King Hussein Cancer Foundation
King Hussein Cancer Center

وزارة الصحة

مكتب مكافحة السرطان
CANCER CONTROL
OFFICE

Jordan Guidelines for Tobacco Dependence Treatment

"Helping Smokers Quit"

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I. Executive summary

The health effects of tobacco use, including the increased risk of non-communicable disease incidence and aggravation, have been well and widely documented; and the public health gains of eliminating tobacco use are irrefutable. Unfortunately, tobacco use rates in Jordan currently rank among the highest in the Middle Eastern region and the world, both among adults and youth. Furthermore, Jordan faces additional challenges with its tobacco burden: namely a high prevalence of other lifestyle factors associated with non-communicable diseases, such as poor nutrition, obesity and physical inactivity. As such, it is not surprising that cardiovascular diseases and cancer are the main causes of death in the country. It is thus timely that the Ministry of Health and its partners are seeking to expand their efforts to combat tobacco and to reduce its health and financial burdens through the use of WHO's MPOWER framework; the development of national tobacco dependence treatment (TDT) guidelines are an important part of these efforts.

These guidelines were developed to promote, educate about, and standardize treatment of tobacco dependence, the most preventable risk factors for numerous acute and chronic health conditions and diseases in Jordan today. TDT in Jordan is currently available in a handful of clinics in the country, and treatment is thus not widely accessible. Data are scare regarding tobacco use screening by healthcare professionals and offering of treatment to smokers. However, the high tobacco use rates in the country and the normalization of tobacco use locally (even among healthcare practitioners), suggest that tobacco use screening and treatment require more concerted and wide-scale promotion efforts so that these (screening, treatment) steps begin to be integrated in existing service-providing systems in Jordan (healthcare clinics, educational settings, and workplaces).

This guideline can serve as a reference for healthcare providers and educators interested in tobacco control and TDT. The purpose of the guideline is to provide an overview of TDT in Jordan, and describe evidence-based interventions that have demonstrated their value in TDT, and that can be used in Jordan. In order to ensure that reliable clinical information is being promoted, the Jordanian guideline relies throughout on several previously developed international evidence-based guidelines and reports as well as published scientific studies. Furthermore, where appropriate, content has been customized to apply to the local situation in the country. For example,

pharmacotherapies currently available in Jordan are described in detail, rather than all possible TDT pharmacotherapies.

International experts also have reviewed the guidelines, and endorsement by local health experts involved in TDT in Jordan has been obtained.

With regards to the specific content of these guidelines, an attempt has been made to cover the main topics relevant to applying TDT in Jordan. An overview of the situation in Jordan is provided, followed by a description of the two most important forms of smoker-healthcare provider (or smoker-educator) interactions for tobacco dependence management: 1) Brief advice, which can be applied by educators and healthcare practitioners with insufficient expertise or time to conduct intensive counseling – the guidelines describe two forms of brief advice: AAR, which involves **A**sking about tobacco use, **A**dvising smokers to quit, and **R**eferring them for further help; or 5As, which involve **A**sking about tobacco use, **A**dvising smokers to quit, **A**ssessing smokers' readiness to quit, **A**ssisting smokers to quit by setting a quit plan or referring them for further help, and **A**rranging for follow-up. 2) The second form of interaction for tobacco dependence counseling and treatment is face-to-face support, which involves additional interaction with the smoker through intensive counseling sessions possibly accompanied by medication use – in Jordan only physicians are authorized to prescribe medications, and therefore face-to-face support involving pharmacotherapies is anticipated to be performed by physicians only. Given the importance of pharmacotherapy in TDT, a separate section is included to address this topic. Other topics addressed in the guideline include waterpipe use, and tobacco use in children, two equally concerning public health issues in Jordan. For each topic, a concise description is given, and recommendations or main points of interest surrounding the topic are emphasized. Where implementation details are needed, flowcharts have also been included (flowcharts for AAR; 5As; face-to-face support; and medication use are available), and a series of appendices further provide clinical details for healthcare providers and educators interested in playing an active role in TDT. Topics in the appendices include the health consequences of smoking and tobacco use as well as the benefits of quitting; the nature of nicotine dependence and withdrawal symptoms when stopping tobacco use; assessment of motivation to quit smoking and nicotine dependence severity; designing a quit plan for smokers; using CO testing to assist TDT efforts; relapse to smoking and its prevention; specific instructions regarding the use of TDT

pharmacotherapies; and the principles of motivational interviewing. The issue of weight management during cessation also is included as an individual topic. Finally, TDT interventions that are marginally useful or whose efficacy is yet to be acknowledged widely in the medical field (e.g. use of self-help material; hypnosis), are mentioned briefly for those interested in knowing which methods are not currently endorsed by the Jordanian guideline.

These guidelines represent a starting point in Jordan's TDT efforts, and their development as well as revision will be on-going as TDT efforts expand and the guidelines become more integrated and used in Jordan.

II. Introduction

Jordan is a developing country with a population of about six million. In recent years, Jordan has recognized tobacco as a major health problem and has taken various steps to address tobacco control. However, statistics indicate that Jordan's tobacco problem, in comparison to other countries in the region, ranks high.[1]

According to a report of the prevalence of lifestyle related risk factors in Jordan, the prevalence of cigarettes and waterpipe (Argilla) smoking among adults was shown to be 32% and 8.7% respectively;[2] in Jordan's GYTS for 2009, current cigarette smokers and waterpipe smokers were reported at 11.5% and 20.7% respectively;[3] while the GHPS in 2004 stated that 34% of Jordanian physicians smoke cigarettes.*

Among adult smokers, roughly 63% have tried to quit smoking but did not succeed. There was a slightly higher percentage of male smokers trying to quit (66%) compared to female smokers (63%); however, when they tried to quit, a higher percentage of women were successful (13%) compared to men (8%).[2] Predictors of intention to quit cigarette smoking among Jordanian adults in Jordan were found to include: lightness of smoking (those who smoked less were more likely to report intention to quit), exposure to media antismoking messages, having a medical education, previous quit attempts, and smoker's mental health (those reporting unhappiness were more likely to have a quit intent).[4] It is also noteworthy that among adolescent smokers, 51.6% have the desire to quit smoking.[3]

Jordan ratified the World Health Organization's Framework Convention on Tobacco Control (WHO FCTC) in August 2004, and committed to the implementation of FCTC, its obligations and guidelines. The WHO FCTC, Article 14 (Demand reduction measures concerning tobacco dependence and cessation) recommends that countries design and implement effective programs to promote the cessation of tobacco use, including diagnosis, treatment and counseling services on cessation in national health programs, plans and strategies'.[5] Additional guidance contained in the FCTC Article 14 guidelines recommends that governments strengthen or create a sustainable infrastructure that motivates quit attempts, ensures wide access to cessation support, and provides sustainable resources to guarantee that such support is always available.[6]

* Unpublished statistics, provided by the Jordanian Ministry of Health

TDT Services in Jordan

Clinics: The Ministry of Health has three smoking cessation clinics at Primary Health Care centers (one clinic in each region: middle, north and south). They offer counseling and pharmacotherapy free of charge to smokers who desire to quit. These are the only available public health care sites for treatment. At King Hussein Cancer Center, there is another smoking cessation clinic that provides counseling and pharmacotherapy to cancer patients mainly, as well as smokers from the general population. No telephone support (Quitlines) has been established so far.

Pharmaceutical Treatment: TDT medications registered and available are Nicotine Replacement Therapies (NRTs), specifically patches, gums and lozenges; and varenicline. While Bupropion is not registered at the JFDA, it is available at KHCC.

Tobacco Treatment Training: Over the recent years, TDT training in Jordan has increased. Thus far, since 2011, about 200 healthcare professionals (physicians, dentists, pharmacists, nurses) were trained on TDT in Jordan, and an additional 327 health educators (school counselors and teachers) were trained in tobacco control and TDT basic principles.

Summary of TDT services: Despite the high level of interest in quitting, access to available treatment is still very limited when considering the high smoking rates prevalent in the country and there is a growing need to develop smoking cessation services. The MOH plans to expand these services by establishing more clinics, increasing the number of knowledgeable and trained health professionals; and making the pharmaceutical treatment products continuously available.

III. About Jordan's TDT Guidelines

- The Jordanian TDT Guidelines were developed to provide guidance for health professionals on how to help tobacco smokers stop smoking. They contain a set of actions and recommendations that a variety of health professionals (nurses, physicians, dentists, pharmacists, midwives) and educators can utilize for their patients, in order to identify those who smoke and provide them with the appropriate management and treatment for their tobacco dependence. The guidelines also provide information for healthcare decision makers with regards to the necessary tools and resources to provide treatment.
- The guidelines are available for all health professionals to use, with the intention of integrating TDT services into the national health care system. All health professionals can conduct the brief intervention to counsel patients (Ask, Advise and Refer; or Ask, Advise, Assess, Assist, and Arrange for follow-up), while face-to-face support can be performed by physicians, who are the only health professionals licensed to prescribe medications. School teachers and counselors can also benefit from these guidelines, particularly the section on support for tobacco dependence in children and adolescents. However, the guidelines will be updated and improved, in the light of the experience working with them.
- The guidelines are based on an updated comprehensive literature review. Yet, they are designed in accordance with the resources available in the country, in terms of expertise and manpower, pharmaceutical products and clinics providing the service.
- The guidelines cover the main forms of treatment and support for tobacco dependence (brief advice, face-to-face support, pharmacotherapy); and also include a special section on supporting children and adolescents, and waterpipe users. A concise overview of each subject is included and important points regarding each topic are summarized. Detailed notes or guides are provided through appendices and flowcharts.
- The guidelines were developed over several stages:
  i. Forming the Jordan Tobacco Dependence Treatment Guidelines Group: the group was formed through the Cancer Control Office (CCO) at KHCC (including tobacco control unit and TDT clinic); the focal point for tobacco control in the Jordanian Ministry of Health (MOH); and international experts. A plan was set and approved by the group with regards to how the guidelines should be developed and reviewed.
  ii. Conducting National Situation Analysis for TDT practices in Jordan: a situation

analysis regarding the current TDT practices in Jordan was conducted (by KHCC and the MOH) through a review of available data in Jordan. The fact that two thirds of adult smokers tried to quit in the past year, and over half of the adolescent smokers have the desire to quit, and the fact that limited resources are available for TDT in Jordan, showed that a wide gap exists between what smokers desire and what is actually available of TDT support in Jordan. The situation analysis suggests a need to expand service provision in both public and private sectors, and the need to empower health professionals to treat tobacco dependence.

iii. Designing the guidelines outline and contents: a review of the most up-to-date information available on TDT was first performed, focusing largely on internationally available TDT guidelines, relevant published literature reviews, and successful TDT models used in other countries. Following this review, and factoring in national resources available, the target audience for the guidelines, the actions expected to be accomplished by the target audience, and the challenges foreseen, the topics to be included in the national guidelines were selected and content developed as well as customized for each topic.

iv. Guidelines Review: the first draft prepared was preliminarily reviewed by Jordan Tobacco Dependence Treatment Guidelines Group; reviewed by national stakeholders (healthcare professionals representing the major health service providing entities in the country); and finally by a group of national, regional and international tobacco control experts attending a TDT workshop in Amman[†], where the guidelines were presented and discussed. After each review, the draft guidelines were modified according to the feedback received.

- The final approved guideline is also available in Arabic.

[†] "Towards strengthened tobacco dependence treatment in the Eastern Mediterranean Region: addressing Framework Convention on Tobacco Control (FCTC)'s Article 14". Amman, November 2013

IV. TDT interventions

1. Brief advice

- More than one model has been proposed to provide brief advise to smokers (e.g. the "AAR model" of Ask, Advise, Refer; and the "5 As model" of Ask, Assess, Advise, Assist and Arrange follow-up).
- Brief advice increases the overall tobacco abstinence rates. Even when patients are not willing to make a quit attempt, clinician-delivered brief interventions enhance motivation and increase the likelihood of future quit attempts.[7]
- When given by a physician to smokers attending a consultation for some other condition, brief advice has been found to increase 6-12 month continuous abstinence rates by an average of 2 percentage points compared with doing nothing or usual care.[8]
- Brief advice is intended to help patients realize the risks they are exposed to as a result of their tobacco use, and the benefits they will gain once they quit. On its own, it does not treat tobacco dependence, but it motivates tobacco users to make a quit attempt. For those who are heavy tobacco users, brief advice can also encourage them to seek and accept referral for treatment.[9]

AAR Model[10-12]

- The "AAR" model is recommended in primary medical care, where the health-care provider (physician, nurse, dentist, pharmacist, midwife) asks or identifies smoking patients, advises them to quit, adds some information about harmful effects of smoking, and refers them to a TDT clinic or quitline, or provides other resources such as printed materials.
- It is composed of three steps that would normally take around 3 minutes in total: Ask, Advise, and Refer.

A: Ask about tobacco use

- Ask every patient about tobacco use at every visit (at least once a year) to determine if patient is current, former, or never tobacco user.
- Determine what form of tobacco is used.
- Determine frequency of use (e.g. number of cigarettes or waterpipes smoked daily/weekly).
- Document tobacco use status in patient's clinical record.

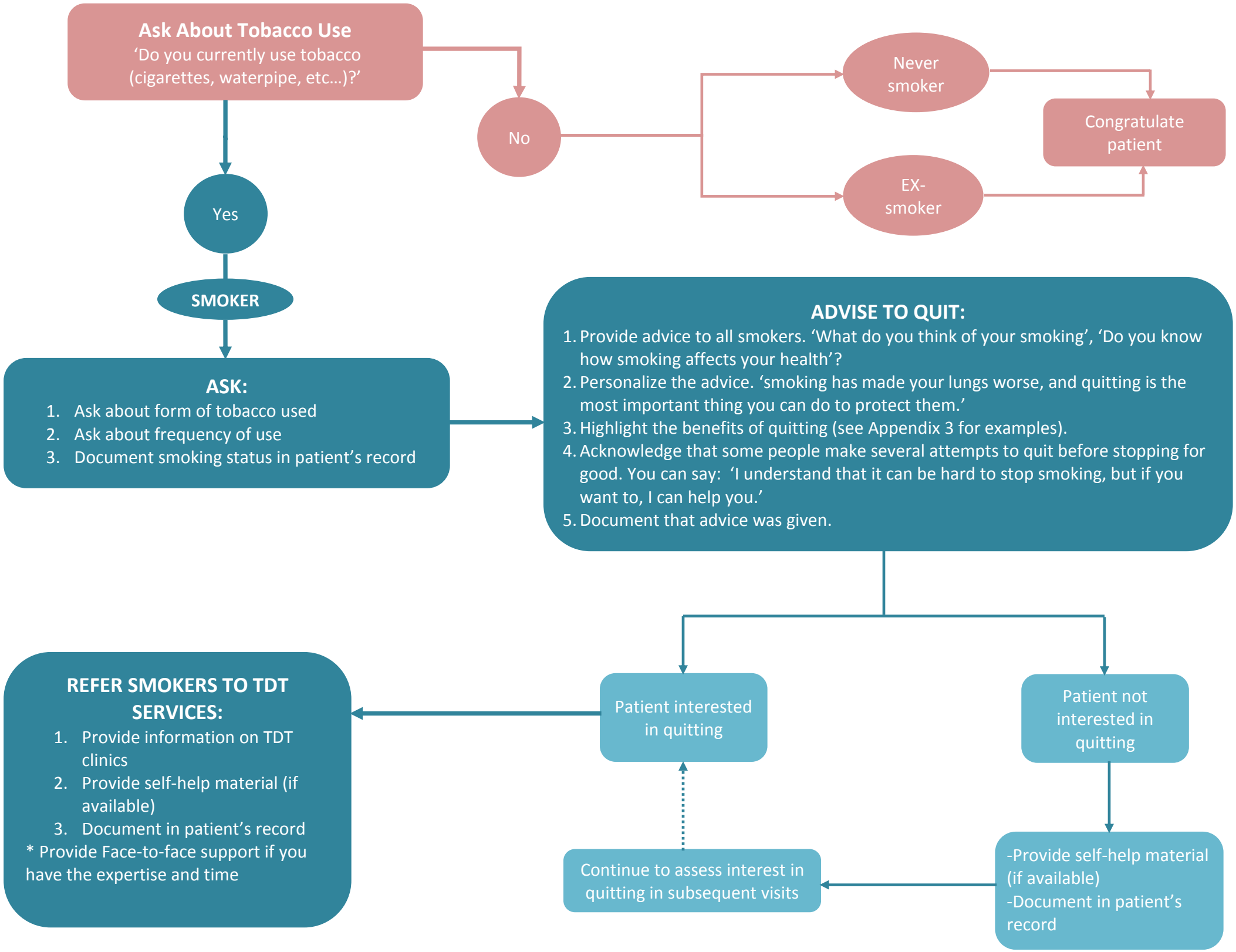
A: Advise to quit.

- In a clear, strong, and personalized manner, urge every tobacco user to quit.
- If relevant, explain how smoking is related to the existing health problems and how stopping smoking might help.
- Highlight the benefits of quitting smoking.
- Tobacco users who have not succeeded in previous quit attempts should be told that most people try repeatedly before permanent quitting is achieved.
- Document advice given in patient's clinical record.

R: Refer patient to TDT clinics

- Assist those interested in quitting by providing information on TDT clinics. If you do not have the expertise or time to help people to stop smoking, refer smokers to smoking cessation services. If you do have expertise and are thus able to, provide Face-to-Face support.
- For all smokers, provide self-help material (if available).
- Document what was done for the patient in patient's record.

Flowchart 1. Ask, Advise, Refer (AAR Model)



5A's Model[7, 9]

- An alternative model for the brief advice that can be used routinely by primary medical care is the 5A's model; where the health-care provider (physician, nurse, dentist, pharmacist, midwife) asks or identifies smoking patients, advises them to quit, adds some information about harmful effects of smoking, determines their readiness to quit, assists them with a quit plan or provides information on specialist support, and arranges for follow up or referral to TDT services.
- To be performed adequately, the 5A's model requires slightly more time, and more experience, than the AAR model.
- It is composed of five steps that would normally take around 5 minutes in total: **Ask, Advise, Assess, Assist, and Arrange**

A: Ask about tobacco use

- Ask every patient about tobacco use at every visit (at least once a year).
- Determine if patient is current, former, or never tobacco user.
- Determine what form of tobacco is used.
- Determine frequency of use.
- Document tobacco use status in patient's clinical record.

A: Advise to quit.

- In a clear, strong, and personalized manner, urge every tobacco user to quit.
- If relevant, explain how smoking is related to the existing health problems and how stopping smoking might help.
- Highlight the benefits of quitting smoking.
- Tobacco users who have not succeeded in previous quit attempts should be told that most people try repeatedly before permanent quitting is achieved.
- Document advice given in patient's clinical record.

A: Assess willingness to make a quit attempt

- Asses if patient is interested in quitting and wants to become a non-smoker (assess importance of quitting).
- Determine whether patient thinks he has any chance of quitting successfully (assess confidence in quitting).

- Document willingness to quit in patient's clinical record.

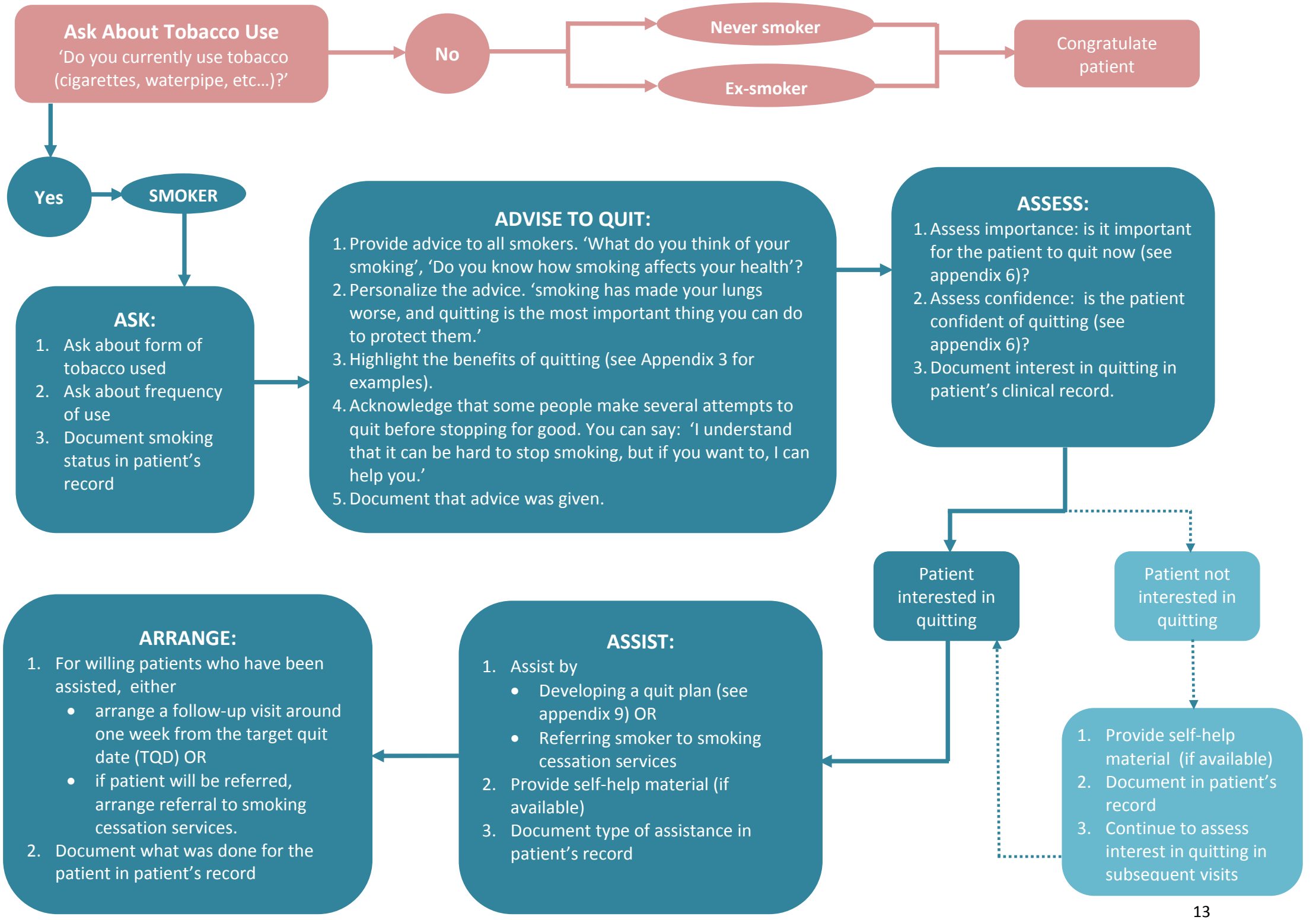
A: Assist in quit attempt

- Assist those interested in quitting by developing a quit plan. If you do not have the expertise or time to help people to stop smoking, refer smokers to smoking cessation services. If you do have expertise and are thus able to, provide Face-to-Face support.
- For all smokers, provide self-help material (if available).
- Document what was done for the patient in patient's record.

A: Arrange follow-up

- If the patient is willing to quit and you have provided assistance, arrange a follow-up visit in around one week from the target quit date (TQD).
- If the patient is willing to quit and you do not have the expertise or time to provide assistance, arrange referral to smoking cessation services.
- Document what was done for the patient in patient's record.

Flowchart 2. Ask, Assess, Advise, Assist and Arrange (5As model)



Summary points[7]

- The first step in treating tobacco and dependence is to identify tobacco users.
- All clinicians are in a position to intervene with patients who use tobacco.
- Brief advice should be offered to every patient who uses tobacco, and recorded at every visit.
- Providing a brief period of counseling is more effective than simply advising the patient to quit, and doubles the cessation rate, as compared with no intervention.

2. Face-to-Face Support

- Face-to-face support is a form of treatment health professionals can provide for smokers interested in quitting. Face-to-face support involves assisting the smoker in quitting by providing counseling and advice, prescribing appropriate pharmacotherapy, and subsequently following-up with the smoker with regards to outcomes of such support. Face-to-face support can take place in a one-to-one setting (health professional supports one patient) or a one-to-group setting (health professional supports more than one patient simultaneously).
- There is clear and consistent evidence that face-to-face support increases smoking cessation rates over that of minimal support.[13, 14] When given to smokers setting a quit date and willing to receive such help, individual face-to-face behavioral support has been found to increase 6-12 month continuous abstinence rates by 4 percentage points compared with provision of written materials or brief advice.[8]
- The evidence indicates that quit rates are generally higher when medication is used in combination with face-to-face support. Conversely, there is good evidence that adherence to smoking-cessation medication tends to be low without some form of behavioural support, and low adherence is associated with lower quit rates.[7] Thus in ideal circumstances, face-to-face support and medication use should be used in conjunction with one another.
- The basic principles of setting a quit date, emphasizing the importance of complete abstinence and providing multi-session support after smoking cessation are important.[7]
- More intensive support in terms of frequency and duration of contacts with smokers is associated with higher abstinence rates.[7]
- Delivering support for this purpose in a time set aside from general duties of the physicians can give even better results.[7]

Flowchart 3. Face-to-face support

Patient was given brief advice then referred by health professional

Patient was given brief advice by health professional and latter can provide further support

Patient self-referral

Smoker interested in quitting can be given Face-to-Face Support

1. INITIAL ASSESSMENT: Gather information on

i. Demographic factors that can assist in customizing advice
- Age
- Gender
- Marital status
- Number of children
- Education

ii. Tobacco use factors
- Age of onset of smoking
- Forms of tobacco used
- Number of cigarettes (or other forms) smoked/day or week
- Previous quit attempts (duration, treatments used, reasons for failure)

iii. Clinical factors
- All co-morbidities (DM, CVD, …) including psychiatric and substance abuse disorders
- Use of other medications
- Vital signs and body weight
- CO level

iv. Non-clinical factors
- Degree of social support
- Smoking patterns at home/work
- Personal reasons motivating quitting
- Perceived barriers or enabling factors

2. DETERMINE:

Level of Dependence: Fagerstrom Test for Nicotine Dependence (see appendix 5 for details)

Reasons for Smoking and Quitting

Level of Motivation (see appendix 6)
- Importance: 'on a scale of zero to 10, how important is it to you to quit smoking today?'
- Confidence: 'On a scale of zero to 10, how confident are you in your ability to quit smoking today?'

Carbon Monoxide Level (see appendix 10 for details)

3. Provide treatment

3. Provide treatment

Quit Plan

- Set TQD
- Discuss pharmacotherapy
- In week before TQD, encourage substantial effort to start quitting process.
- Emphasize importance of pre-quitting changes
- Provide support and encouragement
- Provide any necessary information needed by patient
- See Appendix 9 for details

Pharmacotherapy

Determine best pharmacotherapy for patient (see flowchart 4)

- Instruct patient on how to start medications (oral) in the week before TQD
- Instruct patient on how to start NRTs on TQD
- Advise patient on major side effects for medications
- See Appendix 11 for details

Relapse Prevention

- Address relapse at the initial assessment
- Identify situations that can cause relapse
- Build subject's confidence
- Use imagery
- Individualize the medication plan (see Appendix 8 for details)

4. Arrange for follow-up

Action during follow-up contact

- Determine abstinence status
- Identify any problems encountered by patient (e.g. withdrawal challenges)
- Assess medication use and problems (supply, side effects)
- Anticipate and talk about challenges in the immediate future (prevent relapse)
- If tobacco use has occurred, review circumstances and elicit recommitment to total abstinence.
- Provide self-help methods
- Document in patient record

Summary points[7]

- General Practitioners treat many cases of chronic diseases, and tobacco dependence is a chronic relapsing disease that requires treatment, same as other chronic diseases. It takes 20-25 minutes to help a smoker to quit (5-10 minutes at an initial visit and then several minutes at subsequent follow-up visits).
- Clinicians should encourage all patients who smoke to use medications as medically appropriate for treating tobacco dependence. When it is not possible to use pharmacological treatment, using non-pharmacological therapy such as counseling sessions remains recommended, so that all smokers receive therapeutic support.
- Clinicians should provide all smokers willing to quit with treatment in a format of minimum four face-to-face support sessions. This has proven efficient in increasing the abstinence rates.
- Clinic follow-up for pharmacotherapy should be at least for three months, and evidence shows that use of pharmacotherapy for longer than 3 months increases quit rates.
- Patients who use a pharmacotherapy should be strongly encouraged to use their medications precisely as directed.

3. Pharmacotherapy for Tobacco Dependence:

General principles of pharmacotherapy

- Pharmacotherapies for smoking cessation have generally been shown to be safe and cost-effective. Thus, when there are no contraindications, pharmacotherapy should be offered to any tobacco user who wants to quit.[7, 15]
- All pharmacotherapeutic regimens should be accompanied by counseling. Counseling and pharmacotherapy together are more effective than each given alone.[7]
- Pharmacotherapeutic management of tobacco dependent patients should be addressed in a similar manner to that of chronic disease management: multiple pharmacotherapeutic attempts may be needed to achieve and maintain abstinence.[15]
- It is particularly important that patients' report of withdrawal symptoms be inquired about and used to appropriately adjust medication doses during therapy. While dosing frequencies are detailed in appendix 11, individual therapy may require deviation from such dosing schedules in order to better meet individual patient needs.
- The start of tobacco dependence treatment presents a particularly challenging period for the smoker. Thus, intensive use of medications is important to ensure they are being used to achieve their maximum effect. The underuse of therapy (lower doses or single agents when combinations are more appropriate) can lead to poorer treatment outcomes and an inefficient use of medications.
- Increasingly, evidence is suggesting that more intensive pharmacotherapeutic interventions (particularly for highly dependent smokers) are safe and can improve cessation outcomes such as the achievement of abstinence or sustaining it.[7] Examples of intensive pharmacotherapeutic interventions include
    - Longer duration of therapy
    - Higher doses of conventional agents
    - Combination therapy with multiple agents (e.g. long-acting with short-acting NRTs; oral agents with long or short-acting NRTs)
        - In situations where oral agents are not available, combination NRTs should be used and optimal (generous) dosing provided.

A. Monotherapies

- The following medication categories are used for the treatment of tobacco dependence. Prescribing details regarding individual medication use are attached separately (see Appendix 11 for details).

I. Nicotine replacement therapies (NRTs)[7, 15, 16]

- One of the first-line therapies used for smoking cessation
- Mechanism: With smoking abstinence, nicotinic receptor occupancy in the brain declines, creating cravings. NRTs can control these cravings by occupying these receptors, thereby reducing withdrawal symptoms while nevertheless reducing the reinforcing effects of tobacco-delivered nicotine.
- Two- types of NRTs:
    i. Long-acting – nicotine patch
    ii. Short-acting – nicotine lozenge, gum, inhaler[‡], nasal spray[‡], sublingual tablet[‡], mouth mist/spray[‡]
- All NRTs deliver lower concentrations of nicotine than cigarettes. The nasal spray delivers the highest and fastest peak in nicotine (relative to other formulations), and thus most closely mimics but does not replicate the effect of a cigarette.
- General misconceptions about the use of NRTs have deterred their use and need to be noted. They include:[17]
    i. Erroneous perception regarding harms of NRTs - any risks that are associated with nicotine delivered by NRTs are much lower than the risks associated with smoking.
    ii. Concerns regarding abuse with and dependence on NRTs are exaggerated. In fact, such issues are rare to arise; rather NRT under-use is a bigger problem. Using lower than recommended doses of NRTs, particularly at the start of treatment when withdrawal symptoms are most severe, can reduce the chances of successful treatment.
    iii. NRTs can be safely used in cardiovascular patients (with the exception of those who are hemodynamically unstable, for example have suffered from a recent attack).

[‡] Formulations not currently licensed in Jordan

II. Varenicline[18-21]

- One of the first-line therapies used for smoking cessation.
- Mechanism: It is a nicotinic acetylcholine receptor (α4ß2 receptor) partial agonist and binds to nicotinic receptors in the brain. As a result, symptoms of craving and withdrawal are alleviated because varenicline's binding prevents binding of nicotine from tobacco, thereby reducing the rewarding and reinforcing effects of tobacco; and because varenicline also acts as an agonist and induces dopamine release in a similar manner to nicotine..
- The following rare side effects have raised concern regarding use of varenicline. However, such side effects occur infrequently, and pharmacovigilance studies have been inconclusive. While prescribers should be aware of these rare side effects (addressed below), varenicline generally is a safe medication and its side effect profile should not discourage it's selection as a TDT medication:
    i. Cardiovascular safety: studies are inconsistent with regards to the significance in cardiovascular event incidence between varenicline and non-varenicline users. However, all studies show that the rate of events is very low (rates in varenicline users have varied in studies from 0.3% to 1.06%).
    ii. Varenicline's label contains boxed warning about suicidal ideation and other neuropsychiatric adverse events. However, these events are rare to occur (in patients with and without pre-existing psychiatric disease) and there is no conclusive evidence regarding varenicline use, particularly because some of these events may actually be symptoms of nicotine withdrawal rather than a medication side effect. Nevertheless, varenicline users should be observed for symptoms such as changes in behavior, hostility, agitation, depressed mood, and suicide-related events.

III. Bupropion[22, 23]

- First-line medication.
- Bupropion is not not currently licensed in Jordan but is available at KHCC
- As a [monocyclic] antidepressant, bupropion inhibits the reuptake of norepinephrine and dopamine; bupropion may inhibit nicotinic acetylecholine

receptor function but its precise mechanism of action as a smoking aid is not clear.

- Bupropion's label contains a boxed warning about suicidal ideation and other neuropsychiatric adverse events. Some people have had changes in behavior, hostility, agitation, depression, and suicidal thoughts or actions while taking bupropion to help them quit smoking. However, as with varenicline, these events are rare to occur and there is no conclusive evidence. Bupropion users should nevertheless be observed for symptoms such as changes in behavior, hostility, agitation, depressed mood, and suicide-related events.
- A dose-related risk of seizures occurs with bupropion (the risk is 1:1000 or 0.1% at doses of upto 300 mg daily). Thus seizure risk is assessed and bupropion avoided if the patient appears to have an increased risk of seizures (e.g. recovering from head trauma).

IV. Other agents:

Nortriptyline[7, 23, 24]

- Second-line medication.
- Tricyclic antidepressant but its precise mechanism of action as a smoking aid not clear.
- Like most antidepressants, a warning regarding suicidality is included: thus patients should be observed for clinical worsening, suicidality, or unusual changes in behavior.

Cytisine[§]

- Cytisine bears similar pharmacological properties to varenicline, is currently licensed in some Eastern European markets, and is less costly than varenicline, rendering it a potential agent to be licensed in the future in Jordan.[8, 25, 26]

Clonidine

- Second-line medication.
- Clonidine is an α-2-adrenergic agonist and is used as an anti-hypertensive, but is also a second-line medication for tobacco dependence (it is thought that

[§] Medications not currently licensed in Jordan

clonidine counteracts centrally the features of nicotine withdrawal such as craving and anxiety).[7]

A. Combination therapies:

- Medical evidence suggests that the use of combination therapy is more effective than the use of single agents alone in tobacco dependence treatment. The following combination regimens can be used: (short-acting NRT + nicotine patch) or (short and/or long-acting NRT + oral agent). Specifically:

    i. Nicotine patch + (nicotine lozenge or nicotine gum or nicotine inhaler** or nicotine nasal spray**)[15-17]
    ii. Bupropion + either (nicotine lozenge or nicotine gum or nicotine inhaler** or nicotine nasal spray**) or (nicotine patch) or (both short and long acting NRT).[7, 27, 28]
    iii. Varenicline + either (nicotine lozenge or nicotine gum or nicotine inhaler** or nicotine nasal spray**) or (nicotine patch) or (both short and long acting NRT). The combination of varenicline and NRT has not been shown to be more effective regimen than varenicline monotherapy. However, the combination is tolerable, and is used in some clinical practices.[29, 30]

Medications – Cessation outcomes

- The abstinence rates for the pharmacological agents listed above are presented in Appendix 11 (Medications for treating tobacco dependence).

** Medications not currently licensed in Jordan

Flowchart 4. Medication use for tobacco dependence treatment

- Assess dependence severity
- Assess medical history, co-morbidities, medication use
- Assess patient preferences regarding cessation medications

Overall dependence can be considered mild to moderate (e.g. cigarette use per day is less than ten; Fagerstrom score is 5 or less; patient reports taking first cigarettes after 30 minutes from waking; or patient reports confidence in handling withdrawal symptoms when probed about their experience when tobacco use was reduced

Consider the following
1. Nicotine replacement monotherapy
2. Combination nicotine replacement therapy
3. Bupropion alone

Overall dependence can be considered medium to high (e.g. cigarette use per day is atleast ten and Fagerstrom score is 5 or more; patient reports taking first cigarettes within 30 minutes of waking; or patient reports difficulties (strong cravings / other withdrawal symptoms) when probed about their experience when tobacco use was reduced

Consider the following
1. Varenicline alone
2. Combination nicotine replacement therapy
3. Combination nicotine replacement therapy with bupropion
4. Combination nicotine replacement therapy with varenicline

RELAPSE

YES

NO

CONTINUED FOLLOW-UP

- Counsel patient to ensure proper dosage and administration techniques were used
- If proper dosages and administration techniques used, consider combination therapy if this was not used before
- If patient has been able to abstain while on medication and relapse occurs after treatment with medication has been completed, consider reinstating and/or prolonging previously used medications
- Counsel patient in problem-solving skills (avoiding triggers, responding to stressors appropriately, seeking support)
- See appendix 8

V. Support for tobacco dependence in children and adolescents

- In the US, among adults who ever smoked daily, 88% have tried their first cigarette before the age of 18, and as such, the issue of tobacco use in children is considered a pediatric disease that should not be overlooked by physicians and other health care providers.[31] In Jordan, roughly 57% of smokers (2007 data) began smoking by the age of 18, indicating that the problem of tobacco use among youth in Jordan is also pressing and requires specific focus.[††]
- The younger the age of onset of tobacco use, the more the problems caused by tobacco use. People who start smoking at a younger age have a more difficult time quitting, and those who continue to smoke risk earlier death from a smoking-related disease. Moreover, teen smokers are more likely to use alcohol and illegal drugs, and more likely to have panic attacks, anxiety disorders and depression.[31-33]
- Tobacco use affects brain maturation and even exposure to low nicotine levels may lead to changes in the brain that encourage continued use of nicotine and possibly other substances of abuse.[31] Addiction typically begins in childhood or adolescence. While the brain continues to develop into adulthood and undergoes dramatic changes during adolescence, the prefrontal cortex (the part of the brain that enables us to assess situations, make sound decisions, and keep our emotions and desires under control) is still a work-in-progress,[34] which puts adolescents at increased risk for poor decisions (such as trying drugs or continued illicit substance abuse).
- There is no particular intervention that has proven superior in treating tobacco dependence in young people.[35]

Risk factors for initiating tobacco use include:[31]

- Friends who smoke
- Parents behaviors and attitudes
- Co-morbid psychiatric disorders
- Exposure to advertising
- Others: Low self-esteem, low socio-economic status, health consequences seem far off, and desire to lose weight

How to assist children and adolescents in quitting:[7]

[††] Data provided from the Ministry of Health, 2007 Behavioral Risk Factor Survey – unpublished data

- Provide a strong message regarding the importance of abstaining from tobacco use
- Use counseling interventions that have generally been shown to be effective. The greater the intensity, the better the results achieved. Interventions include:
  - Brief advice especially when repeated.
  - Self-help pamphlets, reading materials or a referral.
  - Addressing matters of importance to this age group such as pocket money, appearance and beauty, and impotence
- Pharmacotherapy for this age group: while NRT is safe, efficacy is not established for NRT or bupropion in adolescents. Thus, medications are generally not recommended to be used with young people.
- Intervene in a manner that respects confidentiality and privacy (e.g., interview young people without parents' presence).
- Offer brief advice and cessation support to family members who smoke to limit the exposure to secondhand smoke, which can be a reason for failure to quit.

Summary points

- Health professionals should ask about smoking and provide a strong message against it.
- Counseling is crucial in this age group.
- Medications are not recommended. If to be used, only with precautions.
- Treating parents for tobacco dependence provides a suitable environment for quitting.

VI. Support for Tobacco Dependence Treatment in Waterpipe users:

- Waterpipe (Argilla) is becoming popular throughout the world, the rates of waterpipe smoking are increasing, with a peak among young people. Increased use is thought to be partly as a result of misperceptions about waterpipe smoking: It is thought to be less addictive & less harmful than cigarettes; users can quit at any time; the primary motives for waterpipe smoking are outings with friends, boredom and passing time.[36, 37]
- Waterpipe use in common in Jordan and although there are no evidence-based interventions for treatment, some key points can be provided for health professionals when treating waterpipe smokers:

Waterpipe effects

- Due to the various toxic substances found in waterpipe smoke,[38] waterpipe use has been associated with many acute as well as long-term detrimental effects.
    - Acute deterioration in cardiopulmonary measures
    - Increased risk of respiratory diseases and lung cancer

For further information regarding the specific health hazards of waterpipe use, see Appendix 2 for more details.

Waterpipe Dependence

- One session of waterpipe smoking (10 gm waterpipe tobacco) produces an amount of nicotine that is 4 times the amount produced in one cigarette.[39]
- Factors like time to the first smoke of the day, smoking even when ill, time to tobacco craving, and hating to give up the first smoke of the day, have been shown to be significantly associated with the number of hagars (sessions) smoked per day.[40] Thus, inquiring about these factors can give healthcare providers a better idea of the extent to which a waterpipe smoker is addicted.

Tobacco Dependence Treatment for Waterpipe Smokers

- Waterpipe smokers are not as interested as cigarette smokers in quitting smoking, only 28.4% of subjects express interest in quitting.[41]
- There are currently no guidelines, and data is limited regarding treatment of waterpipe dependence.[42] However, the following suggestions should be attempted with all waterpipe users:
    - Inquire about detailed patterns of use (regular vs. occasional)

- Provide counseling and motivational interviewing (creating interest to quit)
- Avoid comparing cigarettes to waterpipe (both are bad)
- Using pharmacotherapy: There is insufficient evidence regarding the use of pharmacotherapies [approved for cessation from cigarette smoking] in waterpipe users seeking to quit. Health professionals with sufficient expertise in these pharmacotherapies may choose to use them at their discretion.
- Dealing with relapse – relapse should be addressed in a similar manner to relapse in cigarette users.

VII. Appendices

Appendix 1: Tobacco Control

The MPOWER is a group of strategies that have been shown to reduce tobacco use. They have been successful in many countries, and there are indications that these strategies have a synergistic impact.[1]

MPOWER

- **M**onitor tobacco use and prevention policies
- **P**rotect people from tobacco smoke
- **O**ffer help to quit tobacco use
- **W**arn about the dangers of tobacco
- **E**nforce bans on tobacco advertising, promotion and sponsorship
- **R**aise taxes on tobacco

Appendix 2: Health consequences of smoking and tobacco use

Cigarette smoking[43]

Cancers associated with tobacco use:

- Lung cancer
- Oral cancer
- Laryngeal cancer
- Esophageal cancer
- Kidney and bladder cancers
- Cervical cancer
- Pancreatic cancer
- Stomach cancer
- Colorectal cancer
- Acute Myelod Leukemia
- Liver cancer

Cardiovascular Effects

- Heart attack (coronary heart disease)
- Stroke (cerebro-vascular disease)
- Peripheral arterial disease, resulting in increased risk of amputations

Respiratory Effects

- **COPD:** permanent loss of lung function occurs in some smokers, resulting in shortness of breath, impaired exercise capacity, and the frequent need for oxygen
- **Emphysema:** permanent dilation and destruction of the alveoli
- **Chronic bronchitis:** chronic mucus hypersecretion
- **Tuberculosis**

Smoking and diabetes

- Smoking raises blood glucose, increases the body's resistance to insulin, and causes changes in LDL and HDL profiles. Smoking is thus an important risk factor for diabetes.[‡‡]

Smoking and infertility

- Smoking is associated with impotence and infertility and is a probable cause of unsuccessful pregnancies

[‡‡]There is insufficient evidence that smoking *cessation* leads to higher short-term risk of DM in people with overweight, and an increased long-term risk of DM regardless of body weight or weight gain after cessation.

- Smoking increases frequency of menstrual abnormalities
- Smoking increases the risk of erectile dysfunction

Smoking and women's health effects

- Smoking causes intrauterine growth retardation, leading to low birth weight babies
- Smoking contributes to cervical cancer
- Smoking causes ectopic pregnancy

Smoking and other health effects

- Rheumatoid arthritis
- Impaired immune function
- Age-related macular degeneration

Waterpipe smoking

- Besides the enormous number of toxins known to be present in tobacco (CO, nicotine), waterpipe tobacco smoke contains polyaromatic hydrocarbons (PAH), nitrosamines (TSNA), and heavy metals (such as Arsenic, Beryllium and Lead), due to the use of coal to light up the waterpipe tobacco.[39, 44-49]
- Waterpipe smoking is associated with lung cancer, respiratory illness, bladder cancer, nasopharyngeal cancer, esophageal cancer.[50]
- Acute WTS appears to induce impairment in lung function and exercise capacity.[51] WTS also is associated with a significant reduction in FEV1, trend towards lower FVC, and a lower FEV1/ FVC.[52]
- Waterpipe smoking may be linked to COPD.[52]

Appendix 3: Benefits of Quitting

There are benefits that one will notice right after quitting and some will develop over time.[53, 54]

A. Immediate gains

- Heart rate and blood pressure begin to normalize
- CO levels drop within hours
- Within weeks, circulation has improved, and coughing and phlegm production decreased
- Within months, lung function and sense of smell/taste have improved

B. Long-term benefits

- Coronary heart disease risk is substantially reduced within 1 to 2 years of cessation
- Reduced risk of developing and dying from cancer (e.g. lung, oesophageal, bladder). However
    - Decline in risk of cancer takes a number of years after quitting but benefit increases the longer a person remains smoke free
- Risk of diseases such as PVD and COPD decreases

Appendix 4: Nicotine Dependence

Biological basis:[55, 56]

- Nicotine: is one substance recognized under the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) to be addictive. It is ranked third in substance dependence after heroin and cocaine.
- The binding of Nicotine to the Nicotonic Acetylcoline Receptors in the brain, leads to the release of dopamine.
- Dopamine is a neurotransmitter present in the regions of the brain that regulate movement, emotion, cognition, motivation, and feelings of pleasure.
- Initiation of drug abuse (tobacco use) is most of the times voluntary, but when addiction is developed, self-control can be impaired and quitting becomes difficult. Tobacco dependence can become in many smokers a chronic disease.

Factors Predicting More Intensive Tobacco-Dependence Treatment Requirements or higher risk of relapse[57-60]

- Higher level of physical nicotine dependence (Fagerström Test for Nicotine Dependence Score ≥ 5/10 points)
- Heavy cigarette smoker (≥25 cigarettes/day (cpd))
- Short time to first cigarette of the day (≤ 5 minutes)
- Female gender
- Starting regular tobacco use at young age (≤17 years old)
- Multiple previous quitting attempts
- Another cigarette smoker in the household
- Current psychiatric state
- Current alcohol or substance abuse
- Low motivation to quit

Appendix 5: Assessing Nicotine Dependence

Measuring the degree of nicotine dependence can help identify smokers who would benefit from more intensive assistance to quit. One of the most frequently used tools for assessing nicotine dependence is the Fagerström Test for Nicotine Dependence (FTND), which is composed of six questions. The Fagerstrom scale is a validated tool and widely used. The total test score determines level of dependence:[61]

- 0-2 Very low dependence
- 3-4 Low dependence
- 5 Medium/moderate dependence
- 6-7 High dependence
- 8-10 Very high dependence

The following questions comprise the Fagerstrom Test for Nicotine Dependence on Cigarettes, and the total test score is calculated by summing the score of each selected answer:

	SCORE
1. How soon after you wake up do you smoke your first cigarette?	
Within 5 minutes	3
6–30 minutes	2
31–60 minutes	1
After 60 minutes	0
2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in places of religious worship, at the library, cinema, etc.)?	
Yes	1
No	0
3. Which cigarette would you hate most to give up?	
The first one in the morning	1
Any other	0
4. How many cigarettes a day do you smoke?	
10 or less	0
11–20	1
21–30	2
31 or more	3
5. Do you smoke more frequently during the first hours after waking than during the rest of the day?	
Yes	1
No	0
6. Do you smoke if you are so ill that you are in bed most of the day?	
Yes	1
No	0

Appendix 6: Assessing level of motivation to quit

Assessing importance:[62]

On a scale of 0 to 10, how important is it for you to quit smoking today?

Assessing confidence:[62]

On a scale of 0 to 10, how confident are you in your ability to quit smoking today?

Appendix 7: Nicotine Withdrawal Symptoms

The following are symptoms that a smoker may experience upon reduction of or quitting tobacco use. Symptoms can vary in severity from one smoker to another and most of them disappear within four weeks of abstinence.

Symptoms include:[63]

- Irritation
- Anger
- Weight gain
- Insomnia
- Concentration difficulties
- Anxiety
- Restlessness
- Dysphoria
- Decreased heart rate
- Performance deficits
- Craving for smoking
- Headache

Appendix 8: Relapse and prevention

Relapse to smoking

- Relapse is resuming the use of tobacco after a period of abstinence.
- It is very common in tobacco dependence and does not mean failure of treatment.
- Relapse rates are similar to chronic medical illnesses (diabetes, hypertension, and asthma) which also have both physiological and behavioral components.[64]
- Relapse is associated with the severity of withdrawal symptoms, and the association of factors (such as stress and weight gain) with the process of quitting tobacco. Therefore, most smokers make repeated quit attempts before finally achieving long term abstinence.[65, 66]

Relapse prevention

There is no evidence of effectiveness of a specific intervention to prevent relapse.[67] However, the physician or counselor should exert all possible efforts to prevent relapse. The following points below are specific techniques that can be used to lower the chances of relapse.[7, 15, 65]

1. Address relapse at the initial assessment
2. Identify with the patient situations that can cause relapse.:
    - Triggers to relapse
        a. Negative emotions: anger, frustration, boredom
        b. Interpersonal conflicts: marriage, employer-employee
        c. Social pressure: other tobacco users
    - Pattern of use: morning, work, etc…
    - Exposure to SHS and smoking cues
    - Urge stimulants such as alcohol and coffee
    - Note that not all relapse triggers are stressful or negative situations: For example, Although relapse tends to occur in a high-stress situation, it can also occur in celebratory settings (particularly, in either situation, when the patient is using a alcohol).
3. Build patient's confidence by developing ways to guide them safely through such situations:
    - Build patient's coping skills:
        a. Cognitive: things patient can tell him or herself (see below)

        b. Behavioral: things patient can do (see below)
    - Teach them how to reduce the urge in trigger situations
    - Remind them of how they avoided relapse in similar situations
4. Use of imagery
    - Rehearse with patient his or her being in a triggering situation or problem – and mentally work it through without smoking
    - Instruct patient to do this (use of imagery) as often as they need
5. Individualize the medication plan – reinstate, adjust or combine medications.

Examples: building patient's cognitive coping skills

- Tell myself, "I can do this."
- Recall the reasons I want to quit.
- Tally the progress I've made so far.
- Remind myself smoking will not solve the problem(s) I'm facing right now.
- "I'm not smoking today."
- Play the cigarette through to the end.

Examples: building patient's behavioral coping skills

- Leave the situation
- Take a deep breath
- Use a strong mint
- Eat something
- Go for a walk
- Call a friend
- Exercise

Appendix 9: Designing a Quit Plan

Following the initial assessment, during the first consultation the smoker has with physician, the visit will typically involve:

1. Setting a target quit date (TQD)
    - Patients given a week (maximum 2 weeks if nicotine dependence is high)
2. Determine best pharmacotherapy for patient
    - Instruct patient on how to start medications (oral - Bupropion, Varenicline) in the week before TQD
    - Instruct patient on how to start NRTs on TQD
    - Advise patient on major side effects for medications.
3. During the week before TQD, patient must put in substantial effort to start the quitting process. Advise your patients to:
    - Learn not to smoke in closed places
    - Change favorite location to smoke
    - Remove all ashtrays from house to avoid visual triggers
    - keep in-door air free from smoke
    - Learn how to deal with acute urges: Manage the urge by:
        - ✓ Drinking water
        - ✓ Changing place: go out and walk
        - ✓ Going to bed early if urge is around bedtime
        - ✓ Taking a hot shower
        - ✓ Going to the gym
        - ✓ Chewing or sucking on items with strong taste as a minty sugarless gum or miswak
        - ✓ Staying away from alcohol or coffee/tea

- Cut back gradually in number of cigarettes smoked

4. Emphasize to patients that these changes in the week before the TQD are important to commit to and will help increase chance of success
5. Provide support and encouragement.
6. Provide any needed information.

Appendix 10: Carbon Monoxide Testing

The Breath CO Monitor (Smokerlyser):

- Simple, non-invasive screening test.
- Effective test to confirm the patient's smoking status.
- Provides the smoker with a direct, immediate feedback and motivation to quit.
- Monitors progress toward abstinence.

Instructions:

- Explain the procedure to the patient:
    1. Take a deep breath and hold it for 15 seconds
    2. Blow into the monitor (using a hygienic disposable mouthpiece)
- Read the CO level in PPM and COHb% that is shown within seconds on the display.

Carbon Monoxide Measurements:[68]

Smoking Status	**COHb**[§§]
Non-smokers living in a town	0.7%
Non-smokers living in a busy industrial setting or around smokers	1.5–2%
Cigarette smoker	5% or more (>10 ppm)
Smoker of 20 cigarettes per day	3–6% (15–34 ppm)
Smoker of 40 cigarettes per day	6–10% (15–60 ppm)
Smoker of >40 cigarettes per day	Up to 20%
Cut-off breath CO level for determination of smoking status is 2.5% COHb (10 PPM)	

[§§] CO readings are influenced by many factors such as the device brand, the cigarette brand, the number of cigarettes smoked, time elapsed since the last cigarette smoked, occupation, time of day…

Appendix 11: Pharmacotherapies for TDT

Medications for treating tobacco dependence[69, 70]

Varenicline (first-line agent)[18, 71-73]				
Tips for use; Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Pill form – convenient and easy • Generally well tolerated • No known drug interactions **Cons** • Nausea, abnormal dreams and sleep disturbances are common adverse effects	Available as 0.5mg and 1mg tablets 1. Start one week before target quit date. Instruct patient to try to gradually reduce tobacco consumption during this week. 2. On days 1 to 3 take 0.5mg daily (preferably evening) 3. On days 4 to 7 take 0.5 mg twice daily (morning and evening) 4. On target quit date (day 8), quit smoking and continue using 1.0mg varenicline twice daily for atleast 12 weeks ***Additional notes*** • Take with food and full glass of water to minimize nausea • Dosage can be temporarily reduced to 0.5mg twice daily to improve tolerability • Dose adjustment in renal insufficiency (CrCl<30): do not exceed 0.5mg bid • Dose adjustment in ESRD patients undergoing hemodialysis: 0.5mg qd. • In patients who maintain abstinence by end of first 12 weeks, an additional course of 12 weeks treatment at 1.0 mg twice daily may be considered to prevent relapse if patient indicates need to continue medication. • May stop abruptly; no need to taper. However, in smoking cessation therapy, risk for relapse to smoking is elevated in the period immediately following the end of treatment. In patients with a high risk of relapse, dose tapering may be considered. • Varenicline exerts a dose dependent effect. However, recommended doses are in place to avoid intensification of side effects, particularly risk of nausea. • Patients should exercise caution before driving or use of machinery until they are reasonably certain the therapy does not adversely affect their performance	Use with caution in patients: • With significant renal impairment or undergoing dialysis • With serious psychiatric illness	• Nausea • Abnormal (e.g., vivid, unusual, or strange) dreams • Constipation • Flatulence **Rare side effects:** i. Cardiac safety: data have demonstrated that cardiovascular events were infrequent overall, but some were reported more frequently in patients treated with varenicline (primarily in patients with known cardiovascular disease). Patients should be instructed to notify their health care providers of new or worsening cardiovascular symptoms and to seek immediate medical attention if they experience signs and symptoms of myocardial infarction or stroke. ii. Label contains black box warning about mood changes, suicidal ideation and attempts, and aggressive behavior.	• Average quit rate for varenicline was 46.5% compared to 18% for placebo at 9-12 weeks (pooled RR 2.57, 95% CI 2.33 to 2.84) • Average quit rate for varenicline (standard dose) was 24% compared to 11% for placebo at 6 months or longer (pooled RR 2.31, 95% CI 2.01 to 2.66)

Bupropion (first-line agent)[22, 23, 74, 75]				
Tips for use; Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Pill form – convenient and easy • May be used in combination with NRT (see combination regimens) • May be particularly useful in patients with a past history of depression or those suffering from depression • Good side effect profile • May attenuate weight gain associated with quitting **Cons** • Contraindicated with certain medical conditions and may interact adversely with MAO inhibitors	Available as 150mg tablets 1. Start one week before target quit date. Instruct patient to try to gradually reduce tobacco consumption during this week. 2. On days 1 to 3 take 150 mg daily (preferably morning) 3. On days 4 to 7 take 150 mg twice daily (leave atleast 8 hours between doses) 4. On target quit date (day 8), quit smoking and continue using bupropion 150 mg twice daily for atleast 12 weeks ***Additional notes*** • Treatment for as long as 12 months may be effective for reducing relapse. • Patients with cirrhosis need adjusted dose: 150mg every other day. • May stop abruptly; no need to taper. However, in smoking cessation therapy, risk for relapse to smoking is elevated in the period immediately following the end of treatment. In patients with a high risk of relapse, dose tapering may be considered. • Bupropion exerts a dose dependent effect. However, recommended doses are in place to avoid intensification of side effects, particularly risk of seizures. • Patients should exercise caution before driving or use of machinery until they are reasonably certain the therapy does not adversely affect their performance.	**Drug-drug interactions** • May interact adversely with MAO Inhibitors: Concomitant use of bupropion and MAOIs is contraindicated. At least 14 days should elapse between last dose of irreversible MAOI and first dose of bupropion. For reversible MAOIs, a 24 hour period is enough • Bupropion inhibits CYP2D6 so medications that are metabolized (deactivated) by this enzyme and have a narrow TI should be used at lower end of dose range. Examples of such medications include o certain antidepressants (e.g. desipramine, imipramine, paroxetine) o antipsychotics (e.g. risperidone, thioridazine) o beta-blockers (e.g. metoprolol) o Type 1C antiarrhythmics (e.g. propafanone, flecainide) • Drugs that are activated by CYP2D6 such as tamoxifen may have lower efficacy. • Bupropion is metabolized to its major active metabolite hydroxybupropion primarily by CYP2B6. Caution is advised when using bupropion with drugs that induce its metabolism (e.g. carbamazepine, phenytoin, ritonavir, phenobarbital) or drugs that inhibit its metabolism (e.g. sertraline, paroxetine, valproate) • Bupropion should not be used in patients taking other bupropion-containing medications (because the incidence of seizures is dose-dependent, and to avoid overdosage). **Drug-disease interactions** • Avoid in patients with hepatic failure • Bupropion is contraindicated in patients with a history of bipolar disorder as it may precipitate a manic episode during the depressed phase of their illness.	• Dry mouth • Insomnia **Rare side effects:** i. A dose-dependent risk of seizures (1:1000 at 300 mg daily); Asses seizure risk and avoid bupropion if risk is increased, e.g.: o Personal history of seizures o Significant head trauma/brain injury o Anorexia nervosa or bulimia o Concurrent use of medications that lower the seizure threshold o Patients undergoing abrupt withdrawal from alcohol or any medicinal product known to be associated with risk of seizures on withdrawal (in particular benzodiazepines and benzodiazepine-like agents) ii. Label contains boxed warning about mood changes, suicidal ideation and attempts, and aggressive behavior.	• Average quit rate for bupropion (standard dose) was 22% compared to 12% for placebo at 6 months (pooled RR 1.81, 95% CI 1.51 to 2.16). • Average quit rate for bupropion (standard dose) was 18% compared to 10% for placebo at 12 months (pooled RR 1.64, 95% CI 1.46 to 1.84).

Nortriptyline (second-line agent)[23, 24, 76, 77]				
Tips for use; Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Inexpensive **Cons** • Although studies have documented its effectiveness in TDT, dosages as well as length of treatment have varied. • Unlike bupropion and varenicline, nortriptyline should be started 10–28 days before the quit date to allow it to reach steady state at the target dose. However, most studies evaluating nortriptyline as a smoking cessation aid have initiated therapy ten days before the target quit date.	Dosage of 25mg tablets available. Studies of nortriptyline have started at a dose of 25 mg/day, increasing gradually to a target dose of 75–100 mg/day. Specifically, therapy can be initiated 10-28 days before the quit date to allow nortriptyline to reach therapeutic doses. Possible regimen to use: 1. 25 mg/day for 3 days 2. Increase dose to 50 mg/day for 11 days 3. Increase dose to 75 mg/day at week 3 4. At week 4, assess serum levels to confirm a therapeutic level (50-150 ng/ml serum). If level not yet reached, increase nortriptyline dose to 100 mg/day. 5. Reassess serum levels ***Additional notes*** • Should not be discontinued abruptly. • While length of treatment has been approximately 12 weeks, clinicians may extend therapy up to 24 weeks. • Patients should exercise caution before driving or use of machinery until they are reasonably certain the therapy does not adversely affect their performance	• Because of the risk of arrhythmias and impairment of myocardial contractility, use with caution in patients with cardiovascular disease. • Do not co-administer with MAO inhibitors.	• Sedation • Dry mouth • Blurred vision • Urinary retention • Lightheadedness • Shaky hands **Rare side effects** i. Label contains boxed warning – antidepressants may increase risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults. Therefore all patients should be observed for clinical worsening, suicidality, or unusual behavior changes.	• Average quit rate for nortriptyline was 20% compared to 10% for placebo at 6-12 months (pooled RR 2.03, 95% CI 1.48 to 2.78).

*Proportions calculated from Cochrane Reviews as [number of quitters in intervention or placebo group] / [number randomized to intervention or placebo group]; pooled RRs are adjusted for study heterogeneity

Nicotine replacement therapy (first-line therapies): Nicotine patch - delivers nicotine through the skin[16, 69, 70, 78]				
Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Easy to use • Only needs to be applied once a day • Few side effects **Cons** • Slower onset of delivery than other NRTs (however, the patch provides a more stable dosing of nicotine than other NRTs)	Available in 5mg, 10mg and 15mg [16-hour patches]; 15mg, 10mg and 5mg patches also known as step 1, step 2, and step 3 patches, respectively Patients should be encouraged to stop smoking before initiating NRTs. However, some patients cannot quit completely, particularly at the start of treatment. In such cases, instruct patient to cut down gradually; the use of NRTs before complete abstinence should not be encouraged, but is not contraindicated or alarming should it occur. An approximate dosing and time-frame for use is provided below. However, dosing of NRT should be adjusted primarily based on patient reports of withdrawal symptoms, cravings, or bothersome side effects. Thus, in clinical practice, healthcare providers may need to adjust the dosing provided below at their discretion. i.e. use higher NRT dose/longer duration therapy if withdrawal symptoms persist or use lower NRT dose/shorter duration therapy if use of NRTs is bothering patient: 1. Instruct patient to start NRT on day patient stops smoking. 2. Explain to patient how to apply the patch: apply the patch each morning and replace it the next day (in the event of sleep problems being reported when the patch is used over night, instruct the patient to apply the patch in the morning remove it before sleep; and apply a new patch immediately after waking the next morning) 3. Determine the patch dosages according to the following: ○ >40 cpd = 42 mg/day of NRT = two "15 mg patches" ○ 21-39 cpd = 28-35 mg/day of NRT = one "15 mg patch" plus one "10 mg patch" OR one "15 mg patch" plus one "5 mg patch" ○ 10-20 cpd = 14-21 mg/day of NRT = one "15 mg patch" OR one "10 mg patch" ○ <10 cpd = 14 mg/day of NRT = one "10 mg patch" 4. After 4-6 weeks of continued abstinence, reduce dose of patch every 2 to 4 weeks by 5 to 10 mg increments (patches), as tolerated. i.e. Adjustments should be made such that withdrawal symptoms and urges continue to be controlled. If reducing the dose increases withdrawal symptoms, gradual reduction of patch dosage could be delayed. ***Additional notes*** Apply to clean, dry intact areas of hairless skin (e.g. hip, upper arm, back). Rotate the patch – do not put on the same site on consecutive days.	**General to all NRTs** • In stable cardiovascular disease using NRT presents a lesser hazard than continuing to smoke. However NRTs should be avoided in patients who are haemodynamically unstable: e.g. those in the immediate (within 2 weeks) post-MI period; those with serious arrhythmias; and those with unstable angina pectoris. • Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely. • NRTs should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment - clearance of nicotine or its metabolites may be decreased (and therefore the potential for increased adverse effects).	• Skin irritation • Dizziness, headache • Gastrointestinal discomfort • Nausea, vomiting	• Average quit rate for patch (standard dose) was roughly 16% compared to 10% for placebo at 6 months or longer follow-up (pooled RR 1.81, 95% CI 1.51 to 2.16).

Nicotine replacement therapy (first-line therapies): Nicotine gum - delivers nicotine through lining of the mouth[16, 69, 70, 78]				
Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Easy to use • Can easily titrate based on intensity of withdrawal symptoms **Cons** • Compliance may be an issue since frequent dosing is needed • Inappropriate for people with dental or jaw problems • Proper chewing technique, which may not be easy for some to perform, is important in ensuring effective release of nicotine and minimal side effects. • The name ("gum") is misleading, since it is not chewed like a regular gum.	Available in 2mg and 4mg dosage. Patients should be encouraged to stop smoking before initiating NRTs. However, some patients cannot quit completely, particularly at the start of treatment. In such cases, instruct patient to cut down gradually; the use of NRTs before complete abstinence should not be encouraged, but is not contraindicated or alarming should it occur. Instruct patient to self-administer gum in response to nicotine craving. An approximate dosing An approximate dosing and time-frame for use is provided below. However, dosing of NRT should be adjusted primarily based on patient reports of withdrawal symptoms, cravings, or bothersome side effects. Thus, in clinical practice, healthcare providers may need to adjust the dosing provided below at their discretion. i.e. use higher NRT dose/longer duration therapy if withdrawal symptoms persist or use lower NRT dose/shorter duration therapy if use of NRTs is bothering patient: Instruct patient to start NRT on day patient stops smoking. *Smokers: less than a pack (<15 CPD):* 1. Week 1-6: chew one 2mg gum every 1-2 hours (10-15 pieces/day) 2. Week 7-9: chew one 2mg gum taken every 2-4 hours 3. Week 10-12: chew one 2mg gum taken every 4-8 hours *Smokers: one pack (15-20 CPD)* 1. Week 1-6: take one 4mg gum every 1-2 hours (10-15 pieces/day) 2. Week 7-9: take one 4mg gum taken every 2-4 hours 3. Week 10-12: take one 4mg gum taken every 4-8 hours *Smokers: >21 CPD* It is not advised that nicotine gum alone should be used for heavy smokers. However, in situations where only gums are available, the dosing regimen specified for smokers of 15-20 CPD should be referred to. *Additional notes* Instructions for patients: • Administer gum in response to nicotine craving. • Taste may be unpleasant at start but advise continued use • Do not eat or drink 15 minutes before use or during use • Avoid acidic beverages • Advise patients to chew gum as follows: ○ Chew slowly for 15–30 chews then when peppery or tingling sensation appears park between cheek and gum ○ Resume chewing when taste or tingle fades (about one minute) and rotate to different sites of the mouth when chewing is resumed ○ Try to minimize swallowing to increase the availability of nicotine to be delivered through lining of the mouth ○ Repeat chew/park steps until taste or tingle does not return at all (about 30 minutes) ○ Do not use more than one gum simultaneously or take gums directly after one another as this may increase possibility of side effects	• General to all NRTs • In stable cardiovascular disease using NRT presents a lesser hazard than continuing to smoke. However NRTs should be avoided in patients who are haemodynamically unstable: e.g. those in the immediate (within 2 weeks) post-MI period; those with serious arrhythmias; and those with unstable angina pectoris. • Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely (catecholamines released by nicotine can affect carbohydrate metabolism). • NRTs should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment - clearance of nicotine or its metabolites may be decreased (and therefore the potential for increased adverse effects). • Swallowed nicotine may exacerbate symptoms of oesophagitis, gastritis or peptic ulcers – use oral NRTs with care in these conditions.	• Mouth soreness, hiccups (from excessive swallowing of nicotine at first), dyspepsia, and jaw ache. • Side effects are mild and transient and often avoided by correcting chewing technique.	• Average quit rate for gum was roughly 18% compared to 11% for control at 6 months or longer follow-up (pooled RR 1.43, 95% CI 1.33 to 1.53). • In the case of highly dependent smokers, there was a significant benefit of 4 mg gum compared with 2 mg gum, but evidence is lacking with regards to the benefit of higher doses of patch.

Nicotine replacement therapy (first-line therapies): Nicotine gum - delivers nicotine through lining of the mouth[16, 69, 70, 78]				
Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
	Tips to taper dose (at roughly 7th week of treatment) • Decrease total number of pieces used per day by about 1 piece every 4 to 7 days. • Decrease the chewing time with each piece from the normal 30 minutes to 15 minutes. Substitute one or more pieces of sugarless gum for an equal number of pieces of nicotine gum and gradually increase number of pieces of sugarless gum.			

Nicotine replacement therapy (first-line therapies): Nicotine lozenge - delivers nicotine through lining of the mouth[16, 69, 70, 78]				
Pros and Cons	**Dosage and instructions for use**	**Warnings and contraindications**	**Side effects**	**Abstinence rates in literature***
Pros • Easy to use • Can easily titrate based on intensity of withdrawal symptoms • Nicotine concentrations delivered are roughly 25% higher than those of nicotine gum **Cons** • Compliance may be an issue since frequent dosing is needed	Available in 1mg dosage. Patients should be encouraged to stop smoking before initiating NRTs. However, some patients cannot quit completely, particularly at the start of treatment. In such cases, instruct patient to cut down gradually; the use of NRTs before complete abstinence should not be encouraged, but is not contraindicated or alarming should it occur. Instruct patient to self-administer lozenge in response to nicotine craving. An approximate dosing and time-frame for use is provided below. However, dosing of NRT should be adjusted primarily based on patient reports of withdrawal symptoms, cravings, or bothersome side effects. Thus, in clinical practice, healthcare providers may need to adjust the dosing provided below at their discretion. i.e. use higher NRT dose/longer duration therapy if withdrawal symptoms persist or use lower NRT dose/shorter duration therapy if use of NRTs is bothering patient: Instruct patient to start NRT on day patient stops smoking. *Smokers: less than a pack (<15 CPD):* 1. Week 1-6: take one 1 mg lozenge every 1-2 hours (10-15 pieces/day) 2. Taper as tolerated (roughly by week 7-9): take one 1 mg lozenge taken every 2-4 hours 3. Continue to taper as tolerated (roughly by week 10-12): take one 1 mg lozenge taken every 4-8 hours *Smokers: >14 CPD* It is not advised that 1 mg nicotine lozenges alone should be used for smokers of 15 CPD or more. *Additional notes* • At least 9 lozenges should be used daily for the first 6 weeks to improve chances of quitting. However, do not exceed 20 lozenges daily. • Do not eat or drink 15 minutes before use or during use • Avoid acidic beverages • Advise the patients to use the lozenge as follows: o Allow lozenge to dissolve slowly in the mouth over 20–30 minutes, periodically moving the lozenge within mouth to different areas, and try to minimize swallowing o Nicotine release may cause a warm, tingling sensation. This o is normal o Do not chew, bite or swallow lozenge o Do not use more than one lozenge simultaneously or take lozenges directly after one another as this may increase possibility of side effects Tips to taper dose (at roughly weeks 7 to 12) • Decrease total number of lozenges used per day by about 1 piece every 4 to 7 days. • Substitute one or more pieces of mint lozenges for an equal number of nicotine lozenges and gradually increase number of mint lozenges.	• General to all NRTs • In stable cardiovascular disease using NRT presents a lesser hazard than continuing to smoke. However NRTs should be avoided in patients who are haemodynamically unstable: e.g. those in the immediate (within 2 weeks) post-MI period; those with serious arrhythmias; and those with unstable angina pectoris. • Patients with diabetes mellitus should be advised to monitor their blood sugar levels more closely (catecholamines released by nicotine can affect carbohydrate metabolism). • NRTs should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment - clearance of nicotine or its metabolites may be decreased (and therefore the potential for increased adverse effects). • Swallowed nicotine may exacerbate symptoms of oesophagitis, gastritis or peptic ulcers – use oral NRTs with care in these conditions.	• Hiccups • Heartburn • Nausea	• Average quit rate for lozenge was roughly 16% compared to 8% for control at 6 months or longer follow-up (pooled RR 2.00, 95% CI 1.63 to 2.45).

Combinations

Medication	Tips for use; Pros and Cons	Dosage and instructions for use	Warnings and contraindications	Common side effects	Abstinence rates in literature*
Short and long-acting NRTs[70]	**Pros** • Permits sustained levels of nicotine (through the patch) with rapid adjustment for acute needs (through gum or lozenge) • More efficacious than monotherapy **Cons** • Cost	• Dose the patch as according to daily smoking frequency as described in individual NRT sections • Prescribe the nicotine gum or lozenge every 1-2 hours and as needed when acute withdrawal symptoms occur. • Adjust dose of patch upward if unusually frequent use of immediate-release NRT is needed. The goal is to minimize need for short-acting NRT dosing. • Taper NRTs as described in individual NRT sections	See individual medication warnings.	See individual medication warnings. Warn patient about common side effects between agents since these can increase in intensity when agents are combined (e.g. nausea, vomiting, insomnia).	• Average long-term quit rate for combination NRT was 15% compared to 9.8% for no or single NRT (pooled RR 1.35, 95% CI 1.11 to 1.63)
Bupropion and NRTs[27, 28, 70]	**Pros** • In addition to bupropion's advantages, this combination permits rapid nicotine adjustment for acute needs (if gum or lozenge used) as well as sustained levels of nicotine (if patch is used) • More efficacious than monotherapy **Cons** Cost	• Bupropion may be prescribed with the patch and short-acting NRT in some patients, if dependence is very high. • Begin bupropion 1 week before TQD as instructed when using bupropion alone. • Select nicotine patch based on smoking frequency and begin using on TQD. • Taper patch based on response or as usual (typically within 4 to 6 weeks). • Short-acting NRTs may also be prescribed if cravings are strong. • Patients should exercise caution before driving or use of machinery until they are reasonably certain the therapy does not adversely affect their performance.	See individual medication warnings.	See individual medication warnings. Warn patient about common side effects between agents since these can increase in intensity when agents are combined (e.g. insomnia).	• Abstinence at longest follow-up was 22.4% for bupropion + patch versus 9.8% for patch alone (RR = 2.28, 95% CI 1.46 to 3.56)
Varenicline and NRTs[29, 30],***	**Pros** • In addition to varenicline's advantages, this combination permits rapid nicotine adjustment for acute needs (if gum or lozenge used) as well as sustained levels of nicotine (if patch is used). **Cons** • Cost	• Begin varenicline 1 week before TQD as instructed when using varenicline alone. • Select nicotine patch based on smoking frequency and begin using on TQD. • Taper patch based on response or as usual (typically within 4 to 6 weeks). • Short-acting NRTs may also be prescribed if cravings are strong. • Patients should exercise caution before driving or use of machinery until they are reasonably certain the therapy does not adversely affect their performance.	See individual medication warnings.	See individual medication warnings. Warn patient about common side effects between agents since these can increase in intensity when agents are combined (e.g. nausea, insomnia).	• Limited studies on this combination. However, practitioners may find this combination of benefit in patients who are highly dependent and use varenicline, but require an additional means of acute withdrawal symptom control.

*** King Hussein Cancer Center – Smoking Cessation Clinic, personal communication, October 8, 2013.

Appendix 12: Motivational Interviewing

Motivational interviewing (MI)[62]

- MI is a person-centered counseling style, recommended for substance-abuse patients (smokers), that requires more time than brief intervention.
- It is a collaborative goal-oriented method of communication, where the provider helps the smoker through the change process. It is intended to strengthen personal motivation for and commitment to a target behavior change, by eliciting and exploring an individual's own arguments for change.
- MI is based on collaboration rather than confrontation, evocation rather than education and autonomy instead of authority.
- Across many studies and reviews MI showed a consistent, moderate effect in promoting a variety of behavior change

Appendix 13: Self-help materials

- Using materials such as a self-help manual, a handout, internet sites and booklets, to provide support and advice for smokers, and to provide information on tobacco dependence treatment and related pharmacotherapies, without the help of health professionals, counselors or group support.
- Self-help strategies marginally affect quit rates, especially when offered without any form of counseling.[79]
- There is evidence that materials tailored for individual smoker groups (e.g. pregnant women or patients with heart disease) are more effective than generic materials.[9]

Appendix 14: Weight Gain after Stopping Smoking

The following points need to be considered:[7, 80]

- Concerns about weight gain can be barriers to smoking abstinence.
- The majority of smokers gain weight fewer than 5 kilograms.
- Women tend to gain more weight than men do, and heavy smokers (more than 25 cigarettes per day) are at higher risk for major weight gain.
- Weight gain appears to be caused both by increased intake and by decreased metabolism.

Summary points

- Recommend starting/increasing physical activity and adopting a healthy diet
- Reassure patient that weight gain after quitting is common and usually self-limiting.
- Counsel on health benefits of quitting relative to the health risks of modest weight gain and health risks of continued smoking.
- Dieting at the same time as stopping smoking may increase the risk of relapse, therefore people should concentrate on achieving and maintaining abstinence from smoking first and then tackle the issue of weight gain.
- Use medications known to attenuate weight gain (e.g. nicotine gum and bupropion attenuate weight gain during therapy).

Appendix 15: Other approaches to smoking cessation in Jordan

A) Alternative methods for treating tobacco dependence

- There is no consistent evidence that acupuncture and related techniques (acupressure, laser therapy and electrostimulation) are effective for smoking cessation.[81]
- Hypnotherapy has not been shown to have greater effect on quit rates than other interventions or no treatment.[82]

B) Electronic Nicotine Delivery Systems (ENDS, or E-cigarettes)

- ENDS are electronic devices that contain nicotine and substances (eg: propylene glycol and glycerine) that when heated help to deliver nicotine to the user. Some also contain flavorings, like menthol.[83]
- ENDS are currently a topic of wide debate:[84] Some reports suggest they can help smokers quit by reducing cravings and withdrawal symptoms. Others have shown immediate harmful effects on pulmonary function, despite the fact that the exposure to toxic substances (as tar) is found to be less in e-cigarettes compared to conventional ones. However, the evidence is still insufficient regarding ENDS efficacy in cessation and its harms on health, and more studies are needed in this field.

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