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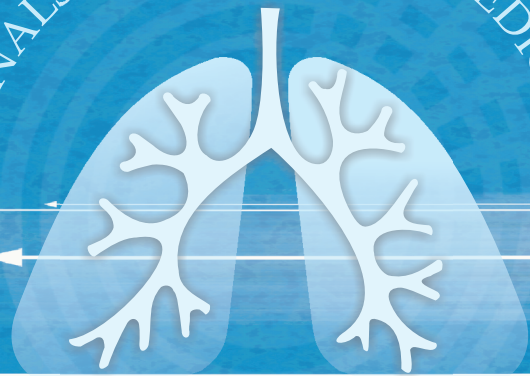
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Saudi lung cancer prevention and screening guidelines

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Abstract:

BACKGROUND: While lung cancer is the leading cancer cause of death, it is largely preventable. Furthermore, early diagnosis enhances the chance of cure. Therefore, we developed guidelines for lung cancer prevention and early detection.

METHODS: A multidisciplinary team of experts in lung cancer representing different health-care sectors was assembled based on the National Cancer Center request and in coordination with the Saudi Lung Cancer Association of Saudi Thoracic Society. The team reviewed various reliable international guidelines and the data and experience in the Kingdom and formulated guidelines that address the primary and secondary prevention approaches in lung cancer, including tobacco control, early diagnosis, and lung cancer screening.

RESULTS: The team developed guidelines to assist healthcare professionals in the Kingdom manage the different aspects of lung cancer prevention. Primary prevention through tobacco control: the recommendations encourage all healthcare professionals in all practice settings to screen their patients for smoking and to provide counseling and if needed referral to smoking cessation programs for current smokers. For early diagnosis of patients with symptoms suspicions of lung cancer, it is expected standard of care to investigate, work up, and refer the patients appropriately. Mass screening of patients at high risk for developing lung cancer: the recommendations listed the program requirements, eligible patients, and algorithm to manage findings. However, the team does not recommend that national screening program be mandated or implemented for lung cancer at this stage until more data and studies provide stronger evidence to justify adopting a national program.

CONCLUSIONS: Physicians can play an important role in preventing lung cancer by tobacco control and also detect lung cancer at earlier presentation. However, national mass screening programs require further study.

Keywords:

Guidelines, lung cancer, lung cancer guidelines, lung cancer prevention, lung cancer screening, prevention, Saudi lung cancer, screening

Lung cancer is the number one cancer killer worldwide afflicting the lives of 1.8 million annually.^[1] In Saudi Arabia, lung cancer is on the rise increasingly claiming lives as the major risk factor causing it, namely smoking in various forms, and is on the rise in all age groups and genders.^[2] In 2014, lung cancer ranked fourth among Saudi males and seventeenth among Saudi

females. There were 452 documented cases of lung cancer accounted for 3.9% of all newly diagnosed cases among Saudis in 2014. Lung cancer affected 354 (78.3%) males and 98 (21.7%) females, with a male-to-female ratio of 361:100. The Age standardized rate (ASR was 5.3/100,000 for males and 1.4/100,000 for females.^[2] In Canada, lung cancer is the most commonly diagnosed form of cancer (26,600 new cases in 2015; 51.9 per 100,000) as well as the main cause of cancer-related mortality among

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Canadians (21,100 estimated deaths in 2017; 51.4 per year 100,000).^[3] In the United States, the incidence of lung cancer (estimated 234,030; 54.6 per 100,000, data for 2011–2015) is second only to the incidence of breast cancer but tops all other forms as the leading cause of cancer deaths (estimated 154,050; 43.4 per 100,000, data for 2011–2015). In both countries, almost all (>90%) new cases of lung cancer in 2016–2017 are expected to be identified in adults aged 50 years and older.^[3,4]

Smoking causes cancer not only among smokers themselves but also among exposed individuals at workplace or home. Other industrial/environmental risk factors such as asbestos exposure and others account for smaller fraction of cancer cases.

When diagnosed, lung cancer kills 85% of its victims. However, what is promising in the fight against lung cancer is the fact that it is largely preventable.^[5] Avoiding tobacco will eliminate 85% of lung cancer cases.

Therefore, the primary prevention of lung cancer by avoiding tobacco is a very effective strategy. On the other hand, cure rate for cases diagnosed early in Stage I can be up to 85% which steps down to 1% in Stage IV.

In conclusion, detection of lung cancer at earlier stage does improve the overall survival of patients. Finally, major efforts should be directed toward preventing lung cancer from occurring in the first place by tobacco control and in high risk patients, detect cancer in early, highly curable stage.

Methods

A multidisciplinary team including consultants from different disciplines was invited by National Cancer Center at Saudi Health Council to form the Lung Cancer Prevention and Screening Committee. The Committee included consultants in thoracic surgery, pulmonary medicine, medical imaging, oncology, and primary care representing different healthcare sectors in the Kingdom of Saudi Arabia. The committee worked in collaboration with Saudi Lung Cancer Association (SLCA) of the Saudi Thoracic Society.

The team set the objective of the guidelines and decided to follow the previously established format and same categories of level of evidence by the SLCA when published in the Saudi Lung Cancer Guidelines 2017.^[6]

The guidelines level is as follows:

1. (EL-1) High level: Well-conducted phase III randomized studies or meta-analysis
2. (EL-2) Intermediate level: Good phase II data or phase III trials with limitations

3. (EL-3) Low level: Observational/retrospective study/expert opinion.

The guidelines are divided into primary prevention, early detection, and screening. Various guidelines were reviewed from the literature of local data and then constructed the guidelines. The guidelines were reviewed internally by all members and externally by the Director of National Cancer Center.

Lung cancer primary prevention

The prevention of lung cancer is centered around tobacco control. This daunting task is the responsibility of multiple entities from national governing bodies all the way down to the individual level as shown in Table 1. These guidelines focus on the healthcare professionals' role in prevention.

In this monograph, our multidisciplinary multicenter national group provides guidelines for primary lung cancer prevention and lung cancer screening.

Management Guidelines for Tobacco Control for Healthcare Providers

Overview

Stop smoking cessation interventions and services should be available in primary care and community settings for everyone over the age of 12 years.^[7] The aim of these guidelines is to ensure that everyone who smokes is screened for smoking and is given the required advice and motivation to stop and all the assistance they might need for quitting and preventing relapse.^[8]

General measures

1. Use local statistics to estimate smoking prevalence among the local population^[9]
2. Prioritize specific groups who are at high risk of tobacco-related harm
3. Assure that your facility is smoke-free facility and your patient and staff are not smoking in areas that are not designated for smoking
4. If you are a smoker, stop smoking, seek help if needed. It is advisable for your own, your family's, and your patients' health. You will be a good role model to your patients. It was found that smoking physicians are less likely to counsel their patients about smoking^[10]
5. Acquire and provide smoking cessations tools and materials in your facility
6. Attend smoking cessations training workshop, if possible
7. Identify local/community resources to refer your patients, when needed.

Screening patients for smoking

1. Ask all your patients systematically if they smoke or not. Make it part of their vital signs^[11] (EL-1)

2. Monitor stop smoking services by setting targets, including the number of people using the service and the proportion who successfully quit smoking^[7]
3. If a smoker is identified, implement smoking cessation guidelines of point 3.
6. Self-management technique should be used (such as print and web-based materials)^[13] (EL-2)
7. Enlist the help of available resources in your community
8. For all adults, use varenicline, bupropion or nicotine replacement therapy (NRT). Except where contraindicated or for specific populations for which there is insufficient evidence of effectiveness (i.e., pregnant women, smokeless tobacco users, light smokers, and adolescent) (EL-1)

Smoking cessation intervention

If a patient is identified as a current smoker, counseling should be provided.

1. Provide smoking cessation counseling using the 5A technique (Ask, Advise, Assess, Assist, and Arrange) or any other proven approach (EL-1)^[8] [Table 2]
2. Once a tobacco user is identified and advised to quit, a clinician should assess the patient’s willingness to quit at this time
3. Tobacco dependence treatment (such as medication) is effective and should be delivered to every individual even if the specialized assessment is not used or available (EL-1)
4. If the patient is not ready to quit, use motivational intervention. To motivate the patient, consider quit attempt with the “5 R’s” (Relevance, Risk, Reward, Roadblocks, and Repetition) (EL-2)^[8,12] [Table 3]
5. Cognitive behavioral therapy and support (counseling) involves delivering evidence-based behavior change techniques, most commonly provided face-to-face individual or groups (EL-1)
9. Agree a quit date set within the first 2 weeks of bupropion treatment and within 1–2 weeks of varenicline treatment (EL-1)
10. Agree a quit date if NRT is prescribed. Ensure that the person has NRT ready to start the day before the quit date (EL-1)
11. Ensure follow-up and behavioral support is provided
12. Ensure at least a very brief advice is delivered
13. Monitor compliance by auditing patients’ self-reported abstinence records, using objective measures such as carbon monoxide monitoring. Success is defined as less than 10 parts per million (ppm) at 4 weeks after the quit date. This should not imply that treatment should stop at 4 weeks^[7]
14. In relapsed patients, assessment has to be done to determine if they are willing to quit again (EL-3)

Table 1: Roles of various entities in tobacco control

Entity	Roles in Tobacco control
Government	Enacts and enforces laws to reduce tobacco use and minimize its harm
Society/public	Avoid normalizing smoking as a socially acceptable habit
MOH	Train adequate number of professionals and provide smoking cessation services
Health care facilities	Offer smoking cessation services to smokers and ban smoking in facility
Public/private businesses	Ban smoking in public places outside designated areas
Health care professionals	Actively identify current smokers, provide counseling, guidance, refer active smokers. Avoid smoking themselves

MOH=Ministry of health

Table 2: The “5 A’s” model for treating tobacco use and dependence

Action	What to Do
Ask	Identify and document tobacco use status for every patient at every visit
Advise	In a clear, strong, and personalized manner, urge every tobacco user to quit. (EL- 1)
Assess	Is the tobacco user willing to make a quit attempt at this time? (EL- 3)
Assist	For the patient willing to make a quit attempt, offer medication and provide or refer for counseling or additional treatment to help the patient quit (EL-1) For patients unwilling to quit at the time, provide interventions designed to increase future quit attempts
Arrange	For the patient willing to make a quit attempt, arrange for follow up contacts, beginning within the first week after the quit date For patients unwilling to make a quit attempt at the time, address tobacco dependence and willingness to quit at next clinic visit

Table 3: Enhancing motivation to quit tobacco, the “5 R’s”

Factor	What to Do
Relevance	Encourage the patient to identify reasons to stop smoking that are personally relevant
Risks	Advise the patient of the harmful effects of continued smoking, both to the patient and to others, incorporating aspects of the personal and family history whenever possible
Rewards	Ask the patient to identify the benefits of smoking cessation
Roadblocks	Explore the barriers to cessation that the patient may encounter
Repeat	Include aspects of the five R’s in each clinical contact with unmotivated smokers

15. If the patient is willing to make another quit attempt, offer behavioral support, medication, and arrange for follow-up.

Lung cancer early detection

Early detection of lung cancer means to discover cancer as early as possible by recognition of the possible early signs and symptoms of cancer and doing the proper workup or referral to confirm or rule out cancer. Early detection may occur proactively by screening asymptomatic patients for cancer. This section will focus on patients who present with symptom, signs, or findings suggestive of lung cancer, which should trigger “early diagnosis” of the disease.

All patients

1. If a patient is asymptomatic and older than 55 with 30 pack-year (PY) history of smoking, follow Guidelines on Section III
2. Keep in mind that nonsmokers and females can get lung cancer too.

Findings that are suspicious suggestive of lung cancer

1. Symptoms: new onset of
 - New cough lasting more than 3–4 weeks or a change in the “smoker’s chronic cough”
 - Hemoptysis: especially not accompanying upper respiratory infection or bronchitis, symptoms >4 weeks
 - Chest pain
 - Shortness of breath
 - Poor appetite/weight loss
2. Signs of physical examination findings include:
 - Cachexia
 - Respiratory distress
 - Clubbing
 - Facial and neck edema and neck venous distension
 - Signs of pleural effusion
 - Signs of mediastinal shift
 - Supraclavicular or cervical adenopathy
3. Imaging findings in asymptomatic and symptomatic patients (incidental findings):
 - Mass with or without cavitation
 - Pleural effusion
 - Atelectasis/volume loss
 - Mediastinal deviation or widening
 - Lytic bone lesions
 - Normal X-ray
 - Keep in mind that chest X-ray can be normal in patients with lung cancer. Therefore, if a patient had symptoms such as hemoptysis >4 weeks and chest X-ray is normal, obtain computed tomographic (CT) of the chest and even if the CT is normal, patient may need bronchoscopy to diagnose an endobronchial small lesion.
 - Recurrent pneumonia in the same lobe

4. Laboratory findings include:

- Hypercalcemia
- Hyponatremia.

Workup

1. Obtain good-quality chest X-ray to rule out other causes of symptoms such as pneumonia or Tuberculosis.
2. Obtain CT scan of the chest for the following indications
 - Abnormal chest X-ray, suspicious of cancer
 - Persistent infiltrate despite antibiotic treatment for a pneumonia
 - Normal chest X-ray with concerning complaints such as persistent hemoptysis or cough >4 weeks
3. Thoracentesis: For a pleural effusion in the setting of suspected malignancy
4. Bronchoscopy
 - If normal CT scan with suspicion of endobronchial lesions
 - If there is accessible lesion
 - Include endobronchial ultrasound staging for hilar and mediastinal nodes if possible in the absence of distant metastasis
5. CT-guided biopsy: For peripheral nodules or masses not accessible by bronchoscopy.

Lung cancer screening

Lung cancer screening is proven to save lives and became the standard of care in the United States especially after National Lung Cancer Screening Trial. However, screening studies were done among a Western population where lung cancer is very prevalent and kills more people than breast, prostate, and colon cancer combined. However, given the lower prevalence in our population, such screening cannot be automatically presumed to be successful or cost-effective to be adopted. However, since we are practicing most of our medicine, based on published evidence, we propose here stringent guidelines to provide to our healthcare professionals who might like to take care of their patients based on available evidence in the literature and consider providing them with lung cancer screening.

It is very prudent that healthcare professional be aware of all the requirements [Table 4] and challenges of doing screening program before launching screening to all his/her patients.

Requirements for lung cancer screening program

These requirements should be considered before starting screening patients [Table 4].

1. Who should be screened (Section 2)
2. Where will CT scan of chest done, would a radiologist be willing to do it, who will pay for it, will the report

Table 4: Requirements for local lung cancer screening program or individual requests

Step	Requirement
Identifying eligible patients	Identifying high risk group Provide counseling about the process, risks and benefits and how the findings will be managed
Obtaining LDCT	Assure willingness of the radiologist to perform LDCT and report it according to guidelines
Recall the patient	Be responsible for following the test results and counselling the patient about the finding and next step.
Manage positive findings	Secure consulting service to work up the positive findings of your patients (pulmonary physicians or thoracic surgeons) Assure ability to manage or refer diagnosed cases of lung cancer
Supportive services	Be ready to provide smoking cessation counseling and emotional support and access to respond to patients' questions and concerns

LDCT=Low dose chest CT scan, CT=Computed tomography

be standardized, who responded to do follow-up plan based on the report?

3. What would ordering physician do if there were abnormal CT scan findings? Do they have multidisciplinary team with expertise to manage suspicious findings or have access to tertiary center that one can refer the patient to them for further workup? Confirm with the center if they accept all your referrals and how many and who is eligible for referral and the referral process? [Figure 1 as prototype]
4. Who would call the patient and report the result and follow-up on the patient workup?
5. Who would counsel the patient for medical and psychological issues?
6. Must have access to/or offer smoking cessation counseling to smokers?
7. If diagnosed with cancer, where will the patient be treated?
8. If there was incidental finding such as coronary artery disease or emphysema, where would physician refer patient?

Whom to screen

The following are candidates for lung cancer screening:

1. Asymptomatic patients (symptomatic patients should be worked up properly according to standards of care)
2. Age 55–77 years^[14]
3. Smoking history >30 PY (number of packs smoked per day X year of smoking)
4. Active smoker or quit smoking less than 15 years ago.
5. Did not have chest CT scan the last year
6. Do not perform screening for individuals with comorbidities that could adversely influence their ability to tolerate the evaluation of screen-detected findings or tolerate treatment of early-stage screen-detected lung cancer or that substantially limit their life expectancy. We recommend that low-dose CT (LDCT) screening should not be performed in these situations (strong recommendation, low-quality evidence) (e.g., advanced liver disease, COPD with hypoventilation and hypoxia, NYHA class IV heart failure).^[14]

What to do?

1. Explain to patient the screening process and potential risks and benefits and follow-up plans in case the patient opts for screening.
2. Obtain LDCT scan of the chest^[15]
 - CT examinations should be acquired using multidetector scanners with at least 16 detector rows, in a helical technique
 - Intravenous contrast material should not be used
 - Field of view: From the lung apices to the costophrenic angles
 - Section thickness should be 2.5 mm or less, with less than 1 mm preferred
 - Gantry rotation should be 500 msec per rotation or faster
 - Dose: Maximum dose threshold as a volumetric CT dose index of 3 mGy for a standard-sized patient (height [170 cm]; weight 70 kg) with “appropriate dose reduction” for smaller patients and an appropriate increase for larger patients
 - Optimum low-dose protocol are established separately depending on vendor specific parameters and adjustments to match dose threshold of CT dose index of 3 mGy
3. Lung-RAD lung imaging reporting and data system is to be used in reporting as established by the American College of Radiology^[15]
4. Based on the report, decide next step (Section 4 and 5)
5. A positive test is defined as a test that leads to a recommendation for any additional testing other than to return for the annual screening examination.^[14]

Managing findings on the screening computed tomographic scan (for primary care/nonspecialist)

1. Normal CT scan: after 1 year and then annually repeat CT scan^[12,14,16]
2. If CT scan is positive per 3.4, compare with previous imaging, if available^[12,14,16]
3. New lung lesions <5 mm repeat in 12 months (later should depend on the 12 months CT)^[12,14,16]
4. New lesions 6–7 mm repeat CT scan in 6 months^[12,14,16]
5. New lesions >8 mm refer to pulmonary/thoracic surgeon for workup^[12,14,16]

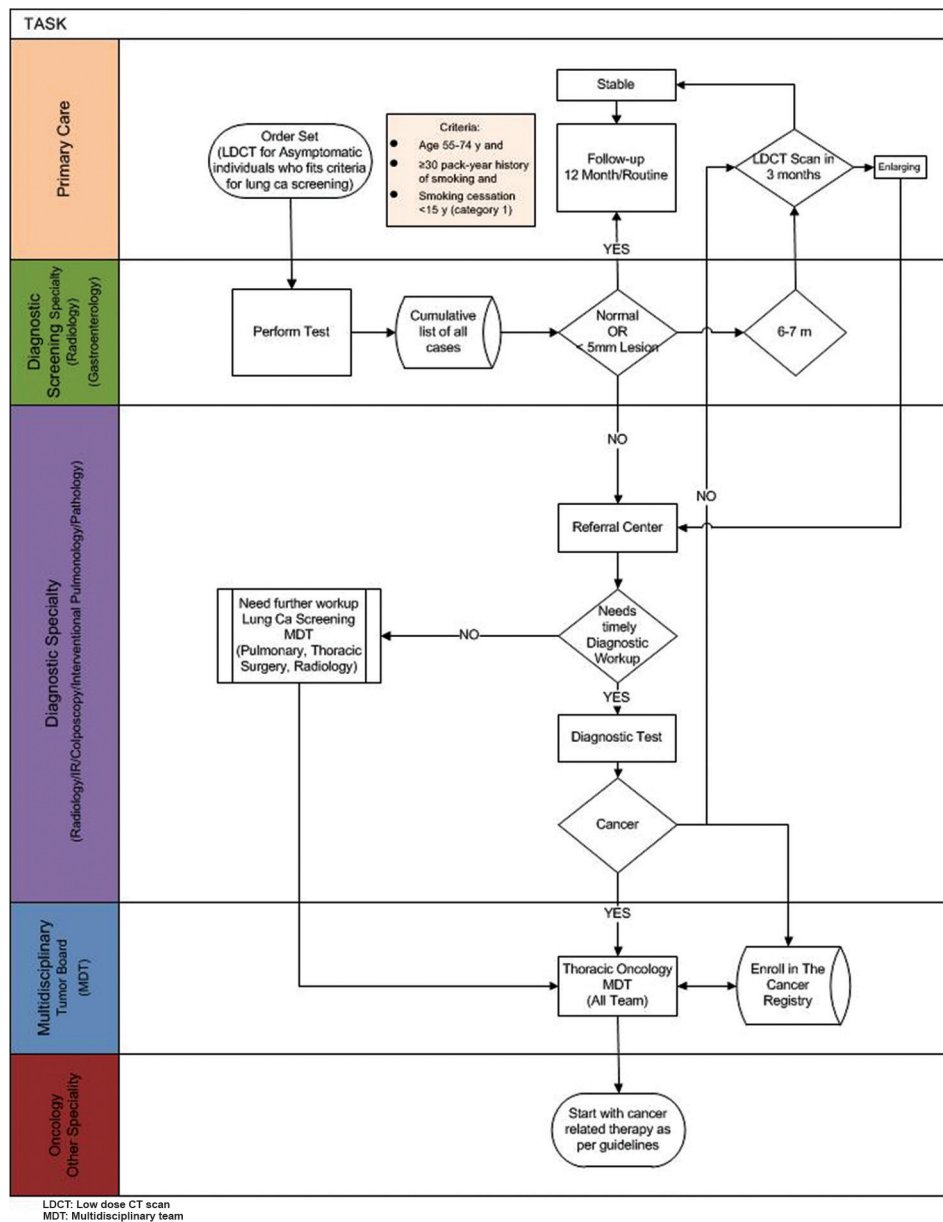


Figure 1: Process map of Saudi lung cancer screening program

6. Other findings [12,14,16]

- Coronary artery disease – refer to cardiology
- Chronic obstructive pulmonary disease – assess need to refer to pulmonary
- Other finding – act based on findings

Workup of lung cancer nodules (to be done by consultant with access to multidisciplinary team)

1. A multidisciplinary team including at least one consultant from each of the following specialties: radiology/interventional radiology, pulmonary/interventional, pulmonary, and thoracic surgeon. Team should review all the cases and take consensus approach to decision making.

2. New solid lesion >8 mm obtain CT scan with IV contrast or positron emission tomography (PET)/CT scan

- PET positive or suspicious CT scan obtains CT-guided or surgical excisional biopsy (resection)
- PET negative or low suspicion, repeat LDCT in 3 months, if still stable, repeat LDCT in 6 months, if still stable, do LDCT scan annually. If it grew, do biopsy or surgical resection

3. Management of part-solid lung nodules

- <5 mm: annual LDCT
- >6 mm with <5 mm solid component: LDCT in 6 months
- >6 mm with 6–7 mm solid component: LDCT in 3 months or PET scan

- >8 mm solid component: CT chest with IV contrast, if highly suspicious: biopsy or surgical excision^[17]
4. New nonsolid lesion:
 - <19 mm repeat LDCT in 6 months, if stable annual LDCT, if grew, biopsy or surgical resection
 - >20 mm repeat LDCT in 3 months, if stable repeat in 6 months, then annual. If grew, do biopsy or surgical resection
 5. Management of multiple lung nodules:
 - Purely solid: Measure and manage the largest and as solid nodules
 - Nodules with partly solid component: Measure and manage the largest as part-solid nodule.

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Conflicts of interest

There are no conflicts of interest.

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