only included studies of general populations of smokers not yet ready to quit, future reviews would be required to establish the evidence for how to meet the needs of more vulnerable smokers. Finally, we identified only two interventions that estimated cost-effectiveness, both of which reported no evidence of effect. Future research should therefore include estimates of the health economic impact of adding in additional features to smoking cessation services to meet the needs of smokers not yet willing to commit to a quit.

6. Conclusions

Based on the totality of the evidence identified in this rapid review, approaches to smoking harm reduction remain in line with NICE guidance, which recommends offering an alternative pathway to support smokers not yet ready to quit to reduce their smoking before attempting to quit, making use of medically-licensed nicotine replacement products to substitute for cigarettes.

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8. Additional information

8.1 Appendix 1.

Supplementary table 1: Summary of approaches to smoking reduction and their effectiveness in interventions synthesised in Lindson *et al.*, 2019.

Approach to reduction	Number of trials	RR of abstinence vs. an abrupt quit	RR of abstinence vs. reduction only
All interventions	51 trials in total 22 trials in meta-analysis	1.01 (0.87, 1.17)	Not estimated
Replacing cigarettes with nicotine replacement therapy	24 trials in total 9 trials in meta-analysis 9 - Choice of product 11 - Fast-acting product 4 - Patches	0.91 (0.72, 1.16) Not estimated Not estimated Not estimated	Not estimated 1.02 (0.61,1.69) 2.56 (1.93, 3.39) 0.34 (0.02, 5.31)
Supporting reduction with prescribed medication	3 trials in total 2 - Varenicline 1 - Bupropion	Not estimated 1.48 (1.16, 1.90) Not estimated	Not estimated 3.99 (2.93, 5.44) 1.27 (0.67, 2.40)
Setting a goal number of cigarettes per day to work toward	14 trials in total	1.05 (0.89,1.23)	Not estimated
Setting smoke-free time periods or locations such as at home or work	4 trials in total	0.82 (0.39,1.7)	Not estimated
Gradually increasing the time between cigarettes	7 trials in total	Not estimated	Not estimated
Eliminating routine or least preferred cigarettes smoked at specific times	5 trials in total	Not estimated	Not estimated
Gradually increasing the time between waking and first cigarette	1 trial in total	Not estimated	Not estimated

Supplementary table 2: Inclusion and exclusion criteria for the rapid review

	Include	Exclude
Population	• Adult smokers in the general population who are not willing or able to commit to a quit date • Participants from any gender, ethnicity, or socioeconomic group provided they are part of a general population • Community-dwelling individuals (non-institutionalised)	• Pregnant or breastfeeding individuals • People living in institutions (e.g. hospitals, care homes, correctional facilities) • Adults with severe mental health conditions (at risk of institutionalisation) • Adults with other diagnosed disease or clinically managed conditions e.g. HIV, chronic lung conditions, etc (unless part of a general population) • Other specific populations – including subsets of the general population like only

		males, or young adults, or low income, or ethnic groups, etc.
Intervention	• Interventions aimed at reducing the amount smoked or reducing harm with or without cessation. These may be offering support or advice • Nicotine replacement therapy products (such as NRT patches, gum, inhalers) • Only include vapes (e-cigarettes) if they are not provided as part of the intervention, but advice on their use is given • Behavioural • Psychological • Pharmacology licenced within the UK i.e. varenicline, cytisine [aka cytisinicline], Bupropion) • Generic interventions designed for general populations	• Provision of free vapes as part of intervention • Tobacco based products (including heated products and snus) • Interventions tailored to a specific population group (likely to be less applicable to the general population)
Comparator	• No intervention or • Waitlist control or • Smoking cessation interventions without smoking reduction prior to a quit attempt i.e. an abrupt quit	
Outcome	• Smoking reduction: change in smoking use per day between baseline and follow-up • Smoking cessation or abstinence: Carbon monoxide confirmed self-reported abstinence at any time point at least 4 months after a quit attempt • Biochemical objective measures indicating tobacco use • Validated subjective self-report measures • Cost-effectiveness outcomes	• Quit attempt at or less than 4 months • Unvalidated subjective self-report measures
Research type	• Systematic Reviews of randomised controlled trials published from Oct 2015 onwards in English • Primary studies involving parallel randomised controlled trials published since Oct 2015	• Cross-over RCTs • Non-systematic literature reviews • Non-randomised primary studies, quasi experimental, observational • Pre-prints; Conference abstracts, posters, editorials and opinion pieces, book chapters
Other Study Considerations		
English Language only No country restrictions Published since 2015		

OVID Search strategy

1 ((stop* or quit* or ceas* or cessation or abstain* or abstinence or "giv* up" or reduc* or gradual* or slow* or substitut* or schedul* or "cut* down" or "cut* back" or swap* or substitut* or fade or fading or taper* or "phas* out") adj4 (smok* or tobacco or cigar* or nicotine)).ti,ab. 66342

2 ("controlled smok*" or "controlled tobacco use" or "controlled tobacco usage" or "scheduled smok*" or "scheduled reduced smok*" or "controlled cigar*" or "reduce to quit" or "dual use" or "induction phase*" or "cessation induction*" or "smoking induction*" or "pre quit*" or prequit* or "quit* attempt*" or ((smok* or nicotine) adj3 (preload* or "pre load*")) or "e-cig*" or vape* or vaping or ecig* or "electronic cig*" or "electronic nicotine delivery system*" or "potential reduced exposure product*" or (pod* adj2 vap*) or (mod* adj2 vap*)).ti,ab. 23277

3 Smoking Cessation/ or *Smoking Reduction/ or Smoking Cessation Agents/ 34827

4 (((harm adj2 reduc*) or (risk adj2 reduc*)) adj5 (smok* or tobacco or cigar* or nicotine)).ti,ab. 2513

5 Risk Reduction Behavior/ and ("Tobacco Use"/ or "Tobacco Use Disorder"/ or Cigarette Smoking/ or Smoking/ or Tobacco Smoking/ or Cigar Smoking/ or Craving/) 761

6 or/1-5 90028

7 (unwilling* or unmotivat* or uninterested or reluctan* or unable or "can't" or cannot or denial or avoid* or fear* or ((no or "not" or "not yet" or none or without or lacks or lacking) adj3 (willing* or motiv* or interest* or intent* or intend* or plan* or try* or tries or attempt* or ready or readiness or able or seek* or desir* or wish* or hope or hoping or "self-efficacy" or "self confidence"))).ti,ab. 1298417

8 Motivation/ or Self Efficacy/ 111803

9 7 or 8 1397883

10 6 and 9 9929

11 limit 10 to yr="2015 - 2025" 4660

12 ("systematic review*" or "controlled clinical trial*" or "randomi?ed controlled trial*").ti. 432265

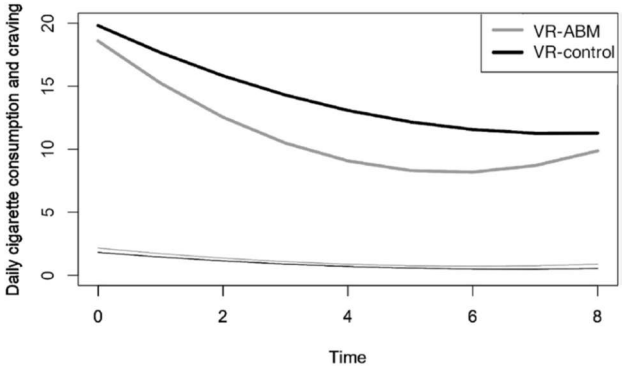
13 (systematic review or controlled clinical trial or randomized controlled trial).pt. 1040927

14 12 or 13 1167160

15 11 and 14 791

8.2 Appendix 2

Supplementary table 3: Summary of included studies

Reference, Key characteristics	Study details	Results
Behavioural only interventions (n= 3 studies)		
Machulska, A. et al. (2021) Approach bias retraining through virtual reality in smokers willing to quit smoking: A randomized-controlled study. Behaviour research and therapy, 141, 103858. https://doi.org/10.1016/j.brat.2021.103858 **Type of intervention:** Behavioural only **Design:** two-arm, randomised controlled trial **Country:** Germany **Eligibility:** •≥18 yrs •Smokes >=6 cpd during the last six months •No criteria on exhaled CO •Self-reported motivation to quit in next six months	**Study aim:** to investigate whether virtual reality technology into Approach Bias Modification (VR-ABM) can modify existing cognitive biases for smoking and/or changing smoking behaviour. **Intervention/Control groups:** 1. VR-ABM – in VR setting asked to put red bordered items in trash; blue-bordered items in the box. Red-border linked to smoking related items and blue-border linked to non-smoking related items 2. VR-control training – asked to put, red-bordered items in right-hand box and blue-bordered items in left-hand box, no link between smoking related-items and border colour Both groups did six sessions over two weeks; received short behavioural counselling for smoking cessation and had access to an app to track cigarettes smoked. **Data collection and methods:** Self-reported in questionnaires and CO at baseline, post-test (2 weeks) and follow-up (7-8 weeks) **Outcomes (relevant):** **Reduction:** reductions in daily cigarette consumption reported 9 times over 7/8 weeks **Cessation:** abstinence rates at 3 or 7 weeks (not further defined). **Verification:** expired CO (no cut-off to define abstinence).	**Summary:** No evidence of any effect on reduction or cessation outcomes at 8 weeks. There were no differences by expired CO by group. Evidence that VR-ABM reduces smoking more than VR-control short-term (up to 4 weeks). However, the size of the effect gets smaller over time so that by 8 weeks cigarettes per day smoked in both groups are similar. The intervention lasted 2 weeks and the biggest difference between groups at around 4 weeks, thus the results suggest that the effect of VR-ABM training wears off after a couple of weeks **Smoking Reduction:** For both groups, there was a decrease in daily smoked cigarettes across time by 8-10 cigarettes over 8 weeks (figure 2).  Figure 2: Change in daily cigarette consumption by group (*light line is VR-ABM; dark line is VR-control*)

Reference, Key characteristics	Study details	Results
	Sample size: 96 Size (n) Male (%) Age mean (SD) Intervention 47 51% 50.53 (12.44) years Control 49 51% 50.12 (10.94) years **Incentive:** participants were not paid for participation	The VR-ABM group, initially reduced smoking faster (-1.36 SE 0.43 cigarettes per day faster, p=0.001) than the VR-control group. However, the rate of decline in smoking reduced over time, meaning that between 4 and 8 weeks, the count of daily smoked cigarettes started to rise again especially in the experimental group. At 8 weeks smoking rates in both groups were again very similar. **Smoking Cessation:** % smokers that had ceased at 3 weeks 27% vs. 16%, P=0.674 (Intervention vs. Control) % smokers that had ceased at 7 weeks 22% vs. 23%, P=0.754 (Intervention vs. Control) ANOVAs did not reveal a main effect for condition, nor a condition by time interaction for expired CO (p=0.807)
Taylor, A. H., et al. (2023). Effectiveness and cost-effectiveness of behavioural support for prolonged abstinence for smokers wishing to reduce but not quit: Randomised controlled trial of physical activity assisted reduction of smoking (TARS). Addiction, 118(6), 1140–1152. https://doi.org/10.1111/add.16129 Taylor, A.H., et al. (2023a) Motivational support intervention to reduce smoking and increase physical activity in smokers not ready to quit: the TARS RCT. NIHR, 27 (4). https://www.journalslibrary.ni	**Study aim:** To assess the effectiveness and cost effectiveness of behavioural support to reduce smoking and increase physical activity on prolonged abstinence. **Intervention/Control groups:** 1. Behavioural support to reduce smoking and increase physical activity 2. Support as usual – brief advice on smoking cessation **Data collection and methods:** Self-reported smoking collected in person or via telephone. Those reporting a quit attempt at 3 and 9 months provided exhaled CO. Those verified abstinent at 9 months provided exhaled CO at 15 months. **Outcomes (relevant):** **Reduction:** Proportion of participants reducing the number of cigarettes smoked by ≥50% between baseline and 3 and 9 months **Cessation:** floating biochemically verified prolonged	**Summary:** There was no evidence that compared with brief advice on smoking cessation that behavioural support to reduce smoking and increase physical activity affected sustained abstinence at 6 or 12 months or was cost-effective. There was evidence that the intervention led to more participants reducing their baseline smoking by 50% at 3 and 9 months compared with brief advice. The intervention group smoked 5.6 (1.4, to 9.8) fewer cigarettes per day at 3 months than the control group. **Smoking Reduction:** Reduced smoking by ≥50% between baseline and 3 months: 18.9% vs. 10.5%, p = 0.009 (Intervention vs. Control) Odds ratio (OR (95% CI)): 1.98 (1.35, to 2.90), p<0.0004 Adjusted mean difference in cigarettes per day at 3 months: −5.62 (−9.80 to −1.44), p=0.0085 (favours intervention) Reduced smoking by ≥50% between baseline and 9 months

Reference, Key characteristics	Study details	Results
hr.ac.uk/hta/KLTG1447 **Type of intervention:** Behavioural only **Design:** two-arm, randomised controlled trial **Country:** UK **Eligibility:** •≥18 years •Smokes ≥10 cpd (for at least 1 year), •No criteria for exhaled CO •Wishes to reduce but not quit smoking immediately	smoking abstinence (since individual quit date) at 6-months and 12 months; a quit attempt (self-reported as at least 24 hours without a puff) at 3 and 9 months **Verification:** exhaled CO < 10 ppm at 3 and 9 months were deemed abstinent at 6 months; exhaled CO < 10 ppm at 9 and 15 months were deemed abstinent at 12 months. **Cost-effectiveness**: direct cost of intervention delivery **Sample size:** 915 Intervention: Size (n) 457; Male (%) 46.6%; Age mean (SD) 49.5 (14.1) years Control: Size (n) 458; Male (%) 42.6%; Age mean (SD) 50.0 (13.6) years **Incentive:** £20 love2shop voucher for participation	14.4% vs. 10.0%, p = 0.044 (Intervention vs. Control) Odds ratio (OR (95% CI)): 1.52 (1.01, to 2.29), p=0.043 Adjusted mean difference in cigarettes per day at 9 months: −0.95 (−5.37 to 3.46), p=0.67 (no evidence of effect) **Smoking Cessation:** % abstinent at 6 months: 2.0% vs. 0.9% (Intervention vs. Control) Odds ratio (OR (95% CI)): 2.30 (0.70, to 7.56), p=0.17 % abstinent at 12 months: 1.3% vs. 0.2% (Intervention vs. Control) Odds ratio (OR (95% CI)): 6.33 (0.76, to 53.10), p=0.09 **Cost effectiveness:** The direct intervention cost was £239.18 (£204, to £292) per person, with no evidence of cost-effectiveness.
Weng, X. et al. (2020). Effects of simple active referrals of different intensities on smoking abstinence and smoking cessation services attendance: a cluster-randomized clinical trial. Addiction (Abingdon, England), 115(10), 1902–1912. https://doi.org/10.1111/add.15029 **Type of intervention:** Behavioural only **Design:** three arm, cluster randomised controlled trial	**Study aim:** compare the effect of two modified approaches to referrals on the cessation outcomes in community smokers. **Intervention/Control groups:** 1. on-site referral (OSR): counsellor helped willing participants make appointments at a smoking cessation service with reminders tailored to date of appointment and daily text messages for 1 month 2. text messaging referral (TMR): no on-site referral, 16 fixed schedule text messages over 2 months 3. brief cessation advice (BCA): 12-page self-help smoking cessation booklet. OSR and TMR groups also received: a 12-page self-help booklet; a smoking harms health warning leaflet; a referral card to utilise smoking cessation services; prompts to use smoking cessation services during telephone follow-up at 1, 2, and 3 months.	**Summary**: No evidence of effect of either on-site referral or text-message reminders compared with brief advice on verified smoking abstinence at 6 months. Evidence of an effect on reducing smoking by 50% from baseline at 18 months for on-site referral vs brief advice. But no evidence of effect at 1, 2, 3, or 6 months for either experimental group vs. control. Evidence of an effect on self-reported abstinence at 1, 2, and 6 months for on-site referral vs brief advice. But no evidence of effect at 3, or 18 months. For text-message referral vs. control there was an effect at 1 month but not at 2, 3, 6, or 18 months. Evidence that the costs per participant reporting abstinence at 6 months was 30% lower than control for on-site referral or text message reminders, but the precision of the effect is not estimated.

Reference, Key characteristics	Study details	Results
(clustered by 68 community sites) **Country:** Hong Kong **Eligibility:** •Hong Kong residents • ≥ 18 yrs •Smokes ≥ 1 cpd over the past 3 months •Exhaled CO ≥ 4 ppm •Willing to quit or reduce smoking	**Data collection and methods**: self-report via questionnaire at baseline and telephone at 1, 2, 3, 6, 18 months. Exhaled carbon monoxide (CO) in-person from all at baseline, but only those reporting a quit for 7+days at 3, 6, and 18 months were verified. **Outcomes (relevant):** **Reduction:** Reduced baseline smoking amount by 50% **Cessation:** 7-day point-prevalence abstinence (PPA) **Verification:** exhaled CO (< 4 parts per million) and salivary cotinine (< 10 µg/l) tests **Cost-effectiveness**: direct cost of intervention delivery **Sample size**: 1163 Size (n) / Male (%) / Age mean (SD) OSR 396 / 78.7% / 40.9 (16.3) years TMR 385 / 78.2% / 41.0 (16.7) years BCA 383 / 76.2% / 42.3 (17.1) years **Incentive:** The trial was nested within a 'Quit to Win' contest for smoking cessation conducted in all 18 districts in Hong Kong. Participants received a small cash incentive (HK $500 ≈ US$64) for passing each validation test	**Smoking Reduction:** 50% reduction at 3 months 18.7% or 16.9% vs. 16.2% (OSR or TMR vs. BCA) Adjusted odds ratio (aOR) (95% CI): 1.21 (0.79 to 1.85) (OSR vs. BCA) aOR (95% CI): 1.29 (0.85 to 1.97) (TMR vs. BCA) 50% reduction at 6 months 20.3% or 16.1% vs. 19.3% (OSR or TMR vs. BCA) aOR (95% CI): 0.90 (0.60 to 1.33) (OSR vs. BCA) 0.84 (0.56 to 1.26) (TMR vs. BCA) 50% reduction at 18 months 14.2% or 10.4% vs. 10.4% (OSR or TMR vs. BCA) aOR (95% CI): 1.75 (1.05 to 2.91)* (OSR vs. BCA) aOR (95% CI): 1.33 (0.79 to 2.26) (TMR vs. BCA) **Smoking Cessation:** 7 day PPA at 3 months 14.4% or 13.0% vs. 8.6% (OSR or TMR vs. BCA) aOR (95% CI): 1.54 (0.96 to 2.49) (OSR vs. BCA) aOR (95% CI): 1.32 (0.81 to 2.15) (TMR vs. BCA) 7 day PPA at 6 months 17.7% or 17.1% vs. 12.0% (OSR or TMR vs. BCA) aOR (95% CI): 1.56 (1.00 to 2.42)* (OSR vs. BCA) aOR (95% CI): 1.40 (0.90 to 2.19) (TMR vs. BCA) Verified abstinence at 6 months 7.6% or 7.8% vs. 3.9% (OSR or TMR vs. BCA) aOR (95% CI): 1.83 (0.95 to 3.53) (OSR vs. BCA) aOR (95% CI): 1.82 (0.94 to 3.52) (TMR vs. BCA) *P<0.05 All aORs are adjusted for baseline covariates including age, sex, marital status, nicotine dependency, quit attempt, reduction

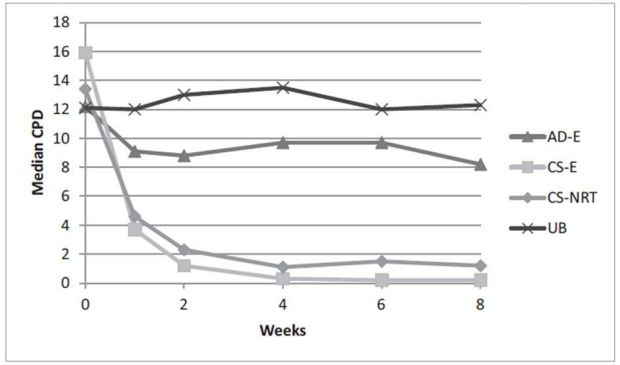
Reference, Key characteristics	Study details	Results
		attempt and intention to quit. The cost per participant with the self-reported PPA at 6 months was similar for the OSR (US$124.8) and TMR (US$131.9) groups, which were both approximately 30% lower than that of the control group (US$180.7).
Behavioural & Pharmacological (Varenicline) (n= 2 studies)		
Ebbert, J, O. et al., (2015) Effect of varenicline on smoking cessation through smoking reduction: a randomized clinical trial. *JAMA*, *313*(7), 687–694. https://doi.org/10.1001/jama.2015.280 Nakamura, M. et al. (2017). Efficacy of Varenicline for Cigarette Reduction Before Quitting in Japanese Smokers: A Subpopulation Analysis of the Reduce to Quit Trial. Clinical therapeutics, 39(4), 863–872. https://doi.org/10.1016/j.clinthera.2017.03.007 **Type of intervention:** Behavioural and pharmacological (varenicline) **Study design:** two-arm randomised controlled trial **Country:** Multi-national **Eligibility:**	**Study aim:** To determine the efficacy of varenicline for increasing smoking abstinence through smoking reduction. **Intervention/Control groups:** 1.Varenicline for twenty-four weeks, titrated to 1 mg twice daily 2.Placebo **Data collection and methods:** Self-reported tobacco use at 18 weekly clinic visits and 10 telephone calls. Exhaled carbon monoxide (CO) measurements were obtained at all clinic visits. **Outcomes (relevant):** **Reduction:** Change in cigarettes per day from baseline •Reduced smoking by 50% at 4 weeks •Reduced smoking by 75% at 8 weeks; **Cessation:** Continuous abstinence rate (CAR) •15 to 24 wks after baseline •21 to 24 wks after baseline •21 to 52 wks after baseline **Verification:** Weekly exhaled CO; Abstinent defined as exhaled CO ≤ 10 ppm each visit in wks 15-24 **Sample size:** 1510 Varenicline 760 55.9% 44.7 (11.8) years. Placebo 750 56.8% 44.4 (12.0) years	**Summary:** Evidence that varenicline reduces smoking, induces continuous abstinence sooner and increases continuous abstinence rates More participants on varenicline vs. placebo had reduced smoking by 50% at 4 weeks (higher by 16% (11%, 21%) percentage points); median time to abstinence was 50 vs. 85 days (p<0.0001) and more were continuously abstinent in weeks 15-24 (higher by 25% (21, 29%) percentage points). **Smoking Reduction**: Reduced smoking >=50% from baseline at 4 weeks: 47.1 % vs. 31.1% (Varenicline vs. Placebo) Risk difference (RD (95% CI)): 16.0%; (95% CI:11.2% to 20.9%) Relative Risk (RR: (95% CI)): 1.5; (95% CI:1.3 to 1.7) Reduced smoking >=75% from baseline at 8 weeks: 26.3% vs. 15.1% (Varenicline vs. Placebo) RD: (95% CI) 11.3 (95% CI: 7.2% to 15.3%) RR: (95% CI) 1.8 (95% CI: 1.4 to 2.2). **Smoking Cessation**: continuous abstinence at 15 to 24 weeks 32.1% vs 6.9% (Varenicline vs. Placebo) RD: (95% CI) 25.2% (95% CI: 21.4% to 29.0%). RR: (95% CI) 4.6 (95% CI: 3.5 to, 6.1). Among participants abstinent during weeks 15-24, the median time to abstinence was 50 vs. 85 days for varenicline vs. placebo

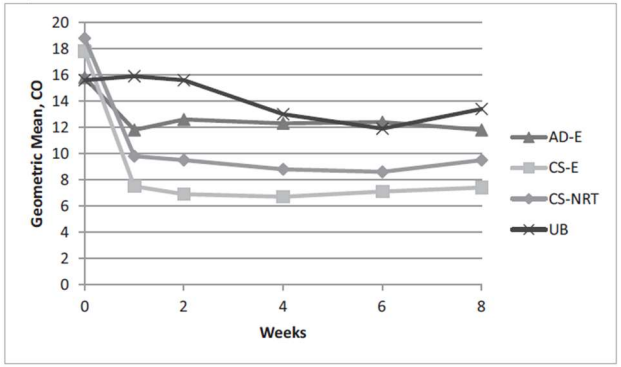
Reference, Key characteristics	Study details	Results
•>=18 yrs •Smokes >=10 cpd • Exhaled CO >10 ppm •Not ready to quit within 1 month but will reduce and try quitting within 3 months	**Incentive:** No incentive described	(P < .0001).
Steinberg, M. L. et al. (2018) Varenicline for smoking reduction in smokers not yet ready to quit: A double-blind, proof-of-concept randomized clinical trial. Addictive behaviors, 84, 20–26. https://doi.org/10.1016/j.addbeh.2018.03.026 **Type of intervention:** Behavioural and pharmacological (varenicline) **Study design:** two-arm, randomised controlled trial (proof of concept) **Country:** USA **Eligibility:** • ≥ 18 yrs • Smokes ≥ 10 cpd for past 6 months • No criteria for exhaled CO • Interested in cutting down, but not quitting within 30 days	**Study aim:** Investigate the use of varenicline for smokers willing to reduce but not quit smoking. **Intervention/Control groups:** 1. Varenicline (1mg/day titrated over 1 week) 2. Placebo Both groups received four weekly brief counselling visits **Data collection and methods:** Self-report (Timeline Follow back procedure) for cigarettes per day and carbon monoxide (CO); follow-up at 1, 3 and 6 months after baseline **Outcomes (relevant):** **Reduction:** Change in cigarettes per day from baseline Reduced baseline smoking amount by 50% (y/n) **Cessation**: Quit attempts (y/n) defined by participant self-report of a "serious quit attempt." **Verification**: exhaled CO (no cut-off to define abstinence). **Sample size:** 64 Varenicline: Size (n) 31; Male (%) 46.2%; Age mean (SD) 46.08 (9.07) years Placebo: Size (n) 33; Male (%) 44.4%; Age mean (SD) 43.68 (12.39) years **Incentive:** Participants were paid up to $170 if all assessments were completed.	**Summary:** No evidence that varenicline for 28 days differed from placebo with respect to quit attempts by 6 months, cigarettes per day at 6 months, CO or reductions in smoking by 50% at 1, 3 or 6-month follow-up. **Smoking Reduction:** % reduced baseline smoking amount by 50% at 6 months: 38% vs. 20% (Varenicline vs. Placebo) Odds ratio (OR (95% CI)): 2.45 (0.53 to 11.38), p=0.26. Mean cigarettes per day at 6 months: 10 vs. 11 (p=0.36) (Varenicline vs. Placebo) **Smoking Cessation:** % making quit attempts by 6 months: 32% vs. 14% (Varenicline vs. Placebo) Odds ratio (OR (95% CI)): 2.44 (0.65 to 9.12), p=0.187 Both groups reduced CO levels between baseline and end-of-treatment (p < 0.001), 1-month (p=0.035), and 6-month (p=0.045) follow-up. But there were no differences between groups at the 6-month follow-up, (ratio=1.04 (95% CI: 0.78–1.38), p=0.812)

Reference, Key characteristics	Study details	Results
Behavioural & Pharmacological (Nicotine replacement therapy) (n= 4 studies)		
Farley, A. et al., (2017) A mixed methods feasibility study of nicotine-assisted smoking reduction programmes delivered by community pharmacists - The RedPharm study. BMC public health, 17(1), 210. **Type of intervention:** Behavioural and pharmacological (Nicotine replacement therapy) **Study design:** four-arm, randomised controlled trial (feasibility study) **Country:** UK **Eligibility:** •>=18 yrs •Smokes >=10 cpd •Exhaled CO >10 ppm •Not planning to quit smoking within 1 month but were wanting to reduce. •No abstinence for >3 months in last yr	**Study aim:** to investigate the feasibility of a community pharmacy programme and the effectiveness of behavioural support vs. self-help methods and of shorter vs. standard length reduction programmes. **Intervention/Control groups:** Behavioural support and standard length 16 weeks Behavioural support and short length 4 weeks Self-help and standard length 16 weeks Self-help and short length 4 weeks All groups had access to NRT for up to 9 months and were given advice on reduction. **Data collection and methods:** Self-reported cigarette consumption monthly via online questionnaires, telephone or pharmacy visits. Exhaled CO at 4 weeks or 6 months post quit for those that declared abstinence. **Outcomes (relevant):** **Reduction:** Change in cigarettes per day from baseline •Reduced smoking by 50% at 9-12 months •Reduced smoking at all (>0) at 9-12 months **Cessation:** Floating sustained abstinence for 4 wks from 15 days after quit date **Verification:** Abstinence defined as exhaled CO ≤ 10 ppm **Sample size:** 70 Support and standard: Size (n) 17, Male (%) 65%, Age mean (SD) 44 (12) years Support and short: Size (n) 19, Male (%) 32%, Age mean (SD) 44 (12) years Self-help and short: Size (n) 17, Male (%) 67%, Age mean (SD) 43 (13) years Self-help and standard: Size (n) 17, Male (%) 41%, Age mean (SD) 44 (17) years **Incentive:** £20 for verification of abstinence.	**Summary:** No evidence of any differences in smoking reduction or cessation between groups. There was strong evidence that a future trial of this kind of intervention would be unfeasible. There was insufficient evidence to assess whether support or speed of reduction enhanced cessation or reduction but cessation and reduction were less common overall than in the pivotal trials for licensing NRT for this indication. **Smoking Reduction:** Rate of >=50% sustained reduction: 8.8% vs. 2.9% (Short 4 weeks vs. Standard 16 weeks) RR (95% CI) 3.00 (0.45 to 20.44) (favours short but imprecise) 8.3% vs. 3.1% (Support vs. Self-help) RR (95% CI) 2.67 (0.40 to 18.19) (favours support but imprecise) Mean (SD) cpd change 0-12 months: −2.29 (7.9) vs. −2.26 (5.4) (Short 4 weeks vs. Standard 16 weeks) −1.58 (7.2) vs. −3.36 (6.1) (Support vs. Self-help) **Smoking Cessation:** Floating sustained abstinence for 4 wks 8.8% vs. 8.8% (Short 4 weeks vs. Standard 16 weeks) RR (95% CI): 1.00 (0.24 to 4.10) (imprecise evidence of no effect) 5.5% vs. 12.5% (Support vs. Self-help) RR (95% CI): 0.44 (0.10 to 1.95) (favours self-help but imprecise)

Reference, Key characteristics	Study details	Results
Guo, N., et al. (2023). Effect of mobile interventions with nicotine replacement therapy sampling on long-term smoking cessation in community smokers: A pragmatic randomized clinical trial. Tobacco induced diseases, 21, 44. DOI: 10.18332/tid/160168 **Type of intervention:** Behavioural and pharmacological (Nicotine replacement therapy) **Study design:** two-arm, randomized controlled trial **Country:** Hong Kong **Eligibility criteria:** •>=18 yrs •Smokes >=1 cpd •Exhaled CO >4 ppm •No use of smoking cessation services, medication, or NRT •No criteria based on motivation to quit. .	**Study aim:** Evaluate the effect of personalised behavioural support through mobile phone interventions plus NRT sampling on smoking cessation in Hong Kong community smokers. **Intervention/Control groups:** Intervention: 1-week supply of gum or patch; dosage varied according to time of first cigarette. Behavioural support from smoking cessation advisor via Instant Messaging and an automated chatbot. Personalised support to readiness to quit (within 7, 30, 60 days or undecided) Control: Regular text messages regarding healthy lifestyles at a similar frequency. Both groups received brief advice and active referral to smoking cessation services at recruitment. **Data collection and methods:** Self-report in telephone interviews at 3, 6 and 12 months. Carbon monoxide tests at 6 and 12 months for participants reporting a 7+ day tobacco use quit **Outcomes (relevant):** **Reduction:** 50% reduction in the number of cigarettes per day vs. baseline at 6 and 12 months. **Cessation:** Verified abstinence at 6 or 12 months after baseline. Quit attempts made at 6 months **Verification:** Abstinence defined as exhaled CO ≤ 4 ppm **Sample size:** 664 **Incentive:** 7 day abstinence reporters doing a carbon monoxide test received HK$300 (approximately US$38)	**Summary:** No evidence that NRT-S and personalised messages vs. general health messages for 12 weeks affect smoking abstinence or reduction at 6 or 12 months. Evidence that more participants in the intervention group made a quit attempt by 6 months **Smoking Reduction:** Reduced cpd by 50% of baseline amount at 6 months: 19.7% vs. 17.8% (Intervention vs. control) OR (95% CI): 1.13 (0.75 to 1.71) Reduced cpd by 50% of baseline amount at 12 months: 26.9% vs. 22.3% (Intervention vs. control) OR (95% CI): 1.28 (0.88 to 1.85) **Smoking Cessation:** Abstinence at 6 months: 3.9% vs 3.0% (Intervention vs. control) OR (95% CI): 1.31 (0.57 to 3.04) Abstinence at 12 months: 5.4% vs 4.5% (Intervention vs. control) OR (95% CI) 1.21 (0.60 to 2.45) % that made a quit attempts by 6 months: 47.0% vs 38.0% (Intervention vs. control) OR (95% CI) 1.45 (1.06 to 1.97, p=0.019) **Subgroup analyses**: Authors conducted subgroup analyses and identified that the intervention effect was greater in females and in those not ready to quit within 30 days. However, these findings were not statistically significant, and the clinical significance of these findings is unknown.

	Size (n)	Male (%)	Age, largest category
Intervention	332	75%	31% aged 30-39 years
Control	332	74%	34% aged 30-39 years

Reference, Key characteristics	Study details	Results
Hatsukami, D. K. et al., (2020). A Randomized Clinical Trial Examining the Effects of Instructions for Electronic Cigarette Use on Smoking-Related Behaviors and Biomarkers of Exposure. Nicotine & tobacco research: official journal of the Society for Research on Nicotine and Tobacco, 22(9), 1524–1532. https://doi.org/10.1093/ntr/ntz233 **Type of intervention:** Behavioural and pharmacological (Nicotine replacement therapy) **Study design:** four-arm, randomised controlled trial (only 2 arms meeting inclusion criteria are summarised) **Country:** US **Eligibility:** •>=18 yrs •Smokes >=5 cpd •Exhaled CO >10 ppm •no serious quit attempt in the past 3 months or planning to quit smoking in the next 3 months.	**Study aim:** To examine cigarette use when smokers were instructed and incentivized to completely switch to e-cigarettes compared to instructions to use the product ad libitum. **Intervention/Control groups:** 1.Complete substitution with nicotine replacement therapy (4mg) (CS-NRT) 2.Usual brand of cigarettes (UB) **Data collection and methods**: Two-week baseline period (weeks −1 and 0) and eight-weeks of product assignment. Self-reported daily smoking for the previous day using an Interactive Voice Recording (IVR) system that called participants each day. Clinic visits at weeks 1, 2, 3, 4, 6, and 8. Expired CO was collected at each visit. First void urines were collected at baseline, 4 and 8 weeks **Outcomes (relevant):** **Reduction**: Cigarettes per day (cpd) 0-8 weeks. **Cessation:** 7-day point prevalence abstinence rate at 8 weeks **Verification:** CO (no cut-off to define abstinence). Urinary biomarkers e.g. total nicotine equivalents (TNE). **Sample size:** 292 randomised, 264 started the study CS-NRT 76 49% 51 years UB 36 53% 47 years **Incentive:** Participants received compensation for research participation and adherence to protocol. Smokers in the complete substitution groups (CS-NRT) also had to have a CO <= 4 ppm at the visit for the bonus payment. Total compensation was equivalent across all	**Summary:** Evidence that complete substitution of smoking with nicotine replacement therapy (CS-NRT) reduced self-reported smoking more at week 8 compared with usual brand (UB) (figure 1a). Abstinence was 17% at 8 weeks for complete substitution by NRT, suggesting complete substitution was difficult to achieve. Smaller of differences for carbon monoxide between groups supports (figure 1b) that complete substitution was difficult and that differences between groups based on self-report (figure 1a) are exaggerated. **Smoking Reduction:** Reduction of cigarettes per day over 8 weeks significantly different to baseline for CS-NRT but not UB (see figure 1a).  Figure 1a: Change in median cigarettes per day from week 0 to 8 Comparison of change in median cigarettes per day from baseline to week 4 or week 8 across all 4 arms showed a difference p<0.001. Pairwise comparison of CS-NRT vs. UB is not reported. Median (min/max) reduction in cigarettes per day over 8 weeks:

Reference, Key characteristics	Study details	Results
	groups if all study requirements (including the additional CO levels for CS-NRT arms) were met by the participant.	CS-NRT: 9.6 [0.9 to 40.7] cpd UB: 0.7 [-3.6 to 12.0] cpd **Smoking Cessation:** 7-day abstinence verified by CO at 8 weeks CS-NRT 17% UB abstinence not reported **Carbon monoxide (CO):** Reduction of CO over 8 weeks significantly different to baseline for CS-NRT but not UB (see figure 1b). Differences were observed between groups for change in CO from baseline to 4 weeks, but they were smaller than the effect observed for self-reported data.  Figure 1b: Change in geometric mean carbon monoxide from week 0 to 8 Comparison of change in CO from baseline to week 4 or week 8 across all arms showed a difference p<0.0001. Specific pairwise comparison of CS-NRT vs. UB comparisons not reported. Geometric mean (95% CI) change in CO over 8 weeks (smaller number means larger reduction): CS-NRT: 0.55 (0.43, 0.69) UB: 0.85 (0.69, 1.06).

Reference, Key characteristics	Study details	Results
Zhao, S. Z. et al. (2021). Mobile chat-based support plus nicotine replacement therapy sampling to promote smoking cessation for community smokers: A randomized controlled trial. Tobacco induced diseases, 19, 32. https://doi.org/10.18332/tid/133373 **Type of intervention::** Behavioural and pharmacological (Nicotine replacement therapy) **Study design:** two-arm, randomised controlled trial (pilot study) **Country:** Hong Kong **Eligibility criteria:** • ≥18 years •Smokes ≥1 cpd in the past 3 months cpd •Exhaled CO ≥4 ppm ppm •No criteria based on motivation to reduce or quit **Incentive:** Participants in both groups received a small cash incentive of HK$200 (about US$25.6) for passing each validation at 3 and 6 months	**Study aim:** To assess the feasibility of mobile chat-based intervention combined with NRT sampling on quitting. **Intervention/Control groups:** 1. Scheduled personalised text messages (approx. 14 over 2 months) with 1-to-1 chat support via instant messaging; Brief (1 to 2 minutes) smoking cessation advice via telephone at 1- and 2-months follow-up. 2. General stop smoking text messages (approx. 14 over 2 months), not personal, no counsellor response Both groups received brief smoking cessation advice; Nicotine replacement therapy sampling (NRT-S): One week of NRT (gum, patch or lozenge); Active referral to smoking cessation services **Data collection and methods:** Self-reported via phone calls, cigarettes per day at baseline, 1,2,3 and 6 months. Participants reporting abstinence (not even a puff) in the past 7 days, at 3 and 6 months, were invited for biochemical verification **Outcomes (relevant):** **Reduction:** smoking reduction by at least 50% of baseline cigarette consumption **Cessation:** Self-reported and verified 7-day point prevalence abstinence at 3 or 6 months; quit attempt (abstinence for ≥24 h) (yes/no) **Verification:** exhaled CO of <4 ppm and saliva cotinine concentration of <10 µg/L **Sample size:** 119 | | Size (n) | Male (%) | Age, largest category | | --- | --- | --- | --- | | Intervention | 62 | 88.7% | 33.9% aged 30-39 yrs | | Control | 57 | 77.9% | 28.3% aged 30-39 yrs |	**Summary**: No evidence that personalised text message and chat support compared with general text messages about smoking cessation affected smoking reduction, cessation or quit attempts. **Smoking Reduction:** 50% reduction at 3 months 24.2% vs. 24.6% (Intervention vs. Control) aOR (95% CI): 0.80 (0.32–2.01), p=0.64 50% reduction at 6 months 32.3% vs. 19.3% (Intervention vs. Control) aOR (95% CI): 1.74 (0.71–4.26), p=0.22 **Smoking Cessation**: Verified abstinence at 3 months 3.2% vs 1.8% (Intervention vs. Control) aOR (95% CI): 1.07 (0.08 to 13.65), p=0.960 Verified abstinence at 6 months 1.6% vs 0% (Intervention vs. Control) aOR (95% CI): No estimate, lack of data Self-reported abstinence at 3 months 12.9% vs 10.5% (Intervention vs. Control) aOR (95% CI): 1.12 (0.34 to 3.71), p=0.856 Self-reported abstinence at 6 months 16.0% vs 5.3% (Intervention vs. Control) aOR (95% CI): 2.82 (0.70 to 11.30), p=0.144 Quit attempt by 6 months 90.3% vs. 77.2 (Intervention vs. Control) aOR (95% CI): 2.61 (0.88 to 7.82), p=0.085 All aORs are adjusted for sex and perceived importance of quitting at baseline

Supplementary table 4: Description of the intervention and control groups in included studies

Citation and characteristics	Description of the context, intervention and control conditions	
Behavioural only interventions (n= 3 studies)		
Machulska et al. (2021) **Country:** Germany **Setting:** Laboratory **Mode of delivery:** Novel virtual reality set-up on a PC with joystick. Training sessions took about 15 minutes to complete. **Duration:** Six sessions over two-weeks **Reduction aims:** No target, no advice **Cessation aims:** No target, self-help book **Behaviour change technique/theory:** Controlled, goal-directed and reflective processes **BCTs:** 2.3, 2.7, 4.1, 5.1, 8.4	**Context:** The VR scenario placed participants inside a virtual office space in which they were instructed to interact with virtual smoking-related and nonsmoking control objects using their dominant hand. Ten different objects appeared consecutively in the middle of a virtual desk and were bordered in either red or blue. All participants were instructed to ignore item content and to respond only to border colour by using their own hand. Participants had to execute the correct movement to make the item disappear. Each of the 20 items was shown 6 times for a total of 120 times per training. All participants attended behavioural counselling for smoking cessation prior to randomisation. Afterwards, smokers received a self-help book (a German copy of "The Easy Way to Stop Smoking" by Allen Carr) to aid smoking cessation and were instructed to self-track smoked cigarettes by means of a mobile phone application specifically developed for this study (Cigarette Tracking List, SenseAble UG). **Intervention:** Virtual reality approach bias modification (VR-ABM) For approach bias modification, a contingency existed between object content (smoking related or not), border colour(red or blue) and expected action (trash or box): All smoking-related objects were bordered in red and had to be thrown away/avoided, whereas all control objects were bordered in blue had to be grasped/approached. Hence, an indirect instruction was employed, meaning that participants were not directly instructed to respond to item content, but to a content-irrelevant feature (border colour). Participants were instructed to respond to red-bordered objects by making a warding arm movement and throwing those objects as quickly as possible into a trashcan placed behind the desk. Similarly, participants responded to blue-bordered objects by making a grasping movement and placing them as quickly as possible into a box in front of the desk.	**Control:** Virtual reality control training (VR-Control) No contingency between item content, border colour and expected action existed. Participants were instructed to respond to red-bordered objects by making a warding arm movement and throwing those objects as quickly as possible into a box on the right-hand side of the desk. Similarly, participants responded to blue-bordered objects by making a grasping movement and placing them as quickly as possible into a box positioned on the left-hand side of the desk.
Taylor et al. (2023)	**Context:** Following randomisation, all participants received standardised written guidance on smoking reduction and	

Citation and characteristics	Description of the context, intervention and control conditions	
Country: UK **Setting:** Primary care Trial was run at four sites: East Midlands; South Central England; Devon and Cornwall; and London **Mode of delivery:** Sessions lasting 10- 60 minutes in-person or telephone by health trainers **Duration:** Eight weekly sessions with additional 6-weeks support for those wishing to quit **Reduction aims:** Increase motivation to reduce smoking **Cessation aims:** Increase motivation to make a quit attempt **Behaviour change technique/theory:** Motivational interviewing, Self-determination theory **BCTs:** 1.1, 1.2, 2.3, 2.7, 3.2, 3.3, 4.1, 12.2, 13.5, 15.1	cessation from researchers, with signposting to the support offered at local level. In the absence of formal programmes for use of e-cigarettes or licensed nicotine-containing products (LNCPs) to support reduction, for participants not wanting to immediately quit, all participants purchased their own products.	
	Intervention: Multi-component community-based behavioural support. The client-centred intervention was designed to engage with those living in disadvantaged communities and was informed by motivational interviewing and self-determination theory. It aimed to enhance participants' sense of importance and confidence to autonomously change behaviours while connecting with others. The content had some overlap with interventions with a focus on smoking reduction for those smokers unmotivated to quit. Participants were encouraged to self-monitor and set goals for both smoking and physical activity, problem-solve to overcome barriers for changing both behaviours, identify links between how physical activity may influence smoking acutely and chronically and vice versa and manage social influences that influenced the two behaviours. For example, with personal experimentation, participants were encouraged to use physical activity to manage cravings and weight gain and shift to a healthier self-identity. For participants wishing to quit, additional health trainer support sessions were provided to help maintain abstinence and to also access support as usual.	**Control:** Brief advice on smoking cessation, in line with UK guidelines for smokers not wishing to quit. 1. Health experts agree that the best thing to improve health and prevention of many diseases in the future is to quit smoking. 2. To quit smoking the best approach is to set a quit date, and use the local Stop Smoking Services [local website link here] who can provide behavioural support and nicotine replacement therapy i.e., gum, patches, lozenges), or can refer to a GP to prescribe Champix or Zyban. Alternatively, you may ask your GP/nurse/pharmacist about the options. 3. You may also be interested in the use of e-cigarettes and vaping which can help smoking reduction and cessation. Local e-cigarettes and vaping shops, as well as the internet can provide more information. The charity ASH provides some guidance on their use at: [ASH link here]. Please contact your local TARS researcher if you would like to receive a paper copy of this guidance. 4. Physical activity can help prevent weight gain when quitting smoking and reduce cravings, as well as helping to deal with stress and low mood.
Weng et al. (2020) **Country:** Hong Kong **Setting:** Community-based smoking hotspots	All participants received a 12-page self-help smoking cessation booklet at baseline	
	Intervention arm 1: On-site active referral (OSR group) Counsellor provided advice based on AWARD: Ask – inquired about smoking behaviours; Warning – given a leaflet on harms of smoking to health;	**Intervention arm 2:** text messaging referral (TMR) Counsellor provided advice based on AWARD: Ask – inquired about smoking behaviours; Warning – given a leaflet on harms of smoking to

Citation and characteristics	Description of the context, intervention and control conditions	
Mode of delivery: Smoking cessation counsellor, in person and/or via text messages. **Duration:** 12 weeks **Reduction aims**: No target; specific advice for reducing smoking not reported **Cessation aims:** No target; Active referral or advice to use smoking cessation services **Behaviour change technique/theory:** Not reported **BCTs:** 1.1, 2.7, 3.2, 3.3, 4.1, 5.1, 10.8, 10.10, 15.1	Advice - to quit or reduce smoking; Referral – given referral card and offered to make an appointment for a free smoking cessation service of their choice including individual counselling; NRT; group therapy; medication or acupuncture; Do-it-again – daily text messages over 1 month. For willing participants, the ambassadors immediately called the service provider, made appointments and relayed the appointment details to participants. Text message appointment reminder 1 to 3 days before appointment. Daily messages were tailored to whether an appointment had been made and if they had attended a smoking cessation service. Messages covered the harms of smoking and benefits of quitting, encouragements to quit and the use of smoking cessation services and reminders to attend their appointment; these were aimed to increase the participants' motivation to use the services. Telephone calls at 1, 2 and 3 months, participants who refused referral were advised to use a smoking cessation service and offered referral to one.	health; Advice - to quit or reduce smoking; Referral – given referral card and motivated to use free smoking cessation services but no offer to make appointment; Do-it-again – 16 fixed schedule text messages over 2 months Text messages mainly focused on encouraging the participants to use and make appointments with a smoking cessation service. Telephone calls at 1, 2 and 3 months, participants were advised to use a smoking cessation service but not offered referral to one. **Control arm:** brief cessation advice (BCA) Participants were asked about their smoking status, advised to quit or reduce smoking and provided with a 12-page self-help smoking cessation booklet.
Behavioural & Pharmacological (Varenicline) (n= 2 studies)		
Ebbert et al. (2015) **Country**: Multi-national (Australia, Canada, Czech Republic, Egypt, Germany, Japan, Mexico, Taiwan, U.K., and U.S) **Setting:** Health trainers at 61 sites in outpatient, clinical trial or academic centres	**Context**: The first 12 weeks of treatment were the reduction phase and the next 12 weeks were the abstinence phase. Counselling was tailored to the participant's needs during the reduction, abstinence, and posttreatment phases. A quit attempt was expected by the 12 week visit, but, participants could reduce their smoking faster and could make a quit attempt prior to week 12. All participants received smoking cessation counselling and a *Clearing the Air: Quit Smoking Today* booklet. Counselling was consistent with recommendations of the "Treating Tobacco Use and Dependence" clinical practice guidelines 2008. http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/index.html Counsellors were urged to be consistent and brief, to focus on problem solving (eg, what triggers the urge to smoke) and skills training (eg, practical actions to avoid smoking), and to highlight successes not failures.	

Citation and characteristics	Description of the context, intervention and control conditions	
Mode of delivery: 18 clinic and 10 telephone sessions lasting 10 min or less. **Duration:** 24-weeks **Reduction aims**: Target reduction of cigarettes by ≥ 50% baseline to 4 weeks ≥ 75% baseline to 8 weeks **Cessation aims:** Quit attempt by 12 weeks. **Behaviour change technique/theory:** Not reported **BCTs:** 1.1, 1.2, 1.3, 1.7, 2.7, 4.1, 8.7, 11.1, 12.3, 15.3	Reduction advice included Increasing time between cigarettes; and rank-ordering cigarettes from easiest to hardest to give up and giving up the easiest to the hardest Participants who had not reduced or made a quit attempt by week 12 were encouraged to continue medications and visits and make quit attempts, and participants who relapsed after week 12 were encouraged to make new quit attempts.	
	Intervention: Varenicline + counselling Self-administered Varenicline tablet (or matching placebo) dosage of 0.5 mg once daily for 3 days, increasing to 0.5 mg twice daily for days 4 to 7, and then to the maintenance dose of 1 mg twice daily.	**Control:** Placebo + counselling
Steinberg et al. (2018) **Country:** U.S **Setting:** Not described **Mode of delivery:** In-person with trained MSc or PhD therapists; Weekly counselling lasting 0 to 35 minutes. **Duration:** 4 weeks **Reduction aims**: Target reduction of cigarettes by ≥ 50% from baseline to 4 weeks; Advice on how to reduce not	**Context:** Following randomization, participants were provided with medication (active or placebo) and provided information regarding medication use and strategies for reducing their cigarettes per day to 50% of baseline levels (loosely based on a treatment manual by Carpenter et al. (Carpenter, Hughes, Solomon, & Callas, 2004)). Both groups were instructed to use the Food and Drug Administration recommended dosing schedule. Participants attended four weekly counselling visits (identical for both groups) consisting of: Visits one to three: up to 20 min when participants were encouraged to reduce the number of cigarettes smoked by 50% by end-of-treatment. Visit 4: up to 35-minute adaptation of motivational interviewing intervention followed by advice to quit (rather than to reduce). The new suggested goal was based on the anticipation that substantially reducing one's cigarettes smoked per day would increase self-efficacy for quitting. Additionally, there is no completely safe level of tobacco use; cessation, rather than reduction, is associated with health benefits, and should be the ultimate goal of treatment.	
	Intervention: Varenicline plus counselling 0.5 mg once daily on days 1–3, 0.5 mg twice daily on days 4–7, and 1 mg twice daily for the remainder of treatment	**Control:** Placebo plus counselling

Citation and characteristics	Description of the context, intervention and control conditions	
described **Cessation aims:** No target; Advice to quit provided at week 4 **Behaviour change technique/theory:** Motivational interviewing **BCTs:** 1.1, 1.3, 2.7, 4.1, 5.1, 11.1		
Behavioural & Pharmacological (Nicotine replacement therapy) (n= 4 studies)		
Farley et al. (2017) **Country:** UK **Setting:** Pharmacies **Mode of delivery:** eight pharmacy visits (lasting 10 min) or self-help booklet. **Duration:** Four or 16 weeks with NRT for up to 9 months. **Reduction aims**: Reduce cigarettes in 4 steps. Step 1: by 25% of baseline Step 2: by 50% of baseline	**Context:** The rationale for the programme by suggesting that learning a new pattern of smoking would prevent consumption increasing again by disrupting learnt associations between cues and smoking behaviour. Programmes contained 4 steps for reducing smoking before stopping then 4 steps to maintain abstinence. Three methods of reduction were advised: 1. Timer method: participants used a timer e.g. a mobile phone, to signal when they could smoke and agreed to smoke only when allowed. The time lengthened on each occasion a person wanted to reduce smoking more. 2. Smoke-free periods: the day was divided into hours and participants progressively eliminated hours they could smoke by designating them smoke-free and agreeing not to smoke in smoke-free hours. 3. Unstructured: participants were free to smoke whenever but set aside each day's cigarette ration in a pack. All groups were prescribed NRT, including a patch and a short acting NRT (2 mg gum, 2 mg sublingual tablets, 2 mg lozenge, inhalator or nasal spray) to replace each 'missing' cigarette.	

Citation and characteristics	Description of the context, intervention and control conditions	
Step 3: by 75% of baseline Step 4: by 100% of baseline **Cessation aims:** Quit attempt at step 4, steps 5-8 support maintenance of abstinence maintenance. **Behaviour change technique/theory:** Not reported **BCTs:** 1.1, 1.3, 1.7, 2.7, 4.1, 8.4, 8.7, 10.10, 11.1	**Intervention arm 1**: Behavioural support + standard length Step 1 in 2 weeks; Step 2 in 6 weeks; Step 3 in 10 weeks; Step 4 in 16 weeks; Steps 5 to 8 in 34 weeks. Smoking reduction methods explained by pharmacists. Preference given for use of structured methods because there is evidence that they are more effective. Willingness to quit asked regularly and referral to a standard smoking cessation service made if ready. Anyone not abstinent at step 4 was offered additional visits were to motivate further reduction or quit attempts. **Intervention arm 2**: Behavioural Support + short length Step 1 in 1 weeks; Step 2 in 2 weeks; Step 3 in 3 weeks Step 4 in 4 weeks; Steps 5 to 8 in 16 weeks. Behavioural support as described in arm 1	**Control arm 3**: Self-help booklet + standard length Step 1 in 2 weeks; Step 2 in 6 weeks; Step 3 in 10 weeks Step 4 in 16 weeks; Steps 5 to 8 in 34 weeks. Smoking reduction methods explained in a written booklet. Pharmacists to handed out booklets with no further advice or interaction. Readers prompted to consider willingness to quit smoking in booklet. Referral to smoking cessation service available to those ready. **Control arm 4:** Self-help booklet + short length Step 1 in 1 weeks; Step 2 in 2 weeks; Step 3 in 3 weeks Step 4 in 4 weeks; Steps 5 to 8 in 16 weeks. Self-help as described in arm 3
Guo et al. (2023) **Country:** Hong Kong **Setting:** Community-based smoking hotspots **Mode of delivery:** Smoking cessation advisors via text messages and chat bot **Duration:** 12 weeks **Reduction aims**: No specific reduction targets set.	**Context:** Both groups received brief advice using the AWARD model (Ask, Warning, Advice, Referral, Do-it-again) at baseline. **Intervention:** Nicotine replacement therapy sampling (NRT-S) + personalised messages and chatbot. NRT: 1 week sample (7 NRT patches or 84 pieces of gum). Participants new to NRT and that smoked >30 minutes after waking up received 2 mg gum or 14 mg patch, while those who smoked ≤30 minutes were given 21 mg nicotine patch (4 mg NRT gum is not available in Hong Kong). Real-time behavioural support via instant messaging on knowledge and skills of quitting, benefits of quitting, strategies to manage urges to smoke for self-efficacy, and smoking cessation services. Message schedule was personalised by baseline readiness to quit and target quit	**Control:** regular SMS messages regarding general health at a similar frequency to intervention group. **AWARD model details:** Ask – inquired about smoking behaviours; Warning – given on smoking harms using exhaled carbon monoxide test results and a leaflet with shocking pictures of smoking-induced diseases; Advice - to quit promptly using NRT or smoking cessation services; Referral - offered a free smoking cessation service (participant contact details sent to service providers in active referral); Do-it-again - advice was repeated at each follow-up.

Citation and characteristics	Description of the context, intervention and control conditions	
Cessation aims: Quit attempt within 12 weeks. Active referral to smokers if they expressed the need for smoking cessation services. **Behaviour change technique/theory:** Social Cognitive Theory; Transtheoretical Model **BCTs:** 1.1, 1.2, 1.3, 1.7, 2.7, 4.1, 5.1, 5.2, 6.2, 8.4, 10.10, 11.1, 12.2, 12.3, 15.1	date. Initially once weekly to initiate an instant messaging conversation, which increased to once daily closer to quit date and twice weekly immediately before and after quit date. Proactive instant messages such as asking about the recent progress of smoking cessation were used to initiate the conversation, for example, '*I have heard lots of good news one after another. Some people said that they had completely quit smoking, and some had reduced smoking. How about your progress? You can share it with me*'. A total of 6 reminders of chatbot URL were sent every two weeks over 12-weeks. The chatbot answered common queries related to cessation like quitting methods, craving management, self-efficacy to quit, novel tobacco products, and a free text box to text their own queries.	
Hatsukami et al. (2020) **Country:** U.S.A **Setting:** Clinics **Mode of delivery:** NRT provided for free at clinics by researchers **Duration:** 8 weeks **Reduction aims**: Complete substitution of smoking cigarettes with NRT; no targets for usual brand arm **Cessation aims:** No aims to quit during the trial (although achieving complete substitution would be equivalent to quitting)	**Context:** All participants completed daily diaries on cigarettes and assigned product use via Interactive Voice Recording that called participants on a daily basis for the duration of the clinical trial. Initial weekly intervention visits were followed by biweekly visits (weeks 1, 2, 3, 4, 6, and 8) for all groups. All subjects were strongly encouraged to quit using all tobacco products at the end of their study participation; a treatment manual and resources were provided. Participants received compensation for attendance at each clinic visit, submission of biological samples, and completion of visit forms.	
	Intervention: complete substitution with NRT Complete substitution with 4 mg nicotine gum or lozenge, with the participant choosing what product they would like to use i.e. "you will stop smoking cigarettes and use only nicotine gum or lozenge"CS-NRT). During the study participants received brief counselling on how to avoid smoking cigarettes. Participants received an incentive if they were protocol compliant i.e. provided records of product use; daily diaries; and returned unused products. A CO result of not more than 4 ppm at a clinic visit was an additional requirement to receive all bonus payments. Nicotine gum or lozenge (participant's choice) was provided	**Control:** continued smoking with usual brand cigarettes At the end of the clinical trial phase (week 8), smokers in the UB cigarette condition were offered e-cigarettes or NRT for up to 8 weeks, with a choice of product and no specific instructions for use. Participants received an incentive if they were protocol compliant i.e. provided records of product use; and completion of daily diaries.

Citation and characteristics	Description of the context, intervention and control conditions	
Behaviour change technique/theory: Not reported **BCTs:** 2.3, 2.7, 4.1, 8.4, 10.8, 10.10, 11.1	in the 4 mg dose but down-titrated to 2 mg if adverse side effects were experienced. Nicotine gum came in mint, cinnamon, and fruit flavours, while the nicotine lozenge was mint or cherry flavours.	
Zhao et al. (2021) **Country:** Hong Kong **Setting:** Community-based smoking hotspots **Mode of delivery:** University students trained as smoking cessation ambassadors and trained smoking cessation counsellor with two years of experience in smoking cessation research **Duration:** 8 weeks **Reduction aims**: No target;	**Context:** Both groups received brief smoking advice, nicotine replacement sampling, and an active referral. Brief advice (lasting 2 minutes) was based on AWARD: Ask – inquired about smoking behaviours; Warning – given a leaflet on harms of smoking to health; Advice - to quit or reduce smoking as soon as possible and set an initiation date; Referral – actively referred to smoking cessation service Do-it-again – repeat the intervention during the chat-based interaction and follow-up calls. Nicotine replacement therapy: A 1-week sample of NRT given to smokers willing to try it, an NRT use card containing the instructions and potential side effects were given with a brief oral explanation. NRT-S was 14/21 mg patch, 2 mg gum, and 1/2 mg lozenges, provided according to preferences and daily cigarette consumption. Participants who consume ≤20 cigarettes daily received the 14 mg patch, 2 mg gum, or 1 mg lozenges while participants who consume >20 cigarettes daily received 21 mg patch, 2 mg gum, or 2 mg lozenges. Active referral: Ambassadors introduced the smoking cessation services (free-of-charge) using an information card. Names and telephone contacts of the agreed participants were sent to the service provider for appointment booking of clinical treatment within a week of enrolment.	

Citation and characteristics	Description of the context, intervention and control conditions	
specific advice for reducing smoking not reported **Cessation aims:** No target; Active referral to smoking cessation services **Behaviour change technique/theory:** motivational interviewing **BCTs:** 1.1, 2.7, 3.2, 3.3, 4.1, 5.1, 10.10, 11.1, 15.1	**Intervention:** personalized text messages and chat-based support via instant messaging. Fourteen messages over 2 months. Twice per week for four weeks then once per week for four weeks plus two additional reminders prior to calls at 3 and 6 months. Each message was personalized according to sex, age, and smoking pattern of the participants. Message content and conversation initiation and facilitation similar to Guo 2023. Non-engaged participants sent 3 additional prompts. Booster (1 to 2 minutes) by telephone at 4 and 8 weeks.	**Control:** general smoking cessation text messages Message frequency similar to the regular instant messaging received by the intervention group. The SMS contents included brief smoking cessation advice, tips for coping with craving and reminders for follow-up calls. Counsellors did not respond to any messages from participants and no telephone booster was given at follow-up.

ISBN: 978-1-83766-863-2

Acknowledgement to Public Health Wales NHS Trust to be stated.

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