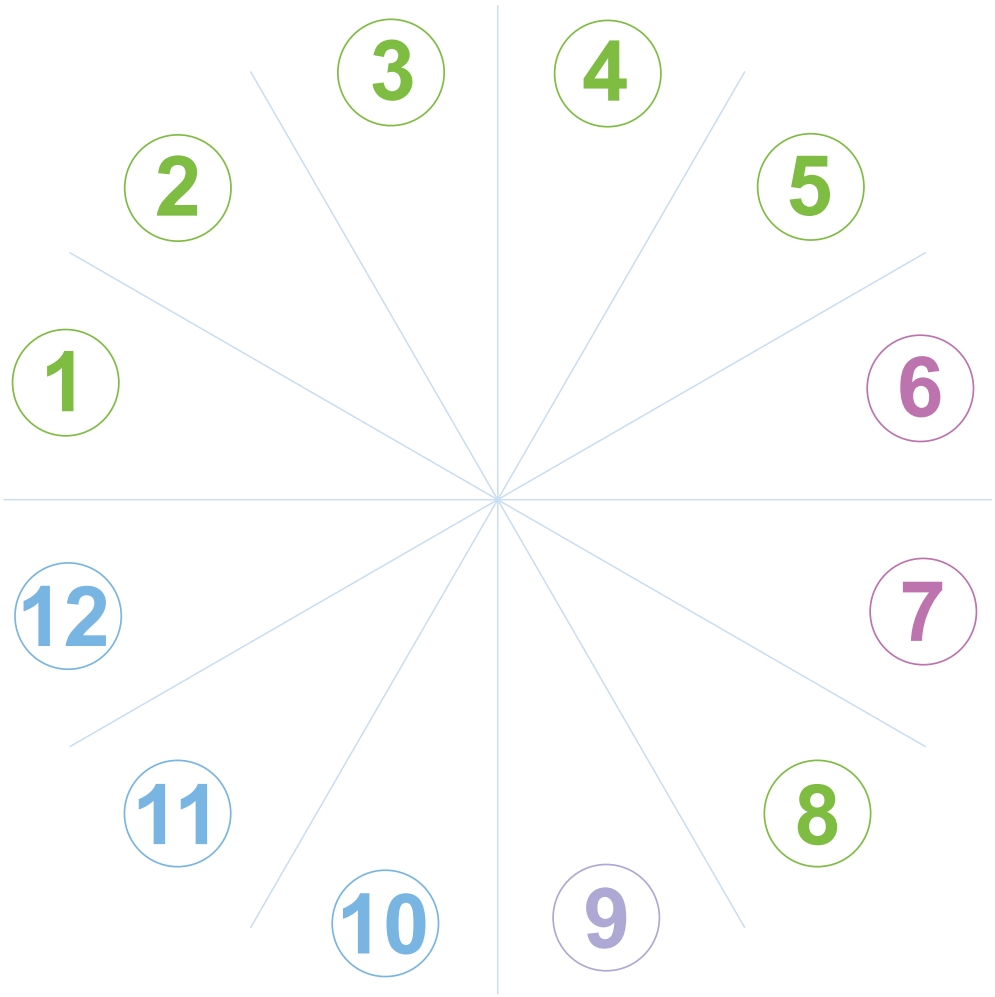
WHO clinical treatment guideline for tobacco cessation in adults



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2
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6
12
7
11
8
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Table of Contents

Acknowledgements iii

Abbreviations and acronyms v

Glossary of terms vii

Executive summary xi

Background xi

Rationale and objectives xi

Guideline development process and methods xi

Target audience xi

Summary of recommendations xii

Behavioural support delivered in both clinical and community settings xiii

Digital tobacco cessation interventions xiii

Pharmacological interventions delivered in both clinical and community settings xiii

Interventions for smokeless tobacco use cessation xiv

Combination of behavioural and pharmacological treatments xiv

Traditional, complementary and alternative therapies xiv

System-level interventions and policies xiv

1. Introduction 1

1.1. Existing WHO guidelines 1

1.2. Rationale and objectives 2

1.3. Target audience 3

2. Methods 5

2.1. Scope of the guideline and questions of interest 5

2.2. Evidence reviews 6

2.3. Assessment of evidence and its grading 8

2.4. Going from evidence to recommendations 8

3. Recommendations 11

3.1. Behavioural support delivered in both clinical and community settings 11

3.1.1. Recommendations 11

3.1.2. Overall questions 11

3.1.3. Justification and evidence 11

3.1.4. Implementation considerations 13

3.2. Digital tobacco cessation interventions 14

3.2.1. Recommendation 14

3.2.2. Overall questions 14

3.2.3. Justification and evidence 14

3.2.4. Implementation considerations 16

3.3. Pharmacological interventions delivered in both clinical and community settings 17

3.3.1. Recommendations 17

3.3.2. Overall questions 17

3.3.3. Justification and evidence 17

3.3.4. Implementation consideration 21

3.4. Interventions for smokeless tobacco use cessation 22
3.4.1. Recommendations 22
3.4.2. Overall questions 22
3.4.3. Justification and evidence 22
3.4.4. Implementation considerations 23
3.5. Combination of behavioural and pharmacological treatments 23
3.5.1. Recommendation 23
3.5.2. Overall questions 23
3.5.3. Justification and evidence 23
3.5.4. Implementation considerations 24
3.6. Traditional, complementary and alternative therapies 25
3.6.1. Statement 25
3.6.2. Overall questions 25
3.6.3. Justification and evidence 25
3.6.4. Implementation considerations 25
3.7. System-level interventions and policies 26
3.7.1. Recommendations 26
3.7.2. Overall questions 26
3.7.3. Justification and evidence 26
3.7.4. Implementation considerations 28
3.8. Overarching guideline implementation considerations 29
4. Evidence to recommendations 31
4.1. Assessment of the certainty of evidence 31
4.2. Benefits and harms 31
4.3. Values and preferences 32
4.4. Cost-effectiveness and resource requirements 32
4.5. Equity, acceptability and feasibility 33
5. Research needs 34
6. Adoption, dissemination, implementation and evaluation 36
References 37
Annexes
Annex 1: Management of guideline development process 42
Contributors to guideline development 42
Declarations of interest 46
Annex 2: Additional information for implementing the recommendations 47
Brief advice 47
Intensive behavioural support 47
Digital tobacco cessation interventions 48
Pharmacological interventions 48
Traditional, complementary and alternative therapies 50
Financial interventions 51
References 51
Annex 3: Summary of declarations of interest and how these were managed 52

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Abbreviations and acronyms

AE	adverse event
AI	artificial intelligence
App	application
CI	confidence interval
EHR	electronic health record
ERG	External Review Group
EtD	Evidence to Decision
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
LMICs	low- and middle-income countries
MPOWER	
	M: Monitor tobacco use and prevention policies
	P: Protect people from tobacco smoke
	O: Offer help to quit tobacco use
	W: Warn about the dangers of tobacco
	E: Enforce bans on tobacco advertising, promotion and sponsorship
	R: Raise taxes on tobacco
NCD	noncommunicable disease
NNH	number needed to harm
NNT	number needed to treat
NRT	Nicotine Replacement Therapy
OR	odds ratio
PICO	Population, Intervention, Comparator and Outcomes
RCT	randomized controlled trial
RR	risk ratio/relative risk
SAE	serious adverse event
SG	Steering Group
SHS	second-hand smoke
WHO	World Health Organization
WHO FCTC	World Health Organization Framework Convention on Tobacco Control

Glossary of terms

Term	Definition
Artificial intelligence (AI)-based tobacco cessation software interventions	Conversational AI, typically referred to as a chatbot or online dialogue system, used to provide tobacco cessation support. It enables two-way communication with users via text and/or audio without human input by employing natural language processing and machine learning algorithms.
Behavioural support	Support, other than medications, aimed at helping people stop their tobacco use. It can include all cessation assistance that imparts knowledge about tobacco use and quitting, provides support, and teaches skills and strategies for changing behaviour. It includes brief advice and intensive behavioural support.
Brief advice	Advice to stop using tobacco – usually taking only a few minutes – given to all tobacco users, usually during a routine consultation or interaction.
Bupropion	Bupropion sustained release (bupropion SR) is an antidepressant agent with a demonstrated efficacy for use in tobacco cessation. It is a non-nicotine-based treatment and helps to alleviate withdrawal and craving in tobacco cessation. It has both dopaminergic and adrenergic actions, and appears to be an antagonist at the nicotinic acetylcholine receptor. It has been licensed as a prescription aid to tobacco cessation in many countries.
Combination pharmacotherapy for tobacco cessation	Any combination between the three main categories of medication recommended for tobacco cessation: combinations of Nicotine Replacement Therapies (NRTs), of an NRT and varenicline/bupropion, or of bupropion and varenicline.
Cytisine	An alkaloid that occurs naturally in several plant genera. It has been used medically to help with tobacco cessation. Its molecular structure has some similarity to that of nicotine and varenicline, and it has similar pharmacological effects. Cytisine is a partial agonist of nicotinic acetylcholine receptors. It decreases the urge to use tobacco and reduces the severity of nicotine withdrawal symptoms, while also reducing the reward experience of using tobacco.
Digital tobacco cessation interventions	Tobacco cessation interventions delivered through digital technologies and can involve the following modalities: mobile text messaging, internet-based interventions, smartphone applications (apps) and AI-based software interventions.
First-line medications	Medications that are strongly recommended, have high certainty of evidence, are legally available in most countries, and have been reviewed and approved by multiple country-level regulatory bodies.
Health systems interventions	Specific strategies that policy-makers and health-care service managers can implement to promote tobacco cessation. They involve systematic identification of tobacco users and subsequent offering of evidence-based tobacco cessation interventions or treatments, providing education, resources and feedback to promote provider interventions, and covering the cost of effective tobacco cessation services and their delivery.
Intensive behavioural support	Multiple sessions of individual, group or telephone counselling aimed at helping people stop their tobacco use. It includes all cessation assistance that imparts knowledge about tobacco use and quitting, and provides support and resources to develop skills and strategies for changing behaviour.
Intensive individual behavioural counselling	Personalized, face-to-face interactions between a trained health-care provider and a tobacco user. It encompasses various evidence-based techniques and strategies to assist the individual in quitting tobacco, including motivational interviewing, cognitive behavioural therapy and relapse prevention.
Intensive group behavioural counselling	A group therapy approach that brings together individuals who want to quit tobacco use. Facilitated by a trained health-care provider or counsellor, these sessions offer participants a supportive environment to learn from each other, develop coping skills and receive evidence-based guidance on quitting tobacco.

Term	Definition
Intensive telephone counselling	Typically refers to the telephone counselling service provided by a national toll-free quit line. It is a form of remote support that connects individuals with trained counsellors via telephone. These counsellors assist participants in quitting tobacco by providing information, enhancing motivation, and using evidence-based techniques and personalized strategies for cessation through scheduled phone sessions and follow-up calls. Telephone counselling is especially useful for those who may face barriers to accessing in-person counselling services.
Internet-based tobacco cessation interventions	Interventions offered through a diverse set of tools and resources including web-, email- and mobile phone-delivered components, online social networks (such as Facebook, X, and WeChat), online forums and support groups.
Mobile text-messaging tobacco cessation programme	A programme involves the delivery of text messages from a preconstructed bank of content within a framework that determines what content and when content is delivered to help people stop tobacco use.
Nicotine replacement therapy (NRT)	A medical product that supplies a controlled amount of nicotine to the body for a limited period, to help quit tobacco use completely. NRT is used to replace the nicotine the body receives through smoking cigarettes or using other tobacco products, and they deliver nicotine without the harmful chemicals present in tobacco smoke or smokeless tobacco. NRT helps to reduce the craving for tobacco and lessens the severity of nicotine withdrawals, thus making it easier for users to quit tobacco use. NRT products include nicotine gum, patches, lozenges, inhalers, and nasal or mouth sprays.
Promotion of tobacco cessation	Population-wide measures and approaches that contribute to stopping tobacco use, including tobacco dependence treatment.
Smartphone applications (apps) for tobacco cessation (tobacco cessation apps)	Discrete pieces of software that can be used on a smartphone to perform specific sets of tasks to support individuals in their efforts to quit tobacco. These apps typically provide a range of features, such as assessing tobacco use, personalized quit plans, tracking of tobacco use triggers, coping strategies and social support.
Smokeless tobacco user	A person who uses any smokeless tobacco products.
Tobacco addiction/ dependence	A cluster of behavioural, cognitive and physiological phenomena that develop after repeated tobacco use and that typically include: a strong desire to use tobacco, difficulties in controlling its use, persisting in its use despite the harmful consequences, giving higher priority to tobacco use than to other activities and obligations, increased tolerance, and sometimes experiencing a physical withdrawal state.
Tobacco cessation	The process of stopping the use of any tobacco product, with or without assistance. May also be referred to as abstinence or quitting. There are multiple technical definitions that vary from study to study. The strictest definition is “no use of combustible or smokeless tobacco products or any other nicotine and tobacco products for at least 6 months”. Abstinence/quitting can be measured by “point prevalence abstinence” meaning the person has complete abstinence during a designated time period (for example, 7 or 30 days) prior to assessment, or prolonged abstinence (complete abstinence after an initial grace period), or continuous abstinence (complete abstinence beginning on the target quit day and lasting until the assessment).
Tobacco dependence treatment	The provision of behavioural support or medications, or both, to tobacco users to help them stop their tobacco use.
Tobacco products	Products entirely or partly made of the leaf tobacco as raw material that are manufactured to be used for smoking, sucking, chewing or snuffing.
Tobacco user	A person who uses any tobacco products.

Term	Definition
Traditional, complementary or alternative therapy for tobacco cessation	Therapies such as acupuncture; laser therapy or electrical stimulation; hypnotherapy; yoga; herbs; traditional Indian medicine; traditional herbal medicine; traditional Chinese medicine exercise, such as Tai Chi, Qigong, Baduanjin or Wuqinxi; mindfulness meditation; homeopathy; and chiropractic therapy to aid in smoking cessation.
Varenicline	A medication used for tobacco cessation. It is a partial agonist of nicotinic acetylcholine receptors. When activated, these receptors release dopamine in the nucleus accumbens, the brain's reward centre, thereby reducing cravings and other withdrawal symptoms. It also reduces the reward experience from using tobacco by preventing the binding of nicotine to these receptors.

Executive summary

Background

Tobacco kills more than 8 million people per year and imposes a significant economic burden throughout the world. Globally, there are still 1.25 billion people who use tobacco. Intensive and sustained efforts are needed to end this global epidemic. As tobacco control policy efforts increase, the scaling up of comprehensive tobacco cessation services to support current tobacco users to quit is imperative.

Rationale and objectives

The need to help tobacco users quit as a key component of a comprehensive tobacco control approach has been reflected in the actions recommended by the *Guidelines for implementation of Article 14* of the World Health Organization Framework Convention on Tobacco Control (WHO FCTC). Over 60% of the world's 1.25 billion adult tobacco users want to quit, but around 70% of them have no access to comprehensive tobacco cessation services due to the challenges that face health systems, such as limited human and financial resources, and limited capacities of tobacco cessation services at the country level. National clinical treatment guidelines for tobacco dependence are recommended by the WHO FCTC Article 14 guidelines as basic infrastructure for promoting tobacco cessation and providing effective tobacco dependence treatment. However, national clinical treatment guidelines for tobacco dependence do not exist in nearly 60% of World Health Organization (WHO) Member States. Therefore, there is an urgent need to develop a standard evidence-based WHO clinical treatment guideline to guide WHO Member States on tobacco cessation and tobacco dependence treatment in adults.

The objective of this guideline is to provide technical guidance on tobacco cessation in adults that can be used by WHO Member States, and to support the use of evidence-based behavioural interventions and pharmacological treatments for tobacco cessation as part of a comprehensive tobacco control approach.

Guideline development process and methods

This guideline was developed following WHO guideline development processes and methods outlined in the *WHO handbook for guideline development (2nd edition)*. The WHO Department of Health Promotion oversaw the guideline development process with a dedicated WHO Steering Group and a guideline methodologist. A Guideline Development Group (GDG) was established – comprising 13 external experts with a range of expertise and perspectives – to determine the key guideline questions, review the evidence and formulate recommendations.

Evidence to inform the guideline recommendations was derived from 20 existing or newly commissioned systematic reviews. The GDG reviewed the evidence and made recommendations. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to determine the certainty of evidence and formulate the recommendations. The External Review Group reviewed the draft guideline.

Target audience

The primary audience for the guideline is health-care providers working in clinical and community settings, where tobacco users may present and be managed. The recommendations on system-level interventions and policies contained in this guideline are intended to inform policy-makers and health service managers on how to provide more-effective tobacco cessation approaches and services.

Summary of recommendations

This guideline provides recommendations on the use of behavioural support, delivered in both clinical and community settings, including: digital tobacco cessation interventions, pharmacological interventions, and system-level interventions and policies to enhance the adoption and implementation of tobacco cessation interventions. No recommendation is made on the use of traditional, complementary and alternative therapies for tobacco cessation due to insufficient evidence. The WHO recommendations on tobacco cessation in adults are outlined below.



Behavioural support delivered in both clinical and community settings

1. WHO recommends brief advice (between 30 seconds and 3 minutes per encounter) be consistently provided by health-care providers as a routine practice to all tobacco users accessing any health-care settings.

   Strong recommendation;
   moderate certainty



2. WHO recommends more-intensive behavioural support be offered to all tobacco users interested in quitting. Options for behavioural support are individual face-to-face counselling, group face-to-face counselling or telephone counselling; multiple behavioural support options should be provided.

   Strong recommendation;
   high certainty (individual counselling)/
   moderate certainty (group counselling and telephone counselling)



Digital tobacco cessation interventions

3. Digital tobacco cessation modalities[1] (text messaging, smartphone applications, artificial intelligence-based interventions or internet-based interventions), individually or combined, can be made available for tobacco users interested in quitting, as an adjunct to other tobacco cessation support or as a self-management tool.

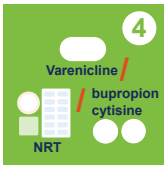
   Conditional recommendation;
   moderate certainty (text messaging)/
   low certainty (smartphone applications/artificial intelligence-based interventions)/
   very low certainty (internet-based interventions)



Pharmacological interventions delivered in both clinical and community settings

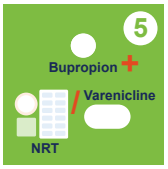
4. WHO recommends varenicline, Nicotine Replacement Therapy (NRT), bupropion and cytisine[2] as pharmacological treatment options for tobacco users who smoke and are interested in quitting. Varenicline, NRT or bupropion are recommended as first-line options; combination NRT (a patch plus a short-acting form, such as gum or a lozenge) is an option for tobacco users interested in quitting who will use NRT.

   Strong recommendation;
   high certainty (varenicline, NRT and bupropion)/
   moderate certainty (combination NRT, cytisine)



5. Bupropion in combination with NRT or varenicline may be offered to tobacco users interested in quitting when there is inadequate response to first-line treatments.

   Conditional recommendation;
   moderate certainty (bupropion plus varenicline)/
   low certainty (bupropion plus NRT)



1 WHO observes a rapid innovation cycle in digital technologies that necessitate reviews as new evidence emerges.
2 Although cytisine is as effective as other so-called first-line medications, it is listed separately because evidence certainty is moderate, it is currently only legally available in some countries, has more variability in dosing regimen, and less review and approval by country-level drug regulatory bodies. However, all medications carry strong recommendations and any of these medications can be used.

Interventions for smokeless tobacco use cessation

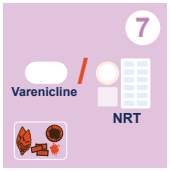
6. WHO recommends providing intensive behavioural support interventions (individual face-to-face counselling, face-to-face group counselling or telephone counselling) for smokeless tobacco users interested in quitting.

Strong recommendation;
moderate certainty



7. WHO recommends varenicline or NRT as pharmacological options for smokeless tobacco users interested in quitting.

Strong recommendation;
moderate certainty (varenicline)/
low certainty (NRT)



Combination of behavioural and pharmacological treatments

8. WHO recommends combining pharmacotherapy and behavioural interventions to support tobacco users interested in quitting.

Strong recommendation;
high certainty



Traditional, complementary and alternative therapies

9. Evidence is insufficient to make a recommendation for or against traditional, complementary and alternative therapies for tobacco users interested in quitting. If these therapies are utilized by tobacco users interested in quitting, ensure that they are offered a comprehensive approach to support tobacco cessation, including behavioural support and/or pharmacotherapy.



System-level interventions and policies

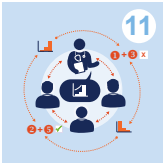
10. WHO recommends that all health-care facilities include tobacco use status and use of tobacco cessation interventions in their medical records (including electronic health records), to facilitate provider interaction with tobacco-using patients and increase adoption and maintenance of evidence-based treatment interventions.

Strong recommendation;
moderate certainty



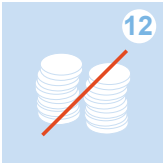
11. WHO recommends training of all health-care providers on delivery of evidence-based cessation interventions, with ongoing prompting and feedback, in their routine medical practices at all levels of health-care settings.

Strong recommendation;
moderate certainty



12. WHO recommends that evidence-based tobacco cessation interventions be provided at no or reduced cost to all tobacco users interested in quitting. No cost is strongly preferred over reduced cost.

Strong recommendation;
moderate certainty



1. Introduction

The tobacco epidemic is one of the biggest public health threats the world has ever faced. Globally, 1.25 billion people use tobacco, and 80% of them live in low- and middle-income countries (LMICs), where the burden of tobacco-related illness and death is heaviest *(1)*. Tobacco use kills more than 8 million people per year *(2)*. Furthermore, tobacco use imposes a heavy economic burden throughout the world. It is estimated that the total global economic cost of tobacco smoking was $US 1436 billion in 2012, equivalent to 1.8% of the world's annual gross domestic product, with about 40% of the total economic cost borne by LMICs *(3)*.

The World Health Organization Framework Convention on Tobacco Control (WHO FCTC) provides a comprehensive set of recommendations and obligations for countries to markedly decrease, and ultimately eradicate, the harms caused by tobacco, including the elimination of predatory marketing practices by the tobacco industry. Many of these recommendations focus on country-level and institutional policies and programmes, such as the elimination of second-hand smoke (SHS) exposure; curtailment of tobacco advertising, promotion and sponsorship; increases in pricing, such as through taxation; anti-tobacco mass media campaigns; and product regulation. These policies and programmatic interventions have been shown to decrease initiation and the prevalence of tobacco use. However, the Parties to the WHO FCTC also have obligations to support tobacco users to quit under Article 14 of the WHO FCTC, which contains measures concerning tobacco dependence and cessation *(4)*.

The WHO FCTC Article 14 guidelines emphasize that it is important to implement tobacco dependence treatment measures synergistically with other tobacco control measures. Implementing cessation and treatment measures in conjunction with population-level interventions covered by other articles of the WHO FCTC will have a synergistic effect, and thus maximize their impact *(5)*.

Over 60% of the world's 1.25 billion adult tobacco users want to quit *(6)*. However, around 70% of them have no access to comprehensive tobacco cessation services due to the challenges that face health systems, such as limited human and financial resources – including limited capacity to deliver tobacco cessation services – as well as tobacco user- and policy-related obstacles to the promotion of tobacco cessation services in LMICs *(7,8)*. Providing access to adequate cessation support and tobacco dependence treatment benefits all tobacco users, and is particularly important for those who are dependent on tobacco. Tobacco or nicotine dependence is considered a chronic condition or disease *(9)*, which often requires repeated intervention and multiple attempts to quit, so the need for ongoing support is critical *(10–12)*. However, national clinical treatment guidelines for providing tobacco cessation support and tobacco dependence treatment do not exist in around 60% of World Health Organization (WHO) Member States *(13)*.

1.1. Existing WHO guidelines

The need to provide interventions and supportive systems to help tobacco users quit as a key component of a comprehensive tobacco control approach to reduce the prevalence of tobacco use has been reflected in the actions recommended by the *Guidelines for implementation of Article 14* of the WHO FCTC *(5)*. The WHO FCTC Article 14 guidelines contain recommendations for promoting tobacco cessation and tobacco dependence treatment, as well as developing a comprehensive tobacco cessation and treatment system *(5)*.

The importance of tobacco cessation as part of the management of mental and physical health conditions has been addressed in other WHO guidelines. The *WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy (14)* provide evidence-based recommendations to health-care providers on the identification, management, and prevention of tobacco use and SHS exposure in pregnant women (and, where relevant, advice for other members of their households on how to reduce the SHS exposure of pregnant women). The *guidelines for the management of physical health conditions in adults with severe mental disorders (15)* recommend that a directive and supportive behavioural intervention programme, varenicline, bupropion, Nicotine Replacement Therapy (NRT), and combined pharmacological and nonpharmacological interventions may be considered for tobacco cessation in people with severe mental

disorders. The *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (16)* provides a protocol for counselling on cessation of tobacco use (the 5As) as an essential noncommunicable disease (NCD) intervention in primary care.

The recommendations in this clinical treatment guideline are closely aligned with the WHO FCTC Article 14 guidelines and other existing WHO guidelines. Together, they provide a comprehensive set of global guidance on how to effectively support 1.25 billion adult tobacco users to quit.

1.2. Rationale and objectives

National clinical treatment guidelines are recommended by the WHO FCTC Article 14 guidelines as basic infrastructure needed to promote tobacco cessation and provide effective tobacco dependence treatment. The 2019 WHO report on the global tobacco epidemic survey *(13)* revealed that only 82 countries (42% globally) had national tobacco cessation guidelines, and that most of those 82 national guidelines were developed more than 5 years before 2019 and required updating. Furthermore, three types of tobacco cessation medicine (NRT, bupropion and varenicline) have been included in the *WHO Model Lists of Essential Medicines (17)*. WHO Member States have requested that WHO provide technical guidance on rational and appropriate use of these three essential medicines. Therefore, there is an urgent need to develop a standard evidence-based WHO clinical treatment guideline to advise WHO Member States on tobacco cessation and tobacco dependence treatment.

Scaling up tobacco cessation services is a core WHO FCTC demand-reduction measure and a key component of the MPOWER policy package *(18)* that is crucial for the achievement of Sustainable Development Goal target 3.a: "Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate". This guideline will also contribute to the achievement of WHO's Global Programme of Work Triple Billion targets *(19)* through improvement of the quality, efficiency and coverage of effective tobacco cessation services in all countries. It is important to emphasize the importance of continuing to maintain and strengthen the implementation of the other MPOWER measures as countries scale up their tobacco cessation services.

The objective of this guideline is to provide technical guidance on tobacco cessation in adults, which can be used in WHO Member States to support the use of evidence-based behavioural interventions and pharmacological treatments for tobacco cessation as part of a comprehensive tobacco control approach.

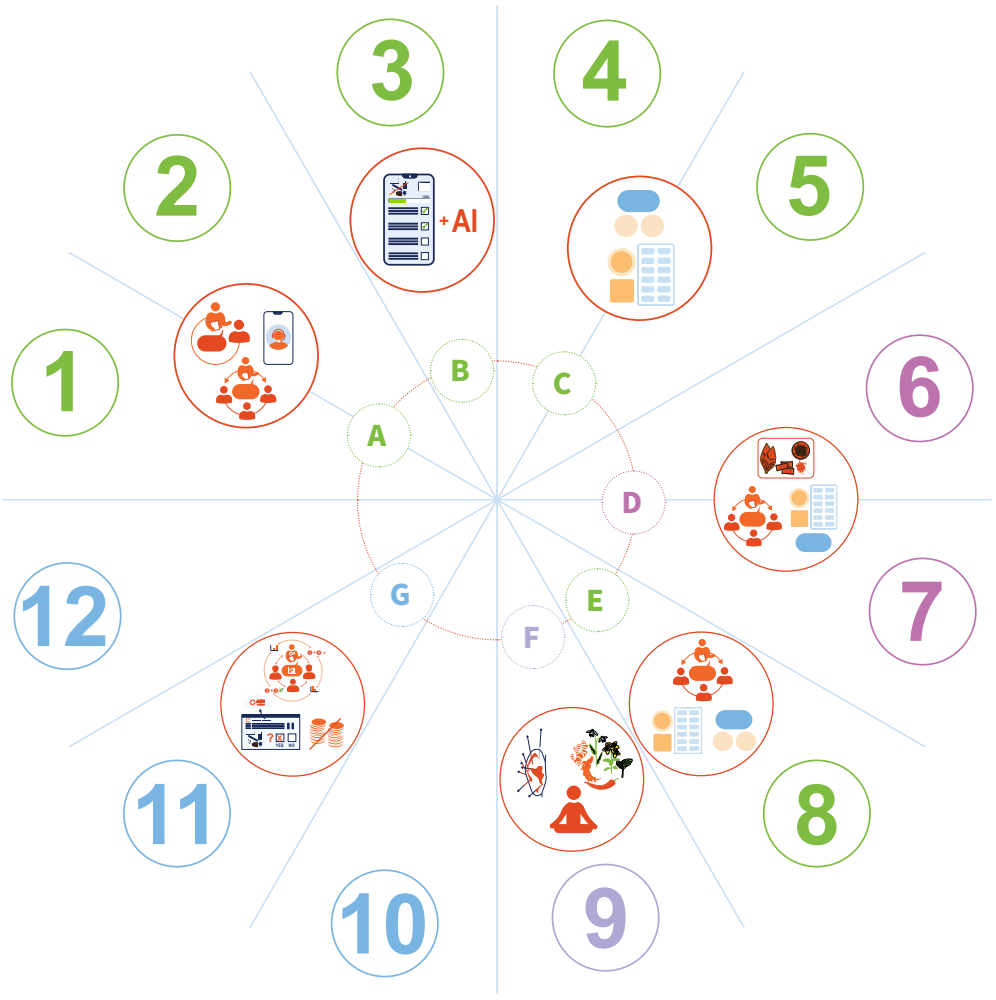
This guideline provides recommendations for supporting adults (individuals aged 18 years and older) to quit the use of any types of tobacco products, including: cigarettes, waterpipe (hookah, shisha) tobacco, various smokeless tobacco products, cigars, cigarillos, roll-your-own tobacco, pipe tobacco, bidis, kreteks and heated tobacco products. E-cigarettes are beyond the scope of this guideline because the potential benefits and harms of using these products are complex, and are addressed in a separate body of literature. These products may be addressed in the future as evidence accumulates.

This guideline includes recommendations on behavioural support, including digital tobacco cessation interventions; pharmacological interventions; and system-level interventions and policies that enhance the adoption and implementation of tobacco cessation interventions. No recommendation is made regarding traditional, complementary and alternative therapies for tobacco cessation due to insufficient evidence. This guideline does not provide recommendations on population-level policies and initiatives that may promote tobacco cessation, such as raising tobacco tax, implementing smoke-free environments, anti-tobacco mass media campaigns or the enforcement of pictorial health warnings *(20–24)*. However, the critical importance of these policies and initiatives, and their roles in complementing individual-level and clinical support for people attempting to quit tobacco, are recognized in this guideline and are discussed as key implementation considerations.

1.3. Target audience

The guideline is primarily designed for use by health-care providers working in clinical (primary, secondary and tertiary care settings) and community settings where tobacco users may present and be managed. The term health-care provider includes – but is not limited to – doctors, nurses, pharmacists, dentists, physical therapists, counsellors, community health workers and other health-care providers. The recommendations on system-level interventions and policies contained in this guideline are intended to inform policy-makers and health service managers about how they can provide more-effective tobacco cessation approaches and services. The expectation is that recommended interventions and policies will be adapted to local circumstances.




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2. Methods

This guideline was developed following WHO processes and methods outlined in the *WHO handbook for guideline development (2nd edition) (25)*, and with the oversight of the WHO Guidelines Review Committee. A WHO Steering Group (SG), led by the Department of Health Promotion, was established, with representation from WHO regional offices and relevant WHO departments. A Guideline Development Group (GDG) was also formed that consisted of 13 experts, reflecting gender and geographical balance, as well as community, clinical, methodological, public health and patient perspectives. The majority of GDG members were from LMICs. In accordance with WHO processes, there was an external GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodologist. The draft guidelines were reviewed by an External Review Group (ERG) consisting of 14 independent reviewers, who provided feedback on the scientific evidence and its interpretation and content. Inputs from members of the ERG were used by the SG to revise the guideline prior to its finalization. Full details of the makeup of the SG, GDG and ERG, as well as the management of the guideline development process, are available in Annex 1.

2.1. Scope of the guideline and questions of interest

The scope of the guideline was established by researching existing WHO and national guidelines (as described above), and the needs of the target population. The GDG reviewed the scope of the guideline and, at their first two virtual meetings, agreed on the key questions using the PICO (Population, Intervention, Comparison, Outcome) framework. The key questions addressed seven categories of intervention:

A. Behavioural support delivered in both clinical and community settings

B. Digital tobacco cessation interventions

C. Pharmacological interventions delivered in both clinical and community settings

D. Interventions for smokeless tobacco use cessation

E. Combination of behavioural and pharmacological treatments

F. Traditional, complementary and alternative therapies

G. System-level interventions and policies

Long-term quit rates (continuous or point prevalence abstinence measured at 6 months or longer after the start of intervention) were a critical outcome (an outcome that is critical to decision-making) for all interventions. For system-level interventions, other critical outcomes included various process measures (the frequency of identifying people who use tobacco, frequency of advising patients who use tobacco to quit and frequency of patients receiving brief advice and/or medication support). Short-term quit rates (continuous or point prevalence abstinence measured at less than 6 months from the start of intervention) were included as important outcomes (an outcome that is important, but not critical to decision-making) for behavioural interventions; digital tobacco cessation interventions; traditional, complementary and alternative therapies; and system-level interventions and policies. Harms, adverse events (AEs) and side-effects were important outcomes for pharmacological interventions; the combination of behavioural and pharmacological treatments; and traditional, complementary and alternative therapies. Although harms were not prioritized for nonpharmacological interventions, the GDG did look at them for the purpose of informing the Evidence to Decision (EtD) framework (that is, the balance of benefits against harms).

The details of each PICO question are in the relevant section of the Web Annex: Evidence profiles.

2.2. Evidence reviews

Evidence to inform the guideline recommendations was derived from existing or newly commissioned systematic reviews. For all interventions, existing Cochrane systematic reviews that addressed the PICOs were utilized as the primary source of evidence when available. If multiple relevant Cochrane reviews addressed the same PICO, the most recent review was utilized. For interventions and PICOs not addressed in existing Cochrane reviews, new systematic reviews were commissioned to address these gaps.

An extensive body of recent Cochrane systematic reviews on tobacco cessation interventions that addressed the PICOs was available. High-quality, existing Cochrane systematic reviews were selected if they met all of the following four criteria: i) the evidence reviews had been conducted according to standard and well-documented systematic processes; ii) assessment of the certainty of the evidence was conducted using the GRADE approach *(26)*; iii) the evidence reviews addressed the interventions of interest with no restrictions regarding countries or country income levels; and iv) the review was current enough and/or the findings stable enough that the SG judged that new evidence was unlikely to change conclusions. The PICO questions, and the critical and important outcomes, were mapped against existing systematic reviews and, where needed, additional new reviews were commissioned to address gaps. The GDG reviewed the existing evidence and determined which PICOs required new systematic reviews.

The following Cochrane reviews met the four criteria outlined above and were utilized.

- A Cochrane systematic review conducted by Lancaster and Stead in 2017 on individual behavioural counselling in adults who use tobacco *(27)*.
- A Cochrane systematic review conducted by Stead et al. in 2017 on group behavioural counselling in adults who use tobacco *(28)*.
- A Cochrane systematic review conducted by Matkin et al. in 2019 on telephone counselling in adults who use tobacco *(29)*. In addition, a Cochrane systematic review conducted by Tzelepis et al. in 2019 was considered, to compare telephone counselling with real-time video counselling for tobacco cessation *(30)*.
- A Cochrane systematic review conducted by Whittaker et al. in 2019 to determine whether mobile phone text message-based smoking cessation interventions increase smoking cessation rates in people who smoke *(31)*.
- A Cochrane systematic review conducted by Hartmann-Boyce et al. in 2018 on NRT versus control for smoking cessation *(32)*. A separate Cochrane systematic review conducted by Lindson et al. in 2019 provided supplemental information on the effectiveness and safety of different forms, deliveries, doses, durations and schedules of NRT for achieving long-term smoking cessation, compared with one another *(33)*.
- A Cochrane systematic review conducted by Hajizadeh et al. in 2023 on the safety, tolerability and effectiveness of bupropion versus placebo or no pharmacological treatment *(34)*.
- A Cochrane systematic review conducted by Livingstone-Banks et al. in 2023 on the effectiveness of varenicline for smoking cessation *(35)*.
- A Cochrane systematic review undertaken by Stead et al. in 2016, which provided evidence on the effect of combining behavioural support and medication to aid smoking cessation, compared with a minimal intervention or usual care, and that identified whether there are different effects depending on characteristics of the treatment setting, intervention, population treated or take-up of a treatment *(36)*. A separate Cochrane systematic review conducted by Hartmann-Boyce et al. in 2019 provided supplementary information on the effect of additional behavioural support as an adjunct to pharmacotherapy for smoking cessation *(37)*.
- A Cochrane systematic review with seven cluster-randomized controlled trials (RCTs) conducted by Thomas et al. in 2017, which assessed the effectiveness of system change interventions within health-care settings for increasing smoking cessation or the provision of smoking cessation *(38)*. Separately, Boyle R et al. in 2014 conducted another Cochrane system review with 16 studies to assess the effectiveness of electronic health record (EHR)-facilitated interventions on smoking cessation support actions by clinicians, clinics and health-care delivery systems, and on patient smoking cessation outcomes *(39)*.

- A Cochrane systematic review with 17 RCTs conducted by Carson et al. in 2013, which provided information on the effectiveness of training health-care providers in the delivery of smoking cessation interventions to their patients *(40)*.
- A Cochrane systematic review undertaken by van den Brand et al. in 2017, which provided information on the impact of reducing the costs for tobacco smokers or health-care providers to use or provide smoking cessation treatment through health-care financing interventions on long-term smoking cessation rates *(41)*.

Between October 2021 and May 2023, WHO commissioned three independent academic groups to conduct six evidence reviews addressing the following questions.

- For adult tobacco users, what is the effect of brief advice by health-care providers on quitting compared with no advice/contact? Does the effect vary according to types of tobacco used, the quantity of tobacco used, the frequency and intensity of advice delivery, readiness to quit and gender?
- For adult tobacco users, do internet-based cessation interventions increase the chance of successful quitting? Does the effect vary according to the intensity or duration of the intervention, tailoring/personalization, interactivity, types of tobacco used, the quantity of tobacco used, readiness to quit and gender?
- For adult tobacco users, do tobacco cessation smartphone applications (apps) increase the chance of successful quitting? Does the effect vary according to the content, intensity or duration of the intervention, tailoring/personalization, interactivity, types of tobacco used, quantity of tobacco used, readiness to quit and gender?
- For adult tobacco users, what effects do conversational artificial intelligence (AI)-based software interventions have on quitting compared with usual care or no intervention? Do the effects vary according to the intensity or duration of the intervention, the types of tobacco used, the duration of tobacco use since initiation, quantity of tobacco used, readiness to quit and gender?
- For adults who smoke tobacco, does cytisine increase the chance of successful quitting? Does the effect vary by dose or duration of its use, the types of tobacco smoked, quantity of tobacco smoked, level of nicotine dependence and gender?
- For adult tobacco users, do traditional, complementary and alternative therapies increase the chance of successful quitting? Does the effect vary according to the types of tobacco used, the duration and quantity of tobacco use, and gender?

In addition, Jonathan Livingstone-Banks at the University of Oxford provided the results of an unpublished updated Cochrane systematic review on behavioural and pharmacological interventions for smokeless tobacco use cessation.

2.3. Assessment of evidence and its grading

The GRADE approach *(26)* was used to rate the certainty of the evidence for each PICO, based on the underlying evidence in the reviews, as summarized in the GRADE Evidence Profiles or Summary of Findings tables from each review. The certainty of the evidence is categorized into four levels (Table 1), based on the study limitations (risk of bias), consistency, precision, directness and other issues (for example, publication or reporting bias). The criteria used by each systematic review to determine the certainty of evidence are summarized in the GRADE tables. The GRADE judgements from the reviews provided the benefits and harms estimates, as well as certainty of findings for each key question/PICO, as summarized in the EtD tables (see Web Annex: Evidence profiles).

Table 1. Certainty of the evidence

Certainty of the evidence	Definition
⊕ High	Further research is very unlikely to change our confidence in the estimate of effect
⊕ Moderate	Further research is likely to have an important impact on our confidence in the effect and may change the estimate
⊕ Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
⊕ Very low	Any estimate of effect is very uncertain

2.4. Going from evidence to recommendations

The GDG employed the GRADE EtD framework to generate question-specific recommendations *(42)*. The EtD framework is a systematic and transparent approach that is used to guide decision-making. The framework is based on a set of domains that are important to consider when developing guideline recommendations. The domains include whether the problem is a priority, the magnitude of the desirable and undesirable effects, the certainty of the evidence, the balance between desirable and undesirable effects, the impact of patient values and preferences regarding outcomes on decisions, resource and cost considerations, and the potential impact on equity, acceptability and feasibility *(42)*. The GDG made each recommendation on the basis of their considerations of all these domains. The Web Annex: Evidence profiles includes the EtD framework developed for each recommendation.

The "Justification and evidence" for each recommendation summarizes the benefits, harms, certainty of evidence and balance of benefits against harms, as well as other EtD judgements important for informing the recommendation. Additional reviews and surveys were not commissioned to inform the other EtD domains, and judgements relating to them were based on GDG expertise and experience, with the exception of costs (where the costs of some interventions – for example, behavioural, pharmacological and financial interventions – are known at least to some extent, and supplemental evidence/data on cost-effectiveness was sought). There is a separate "Evidence to recommendations" section (Section 4) discussing overarching issues related to the EtD domains at the end of the guideline.

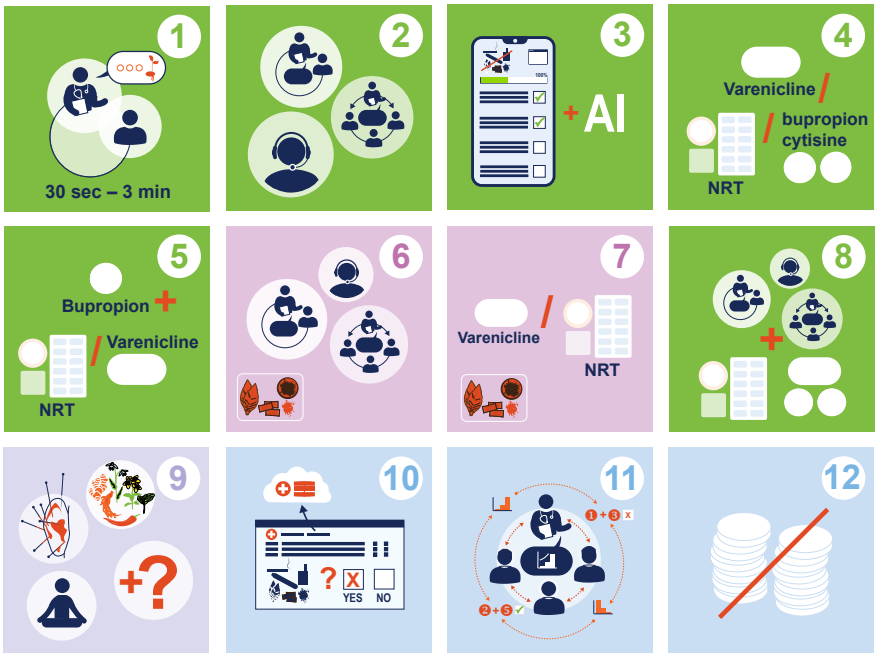
All decisions about the recommendations were reached by discussion and consensus. The chairs of the GDG facilitated the discussions during the meeting using an informal consensus process. Consensus was attained for all recommendations and their assigned strength; voting was not required for any recommendation. For each recommendation, the GDG chairs also facilitated discussion to identify key implementation considerations.

Each recommendation in this guideline has been assigned a strength, as well as the certainty of the evidence on which it is based. Regarding recommendation strengths, recommendations were either strong or conditional. For strong recommendations, the GDG was confident that the desirable effect of following the recommendation outweighed any potential undesirable effects. Other factors that supported strong recommendations were whether the balance of benefits to harms is sensitive to variability in patient values/preferences regarding outcomes; lower costs or resources and/or high cost-effectiveness; high acceptability and feasibility in the intended populations and settings; and anticipated positive impacts on equity. For conditional recommendations, the GDG determined that the balance of desirable against undesirable effects

favoured the recommendation being followed, but to a relatively small extent; there was more uncertainty about anticipated effects; and/or the decision to follow the recommendation was preference sensitive, costly or cost-ineffective, or there were important feasibility, acceptability or equity concerns. The strength of a recommendation has different implications for the individuals affected by this guideline (Table 2).

Table 2. Implications of the strength of a recommendation for different users

Perspective	Strong recommendation	Conditional recommendation
Patients/tobacco users	Most people in this situation would want the recommended course of action and only a small proportion would not	Most people in this situation would want the recommended course of action, but many would not
Clinicians	Most people should receive the recommended course of action	Recognize that different choices will be appropriate for individual patients
Policy-makers	The recommendation can be adopted as policy in most situations	Require substantial debate with all stakeholders before this can be adopted as policy


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3. Recommendations

3.1. Behavioural support delivered in both clinical and community settings

3.1.1. Recommendations

1. WHO recommends brief advice (between 30 seconds and 3 minutes per encounter) be consistently provided by health-care providers as a routine practice to all tobacco users accessing any health-care settings.



Strong recommendation;
moderate certainty

2. WHO recommends more-intensive behavioural support be offered to all tobacco users interested in quitting. Options for behavioural support are individual face-to-face counselling, group face-to-face counselling or telephone counselling; multiple behavioural support options should be provided.



Strong recommendation;
high certainty (individual counselling)/
moderate certainty (group counselling and telephone counselling)

3.1.2. Overall questions

In adults who use tobacco, what are the effects of brief advice by health professionals, individual behavioural counselling, group behavioural counselling and telephone counselling on quitting compared with no intervention or usual care? Does the effect vary according to types of tobacco used; the quantity of tobacco used; the frequency, intensity, duration or type of the interventions; readiness to quit; and gender?

3.1.3. Justification and evidence

For these recommendations on behavioural support delivered in both clinical and community settings, one newly commissioned systematic review, which is now published *(43)*, and four Cochrane systematic reviews *(27–30)* were used. Full details of the EtD tables can be found in the Web Annex: Evidence profiles.

A systematic review and meta-analysis, which included 24 352 participants in 13 RCTs, conducted by Cheng et al. showed that, in comparison with no advice being given, the average treatment effect of brief advice for long-term tobacco abstinence was modest and significant (risk ratio/relative risk [RR]: 1.17; 95% confidence interval [CI]: 1.07–1.27) *(43)*. The average treatment effect of brief advice for short-term tobacco abstinence was also modest and significant (RR: 1.22; 95% CI: 1.01–1.47). The average treatment effect of brief advice for a quit attempt was insignificant when only studies with lower risk of bias were included (RR: 1.03; 95% CI: 0.97–1.08). Subgroup analyses on age, high- versus low-income countries, types of health-care providers, clinical versus community settings and outcome characteristics (for example, duration of follow-up) were conducted. No significant heterogeneity of treatment effects on long-term or short-term abstinence was detected between the subgroups.

The evidence relating to individual behavioural counselling was based on a Cochrane systematic review published by Lancaster et al. *(27)*. The evidence showed that: there was high-quality evidence that individual counselling was more effective than a minimal contact control (which included brief advice, usual care or provision of self-help materials) when pharmacotherapy was not offered to any of the participants (RR: 1.57; 95% CI: 1.40–1.77; 27 studies; 11 100 participants); there was moderate-quality evidence of a benefit of counselling when all participants received pharmacotherapy (RR: 1.24; 95% CI: 1.01–1.51; 6 studies; 2662 participants); and there was moderate-quality evidence for a small benefit of more-intensive counselling when compared with brief counselling (RR: 1.29; 95% CI: 1.09–1.53; 11 studies; 2920 participants). No significant differences were reported by five studies that compared different types of counselling.

For group behavioural counselling, the evidence from a Cochrane systematic review that included 66 RCTs *(28)* indicated that, compared with a self-help programme, the group-based approach resulted in a benefit, with the chance of long-term quitting increased by 50% to 130% (RR: 1.88; 95% CI: 1.52–2.33; 4395 participants); a small increase in long-term quitting compared with brief support delivered by a health-care provider (RR: 1.22; 95% CI: 1.03–1.43; 7286 participants); and there was also low-quality evidence of benefit of a group programme compared with no-intervention controls (RR: 2.60; 95% CI: 1.80–3.76; 9 trials; 1098 participants). The review did not identify evidence that group therapy was more effective than individual counselling of similar intensity (RR: 0.99; 95% CI: 0.76–1.28; 6 trials; 980 participants). Programmes that included components to increase cognitive and behavioural skills were not shown to be more effective than same-length or shorter programmes without these components.

A Cochrane systematic review of 104 trials, which included 111 653 participants, evaluated the effect of telephone counselling to help people quit smoking cigarettes *(29)*. The review showed that, compared with a control condition in which self-help materials or brief counselling in a single call were provided, multiple sessions of proactive counselling increased long-term quit rates for people who contacted helplines (RR: 1.38; 95% CI: 1.19–1.61; 14 trials; 32 484 participants); for people who did not call a helpline, the provision of telephone counselling increased quit rates (RR: 1.25; 95% CI: 1.15–1.35; 65 trials; 41 233 participants); and in studies that compared more versus fewer calls directly, people who were offered more calls (three to five) tended to be more likely to quit than those who received only one call (RR: 1.27; 95% CI: 1.12–1.44; 2602 participants). Subgroup analysis identified no evidence that the effect of telephone counselling depended upon whether or not other interventions were provided, that more-intensive support was more effective than less-intensive support, or that the effect of telephone support depended upon whether or not people were actively trying to quit smoking. However, meta-regression demonstrated that telephone support was more effective for people who were motivated to try to quit smoking; telephone counselling was associated with greater effectiveness when provided as an adjunct to self-help written support or to a brief intervention from a health-care provider; and telephone counselling was less effective when provided as an adjunct to more-intensive counselling. Separately, another Cochrane systematic review compared real-time video counselling with telephone counselling *(30)*. The review indicated that there was no statistically significant difference regarding the treatment effect between video counselling and telephone counselling in assisting people to quit smoking (RR: 2.15; 95% CI: 0.38–12.04; 2 studies; 608 participants).

The GDG reached the following conclusions.

- There is moderate-certainty evidence that brief advice increases long-term abstinence, and high-certainty evidence for short-term abstinence; long-term abstinence was considered the more important clinical outcome.
- The balance of benefits against harms favours brief advice on the basis of:
  - small benefits at the individual level (number needed to treat [NNT]: 91 to achieve one more case of long-term abstinence), moderate to large population-level benefits of brief advice (given the low cost, feasibility, acceptability and the high number of individuals potentially impacted); and
  - trivial harms (judged according to the nature of the intervention and the absence of harms reported in the trials).
- Decisions regarding brief advice are not preference sensitive (due to trivial harms), and brief advice is low cost, feasible and acceptable, with potential positive impact on equity.
- There is high-certainty evidence for long-term abstinence following individual behavioural counselling delivered without pharmacotherapy, and moderate-certainty evidence when delivered with pharmacotherapy (this applies to the incremental added benefit, even though the overall benefit of combining the two is greater). There is high-certainty evidence that more-intensive individual behavioural counselling is more effective than less-intensive individual behavioural counselling.

- The balance of benefits against harms favours individual behavioural counselling over minimal contact and more- versus less-intensive counselling on the basis of:
  - moderate to large benefits (individual behavioural counselling with or without pharmacotherapy versus minimal contact, NNT: 25–50 to achieve one more case of long-term abstinence; more- versus less-intensive counselling, NNT: 6–33 to achieve one more case of long-term abstinence); and
  - trivial harms (judged according to the nature of the intervention and the absence of harms reported in the trials).
- Decisions regarding individual behavioural counselling are probably not preference sensitive (due to trivial harms); it requires moderate cost, and it is probably feasible and acceptable, with potentially increased equity.
- There is moderate-certainty evidence that group behavioural counselling increases long-term quitting, compared with a self-help programme; there is low-certainty evidence that a group programme is more effective than brief support or no intervention.
- The balance of benefits against harms favours group behavioural counselling over self-help programmes, brief support or no intervention on the basis of:
  - large benefits (group counselling versus no intervention or self-help programme, NNT: 8–25 to achieve one more case of long-term abstinence); trivial to small benefits (group counselling versus face-to-face individual intervention or brief group support, NNT: 100 to achieve one more case of long-term abstinence); and
  - trivial harms relative to other counselling interventions or usual care (based on the nature of the intervention and the absence of harms reported in the trials).
- The benefits and harms of group counselling and individual counselling are closely balanced, with similar effectiveness and no anticipated differences in harms.
- Decisions regarding group behavioural counselling are probably not preference sensitive (due to trivial harms); it requires moderate cost, and its feasibility and acceptability may vary in different stakeholders and in different settings, with potentially increased equity.
- There is moderate-certainty evidence that telephone counselling increases long-term tobacco abstinence.
- The balance of benefits against harms favours proactive telephone counselling on the basis of:
  - moderate benefits (multisession proactive counselling versus self-help materials or brief counselling at single call, NNT: 36 to achieve one more case of long-term cessation); and
  - trivial harms (judged on the basis of the type of intervention provided and absence of harms reported in the trials).
- Decisions regarding telephone counselling are not preference sensitive (due to no known harms), it requires small to moderate cost, and it is feasible and acceptable, with probably increased equity.

3.1.4. Implementation considerations

Brief advice can help all tobacco users regardless of interest in quitting. Routine provision of brief advice in all health-care settings is critical to achieve a high level of population reach and serve as an entry point for the provision of additional evidence-based cessation support.

Multiple modalities are available for the provision of additional, more-intensive behavioural support to tobacco users. Since none of the different live support modality options (individual, group or telephone) is clearly superior to the others in terms of effectiveness, more than one modality being available may increase patient and provider choice and utilization (see Annex 2 for additional details on modality characteristics).

All behavioural support options may be augmented by digital tobacco cessation interventions for additional support (see Section 3.2).

Making behavioural support, including of longer duration and intensity, available to tobacco users is especially important in settings where they have minimal or no access to pharmacotherapy.

Behavioural support is provided by personnel who have received sufficient training in knowledge and skills to aid tobacco users who are attempting to quit. These personnel can be either hired and trained specifically to provide cessation support, or they can be existing staff who already provide counselling to people with other health conditions. Trained cessation counsellors can support different populations in quitting, including those with mental health conditions. Counselling support that is culturally sensitive and available in the primary language of tobacco users is important. It is useful to have support materials and training available in local languages, and to include examples that are inclusive of smokeless tobacco and other products, such as waterpipes (hookah, shisha) and bidis, especially in areas of high prevalence.

3.2. Digital tobacco cessation interventions

3.2.1. Recommendation

3. Digital tobacco cessation modalities[3] (text messaging, smartphone apps, AI-based interventions or internet-based interventions), individually or combined, can be made available for tobacco users interested in quitting, as an adjunct to other tobacco cessation support or as a self-management tool.



Conditional recommendation;
moderate certainty (text messaging)/
low certainty (smartphone apps/AI-based interventions)/
very low certainty (internet-based interventions)

3.2.2. Overall questions

For adult tobacco users, do mobile phone text-messaging cessation interventions, internet-based cessation interventions, tobacco cessation smartphone apps and conversational AI-based software interventions increase the chance of successful quitting? Does the effect vary according to content, the intensity or duration of the intervention, tailoring/personalization, interactivity, types of tobacco used, the quantity of tobacco used, readiness to quit and gender?

3.2.3. Justification and evidence

The evidence on digital tobacco cessation interventions presented to the GDG was based on a Cochrane systematic review *(31)* and three newly commissioned systematic reviews conducted by Gartner et al. The systematic review on AI-based software interventions has now been published *(44)*. Full details of the EtD tables can be found in the Web Annex: Evidence profiles.

The Cochrane systematic review suggested that automated text-messaging interventions were more effective than minimal smoking cessation support (RR: 1.54; 95% CI: 1.19–2.00; 13 studies; 14 133 participants), and that text messaging added to other smoking cessation interventions was more

effective than the other smoking cessation interventions alone (RR: 1.59; 95% CI: 1.09–2.33; 4 studies; 997 participants). Two studies comparing text messaging with other smoking cessation interventions, and three studies comparing high- and low-intensity messaging, did not show significant differences between groups (RR: 0.92; 95% CI: 0.61–1.40; 2 studies; 2238 participants and RR: 1.00; 95% CI: 0.95–1.06; 3 studies; 12 985 participants, respectively).

The newly commissioned systematic reviews showed that: compared with no or minimal intervention, internet-based interventions were not significantly more effective for long-term tobacco abstinence (RR: 1.11; 95% CI: 0.90–1.36; 7 studies; 12 970 participants); there was no statistically significant treatment effect between smartphone apps and minimal intervention for assisting people to quit tobacco use (RR: 0.93; 95% CI: 0.79–1.09; 6 studies; 5424 participants); and that compared with standard/usual care, conversational AI-based

3 WHO observes a rapid innovation cycle in digital technologies that necessitate reviews as new evidence emerges.

software interventions significantly increased long-term tobacco abstinence rates (RR: 1.29; 95% CI: 1.13–1.46; 3 trials; 1486 participants) *(44)*. Eight studies comparing smartphone apps with more versus fewer functions for smoking cessation suggested that people who were offered more-functional smartphone apps were more likely to quit than those who were offered less-functional ones (RR: 1.33; 95% CI: 1.01–1.74; 10 235 participants). Five studies that examined smartphone app use delivered with pharmacotherapy versus pharmacotherapy and minimal behavioural support showed that there was moderate-quality evidence of increased long-term tobacco abstinence following smartphone app use when used as an adjunct to pharmacotherapy (RR: 1.28; 95% CI: 1.12–1.47; 1798 participants).

The GDG concluded the following.

- There is moderate-certainty evidence that automated text-messaging interventions are more effective than minimal smoking cessation support. Isolated texting programs may have less impact in current digital environments given the proliferation of other forms of smartphone and social media interaction, and increased levels of nonelective political and commercial messaging that was not prevalent when the research was conducted.
- The balance of benefits against harms favours text-messaging cessation interventions on the basis of:
  - moderate benefits (text messaging versus minimal smoking cessation support, NNT: 33; text messaging plus other smoking cessation support versus other smoking cessation support, NNT: 25 to achieve one more additional case of long-term cessation); and
  - trivial or minimal harms (judged according to the nature of the intervention; there is some risk of indirect harms if mobile text messaging is used as the sole option for cessation support: interventions with higher effectiveness are thus not used as a result).
- Decisions regarding cessation interventions delivered via text messaging are not preference sensitive (due to no known harms), text-messaging interventions require small to moderate cost, and they are probably feasible and acceptable, with the impact on equity varying (if digital access varies).
- There is very low-certainty evidence suggesting that internet-based interventions are not significantly more effective for long-term tobacco abstinence than no or minimal intervention, due to risk of bias, inconsistency and potential publication bias.
- The balance of benefits against harms is uncertain for internet-based interventions on the basis of small benefits with low certainty (NNT: 31–111 to achieve one more case of continuous abstinence at 6–13 months) and trivial/minimal harms (judged on the basis of the nature of the intervention and there is some risk of indirect harms if internet-based intervention is used as the sole option for cessation support: interventions with higher effectiveness are thus not used as a result).
- There is low-certainty evidence supporting any significant differences in long-term tobacco abstinence between tobacco cessation smartphone apps and minimal intervention, due to risk of bias, imprecision and inconsistency; there is moderate-certainty evidence that more-interactive apps have a greater effect and improve effectiveness when added to pharmacotherapy. In addition, outcomes were variably defined and the apps varied widely.
- The balance of benefits against harms probably favours tobacco cessation smartphone apps on the basis of:
  - moderate benefits (smartphone apps more versus fewer functions, and app use with pharmacotherapy versus pharmacotherapy plus minimal behavioural support, NNT: 14–29 for one more case of long-term abstinence), but there are no additional benefits versus minimal intervention control; and
  - trivial or minimal harm (harms were reported in only one trial, and there is some risk of indirect harms due to the lower efficacy of apps relative to other forms of behavioural interventions for tobacco cessation if a smartphone-based intervention is used as the sole option for cessation support: interventions with greater effectiveness are thus not used as a result).

- Certainty regarding internet-based interventions and tobacco cessation smartphone apps is too low to enable the determination of sensitivity to preference, they require small to moderate costs, and they are probably feasible and acceptable, with the impact on equity varying (if digital access varies).
- There is low-certainty evidence that conversational AI-based software interventions significantly increase long-term tobacco abstinence rates, due to risk of bias. In addition, only three RCTs compared conversational AI-based software interventions with standard/usual care.
- The balance of benefits against harms probably favours conversational AI-based interventions on the basis of:
  - large benefits (conversational AI-based software intervention versus control, NNT: 12 for one more case of smoking cessation at 6 months); and
  - trivial or minimal harms (there is some risk of indirect harms if conversational AI-based software interventions are offered as the sole option for cessation support: interventions with greater effectiveness are thus not used as a result).
- Decisions regarding conversational AI-based software interventions are not preference sensitive, they require small to moderate cost, and they are probably feasible and acceptable, with a positive impact on equity.

3.2.4. Implementation considerations

Digital tobacco cessation interventions have the potential to reach millions of tobacco users and can serve as an entry point through which they can access other recommended tobacco cessation interventions.

Digital tobacco cessation interventions can be implemented as a standalone service to support people to stop using tobacco. When offered as a standalone service to support self-management, it is important to advise potential users on the full range of recommended and available tobacco cessation interventions, including information on their effectiveness.

Digital tobacco cessation interventions may also be implemented as an add-on support to other recommended tobacco cessation interventions. More evidence is needed to suggest specific combinations of interventions that are especially effective or efficient. For tobacco users who are interested in using other recommended and available tobacco cessation interventions, digital interventions may be used to complement but not replace those interventions.

Careful content design, and ongoing monitoring and evaluation, is required to develop and maintain new digital tobacco cessation programmes (see Annex 2 for design, adaptation and choice considerations).

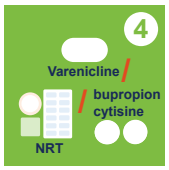
Digital tobacco cessation interventions with interactive content and responses tailored on the basis of user replies are most likely to be effective.

- The place of digital tobacco cessation interventions within digital and social media has evolved over the past decade, and will continue to evolve rapidly. It is important to conduct monitoring and evaluation when incorporating them into new digital platforms.
- Different modalities of digital tobacco cessation interventions can be made available for tobacco users, and can often be combined (for example, a smartphone app could link to an internet-based website, have built-in texting and include AI systems). Across modalities, tobacco cessation interventions via mobile text messaging currently have the strongest evidence (see Annex 2 for considerations regarding specific digital modalities).

3.3. Pharmacological interventions delivered in both clinical and community settings

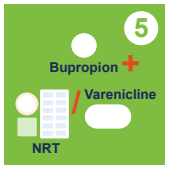
3.3.1. Recommendations

4. WHO recommends varenicline, NRT, bupropion and cytisine[4] as pharmacological treatment options for tobacco users who smoke and are interested in quitting. Varenicline, NRT or bupropion are recommended as first-line options; combination NRT (a patch plus a short-acting form, such as gum or a lozenge) is an option for tobacco users interested in quitting who will use NRT.



Strong recommendation;
high certainty (varenicline, NRT and bupropion)/
moderate certainty (combination NRT, cytisine)

5. Bupropion in combination with NRT or varenicline may be offered to tobacco users interested in quitting when there is inadequate response to first-line treatments.



Conditional recommendation;
moderate certainty (bupropion plus varenicline)/
low certainty (bupropion plus NRT)

3.3.2. Overall questions

For adults who smoke, do NRT, bupropion, varenicline and cytisine increase their chance of successful quitting? For adults who smoke, is combination therapy better than monotherapy in smoking cessation treatment? Does the effect vary by form, dose and duration of use; the types and quantity of tobacco smoked; level of nicotine dependence; and gender?

3.3.3. Justification and evidence

The evidence for pharmacological interventions delivered in both clinical and community settings was obtained from four Cochrane systematic reviews *(32–35)* and one newly commissioned systematic review on cytisine. Full details of EtD tables can be found in the Web Annex: Evidence profiles.

3.3.3.1. NRT

For the effects of NRT as monotherapy compared with a placebo or non-NRT control group, a Cochrane systematic review of 133 studies that included 64 640 participants showed that the RR of long-term abstinence for any form of NRT relative to control was 1.55 (95% CI: 1.49–1.61) *(32)*. The pooled RRs for each type were 1.49 (95% CI: 1.40–1.60; 56 trials; 22 581 participants) for nicotine gum, 1.64 (95% CI: 1.53–1.75; 51 trials; 25 754 participants) for nicotine patches, 1.52 (95% CI: 1.32–1.74; 8 trials; 4439 participants) for oral tablets or lozenges; 1.90 (95% CI: 1.36–2.67; 4 trials; 976 participants) for nicotine inhalators, 2.02 (95% CI: 1.49–2.73; 4 trials; 887 participants) for nicotine nasal sprays and 2.48 (95% CI: 1.24–4.94; 1 trial; 542 participants) for nicotine oral sprays. The evidence was judged by the authors to be of high quality. The effects were largely independent of the definition of abstinence, the intensity of additional support provided and the setting in which the NRT was offered.

Subgroup analysis in a separate Cochrane systematic review (33) suggested that: for (24-hour) patches, 42/44 mg is as effective as 21/22 mg per patch (RR: 1.09; 95% CI: 0.93–1.29; 5 studies; 1655 participants), and 21 mg is more effective than 14 mg (RR: 1.48; 95% CI: 1.06–2.08; 1 study; 537 participants); and that for 16-hour patches, 25 mg is more effective than 15 mg (RR: 1.19; 95% CI: 1.00–1.41; 3 studies; 3446 participants). Five studies comparing 4-mg gum with 2-mg gum reported that smokers who are highly dependent may benefit from the higher dose (RR: 1.43; 95% CI: 1.12–1.83; 5 studies; 856 participants). High-certainty evidence from

4 Although cytisine is as effective as other so-called first-line medications, it is listed separately because evidence certainty is moderate, it is currently only legally available in some countries, has more variability in dosing regimen, and less review and approval by country-level drug regulatory bodies. However, all medications carry strong recommendations and any of these medications can be used.

eight studies suggests that the use of either a form of fast-acting NRT or a nicotine patch results in similar long-term quit rates (RR: 0.90; 95% CI: 0.77–1.05; 8 studies; 3319 participants). The authors identified no evidence of effects of: duration of nicotine patch use; 16-hour versus 24-hour daily patch use; tapering of patch dose versus abrupt patch cessation; fast-acting NRT type; duration of nicotine gum use; ad lib versus fixed dosing of fast-acting NRT; free versus purchased NRT; length of provision of free NRT; ceasing versus continuing patch use on lapse; and participant versus clinician-selected NRT. However, in most cases these findings were based on very low- or low-certainty evidence, and were findings from single studies.

AEs from using NRT were related to the type of product, and included skin irritation following the use of patches, and irritation to the inside of the mouth following the use of gum and tablets. Cardiac AEs like chest pains and palpitations were rare, and serious adverse events (SAEs) were extremely rare. The odds ratio (OR) of chest pains or palpitations for any form of NRT relative to control was 1.88 (95% CI: 1.37–2.57; 11 074 participants). Most comparisons identified no evidence of effects on cardiac AEs, SAEs or withdrawals due to treatment. Rates of these were low overall. Significantly more withdrawals due to treatment were reported for participants using nasal sprays compared with patches in one trial (RR: 3.47; 95% CI: 1.15–10.46; 922 participants), and for participants using 42/44-mg patches compared with 21/22-mg patches across two trials (RR: 4.99; 95% CI: 1.60–15.50; 544 participants).

3.3.3.2. Bupropion

In terms of the evidence for bupropion regarding long-term tobacco cessation, a Cochrane systematic review of 124 studies that included 48 832 participants demonstrated that there was high-certainty evidence that bupropion increased smoking cessation rates when compared with placebo or no pharmacological treatment (RR: 1.60; 95% CI: 1.49–1.72; 50 studies; 18 577 participants) (34). Bupropion resulted in inferior smoking cessation rates when compared with varenicline (RR: 0.73; 95% CI: 0.67–0.80; 9 studies; 7564 participants) and with combination NRT (RR: 0.74; 95% CI: 0.55–0.98; 2 studies; 720 participants). However, there was no clear evidence of a difference in efficacy between bupropion and single-form NRT (RR: 1.03; 95% CI: 0.93–1.13; 10 studies; 7613 participants).

There was moderate-certainty evidence that participants taking bupropion were more likely to report SAEs than those taking placebo or receiving no pharmacological treatment. However, results were not significantly different (RR: 1.16; 95% CI: 0.90–1.48; $I^2 = 0\%$; 23 studies; 10 958 participants). There was high-certainty evidence that bupropion resulted in more trial dropouts due to AEs than placebo or no pharmacological treatment (RR: 1.44; 95% CI: 1.27–1.65; 25 studies; 12 346 participants).

3.3.3.3. Varenicline

A Cochrane systematic review of 75 trials with 45 049 participants (35) published in 2023 found high-certainty evidence that varenicline helps more people to quit than placebo (RR: 2.32; 95% CI: 2.15–2.51; 41 studies; 17 395 participants); helps more people to quit than bupropion (RR: 1.36; 95% CI: 1.25–1.49; 9 studies; 7560 participants); and helps more people to quit than a single form of NRT (RR: 1.25; 95% CI: 1.14–1.37; 11 studies; 7572 participants). There was no clear evidence of a difference in quit rates between participants taking varenicline and combination NRT (RR: 1.02; 95% CI: 0.87–1.20; 5 studies; 2344 participants). Pooled results from studies comparing cytisine with varenicline showed that more people taking varenicline quit smoking than those receiving cytisine (RR: 0.83; 95% CI: 0.66–1.05; 2 studies; 2131 participants).

The authors found moderate-certainty evidence that people taking varenicline are more likely to report SAEs than those not taking it (RR: 1.23; 95% CI: 1.01–1.48; 26 studies; 14 356 participants). Comparing varenicline with bupropion, there was no clear evidence of a difference in rates of all SAEs (RR: 0.89; 95% CI: 0.61–1.31; 5 studies; 5317 participants), neuropsychiatric SAEs (RR: 1.05; 95% CI: 0.16–7.04; 2 studies; 866 participants) or cardiac SAEs (RR: 3.17; 95% CI: 0.33–30.18; 2 studies; 866 participants). When compared with combination NRT, people taking varenicline had increased risk of SAEs (RR: 2.15; 95% CI: 0.49–9.46; 4 studies; 1852 participants) and neuropsychiatric SAEs (RR: 4.69; 95% CI: 0.23–96.50; 2 studies; 764 participants), and reduced risk of cardiac SAEs (RR: 0.32; 95% CI: 0.01–7.88; 2 studies; 819 participants). In all these cases, evidence was of low certainty and CIs were very wide, encompassing both substantial harm and benefit. There was low-certainty evidence that more people taking varenicline reported SAEs when compared with those taking cytisine (RR: 0.67; 95% CI: 0.44–1.03; 2 studies; 2017 participants).

3.3.3.4. Cytisine

A systematic review of 14 studies commissioned by WHO showed that participants who received cytisine were significantly more likely to quit smoking for at least 6 months than those who received placebo/no intervention/usual care (RR: 2.61; 95% CI: 1.50–4.67; 6 trials; 5194 participants) and significantly more likely to have higher long-term abstinence rates than participants who received NRT (RR: 1.36; 95% CI: 1.06–1.73; 2 trials; 1511 participants). There was no significant difference in the likelihood of quitting tobacco use between participants taking cytisine and varenicline (RR: 0.96; 95% CI: 0.63–1.45; 3 trials; 2127 participants). Two trials that examined the impact of longer versus shorter treatment durations of cytisine found high abstinence rates with longer treatment (RR: 1.29; 95% CI: 1.02–1.63; 1009 participants).

While seven studies reported more AEs among those receiving cytisine compared with those who received placebo, NRT or counselling, there was little evidence of SAEs associated with cytisine use.

3.3.3.5. Combination pharmacotherapy

There was high-certainty evidence that combination NRT (a fast-acting form plus a patch) results in higher long-term quit rates than single-form NRT (RR: 1.25; 95% CI: 1.15–1.36; 14 studies; 11 356 participants) (33). The authors found no evidence of an effect of duration of combination NRT use. There was moderate-certainty evidence that a combination of bupropion and varenicline may have resulted in superior quit rates compared with varenicline alone (RR: 1.21; 95% CI: 0.95–1.55; 3 studies; 1057 participants) (34). However, there was insufficient evidence to establish whether a combination of bupropion and NRT resulted in superior quit rates compared with NRT alone (RR: 1.17; 95% CI: 0.95–1.44; 15 studies; 4117 participants) (34).

There was no evidence of an effect on cardiac AEs, and all SAEs and withdrawals when combination NRT was compared with single-form NRT (33). Results were also imprecise when comparing SAEs between people randomized to a combination of bupropion and NRT versus NRT alone (RR: 1.52; 95% CI: 0.26–8.89; 4 studies; 657 participants), and randomized to bupropion plus varenicline versus varenicline alone (RR: 1.23; 95% CI: 0.63–2.42; 5 studies; 1268 participants) (34). However, there was insufficient evidence that bupropion combined with NRT versus NRT alone, or bupropion combined with varenicline versus varenicline alone, had an impact on the number of dropouts due to treatment (34).

3.3.3.6. Conclusions

The GDG concluded the following.

- There is high-certainty evidence that all forms of NRT are more effective in achieving long-term tobacco abstinence compared with a placebo or non-NRT control group.
- The balance of benefits against harms favours NRT on the basis of moderate to large benefits (NRT versus placebo/no NRT, NNT: 12–45 for one additional long-term abstinence depending on level of baseline behavioural support) and small harms (the most common AEs with NRT included hiccups, jaw pain, sore throat, mouth ulcers, gastrointestinal disturbance and local irritation, but were usually not severe; NRT was reportedly associated with increased risk of chest pains and heart palpitations with number needed to harm [NNH]: 91, but were uncommon).
- Decisions regarding NRT are probably not preference sensitive (small harms that do not appear serious), it requires small cost, and it is feasible and probably acceptable, with probably increased equity.
- There is high-certainty evidence that bupropion increases long-term smoking cessation rates when compared with placebo or no pharmacological treatment.
- The balance of benefits against harms favours bupropion on the basis of large benefits (bupropion versus placebo/no pharmacotherapy, NNT: 14 for one more case of long-term abstinence) and moderate harms (SAEs included anxiety, insomnia and psychiatric AEs, NNH: 100 to cause one additional SAE; dropouts due to AEs, NNH: 33 to cause one dropout).

- Decisions regarding bupropion are probably preference sensitive (moderate harms with some uncertainty regarding serious harms), it requires small cost, and it is feasible and probably acceptable, with probably increased equity.
- There is high-certainty evidence that varenicline is more effective than placebo, bupropion or NRT in achieving long-term smoking abstinence. For varenicline versus placebo, there is moderate-certainty evidence that use of varenicline causes SAEs and low-certainty evidence that it causes cardiac SAEs.
- The balance of benefits against harms favours varenicline on the basis of:
  - large benefits (varenicline versus placebo, NNT: 7.6 to achieve one more case of continuous/sustained abstinence at 6 months or longer; varenicline versus bupropion or NRT, NNT: 16–22 for one additional case of long-term abstinence); and
  - moderate harms (varenicline versus placebo, NNH: 167 to cause one more SAE; NNH: 500 [range: 111–333] to cause one more cardiac SAE; RR: 2.61 [range: 2.44–2.80] for nausea; RR: 1.37 [range: 1.27–1.47] for insomnia; RR: 1.82 [range: 1.67–1.97] for abnormal dreams; RR: 1.11 [range: 1.03–1.19] for headache; varenicline was not associated with increased risk of depression, suicidal ideation or neuropsychiatric SAEs).
- Decisions regarding varenicline are probably preference sensitive (moderate harms including some serious harms), it requires moderate cost, and it is feasible and probably acceptable, with no impact on equity.
- There is moderate-certainty evidence that cytisine is more effective than placebo/no intervention/usual care in supporting smokers to quit smoking for 6 months or longer; there is very low- to low-certainty evidence for a significant difference in the likelihood of quitting smoking between cytisine and varenicline, and between cytisine and NRT.
- The balance of benefits against harms favours cytisine on the basis of large benefits (cytisine versus placebo, NNT: 15 for one more case of continuous long-term abstinence; cytisine versus NRT, NNT: 18 to achieve one additional case of long-term abstinence) and small harms (more harms than placebo were reported in five out of six trials; however, differences were not statistically significant in most trials and no serious harms were reported).
- Decisions regarding cytisine are not preference sensitive (small harms that do not appear serious), it requires small cost, and it is feasible and probably acceptable, with probably increased equity.
- There is high-certainty evidence that combination NRT is more effective than single-form NRT for long-term smoking cessation; there was no evidence of an effect on cardiac AEs, and all SAEs and withdrawals when combination NRT was compared with single-form NRT.
- The balance of benefits against harms favours combination NRT on the basis of moderate benefits (combination NRT versus monotherapy, NNT: 29 to achieve one more case of long-term abstinence) and small harms (combination NRT versus monotherapy, NNH: 500 for SAEs, NNH: 500 for treatment withdrawal).
- Decisions regarding combination NRT are probably preference sensitive (small increased risk of SAEs and treatment withdrawals), it requires small cost, and it is probably feasible and acceptable, with increased equity.
- There is moderate-certainty evidence that a combination of bupropion and varenicline may result in superior long-term quit rates compared with varenicline alone; there is insufficient evidence that a combination of bupropion and NRT results in superior long-term quit rates compared with NRT alone. There is low-certainty evidence for an effect of SAEs and dropout rates for bupropion combined with NRT versus NRT alone, or bupropion combined with varenicline versus varenicline alone.
- The balance of benefits against harms probably favours bupropion plus NRT and bupropion plus varenicline combinations on the basis of:
  - moderate benefits (bupropion plus NRT versus NRT, NNT: 33 for one additional case of long-term smoking cessation; bupropion plus varenicline versus varenicline, NNT: 20 to achieve one more case of long-term smoking cessation); and

  - small but nontrivial harms with low certainty (bupropion plus NRT versus NRT: imprecise estimates for SAEs, RR: 1.52 [range: 0.26–8.89], statistically nonsignificant increased risk of study withdrawals due to AEs, increased risk of insomnia and anxiety; bupropion plus varenicline versus varenicline: imprecise estimates for SAEs, RR: 1.23 [range: 0.63–2.42], study withdrawals due to drug AEs and increased risk of any AE, psychiatric AEs, anxiety and insomnia).
- Decisions regarding bupropion plus NRT and bupropion plus varenicline are probably preference sensitive (small harms with uncertainty regarding SAEs), they require moderate costs and they are probably feasible, with uncertain acceptability and probably increased equity.

3.3.4. Implementation consideration

It is critical to minimize or ideally eliminate the cost of medication, and other access barriers, to increase tobacco users' medication use, compliance with dose and duration recommendations, and maximize population-level impacts on prevalence (see Section 3.7). Given that health insurance is only available to a minority of tobacco users in LMICs, other mechanisms may need to be deployed to decrease or eliminate cost and access barriers. Where health insurance exists, both public and private insurers may consider providing full-cost coverage and availability, without preauthorization, for counselling and tobacco cessation medications.

The inclusion of medications recommended in this guideline in the National List of Essential Medicines of a country can help increase tobacco users' access to these medications.

Because tobacco cessation medications have different advantages and disadvantages, with potential impacts on adherence, individuals and clinicians may prefer one medication over another or a particular combination. Thus, where feasible, having multiple medications available is preferable to increase patient and clinician choice.

Varenicline and combination NRT both have greater effectiveness compared with NRT monotherapy and bupropion. Where resources allow, countries may make the following options, which have higher likelihoods of quit success associated with their use, available for all tobacco users:

- single-agent varenicline or cytisine
- combination NRT (a long-acting and a short-acting agent)
- combination of any medication(s) and behavioural support.

Health-care providers should consider recommending these more-effective therapies routinely, without preconditions, but especially for selected patients, such as more-dependent tobacco users (for example, those who smoke more than 10 cigarettes per day) and those who have not been able to quit despite multiple attempts.

Tobacco cessation medications are effective in most adult tobacco users (see Annex 2 for special considerations regarding pregnant, less-dependent and hospitalized tobacco users).

It is important to advise all users of cessation medications to seek concurrent behavioural support; to provide them with instruction and follow-up to ensure proper use and adherence to the recommended duration of therapy; and to assist with the management of any side-effects or withdrawal symptoms (see Annex 2 for additional considerations regarding minimal availability, specific situations where shorter medication courses may be reasonable, the benefits of training and cost comparisons).

Because of the high negative impact of continued tobacco use on health and the challenges associated with quitting, minimizing withdrawal symptoms and maximizing the chances of success is important. Encouraging the use of combination pharmacotherapies that have higher effectiveness and providing instructions for the use of combination therapy (the potential additive side-effects and relevant coping strategies) to patients and health-care providers is an important clinical strategy.

Providing cost coverage without preconditions, such as requiring relapse on monotherapy, is also important to increase the proper use of combination therapy.

3.4. Interventions for smokeless tobacco use cessation

3.4.1. Recommendations

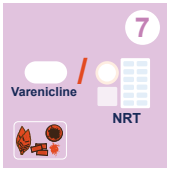
6. WHO recommends providing intensive behavioural support interventions (individual face-to-face counselling, face-to-face group counselling or telephone counselling) for smokeless tobacco users interested in quitting.

Strong recommendation;
moderate certainty



7. WHO recommends varenicline or NRT as pharmacological options for smokeless tobacco users interested in quitting.

Strong recommendation;
moderate certainty (varenicline)/
low certainty (NRT)



3.4.2. Overall questions

For adults who use smokeless tobacco, do behavioural support interventions or pharmacotherapies increase the chance of successful quitting? Does the effect vary by dose or duration of use, intervention/pharmacotherapy type, level of nicotine dependence, the quantity of smokeless tobacco used and gender?

3.4.3. Justification and evidence

The results of an updated Cochrane systematic review provided by Jonathan Livingstone-Banks (not yet published) showed that behavioural counselling, including telephone counselling, was more effective for long-term smokeless tobacco use cessation than usual care/minimal support (RR: 1.76; 95% CI: 1.43–2.16; 20 studies; 8252 participants). There was moderate-certainty evidence that varenicline helps more people to stop using smokeless tobacco products than placebo (RR: 1.35; 95% CI: 1.08–1.68; 2 studies; 508 participants), and low-certainty evidence that NRT helps more people stop using smokeless tobacco products than placebo or no medication (RR: 1.18; 95% CI: 1.05–1.33; 11 studies; 2562 participants). There was no clear evidence of a difference in smokeless tobacco use cessation rates between people taking bupropion and placebo (RR: 0.89; 95% CI: 0.54–1.44; 2 studies; 293 participants). Full details of the EtD tables can be found in the Web Annex: Evidence profiles.

The GDG concluded the following.

- There is moderate-certainty evidence that behavioural counselling, including telephone counselling, is more effective than usual care/minimal support for long-term smokeless tobacco use cessation, and that varenicline helps more people to stop using smokeless tobacco products than placebo. There is low-certainty evidence that NRT is more effective for smokeless tobacco use cessation than placebo or no medication. There is no clear evidence for any difference in smokeless tobacco use cessation rates between people taking bupropion and placebo.
- The balance of benefits against harms favours behavioural counselling for smokeless tobacco use cessation on the basis of large benefits (behavioural counselling versus usual care/minimal support, NNT: 9 for one additional case of long-term tobacco cessation) and trivial harms (due to the nature of the intervention and absence of harms reported in the trials).
- Decisions regarding behavioural counselling for smokeless tobacco use cessation are probably not preference sensitive (due to trivial harms), it requires moderate cost, and its feasibility and acceptability may vary for different stakeholders and in different settings, with potentially increased equity.
- The balance of benefits against harms favours varenicline over placebo/no medication for smokeless tobacco use cessation on the basis of large benefits (NNT: 9 for one more case of long-term tobacco cessation) and moderate harms (harms of pharmacotherapies previously reviewed and judged to be moderate).

- The balance of benefits against harms probably favours NRT over placebo/no medication for smokeless tobacco use cessation on the basis of moderate benefits (NNT: 20 for one additional case of long-term tobacco cessation) and small harms (harms previously reviewed and judged as small), and placebo/no medication over bupropion for smokeless tobacco use cessation on the basis of no benefit and moderate harms.
- Decisions regarding pharmacotherapy for smokeless tobacco use cessation are probably preference sensitive for varenicline and NRT (due to potentially significant benefits and harms), and not preference sensitive for bupropion; they require small to moderate costs and they are probably feasible; and varenicline and NRT are acceptable, with potentially increased equity.

3.4.4. Implementation considerations

It is important to raise awareness about the effectiveness of behavioural and pharmacological interventions for quitting smokeless tobacco use, the availability of such medications, and the recommended medications (NRTs and varenicline) among smokeless tobacco users and health-care providers. Because the evidence for the effectiveness of medications is not as certain for smokeless tobacco products as for cigarettes, behavioural support remains the primary intervention that should be offered to smokeless tobacco users, with and without medication use.

Support materials and training to health-care providers can be made available in local languages and include examples of smokeless tobacco use, especially in areas of high prevalence.

Dosing/duration and other tailoring considerations need to be developed for smokeless tobacco users.

3.5. Combination of behavioural and pharmacological treatments

3.5.1. Recommendation

8. WHO recommends combining pharmacotherapy and behavioural interventions to support tobacco users interested in quitting.

Strong recommendation;
high certainty



3.5.2. Overall questions

For adult tobacco users, are combined behavioural and pharmacological treatments more effective than behavioural interventions or pharmacological treatments alone? Does the effect vary by types of tobacco used, level of nicotine dependence, the quantity of tobacco used and gender?

3.5.3. Justification and evidence

A Cochrane systematic review of 83 studies published in 2019 *(37)*, which represented 29 536 participants, demonstrated a statistically significant benefit of behavioural support in addition to pharmacotherapy (RR: 1.15; 95% CI: 1.08–1.22; 65 studies; 23 331 participants) for long-term abstinence from tobacco, and this effect did not differ when subgroups were compared by type of pharmacotherapy or intensity of contact. This effect was similar in a subgroup of eight studies in which the control group received no behavioural support (RR: 1.20; 95% CI: 1.02–1.43; 4018 participants). Seventeen studies compared interventions matched by contact time, but that differed in terms of the behavioural components or approaches employed. Of the 15 comparisons, all included small numbers of participants and events, and only one detected a statistically significant effect, favouring a health education approach (which the authors described as standard counselling including information and advice) over a motivational interviewing approach (RR: 0.56; 95% CI: 0.33–0.94; 378 participants).

A Cochrane systematic review published in 2016 *(36)*, which examined 53 studies with a total of more than 25 000 participants, found high-quality evidence for a benefit of combined pharmacotherapy and behavioural support compared with usual care, brief advice or less-intensive behavioural support (RR: 1.83; 95% CI: 1.68–1.98). The pooled estimate for 43 studies that recruited participants in health-care settings (RR: 1.97; 95% CI: 1.79–2.18) was higher than the pooled estimate for 8 studies with community-based recruitment (RR: 1.53; 95% CI: 1.33–1.76).

The authors of the reviews did not detect differences between subgroups defined by motivation to quit, treatment provider, number or duration of support sessions, or take-up of treatment.

The GDG concluded the following.

- There is high-certainty evidence of a significant benefit of combined pharmacotherapy and behavioural support compared with usual care, brief advice or less-intensive behavioural support, and a significant benefit of behavioural support when given in addition to pharmacotherapy.
- The balance of benefits against harms favours combined intervention versus behavioural support or pharmacotherapy alone on the basis of moderate to large benefits (combination intervention versus usual care/brief intervention, NNT: 14 to achieve one additional case of long-term abstinence; combination intervention versus pharmacotherapy, NNT: 38 for one more case of long-term abstinence) and trivial harms (harms of the added behavioural component intervention expected to be trivial).
- Decisions regarding combination interventions are not preference sensitive (trivial harms versus pharmacotherapy alone), they require moderate costs and they are probably feasible, with the acceptability varying (depending on the willingness of patients to receive, and clinicians and health systems to provide, multiple treatments), and potentially increased equity.

3.5.4. Implementation considerations

Developing or increasing the capacity of health-care providers, health systems and population-level services – such as quit lines – to provide both medication and behavioural support is essential for the delivery of interventions. Wide availability and access to both treatment options needs to be ensured, including cost coverage. It is important that health-care providers are informed about the benefits of concurrent use of behavioural support and medications, so that they can encourage their patients to use them if they are not able to provide them directly.

Combination treatment is also optimal for smokeless tobacco users.

Although the evidence for their effectiveness is not as strong, countries may also benefit by providing adjunct mobile phone apps, websites, and AI-supported and text-based interventions that include behavioural support and information regarding the proper use of medications, in addition to individual, telephone and group counselling.

3.6. Traditional, complementary and alternative therapies

3.6.1. Statement

9. Evidence is insufficient to make a recommendation for or against traditional, complementary and alternative therapies for tobacco users interested in quitting. If these therapies are utilized by tobacco users interested in quitting, ensure that they are offered a comprehensive approach to support tobacco cessation, including behavioural support and/or pharmacotherapy.



3.6.2. Overall questions

For adult tobacco users, do traditional, complementary and alternative therapies increase the chance of successful quitting? Does the effect vary by types of tobacco used, duration of use, quantity of tobacco used and gender?

3.6.3. Justification and evidence

An updated systematic review of 71 studies found low-certainty evidence that traditional filiform needle acupuncture, acupressure, laser acupuncture, and acupoint catgut embedding appear to be safe and effective in achieving short-term smoking cessation: filiform needle acupuncture versus sham acupuncture (RR: 1.44; 95% CI: 1.02–2.02; 1358 participants); acupressure versus conventional therapy (RR: 1.46; 95% CI: 1.14–1.87; 595 participants); acupressure versus sham acupressure (RR: 2.44; 95% CI: 1.13–5.25; 210 participants); laser acupuncture versus sham laser acupuncture (RR: 2.25; 95% CI: 1.23–4.11; 160 participants); and acupoint catgut embedding versus bupropion/varenicline (RR: 0.99; 95% CI: 0.70–1.40; 177 participants). There was low-certainty evidence suggesting that mindfulness, hypnotherapy and yoga fail to show a better effect than matched-intensity or less-intensive behavioural therapy in improving short-term abstinence rates: mindfulness versus matched-intensity behavioural therapy (RR: 0.97; 95% CI: 0.71–1.33; 955 participants) or less-intensive behavioural therapy (RR: 1.19; 95% CI: 0.65–2.19; 813 participants); hypnotherapy versus attention-matched behavioural therapy (RR: 1.21; 95% CI: 0.91–1.61; 957 participants), brief behavioural interventions (RR: 0.98; 95% CI: 0.57–1.69; 269 participants) or pharmacotherapy (RR: 1.68; 95% CI: 0.88–3.20; 197 participants); and yoga versus matched-intensity smoking cessation treatment (RR: 1.62; 95% CI: 0.53–4.94; 98 participants).

The GDG concluded the following.

- There is moderate-certainty evidence that acupressure does not increase long-term tobacco abstinence rates compared with sham acupressure; there is very low-certainty evidence that mindfulness does not improve long-term tobacco abstinence rates compared with less-intensive behavioural therapy. There is low-certainty evidence for all other comparisons and outcomes.
- The balance of benefits against harms probably favours acupuncture or acupressure versus sham acupressure on the basis of moderate short-term benefits and trivial harms, and the balance of benefits against harms is uncertain for long-term benefits of acupuncture and acupressure, and for other interventions.
- There is insufficient evidence to make a recommendation for or against traditional, complementary and alternative therapies for tobacco cessation.

3.6.4. Implementation considerations

Evidence for the efficacy of acupuncture, hypnotherapy, Chinese herbal medicines, mindfulness and yoga for tobacco cessation treatment was systematically examined. Evidence was found to be insufficient to make a recommendation for or against these therapies.

In countries where these therapies are used by tobacco users interested in quitting, use of complementary, alternative and traditional therapies may benefit from being embedded within a comprehensive approach to support tobacco cessation, including behavioural support, digital interventions and/or pharmacotherapy.

3.7. System-level interventions and policies

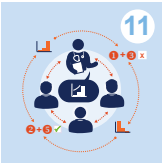
3.7.1. Recommendations

10. WHO recommends that all health-care facilities include tobacco use status and use of tobacco cessation interventions in their medical records (including EHRs), to facilitate provider interaction with tobacco-using patients and increase adoption and maintenance of evidence-based treatment interventions.



Strong recommendation;
moderate certainty

11. WHO recommends training of all health-care providers on delivery of evidence-based cessation interventions, with ongoing prompting and feedback, in their routine medical practices at all levels of health-care settings.



Strong recommendation;
moderate certainty

12. WHO recommends that evidence-based tobacco cessation interventions be provided at no or reduced cost to all tobacco users interested in quitting. No cost is strongly preferred over reduced cost.



Strong recommendation;
moderate certainty

3.7.2. Overall questions

Can including tobacco use status in medical records increase the performance of health-care providers in identifying and intervening with patients who use tobacco and advising them to quit? Is identification more effective if coupled with other clinic-based care components that remind and incentivize providers to provide brief advice, and assistance or referral? Can training health-care providers on tobacco cessation increase offers of advice and help patients quit? Do interventions that reduce the cost of tobacco cessation services for patients increase quit rates, the likelihood of quit attempts or the use of services among adult tobacco users?

3.7.3. Justification and evidence

A Cochrane systematic review, which looked at seven cluster RCTs *(38)*, demonstrated that organizational changes helped people to quit smoking for at least 6 months (two studies); there were significant improvements in the documentation of smoking status (one study), quit-line referral (two studies) and quit-line enrolment (two studies). Positive effects were also indicated for other secondary end-points, such as asking about tobacco use (three studies), advising to quit (three studies), provision of cessation counselling (four studies), and provision of NRT or other pharmacotherapy (two studies).

A separate Cochrane systematic review of 16 studies tested the use of EHRs for smoking cessation support actions by clinicians *(39)*. The authors found only modest improvements in some of the recommended clinician actions on tobacco use including documenting smoking status, giving advice to quit, assessing interest in quitting and providing assistance (including referral). None of the studies examined the direct effect on cessation outcomes.

In terms of the effectiveness of training health-care providers in smoking cessation, a Cochrane systematic review of 17 studies *(40)* demonstrated that smokers treated by trained health-care providers had a statistically significantly higher chance of quitting for at least 6 months, with increased point prevalence of smoking cessation (OR 1.41; 95% CI: 1.13–1.77; 14 studies; 13 459 participants) and increased continuous abstinence (OR 1.60; 95% CI: 1.26–2.03; 8 studies; 9443 participants). The subgroup analysis found that health-care providers who had received training were more likely to perform tasks of smoking cessation than untrained controls, including: asking patients to set a quit date (OR 4.98; 95% CI: 2.29–10.86; 8 studies; 4332 participants), making follow-up appointments (OR 3.34; 95% CI: 1.51–7.37; 7 studies; 3114 participants), counselling of

smokers (OR 2.28; 95% CI: 1.58–3.27; 14 studies; 8531 participants), provision of self-help material (OR 3.52; 95% CI: 1.90–6.52; 9 studies; 4925 participants) and prescribing a quit date (OR 14.18; 95% CI: 6.57–30.61; 3 studies; 1172 participants). No evidence of an effect was observed for the provision of nicotine gum/ replacement therapy (OR 1.57; 95% CI: 0.87–2.84; 9 studies; 5073 participants).

A Cochrane systematic review of 17 studies examined the effect of financial interventions directed at smokers, health-care providers, or both *(41)*. The results showed that full financial interventions directed at smokers had a favourable effect on abstinence at 6 months or longer when compared with no intervention (RR: 1.77; 95% CI: 1.37–2.28; 9333 participants); an increased number of participants attempted to quit when compared with no interventions (RR: 1.11; 95% CI: 1.04–1.17; 9065 participants); and there was increased use of smoking cessation treatments when compared with no interventions with regard to various pharmacological and behavioural treatments: NRT (RR: 1.79; 95% CI: 1.54–2.09; 9455 participants), bupropion (RR: 3.22; 95% CI: 1.41–7.34; 6321 participants) and behavioural therapy (RR: 1.77; 95% CI: 1.19–2.65; 9215 participants). The partial-coverage financial interventions directed at smokers were more effective in increasing abstinence than no intervention (RR: 1.27; 95% CI: 1.02–1.59; 7108 participants) and had a small positive effect on the use of bupropion when compared with no coverage (RR: 1.15; 95% CI: 1.03–1.29; 6765 participants), but there was insufficient evidence that partial-coverage financial interventions increased quit attempts compared with no interventions (RR: 1.13; 95% CI: 0.98–1.31; 6944 participants). There was no evidence that full-coverage financial interventions increased smoking abstinence compared with partial-coverage interventions (RR: 1.02; 95% CI: 0.71–1.48; 5914 participants).

There was no clear evidence of an effect on smoking cessation when we pooled two trials of financial incentives directed at health-care providers (RR: 1.16; 95% CI 0.98–1.37; 2311 participants). Financial interventions directed at health-care providers increased the use of behavioural therapy (RR: 1.69; 95% CI: 1.01–2.86; 25 820 participants), but not the use of NRT and/or bupropion (RR: 0.94; 95% CI: 0.76–1.18; 2311 participants).

The GDG concluded the following.

- There is moderate-certainty evidence for positive effects of using EHRs on process outcomes (smoking cessation support actions) including documenting smoking status, giving advice to quit, assessing interest in quitting and providing assistance including referral; there is very low-certainty evidence that the use of EHRs improves smoking cessation outcomes.
- The balance of benefits against harms favours the use of health records, including EHRs, on the basis of moderate improvement in process outcomes (but effects on cessation outcomes are unknown), but there was insufficient evidence to directly determine the effects on smoking cessation and trivial harms (the systematic reviews did not assess harms but, given the type of interventions, harms were judged likely to be trivial).
- Decisions regarding the use of medical records, including EHRs, to support tobacco cessation are not preference sensitive (due to trivial harms), their required costs vary (depending on the type of medical records and how they are used), and they are probably feasible and acceptable, with probably increased equity.
- There is moderate-certainty evidence that training health-care providers in tobacco cessation helps improve long-term quit rates among smokers treated by trained health-care providers; there is low-certainty evidence that training health-care providers improves their performance when carrying out smoking cessation tasks.
- The balance of benefits against harms favours training of health-care providers in tobacco cessation on the basis of:
  - moderate to large benefits (training health-care providers, including prompting and feedback versus no training, NNT: 34–67 for one additional long-term smoking cessation; training associated with increased number of smokers counselled, NNT: 5.0; asked to make a follow-up appointment, NNT: 4.3; receiving self-help material, NNT: 4.6; and receiving NRT, NNT: 10.4); and
  - trivial harms (the systematic reviews did not assess harms but given the type of intervention harms were judged trivial).

- Decisions regarding the use of training of health-care providers for tobacco cessation are not preference sensitive (due to trivial harms), it requires small to moderate costs (depending on the type of training, how many health-care providers are trained, and the degree of ongoing prompting and feedback), and it is probably feasible and acceptable, with potential positive impact on equity.
- There is moderate-certainty evidence that full-coverage financial interventions directed at smokers increase the proportion of smokers who attempt to quit and succeed in long-term quitting. Partial-coverage interventions are also more effective in increasing abstinence than no intervention.
- The balance of benefits against harms favours financial coverage directed at individuals on the basis of small to large benefits (full financial coverage versus no coverage, NNT: 15 to achieve one more case of long-term smoking cessation; for partial coverage versus no coverage: smaller benefit observed) and trivial harms (the systematic reviews did not assess harms, but given the type of interventions harms were judged likely to be trivial).
- Decisions regarding cost coverage of tobacco cessation services are not preference sensitive (due to trivial harms), it requires small to moderate costs (depending on the degree of financial coverage, types of treatment covered and utilization rate), and it is probably feasible and acceptable, with probably increased equity.

3.7.4. Implementation considerations

3.7.4.1. Using medical records

Many countries are in the process of implementing EHRs in multiple health-care settings. This provides an important opportunity to facilitate tobacco cessation interventions and ensure that the collection and recording of tobacco use status are incorporated in the new systems. This will enhance both the delivery of cessation support and health-care delivery in general, given that tobacco use impacts a host of conditions.

All health-care facilities can develop mechanisms for the integration of tobacco use status collection into their electronic health information systems. This can include enhancements to facilitate and document provider interactions with patients who use tobacco, as well as facilitating follow-up (such as cessation medication prescription generation, patient cessation materials embedded in follow-up instructions, and referrals to clinic and community counselling resources). These EHR enhancements can help ensure the adoption and maintenance of evidence-based tobacco cessation interventions.

Where EHRs are not in place or are in the process of being implemented, similar paper-based documentation and prompting systems can be effective at increasing provider delivery of brief advice, assistance and follow-up.

The evidence for medical record effectiveness generally included additional support for providers (see the Section 3.7.4.2 below).

3.7.4.2. Training health-care providers

The health-care setting provides an ideal opportunity to encourage tobacco users seeking health care to quit tobacco use. Integrated cessation advice by trained health-care providers will ensure all patients are assessed, counselled, advised on quitting tobacco use and referred to intensive tobacco cessation services (for example, national toll-free quit lines).

Health-care providers at all levels can offer brief cessation advice; training them ensures the advice is more effective and evidence-based, and that they are aware of additional cessation support resources such as intensive counselling and medications. These trainings can be brief, but are more impactful and the effects more sustainable when combined with additional health systems support.

- EHRs and/or paper health records and clinic routines capture tobacco status, and prompt advice to quit tobacco.

- Clinic and hospital systems integrate tobacco cessation into routine care by using a team approach. For instance, if patients are in an examination room or have their blood pressure or temperature taken by a medical assistant or aide, that person may ask about tobacco use status and record information on a chart. More-intensive follow-up or referral may be provided by other personnel.
- Availability of cessation tools (medications, referral to support groups, screening tools) to enhance cessation interventions by trained health-care providers.

Here are links to training materials developed by WHO.

- WHO e-learning course on brief tobacco interventions for primary care providers. https://www.campusvirtualsp.org/en/node/30781
- WHO training package: *Strengthening health systems for treating tobacco dependence in primary care*. https://www.who.int/publications/i/item/strengthening-health-systems-for-treating-tobacco-dependence-in-primary-care
- WHO training package: *Training for tobacco quit line counsellors: telephone counselling*. https://iris.who.int/bitstream/handle/10665/113145/9789241507264_eng.pdf?isAllowed=y&sequence=1

3.7.4.3. Reducing tobacco user treatment costs

Countries vary widely in how and by whom medical costs are paid. Whatever the cost support systems for health-care treatments are in a country, it is important to remove cost barriers to increase the utilization of tobacco cessation services.

Since health insurance is only available to a minority of tobacco users in most LMICs, other mechanisms may need to be deployed to decrease or eliminate cost and access barriers. Countries may consider using a portion of tobacco tax revenues to pay for some tobacco cessation services, such as national toll-free quit lines. Where health insurance exists, both public and private insurers may consider providing full-cost coverage and availability, without preauthorization, for counselling and cessation treatment medications.

In countries or systems with resource scarcity concerns regarding the covering of the cost of tobacco dependence treatments, it is important to raise awareness of the powerful benefits to be gained from making tobacco dependence treatments available (for example, viewing tobacco dependence and treatment from a chronic disease paradigm) among fiscal decision-makers. A chronic disease perspective suggests that coverage and accessibility should be determined by recognizing tobacco dependence as a very serious condition that causes major excess morbidity, mortality, health-care costs and societal costs, and recognizes that effective treatments exist with modest costs compared with comparable chronic conditions (see Annex 2 for details on the case for cost coverage and additional considerations to increase policy effectiveness).

3.8. Overarching guideline implementation considerations

Tobacco users will be more interested in attempting to quit, and more successful in quit attempts, when countries implement comprehensive tobacco control measures, as outlined in MPOWER, that make the environment more conducive to quitting. Furthermore, for countries who are investing in tobacco use cessation, comprehensive tobacco control measures will improve the effectiveness and efficiency of these efforts by supporting people who use tobacco to remain abstinent. These measures, known as MPOWER, include protecting people from tobacco smoke; warning about the dangers of tobacco; enforcing bans on tobacco advertising, promotion and sponsorship; and raising taxes on tobacco *(18)*.

- Thus, in addition to working to increase access to tobacco cessation interventions, countries, health systems and health-care providers can actively support programmes and policies likely to promote tobacco cessation.
- Interventions designed to increase equity and the impact of tobacco cessation services should take into consideration not only the effectiveness of interventions but also their reach (total percentage of tobacco users who utilize an intervention), especially across vulnerable populations.

Tobacco cessation interventions are more likely to be adopted if policy-makers develop policies that remove barriers and encourage their use.

- Increased availability, reimbursement, and cost support for behavioural and pharmacological interventions.
- Training and system support to facilitate the routine identification, assessment and provision of tobacco cessation services.
- Quality assurance and improvement metrics and feedback, similar to those used to improve chronic disease outcomes.

Individuals interested in quitting may be informed about which interventions can maximize their chance of success, taking into account individual preferences where relevant.

- There are four treatments with a higher rate of quit success:
  - combining any medication with counselling;
  - combining two medicines, such as two forms of NRT (longer-acting and shorter-acting), or bupropion in combination with NRT or varenicline;
  - using partial agonists of $\alpha 4\beta 2$ nicotinic receptors (varenicline and cytisine); and
  - increasing the intensity of counselling above a minimal level (benefits increase for with multisession counselling of up to five sessions, and for a duration of up to at least 10 minutes per session).
- Wherever feasible and acceptable, clinicians and tobacco users interested in quitting should be encouraged to use treatments associated with the highest success rates.
- However, the chances of quit success are increased by the use of any of the individual medications endorsed by this guideline.
- Chances of success are increased by using any form of counselling, with similar effects.
- Chances of success may be increased by using certain forms of digital support (text messaging, website, apps and AI software programs), but this may depend on the characteristics of the specific programme, and the effect may be smaller than with medications or live counselling.

Promoting tobacco cessation services.

- If treatment accessibility is built into public health campaigns, such as the inclusion of a quit-line number in media campaigns or on tobacco product packaging, the promised form of cessation support should be reliably provided.
- Where the primary campaign aim is to increase quit attempts, the dose of cessation support can be more modest to enable resources to be available to larger numbers of tobacco users. Examples include providing brief single-session telephone counselling or 1–2-week so-called starter kits of medications, rather than multisession counselling or full-course medication. Providing digital support, such as a link to a mobile text-messaging tobacco cessation programme or a website, to quit-line callers is another option. Triaging of intervention intensity during periods that a quit line has high call volumes may enable all callers to receive at least some support.

4. Evidence to recommendations

In accordance with the GRADE approach, the GDG made each recommendation on the basis of their assessments or judgements of all these criteria: whether the problem is a priority, the magnitude of the desirable and undesirable effects, the certainty of the evidence, the balance between desirable and undesirable effects, consideration of how people value the intervention, resource requirements, the certainty of the evidence for the costs, cost-effectiveness, consideration of impacts on equity, and acceptability and feasibility *(42)*. Given the similarity of the issues, the considerations discussed are consolidated and presented here.

The strengths of the recommendations were primarily based on the assessed certainty of evidence and the balance of benefits against harms. Recommendations were graded strong if the certainty of evidence was high or moderate, and the balance of benefits against harms was judged to be "favours intervention"; and conditional if the certainty of evidence was low or very low, and the balance of benefits against harms was judged as "probably favours intervention" or "uncertain".

All decisions about the recommendations were reached by consensus through discussion. The GDG reached consensus on each recommendation, including on the strength of the recommendations; voting was not required.

4.1. Assessment of the certainty of evidence

The GRADE framework was used by the GDG to examine the certainty or quality of evidence for each outcome identified in the PICOs *(26)*. The overall certainty of the evidence for each intervention was assessed, taking into consideration the risk of bias, inconsistency, imprecision, indirectness of the evidence and publication bias across each outcome. The long-term quit rate was prioritized as the most critical outcome, followed by outcomes related to the provision of tobacco cessation interventions (identifying patients who use tobacco, advising tobacco users to quit, and the provision of behavioural counselling or medication support), and then other important outcomes (for example, the short-term quit rate and quit attempt rate) as well as harms. EtD tables detailing this information for each PICO are available in the Web Annex: Evidence profiles.

4.2. Benefits and harms

The development of the recommendations included an assessment of the benefits and harms (AEs or risks). Where there was limited evidence, decisions were based on the expertise of the GDG. Overall, for tobacco cessation interventions it was concluded that the benefits outweighed the potential harms.

The benefits of the behavioural tobacco interventions (including digital modalities) were judged to be large or moderate, except for internet-based tobacco cessation interventions (for which the benefits were judged to be small). Their harms were not addressed in systematic reviews and the GDG judged their harms to be trivial/minimal on the basis of the types of interventions provided. Pharmacological interventions were judged to have large or moderate benefits compared with placebo or no intervention. The harms of NRT were judge to be small with mild AEs. Bupropion and varenicline were judged to have moderate harms with some SAEs reported, and the harms of cytisine were judged to be trivial with no SAEs reported. The traditional, complementary and alternative therapies for tobacco cessation were judged to have uncertain long-term benefits and trivial harms, with no SAEs reported. The GDG judged the system-level interventions and policies to have large or moderate benefits and trivial harms.

4.3. Values and preferences

Overall, The GDG judged that there was little or no uncertainty about preferences regarding the main outcomes, including long-term quit rates and the provision of tobacco cessation interventions and, as such, the GDG judged that decisions to utilize most recommended interventions were not sensitive to values or preferences regarding outcomes, because harms were minimal/trivial and/or benefits greatly outweighed harms. The GDG considered that decisions regarding pharmacotherapy (bupropion, varenicline, combination NRT, bupropion plus NRT and bupropion plus varenicline) were "probably preference sensitive" because of "moderate harms with some uncertainty regarding serious harms", "small increased risk of SAEs and treatment withdrawals", or "small harms with uncertainty regarding SAEs".

4.4. Cost-effectiveness and resource requirements

Judgements on costs/resources were based on GDG expertise/experience in the interventions as well as known costs (for example, the costs of pharmaceutical products). The cost-effectiveness of financial interventions was the only type of intervention assessed for cost-effectiveness in a systematic review *(41)*. The economic evaluation showed that costs per additional quitter were low or moderate, ranging from US$ 97 to US$ 7646 for a comparison of full coverage with partial or no coverage. Some individual studies on cost-effectiveness of pharmacological and behavioural interventions, including analysis from WHO, were identified and informed discussion of the resource implications of the recommendations in different settings. The costs per life year saved for different interventions were estimated as follows: 174–212 pounds sterling for brief advice *(45)*; 30–50 US dollars (Thailand) *(46)* and 139 Australian dollars (Australia) *(47)* for quit-line services; 141–176 pounds sterling for cessation interventions delivered via mobile text-messaging *(48)*; 2229–9811 US dollars for intensive individual or group counselling *(49)*; 1447–11 374 US dollars for NRT (often combined with counselling) *(49)*; 1438–4743 US dollars for bupropion (often combined with counselling) *(49)*; and 1696 US dollars for varenicline *(50)*. Cytisine was estimated to be less cost-effective than brief advice, but more cost-effective than varenicline *(51,52)*. In addition, to support WHO Member States to achieve the global targets for NCD prevention and control by 2030, WHO updated Appendix 3 of the WHO *Global action plan for the prevention and control of noncommunicable diseases 2013-2030*, through which WHO recommended a list of very cost-effective (so-called best-buy) and affordable interventions, including six tobacco cessation interventions: brief advice, national toll-free quit-line services, cessation interventions delivered via mobile text messaging (mCessation), NRT, bupropion and varenicline *(53)*. WHO-CHOICE economic analysis indicated that the three population-wide behavioural interventions are very cost-effective in LMICs with banded cost-effective ratios of less than 100; NRT, bupropion and varenicline are also affordable in LMICs (banded cost-effective ratios less than 100 in low-income countries and 100–500 in middle-income countries) *(53)*.

The available evidence and the expert opinion of the GDG recognize that cost-effectiveness favours the use of brief advice; intensive individual, group or telephone counselling; text-messaging cessation interventions, pharmacological interventions; a combination of behavioural and pharmacological treatments; and financial interventions. The GDG judged that the cost-effectiveness of three digital tobacco cessation interventions (internet-based, smartphone apps and AI-based software interventions); traditional, complementary and alternative therapies for tobacco cessation; the use of health records and the training health professionals in tobacco cessation was uncertain because there was no information available. Further, it was acknowledged that the resources required for brief advice are negligible given the nature and intensity of the intervention; the resources required for intensive individual, group or telephone counselling; pharmacological interventions; a combination of behavioural and pharmacological treatments; and system-level interventions are moderate to small because of variability in the type and intensity of interventions and different settings. The GDG judged that the costs of developing digital tobacco cessation interventions are moderate, but that intervention delivery costs are small.

The GDG discussed several implementation strategies that could help governments develop and deliver the guideline-recommended tobacco cessation services at a lower cost and maximize efficiency. The first is to implement tobacco cessation measures in conjunction with other demand-reduction tobacco control policies. These policies promote tobacco cessation by encouraging quitting and creating a supportive environment. A typical example of synergistic efforts is including a quit-line number on cigarette packs and mass media

anti-tobacco campaigns, resulting in a significant increase in demand for tobacco cessation services. The second is to use existing infrastructure to develop cessation support. Integrating brief advice into health-care programmes in primary care has the potential to reach around 80% of all tobacco users in a country *(54)*, which is both practical and economical. Utilizing pre-existing infrastructure (for example, existing call centres) to implement national toll-free quit-line services can help governments minimize the costs of development and operation. Finally, prioritizing population-level tobacco cessation interventions is an important strategy to reach as many tobacco users as possible at the lowest possible cost, and to have the greatest impact on reducing the prevalence of tobacco use at the population level. *Updating Appendix 3 of WHO Global NCD Action Plan 2013-2030* recommended integrating brief advice into primary care, national toll-free quit-line services and mCessation as three best-buy interventions *(53)*. In 2021, WHO developed the global investment case to explain why countries should invest in tobacco cessation from health and economic perspectives. A return-on-investment analysis of 124 LMICs showed that these population-level interventions cost little but have significant returns *(55)*. On average, countries only need to spend US$ 0.21 per person per year on these interventions to witness an estimated 88 million individuals quitting smoking by 2030, leading to 1.4 million lives saved. If countries spend an additional US$ 1.49 per person per year on NRT, bupropion and varenicline, 1.3 million more lives could be saved by 2030. Overall, the GDG concluded that the benefits of implementing the recommendations outweigh the costs.

4.5. Equity, acceptability and feasibility

The GDG discussed each recommendation, considering whether implementing the recommended intervention would impact health equity, whether the intervention is acceptable to all stakeholders and whether the intervention is feasible.

The general approach that the GDG used to assess equity was based on providing access to the recommended interventions for all tobacco users who could benefit, as well as providing additional choices for tobacco users. The GDG's judgements regarding equity require that recommended interventions are not selectively available based on socioeconomic status, insurance status or other social determinants.

The GDG was confident that brief advice; intensive individual, group and telephone counselling; all pharmacological interventions; and system-level interventions may increase equity by providing additional treatment options or increasing the provision of effective tobacco cessation interventions for people who might otherwise have no access to them. Digital tobacco cessation interventions may increase equity in populations with digital access, but may reduce equity in populations without digital access. Traditional, complementary and alternative therapies may increase equity for those who otherwise would not have access to proven tobacco cessation services, but they might have no or even negative impact on equity if evidence-based therapies are not provided. In developing this guideline, the decision was taken to explicitly include consideration of vulnerable populations, such as those living with chronic conditions and/or disability. The GDG and SG included members representing such groups. It was noted that a comprehensive approach for implementation of the recommendations to make a variety of treatment options available is the best way to ensure there are always tobacco cessation interventions for all, including people living with disability, and socioeconomically and other disadvantaged people. For example, telephone counselling or digital tobacco cessation interventions that do not require face-to-face meetings are most likely to be accessed and used by individuals with mobility impairments.

The GDG judged that the individual tobacco cessation interventions recommended in this guideline are probably acceptable to all stakeholders. Patient and clinician acceptability of a combination of behavioural and pharmacological interventions – and of traditional, complementary and alternative therapies – depends on willingness, attitudes and beliefs regarding these interventions. In terms of feasibility, the GDG judged that all tobacco cessation interventions are "probably yes" or "yes", except for group counselling and traditional, complementary and alternative therapies, the feasibility of which varies in different settings. The behavioural and pharmacological interventions recommended in this guideline have been widely implemented and shown to be feasible. It was also noted that more-intensive interventions, combination therapies and some of the financial interventions are less feasible. Digital tobacco cessation interventions are less feasible in subpopulations with less access to digital services or technologies.

5. Research needs

The GDGs discussed important evidence gaps for future research, particularly the fact that there remains limited evidence from LMICs. Future research priorities are highlighted as follows.

General

- Explore strategies to increase quit attempts and to maximize the impact of available evidence-based cessation support on tobacco cessation at the population level.
- Examine the enabling factors and barriers to the implementation and adoption of the guideline recommendations in LMICs.
- Monitor, evaluate and report on implementation progress regarding tobacco cessation policies and programmes, especially in LMICs, including the availability and use of tobacco cessation medications, counselling, digital tobacco cessation interventions, community and health systems support, and trainings by country and region.
- Examine the impacts of tobacco cessation service provision or implementation on equity.
- Conduct implementation research in local contexts to identify health system barriers and to develop strategies, aligned with WHO health system building blocks to address the barriers to implementation and scale-up.

Policy

- Explore effective strategies to increase the relative priority of tobacco cessation and policy options.
- Explore strategies to reduce or eliminate the cost of tobacco cessation interventions, and increase availability, reach and equitable access.

Systems

- Assess strategies for the integration of brief advice into public health systems in LMICs.
- Assess the effectiveness of tobacco cessation interventions delivered by community health workers.
- Identify approaches for triaging and tailoring of a combination of interventions to increase efficiency and effectiveness.
- Explore which system-level approaches and policies work best to increase the use of evidence-based tobacco cessation services and increase quit attempts in LMICs.
- Identify the combination of interventions that can achieve goals relating to affordability and impact, and that are administratively feasible to implement and scale up.

Counselling interventions

- Compare different counselling approaches and characteristics to identify any factors that may increase effectiveness or efficiency:
  - theoretical basis, such as: cognitive behavioural therapy, acceptance and commitment therapy, dialectical and behavioural therapy, motivational interviewing, etc.;
  - elements of practical counselling (that is, problem-solving, skills-building) and provision of support;
  - counselling that is tailored to specific sociocultural backgrounds; and
  - timing, duration and frequency of counselling contact (such as weekly or monthly versus quit-date focused).

Digital interventions

- Additional research on smartphone apps, AI-based interventions or internet-based interventions for tobacco cessation.
- Examine which design features and functions across modalities of digital tobacco cessation interventions (interactivity, tailoring, gamification, frequency, duration etc.) maximize the chance of successful quitting.

Medications

- Explore ways to increase medication use (such as over-the-counter strategies) and to increase use of combinations of behavioural support and pharmacotherapy.
- Examine the effectiveness and possible side-effects of higher dosing, as well as longer or shorter durations of pharmacotherapy, on both quit attempts and quit success.
- Explore the role of medication use for less nicotine-dependent tobacco users.
- Systematically collect information on tobacco cessation medication availability and cost coverage policies in countries.
- Monitor AEs among tobacco users who use tobacco cessation medications to quit, especially for medications that are not well studied and for longer durations.

Cost and cost-effectiveness

- Conduct or identify cost-effectiveness analyses of tobacco cessation interventions, including newer medications like cytisine, and modality combinations such as dual pharmacotherapies and counselling/medication delivered together, with special emphasis on conducting analyses relevant to LMICs.
- Examine the effectiveness and cost-effectiveness of strategies that use a chronic disease/addiction model in people who are more dependent on tobacco, and the integration of tobacco cessation into health programmes.
- Conduct studies on the use of financial incentives to promote tobacco cessation.

Strategies and methods

- Identify effective treatment methods for stopping the use of smokeless tobacco products or waterpipes.
- Conduct more well-designed studies of traditional, complementary and alternative therapies for tobacco cessation, including looking at noninferiority to evidence-based behavioural counselling.
- Explore effective tobacco cessation strategies and methods for adolescents, people who are pregnant and people who use e-cigarettes (including dual users), including the use of AI-based interventions.

Products

- Quantify nicotine concentrations for different modes of delivery (for example, waterpipe smoking, e-cigarettes and smokeless tobacco).
- Additional research on the efficacies of pharmacotherapies and behavioural support for smokeless tobacco cessation, especially in LMICs with high prevalence.

6. Adoption, dissemination, implementation and evaluation

This guideline will be launched at a suitable event or date, such as a conference or World No Tobacco Day. A press conference will be organized and social media will be employed to disseminate the recommendations. The launch of the guideline will be widely publicized through regional and country offices, the WHO global and regional websites, and by relevant United Nations agencies and partners. Summary documents and information sheets in six official United Nations languages in the format of infographics, social media elements and web-stories will be developed as a package for rapid and wide dissemination of the guideline.

A practical guide for developing national treatment guidelines for tobacco cessation will be developed to guide WHO Member States on how to adopt and implement this guideline to promote tobacco cessation and tobacco dependence treatment in a variety of settings. In adopting and implementing this guideline, national authorities will need to consider whether local adaptation, including adaptation for specific population groups or settings, is required. This may include the adaptation of practical recommendations for developing comprehensive tobacco cessation and treatment systems using a stepwise approach, and consideration of social and cultural norms, including how to make appropriate provisions of tobacco cessation services in the local setting.

To support national authorities and other stakeholders in implementing the guideline at the country level, the above-mentioned practical guide will provide links to online technical resources and best-practice examples that WHO has developed to promote tobacco cessation in different settings. A series of regional webinars will be organized to raise awareness and support WHO Member States in capacity-building for implementation of the guideline.

WHO has published a report on the global tobacco epidemic every 2 years since 2008 *(18)*. This biennial report allows WHO to assess the adoption of the recommendations into national guidelines and whether these have been implemented at the country level after the guideline publication. The WHO reports also include data on the prevalence of tobacco use in all WHO Member States, which allows evaluation of the impact of the guideline on reducing the prevalence of tobacco use in each country, as well as the tracking of progress relating to the achievement of the WHO's Global Programme of Work Triple Billion targets and Output 3.2.1 Countries enabled to address risk factors through multisectoral actions.

The SG will monitor the literature, particularly in the field of digital tobacco cessation interventions and pharmacotherapies, and assess the need for further reviews of the literature and updating of the guideline. This guideline will be updated after 5 years unless further research in the area provides additional evidence to warrant an earlier update.

References

1. WHO global report on trends in prevalence of tobacco use 2000–2030. Geneva: World Health Organization; 2024 (https://iris.who.int/bitstream/handle/10665/375711/9789240088283-eng.pdf?sequence=1, accessed 16 January 2024).

2. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223–49 (https://doi.org/10.1016/S0140-6736(20)30752-2).

3. Goodchild M, Nargis N, Tursan d'Espaignet E. Global economic cost of smoking-attributable diseases. Tob Control. 2018;27(1):58–64 (https://doi.org/10.1136/tobaccocontrol-2016-053305).

4. WHO Framework Convention on Tobacco Control. Geneva: World Health Organization; 2003 (https://iris.who.int/bitstream/handle/10665/42811/9241591013.pdf?sequence=1, accessed 18 October 2023).

5. Guidelines for implementation of Article 14. WHO Framework Convention on Tobacco Control. Geneva: World Health Organization; 2022 (https://fctc.who.int/publications/m/item/guidelines-for-implementation-of-article-14, accessed 30 June 2022).

6. Asma S, Mackay J, Song SY, Zhao L, Morton J, Palipudi KM, et al. The GATS Atlas. Atlanta (GA): CDC Foundation; 2015 (https://www.gatsatlas.org/, accessed 1 July 2022).

7. WHO report on the global tobacco epidemic 2021: addressing new and emerging products. Geneva: World Health Organization; 2021 (https://iris.who.int/bitstream/handle/10665/343287/9789240032095-eng.pdf?sequence=1, accessed 16 October 2023). Licence: CC BY-NC-SA 3.0 IGO.

8. Abdullah ASM, Husten CG. Promotion of smoking cessation in developing countries: a framework for urgent public health interventions. Thorax. 59:623;2004–30 (https://doi.org/10.1136/thx.2003.018820).

9. 6C4A Disorders due to use of nicotine. In: International statistical classification of diseases and related health problems, 11th edition. Geneva: World Health Organization; 2019 (https://icd.who.int/browse/2024-01/mms/en, accessed 18 October 2023).

10. Divinakumar KJ, Patra P, Prakash J, Daniel A. Prevalence and patterns of tobacco use and nicotine dependence among males industrial workers. Ind Psychiatry J. 2017;26(1):19–23 (https://doi.org/10.4103/ipj.ipj_14_17).

11. Breslau N, Johnson EO, Hiripi E, Kessler R. Nicotine dependence in the United States: prevalence, trends, and smoking persistence. Arch Gen Psychiatry. 2001;58(9):810–6 (https://doi.org/10.1001/archpsyc.58.9.810).

12. Liu Z, Li YH, Cui ZY, Li L, Nie XQ, Yu CD, et al. Prevalence of tobacco dependence and associated factors in China: findings from nationwide China Health Literacy Survey during 2018–19. Lancet Reg Health West Pac. 2022;24:100464 (https://doi.org/10.1016/j.lanwpc.2022.100464).

13. WHO report on the global tobacco epidemic, 2019: offer help to quit tobacco use. Geneva: World Health Organization; 2019 (https://iris.who.int/bitstream/handle/10665/326043/9789241516204-eng.pdf?sequence=1, accessed 1 November 2023). License: CC BY-NC-SA 3.0 IGO.

14. WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy. Geneva: World Health Organization; 2013 (https://iris.who.int/bitstream/handle/10665/94555/9789241506076_eng.pdf?sequence=1, accessed 16 October 2023).

15. Guidelines for the management of physical health conditions in adults with severe mental disorders. Geneva: World Health Organization; 2018 (https://iris.who.int/bitstream/handle/10665/275718/9789241550383-eng.pdf?sequence=1, accessed 18 October 2023). Licence: CC BY-NC-SA 3.0 IGO.

16. WHO package of essential noncommunicable (PEN) disease interventions for primary health care. Geneva: World Health Organization; 2020 (https://iris.who.int/bitstream/handle/10665/334186/9789240009226-eng.pdf?sequence=1, accessed 18 October 2023). Licence: CC BY-NC-SA 3.0 IGO.

17. WHO Model List of Essential Medicines – 22nd list, 2021. Geneva: World Health Organization; 2021 (https://iris.who.int/bitstream/handle/10665/345533/WHO-MHP-HPS-EML-2021.02-eng.pdf?sequence=1, 1 November 2023). Licence: CC BY-NC-SA 3.0 IGO.

18. WHO Report on the global tobacco epidemic, 2008: the MPOWER package. Geneva, World Health Organization;2008 (https://iris.who.int/bitstream/handle/10665/43818/9789241596282_eng.pdf?sequence=1, accessed 16 October 2023).

19. Thirteenth general programme of work, 2019–2023: promote health, keep the world safe, serve the vulnerable. Geneva: World Health Organization; 2019 (WHO/PRP/18.1; https://apps.who.int/iris/handle/10665/324775/, accessed 16 October 2023).

20. Tobacco taxes: a win–win measure for fiscal space and health. Mandaluyong City: Asian Development Bank; 2012 (https://www.adb.org/sites/default/files/publication/30046/tobacco-taxes-health-matters.pdf, accessed 12 December 2023).

21. Ye X, Chen S, Yao Z, Gao Y, Xu Y, Zhou S et al. Smoking behaviors before and after implementation of a smoke-free legislation in Guangzhou, China. BMC Public Health. 2015;15:982 (https://doi.org/10.1186/s12889-015-2353-6).

22. Durkin SJ, Biener L, Wakefield MA. Effects of different types of antismoking ads on reducing disparities in smoking cessation among socioeconomic subgroups. Am J Public Health. 2009;99(12):2217–23 (https://doi.org/10.2105/AJPH.2009.161638).

23. Noar SM, Francis DB, Bridges C, Sontag JM, Ribisl KM, Brewer NT. The impact of strengthening cigarette pack warnings: systematic review of longitudinal observational studies. Soc Sci Med. 2016;164:118–129 (https://doi.org/10.1016/j.socscimed.2016.06.011).

24. Brewer NT, Hall MG, Noar SM, Parada H, Stein-Seroussi A, Bach LE et al. Effect of pictorial cigarette pack warnings on changes in smoking behavior: a randomized clinical trial. JAMA Intern Med. 2016;176:905–12 (https://doi.org/10.1001/jamainternmed.2016.2621).

25. WHO handbook for guideline development – 2nd edition. Geneva: World Health Organization; 2014 (https://iris.who.int/bitstream/handle/10665/145714/9789241548960_eng.pdf?sequence=1, accessed 1 November 2023).

26. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–6 (https://doi.org/10.1136/bmj.39489.470347.AD).

27. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database Syst Rev. 2017;3:CD001292 (https://doi.org/10.1002/14651858.CD001292.pub3).

28. Stead LF, Carroll AJ, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database Syst Rev. 2017;3:CD001007 (https://doi.org/10.1002/14651858.CD001007.pub3).

29. Matkin W, Ordóñez-Mena JM, Hartmann-Boyce J. Telephone counselling for smoking cessation. Cochrane Database Syst Rev. 2019;5:CD002850 (https://doi.org/10.1002/14651858.CD002850.pub4).

30. Tzelepis F, Paul CL, Williams CM, Gilligan C, Regan T, Daly J et al. Real-time video counselling for smoking cessation. Cochrane Database Syst Rev. 2019;10:CD012659 (https://doi.org/10.1002/14651858.CD012659.pub2).

31. Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y, Dobson R. Mobile phone text messaging and app-based interventions for smoking cessation. Cochrane Database Syst Rev. 2019;10:CD006611 (https://doi.org/10.1002/14651858.CD006611.pub5).

32. Hartmann-Boyce J, Chepkin SC, Ye W, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database Syst Rev. 2018;5:CD000146 (https://doi.org/10.1002/14651858.CD000146.pub5).

33. Lindson N, Chepkin SC, Ye W, Fanshawe TR, Bullen C, Hartmann-Boyce J et al. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev. 2019;4:CD013308 (https://doi.org/10.1002/14651858.CD013308).

34. Hajizadeh A, Howes S, Theodoulou A, Klemperer E, Hartmann-Boyce J, Livingstone-Banks J et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2023;5:CD000031 (https://doi.org/10.1002/14651858.CD000031.pub6).

35. Livingstone-Banks J, Fanshawe TR, Thomas KH, Theodoulou A, Hajizadeh A, Hartman L et al. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev. 2023;5:CD006103 (https://doi.org/10.1002/14651858.CD006103.pub8).

36. Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database Syst Rev. 2016;3:CD008286 (https://doi.org 10.1002/14651858.CD008286.pub3).

37. Hartmann-Boyce J, Hong B, Livingstone-Banks J, Wheat H, Fanshawe TR. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database Syst Rev. 2019;6:CD009670 (https://doi.org10.1002/14651858.CD009670.pub4).

38. Thomas D, Abramson MJ, Bonevski B, George J. System change interventions for smoking cessation. Cochrane Database Syst Rev. 2017;2:CD010742 (https://doi.org/10.1002/14651858.CD010742.pub2).

39. Boyle R, Solberg L, Fiore M. Use of electronic health records to support smoking cessation. Cochrane Database Syst Rev. 2014;12:CD008743 (https://doi.org/10.1002/14651858.CD008743.pub3).

40. Carson KV, Verbiest MEA, Crone MR, Brinn MP, Esterman AJ, Assendelft WJJ et al. Training health professionals in smoking cessation. Cochrane Database Syst Rev. 2012;5:CD000214 (https://doi.org/10.1002/14651858.CD000214.pub2).

41. van den Brand FA, Nagelhout GE, Reda AA, Winkens B, Evers SMAA, Kotz D et al. Healthcare financing systems for increasing the use of tobacco dependence treatment. Cochrane Database Syst Rev. 2017;9:CD004305 (https://doi.org/10.1002/14651858.CD004305.pub5).

42. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016 (https://doi.org/10.1136/bmj.i2016).

43. Cheng CCW, He WJA, Gouda H, Zhang MJ, Luk TT, Wang MP et al. Effectiveness of very brief advice on tobacco cessation: a systematic review and meta-analysis. J Gen Intern Med. [in press] (https://doi.org/10.1007/s11606-024-08786-8).

44. Bendotti H, Lawler S, Chan GCK, Gartner C, Ireland D, Marshall HM. Conversational artificial intelligence interventions to support smoking cessation: a systematic review and meta-analysis. Digit Health. 2023;9:20552076231211634 (https://doi.org/10.1177/20552076231211634).

45. Parrott S, Godfrey C, Raw M, West R, McNeill A. Guidance for commissioners on the cost effectiveness of smoking cessation interventions. Thorax. 53;1998:S1–38 (https://thorax.bmj.com/ciontent/53/suppl_5/S2, accessed 28 May 2024).

46. Meeyai A, Yunibhand J, Punkrajang P, Pitayarangsarit. An evaluation of usage patterns, effectiveness and cost of the national smoking cessation quitline in Thailand. Tob Control. 2015;24(5):481–8 (https://doi.org/10.1136/tobaccocontrol-2013-051520).

47. McCaffrey N, Carter R. Economic evaluation of the Victorian Quitline service. 2018 (https://www.researchgate.net/publication/346503057_Economic_evaluation_of_the_Victorian_Quitline_service, accessed 1 November 2023)

48. Guerriero C, Cairns J, Roberts I, Rodgers A, Whittaker R, Free C. The cost-effectiveness of smoking cessation support delivered by mobile phone text messaging: Txt2stop. Eur J Health Econ. 2013;14:789–97 (https://doi.org/10.1007/s10198-012-0424-5).

49. Kahende JW, Loomis BR, Adhikari B, Marshall L. A review of economic evaluations of tobacco control programs. Int J Environ Res Public Health. 2009;6(1):51–68 (https://doi.org/10.3390/ijerph6010051).

50. Madae'en S, Obeidat N, Adeinat M. Using cost-effectiveness analysis to support policy change: varenicline and nicotine replacement therapy for smoking cessation in Jordan. J Pharm Policy Pract. 2020;13:65 (https://doi.org/10.1186/s40545-020-00270-y).

51. Leaviss J, Sullivan W, Ren S, Everson-Hock E, Stevenson M, Stevens JW et al. What is the clinical effectiveness and cost-effectiveness of cytisine compared with varenicline for smoking cessation? A systematic review and economic evaluation. Health Technol Assess. 2014;18(33):1–120 (https://doi.org/10.3310/hta18330).

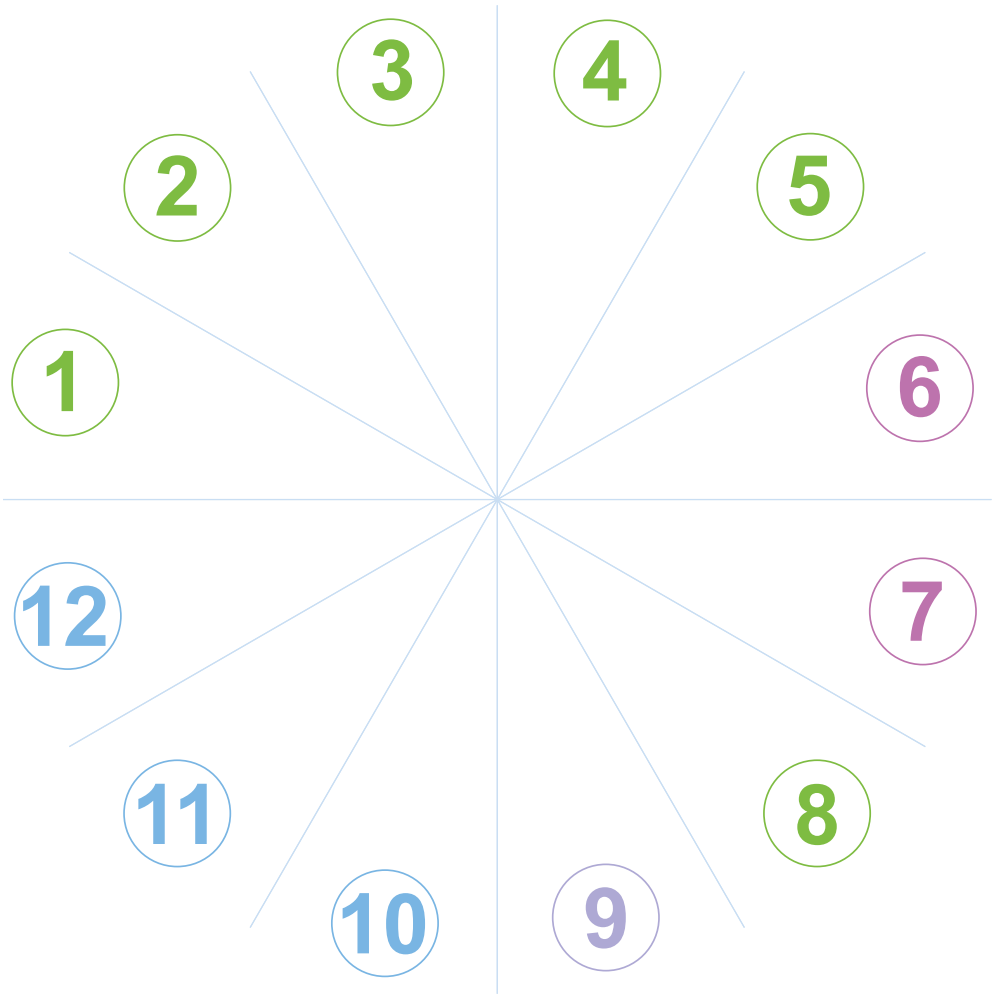
52. Li J, Parrott S, Keding A, Dogar O, Gabe R, Marshall AM et al. Cost-utility of cytisine for smoking cessation over and above behavioural support in people with newly diagnosed pulmonary tuberculosis: an economic evaluation of a multicentre randomized controlled trial. BMJ Open. 2022;12:e049644 (https://doi.org/10.1136/bmjopen-2021-049644).

53. Updating Appendix 3 of the WHO Global NCD action plan 2013–2030. Geneva: World Health Organization; 2022 (https://www.who.int/teams/noncommunicable-diseases/updating-appendix-3-of-the-who-global-ncd-action-plan-2013-2030, accessed 18 October 2023).

54. Strengthening health systems for treating tobacco dependence in primary care. Geneva: World Health Organization; 2013 (https://www.who.int/publications/i/item/strengthening-health-systems-for-treating-tobacco-dependence-in-primary-care, accessed 18 October 2023).

55. It's time to invest in cessation: the global investment case for tobacco cessation. Geneva: World Health Organization; 2021 (https://www.who.int/publications/i/item/9789240039308, accessed 18 October 2023). Licence: CC BY-NC-SA 3.0 IGO.

Annexes



Annex 1: Management of guideline development process

Contributors to guideline development

WHO Steering Group

The Steering Group (SG) included experts in the areas of tobacco cessation, health promotion, tobacco control policy implementation, noncommunicable disease (NCD) risk factor management, epidemiology of tobacco use, communication, surveillance, tobacco control laws, essential medicine, health systems, disability, gender, equity and human rights, from both World Health Organization (WHO) headquarters and regional offices. The members of the SG are listed in Table A1.1.

Table A1.1. Members of the SG

Name	Cluster/department/unit	Expertise
Adriana Bacelar Gomes	Risk Factors and Nutrition Unit, Department of Noncommunicable Diseases and Mental Health, Pan American Health Organization	Tobacco control policy, surveillance and NCD risk factor management
Alarcos Cieza	Sensory Functions, Disability & Rehabilitation Unit, Department of Noncommunicable Diseases, Universal Health Coverage/ Communicable and noncommunicable Diseases Division, WHO Headquarters	Sensory functions, disability and Rehabilitation
Angela Ciobanu	Special Initiative on NCDs and Innovation, Regional Governance, WHO Regional Office for Europe	Tobacco control policy, NCD prevention and control
Fatimah El-Awa	Tobacco Free Initiative, Noncommunicable Diseases and Mental Health, WHO Regional Office for the Eastern Mediterranean	Tobacco control policy, implementation and legal perspective
Dongbo Fu[a]	No Tobacco Unit, Health Promotion Department, Universal Health Coverage/Healthier Populations, WHO Headquarters	Tobacco cessation and health promotion
Hebe Gouda	No Tobacco Unit, Health Promotion Department, Universal Health Coverage/Healthier Populations, WHO Headquarters	Epidemiology of tobacco use and research
Benedikt Huttner	Medicines Selection, IP and Affordability Unit, Department of Health Product Policy and Standards, Access to Medicines and Health Products, WHO Headquarters	Essential medicines and health systems
Jagdish Kaur	Health Risk Factors Unit, Department of Healthier Populations and Noncommunicable Diseases, WHO Regional Office for South-East Asia	Tobacco control policy, tobacco cessation and implementation
Kritika Khanijo	Public Health Law and Policies Unit, Health Promotion Department, Universal Health Coverage/Healthier Populations, WHO Headquarters	Gender, equity and human rights

Name	Cluster/department/unit	Expertise
William Kiberenge Maina	Tobacco and Reduction of other NCD Risk Factors Unit, Department of Universal Health Coverage/Healthier Population, WHO Regional Officer for Africa	Tobacco control policy, implementation
Vinayak Prasad[a]	No Tobacco Unit, Health Promotion Department, Universal Health Coverage/Healthier Populations, WHO Headquarters	Tobacco control policy and management
Xi Yin	Prevention of Noncommunicable Diseases Unit, Department of Building Healthy Communities and Populations, WHO Regional Office for the Western Pacific	Tobacco control policy and communication

[a] Responsible Technical Officer.

The SG drafted the scope of the guidelines and the PICOs (Population, Intervention, Comparator and Outcomes). They reviewed the declarations of interest and drafted the guideline.

Guideline Development Group

The Guideline Development Group (GDG) consisted of a broad group of relevant experts in tobacco cessation in clinical, primary care and community settings, as well as end users of and persons affected by the recommendations. Over one half of the GDG members were from low- and middle-income countries (LMICs). The members of the GDG are listed in Table A1.2.

Table A1.2. Members of the GDG

Name	Affiliation, city, country	WHO region of residence	Gender	Expertise
Ahmad Al Mulla	Tobacco Control Center, Hamad Medical Corporation, Doha, Qatar	WHO Regional Office for the Eastern Mediterranean	Male	Tobacco cessation, public health and community medicine
Vasant Basdeo	South-West Regional Health Authority, San Fernando, Trinidad and Tobago	Pan American Health Organization	Male	Tobacco cessation in primary care
Eduardo Bianco	NextGenU/Frank Foundation for International Health, Chicago, USA	Pan American Health Organization	Male	Clinical cardiology and tobacco cessation
Roger Chou	Departments of Medicine and Medical Informatics and Clinical Epidemiology, Oregon Health and Science University, Portland, USA	Pan American Health Organization	Male	GRADE methodologist
Magdalena Ciobanu	National Institute of Pneumology Marius Nasta, Bucharest, Romania	WHO Regional Office for Europe	Female	Pneumology and tobacco cessation
Lenora Fernandez	University of the Philippines-Philippine General Hospital, Manila, Philippines	WHO Regional Office for the Western Pacific	Female	Pulmonology and tobacco cessation

Name	Affiliation, city, country	WHO region of residence	Gender	Expertise
Gholamreza Heydari	Shahid Beheshti University of Medical Science, Tehran, Iran (Islamic Republic of)	WHO Regional Office for the Eastern Mediterranean	Male	Tobacco control research, tobacco cessation and patient perspective
Sonali Jhanjee	All India Institute of Medical Sciences, New Delhi, India	WHO Regional Office for South-East Asia	Female	Tobacco cessation and substance abuse treatment
Paul Kavanagh	Health Service Executive, Dublin, Ireland	WHO Regional Office for Europe	Male	Community health, health economics and medical education
Tim McAfee[a]	Department of Social and Behavioural Sciences, University of California, San Francisco, USA	Pan American Health Organization	Male	Tobacco control, tobacco cessation and public health
Pratima Murthy[b]	National Institute of Mental Health and Neurosciences, Bangalore, India	WHO Regional Office for South-East Asia	Female	Addiction psychiatry and tobacco cessation
Yvonne Olando	National Authority for the Campaign Against Alcohol and Drug Abuse, Nairobi, Kenya	WHO Regional Office for Africa	Female	Clinical psychology and tobacco cessation
Dan Xiao	China-Japan Friendship Hospital, Beijing, China	WHO Regional Office for the Western Pacific	Female	Tobacco cessation and epidemiology

[a] Chair.

[b] Co-chair.

The first two virtual GDG meetings were held on 23 September and 13 October 2022, at which the GDG reviewed the guideline scope and decided on the PICO questions. The GDG reviewed the existing systematic reviews and identified new or updated systematic reviews required at the third and fourth virtual GDG meetings, held on 22 November and 13 December 2022. The GDG reviewed all available evidence presented in GRADE (Grading of Recommendations Assessment, Development and Evaluation) Evidence to Decision tables at the fifth and sixth virtual meetings held on 20 June and 4 July 2023. The GDG met in-person on between 4 and 6 September 2023. At this last meeting, the process for decision-making on recommendations and the strength of the evidence to be applied were decided, and final recommendations agreed upon by consensus.

Systematic review team

The systematic review team consisted of Coral Gartner, NHMRC Centre of Research Excellence on Achieving the Tobacco Endgame, School of Public Health, Faculty of Medicine, the University of Queensland, Australia; Jianping Liu, Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, China; and Christopher Chi Wai Cheng and Derek Yee Tak Cheung, School of Nursing, The University of Hong Kong, China, Hong Kong Special Administrative Region (SAR). The systematic review team conducted the following updated or new systematic reviews according to the GDG's decision: brief advice by health professionals, digital tobacco cessation interventions, cytisine, and traditional, complementary and alternative therapies for tobacco cessation.

External Review Group

Fourteen peer reviewers were drawn from a list of individuals suggested by the GDG and SG. They provided relevant expertise, including tobacco cessation service delivery and programme implementation, and represented all six WHO regions. External peer reviewers were requested to review the draft guideline and provide comments on issues of clarity, presentation of the evidence and implementation; comments were incorporated as appropriate. External peer reviewers could not change the recommendations decided upon by the GDG. Members of the External Review Group (ERG) are listed in Table A1.3; a summary of declarations of interest is provided in Annex 3.

Table A1.3. Members of the ERG

Name	Affiliation, city, country	WHO region of residence	Gender	Expertise
Lekan Ayo-Yusuf	School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa	WHO Regional Office for Africa	Male	Tobacco use prevention, treatment/cessation and policy
Sophia Chan	University of Hong Kong, China, Hong Kong SAR	WHO Regional Office for the Western Pacific	Female	Tobacco cessation in the community and gender-specific tobacco cessation programme
Smita Deshpande	Independent consultant, Bangalore, India	WHO Regional Office for South-East Asia	Female	Tobacco cessation services and mental health
Mahmoud Elhabiby	Institute of Psychiatry, Faculty of Medicine, Ain Shams University, Cairo, Egypt	WHO Regional Office for the Eastern Mediterranean	Male	Specialized tobacco cessation service delivery in clinical settings and training
Elba Ines Esteves Di Carlo	Tobacco Dependence Treatment Program, National Resources Fund, Montevideo, Uruguay	Pan American Health Organization	Female	Implementation of national tobacco dependence treatment programme
Takashi Hanioka	Department of Preventive and Public Health Dentistry, Fukuoka Dental College, Fukuoka, Japan	WHO Regional Office for the Western Pacific	Male	Public health dentistry and tobacco cessation
Danielle McCarthy	Center for Tobacco Research and Intervention, University of Wisconsin–Madison, Madison, USA	Pan American Health Organization	Female	Clinical psychology and tobacco cessation research
Myra Muramoto	Department of Family Medicine, University of Colorado School of Medicine, Colorado, USA	Pan American Health Organization	Female	Tobacco cessation in community settings and special populations
Galina Sakharova	Smoking Cessation Centre, Pulmonology Research Institute, Moscow, Russian Federation	WHO Regional Office for Europe	Female	Specialized smoking cessation services and training
Donna Shelley	School of Global Public Health, New York University, New York, USA	Pan American Health Organization	Female	Public health policy and implementation science

Name	Affiliation, city, country	WHO region of residence	Gender	Expertise
Kamran Siddiqi	Department of Health Sciences, University of York, York, the United Kingdom	WHO Regional Office for Europe	Male	Tobacco control in LMICs and cessation of smokeless tobacco use
Behzad Valizadeh	National Tobacco Control Secretariat, Ministry of Health and Medical Education, Tehran, Iran (Islamic Republic of)	WHO Regional Office for the Eastern Mediterranean	Male	Implementation of national tobacco control programme
Lin Xiao	Tobacco Control Office, Chinese Center for Disease Control and Prevention, Beijing, China	WHO Regional Office for the Western Pacific	Female	Implementation of national tobacco control programme
Jintana Yunibhand	Thailand National Quitline, Bangkok, Thailand	WHO Regional Office for South-East Asia	Female	Tobacco quit-line operation and nursing science

Declarations of interest

All members of the GDG members and ERG completed and submitted a WHO Declaration of Interests form, and signed confidentiality undertakings prior to attending any GDG meetings. The SG reviewed and assessed the submitted curriculum vitae and declarations of interest, and performed an internet and publications search to identify any obvious public controversies or interests that may lead to compromising situations. The names and brief biographies of all proposed GDG members were published on the WHO Tobacco Control webpage for public consultation for a period of 14 days. No comments were received. If additional guidance on the management of any declaration or conflicts of interest had been required, the SG would have consulted with colleagues in the Office of Compliance, Risk Management and Ethics. If deemed necessary, individuals found to have conflicts of interest, whether financial or nonfinancial, would have been excluded from participation on any topics where interests were conflicting. The management of conflicts of interest was reviewed throughout the process. GDG members were required to update their Declaration of Interest form, if necessary, before each meeting and a verbal declaration of interest was solicited at the beginning of each GDG meeting. Declared interests of the members of the GDG and the ERG are summarized in Annex 3. No conflict of interest was identified.

Annex 2: Additional information for implementing the recommendations

Brief advice

- A supportive system (clear policy with leadership support, tobacco use status included in all medical records, training, structured delivery models like 5As [Ask, Advise, Assess, Assist, Arrange] and 5Rs [Relevance, Risks, Rewards, Roadblocks, Repetition] *(1)*, monitoring and evaluation etc.) will improve and sustain the routine delivery of brief advice.
- Tailored or personalized advice may improve the effectiveness and acceptability.
- In busy health-care settings, a team approach may help improve the efficiency and delivery of brief advice. This could include having tobacco use status determined and recorded by a health-care provider taking patient vital signs, cessation advice being given by the principal health-care provider, and follow-up counselling and medication instruction provided by other personnel.

Intensive behavioural support

Individual face-to-face counselling may be more practical to implement, especially where there is an existing system for delivering counselling on other health issues (such as mental health).

- Increased frequency and duration of counselling sessions, at least up to five sessions and 10 minutes in duration, increases quit success rates, but less is still helpful.

Group face-to-face counselling may increase efficiency and have added benefits (for example, enhanced cohesiveness) compared with individual counselling. However, groups may have challenges regarding availability, sustainability, logistics and participation.

Telephone counselling can reach people without requiring them coming to a specific location, and can be centralized for efficiency and quality control *(2)*.

- A single telephone counselling session can be effective, but evidence is strongest for multisession (three to five sessions) proactive telephone counselling.
- Increasing the reach of telephone counselling may have more population impact than expending more resources on each individual caller.
- Cost-efficient methods used to increase the number of calls have included tagging mass media anti-tobacco advertisements with quit-line numbers, adding quit line numbers to cigarette packs and encouraging referrals from health-care providers.
- There should be sufficient staffing and telephony services to ensure calls to a quit line are answered and not dropped. Use of automated messaging and callbacks may be necessary during very high-volume periods.
- Quit lines can also serve as a portal to digital cessation support and pharmacotherapy access.
- Real-time video counselling may be offered as an option for patient or counsellor preference reasons where desired and feasible, but there is no evidence that it is more effective.

Digital tobacco cessation interventions

In general, digital tobacco cessation programmes found to be effective were carefully developed using well-established behavioural change theories, with large libraries of tobacco cessation text messages and complex decision logic applied as to the frequency, duration and content of intervention. However, there are hundreds if not thousands of digital cessation programmes available that have not gone through a rigorous design, testing and maintenance process.

Countries may consider adapting existing digital tobacco cessation programmes through the process of evaluation/validation and quality assurance by trusted institutions. The limitations and evolving characteristics of digital tools should be kept in mind, and underscores the need to support local implementation with research, monitoring and evaluation.

Countries may also consider the stakeholders involved in the development and operation of digital tobacco cessation interventions, and should ensure there is freedom from tobacco industry interference.

The following considerations regarding specific digital modalities apply.

- **Mobile text messaging** is an older digital modality. While it currently has the strongest evidence, the reach and effectiveness of standalone texting may be diminished due to the evolution of the digital environment. Many digital programmes – such as those that are web-, application (app)- and artificial intelligence (AI)-based – may utilize text responses as a component of their intervention.
- **Smartphone apps** vary widely in interactivity, tailoring, engagement and adherence to effective behavioural theory. They have the potential to provide a more engaging and controlled experience than websites or mobile text messaging, and may include other digital elements, including interactive texting. Careful attention should be paid to the supportive data relating to the quality and evaluation of a specific smartphone app before adoption.
- **Internet-based websites and programmes** may serve as a portal to other cessation services, as well as providing direct cessation assistance. Their capacity to deliver a systematic programme with internal navigation logic may become more challenging as users increasingly rely on search engine queries to lead them to specific subsite webpages.
- **AI-based interventions**: With the rapid evolution of AI systems, elements of AI are likely to be incorporated into existing digital approaches (such as the generation of text-message responses and populating search engine requests) as well as increasingly sophisticated AI-driven chatbots/avatars dispensing cessation advice, referrals and counselling advice. To ensure fidelity to evidence-based approaches, collaborative development and evaluation will be critical.

Pharmacological interventions

General

Special consideration should be exercised with several groups:

- People who are pregnant should not be routinely prescribed or recommended cessation medication due to pregnancy-related safety concerns, including for Nicotine Replacement Therapy (NRT) products. They should receive tobacco-related behavioural cessation support, both delivered in the course of prenatal care visits and as offered by intensive counselling programmes. Because of the urgent danger to the developing fetus of continued tobacco use during pregnancy, NRT products can be cautiously considered on a case-by-case basis, especially if counselling alone has been ineffective.
- The use of cessation medications in less-dependent tobacco users (that is, non-daily, smoking fewer than 5–10 cigarettes/day) is less well studied, suggesting that an individualized approach to the use of medications should be followed in such patients. As in more-dependent tobacco users, brief and intensive behavioural counselling and support should be offered to less-dependent users.
- Hospitalized patients may benefit from routine availability of cessation medication to avoid withdrawal (and encourage long-term cessation), for example through the use of standing admission orders for NRT "as needed". Hospitals should be tobacco-free environments.

- There is insufficient evidence to recommend routinely prescribing or recommending cessation medications for adolescents, although this evidence base was not systematically reviewed for this guideline. Although generally safe, their effectiveness has not been consistently shown.
- Those with psychiatric conditions are at higher risk of relapse and may benefit from longer and more intense interventions, both pharmacological and behavioural. For those taking psychiatric medications, monitoring of symptoms for potential medication adjustment may be beneficial. The existence of a psychiatric condition should not be used as an excuse by clinicians to not provide encouragement and support for quitting tobacco use.

In countries where not all recommended cessation medications will be made available, the following minimal level of medication availability may be considered:

- at least one long-acting NRT and one short-acting NRT;
- at least one $\alpha 4\beta 2$ nicotine receptor agonist (varenicline or cytisine); and
- bupropion (if bupropion is on formulary or the country's essential medication list for depression, authorize use for cessation as well).

Coverage for full courses of treatment should be provided in health-care settings. In some community settings, where the primary objective of a time-limited campaign may be to increase quit attempts, it may be reasonable to offer shorter courses of a medication, such as in so-called Quit-and-Win contests or quit-line promotions. However, these should be framed as so-called starter kits, rather than implying that they represent a full course of treatment.

Effective use of cessation medications can be increased by training and support (such as patient handouts and standing orders in electronic systems and hospital settings) for health-care providers who may prescribe or recommend them.

Any comparisons of relative medication costs should consider other factors in addition to the cost of a course of treatment, especially cost-effectiveness and acceptance/feasibility.

Specific pharmacotherapy

NRT

All forms of NRT reviewed are effective (nicotine patches, gum, lozenges, inhalers, sprays).

The availability of some forms of NRT medications without a prescription (over the counter [OTC]) may facilitate population use by increasing accessibility. However, if available OTC, behavioural support and instruction regarding proper use should be encouraged and available. If OTC medications are generally not covered by health insurance, provisions should be made for coverage despite OTC status.

Having multiple forms of NRT available is preferable to increase patient choice, but as a minimum at least one fast-acting and one long-acting form should be available without cost or accessibility barriers. Combining a fast-acting and a long-acting NRT increases quit success, and this option should be encouraged and available, especially for more-dependent tobacco users and those having difficulty quitting despite multiple attempts.

Bupropion

Many primary care and psychiatric clinicians are familiar with prescribing bupropion as a treatment for depression. Bupropion may already be available as a lower-cost generic drug in countries for this purpose. This may decrease some implementation barriers, but it is important to emphasize that bupropion's effectiveness as a cessation medication is not dependent upon its antidepressant effects, and it can be used for any person who smokes interested in quitting, regardless of their depression status.

Combined use of bupropion with NRTs or varenicline can be considered in individual patients, especially those who are highly dependent or those having difficulty quitting despite multiple attempts. Discontinuation of therapy due to adverse events may be more common with bupropion than other cessation monotherapies.

Varenicline and cytisine (partial agonists of α4β2 nicotinic receptors)

Varenicline

Despite strong certainty regarding the higher degree of effectiveness of varenicline in smoking cessation relative to other cessation monotherapies among tobacco-dependent adults, it is not readily available in many low- and middle-income countries (LMICs) due to cost, manufacturing challenges and other factors. Other measures may need to be instituted in LMICs to increase availability.

Although more expensive per course of treatment than monotherapy NRTs, varenicline's greater effectiveness may make its cost per quitter similar to or lower than monotherapy NRTs. Varenicline is started at a low dose and then increased before tobacco use is discontinued. This initiation regimen may decrease gastrointestinal side-effects and increase successful use.

Cytisine

Cytisine is another agonist of α4β2 nicotinic receptors with a similar molecular structure and mode of action to varenicline. It may be a reasonable and currently less expensive alternative, with moderate-certainty evidence for efficacy that appears similar to varenicline, although head-to-head comparison trials are needed. Since cytisine is associated with large benefits, minimal harms and currently incurs only a small cost, LMICs may consider its use for smoking cessation treatment.

Cytisine is not yet widely available outside a small number of countries. It is often regulated as a herbal product or an OTC medication, rather than a prescription medication. Manufacturing, distribution and pricing may alter as regulatory bodies approve it as a cessation medication in the future. Availability needs to be addressed by the stakeholders concerned.

One challenge regarding cytisine compliance has been a complex dosing regimen (beginning with 1 mg six times per day tapering gradually over 25 days to once per day). However, recent randomized dosing trials support much simpler dosing (3 mg three times per day for 6 or 12 weeks) with similar effectiveness *(3)*.

If neither varenicline nor cytisine are available, combination NRTs are a reasonable alternative providing similar greater effectiveness compared with single NRTs and bupropion.

Traditional, complementary and alternative therapies

- The availability and costs of acupuncture services may be a barrier in some regions outside China. Policy-makers should evaluate local access to qualified acupuncturists.
- Although rare serious adverse events resulting from acupuncture have been reported, policy-makers should ensure proper training and credentialing of acupuncturists

Patient preferences and motivations may impact acupuncture success rates. Evidence-based counselling should be included to maximize patient engagement and compliance.

Financial interventions

Removal of cost barriers may help more tobacco users if:

- both approved cessation medications and counselling are provided at no cost; full-cost support will have greater impact than reduced-cost support on increasing equity;
- access barriers to receiving no-cost treatments are minimized, such as preauthorization requirements or contingency requirements;
- availability of cessation support, including cost support, is communicated effectively and repeatedly to health-care providers and patients;
- nonfinancial barriers to accessing medications and counselling through health-care and community settings are minimized (medicines stocked in pharmacies, toll-free quit lines, etc.); and
- tobacco use status is assessed, and brief advice offered, to identify people interested in quitting.

Support for removal of cost barriers may benefit from the education of decision-makers in payer/insurance/public health systems in countries regarding the rationale for providing treatment cost support, including:

- the high impact of tobacco use on morbidity, mortality and health-care utilization;
- the strong evidence for the effectiveness of cessation interventions;
- evidence regarding the effectiveness of cost support;
- the relative low cost of interventions compared with the medical/surgical costs of treating tobacco-related diseases; and
- may require the inclusion of cessation medications on country essential medicine lists.

References

1. Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care. Geneva: World Health Organization, 2014 (https://iris.who.int/bitstream/handle/10665/112835/9789241506953_eng.pdf?sequence=1, accessed 1 November 2023).

2. Developing and improving national toll-free tobacco quit-line services: a World Health Organization manual. Geneva: World Health Organization, 2011 (https://www.who.int/publications/i/item/developing-and-improving-national-toll-free-tobacco-quit-line-services, accessed 1 November 2023).

3. Rigotti NA, Benowitz NL, Prochaska J, Leischow S, Nides M, Blumenstein B et al. Cytisinicline for smoking cessation: a randomized clinical trial. JAMA. 2023;330(2):152–60 (https://doi.org/10.1001/jama.2023.10042).

Annex 3: Summary of declarations of interest and how these were managed

Declarations of interest for the members of the Guideline Development Group are listed in Table A3.1.

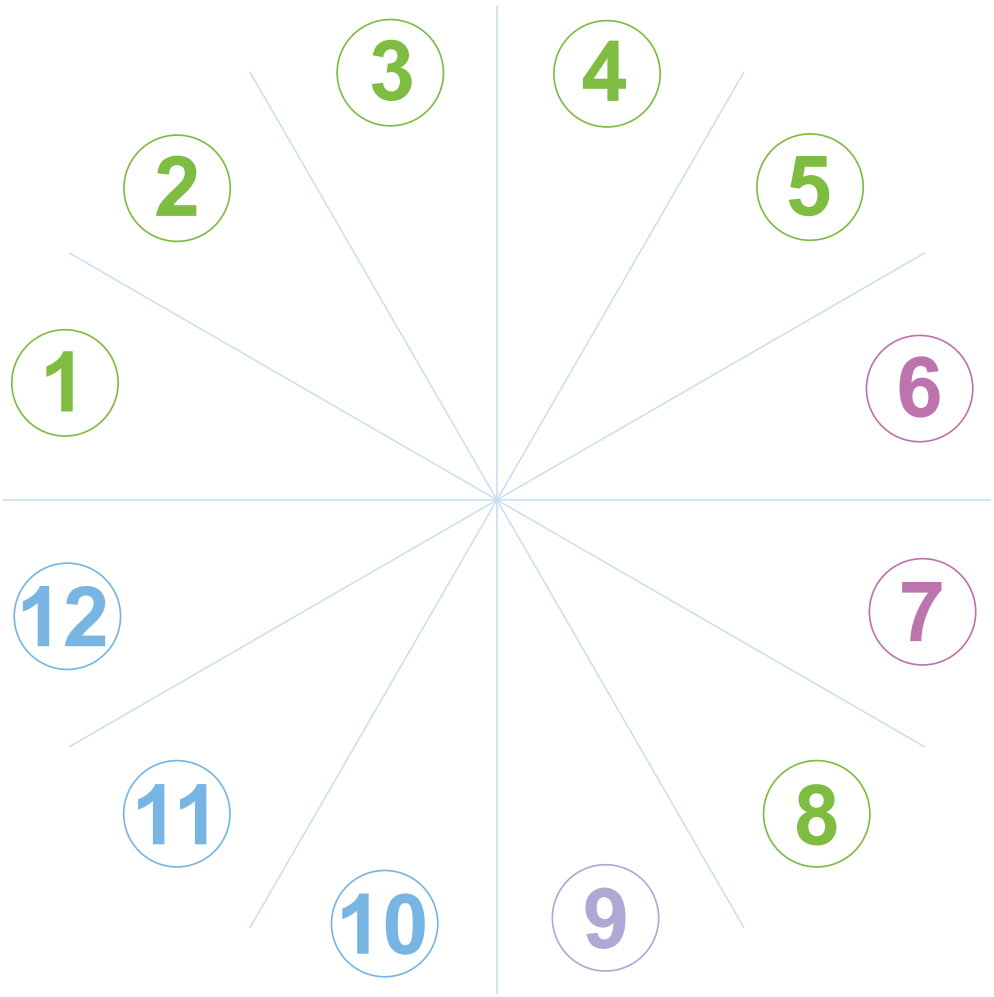
Table A3.1. Guideline Development Group declarations of interest

Name	Disclosure of interest	Conflict of interest and management
Ahmad Al Mulla	None declared	No conflict of interest identified
Vasant Basdeo	None declared	No conflict of interest identified
Eduardo Bianco	None declared	No conflict of interest identified
Roger Chou	Employment with Oregon Health & Science University; consulting for WHO through affiliated institution (Evidence Consulting, LLC)	No conflict of interest identified
Magdalena Ciobanu	Consultancy paid by the National Institute of Public Health, Romania	No conflict of interest identified
Lenora Fernandez	Funding support from the Department of Health in the Philippines to update Philippine smoking cessation guidelines	No conflict of interest identified
Gholamreza Heydari	None declared	No conflict of interest identified
Sonali Jhanjee	None declared	No conflict of interest identified
Paul Kavanagh	None declared	No conflict of interest identified
Tim McAfee	Chapter author/editor and senior scientific reviewer for multiple US Surgeon General Reports; a contractor for the United States Centers for Disease Control and Prevention over the past 3 years developing web content for cessation support	No conflict of interest identified
Pratima Murthy	None declared	No conflict of interest identified
Yvonne Olando	None declared	No conflict of interest identified
Dan Xiao	None declared	No conflict of interest identified

Declarations of interest for the members of the External Review Group are listed in Table A3.2.

Table A3.2. External Review Group declarations of interest

Name	Disclosure of interest	Conflict of interest and management
Lekan Ayo-Yusuf	None declared	No conflict of interest identified
Sophia Chan	None declared	No conflict of interest identified
Smita Deshpande	None declared	No conflict of interest identified
Mahmoud Elhabiby	None declared	No conflict of interest identified
Elba Ines Esteves Di Carlo	None declared	No conflict of interest identified
Takashi Hanioka	Research grants from Pfizer Inc. (USA)	No conflict of interest identified
Danielle McCarthy	Active and placebo varenicline from Pfizer Inc. for clinical trial; Member of National Comprehensive Cancer Network Smoking Cessation Panel in the USA	No conflict of interest identified
Myra Muramoto	None declared	No conflict of interest identified
Galina Sakharova	None declared	No conflict of interest identified
Donna Shelley	Consultancy paid by Memorial Sloan Kettering Cancer Center; research grants from National Institutes of Health	No conflict of interest identified
Kamran Siddiqi	Research grants from the European Union's Horizon Europe initiative, the Medical Research Council, the Wellcome Trust and the National Institute for Health Research	No conflict of interest identified
Behzad Valizadeh	None declared	No conflict of interest identified
Lin Xiao	None declared	No conflict of interest identified
Jintana Yunibhand	None declared	No conflict of interest identified


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