Evidence-to-Recommendations Framework

This document outlines the underpinning evidence and rationale for the recommendation in the ACE Clinical Guidance (ACG) "Promoting smoking cessation and treating tobacco dependence".

In ACGs, the strength of a recommendation reflects the confidence that the desirable effects of the recommended practice outweigh undesirable effects across the range of patients for whom the recommendation applies, based on the best available evidence:

- A strong recommendation is usually made when benefits clearly outweigh the risks, based on at least moderate-certainty evidence.
- A weak or conditional recommendation may be needed when there is a closer balance between benefits and harms, evidence is of low certainty, there is significant variability in patients' values and preferences, or important concerns with resourcing and feasibility of the recommended practice.[1]

It should be noted that vaping is not in scope for this ACG, and is not mentioned within any of the recommendations.

Recommendation 1	**Ask all patients about tobacco use and maintain an up-to-date record of their status.**

Strength of recommendation: **Strong** Weak/conditional

Summary:
The Expert Group agreed that it is important for healthcare professionals to establish a baseline smoking status for all patients as the first step to initiating discussions on tobacco use. They also recognised the value of maintaining an updated record of this status to ensure patients receive ongoing support, as required.

Evidence-to-recommendation considerations

Balance of benefits and harms	**Values and preferences**
Timely identification of people who smoke enables provision of appropriate support and interventions to quit, thereby alleviating the risk, symptoms or progression of related complications. All high-quality reference guidelines agree that healthcare professionals should ask all individuals about their smoking status.[3-8]	A systematic review of qualitative studies found that many patients expect primary care practitioners to proactively address smoking, as some feel too ashamed to admit they smoke.[2]
Certainty of evidence	**Resources and feasibility**
Not applicable.	This recommendation is not expected to impact resources and no significant feasibility concerns were identified; recording smoking status is already part of the recommended components in the Chronic Disease Management Handbook (CDMP), including as risk factor for several associated conditions.
Expert Group deliberation of above factors	
The Expert Group acknowledged that while asking about smoking status at every encounter is ideal, there may be situations where it is not appropriate. For instance, if the patient is a non-smoker or has already quit smoking and has maintained abstinence. Therefore, the recommendation does not provide specific guidance on frequency of subsequent check-ins, but instead encourages clinician discretion based on patient circumstances. They also noted while patients aged below 12 years are unlikely to be smokers, it is still important to identify if a household member is a smoker, to reduce risk of exposure to secondhand smoke or of picking up smoking later in life. Hence the recommendation applies to all patients, not just those above a certain age.	

Recommendation 2	**Advise all people who smoke that effective methods to help them quit are available, and assess willingness to quit based on their response.**

Strength of recommendation: **Strong** Weak/conditional

Summary:
The Expert Group determined that delivering brief advice to patients that strategies are available to help them quit was a non-confrontational and practical approach to implement in a busy practice, and less likely to elicit patient resistance than other approaches (such as advising on the health benefits of quitting).

Evidence-to-recommendation considerations

Balance of benefits and harms	Values and preferences
The approach outlined in this recommendation is adapted from the Very Brief Advice (VBA) intervention. Framing the offer to help using the VBA approach can trigger a quit attempt.[9-11] Conversely, explicitly advising people who smoke to quit or assessing their willingness to quit may cause them to become defensive or feel judged. Assessing the willingness of people who smoke to quit using their response to this advice can then help healthcare professionals provide appropriate support and interventions that align with an individual's motivation for quitting.[9-11] The recommendation is informed by a meta-analysis of 13 randomised controlled trials which found that offering assistance to smokers was associated with more quit attempts than advising them to quit on medical grounds (risk ratio [RR] 1.69, 95% confidence interval [CI] 1.24-2.31 for offering behavioural support; RR 1.39, 95% CI 1.25-1.54 for offering pharmacological treatment).[12]	A systematic review of qualitative studies found that primary care practitioners commonly waited for explicit patient requests before offering smoking cessation advice, to preserve the therapeutic alliance.[2] However, many patients expected practitioners to take an active role in providing information and options for smoking cessation.[2] These findings should be viewed with consideration of clinician-patient relationships in the local context.
Certainty of evidence	**Resources and feasibility**
No significant concerns identified.	This recommendation is expected to encourage healthcare professionals to modify the content of their smoking cessation advice – to inform people who smoke of the various approaches for quitting – and to then assess willingness to quit based on an individual's response to the advice. It is anticipated that the implementation of this recommendation will be feasible, as it is practical and less likely to elicit patient resistance. Most healthcare institutions and clinics already adopt established frameworks (e.g. 2As, 5As or ABC) which still offer a useful structure for implementing the recommendation.
Expert Group deliberation of above factors	
The Expert Group agreed with the evidence findings regarding the initial advice approach to take, and noted that any established framework such as 2As, 5As or ABC could be utilised based on the time available within a consultation. The Expert Group also agreed that the recommendation did not need to differentiate the approach to advising those unwilling to quit. Instead, the supporting text could describe principles of brief advice for the healthcare professional to individualise to the patient, based on the time available.	

Recommendation 3	Individualise behavioural support to maximise engagement and adherence to the quit plan.

Strength of recommendation: **Strong** Weak/conditional

Summary:
The Expert Group assessed that behavioural support was effective in increasing quit rates compared with no support, and that a beneficial outcome was achievable with multiple different interventions. As it was unclear if one form of behavioural support could be recommended over another, it was agreed that weight would be given to using patient values and preferences when deciding which support interventions were most appropriate.

Evidence-to-recommendation considerations

Balance of benefits and harms	Values and preferences
Behavioural support has been established as effective for increasing abstinence rates compared to placebo, albeit lower than receiving both pharmacological treatment and behavioural support.[13] A recent network meta-analysis reported that counselling (OR 1.44, 95% CI 1.22–1.70) and guaranteed monetary rewards (OR 1.46, 95% CI 1.15–1.85) significantly increases the likelihood of quitting smoking for six months or longer compared to minimal intervention.[14] Interventions with the following characteristics were more beneficial compared with no support: delivered by text message; individually tailored; inclusion of motivational content; group-based delivery; and focused on quitting strategies. [14] Another recent meta-analysis found that e-health smoking cessation interventions, (text, telephone, websites, and apps) can increase quit rates (RR 1.86, 95% CI 1.69–2.04) and sustain long-term cessation (RR 1.79, 95% CI 1.60–2.00), compared with more traditional interventions.[15]	In the absence of definitive evidence to recommend one behavioural support over another, healthcare professionals are encouraged to consider the values and preferences of each person who smokes to individualise behavioural support, personalise goal setting and increase chances of a successful quit attempt.
Certainty of evidence	**Resources and feasibility**
The evidence for different components and types of behavioural support for smoking cessation has limited interpretability, due to unclear definitions of the interventions and limited information about the study populations.	Multiple local quit programmes are available for health professionals to refer their patients.
Expert Group deliberation of above factors	
There was strong consensus from the Expert Group that all people who have indicated a willingness to quit smoking should be offered behavioural support tailored to their unique needs and preferences, to increase their chances of quitting.	

Recommendation 4	Offer combination NRT (long-acting nicotine patch and short-acting NRT) or varenicline, alongside behavioural support.

Strength of recommendation: **Strong** Weak/conditional

Summary: The Expert Group decided on a strong recommendation to ensure that all non-pregnant adults willing to quit smoking are provided with the opportunity to access both pharmacological treatment and behavioural support, as this will increase the likelihood of quitting. They acknowledged that guidelines generally recommend varenicline or combination NRT (long- and short-acting NRT) as the first-line pharmacological treatment for smoking cessation. They agreed to mention both in the recommendation but positioned combination NRT first due to cost concerns and local lack of availability of varenicline.

Evidence-to-recommendation considerations

Balance of benefits and harms	Values and preferences
This recommendation builds from the previous one, which encourages the provision of behavioural support for all people who smoke. In non-pregnant adult smokers, multiple systematic reviews show that varenicline or combination NRT have greater efficacy in achieving abstinence and safety compared to placebo and other pharmacological treatments.[16] Evidence for use of pharmacological treatments to support smoking cessation in people who are pregnant or aged 18 years or younger is not clear. The text placed directly following the recommendation explains that it directed at non-pregnant adults who smoke, with additional guidance for other populations provided later in the ACG. A component network meta-analysis of 319 RCTs found that compared with placebo, the most effective pharmacological treatments for smoking were varenicline (OR 2.33, 95% CI 2.02-2.68) and combination NRT (OR 1.93, 95% CI 1.61-2.34).[16] While bupropion is also more effective than placebo for helping non-pregnant adults stop smoking (OR 1.43, 95% CI 1.26-1.62), a Cochrane review found bupropion to be less effective than varenicline (RR 0.73, 95% CI 0.67-0.80; nine RCTs) and combination NRT (RR 0.74, 95% CI 0.55-0.98; two RCTs).[19]	Shared decision making when selecting pharmacological treatment is encouraged, to optimise individualisation and maximise adherence. People who smoke should be informed that some pharmacological treatments may be less effective than others and that long and short acting NRT products vary in their mechanism of action and potential side-effects.
Certainty of evidence	**Resources and feasibility**
There is high-certainty evidence that offering both pharmacological treatment and behavioural support to non-pregnant adults is more effective than minimal support in terms of increased quit rates, and achieving abstinence at six-month follow up.[17,18]	The synchronisation of I-Quit data to the clinic management systems under Healthier SG helps to facilitate the implementation of this recommendation. NRT as a smoking cessation aid is available for subsidy through the Medication Assistance Fund for patients who met the eligibility criteria. While varenicline is locally registered for smoking cessation, it is not currently available on the market. Bupropion is locally registered for treating depression, and use for smoking cessation would be as off-label treatment.
Expert Group deliberation of above factors	
Although currently unavailable, the Expert Group agreed to include varenicline in the recommendation based on the clinical evidence, reference guidelines recommendations and expectations that supply will resume. Bupropion was not included at the recommendation level because of lower efficacy compared to NRT and	

varenicline, and noting that it is not registered in Singapore for this use. Information about this medication was provided in the supporting text, recognising that there may be some circumstances where it is preferred over other treatments.

The Expert Group agreed that the supporting text should mention shared decision making when selecting pharmacological treatment, to optimise individualisation and maximise adherence.

Recommendation 5	**Follow up within the initial weeks after the quit date.**

Strength of recommendation: **Strong** Weak/conditional

Summary: The Expert Group acknowledged the importance of follow-up with a patient in the weeks soon after quitting. However, they also recognised that the recommendation needed to be practical and allow for flexibility to make it a sustainable approach for busy practices that may have limited time and resources. Hence, the recommendation is strong but does not provide strict time frames, instead leaving the details for the supporting text.

Evidence-to-recommendation considerations

Balance of benefits and harms	**Values and preferences**
Most high-quality reference guidelines emphasised the importance of scheduling a follow-up appointment, with some recommending a follow-up appointment one week after the quit date. The National Centre for Smoking Cessation and Training recommends that all stop-smoking services provide one or more sessions per week for at least four weeks following the quit date.[20] Locally, there is limited evidence to recommend a specific frequency or follow-up modality that will work for all practice settings and smokers. Although a practice article for primary care recommended arranging a follow-up visit within three months.[21]	Follow up can be conducted in-person or via telephone, increasing the flexibility for the patient, to better meet their needs.
Certainty of evidence	**Resources and feasibility**
Not applicable.	If the healthcare professional or their clinical staff are unable to arrange a follow-up within one to two weeks from the quit date due to practical limitations, referral to the I-Quit programme is a viable option. The I-Quit programme follows up with people who smoke one week after the quit date via SMS or telephone call, with outcomes reflected automatically on Healthier SG-compatible clinic management systems.
Expert Group deliberation of above factors	
The Expert Group agreed that follow up was a key component of support for people willing to quit smoking. However they recognised the need for flexibility in terms of timing, method of follow-up and also involvement of staff, to ensure sustainability and practicability within the clinical practice setting.	

Recommendation 6	Consider interventions to prevent relapse, such as extending pharmacological treatment and advising on coping strategies.

Strength of recommendation: Strong | **Weak/conditional**

Summary: The Expert Group supported a conditional statement using 'consider' for relapse prevention interventions. They recognised that while some guidelines recommend extending pharmacological treatment duration and discussing coping strategies, the impact of these interventions on relapse prevention is unclear.

Evidence-to-recommendation considerations

Balance of benefits and harms	Values and preferences
A systematic review found no clear evidence of an effect of duration for combination NRT use on maintaining abstinence for 16 weeks compared to 8 weeks, and for 6 weeks compared to 2 weeks.[22] A Cochrane systematic review also noted that while the effectiveness of varenicline for smoking cessation is well established, substantial questions remain about different doses and durations of treatment, and what impact they have on how effective varenicline is at helping people to quit smoking.[23] Another Cochrane review reported that behavioural interventions may not help for relapse prevention, noting there was unexplained statistical heterogeneity across the included studies.[24]	In the absence of strong evidence, the potential benefits of different strategies will need to be assessed at the individual level taking patient profile, values and needs into consideration.
Certainty of evidence	**Resources and feasibility**
Certainty of the evidence ranged from moderate to very low.	No significant concerns identified. The ACG will provide healthcare professionals with links to existing educational resources hosted on HealthHub.
Expert Group deliberation of above factors	
The Expert Group agreed that a weak recommendation was appropriate given the mixed evidence regarding effectiveness for pharmacological or behavioural strategies as relapse prevention interventions.	

References

1. Schünemann H, Brożek J, Guyatt G, Oxman A. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach [updated October 2013. Available from: https://gdt.gradepro.org/app/handbook/handbook.html#h.1yd7iwhn8pxp.
2. Manolios E, Sibeoni J, Teixeira M, et al. When primary care providers and smokers meet: a systematic review and metasynthesis. npj Primary Care Respiratory Medicine. 2021;31(1):31
3. National Institute for Health and Care Excellence (NICE). Tobacco: preventing uptake, promoting quitting and treating dependence. 2023
4. American Thoracic Society (ATS). Initiating Pharmacologic Treatment in Tobacco-Dependent Adults. An Official American Thoracic Society Clinical Practice Guideline. 2020
5. Royal Australian College of General Practitioners (RACGP). Supporting smoking cessation: A guide for health professionals. 2021
6. Department of Health, Ireland. Stop Smoking: National Clinical Guideline No. 28. 2022
7. Ministry of Health, Malaysia. Treatment of Tobacco Use Disorder. 2016
8. US Preventive Services Task Force (USPSTF). Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons. US Preventive Services Task Force Recommendation Statement. 2021
9. PCRS. Become a Quit Catalyst. Primary Care Respiratory Society. 2019.
10. NCSCT. Local Stop Smoking Services. Service and delivery guidance 2014. National Centre for Smoking Cessation and Training. 2014.
11. Papadakis S, Cole AG, Reid RD, et al. Increasing Rates of Tobacco Treatment Delivery in Primary Care Practice: Evaluation of the Ottawa Model for Smoking Cessation. The Annals of Family Medicine. 2016;14(3):235.
12. Aveyard P, Begh R, Parsons A, et al. Brief opportunistic smoking cessation interventions: a systematic review and meta-analysis to compare advice to quit and offer of assistance. Addiction. 2012;107(6):1066-73.
13. Nian T, Guo K, Liu W, et al. Non-pharmacological interventions for smoking cessation: analysis of systematic reviews and meta-analyses. BMC Med. 2023;21(1):378.
14. Hartmann-Boyce J, Livingstone-Banks J, Ordóñez-Mena JM, et al. Behavioural interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database of Systematic Reviews. 2021(1).
15. Hartmann-Boyce, J., Ordóñez-Mena, J.M., Livingstone-Banks, J., Fanshawe, T.R., Lindson, N., Freeman, S.C., et al. Behavioural programmes for cigarette smoking cessation: investigating interactions between behavioural, motivational and delivery components in a systematic review and component network meta-analysis. Addiction. 2022;117(8):2145-56.
16. Lindson N, Theodoulou A, Ordóñez-Mena JM, et al. Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. Cochrane Database of Systematic Reviews. 2023(9).
17. Hartmann-Boyce J, Hong B, Livingstone-Banks J, et al. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database of Systematic Reviews. 2019(6).
18. Stead LF, Koilpillai P, Fanshawe TR, et al. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database of Systematic Reviews. 2016(3).
19. Hajizadeh A, Howes S, Theodoulou A, et al. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews. 2023(5).
20. NCSCT. Behavioural support for smoking cessation. National Centre for Smoking Cessation and Training. 2019.
21. Lua YHA, How CH, Ng CWM. Smoking cessation in primary care. Singapore Medical Journal. 2024;65(1).
22. Theodoulou A, Chepkin SC, Ye W, et al. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews. 2023(6).
23. Livingstone-Banks J, Fanshawe TR, Thomas KH, et al. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews. 2023(6).
24. Livingstone-Banks J, Norris E, Hartmann-Boyce J, et al Relapse prevention interventions for smoking cessation. Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD003999. DOI: 10.1002/14651858.CD003999.pub6.