Evaluation of Pulmonary Nodules
Clinical Practice Consensus Guidelines for Asia

Chunxue Bai, MD, PhD, FCCP; Chang-Min Choi, MD, PhD; Chung Ming Chu, MD, FCCP; Devanand Anantham, MBBS; James Chung-man Ho, MD, FCCP; Ali Zamir Khan, MD, PhD; Jang-Ming Lee, MD, PhD; Shi Yue Li, MD, PhD; Sawang Saenghirunvattana, MD, PhD; and Anthony Yim, MD, PhD

BACKGROUND: American College of Chest Physicians (CHEST) clinical practice guidelines on the evaluation of pulmonary nodules may have low adoption among clinicians in Asian countries. Unique patient characteristics of Asian patients affect the diagnostic evaluation of pulmonary nodules. The objective of these clinical practice guidelines was to adapt those of CHEST to provide consensus-based recommendations relevant to practitioners in Asia.

METHODS: A modified ADAPTE process was used by a multidisciplinary group of pulmonologists and thoracic surgeons in Asia. An initial panel meeting analyzed all CHEST recommendations to achieve consensus on recommendations and identify areas that required further investigation before consensus could be achieved. Revised recommendations were circulated to panel members for iterative review and redrafting to develop the final guidelines.

RESULTS: Evaluation of pulmonary nodules in Asia broadly follows those of the CHEST guidelines with important caveats. Practitioners should be aware of the risk of lung cancer caused by high levels of indoor and outdoor air pollution, as well as the high incidence of adenocarcinoma in female nonsmokers. Furthermore, the high prevalence of granulomatous disease and other infectious causes of pulmonary nodules need to be considered. Therefore, diagnostic risk calculators developed in non-Asian patients may not be applicable. Overall, longer surveillance of nodules than those recommended by CHEST should be considered.

CONCLUSIONS: TB in Asia favors lesser reliance on PET scanning and greater use of nonsurgical biopsy over surgical diagnosis or surveillance. Practitioners in Asia are encouraged to use these adapted consensus guidelines to facilitate consistent evaluation of pulmonary nodules.

CHEST 2016; 150(4):877-893

KEY WORDS: Asia; diagnosis; lung neoplasms; peripheral pulmonary nodules; solitary pulmonary nodules

ABBREVIATIONS: CHEST = American College of Chest Physicians; ENB = electromagnetic navigation bronchoscopy; TTNA = transthoracic needle aspiration; TTNB = transthoracic needle biopsy

AFFILIATIONS: From Pulmonary Medicine Department (Dr Bai), Zhongshan Hospital, Fudan University, Shanghai Respiratory Research Institute, Shanghai, China; Department of Pulmonary and Critical Care Medicine (Dr Choi), Asan Medical Center, College of Medicine, University of Ulsan, Seoul, South Korea; Respiratory Medicine (Dr Chu), United Christian Hospital, Kwan Tong, Hong Kong SAR, China; Respiratory Medicine and Critical Care Medicine (Dr Anantham), Singapore General Hospital, Singapore; Respiratory Medicine (Dr Chung-man Ho), University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong SAR, China; Minimally Invasive and Robotic Thoracic Surgery (Dr Khan), Medanta The Medicity, Gurgaon, India; Thoracic Surgery (Dr Lee), National Taiwan University Hospital, Taipei, Taiwan; Respiratory Medicine (Dr Li), The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; Respiratory Medicine (Dr Saenghirunvattana), Bangkok Hospital Medical Center, Bangkok Hospital Group, Bangkok, Thailand; and the Minimally Invasive Thoracic Surgery Centre (Dr Yim), Hong Kong SAR, China.
Summary of Recommendations

1.1. In an individual with an indeterminate nodule that is visible on chest radiography, review prior imaging tests.

1.2. In an individual with an indeterminate nodule that has been stable for at least 2 years, annual low-dose CT screening beyond 2 years for high-risk patients for early detection of lung cancer should be individualized.

1.3. In an individual with an indeterminate nodule identified by chest radiography, perform low-dose chest CT (preferably with thin sections through the nodule) to characterize the nodule and assess the likelihood of malignancy.

2.1. Individuals with solid, indeterminate nodules > 8 mm should be referred to a center for management by a multidisciplinary team. Diagnostic capabilities of the center should include CT/PET scans, tests for benign diseases (eg, TB), and biopsy (surgical or minimally invasive).

2.2. In an individual with a solid, indeterminate nodule > 8 mm in diameter, estimate the probability of malignancy using clinical judgement. If possible, make a quantitative assessment using a validated model with appropriate regional caveats.

2.3. In an individual with a solid, indeterminate nodule > 8 mm in diameter, perform surveillance with serial low-dose CT scans in the following circumstances:

- The clinical probability of malignancy is deemed low (< 5%)
- Biopsy is non-diagnostic and the lesion is not hypermetabolic as assessed by PET

2.4. In an individual with a solid, indeterminate nodule > 8 mm in diameter who undergoes surveillance, serial CT scans using thin sections and non-contrast, low-dose techniques should be performed at 3 to 6 months, 9 to 12 months, 18 to 24 months, and, depending on clinical judgement and patient preference, annually thereafter.

2.5. In an individual with a solid, indeterminate nodule > 8 mm in diameter with moderate (5-60%) probability of malignancy, consider functional imaging, preferably with PET, to characterize the nodule before surgical resection or continued radiological surveillance. Consider caveats to PET screening.

2.6. In an individual with a solid, indeterminate nodule > 8 mm in diameter with high (> 60%) probability of malignancy, functional imaging has a greater role in preoperative staging than in characterizing the nodule.

2.7. In an individual with a solid, indeterminate nodule that measures > 8 mm in diameter, the expert panel suggests nonsurgical biopsy in the following circumstances:

- The clinical (pretest) probability of malignancy is moderate (5-60%)
- When the clinical (pretest) probability and the findings on imaging are discordant
- A benign diagnosis such as TB requiring specific medical treatment is suspected
- A fully informed patient desires proof of a malignant diagnosis before surgery, especially when the risk of surgical complications is high.

2.8. In an individual with a solid, indeterminate nodule that measures > 8 mm in diameter, surgical biopsy (and possibly resection) in a patient with suitable surgical risk is suggested in the following circumstances:

- The clinical probability of malignancy is high (> 60%)
- There is clear evidence of growth on serial imaging suggestive of malignancy
- The nodule is intensely hypermetabolic as assessed by PET
- Nonsurgical biopsy is suspicious for malignancy
- A fully informed patient prefers undergoing a definitive diagnostic procedure.

DISCLAIMER: American College of Chest Physician guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at http://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/CHEST-Guidelines.

FUNDING/SUPPORT: Medical writing assistance was provided by Mark Snape, MB BS, and Serina Stretton, PhD, CMPP, of ProScribe – Envision Pharma Group and was funded by Covidien. ProScribe’s services complied with international guidelines for Good Publication Practice (GPP3).

CORRESPONDENCE TO: Chunxue Bai, MD, PhD, FCCP, Pulmonary Medicine Department, Zhongshan Hospital, Fudan University, Shanghai Respiratory Research Institute, No. 180 Fenglin Rd, Shanghai, 200032 China; e-mail: bai.chunxue@zs-hospital.sh.cn

Copyright © 2016 American College of Chest Physicians. Published by Elsevier Inc. All rights reserved.

DOI: http://dx.doi.org/10.1016/j.chest.2016.02.650
2.9. In an individual with a solid, indeterminate nodule > 8 mm in diameter who chooses surgical biopsy, the expert panel recommends minimally invasive surgery where appropriate.

2.10. In an individual with a solid, indeterminate nodule > 8 mm in diameter, clinicians should elicit preferences for management, and consider family input where appropriate before offering management options.

3.1. In an individual with a solid nodule ≤ 8 mm in diameter and low risk for lung cancer, perform low-dose CT surveillance according to the size of the nodule:

- Nodules measuring ≤ 4 mm in diameter: consider ongoing annual CT depending on clinical judgement and patient preference
- Nodules measuring > 4 mm to ≤ 6 mm: re-evaluate by low-dose CT annually if stable depending on clinical judgement and patient preference
- Nodules measuring > 6 mm to ≤ 8 mm: re-evaluate by low-dose CT at 6 to 12 months, 18 to 24 months, and then annually if stable depending on clinical judgement and patient preference.

3.2. In an individual with a solid nodule that measures > 8 mm in diameter who has moderate to high risk for lung cancer, perform low-dose CT surveillance according to the size of the nodule:

- Nodules measuring ≤ 4 mm in diameter: re-evaluate by low-dose CT at 12 months and then consider annual CT surveillance depending on clinical judgement and patient preference
- Nodules measuring > 4 mm to ≤ 6 mm: re-evaluate by low-dose CT between 6 and 12 months and then again between 18 and 24 months if unchanged, and then annually if stable depending on clinical judgement and patient preference.
- Nodules measuring > 6 mm to ≤ 8 mm: re-evaluate by low-dose CT at 3 months, 6 months, 12 months, and then annually if stable depending on clinical judgement and patient preference.

4.1. In an individual with a nonsolid (pure ground glass) nodule measuring ≤ 5 mm in diameter, consider ongoing annual CT surveillance depending on clinical judgement and patient preference.

4.2. In an individual with a nonsolid (pure ground glass) nodule measuring > 5 mm in diameter, re-evaluate by annual CT surveillance for at least 3 years, and then consider ongoing annual CT surveillance depending on clinical judgement and patient preference.

5.1. In an individual with a partsolid nodule measuring ≤ 8 mm in diameter, the expert panel suggests low-dose CT surveillance at approximately 3, 12, and 24 months, with consideration given to ongoing annual low-dose CT surveillance depending on clinical judgement and patient preference. Consideration should also be given to empiric antimicrobial therapy if there are symptoms or signs of bacterial infection at the time of detection.

5.2. In an individual with a partsolid nodule measuring > 8 mm in diameter, repeat CT at 3 months and consider empiric antimicrobial therapy if deemed clinically appropriate at the time of detection. Perform further evaluation with nonsurgical biopsy and/or surgical resection for nodules that persist beyond 3 months, with the additional option of PET scanning for staging of disease before surgical intervention.

6.1. In an individual with a dominant nodule and one or more additional small nodules, the expert panel suggests that each nodule be evaluated individually, curative treatment not be denied, and histopathological confirmation of metastasis be considered where appropriate.

7.1. When considering nonsurgical biopsy, base the choice of technique on factors related to the patient and nodule as well as resources:

- Consider use of TTNA or TTNB for nodules close to the chest wall or deeper lesions especially if fissures do not need to be traversed and there is no surrounding emphysema
- Consider use of bronchoscopy techniques for nodules closer to a patient bronchus and with a visible bronchus sign or for individuals at high risk of pneumothorax
- Consider use of advanced bronchoscopic techniques, if available, over traditional bronchoscopy especially for smaller nodules, and over TTNA or TTNB if there is surrounding emphysema.

Pulmonary nodules are predominantly peripheral solitary or multiple small (≤ 3 cm in diameter), focal radiographic opacities that may signal an early malignancy. Therefore, the task of clinicians is to
accurately characterize pulmonary nodules, especially in relation to their likelihood of malignancy. Based on the estimation of the probability of malignancy, clinicians can develop an appropriate management plan, which typically involves either surveillance or definitive diagnosis and treatment. By definition, peripheral pulmonary nodules are not visible endobronchially and are completely surrounded by lung parenchyma without associated atelectasis, effusion, or enlarged lymph nodes.

Clinical practice guidelines on the evaluation of pulmonary nodules have been published by the American College of Chest Physicians (CHEST). However, implementation of these clinical practice guidelines is often very low among clinicians in Asian countries, even when awareness of those guidelines is high. CHEST has recommended that clinical practice guidelines should be adapted to the local setting by critical review of recommendations against the background of local strengths and challenges. Local adaptation of guidelines is critical for helping to ensure that recommendations are relevant and more likely to be implemented. This multidisciplinary group is committed to following up on the CHEST recommendation to adapt the guidelines to Asia.

In Asia, the incidence of lung cancer is high and rising in many countries, particularly in response to the maturation of the smoking epidemic (Fig 1). There are many unique characteristics of Asian patients related to ethnicity, genetics, risk profile, prevalence of benign diseases that require treatment, prevalence of malignancy, access to diagnostic services, and cultural understanding of disease. TB is highly prevalent, which often means that even the presence of apparently benign lung nodules requires a definitive diagnosis because of both individual treatment and public health implications. Incidence rates of TB in most countries in western Europe, Canada, and the United States are < 10 cases per 100,000 population per year. In contrast, incidence rates in Asian countries are generally several times higher (China, 70; India, 171; Thailand, 119 cases per 100,000 population per year), although rates are lower in a few high-income Asian countries (e.g., Japan).

The existence of local guidelines on the evaluation of pulmonary nodules varies widely throughout different countries in Asia. Local guidelines currently exist in China, Korea, and Japan. However, no national clinical guidelines have been formulated in Singapore, India, or Thailand, where institutional standards are used instead. An informal survey of clinicians in the Asian region has highlighted several points of difference between practices recommended by the current CHEST guidelines and those often carried out in clinical practice.

The primary aim of these clinical practice guidelines was to provide consensus-based expert recommendations adapted from the current CHEST guidelines that are broadly relevant to countries in Asia. Evidence that forms the basis for such adaptation of the CHEST guidelines is presented.

**Methods**

The development of these adapted clinical practice guidelines was based on a modified ADAPTE process that "provides a systematic approach to adapting guidelines produced in one setting to use in a different cultural and organisational context." The key steps of the adaptation phase consisted of: a search for, and screening of, existing guidelines; assessment of these guidelines; a decision and selection phase; and drafting of a guideline report.

**Participants and Evidence Collection**

A panel of experts was assembled consisting of pulmonologists and thoracic surgeons from various countries and regions in Asia. Panel members were individually asked to collect data and evidence regarding local practices. Current CHEST guidelines on the evaluation of pulmonary nodules were reviewed before and during the panel meeting. A consensus was reached on the adaptation of guidelines and the revised guidelines will be published in CHEST soon.
analyzed all recommendations from the CHEST guidelines in two separate groups. The panel as a whole then discussed each recommendation and achieved broad consensus on most recommendations based on expert clinical opinion. Several recommendations regarded as more contentious and difficult to reach consensus on were identified for further investigation of existing evidence. An initial draft of the revised guidelines was developed based on the consensus and on region-specific evidence, and the draft version was circulated to panel members for review. An iterative process of review and redrafting of guidelines was undertaken to develop the final recommendations.

## Recommendations

The main aims of the initial diagnostic approach taken toward a pulmonary nodule are to establish a definitive diagnosis where possible and to avoid invasive procedures in patients with benign disease that does not require treatment. Pulmonary nodules, whether benign or malignant, can be broadly classified radiologically on CT scans as solid or subsolid nodules. In solid nodules, the likelihood of malignancy is influenced by the age of the patient, smoking history, size of the nodule, presence of spiculated edges, hemoptysis, absence of calcification, history of malignancy, history of TB and other benign lung disease, and uptake on PET scans (Table 1).

Subsolid nodules are further classified as either nonsolid (pure ground-glass appearance) or part-solid (containing a solid component but > 50% ground-glass appearance). Subsolid nodules can be associated with either inflammatory causes or various forms of peripheral adenocarcinoma, including premalignant atypical adenomatous hyperplasia, carcinoma in situ, and mixed subtype adenocarcinoma. Subsolid nodules, especially pure ground-glass opacities, often have an indolent course and although malignancy has been linked to size, there is less association with smoking history, especially for pure ground-glass nodules.

The following specific recommendations are intended to be broadly relevant to populations in Asia and represent adapted CHEST recommendations. Additional remarks either relate to the justification for changes made to the original CHEST recommendations or provide additional guidance.

### Individuals With an Indeterminate Nodule (Fig 2)

All newly identified pulmonary nodules are indeterminate until a definitive diagnosis is made. Benign etiology is suggested by radiologic features such as diffuse, central, laminated, and popcorn patterns of calcification. Systematic radiography screening has been common in many Asian countries (eg, for TB and malignancy) and has led to a large number of incidental pulmonary nodules being detected.

1.1. In an individual with an indeterminate nodule that is visible on chest radiography, review prior imaging tests.

This recommendation from CHEST is applicable in Asian countries, although the expert panel noted that the transition to digital radiography has made prior radiographs difficult to assess or compare with digital images. Radiology images are compared to assess stability of nodule size.

1.2. In an individual with an indeterminate nodule that has been stable for at least 2 years, annual low-dose CT screening beyond 2 years for high-risk patients for early detection of lung cancer should be individualized.

### TABLE 1 Radiographic Characteristics of Pulmonary Nodules on CT Scans Suggestive of Malignancy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Characteristics Associated With Malignant Nodules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth rate</td>
<td>Doubling time 20-400 d (&lt; 100 d for most solid nodules); growth rate may be slower with ground-glass and subsolid nodules (&gt; 200 d); very rapid doubling suggests an infectious or inflammatory cause</td>
</tr>
<tr>
<td>Location</td>
<td>Upper lobe is a more common site for malignant nodules, although the diagnostic significance of this finding is reduced in Asia due to the high prevalence of TB</td>
</tr>
<tr>
<td>Margins</td>
<td>Lobulated or speculated margins are strongly associated with malignancy; notches are commonly seen in adenocarcinomas with overt invasion</td>
</tr>
<tr>
<td>Cavitation</td>
<td>Malignant lesions are associated with irregular, thicker walls &gt; 15 mm thick</td>
</tr>
<tr>
<td>Size</td>
<td>Probability of malignancy increases with size (nodules &gt; 2 cm are more likely to be malignant, although smaller size does not exclude malignancy)</td>
</tr>
<tr>
<td>Calcification</td>
<td>Punctate and eccentric (evidence of necrosis within nodule) calcification may occur with malignancy</td>
</tr>
<tr>
<td>Other features</td>
<td>Vascular convergence, dilated bronchus leading into the nodule</td>
</tr>
</tbody>
</table>
There is little evidence to support a longer duration of surveillance for patients with solid nodules once 2 years of stability have been documented. However, patients at high risk for lung cancer should be offered annual screening with low-dose CT surveillance according to national guidelines and local standards of care.

1.3. In an individual with an indeterminate nodule identified by chest radiography, perform low-dose chest CT (preferably with thin sections through the nodule) to characterize the nodule and assess the likelihood of malignancy (Table 1).

Compared with chest radiography, CT scans provide additional information about the location, shape, margins, and attenuation characteristics of pulmonary nodules. The expert panel emphasized that obtaining thin (≤ 1 mm) sections through the nodule increased the ability to radiologically characterize the nodule. Analysis of tumor volume may be of assistance for detecting tumor growth.

**Individual With a Solid, Indeterminate Nodule > 8 mm in Diameter (Fig 3)**

2.1. Individuals with solid, indeterminate nodules > 8 mm should be referred to a center for management by a multidisciplinary team. Diagnostic capabilities of the center should include CT/PET scans, tests for benign diseases (eg, TB), and biopsy (surgical or minimally invasive).

The expert panel developed this new recommendation to accommodate the large variation in practice conditions and resources available in many Asian countries. In addition, the expert panel recommends the involvement of a multidisciplinary team consisting of physicians, surgeons, radiologists, and pathologists to develop an individualized patient plan.

2.2. In an individual with a solid, indeterminate nodule > 8 mm in diameter, estimate the probability of malignancy using clinical judgement. If possible, make a quantitative assessment using a validated model with appropriate regional caveats.

In Asian countries, initial (“pretest”) estimates of the likelihood of malignancy are often made by using clinical judgment. Clinicians who wish to estimate the probability of malignancy by using quantitative models should be aware that these models may not have been validated in Asian populations. Indeed, the CHEST guidelines recommend that the choice of a quantitative model may
be guided by the target population, ease of use, and the extent of validation. The expert panel recommends that regardless of whether clinical judgment or a calculation model is used, clinicians must decide if the clinical probability suggests further imaging studies, biopsy, and/or resection are needed.

2.3. In an individual with a solid, indeterminate nodule > 8 mm in diameter, perform surveillance with serial low-dose CT scans in the following circumstances:

- The clinical probability of malignancy is deemed low (< 5%)
- Biopsy is non-diagnostic and the lesion is not hypermetabolic as assessed by PET
- A fully informed patient prefers this nonaggressive management approach, despite the potential risk of disease progression.

The threshold for what is considered "low probability" may depend on the geographical and cultural context of individuals. Generally, the probability of malignancy of pulmonary nodules is higher in Asian populations than in Western populations. For seemingly benign nodules (ie, low probability of malignancy), an accurate diagnosis may sometimes be necessary rather than surveillance. Examples of relevant scenarios include: (1) TB or other infections requiring specific treatment, and (2) patients who use high-dose immunosuppression (eg, transplant) may need a more aggressive approach.

2.4. In an individual with a solid, indeterminate nodule > 8 mm in diameter who undergoes surveillance, serial CT scans using thin sections and non-contrast, low-dose techniques should be performed at 3 to 6 months, 9 to 12 months, 18 to 24 months, and, depending on clinical judgement and patient preference, annually thereafter.

In Asia, the high prevalence of risk factors for lung cancer and anecdotal reports of the emergence of malignancy in otherwise stable nodules after many years suggest that consideration should be given to extended (3 years and beyond) annual surveillance based on clinical judgment and patient preference. However, the expert panel acknowledged the lack of evidence for this approach and the potential risk of ongoing ionizing radiation. Surveillance may cease in nodules that show progressive shrinkage or disappearance.
2.5. In an individual with a solid, indeterminate nodule > 8 mm in diameter with moderate (5-60%) probability of malignancy, consider functional imaging, preferably with PET, to characterize the nodule before surgical resection or continued radiological surveillance. Consider caveats to PET screening.

In some Asian countries, availability and cost of PET scanning may be an issue. Cost-effective use of PET surveillance is for nodules that have indeterminate CT scan features when the clinical probability of malignancy is relatively low (ie, discordance between the clinical and radiologic features). False-positive and false-negative results may also be an issue with PET scanning because of infections (eg, TB, fungal and parasitic disease) and slow-growing tumors (eg, adenocarcinoma in situ), respectively. For these reasons, PET scans may not always be a highly discriminative tool in Asian countries, and biopsy for other possible causes may also be required.

2.6. In an individual with a solid, indeterminate nodule > 8 mm in diameter with high (> 60%) probability of malignancy, functional imaging has a greater role in preoperative staging than in characterizing the nodule.

When there is a high probability of malignancy, PET scans are useful for disease staging to rule out previously undetected metastases before surgical intervention.

2.7. In an individual with a solid, indeterminate nodule that measures > 8 mm in diameter, the expert panel suggests nonsurgical biopsy in the following circumstances:

- The clinical (pretest) probability of malignancy is moderate (5-60%)
- When the clinical (pretest) probability and the findings on imaging are discordant
- A benign diagnosis such as TB requiring specific medical treatment is suspected
- A fully informed patient desires proof of a malignant diagnosis before surgery, especially when the risk of surgical complications is high.

In Asia, there is variation in practices related to surgical versus nonsurgical biopsy depending on the availability of local expertise. Techniques for minimally invasive biopsy include CT scan-guided transthoracic needle biopsy (TTNB), transbronchial lung biopsy under fluoroscopic guidance, radial probe endobronchial ultrasound (with or without guide sheath), electromagnetic navigation bronchoscopy (ENB), and virtual bronchoscopy navigation. The type of biopsy performed should be selected based on radiologic characteristics (size, location, and relation to airways), potential risk of complications, and expertise of practitioners. For nodules difficult to access with bronchoscopy or TTNB, consider surgical diagnosis for nodules with moderate probability of malignancy if the rates of positive diagnosis with nonsurgical biopsy are low in routine clinical practice. In areas where TB is endemic, use of nonsurgical biopsy may be useful for minimizing unnecessary thoracotomy. However, the expert panel noted that an infectious or inflammatory etiology as the only pathology may be incorrect during the initial diagnosis. Accordingly, implement careful surveillance during therapy and, if the patient fails to respond to treatment, the possibility of a second diagnosis should be considered.

2.8. In an individual with a solid, indeterminate nodule that measures > 8 mm in diameter, surgical biopsy (and possibly resection) in a patient with suitable surgical risk is suggested in the following circumstances:

- The clinical probability of malignancy is high (> 60%)
- There is clear evidence of growth on serial imaging suggestive of malignancy
- The nodule is intensely hypermetabolic as assessed by PET
- Nonsurgical biopsy is suspicious for malignancy
- A fully informed patient prefers undergoing a definitive diagnostic procedure.

Surgical biopsy is different from surgical resection that aims to curatively remove all the malignancy (eg, anatomical lobar resection). Generally, surgical resection and surgical biopsy are simultaneous, providing the gold standard for evaluation and treatment of a lung nodule. A frozen section biopsy can be performed intraoperatively and, if confirmed malignant, curative lung resection will then be performed. In Asia, the high incidence of benign causes of pulmonary nodules such as TB reduces the confidence with which malignant growth can be predicted on serial imaging alone. However, surgical resection is still considered the gold standard for the diagnosis of pulmonary nodules where malignancy is suspected. Clinicians should be mindful of patient preferences and assess both fitness and suitability prior to recommending surgery. Minimally invasive surgery

Downloaded From: http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/935762/ on 06/28/2017
such as video-assisted thoracoscopic surgery is recommended to reduce morbidity.

2.9. In an individual with a solid, indeterminate nodule > 8 mm in diameter who chooses surgical biopsy, the expert panel recommends minimally invasive surgery where appropriate.

2.10. In an individual with a solid, indeterminate nodule > 8 mm in diameter, clinicians should elicit preferences for management, and consider family input where appropriate before offering management options.

In many Asian countries, the roles of patients, family members, and clinicians in decision-making may differ from those in Western countries. Clinicians should consider the cultural norms regarding decision-making in their country or region. However, patient preference on the decision-making process should be elicited. In addition, the expert panel noted that, in many Asian countries, there is commonly an expectation that clinicians will present more than one alternative in rank order from most to least preferred to guide patient decision-making. Multidisciplinary team input can assist in developing the recommended management options.

**Individual With a Solid Nodule ≤ 8 mm in Diameter (Fig 4)**

3.1. In an individual with a solid nodule ≤ 8 mm in diameter and low risk for lung cancer, perform low-dose CT surveillance according to the size of the nodule:

- Nodules measuring ≤ 4 mm in diameter: consider ongoing annual CT depending on clinical judgment and patient preference
- Nodules measuring > 4 mm to ≤ 6 mm: re-evaluate by low-dose CT annually if stable depending on clinical judgement and patient preference
- Nodules measuring > 6 mm to ≤ 8 mm: re-evaluate by low-dose CT at 6 to 12 months, 18 to 24 months, and then annually if stable depending on clinical judgement and patient preference.

No data are available to properly support modifications to the CHEST recommendations. However, solid nodules ≤ 8 mm in diameter have a low, but not negligible, probability of malignancy. In addition, environmental risk factors may make the dichotomy between high and low risk not applicable in many parts of Asia. As a result, the expert panel suggested more frequent and longer term CT surveillance (3 years and beyond depending on clinical judgment and patient preference) for small nodules than recommended by the CHEST with an algorithm that is similar to the “high-risk” group. This approach is aimed at detecting changes such as an increase in size or to confirm that the nodule is stable. One recent study from Thailand also observed a very high prevalence of TB in nodules ≤ 8 mm but especially in smaller nodules (4.5-11 mm). This

---

**Figure 4 – Algorithm for evaluation of a solid solitary pulmonary nodule ≤ 8 mm in diameter. Numbers in parentheses refer to recommendations in text.**
finding highlights the need for careful consideration of nonmalignant causes in the Asian region. Follow-up CT scans should be conducted at the lowest effective dose possible. Clinicians are reminded of the major limitation of PET scans in characterizing nodules ≤ 8 mm in diameter due to the low mass of metabolically active cells.2

3.2. In an individual with a solid nodule that measures ≤ 8 mm in diameter who has moderate to high risk for lung cancer, perform low-dose CT surveillance according to the size of the nodule:

- Nodules measuring ≤ 4 mm in diameter: reevaluate by low-dose CT at 12 months and then consider annual CT surveillance depending on clinical judgement and patient preference
- Nodules measuring > 4 mm to ≤ 6 mm: reevaluate by low-dose CT between 6 and 12 months and then again between 18 and 24 months if unchanged, and then annually if stable depending on clinical judgement and patient preference
- Nodules measuring > 6 mm to ≤ 8 mm: reevaluate by low-dose CT at 3 months, 6 months, 12 months, and then annually if stable depending on clinical judgement and patient preference.

Compared with the CHEST guidelines, the expert panel suggested long-term CT surveillance (3 years and beyond) of small nodules in Asian individuals with a higher risk profile. Although the expert panel acknowledged that there are no data to explicitly support this approach, the recommendation is based on the natural history of slowly growing early-stage adenocarcinoma.

**Individual With a Nonsolid (Pure Ground-Glass) Nodule (Fig 5)**

Nonsolid (pure ground-glass) nodules represent areas of increased lung attenuation that allow normal parenchymal tissue such as blood vessels to be visible. Atypical adenomatous hyperplasia is a premalignant condition with ground-glass features that may lie dormant for many years before becoming malignant.13

4.1. In an individual with a nonsolid (pure ground glass) nodule measuring ≤ 5 mm in diameter, consider ongoing annual CT surveillance depending on clinical judgement and patient preference.

The expert panel noted that ground-glass nodules still have an appreciable potential for premalignant and malignant changes, which justifies an active surveillance approach. Furthermore, ground-glass nodules that are benign will generally disappear over time, again justifying the surveillance approach.

4.2. In an individual with a nonsolid (pure ground glass) nodule measuring > 5 mm in diameter, reevaluate by annual CT surveillance for at least 3 years, and then consider ongoing annual CT surveillance depending on clinical judgement and patient preference.

The expert panel broadly agreed with the suggested approach for nonsolid nodules in Asian countries but acknowledged that there is not strong enough evidence at present for long-term surveillance. However, based on the indolent nature of early-stage adenocarcinoma, consideration should be given to long-term surveillance (ie, beyond 3 years).

**Individual With a Part-Solid Nodule (Fig 5)**

Part-solid nodules have a solid component but also have a > 50% ground-glass appearance.1,2 When more solid components are visible on a CT scan, there is a greater propensity for invasive features.2

5.1. In an individual with a part-solid nodule measuring ≤ 8 mm in diameter, the expert panel suggests low-dose CT surveillance at approximately 3, 12, and 24 months, with consideration given to ongoing annual low-dose CT surveillance depending on clinical judgement and patient preference.

Although empirical antimicrobial therapy is potentially harmful, the expert panel noted that use of empiric antimicrobial therapy can be considered if the patient is at low clinical risk for an alternative diagnosis such as TB.28

5.2. In an individual with a part-solid nodule measuring > 8 mm in diameter, repeat CT at 3 months and consider empiric antimicrobial therapy if deemed clinically appropriate at the time of detection. Perform further evaluation with nonsurgical biopsy and/or surgical resection for nodules that persist beyond 3 months, with the additional option of PET scanning for staging of disease before surgical intervention.
The expert panel noted that, in the appropriate clinical context, allowing an additional 3 months for a repeat CT evaluation for a larger nodule (> 8 mm) with part-solid characteristics may unnecessarily delay definitive diagnosis. In such cases, immediate intervention is suggested. The choice of nonsurgical biopsy or surgical resection should be made based on the availability of relevant expertise at each center, fitness for surgery, and patient preferences. If available, PET scanning is an option for the staging of disease.

**Individual With One or More Nodules**

Individuals may have one or more additional nodules detected on CT scanning. Additional nodules should be considered individually in terms of their likelihood of malignancy. Preoperative PET scanning may help guide further evaluation, although nodules ≤ 8 mm in diameter are difficult to characterize by using PET scans. Newer technologies, such as ENB, may enable biopsy and histopathologic assessment of multiple smaller peripheral lesions during the same procedure.

6.1. *In an individual with a dominant nodule and one or more additional small nodules, the expert panel suggests that each nodule be evaluated individually, curative treatment not be denied, and histopathological confirmation of metastasis be considered where appropriate.*

**Interventional Pulmonology and Future Directions**

Procedures to definitively diagnose and manage pulmonary nodules have expanded with the emergence and refinement of various technologies. Available procedures can be broadly classified as radiologic, cytologic, traditional, or advanced bronchoscopic techniques, and surgical or nonsurgical (eg, bronchoscopy-guided) biopsy procedures. Each procedure type is associated with different benefits, risks, and diagnostic yields (Table 2). Increasingly, procedures are being combined to improve diagnostic accuracy compared with single techniques and potentially to mitigate against risks.

Decisions regarding the choice of technique(s) that maximize diagnostic yield and minimize complications should consider factors related to the patient and pulmonary nodule (eg, location, size), expense, and the availability of local expertise.

Radiologic surveillance via serial CT scanning is appropriate in several situations (see Recommendations 1.2, 2.3, 2.4, 3.1, 3.2, 4.1, 4.2, and 5.1).

Cytologic procedures include sputum cytology and cytologic samples gained via nonsurgical biopsy such as transthoracic needle aspiration (TTNA) cytology. Sputum cytology is completely noninvasive but has...
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
<th>Benefits</th>
<th>Risks/Disadvantages</th>
<th>Diagnostic Yield (Sensitivity)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiologic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serial CT scans</td>
<td>Surveillance by repeat CT scan to detect malignant growth</td>
<td>• Noninvasive</td>
<td>• Variable diagnostic yield</td>
<td>• Highly variable (between and within observers for measuring size differences)¹</td>
</tr>
<tr>
<td>(&quot;radiologic surveillance&quot;)</td>
<td></td>
<td>• Allows detection of nonmalignant causes and other pathology</td>
<td>• Radiologic exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Delay in diagnosis and treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cytologic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sputum cytology</td>
<td>Examines sputum to determine presence of abnormal cells or tumor markers</td>
<td>• Noninvasive</td>
<td>• Limited diagnostic yield, especially for peripheral lesions</td>
<td>• Sensitivity 49% overall for peripheral lesions³⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Low cost</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT-guided TTNA</td>
<td>Thin-walled, flexible aspiration needle is passed under CT guidance to obtain adequate sample for cytologic assessment (via percutaneous/transthoracic route)</td>
<td>• Relatively low cost</td>
<td>• Relatively high rate of physical complications, especially pneumothorax</td>
<td>• High (sensitivity &gt; 80% overall)³⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• High diagnostic yield in appropriately selected cases</td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td>• Higher with larger nodules (&gt; 3 cm) and with immediate cytologic assessment³⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nonsurgical biopsy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transthoracic needle biopsy</td>
<td>Cutting or automated core-biopsy needle is passed under CT/fluoroscopic guidance to obtain tissue for histologic examination</td>
<td>• High diagnostic yield</td>
<td>• High rate of physical complications, especially pneumothorax and hemorrhage</td>
<td>• Sensitivity &gt; 90%³⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Provides tissue for molecular testing</td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td>• Lower diagnostic yield with smaller nodules (&lt; 1.5 cm)³⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsurgical biopsy using conventional bronchoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With fluoroscopic guidance + TBB</td>
<td>Flexible bronchoscope</td>
<td>• Relatively low complication rate</td>
<td>• Limited diagnostic yield with peripheral nodules</td>
<td>• Sensitivity 34% for nodules ≤ 2 cm (63% for nodules &gt; 2 cm)³²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can establish benign diagnosis</td>
<td>• Physical complications</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Nondiagnostic result does not exclude malignancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
<th>Benefits</th>
<th>Risks/Disadvantages</th>
<th>Diagnostic Yield (Sensitivity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsurgical biopsy using advanced bronchoscopic technologies</td>
<td>Generates 360-degree ultrasound image of lung parenchyma in a disposable guide sheath that can also allow biopsy or placement of surgical markers</td>
<td>• Improved targeting of nodules compared with traditional bronchoscopy&lt;br&gt;• Navigation methods may be combined with biopsy techniques (eg, TBB, TBNA, lavage) or with each other to increase diagnostic yield&lt;br&gt;• Low complication rate</td>
<td>• Relatively high cost of acquisition or disposable items (eg, sheaths)&lt;br&gt;• Nondiagnostic result does not exclude malignancy&lt;br&gt;• Nondefinitive management if malignancy present</td>
<td>• EBUS: Overall sensitivity 58.3%-80% (with TBB)&lt;br&gt;• Sensitivity 54.5% for nodules &lt; 2 cm with TBB (66% for nodules &gt; 2 cm with TBB)</td>
</tr>
<tr>
<td>EBUS</td>
<td>Employs magnetic field and sensor to determine location with a CT-generated 3-D image; various tools (TBB, cytology needle brush, TBNA, forceps biopsy) are available to biopsy one or multiple lesions within the same procedure</td>
<td></td>
<td>• ENB: Pooled/weighted diagnostic yield 65%-67% (multiple studies involving various sampling methods)&lt;br&gt;• Diagnostic yield 75.6% for nodules &lt; 2 cm and 89.6% for nodules &gt; 2 cm (with CT-PET and ROSE)</td>
<td></td>
</tr>
<tr>
<td>ENB</td>
<td>Creates computer-simulated roadmap to region of interest from CT scans</td>
<td></td>
<td>• VNB: Weighted diagnostic yield 72% excluding PPL (biopsy via TBB in most included studies)</td>
<td></td>
</tr>
<tr>
<td>VNB</td>
<td>Surgical resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical resection</td>
<td>Wedge resection under VAT is strongly preferred; other techniques include thoracotomy and mediastinoscopy</td>
<td>• High diagnostic yield&lt;br&gt;• Provides definitive management of nodule</td>
<td>• Physical complications&lt;br&gt;• Short-term deterioration of lung function&lt;br&gt;• Possibility of unnecessary surgery in benign disease that does not require treatment</td>
<td>• High (approaches 100%)&lt;br&gt;• Localization of small, deep nodules may be problematic&lt;br&gt;• Yield may be improved by radio guidance, hook and wire, methylene blue, percutaneous microcoils, ultrasound, and fluoroscopy</td>
</tr>
</tbody>
</table>
limited diagnostic yield for peripheral lesions (overall sensitivity, 49%).\textsuperscript{30,31}

Other recommendations in these guidelines provide broad guidance on the use of nonsurgical (see Recommendations 2.7 and 5.2) (Fig 3) versus surgical biopsy (see Recommendations 2.8 and 5.2) (Fig 3). Nonsurgical biopsy options include conventional techniques such as TTNB and traditional bronchoscopy combined with transbrachial biopsy (under fluoroscopic guidance) or one of the newer advanced bronchoscopic techniques.

7.1. When considering nonsurgical biopsy, base the choice of technique on factors related to the patient and nodule as well as resources:

- Consider use of TTNA or TTNB for nodules close to the chest wall or deeper lesions especially if fissures do not need to be traversed and there is no surrounding emphysema
- Consider use of bronchoscopy techniques for nodules closer to a patient bronchus and with a visible bronchus sign or for individuals at high risk of pneumothorax
- Consider use of advanced bronchoscopic techniques, if available, over traditional bronchoscopy especially for smaller nodules, and over TTNA or TTNB if there is surrounding emphysema

TTNB provides high diagnostic yield with sensitivity \( \geq 90\% \) for peripheral nodules except for nodules < 1.5 cm.\textsuperscript{1,2,8,32} Sensitivity is affected by nodule size, needle size, the number of needle passes, and the presence of on-site cytopathologic examination.\textsuperscript{1}

However, complications with TTNB, particularly pneumothorax, may not be tolerated in patients with underlying pulmonary disease. The incidence of pneumothorax with TTNB reported over the last decade has been reported to be between 9% and 54%,\textsuperscript{33} whereas one large cross-sectional analysis of 15,865 adults reported a 15% risk of any pneumothorax.\textsuperscript{34}

When surgical biopsy is considered appropriate, thoracoscopic wedge resection is generally preferable.\textsuperscript{1} However, nodules that are small (< 1 cm), deep, or subsolid in attenuation may be difficult to locate by digital palpation. Diagnostic yield may be improved by various techniques, including use of radio guidance, methylene blue, and ultrasound (Table 2). In addition to allowing biopsy of lesions, ENB may be used during the same procedure to localize lesions with dye marking to facilitate their immediate surgical removal.\textsuperscript{35,36} For the treatment of resectable non-small cell lung cancer, lobectomy and systematic sampling of mediastinal lymph nodes should be conducted.\textsuperscript{1} For small peripheral lesions (< 2 cm), sublobar resection including segmentectomy or wedge resection with mediastinal lymph node sampling or dissection may be another treatment option. However, this option awaits validation from the results of a previous randomized clinical trial.\textsuperscript{37}

Apart from use of procedures, early detection of pulmonary nodules and timely intervention may be facilitated by telemedicine interventions, which include video, telephone, and Internet links among health-care professionals.\textsuperscript{38} Teleradiology, as a specific application of telemedicine technologies, has the potential to improve access to health-care services and expertise in remote areas, although data protection to preserve patient confidentiality must not be compromised.

Hospitals with Internet-based medical technology capabilities should consider applying teleradiology to assist in early diagnosis of lung nodules if necessary. Teleradiology has its own networking, information mining, and monitoring capabilities. These capabilities can be applied not only for lung nodule management and facilitating information collection and storage but can also help facilitate remote expert multidisciplinary consultation and follow-up tracking.\textsuperscript{39}

In this text, we developed clinical practice consensus guidelines for Asia in evaluating pulmonary nodules based on CHEST guidelines and the specific conditions in Asia. The suggested adoption of a standardized size threshold is reasonable but not based on current evidence.

Discussion

These clinical practice guidelines were developed in response to the need for local guidance on the evaluation of pulmonary nodules, especially given the increasing incidence and unique characteristics of lung cancer in many Asian countries. Recommendations based on the CHEST guidelines on the evaluation of pulmonary nodules were adapted by a panel of experts in pulmonary medicine and thoracic surgery from different Asian countries. Some of the considerations (eg, higher prevalence of granulomatous disease) apply equally well to some settings outside of Asia. However, the present consensus emphasizes that the high prevalence of TB in Asia favors lesser reliance on PET scanning.
and greater use of nonsurgical biopsy over surgical diagnosis (at high probabilities) or surveillance (at low probabilities).

The incidence of lung cancer in many Asian countries has risen in response to multiple risk factors, including cigarette smoking, air pollution, and use of coal and biomass fuels. The smoking epidemic in many Asian countries, in contrast to the situation in many Western countries, has only just peaked or is still rising and continues to represent a key risk factor for lung cancer. In China, smoking rates among men were estimated at 52.9% in 2010. In Korea, smoking has been shown to increase the risk of lung cancer by a factor of 4.2. Accordingly, Korea has developed guidelines for the screening of lung cancer among heavy smokers, aged 50 to 74 years, which includes guidance on the evaluation of nodules detected during screening. Several populations in Asia, especially Chinese and Korean men, have higher lung cancer incidence rates than those noted in Asian subjects residing in Western countries such as the United States. This finding may reflect both higher smoking rates and the presence of other risk factors.

Air pollution is considered the largest environmental cause of death worldwide, with mutagenic effects on DNA leading to an increased risk of several cancers, including lung cancer. Air pollution is common and severe in many Asian countries, particularly in large cities in China and India. Occupational exposure to asbestos or other carcinogens can increase the risk for lung cancer. In addition to outdoor air pollution, widespread use of household coal and biomass fuels for heating and cooking leads to indoor air pollution, which has been associated with respiratory tract infections, chronic respiratory diseases, or lung cancer, especially among those with a history of chronic lung disease such as TB and COPD.

In many Asian countries, women who have never smoked also seem to have an increased risk of developing lung cancer compared with women living in Western countries. Adenocarcinoma is the most common form of lung cancer in Asia, particularly in women, and this finding may reflect both genetic differences and other risk factors. In support of a genetic role, a recent genome-wide association analysis in never-smoking Asian women from mainland China, South Korea, Japan, Singapore, Taiwan, and Hong Kong identified three new susceptibility loci and confirmed associations for other loci. Women also seem to be more susceptible to developing lung cancer than men, which may relate to functional genetic differences between the sexes. Risk factors that have been noted among women in Asia include the widespread use of coal and biomass fuels, passive smoking, cooking smoke, and second-hand smoke.

In broad terms, the diagnosis and management of pulmonary nodules in most Asian countries are not substantially different from those performed in Western countries. However, evaluation of pulmonary nodules is likely to be affected by differences between Asian and Western countries, between different countries in Asia, and between different regions within countries. These differences primarily relate to the greater prevalence in Asia of: (1) lung cancer risk factors as discussed earlier, (2) granulomatous and infectious disease that can confound the diagnosis, and (3) genetic predisposition to lung cancer. Moreover, access to diagnostic equipment, religious and cultural beliefs, and the role of family in decision-making may also influence the evaluation of pulmonary nodules. The expert panel acknowledges that guidelines on the evaluation of pulmonary nodules already exist in several Asian countries. The adapted recommendations reported here are not designed to replace these local guidelines but are meant to supplement them with an overview applicable to Asia. One of the key differences between the CHEST recommendations and those suggested here is the consideration to increase the duration of CT surveillance to 3 years and beyond. The panel acknowledged there is insufficient published evidence supporting this practice and that it is based on the greater levels of overall risk in many countries in Asia. The panel experts also acknowledged that the risks of repetitive exposure to ionizing radiation may not be trivial. Another important difference between the CHEST recommendations and those suggested here is the use of quantitative measures for assessing the initial, pretest probability of malignancy. The populations used to validate the models for assessing pretest probability of malignancy (eg, the Mayo Clinic model suggested by CHEST) may be inaccurate when applied to populations in Asia for several key reasons. These reasons include high rates of granulomatous and other infectious diseases, severe air pollution, and lung cancer among nonsmokers. The expert panel agreed there is a need to develop a
locally validated prediction model in different Asian countries. At present, efforts are currently underway in China to update the Mayo Clinic prediction model using local data.

There are several key limitations of these adapted clinical practice guidelines. Most importantly, there is a lack of published evidence to support the suggested changes to the CHEST recommendations. The panel agreed on the importance of updating these recommendations based on new evidence as it emerges and on feedback from end users. In this regard, the process of adapting recommendations highlights deficiencies in the available evidence and suggests areas for future research. Secondly, the wide variations both between countries and regions within individual countries make it difficult to provide recommendations that are universally applicable to the whole of Asia. Therefore, clinicians are urged to apply the recommendations as appropriate to their practice, taking into consideration available resources, expertise, and other constraints. It should be noted that a different recommendation may have been made if a patient, caregiver or primary care physician had been included on the panel.

Conclusions
These clinical practice guidelines used a consensus-based approach to adapt the current CHEST recommendations on the evaluation of pulmonary nodules to be relevant to clinical practice in Asia. Most of the CHEST recommendations are broadly applicable to Asia, with some modification required, mainly to address the increased risk of lung cancer in the region, especially in nonsmokers, as well as the different prevalence of infectious lung disease. In addition, the panel recommended standardization of all future guidelines using a 4-mm threshold (as opposed to 4 mm for solid nodules and 5 mm for nonsolid nodules) for ease of implementation.

Acknowledgments
Author contributions: All authors participated in the drafting, critical revision, and approval of the final version of the manuscript. The consensus was developed primarily from CHEST guidelines, and the original authors reserve all the copyright.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following: D. A. has received accommodation and travel expenses from the sponsor. None declared (C. B., C.-M.C., C. M. C., J. C. H., A. Z. K., J.-M. L., S. Y. L., S. S., A. Y.).

Role of sponsors: Covidien was involved in organizing the consensus meeting. However, the guidelines reflect the expert opinion of the authors.

References
20. Bae J, Gwack J, Park SK, Shin HR, Chang SH, Yoo KY. Cigarette smoking, alcohol consumption, tuberculosis and risk of lung cancer:...