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SUMMARY WITH CRITICAL APPRAISAL

Non-Pharmacological and Pharmacological Interventions for Smoking Cessation Programs in Youth: A Review of Clinical Effectiveness and Guidelines

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Abbreviations

AGREE	Appraisal of Guidelines for Research and Evaluation
AMSTAR	A Measurement Tool to Assess systematic Reviews
CI	Confidence interval
CM	Contingency management
CO	Carbon monoxide
CRD	Centre for Reviews and Dissemination
CTFPHC	Canadian Task Force on Preventive Health Care
FTND	Fagerström Test for Nicotine Dependence
GDG	Guideline Development Group
GRADE	Grading for Recommendations Assessment, Development, and Evaluation
HTA	Health Technology Assessment
ITT	Intention-to-treat
MA	Meta-analysis
MeSH	Medical Subject Headings
NICE	National Institute for Health and Care Excellence
NoT	Not on Tobacco
NRT	Nicotine replacement therapy
NS	Non-significant
OR	Odds ratio
PICO	Population, Intervention, Comparator, Outcome
POP	Put it Out Project
PPA	Point-prevalence abstinence
ppm	Part per million
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
SGM	Sexual and gender minority
SIGN	Scottish Intercollegiate Guidelines Network
SLT	Smokeless tobacco
SMS	Short message service
SR	Systematic review
TSP	Tobacco Status Project
wks	Weeks

Context and Policy Issues

Smoking is one of the most preventable causes of mortality and morbidity among Canadians,[1] yet the use of tobacco remains an important and challenging public health issue.[1,2] The current Canadian youth are one of the first generations that are more likely to be aware than not of the health risks associated with traditional tobacco consumption (e.g., cigarettes, chewing tobacco).[1] Even though the prevalence of traditional tobacco consumption by youth may be lower than previous generations,[1,3] there are added concerns with the most recent invention of vaping devices and e-cigarettes.[4] Vaping is recognized to be associated with significant adverse events with short-term use and the long-term implications of such a novel technology are unknown.[5,6] Taken together, preventing tobacco or nicotine consumption, in any form, among youth is critical.

Pharmacological therapy, such as nicotine replacement therapy (NRT), bupropion, and varenicline, are effective in helping the general population of smokers quit using tobacco.[7] Non-pharmacological therapies may also be useful in assisting patients who are ready to

quit smoking.[7] Examples of non-pharmacological therapies include behavioural therapy, physician advice, telephone-based interventions, and group/peer or individual smoking cessation programs delivered in person or remotely.[8] In certain populations, such as pregnant women, non-pharmacological therapy, specifically cognitive behavioural therapy, can be as effective as NRT.[7] In addition, pharmacological and non-pharmacological therapies can be used alone or as a combined therapy.[9] Overall, there is less evidence regarding which interventions are most effective for youth (defined by the United Nations as 15 to 24 years).[6,10]

To inform policy decisions about using pharmacotherapy and non-pharmacotherapy for smoking cessation among youth, specific evidence is required. As such, this report aims to review the clinical effectiveness of using a combination of pharmacological and non-pharmacological smoking cessation interventions or non-pharmacological smoking cessation interventions alone for youth. The current report also aims to review evidence-based guidelines regarding smoking cessation interventions for youth.

Research Questions

1. What is the clinical effectiveness of pharmacological and non-pharmacological smoking cessation interventions for youth?
2. What is the clinical effectiveness of non-pharmacological smoking cessation interventions for youth?
3. What are the evidence-based guidelines regarding smoking cessation interventions for youth?

Key Findings

Three systematic reviews, nine randomized controlled trials, and two guidelines were identified that addressed the research questions, and the results were mixed.

One randomized controlled trial was identified and provided results regarding the clinical effectiveness of pharmacological and non-pharmacological smoking interventions for youth. Evidence from this randomized controlled trial suggested that there were no significant differences in smoking cessation or smoking frequency outcomes between brief advice, nicotine patch therapy and a 6-week text messaging intervention (intervention) and brief advice and nicotine patch therapy (control).

Three systematic reviews and eight randomized controlled trials were identified and examined the clinical effectiveness a variety of different non-pharmacological smoking interventions for youth. Evidence from the systematic reviews did not reveal improved smoking cessation outcomes for most comparisons; two comparisons via meta-analyses did find improved smoking cessation outcomes in favour of the intervention. Of the seven randomized controlled trials that examined smoking cessation outcomes, three studies found reductions in favour of the smoking cessation intervention, three did not find differences between groups, and one study found improvements at 3-months in favour of the intervention but not at 6-month follow-up. Mixed findings were found for other key clinical outcomes, such as smoking behaviour and quitting outcomes.

Two evidence-based guidelines regarding smoking cessation interventions for youth were identified; one guideline was commissioned by National Institute for Health and Care

Excellence and the other by the Canadian Task Force on Preventive Health Care. The National Institute for Health and Care Excellence guideline recommends the consideration of nicotine replacement therapy for young people who are dependent on nicotine (strength of recommendation: weak); if nicotine replacement therapy is prescribed, the guideline recommends offering it with behavioural support (strength of recommendation: strong). The Canadian Task Force on Preventive Health Care guidelines recommend asking children and youth smokers or their parents about tobacco use by the child or youth and offering brief information and advice during primary care visits (strength of recommendation: weak). Both guidelines used rigorous methodology to inform their recommendations, but the studies included to inform the recommendations were of varying quality, ranging from low to moderate quality.

It may be premature to draw conclusions about pharmacological and non-pharmacological smoking cessation interventions for youth given the mixed findings identified in this report.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were Smoking Cessation and Youth. Search filters were applied to limit retrieval to randomized controlled trials (RCTs), systematic reviews (SRs), and clinical practice guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2017 and January 17, 2020. Internet links were provided, where available.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection criteria

Population	Youth (15 to 24 years of age)[a] who smoke including chewing tobacco, vaping, e-cigarettes
Intervention	Q1: Pharmacological smoking cessation interventions (e.g., Nicotine replacement therapy [NRT]) and non-pharmacological smoking cessation interventions Q2: Non-pharmacological smoking cessation interventions Q3: Pharmacological smoking cessation intervention, non-pharmacological smoking intervention, pharmacological and non-pharmacological combined
Comparator	Q1-2: No treatment, usual care, another pharmacological or non-pharmacological intervention Q3: Not applicable
Outcomes	Q1-2: Clinical effectiveness (e.g., reduction in smoking/vaping, quality of life, relapse, quit attempts, adverse events)

	Q3: Recommendations regarding the use of pharmacological and/or non-pharmacological interventions for smoking cessation
Study Designs	Q1-2: Health technology assessments, systematic reviews, randomized controlled trials Q3: Evidence-based guidelines

[a] Studies that limited inclusion to patients within this age range or with a population mean age within this range were eligible.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2017. Studies examining cannabis cessation were excluded. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included SRs were critically appraised by one reviewer using A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2,[11] RCTs were critically appraised using the Scottish Intercollegiate Guidelines Network (SIGN) II Checklist,[12] and guidelines were assessed with the AGREE II instrument.[13] Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 630 citations were identified in the literature search. Following screening of titles and abstracts, 568 citations were excluded and 62 potentially relevant reports from the electronic search were retrieved for full-text review. Four potentially relevant publications were retrieved from the grey literature search for full text review. Of these 66 potentially relevant articles, 52 publications were excluded for various reasons, and 14 publications met the inclusion criteria and were included in this report. These comprised three SRs, nine RCTs, and two evidence-based guidelines. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14] flowchart of the study selection.

Additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Three SRs were included in this report all of which had broader inclusion criteria than this report. Two reviews were Cochrane SRs with meta-analyses (MAs)[15,16] and one SR did not conduct MAs.[17] One Cochrane SR with MA searched literature published from inception to June 2017.[16] Twenty-six of the 41 RCTs included in the SR fulfilled the eligibility criteria of this report.[16] Of the 26 studies that were relevant to this report, the results for 10 of those were reported separately from other, irrelevant studies; this subset of relevant results is presented in the Summary of Findings section.[16] The other Cochrane SR with MA searched literature published from inception to August 2016.[15] Five of the 34 studies included in the

SR (all RCTs) fulfilled the eligibility criteria this report and four had usable results that are reported in the Summary of Findings sections.[15] The third SR searched literature from inception to 2017.[17] Of the 59 studies included in this SR, one RCT was relevant to this report.[17] Appendix 5 provides a detailed description of the overlap in the primary studies between the two Cochrane SRs.[15,16]

The nine primary studies included in this report were two-arm parallel RCTs.[18-26]

Two evidence-based guidelines were included in this report.[27,28] One guideline was commissioned by the National Institute for Health and Care Excellence (NICE)[28] and one guideline was commissioned by the Canadian Task Force on Preventive Health Care (CTFPHC).[27] The 2018 NICE guideline[28] is an update to a previous guideline (first published in March 2006) and covers smoking cessation interventions and services delivered in primary care and community settings for everyone over the age of 12. The NICE guideline is developed in accordance with the methodology found in the NICE Guidelines Manual.[29] In brief, NICE guidelines include a systematic literature search (or a systematic literature search update if updating a guideline) to identify and synthesize relevant literature and the NICE Guideline Development Group drafts and later finalizes recommendations. Recommendations are based on the trade-off between the benefits and harms of an intervention taking into consideration the quality of the underpinning evidence, among other factors (e.g., costs, current practices, recommendations made in other relevant guidelines, patient preferences, equality issues, stakeholder input). Regular checks are conducted to determine if an update is required.[28,29] The CTFPHC guideline[27] is an update to the US Preventive Services Task Force search with the goal of providing evidence-based recommendations on behavioural interventions for the prevention and treatment of tobacco smoking among children and youth (five to 18 years). To develop the recommendations, a systematic literature search was conducted by an independent organization using a priori framework and updated to identify and synthesize relevant literature, and a working group of independent clinicians and methodologists developed recommendations based on the trade-off between the benefits harms, for specific interventions, patient values and preferences, and resource considerations. Recommendations are formulated based upon this comprehensive assessment of evidence.[27] Both guidelines used GRADE to assess quality of evidence and provide a strength of recommendations.[27,28] Both guidelines were also externally peer-reviewed.[27,28]

Country of Origin

The body of evidence originated from India (one SR),[17] the Netherlands (one RCT),[19] Peru (one RCT),[26] Singapore (one SR),[15] Spain (one RCT),[24] South Africa (one RCT),[22] South Korea (one RCT),[21] the United Kingdom (one SR),[16] and the United States (four RCTs).[18,20,23,25] The NICE guideline originates from the United Kingdom[28] and the CTFPHC originates from Canada.[27]

Patient Population

One Cochrane SR by Fanshawe and colleagues[16] considered studies that included young people, aged 20 years or younger, who regularly smoke. The second Cochrane SR by Taylor et al.[15] included people who smoked, with no exclusions based on age, gender, ethnicity, language or health status. As the current Rapid Response report was focusing on youth, studies within the SR that examined youth smokers (i.e., 15 to 24 years) were eligible for inclusion in this report. The final SR included youth aged 14 to 25 years (mean age 21 years) who used smokeless tobacco products.[17]

All of the primary studies examined youth (other classification names: adolescents, young adults, college students) tobacco smokers with a mean age between 15 and 24 years.[18-26] A few studies focused on more specific populations, such as male college students[21] or participants described by the study authors as sexual and gender minorities (i.e., those who are not heterosexual and/or do not identify with their sex assigned at birth).[18]

The intended users of the 2018 NICE guideline[28] are (i) commissioners and providers of stop smoking interventions or services; (ii) health social care and other frontline staff with links to stop smoking services who engage with people who smoke; (iii) health and wellbeing boards; and (iv) members of the public who want to stop smoking or who want to help others to stop. The target population of the guideline is members of the public who want to stop smoking or who want to help others stop. Specific to this report, the relevant population includes young people over 12 years old.[28] The intended users of the 2017 CTFPHC guideline[27] are individuals who work in Canadian primary care settings and the target population of the guideline are children and youth between the ages of five and 18 years.

Interventions and Comparators

Pertinent to this report, the SR by Fanshawe et al.[16] included a combination of pharmacological and non-pharmacological interventions (e.g., counselling and a pharmacological intervention, behavioural intervention plus nicotine patch) as well as non-pharmacological interventions (e.g., motivational interviewing, interventions based on social cognitive theory, Transtheoretical Model of Stages of Change for adolescents alone, in combination with other non-pharmacological modalities [brief advice, motivational enhancement], in the case of the Project EX set of studies plus yoga and meditation).[16] These interventions were compared to no intervention, delayed intervention, a 'brief' intervention (e.g., information on stopping smoking either delivered to individuals in control groups or as literature), general tobacco education given to all participants in the trial, and different cessation interventions or combinations of interventions. To note, this report does not include results for 16 of the 26 studies that met the eligibility criteria due to the nature of result reporting for those studies (i.e., 16 eligible studies were not synthesized separately from ineligible studies). Thus, the 10 studies with results that could be summarized from this SR evaluated non-pharmacological interventions, which is the reason for the Fanshawe et al. review being located under the subheading non-pharmacological smoking cessation interventions in the Summary of Findings section.[16]

The Taylor and colleagues SR[15] investigated internet interventions (i.e., non-pharmacologic), in all settings and from all types of providers, for the purposes of smoking cessation (e.g., tailored internet-based lifestyle interventions with and without interactive components, virtual reality plus motivational interviewing conducted in real time with a counselor). These interventions were compared to no intervention, a different internet intervention, or a non-internet intervention (e.g., non-tailored and non-interactive internet intervention, brief office intervention consisting of four individual counselling sessions).[15]

Relevant to this report, the SR by Nethan et al.[17] included an RCT focusing on smokeless tobacco cessation which examined a behavioural therapy intervention (enhanced condition) including interactive and multimedia features with functionality to create online lists, watch videos, and a web blog moderated by research staff. Automated email reminders encouraged website use and provided supportive measures. This study compared this intervention to behavioural therapy (basic condition), including static website content

including an 'Enough Snuff' pocket guide, a resource section with informational materials and links to websites offering content for short-term.[17]

One of the RCTs included in this Rapid Response report examined a combination of pharmacological and non-pharmacological smoking cessation intervention.[25] Specifically, the intervention included brief advice, NRT (patch) and a 6-week text messaging program. This was compared to brief advice and NRT (patch) without the text messaging component.[25] The remaining eight RCTs examined non-pharmacological smoking cessation interventions, including the use of internet platforms,[18,20,23] games or text messages on a mobile phone,[19,26] monetary incentives,[22,23] auricular acupressure,[21] and combination interventions (e.g., motivational interviewing with lifestyle interventions [exercise, meditation, anger management]).[24] Some of these interventions were developed using theoretical frameworks (e.g., contingency management, cognitive behaviour therapy).[22,23,26] The RCTs were compared to no intervention,[23,24] educational material,[19,20,22,26] non-tailored interventions,[18] or sham interventions.[21]

Relevant to this report, the NICE guideline explored NRT and behavioural support including motivational enhancement, programs based on social learning theory (e.g., Not on Tobacco or NoT program).[28] The CTFPHC guideline explored NRT and brief information and advice from primary care settings about (unspecified) behavioural interventions.[27]

Outcomes

For the SRs, the outcomes of interest were smoking cessation,[15-17] with MA performed based on type of intervention for the two Cochrane SRs.[15,16]

The RCTs investigated smoking cessation (e.g., biochemically verified and/or self-reported abstinence, self-reported relapse),[19,20,22,23,25,26] smoking behaviour such as intensity/frequency,[19,20,22-25] quitting behaviours, including intention, motivation, stage of change for quitting, and quit attempts[18,20,24] nicotine dependence (i.e., modified Fagerström Test for Nicotine Dependence),[24] and dose response effects.[19] Outcomes were measured in a standard, valid and reliable way for six RCTs[18,20-23,25] and three RCTs used self-report methods.[19,24,26] A common self-reported outcome measure for smoking cessation used was the seven-day point-prevalence abstinence (PPA), used by 3 RCTs,[20,22,25] and involved asking participants at a given time (e.g., 6 months) whether they have used cigarettes or other forms of tobacco in the past seven days. Espada et al. (2017)[24] used a modified Fagerström Test for Nicotine Dependence test, a self-reported method to assess nicotine dependence, that includes eight items where a higher total score implied a higher nicotine dependence (dichotomized into low and high nicotine dependence).

Pertinent to this report, both guidelines examined smoking cessation.[27,28]

Summary of Critical Appraisal

Systematic Reviews

Both Cochrane SRs[15,16] used strong methodology and met the criteria of all of the AMSTAR II checklist[11] with the exception of one criterion. The authors did not justify limiting inclusion to RCTs.[15,16] The third SR by Nethan et al.[17] also did not provide rationale for their selection of eligible study designs. Moreover, this SR did not include important methodological details: did not describe following a prospective protocol, the full search strategy was not provided (i.e., search syntax), the literature search could have been more exhaustive by searching additional databases other than PubMed and Google, it is unclear if data

selection and extraction were conducted independently and in duplicate, a list of excluded studies was not provided, and the risk of bias was not assessed for the included studies.[17] Together, these limitations suggest that this SR may not provide an accurate and comprehensive summary of the available studies that address the research question. Despite these limitations, the SR also included key methodological details that were also described in the two Cochrane reviews: the research question(s) were clear and inclusion criteria for the review were included, broad keywords from the search strategy were provided, reasons for excluding studies were provided, basic details about the included studies were provided, and study authors acknowledged financial support and any potential or actual conflicts of interest.[15-17]

Randomized Controlled Trials

The nine included RCTs all addressed an appropriate and clearly focused question and the assignment of the participants to treatment (intervention) groups was randomized.[18-26] One RCT provided adequate concealment methods (online randomization sequence contained in sealed opaque envelopes);[25] this was uncertain for the other eight RCTs.[18-23] This suggests that it is unclear whether there was a process implemented for the eight RCTs to ensure that the researchers were unaware of which participants were randomly allocated to each group. Moreover, none of the RCTs clearly described keeping the subjects and data assessors blind about treatment allocation.[18-26] Six RCTs[19-23,25] had similar treatment and control groups at the start of the trial and as described, the only difference between groups was the treatment under investigation; however, this was not clear for the other three RCTs.[18,24,26] Outcomes were measured in a standard, valid and reliable way for six RCTs[18,20-23,25] and three RCTs used self-report methods.[19,24,26] Three RCTs[19-21] indicated that they conducted power calculations to inform the sample size whereas the remaining six RCTs did not.[18,22-26]

Seven RCTs[19-22,24-26] provided drop out data but this information was missing for two studies.[18,23] Moreover, two RCTs[20,24] had dropout rates >20% which may introduce bias such as systematic differences between dropouts and participants who completed the study. For three RCTs,[18,19,22] all subjects were analyzed in the groups to which they were randomly allocated, four RCTs[20,21,24,26] were not, and it was unclear for the remaining two RCTs.[23,25] When applicable, it was unclear if results were comparable for all sites.[18,20,21,23-25]

Evidence-based Guidelines

Both guidelines[27,28] fulfilled the criteria for Domain 1 (scope and purpose) of the AGREE II checklist: the overall objectives, health questions, and populations to whom the guidelines apply were specifically described. The NICE guideline[28] fulfilled all of the criteria for Domain 2 (stakeholder involvement): Guideline Development Groups included individuals from all relevant professional groups; the guideline developers sought the views and preferences of the target population (patients, public, etc.); and the target users of the guidelines were clearly defined. In comparison, the CTFPHC guideline[27] partially fulfilled the views and preferences criterion as neither youth nor clinician preferences were examined due to resource limitations, but they did collect input from parents on their preferences and values.[27] Both guidelines[27,28] fulfilled the criteria for Domain 3 (rigour of development) of the AGREE II checklist: systematic methods were used to search for evidence; the criteria for selecting the evidence, the strengths and limitations of the body of evidence, and the methods for formulating the recommendations were described; the health benefits, side effects, and risks were considered in the formulation of the recommendations; the guideline

was externally reviewed by experts prior to its publication; and a procedure for updating the guideline was provided. The NICE guideline[28] provided information about the body of literature used to inform the guideline, including its quality; however, the formal recommendations use a specific syntax to link the quality of evidence with the recommendation. For example, NICE uses "offer" to reflect a strong recommendation and "consider" reflecting a recommendation where the evidence of a benefit is less certain.[28,29] The strength of CTHPHC recommendations[27] was based on the quality of supporting evidence, degree of uncertainty about the balance between desirable and undesirable effects, degree of uncertainty or variability in patient values and preferences, and degree of uncertainty about whether the intervention represents a wise use of resources. For Domain 4 (clarity of presentation), both guidelines presented their key recommendations in a way that is easily identifiable.[27,28] Different options for smoking cessation were clearly presented for the NICE guidelines[28] but were not for the CTFPHC guideline; this guideline described behavioural interventions without much description on what these were and how they differed. Both guidelines[27,28] fulfilled all or most of the criteria for Domain 5 (applicability): they provided advice and/or tools on how the recommendations can be put into practice and the potential resource implications of applying the recommendations have been considered. The NICE guideline[27] described facilitators and barriers to the application and presented monitoring and auditing criteria, but these were unclear for the CTFPHC guideline.[27] The final domain of the AGREE II checklist (Domain 6, editorial independence) identified that both guidelines declared any potential or actual competing interests of the guideline. The CTFPHC guideline[27] acknowledged that the views of the funding body had not influenced the content of the guideline, but this was unclear for the NICE guideline.[28]

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Appendix 4 presents a table of the main study findings and authors' conclusions.

Clinical Effectiveness of Pharmacological and Non-pharmacological Smoking Cessation Interventions

Smoking Cessation

One RCT[25] examined the clinical effectiveness of pharmacological and non-pharmacological smoking cessation interventions. This study compared brief advice, nicotine patch therapy and a 6-week text messaging versus brief advice and nicotine patch therapy. At both six and 12 weeks, there were no significant differences between intervention and comparator for seven-day PPA.[25]

Smoking Behaviour

This same RCT[25] also found no significant differences between intervention and comparator at both six and 12 weeks for cigarettes smoked per day or change in cigarette use per day from baseline.

Clinical Effectiveness of Non-pharmacological Smoking Cessation Interventions

Smoking Cessation

The three SRs[15-17] found the non-pharmacological intervention did not improve smoking cessation outcomes with the exception of two MA comparisons.[15,16] Fanshawe et al.[16] conducted an MA which pooled four studies investigating Project EX (multicomponent

intervention that includes sessions to strengthen students resolve to quit tobacco use) to no intervention (control). The analyses revealed a significant relative risk (RR) of 1.48 (95% confidence interval [CI], 1.05 to 2.1) in favour of the intervention.[16] The second exception was the Taylor et al.[15] SR which conducted a sensitivity analysis for completed cases (i.e., including only participants who were followed up versus intention to treat analysis) and found a significant RR of 1.92 (95% CI, 1.4 to 2.63) in favour of the internet interventions versus non-active control (e.g., printed self-help guides).

Seven RCTs examined smoking cessation outcomes and the results were mixed.[18-23,26] The SGM-tailored Put It Out Project (POP) intervention group outperformed the non-tailored Tobacco Status Project (TSP) comparator group at 6-months in regards to both biomechanically verified abstinence (odds ratio [OR]: 2.00; 95% CI, 0.48 to 8.28) and 7-day self-reported abstinence (OR: 2.50; 95% CI, 1.08 to 5.80).[18] The RCT which examined a complementary and alternative medicine intervention found the auricular acupressure group had significantly lower carbon monoxide levels compared to sham control (P = 0.001), with respondents having higher self-efficacy of smoking cessation (P = 0.048).[21] A pilot RCT (n = 12) compared a short message service (SMS) text message intervention, based on a cognitive behavioural smoking cessation program, to a SMS text message nutrition program (control).[26] The authors descriptively reported that the intervention group may improve self-reported smoking cessation outcomes, but also may have higher self-reported smoking relapse.[26] One RCT found significant differences in seven-day PPA in favour of the intervention (6-week information and monitoring plus contingency management with a financial incentive of $24 per assessment) when compared control (information and monitoring plus $8 incentive at each assessment) at 3-months (P < 0.001), but this difference was not retained at 6-months.[22]

Three RCTs found no differences between groups, for smoking cessation outcomes.[19,20,23] The RCT which compared a social mobile game (*HintRun*) to a psychoeducation brochure found no significant differences in self-reported abstinence at post-test or at follow-up.[19] Similarly, the RCT comparing the TSP Facebook intervention with control (referral to a smoking cessation website) did not find significant differences in biochemically verified 7-day abstinence (P = 0.969) nor self-reported seven-day PPA (P = 0.746).[20] When comparing web-based contingency management plus monetary incentives associated with providing carbon monoxide measurements on schedule *and* below a certain threshold to the same intervention with monetary incentives associated with participants providing carbon monoxide measurements on schedule alone (no set threshold), there were no significant differences in urinary cotinine or carbon monoxide levels at three or six-month follow-up.[23]

Smoking Behaviour

Six RCTs examined smoking behaviour outcomes.[18-20,22-24] The RCT which compared information and monitoring plus contingency management with a $24 financial incentive per assessment to information and monitoring plus $8 at each assessment found no significant differences in smoking intensity (average number of cigarettes smoked per day) between groups, but did find a significant decrease in smoking intensity of non-abstinent treatment and control participants, which was maintained through follow-up.[22] The SGM-tailored POP intervention found 50% or greater reduction in the number of cigarettes smoked per week in favour of the intervention when compared to the non-tailored TSP group (OR: 2.11; 95% CI, 1.09 to 4.08).[18] The RCT which compared Project EX to control (no intervention) found that the intervention group smoked a significantly lower number of cigarettes over the last 30 days (P < 0.001).[24] Moreover, the RCT that examined web-based contingency

management with monetary incentives tied with sending carbon monoxide measurements on time and below a set criterion compared to same program without the set criterion for carbon monoxide measurements found, via self-reported data, the intervention group smoked significantly less during the abstinence phase ($P < 0.05$) and return-to-baseline phase ($P < 0.001$) but not during 3-month and 6-month follow-up.[23] In addition, the RCT which compared TSP Facebook smoking cessation intervention to control (referral to smoking cessation website) found no differences in smoking reduction by 50% or more between groups ($P = 0.533$).[20] The social mobile game (*HitRun*) also did not find any significant differences in weekly smoking behaviour when compared to the psychoeducational brochure (control).[19]

Quitting Behaviours (intention, motivation, stage of change for quitting, quit attempts)

One RCT[24] examined intentions to quit, motivations to quit, and future smoking expectation (differences between questionnaire results between baseline and one-year follow-up). This study found that the intervention (Project EX) had a significant positive influence on all three outcomes in comparison to control (no intervention; $P < 0.001$, $P < 0.01$, and $P < 0.05$, respectively).[24] The study that compared an SGM-tailored POP versus non-tailored TSP found no significant differences between groups for stage of change for quitting smoking (precontemplation/contemplation versus preparation/action) or quit attempts during treatment.[18] Likewise, the RCT which compared TSP Facebook smoking cessation to control (referral to a smoking cessation website) found no differences between groups for ready to quit, quit attempt, and stage of change for quitting smoking over time outcomes.[20]

Nicotine dependence

One RCT[24] examined nicotine dependence and found that the intervention (Project EX) had a significant influence on nicotine dependence compared to the control (no intervention, $P < 0.05$). A second RCT examined nicotine dependence and found no differences in dependence when comparing auricular acupressure to sham control ($P = 0.10$).

Dose Response Effects

For one RCT,[19] a higher dose of the *HintRun* game (intervention, i.e., longer participants played the game) was associated with lower weekly smoking rates. Conversely, a higher dose of brochure (comparator, i.e., more time in reading the brochure) was associated with higher weekly smoking rates.[19]

Guidelines

The NICE guideline[28] recommends the consideration of NRT for young people who are dependent on nicotine (strength of recommendation: weak); if NRT is prescribed, the guideline recommends offering it with behavioural support (strength of recommendation: strong). Behavioural support may be include individual behavioural support (face-to-face meeting between an individual that smokes and a trained counsellor) or group behavioural support (scheduled meetings where people who smoke receive information, advice and encouragement and some form of behavioural intervention like cognitive behavioural therapy). Both types of behavioural support can weekly sessions for four or more weeks after quit date and often combined with pharmacotherapy.[28] These recommendations were based on moderate quality of evidence.[28]

The CTFPHC guidelines[27] recommend asking children and youth (age five to 18 years) or their parents about tobacco use by the child or youth and offering brief information and

advice, as appropriate, during primary care visits to treat tobacco smoking among children and youth. The guidelines describe 'brief' as contact time up to five minutes with primary care clinician and advice may include verbal communication about patient attitudes and beliefs, risks of smoking and strategies for dealing with the influence of peers. Sharing of printed or electronic material (e.g., brochures, newsletters and interactive computer programs) can also be considered. The strength of recommendations is weak and these guidelines are derived from low quality of evidence.[27]

Limitations

There are certain limitations to consider when reviewing the report. The three included SRs[15-17] had eligibility criteria that were broader than this report. Thus, a subset of studies from each SR were included and synthesized. Moreover, only certain MA comparisons from the two Cochrane SRs were relevant for this report.[15,16] Of the 14 studies and guidelines included, there were many different types of smoking cessation interventions and comparators, specifically non-pharmacologic, explored, and it is challenging to compare these findings as they relate to different interventions with different features and construct. No included studies focused on vaping or e-cigarettes. In addition, most of the clinical evidence identified included non-pharmacological interventions and there was a paucity of combination interventions (pharmacological and non-pharmacological) whereby definitive conclusions cannot be made. The majority of included RCTs did not conduct power calculations to inform the sample size,[18,22-26] and inappropriate or small sample sizes may influence the ability to detect significant differences between groups. One guideline was conducted in Canada;[27] therefore, it is unclear how generalizable the results from the other included literature are to the Canadian context (e.g., available interventions, population characteristics). Finally, the guidelines were based on low to moderate quality of evidence. These limitations warrant the use of caution when interpreting the findings of this report.

Conclusions and Implications for Decision or Policy Making

This report identified evidence about the clinical effectiveness of non-pharmacological smoking cessation interventions alone or in combination with pharmacological smoking cessation interventions for youth as well as evidence-based guidelines regarding smoking cessation interventions in this population.

Regarding the clinical effectiveness for pharmacological and non-pharmacological smoking cessation interventions, one RCT[25] was identified in the search. Evidence from this RCT[25] suggested that there were no significant differences in smoking cessation or smoking frequency outcomes when comparing a multicomponent intervention group (brief advice, nicotine patch therapy and a 6-week text messaging intervention) to brief advice and nicotine patch therapy alone. One Cochrane SR[16] included pharmacological and non-pharmacological interventions in the SR, but none of those included studies fulfilled the eligibility criteria for this report and were not summarized.

Three SRs[15-17] and eight RCTs[18-24,26,30] addressed the clinical effectiveness of non-pharmacological smoking cessation interventions research question, and the results were mixed. Evidence from the SRs[15-17] did not reveal improved smoking cessation outcomes for most comparisons; two MAs[15,16] did find improved smoking cessation outcomes in favour of the intervention. Of the seven RCTs[18-23,26,30] that examined smoking cessation outcomes, three studies found reductions in favour of the smoking cessation intervention,[18,21,26] three did not find differences between groups,[19,20,23] and one study found improvements at 3-

months in favour of the intervention but not at 6-month follow-up.[22] Results for other clinical outcomes were also variable. For example, six RCTs[18-20,22-24] investigated smoking behaviours: four studies[18,22-24] found significant differences between groups for certain comparisons differences in favour of the intervention and two studies found no significant differences between groups.[19,20]

Two evidence-based guidelines were identified that provide recommendations regarding smoking cessation interventions for youth, including one Canadian guideline. Generally, the guidelines provide recommendations for the consideration of NRT with behavioural support for young people (12+ years) who are dependent on nicotine (strength of recommendation: weak to strong)[28] and it is recommended that staff from primary care ask children and youth smokers (five to 18 years) or their parents about tobacco use by the child or youth and offer brief information and advice during primary care visits (strength of recommendation: weak).[27] Both guidelines used rigorous methodology to inform their recommendations,[27,28] but the studies included to inform the recommendations were of varying quality, ranging from low to moderate quality.

It may be early to draw conclusions about pharmacological and non-pharmacological smoking cessation interventions for youth given the mixed findings identified in this report. Larger, sufficiently powered comparative studies evaluating pharmacological and non-pharmacological smoking cessation interventions may help reduce this uncertainty.

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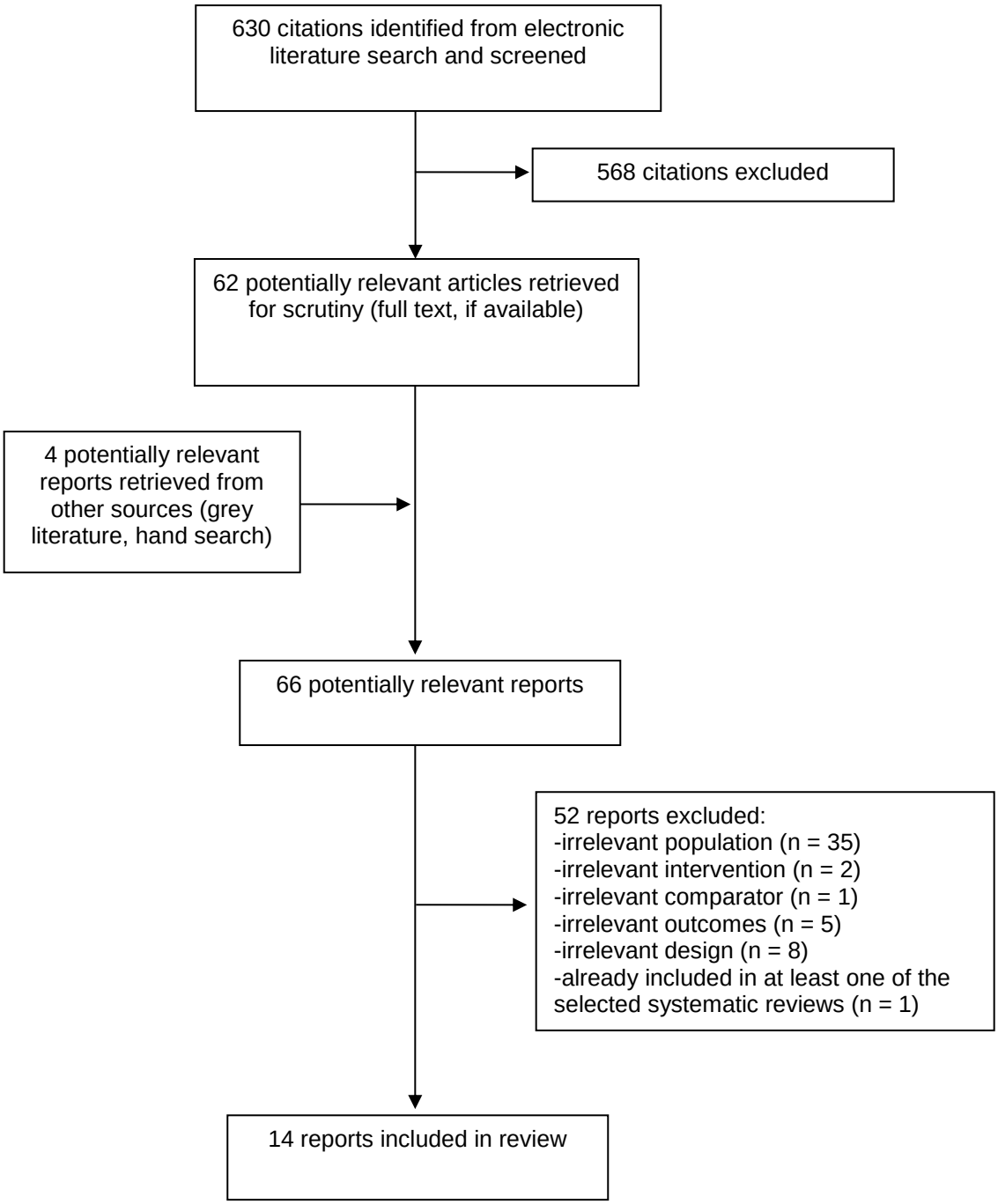
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of included systematic reviews and meta-analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Non-pharmacological Smoking Cessation Interventions				
Nethan, 2018[17] India	59 total studies (RCTs and cohort), 1 RCT relevant to this report	Youth aged 14 to 25 years (mean age: 21 years) that use smokeless tobacco products	Intervention: Behavioural therapy (enhanced condition) including interactive and multimedia features with functionality to create online lists, watch videos, and a web blog moderated by research staff. Automated email reminders encouraged website use and provided supportive measures Comparator: Behavioural therapy (basic condition), including static website content including an 'Enough Snuff' pocket guide, a resource section with informational materials and links to websites offering content for short-term	– Smoking cessation Length of follow-up: 3 and 6 months
Fanshawe, 2017[16] United Kingdom	41 total RCTs, 26 relevant to this report; of these 26 studies, 10 reported results separately from other, irrelevant studies (this subset of relevant results presented in Summary of Findings table)	Young people, aged under 20 years, who regularly smoke	Intervention: combination of pharmacological and non-pharmacological interventions (e.g., counselling and a pharmacological intervention, behavioural intervention plus nicotine patch); non-pharmacological interventions (e.g., motivational interviewing, interventions based on social cognitive theory, Transtheoretical Model	– Smoking cessation – Length of follow-up: minimum 6 months

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
			of Stages of Change for adolescents alone, in combination with other modalities [brief advice, motivational enhancement], in the case of the Project EX set of studies plus yoga and meditation Comparator: no intervention, delayed intervention, information on stopping smoking either delivered to individuals in control groups or as literature ('brief intervention'), general tobacco education given to all participants in trial, different cessation interventions or combinations of interventions	
Taylor, 2017[15] Singapore	34 total RCTs, 5 relevant to this report; relevant to this report; of these 5 studies, 4 reported results separately from other, irrelevant studies (this subset of relevant results presented in Summary of Findings table)	People who smoked, with no exclusions based on gender, ethnicity, language or health status.	Intervention: Internet intervention in all settings and from all types of providers for the purposes of smoking cessation (e.g., tailored internet-based lifestyle interventions with and without interactive components, virtual reality plus motivational interviewing conducted in real time with a counselor) Comparator: no intervention, a different internet intervention, or a non-internet intervention (e.g., non-tailored and non-interactive internet intervention, brief office intervention consisting	– Smoking cessation – Length of follow-up: minimum 4-weeks

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
			of four individual counselling sessions)	

RCT = randomized controlled trial.

Table 3: Characteristics of included primary clinical studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Pharmacological and Non-pharmacological Smoking Cessation Interventions				
Camenga, 2019[25] United States	Two-centre, two-arm parallel RCT Sample size calculation: No	Young adult cigarette smokers (n = 40) Mean age, years (SD): 20.2 (1.6) Age range: not specified % Female: 55 Mean number of cigarettes smoked per day (SD): 7.3 (4.4) Mean age started smoking cigarettes (SD): 16.5 (1.7) Number of previous quit attempts, median (range): 2 (0 to 10)	Intervention: brief advice, NRT (patch) and a 6-week text messaging intervention (n = 20) Comparator: brief advice, NRT (patch) and no text messaging (n = 20)	– 7-day PPA – Cigarettes smoked/day – Change in cigarette per day from baseline Treatment duration: 6-weeks Length of follow-up: 6 and 12 weeks
Non-pharmacological Smoking Cessation Interventions				
Hofmeyr, 2020[22] South Africa	Open-label, single centre, two-arm parallel RCT Sample size calculation: No	Treatment-seeking student smokers (n = 87) Mean age, years (SD): 21.6 (2.99) Age range: not specified % Female: 77.01	Intervention: Information and monitoring plus contingency management and could additionally earn $24 in abstinence-contingent incentives at each assessment (n = 40) Comparator: Information and	– 7-day PPA – Smoking intensity (average number of cigarettes smoked per day) of non-abstinent subjects Treatment duration: 6-weeks Length of follow-up: 3 and 6 months

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		Mean number of cigarettes smoke per day (SD): 9.86 (5.90) Mean years of smoking (SD): 3.38 (2.61) % participants who previously attempted to quit smoking in the past 5 years: 66	monitoring plus $8 at each assessment (n = 47)	
Scholten, 2019[19] The Netherlands	Open-label, single-centre two-arm parallel RCT Sample size calculation: Yes	Young smokers who were motivated to quit smoking Mean age (SD): 19.39 (2.52) years Age range: 16 to 27 years % Female: 54.9 Mean number of cigarettes smoke per week (SD): 70.63 (47.82) Mean years of smoking (SD): 4.16 (2.41) Mean FTND (SD): 2.72 (2.16) % participants who previously attempted to quit smoking: 63%	Intervention: *HintRun* (social mobile game) (n = 72) – "*a game to train inhibitory control through a modified version of a Go-No-Go training to help youth quit smoking*" Comparator: Psychoeducational brochure (n = 72) – a self-help brochure designed to help general public to quit smoking, and to provide resources and supporting methods	– Weekly smoking behaviour – Abstinence (self-reported abstinence in the last 24 hours) – Dose-response effects Treatment duration: 4 weeks Length of follow-up: 3 months
Vogel, 2019[18] United States	Open-label, two-arm parallel RCT Sample size calculation: No	SGM young adult smokers Age range: 18 to 25 years Sexual identity: bi/pansexual (56%), gay (18%), lesbian (18%), other (8%)	Intervention: SGM-tailored (POP; n = 84) Comparator: Non-tailored (TSP; n = 81) Both interventions took place within "secret" Facebook groups and were structurally identical, with daily Facebook posts and weekly "The Doctor Is IN" live group chat sessions. Monetary incentives were given	Primary outcome: – Biochemically verified abstinence Secondary outcomes: – 7-day self-reported abstinence – Reduction by 50% or more – Stage of change for quitting smoking – Quit attempt Treatment end: 3 months

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
			for completion of assignments	Length of follow-up: another 3 months (i.e., 6 months from randomization)
Harvanko, 2018[23] United States	Open-label, two-arm parallel RCT Sample size calculation: No	Adolescent tobacco smokers Mean age (SD): 16.9 (1.4) years % Female: 49.6 Mean number of cigarettes smoked per day (SD): 12.6 (9.1) Mean FTND (SD): 5.2 (1.8) Mean CO (SD): 10.1 (7.2) ppm Mean baseline cotinine (SD): 1182.8 (881.3) ng/mL	Intervention: Web-based contingency management (n = 63) plus participants were reinforced via monetary incentives for providing CO measurements on schedule and below a set criterion Comparator: Web-based contingency management (n = 64) plus participants were reinforced via monetary incentives for providing CO on schedule (with no set criterion) Contingent management phases: Baseline phase (7 days); Shaping phase (4 days); Abstinence phase (21 days); Thinning phase (5 days); Return to baseline phase (5 days). Participants received incentives per day for providing timely samples, with specific criterion CO level	– CO levels – Self-reported smoking behaviours – Urinary cotinine Treatment duration: 42 days Length of follow-up: 3 months or 6 months
Ramo, 2018[20] United States	Open-label, two-arm parallel RCT Sample size calculation: Yes	Young adult smokers Mean age (SD): 20.9 (2.0) years % Female: 54.6 Mean number of cigarettes smoke per day (SD): 11.6 (6.8)	Intervention: TSP Facebook smoking cessation (n = 251) – Implemented entirely to “secret” Facebook groups Comparator: Control (n = 249) – referred to National Cancer Institute’s	Primary outcome: – 7-day PPA over 12 months Secondary outcomes: – Biochemically verified abstinence at treatment end (3 months) – Self-reported 7-day abstinence

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		Mean FTND (SD): 3.2 (2.1)	Smokefree.gov website	– Self-reported reduction of cigarette consumption – Stage of change for quitting smoking (proportions of participants in preparation, action or maintenance stages of change at all time points) Treatment duration: 90 days Length of follow-up: 3 months, 6 months, 12 months
Blitchtein-Winicki, 2017[26] Peru	Open-label, single centre, two-arm parallel RCT Sample size calculation: No (pilot study)	Young adult smokers interested in quitting smoking in the next 30 days Age range: 18 to 23 years % Female: 13% (2 of 15) Smoking at least 4 cigarettes peer day at least 6 days per week	Intervention: SMS text message-based cognitive behavioural smoking cessation program (n = 9) Comparator: SMS text message nutrition program (n = 6) Participants received text messages, which allowed them to self-report smoking cessation data on days 2, 7, and 30 after quit date	– Self-reported smoke-free – Self-reported relapse on day 2 after quit day Length of follow-up: 2, 7, and 30 days after quit smoking date
Espada, 2017[24] Spain	Open-label, multi-center; two-arm parallel RCT Sample size calculation: No (pilot study)	Adolescent smokers Mean age (SD): 17.2 (1.23) years % Female: 51.4	Intervention: Project EX (n = 58) – a program of 8 sessions prepared students to strengthen their resolve to quit tobacco use Comparator: Control (n = 34) – received no formal intervention classes, materials or programs	– Percentage of quitters – Nicotine dependence (FTND) – Number of cigarettes in the last 30 days (active smokers only) – Intention to quit – Motivation to quit Treatment duration: 10 weeks Length of follow-up: 1 year
Lee, 2017[21] South Korea	Single-blinded, multi-center; two-arm parallel RCT	Male college students interested in quitting smoking	Intervention: Auricular acupressure (n = 30) – acupressure on	– Nicotine dependence

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	Sample size calculation: Yes	Mean age (SD): 22.43 (2.02) Mean smoking duration (SD): 67.77 (33.67) months	specific acupoints for smoking cessation Comparator: Control (n = 30) – sham	– Self-efficacy of smoking cessation (9 questions; Total score ranged from 9 to 45) – CO level Treatment duration: once a week for 6 weeks

CO = carbon monoxide; FTND = Fagerström Test for Nicotine Dependence; ITT = intention-to-treat; NRT = nicotine replacement therapy; POP = Put It Out Project; ppm = part per million; PPA = point-prevalence abstinence; RCT = randomized controlled trial; SD = standard deviation; SGM = sexual and gender minority; SMS = short message service; TSP = Tobacco Status Project.

Table 4: Characteristics of included guidelines

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
Pharmacological and Non-pharmacological Smoking Cessation Interventions						
NICE, 2018[28]						
Intended Users: Commissioners and providers of stop smoking interventions or services Health social care and other frontline staff with links to stop smoking services who engage with people who smoke Health and wellbeing boards Members of the public who want to stop	Relevant to this report, NRT, behavioural support (motivational enhancement, programs based on social learning theory such as NoT program)	Smoking cessation	Systematic literature search conducted and updated to identify and synthesize relevant literature	GRADE	NICE GDG makes a recommendation based on the trade-off between the benefits harms, costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues	Draft guidance sent to stakeholders, and is assessed for its impact on quality The guideline developer considers comments from stakeholders and agrees any changes The senior team (Guidance Executive) considers guideline and signs it off for publication

Intended Users, Target Population	Intervention and Practice Considered	Major Outcomes Considered	Evidence Collection, Selection, and Synthesis	Evidence Quality Assessment	Recommendations Development and Evaluation	Guideline Validation
smoking or who want to help others to stop Target Population: Members of the public who want to stop smoking or who want to help others to stop						
CTFPHC, 2017[27]						
Intended Users: Individuals who work in Canadian primary care settings Target Population: children and youth (age 5 to 18 years)	Relevant to this report, NRT, brief information and advice from primary care settings about (unspecified) behavioural interventions	Smoking cessation	Systematic literature search conducted by an independent organization using a priori framework and updated to identify and synthesize relevant literature	GRADE	CTFPHC working group (independent panel of clinicians and methodologists) developed guidelines with support from scientific staff at the Public Health Agency of Canada The work group makes a recommendation based on the trade-off between the benefits harms, for specific interventions, patient values and preferences, and resource considerations. Recommendations are formulated based upon this comprehensive assessment of evidence	Each phase of process includes peer review by methodologists and content experts Stakeholders invited to provide comments at all stages (protocol, systematic review, draft guidelines) All members of the CTFPHC reviews and approve each phase of guideline development

CTFPHC = Canadian Task Force on Preventive Health Care; GDG = Guideline Development Group; GRADE = Grading for Recommendations Assessment, Development, and Evaluation; NICE = National Institute for Health and Care Excellence; NoT = Not on Tobacco; NRT = nicotine replacement therapy.

Appendix 3: Critical Appraisal of Included Publications

Table 5: Strengths and limitations of systematic reviews and meta-analyses using AMSTAR 2[11]

Strengths	Limitations
Non-pharmacological Smoking Cessation Interventions	
Nethan, 2018[17]	
- Research question clear and inclusion criteria for the review included the components of PICO - Broad keywords from search strategy provided - Reasons for excluding studies during full-text screening provided in flow chart - Basic details about the included studies provided - Study authors acknowledged financial support - Study authors reported no conflicts of interest	- Study authors did not describe following a prospective protocol - Did not justify why study authors included certain study designs and not others - Full search strategy not provided (i.e., search syntax) - PubMed and Google were used to identify literature (i.e., search could have been more exhaustive by searching additional academic databases) - Grey literature platforms, such as ClinicalTrials.gov, not searched with the exception of using a Google literature search - It is unclear if data selection and extraction were conducted independently and in duplicate. - List of excluded studies not provided - Risk of bias not assessed for the included studies
Fanshawe, 2017[16]	
- Study authors stated following a prospective protocol and reported differences between the protocol and final review - Research questions clear and inclusion criteria for the - review included the components of PICO - Multiple databases, grey literature, and reference lists of identified studies searched - Full search strategy not provided (i.e., search syntax) in appendix - Data selection and extraction conducted in duplicate and a third reviewer or editorial base was used, when applicable, to settle discrepancies - Meta-analysis plan described - Methods used to combine study findings appropriate - Basic details about the included studies provided - Reasons for excluding studies not explicitly provided in flow chart, but provided in the appendices - Risk of bias assessed using the Cochrane Risk of Bias tool - List of excluded studies provided - Study authors acknowledged financial support - Study authors reported conflicts of interest: one investigator is an author of one of the included studies; one investigator is a co-applicant on a completed trial where nicotine patches were provided free of charge by GlaxoSmithKline; however the trial was funded by the NIHR HTA, and the sponsor was not involved in the running or reporting of the study	- Did not justify why study authors included RCTs and not other study designs

Strengths	Limitations
Taylor, 2017[15]	
- Study authors stated following a prospective protocol and reported differences between the protocol and final review - Research questions clear and inclusion criteria for the - review included the components of PICO - Multiple databases searched as well as clinicaltrials.gov to identify completed and ongoing studies - Full search strategy not provided (i.e., search syntax) in appendix - Data selection and extraction conducted in duplicate and a third reviewer, when applicable, to settle discrepancies - Meta-analysis plan described - Methods used to combine study findings appropriate - Basic details about the included studies provided - Reasons for excluding studies not explicitly provided in flow chart, but provided in the appendices - Risk of bias assessed using the Cochrane Risk of Bias tool - List of excluded studies provided - Study authors acknowledged financial support - Study authors reported no conflicts of interest	- Did not justify why study authors included RCTs and quasi-RCTs and not other study designs

HTA = Health Technology Assessment; NIHR = National Institute for Health Research; PICO = Population, Intervention, Comparator, Outcome; RCT = randomized controlled trial.

Table 6: Strengths and limitations of clinical studies using SIGN II Checklist[12]

SIGN Checklist for Randomized Controlled Trials: Internal Validity[12]	Pharmacological and Non-pharmacological Smoking Cessation Interventions	Non-pharmacological Smoking Cessation Interventions							
	Camenga 2019[25]	**Hofmeyr 2020[22]**	**Scholten 2019[19]**	**Vogel 2019[18]**	**Harvanko 2018[23]**	**Ramo 2018[20]**	**Blitchtein-Winicki 2017[26]**	**Espada 2017[24]**	**Lee 2017[21]**
1. The study addresses an appropriate and clearly focused question.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. The assignment of subjects to treatment groups is randomized.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. An adequate concealment method is used.	Yes	Can't Say	Can't say	Can't say	Can't say	Can't say	Can't say	Can't say	Can't say
4. Subjects and investigators are kept 'blind' about treatment allocation.	No	No	No	No	No	No	No	No	No
5. The treatment and control groups are similar at the start of trial.	Can't say	Yes	Yes	Can't say	Yes	Yes	Can't say	Can't say	Yes
6. The only difference between groups is the treatment under investigation.	Can't say	Yes	Yes	Can't say	Yes	Yes	Can't say	Can't say	Yes
7. All relevant outcomes are measured in a standard, valid and reliable way.	Yes - biochemically verified abstinence	Yes - biochemically verified abstinence	No - self-reported abstinence	Yes - biochemically verified abstinence	Yes - breath CO levels and urinary cotinine	Yes - biochemically verified abstinence	No -self-reported abstinence	No -self-reported abstinence	Yes -breath CO levels

SIGN Checklist for Randomized Controlled Trials: Internal Validity[12]	Pharmacological and Non-pharmacological Smoking Cessation Interventions	Non-pharmacological Smoking Cessation Interventions							
	Camenga 2019[25]	**Hofmeyr 2020[22]**	**Scholten 2019[19]**	**Vogel 2019[18]**	**Harvanko 2018[23]**	**Ramo 2018[20]**	**Blitchtein-Winicki 2017[26]**	**Espada 2017[24]**	**Lee 2017[21]**
8. What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	Experimental: 5% Control: 10%	Experimental: 11.3% Control: 10%; NS difference between groups (P = 0.687)	Experimental: 0% Control: 19%	Can't say	Can't say	Experimental: 32% Control: 27%	Total: 1 of 15 (6.7%) dropped out	Total: 92 of 211 (43.6%) retention	Experimental: 10% Control: 13%
9. All the subjects are analyzed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Can't Say	Yes	Yes	Yes	Can't say	No	No	No	No
10. Where the study is carried out more than one site, results are comparable for all sites.	Can't Say; 1 private and 1 public school	N/A	Can't say	Can't say	Can't say	Can't say	Can't say	Can't say	Can't say

CO = carbon monoxide; NS = non-significant; wks= weeks.

Table 7: Strengths and limitations of guidelines using AGREE II[13]

Item	Guideline	
	Pharmacological and Non-pharmacological Smoking Cessation Interventions	
	NICE, 2018[28]	CTFPHC, 2017[27]
Domain 1: Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	✓	✓
2. The health question(s) covered by the guideline is (are) specifically described.	✓	✓
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	✓	✓
Domain 2: Stakeholder Involvement		
4. The guideline development group includes individuals from all relevant professional groups.	✓	✓
5. The views and preferences of the target population (patients, public, etc.) have been sought.	✓	partially
6. The target users of the guideline are clearly defined.	✓	✓
Domain 3: Rigour of Development		
7. Systematic methods were used to search for evidence.	✓	✓
8. The criteria for selecting the evidence are clearly described.	✓	✓
9. The strengths and limitations of the body of evidence are clearly described.	✓	✓
10. The methods for formulating the recommendations are clearly described.	✓	✓
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	✓	✓
12. There is an explicit link between the recommendations and the supporting evidence.	✓	✓
13. The guideline has been externally reviewed by experts prior to its publication.	✓	✓
14. A procedure for updating the guideline is provided.	✓	✓
Domain 4: Clarity of Presentation		
15. The recommendations are specific and unambiguous.	unclear	✓
16. The different options for management of the condition or health issue are clearly presented.	✓	x
17. Key recommendations are easily identifiable.	✓	✓
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	✓	unclear

Item	Guideline	
	Pharmacological and Non-pharmacological Smoking Cessation Interventions	
	NICE, 2018[28]	CTFPHC, 2017[27]
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	✓	✓
20. The potential resource implications of applying the recommendations have been considered.	✓	✓
21. The guideline presents monitoring and/or auditing criteria.	✓	unclear
Domain 6: Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	unclear	✓
23. Competing interests of guideline development group members have been recorded and addressed.	✓	✓

CTFPHC = Canadian Task Force on Preventive Health Care; NIHR = National Institute for Health Research.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 8: Summary of findings included systematic reviews and meta-analyses

Main Study Findings	Authors' Conclusion
Non-pharmacological Smoking Cessation Interventions	
Nethan, 2018[17]	
Brief advice, nicotine patch therapy and a 6-week text messaging (n = 20) versus brief advice, nicotine patch therapy and no text messaging (n = 20) **Smoking Cessation** • NS. RR (95% CI): 1.07 (0.87 to 1.31)	"Globally, there is limited information available on SLT cessation intervention trials, research on which must be encouraged, specially in the low-resource, high SLT burden countries; behavioural interventions are most suitable for such settings. Appropriate training/sensitization of health care professionals, and school-based SLT use prevention and cessation programmes need to be encouraged." (p. 396)
Fanshawe, 2017[16]	
Combination of pharmacological and non-pharmacological interventions or non-pharmacological interventions versus control (e.g., no intervention, different intervention or combination of interventions) *Smoking Cessation* • NS. Behavioural, computer-based intervention versus control (3 studies): 0.79 (0.5 to 1.24) • NS. Behavioural interventions using messaging versus control (3 studies): 1.18 (0.9 to 1.56) • Significant difference in favour of the intervention, Project EX versus control (4 studies): RR (95% CI): 1.48 (1.05, 2.1)	Not applicable (study authors did not make any conclusions specific to the comparisons of interest for the current report).

Main Study Findings	Authors' Conclusion
Taylor, 2017[15]	
Internet intervention versus control (e.g., no-intervention control, a different internet intervention, or a non-internet intervention) *Smoking Cessation* • NS. Intervention versus active control (e.g., face-to-face counselling) at 6 months+ follow-up (1 study looking at adolescents): RR (95% CI) = 0.44 (0.14 to 1.36) • Significant difference after sensitivity analysis (complete cases) in favour of control. Intervention versus non-active control (e.g., printed self-help guides) at 6 months+ follow-up (1 study looking at young adults): RR (95% CI) = 0.35 (0.12 to 1.02) • NS. Intervention versus active control at 6 months+ follow-up (1 study looking at young adults): RR (95% CI) = 1.42 (0.74 to 2.71) • NS. Intervention versus non-active control at 6 months+ follow-up (1 study looking at adolescents): RR (95% CI) = 0.93 (0.6 to 1.44) • Significant differences in favour of internet. Intervention versus non-active control at 6 months+ follow-up (1 study looking at young adults): RR (95% CI) = 1.95 (1.42 to 2.69) ○ Significant difference after sensitivity analysis (complete cases) in favour of internet. Intervention versus non-active control at 6 months+ follow-up (1 study looking at young adults): RR (95% CI) = 1.92 (1.4 to 2.63)	"Treatment effectiveness in younger people is unknown." (p.2)

CI = confidence interval; NS = non-significant; RR = relative risk; SLT = smokeless tobacco.

Table 9: Summary of findings of included primary clinical studies

Main Study Findings	Authors' Conclusion
Pharmacological and Non-pharmacological Smoking Cessation Interventions	
Camenga, 2019[25]	
Brief advice, nicotine patch therapy and a 6-week text messaging (n = 20) versus brief advice, nicotine patch therapy and no text messaging (n = 20) *7-day PPA* • NS differences at 6 weeks: Intervention (n = 3) versus comparator (n = 5, P = 0.6) • NS differences at 12 weeks: Intervention (n = 5) versus comparator (n = 6, P = 0.7) *Cigarettes smoked per day* • NS differences at 6 weeks: Intervention (mean [SD]: 2.5 [2.4]) versus comparator (2.0 [3.6], P = 0.09) • NS differences at 12 weeks: Intervention (2.7 [2.9]) versus comparator (2.6 [3.7], P = 0.3)	"Text messaging programs may need to be modified to better engage and motivate college-age smokers who participate in evidence-based smoking cessation treatments, such as brief advice and NRT. Future research is needed to continue to refine text messaging interventions to meet the needs of college-age smokers, and to determine how they may help augment existing evidence-based tobacco use disorder treatment practices." (p.7)

Main Study Findings	Authors' Conclusion
Change in cigarette per day from baseline • NS differences at 6 weeks: Intervention (mean [SD]: -4.8 [0.7]) versus comparator (-5.2[0.7], P = 0.7) • NS differences at 12 weeks: Intervention (-4.7 [0.8]) versus comparator (-4.6 [0.8], P = 0.9)	
Non-pharmacological Smoking Cessation Interventions	
Hofmeyr, 2020[22]	
Information and monitoring plus CM and could additionally earn $24 in abstinence-contingent incentives at each assessment (n = 40) versus Information and monitoring plus $8 at each assessment (n = 47) *7-day PPA (abstinence proportion)* • 3 month: significant difference between groups (45% for intervention versus 6% comparator, P < 0.001) • 6 month: NS difference between groups (10% for intervention versus 6% comparator) *Smoking intensity of non-abstinent subjects* • NS difference in smoking intensity between groups • Significant difference in smoking intensity for all non-abstinent participants during the intervention period and the follow-up period (P < 0.001 in all cases) • Significant increase in smoking intensity during the follow-up period versus intervention period (P < 0.001 in all comparisons), but smoking intensity in the follow-up sessions remains below the levels evidenced at baseline.	"In sum, we found that a relatively low-cost, low-intensity CM smoking cessation program, conducted on a sample of treatment-seeking university students in a developing country, had a marked effect on the likelihood of abstinence during the intervention period: by the final intervention session 45% of treatment subjects were abstinent compared to only 6% of control subjects. However, the effects of CM were not sustained, and abstinence rates reverted to baseline at the 3-month and 6-month follow-up sessions. In addition, CM did not reduce smoking intensity compared to the control group, but there was a statistically significant decline in smoking intensity for all non-abstinent subjects that was maintained into the follow-up period. This decline in the smoking intensity of all subjects may make their next quit attempt easier but future research should investigate how to tailor a CM intervention to the unique characteristics and environment of university students. If successful, universities may want to consider offering CM programs as part of their health-care services because promoting smoking abstinence will reduce tobacco-related morbidity and thereby decrease the burden on universities' health-care services." (p.117)
Scholten, 2019[19]	
***HintRun* (social mobile game) (n = 72) versus Psychoeducational brochure (n = 72)** *Weekly smoking behaviour* • NS differences between groups in number of cigarettes smoked per week from pre-test to post-test or from post-test to follow-up *Self-reported abstinence in the last 24 hours* • NS differences between groups in abstinence at post-test or at follow-up *Dose-response effects* • Higher dose of *HintRun game* (i.e., longer participants played the game) was associated with lower weekly smoking rates. • Higher dose of brochure (i.e., more time in reading the brochure) was associated with higher weekly smoking rates.	"In conclusion, the current study revealed equal improvements in weekly smoking behaviour and abstinence rates for the game and brochure groups. Yet, the game group showed a dose-response effect directly after the intervention, which faded over the three-month follow-up." (p. 1939)
Vogel, 2019[18]	
SGM-tailored (Put It Out Project [POP]) (n = 84) versus Non-tailored (Tobacco Status Project [TSP]) (n = 81)	"This pilot study provides preliminary support for the effectiveness of a Facebook smoking cessation intervention tailored to SGM young adults. Culturally tailored intervention

Main Study Findings	Authors' Conclusion
Biochemically verified abstinence • NS. 7.1% versus 3.7%; OR (95% CI) = 2.00 (0.48 to 8.28) *7-day Self-reported abstinence* • Significant differences in favour of the intervention: 23.8% versus 12.3%; OR (95% CI) = 2.50 (1.08 to 5.80) *50% or greater reduction in the number of cigarettes smoked per week* • Significant differences in favour of the intervention: 52.4% versus 39.5%; OR (95% CI) = 2.11 (1.09 to 4.08) *Stage of change for quitting smoking* • NS. 44.0% versus 33.3%; OR (95% CI) = 1.84 (0.95 to 3.57) *Quit attempt during treatment* • NS. 70.2% versus 63.0% ; OR (95% CI) = 2.14 (0.99 to 4.62)	content appeared to boost reported abstinence above that of comparable non-tailored interventions. A smoking cessation intervention delivered entirely on Facebook may be highly beneficial for SGM young adults who lack access to culturally-appropriate smoking cessation resources." (p. 7)
Harvanko, 2018[23]	
Web-based CM (n = 63) versus Control (n = 64) *CO levels* • Treatment adherence (i.e., percentage of CO samples submitted throughout the treatment): 37% versus 51%; P = 0.004 • Baseline: 11.0 ± 6.0 ppm versus 9.9 ± 5.0 ppm • Shaping phase (4 days): 7.8 ± 5.7 versus 8.9 ± 4.7 ppm • Abstinence phase (21 days): 7.8 ± 6.3 ppm versus 9.7 ± 5.1 ppm; P = 0.08 • Thinning phase (5 days): 6.3 ± 6.3 ppm versus 9.6 ± 5.5 ppm; P = 0.03 • Return-to-baseline phase (5 days): 6.8 ± 4.8 ppm versus 8.7 ± 5.1 ppm; P < 0.001 *Self-reported smoking behaviours* • Active treatment reported significantly less smoking during abstinence (P < 0.05) and return-to-baseline phase (P < 0.01), but not during 3-month or 6-month follow-up, compared to control group. *Urinary cotinine* • NS differences between groups in urine cotinine during treatment phases or follow-ups.	"This study replicates feasibility of a remote form of CM for adolescent smoking. CO results suggest active condition reduced smoking within group, but treatment adherence and posttreatment efficacy was poor. Future research should focus on increasing adherence for this type of program among adolescent smokers." (p. 1)
Ramo, 2018[20]	
Tobacco Status Project (TSP) Facebook smoking cessation (n = 251) versus Control (referral to a smoking cessation website) (n = 249) All statistical analyses performed at 12-month follow-up	"Compared with referral to a smoking cessation website, a novel US-focused Facebook smoking cessation intervention did not improve abstinence from smoking over 1 year, but increased abstinence at the end of treatment and was engaging to participants." (p. 2)

Main Study Findings	Authors' Conclusion
Biochemically verified 7-day abstinence • Month 3: 8.3% versus 3.2% • Month 6: 6.2% versus 6.0% • Month 12: 5.9% versus 10.0% • NS. OR (95% CI) = 1.07 (0.23 to 4.97); P = 0.925 *Self-reported 7-day PPA* • Month 3: 13.6% versus 7.5% • Month 6: 18.6% versus 14.5% • Month 12: 21.8% versus 20.8% • NS. OR (95% CI) = 1.29 (0.26 to 6.36); P = 0.746 *Reduction in smoking by 50% or more* • NS. OR (95% CI) = 1.43 (0.45 to 4.54); P = 0.533 *Quit attempt* • NS. OR (95% CI) = 0.94 (0.23 to 3.78); P = 0.929 *Ready to quit or quit* • NS. OR (95% CI) = 0.927 (0.089 to 9.68); P = 0.947 *Stage of change for quitting smoking over time* • NS, differences between groups (P = 0.968)	
Blitchtein-Winicki, 2017[26]	
SMS text message-based cognitive behavioural smoking cessation program (n = 9) versus SMS text message nutrition program (n = 6) *Self-reported smoke free* • 56% (5 out of 9) versus 17% (1 out of 6) *Self-reported relapse on day 2 after quit smoking* • 44% (4 out of 9) versus 33% (2 out of 6)	"This study provides initial evidence that a SMS test message smoking cessation program is feasible and acceptable for young adults residing in Lima." (p. 2)
Espada, 2017[24]	
Project EX (n = 58) versus Control (n = 34) *Future smoking expectation (change in score between baseline and at 1-year follow-up):* • 0.46 ± 0.11 versus -0.16 ± 0.12; P < 0.05 *Intention to quit:* • 0.93 ± 0.15 versus -0.49 ± 0.21; P < 0.001 *Motivation to quit:* • 0.26 ± 0.13 versus 0.09 ± 0.11; *P* < 0.01 *Nicotine dependence:* • 0.59 ± 0.21 versus 0.33 ± 0.14; *P* < 0.05 *Number of cigarettes smoked in the last 30 days:* • -63.94 ± 113.22 versus -29.43 ± 112.19; P < 0.001	"The intervention had a significant influence on future smoking expectation, intention, motivation to quit, and overall level of 30-day smoking. Long-term outcomes of the Project EX clinic-based program are promising for adolescent smokers in Spain" (p. 1067)
Lee, 2017[21]	
Auricular acupressure (n = 30) versus Sham control (n = 30) *Nicotine dependence (Difference of pre-post):* • 1.04 ± 2.01 versus 0.23 ± 1.48; P = 0.10	"Auricular acupressure was effective in smoking cessation by improving self-efficacy of smoking cessation and decreasing exhaled CO among male collage studies." (p. 385)

Main Study Findings	Authors' Conclusion
Self-efficacy of smoking cessation: • 5.71 ± 5.81 versus 3.00 ± 3.51; P = 0.048 *CO levels:* • 12.33 ± 5.28 versus 17.31 ± 6.73; P < 0.001	

CI = confidence interval; CM = contingency management; CO = carbon monoxide; NS = non-significant; OR = odds ratio; POP = Put It Out Project; PPA = point - prevalence abstinence; ppm = part per million; SD = standard deviation; SGM = Sexual and gender minority; SMS = short message service; TSP = Tobacco Status Project.

Table 10: Summary of recommendations in included guidelines

Recommendations	Strength of Evidence and Recommendations
NICE, 2018[28]	
Recommendation 1: "Consider NRT[a] for young people over 12 who are smoking and dependent on nicotine." [28] (p. 9) Recommendation 2: "If this [NRT] is prescribed, offer it with behavioural support. [2018]"[28] (p. 9) Supporting evidence that informed the recommendation: "Stanton & Grimshaw (2013 [++]) focused on strategies that help young people (<20 years) to stop smoking tobacco. The authors concluded that complex interventions including motivational enhancement are effective for smoking abstinence (12 trials, RR of 1.60 [95%CI 1.28 to 2.01]). They also found that the NoT programs for smoking cessation (a structured program based on social learning theory) in young people had a marginally significant effect (6 trials of low-quality evidence, RR of 1.31 [95%CI1.01 to 1.71])])."[31] (p. 9 to 10)	Strength of Recommendations: Weak (recommendation 1) to Strong (recommendation 2) Quality of Evidence: Moderate
CTFPHC, 2017[27]	
"We recommend asking children and youth (age 5 to 18 years) or their parents about tobacco use by the child or youth and offering brief[b] information and advice, as appropriate, during primary care visits[c] to treat tobacco smoking among children and youth. The recommendation for treatment interventions applies to children and youth 5 to 18 years of age who have smoked tobacco within the past 30 days and who do not have cognitive deficits, mental or physical health issues, or a history of alcohol or drug abuse." (p. E312)	Strength of Recommendations: Weak Quality of Evidence: Low

[a] "The UK marketing authorization for NRT products varies for use in children and young people under 18."[28] (p. 15) Thus, this guideline suggests practitioners refer "to the summary of product characteristics for prescribing information on individual NRT preparations. "[28] (p. 15)

[b] "Contact time with primary care clinician of up to five minutes. Advice may include verbal communication about patient attitudes and beliefs, risks of smoking and strategies for dealing with the influence of peers. Sharing of printed or electronic material (e.g., brochures, newsletters and interactive computer programs) could also be considered." (p. E312)

[c] "Appropriate primary care visits include scheduled health supervision visits, visits for vaccinations, medication renewal, episodic care or acute illness, and other visits where the primary care practitioner deems it appropriate. Primary care visits are completed in primary health care settings, including those outside of a physician's office (e.g., public health nurses carrying out a well-child visit in a community setting)." (p. E312)

CTFPHC = Canadian Task Force on Preventive Health Care; CI = confidence interval; NICE = National Institute for Health and Care Excellence; NoT = Not on Tobacco; NRT = nicotine replacement therapy; RR = relative risk.

Appendix 5: Overlap between Included Systematic Reviews

Table 11: Primary study overlap between included systematic reviews

Primary Study Citation	Systematic Review Citation	
	Fanshawe, 2017[16]	Taylor, 2017[15]
An 2013		X
Abroms 2008	X	
Bailey 2013	X	
Berg 2014		X
Brown 2003	X	
Colby 2005	X	
Colby 2012	X	
Dalum 2012	X	
Gungormus 2012	X	
Guo 2014	X	
Harris 2010	X	
Haug 2013	X	
Joffe 2009	X	
Mason 2016	X	
NoT MD 2009	X	
O'Niell 2000	X	
Patten 2006	X	X
Pbert 2011	X	
Perez-Milena 2012	X	
Peterson 2009	X	
Prochaska 2015	X	
Project EX-1 2001	X	
Project EX-4 2007	X	
Project EX Spain 2015a	X	
Project EX Spain 2015b	X	
Scherphof 2014	X	
Skov-Ettrup 2014	X	
Simmons 2011		X
Woodruff 2007	X	X

Appendix 6: Additional References of Potential Interest

Studies with mean age <15 years

1. Blank MD, Ferris KA, Metzger A, Gentzler A, Duncan C, Jarrett T, Dino G. Physical activity and quit motivation moderators of adolescent smoking reduction. *Am J Health Behav*. 2017;41(4):419-27.

2. Gonzálvez MT, Morales A, Orgiles M, Sussman S, Espada JP. Role of smoking intention in tobacco use reduction: a mediation analysis of an effective classroom-based prevention/cessation intervention for adolescents. *Addict Behav.* 2018;84:186-92.

Studies investigating pharmacological interventions alone

3. Gray KM, Baker NL, McClure EA, Tomko RL, Squeglia LM, Saladin ME, Carpenter MJ. Efficacy and safety of varenicline for adolescent smoking cessation: a randomized clinical trial. *JAMA Pediatr*. 2019;173(12):1146-53.

4. Myung SK, Park JY. Efficacy of pharmacotherapy for smoking cessation in adolescent smokers: a meta-analysis of randomized controlled trials. *Nicotine Tob Res*. 2019;21(11):1473-9.

Guidelines with Unclear Methodology

5. ENSP guidelines for treating tobacco dependence. Brussels (BE): European Network for Smoking and Tobacco Prevention; 2017.

Mixed or Unclear Population

6. Alghamdi F, Alhussien A, Alohali M, Alatawi A, Almusned T, Fecteau S, Habib SS, Bashir S. Effect of transcranial direct current stimulation on the number of smoked cigarettes in tobacco smokers. *PloS One.* 2019;14(2).

7. Baskerville NB, Struik LL, Guindon GE, Norman CD, Whittaker R, Burns C, Hammond D, Dash D, Brown KS. Effect of a Mobile phone intervention on quitting smoking in a young adult population of smokers: randomized controlled trial. JMIR mHealth and uHealth. 2018;6(10):e10893.

8. Baskerville NB, Struik LL, Dash D. Crush the crave: development and formative evaluation of a smartphone app for smoking cessation. *JMIR MHealth UHealth*. 2018;6(3):e52.

Related CADTH Reports

9. Pharmacist-led interventions for tobacco smoking cessation: a review of clinical effectiveness and cost-effectiveness. (*CADTH rapid response report: summary with critical appraisal).* Ottawa (ON): CADTH; 2019: https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1174%20Pharm-led%20smoking%20Cessation%20Final.pdf. Accessed 2020 Feb 24.

10. Internet-based brief interventions for substance misuse in youth and young adults: a review of clinical effectiveness, cost-effectiveness and guidelines. (*CADTH rapid response report: summary with critical appraisal)* Ottawa (ON): CADTH; 2018: https://www.cadth.ca/internet-based-brief-interventions-substance-misuse-youth-and-young-adults-review-clinical. Accessed 2020 Feb 24.

11. Pharmacological Agents for Smoking Cessation: Clinical Effectiveness and Cost-Effectiveness. (*CADTH rapid response report: reference list*). Ottawa (ON): CADTH; 2017: https://www.cadth.ca/pharmacological-agents-smoking-cessation-clinical-effectiveness-and-cost-effectiveness-0. Accessed 2020 Feb 24.

12. Integrated Cessation Programs for Adults Who Smoke Cannabis and Tobacco: Clinical Effectiveness and Guidelines. (*CADTH rapid response report: reference list*). Ottawa (ON): CADTH; 2017: https://www.cadth.ca/integrated-cessation-programs-adults-who-smoke-cannabis-and-tobacco-clinical-effectiveness-and. Accessed 2020 Feb 24.

13. Electronic Cigarettes for the Reduction or Cessation of Smoking: Clinical Utility, Safety, and Guidelines (*CADTH rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2017: https://www.cadth.ca/electronic-cigarettes-reduction-or-cessation-smoking-clinical-utility-safety-and-guidelines-0. Accessed 2020 Feb 24.

14. Smoking Cessation Interventions for Patients with Severe Mental Illnesses: A Review of Clinical Effectiveness and Guidelines. (*CADTH rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2017: https://www.cadth.ca/smoking-cessation-interventions-patients-severe-mental-illnesses-review-clinical-effectiveness-and. Accessed 2020 Feb 24.