Lung cancer staging now and in the future

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ABSTRACT
For a long time lung cancer was associated with a fatalistic approach by healthcare professionals. In recent years, advances in imaging, improved diagnostic techniques and more effective treatment modalities are reasons for optimism. Accurate lung cancer staging is vitally important because treatment options and prognosis differ significantly by stage. The staging algorithm should include a contrast computed tomography (CT) of the chest and the upper abdomen including adrenals, positron emission tomography/CT for staging the mediastinum and to rule out extrathoracic metastasis in patients considered for surgical resection, endosonography-guided needle sampling procedure replacing mediastinoscopy for near complete mediastinal staging, and brain imaging as clinically indicated. Applicability of evidence-based guidelines for staging of lung cancer depends on the available expertise and level of resources and is directly impacted by financial issues. Considering the diversity of healthcare infrastructure and economic performance of Asian countries, optimal and cost-effective use of staging methods appropriate to the available resources is prudent. The pulmonologist plays a central role in the multidisciplinary approach to lung cancer diagnosis, staging and management. Regional respiratory societies such as the Asian Pacific Society of Respirology should work with national respiratory societies to strive for uniform standards of care. For developing countries, a minimum set of care standards should be formulated. Cost-effective delivery of optimal care for lung cancer patients, including staging within the various healthcare systems, should be encouraged and most importantly, tobacco control implementation should receive an absolute priority status in all countries in Asia.

Key words: Asia Pacific, challenge, lung cancer, staging.

INTRODUCTION
Lung cancer burden
Lung cancer is the leading cause of cancer death for both men and women worldwide.1 In 2012, there were more than 1.8 million lung cancer diagnoses causing 1.6 million deaths worldwide.2 With the current high
and ever increasing rate of smoking in many Asian and developing countries, the incidence of lung cancer and consequent deaths from this disease is anticipated to increase over the next decades. It is estimated that by 2030, 70% of tobacco-related deaths will occur in developing and low-income countries. The tobacco smoking epidemic in China exemplifies a shift in the global burden of lung cancer from high-income western countries to low- and middle-income countries. In the 1980s one-third of lung cancer cases occurred in developing countries while currently 55% of the new lung cancer cases are diagnosed in the developing world, and this trend is expected to continue in the next decades. Although developing countries are heterogeneous in terms of ethnicity, prevalence of smoking and incidence of lung cancer, they share in common the limited and suboptimal access of lung cancer patients to the healthcare system. In Asia, it is noteworthy that a significant proportion of people who develop lung cancer are lifelong non-smokers. 

The mortality rate of lung cancer is high compared with other cancers because only about 15% of lung cancer cases are diagnosed at an early stage allowing curative treatment. In the United States, 5-year survival figures range from 52% to 4% for local, loco-regional and distant disease, respectively. However, meta-analytic studies suggest that the survival of Asian lung cancer patients is better than that of their Caucasian counterparts. The reasons behind a more favourable prognosis of Asian lung cancer patients might be explained by the relatively high prevalence of epidermal growth factor receptor (EGFR) mutations predicting altered biology and more favourable response to EGFR tyrosine kinase inhibitors.

Reasons for optimism
For many years, the diagnosis of lung cancer has been accompanied by a nihilistic attitude of many healthcare professionals. This nihilism has also negatively affected research funding which has been very modest in comparison with research funding for other cancers. However, the recent advances in lung cancer diagnosis and management have rapidly transformed this landscape. Apart from improved diagnostic techniques, novel treatment opportunities such as stereotactic and 4D radiation therapy, radiofrequency ablation, adjuvant chemotherapy and targeted therapies have become more widely available. With new screening strategies early diagnosis is coming into sight.

LUNG CANCER STAGING

Advances in lung cancer staging
The tumour-node-metastases (TNM) staging of lung cancer describes the extent of the disease in terms of the size, location and extent of the primary tumour (T descriptor), the presence and location of lymph node involvement (N descriptor) and the presence or absence of distant metastatic disease (M descriptor).

The revised classification system for lung cancer by the International Association for the Study of Lung Cancer (IASLC) represents a major advancement which has resulted in a significantly improved stratification of survival among the staging subgroups. Briefly, in the revised classification, the stage of lung cancer is determined by the size and local invasion of the primary tumour (T1-4); whether the ipsilateral hilar (N1) and mediastinal lymph nodes (N2), contralateral hilar or mediastinal nodes (N3) or supraclavicular nodes (N3) are involved; and whether intrathoracic (M1a) or distant metastases (M1b) are present. The National Comprehensive Cancer Network (NCCN) Guidelines and the American Joint Committee on Cancer (7th edition) staging system for lung cancer adopt the revised IASLC classification and recommend TNM staging for both NSCLC and small cell lung cancer (SCLC).

The importance of lung cancer staging
Proper and precise staging to assess the extent of the disease is of paramount importance to patients diagnosed with lung cancer for appropriate treatment recommendations. An incorrect or insufficient cTNM classification can lead to a wrong decision on potential curative as well as palliative treatment options. While patients with stage IA, IB, IIA and IIB NSCLC can benefit from curative surgical resection, those with stage IIIA, IIIB and IV disease rarely benefit from surgery. In patients with SCLC, except in rare cases of surgically operable limited-stage disease, the purpose of staging is to determine whether treatment is with chemotherapy and radiation for limited disease or with chemotherapy alone for extensive disease.

While clinical evaluation and computed tomography (CT) provide an initial estimation of the extent of the disease, in most cases, stage needs to be confirmed with additional tests. Pathological staging (pTNM) uses clinical staging (cTNM) and the additional pathological information obtained by surgical procedures (including the examination of mediastinal lymph nodes by mediastinoscopy and/or thoracotomy). The pTNM stage is considered to be the ‘true’ stage, and the degree of agreement between cTNM and pTNM is one of the most important indicators of the quality of the diagnostic and staging workup.

Imaging modalities for lung cancer staging
Imaging modalities for staging lung cancer include chest radiography, CT, magnetic resonance imaging (MRI), and whole body 18-fluorodeoxyglucose (FDG) positron-emission tomography (PET) and fused or integrated PET/CT. CT is the most common imaging procedure for staging in most institutions because it is widely available and relatively non-expensive. While chest CT is useful in identifying tumour location and the presence of mediastinal lymph node involvement, it is limited in its ability to differentiate benign from malignant pulmonary nodules and lymph nodes. FDG-PET scanning is more accurate in
identifying mediastinal lymph node metastases. In a systematic review comprising 45 studies sensitivity, specificity, positive predictive and negative predictive values of 80%, 88%, 75% and 91%, respectively, were reported.19 PET is also more sensitive in detecting extrathoracic metastases. However, there is a notable exception: the detection of brain metastases which often requires imaging with contrasted brain CT or MRI. Because FDG-PET cannot differentiate benign (e.g., inflammation) from malignant disease, tissue sampling of ‘decisive’ lesions is mandatory. The specificity of PET depends on the prevalence of other PET-avid diseases in the population such as tuberculosis and sarcoidosis and may not exceed 90%.19

The use of PET imaging is limited because of its high cost and limited availability. If PET scintigraphy is not available, a CT of the chest extending to the upper abdomen to include the liver and adrenal glands, and bone scan are reasonable alternatives.19 However, the sensitivity and specificity of CT scanning to detect mediastinal lymph node metastases are relatively low at 55% and 81%, respectively.19 Consequently mediastinal metastases may remain undetected (false negatives), leading to futile thoracotomies or enlarged benign lymph nodes may exclude patients from potentially curative surgery (false positive).

The high negative predictive value of FDG-PET means curative surgery may be undertaken and invasive diagnostic procedures may be omitted if there is no extra FDG-uptake in the mediastinum, except when the tumour is centrally located, or in the case of adenocarcinoma-in-situ and PET N1 disease. On the other hand, the high false-negative rate means a positive FDG-PET examination requires pathological confirmation. In addition, it should be noted that PET is also associated with a significant false-negative rate.22 PET scanning becomes less sensitive when lymph nodes are not or are moderately enlarged, and with invasive diagnostic procedures such as mediastinoscopy, endobronchial ultrasound (EBUS), and endoscopic ultrasound (EUS), metastases in normal-sized and non-FDG-avid lymph nodes could be detected.23,24 About 4% of patients presenting with what is expected to be stage I disease and a normal PET scan turn out to have N2 disease. Larger lymph nodes on CT with no FDG-uptake may require tissue sampling because these nodes have a higher probability for N2 disease. The presence of N2-positive lymph nodes substantially increases likelihood of positive N3 lymph nodes and therefore it is advised that pathological evaluation of the mediastinum must include the subcarinal and contralateral lymph node stations.18

In Asian countries, where the prevalence of tuberculosis (TB) is high, the accuracy of PET/CT in lymph node staging may be less than reported elsewhere. A meta-analysis of seven studies on the diagnostic performance of PET/CT in lymph node staging of patients with NSCLC in TB and non-TB endemic regions found the pooled sensitivity, specificity, positive likelihood ratio and negative likelihood ratio for patient-based analyses were 66%, 92.7%, 5.86% and 0.41%, respectively, and those for lesion-based analyses were 59.4%, 96.5%, 9.37% and 0.31%, respectively.25

Minimally invasive techniques for lung cancer staging

Transbronchial needle aspiration (TBNA) can be used to sample either suspected lesions or enlarged paratracheal and subcarinal lymph nodes identified by CT. The diagnostic yield of blind TBNA procedure is around 40%. Therefore this procedure is gradually being superseded by EBUS and EUS that have shown diagnostic yields as high as 90%. EBUS-TBNA allows real-time controlled sampling of paratracheal, subcarinal and hilar lymph nodes, and EUS-fine needle aspiration (FNA) sampling of the mediastinal nodes located adjacent to the oesophagus, including those in the inferior mediastinum as well as the liver and the left adrenal metastases. With the complementary reach of EBUS-TBNA and EUS-FNA in assessing different regions of the mediastinum, more complete mediastinal staging can be achieved by the combination of both procedures. EBUS-NA, EUS-NA and combined EBUS/EUS-NA procedures have sensitivities of approximately 89%, 89% and 91%, respectively. In experienced hands, these minimally invasive biopsy techniques are at least as accurate as mediastinoscopy26,27 and can reduce the need for surgical staging.

For patients presenting with discrete mediastinal lymph node enlargement with or without PET uptake and in the absence of distant metastases, invasive staging of the mediastinum is recommended.19 It is also recommended that patients with a central tumour or hilar lymph node enlargement and an otherwise radiographically normal mediastinum should undergo invasive staging by a needle aspiration (NA) technique (EBUS-NA, EUS-NA or combined EBUS/EUS-NA) if this technology and a skilled operator are available.19

It is obvious that pathological confirmation of suspected mediastinal lymph nodes is not necessary in patients with overwhelming radiographic evidence of extensive mediastinal tumour infiltration or multiple distant metastases.19 For patients with a peripheral lesion of 3 cm or less and ‘normal’ lymph nodes by CT and PET, further preoperative mediastinal staging may be omitted.19

Invasive surgical techniques for lung cancer staging

In patients in whom the clinical suspicion of mediastinal node involvement remains high despite a negative result of FNA, surgical staging such as mediastinoscopy, mediastinotomy or video-assisted thoracic surgery (VATS) is advised.19

For patients presenting with a left upper lobe tumour in whom invasive mediastinal staging is indicated, invasive assessment of the aortopulmonary window nodes via video-assisted thoracoscopy, an extended cervical mediastinoscopy or a Chamberlain procedure maybe considered if other mediastinal node stations do not seem to be involved.19
Implication of these advances and the challenges of implementing them from the perspective of higher compared to lower income countries

The applicability of evidence-based guidelines for the staging and treatment of lung cancer depends on the resources available. Advancement in diagnosis, staging and treatment of lung cancer remains inaccessible for the vast majority of people living in low- and middle-income countries because of limited resources. There is a paucity of published literature on lung cancer staging practices in the Asia-Pacific region. Given the diversity of healthcare infrastructure and economies in Asian countries, optimal and cost-effective use of these staging methods appropriate to the resource availability is prudent.

Variations and disparities in practice

Not unlike the situation in other parts of the world, variations in practice, infrastructure, resource availability and standards of care for lung cancer are present across countries and also within the same countries in the Asia-Pacific region. For example, in Hong Kong, despite the availability of EBUS service in most respiratory units of public hospitals, clinical practice varies from sampling only the FDG-avid mediastinal lymph nodes only to systematic sampling. Performance including the thoroughness of staging and care provided may vary according to the characteristics of the healthcare facility such as academic affiliation, for-profit status and staffing.

Challenges of implementing evidenced-based advances in lower income countries

Increasingly, lung cancer is more likely to occur in poorer and less-educated populations, primarily reflecting the increasing gradient of smoking with socioeconomic indicators that include income, education and occupation. This pattern, noted for the first time several years ago in the United States, is currently being observed in many other countries worldwide. Despite the availability of universal healthcare, lower socioeconomic status has been shown to be also associated with poorer lung cancer survival and more advanced cancer stage at diagnosis.

Oncology practice in most parts of the developing world lags behind the rest of the world by several years. As much as they are enthusiastic about embracing evidence-based advances and recommendations by international guidelines, resource-constrained countries face many barriers and challenges in adopting new staging technologies as well as implementing the recommendation. Such challenges include financial constraints, the lack of epidemiological data to guide resource planning, deficiency of diagnostic and staging capabilities/facilities, shortage of trained healthcare professionals, competing healthcare priorities and political uncertainty.

Impact of funding and reimbursement

Funding and reimbursement are key factors in driving policy and practice changes. In most low- and middle-income countries, national healthcare financing is far from universal. Often, only the small proportion of the population can afford the cost associated with private healthcare. The actual cost of investigations and lack of comprehensive health insurance seem to determine the access to and the extent of staging investigations. Private for-profit insurers target only the better-off section of the society with expensive healthcare packages. Out-of-pocket payment for diagnostic and staging procedures can be a major drain on the patients’ finances, causing severe indebtedness and financial distress. Lack of financial resources may cause patients to avoid recommended procedures.

Even in affluent parts of the Asia-Pacific region such as Hong Kong where the public healthcare sector takes care of over 90% of the population, only two out of around 10 PET imaging centres are located in public hospitals. Even in the public sector PET-CT is a self-financed investigation for most of the patients. Despite the wide availability of advanced diagnostic techniques and equipment such as EBUS and PET-CT, the lack of wide medical insurance coverage limits the utilization of such techniques for thorough clinical staging in a significant proportion of newly diagnosed lung cancer patients. The situation in Malaysia, a middle-income country lacking a national health insurance coverage, is similar where only three of a dozen PET/CT imaging centres are located in public facilities while the rest is in the private sector. In Thailand, the national guideline on lung cancer staging recommends chest CT for the evaluation of mediastinal lymphadenopathy. While lung cancer staging workup as recommended by the guideline is funded under the national universal health coverage policy in Thailand, PET/CT for lung cancer staging is not reimbursable because of its limited availability, and its use is limited to self-paying patients. In Indonesia, a lower-middle income country, the implementation of universal social security programme has increased the scope for lung cancer diagnosis and therapy. Diagnostic procedures such as EBUS but not PET/CT and treatments such as chemotherapy and targeted therapy with EGFR-TKI are available at referral hospitals but are inaccessible to the vast majority of the people. PET/CT centres are mostly located in private hospitals and are not covered by the universal social security programme. In Indonesia where the population is widely dispersed over 16 000 islands, the availability of universal social security programmes is not sufficient to solve the problems. An imbalanced distribution of lung centres, a complex referral system and inconvenient inter-island transport are the major obstacles in the diagnosis and management of lung cancer.

Mainland China, for example, is a geographically huge and a fast-growing developing country where the medical care standard and accessibility are heterogeneous and inequitable across different provinces. The payment modalities of the healthcare
system varies across districts for cancer patients. For instance, the cost of chemotherapy and radiation for citizens living in Beijing is fully covered, while those living in other provinces are only partially covered with different reimbursement proportions.42 A recent cost-effectiveness study has examined the role of PET/CT in pre-operative staging of NSCLC in China.42 With a strategy of including a whole-body PET after CT scan for all patients with potentially resectable lung cancer, the incremental cost-effectiveness ratio was around US$ 3500/life year saved (LYS) in 2010, which was well below the threshold of US$ 50 000/LYS in Europe to be considered cost-effective. Wider availability and national insurance coverage of PET/CT in lung cancer staging in China will likely improve the overall staging and management of lung cancer in the future.42

Establishing specialized cancer centres is often not feasible in less-developed countries due to financial constraints, insufficient resources, inadequate planning and management issues. Non-existent budgets for cancer control, detection and treatment, and failure to prioritize cancer as a health problem will have to be overcome to effectively address these issues. Policy barriers are often among the most difficult to overcome. The low priority assigned to cancer control in low-income countries has created a ‘triple penalty’ comprising poor access to care, late presentation with advanced disease thereby greatly increasing both the cost and toxicity of treatment as well as lowering survival outcomes.43 The poor outcomes, in turn, erroneously support the argument that cancer care is unaffordable, unachievable and inappropriate in low-income countries and should not be a priority on their health agendas because it diverts precious resources from other more deserving and burdensome health priorities.43 Even in the case of lung cancer, the stigma of it being thought of as an avoidable smoking-related cancer has adversely affected its awareness and research funding.

Limited access to specialist care and state-of-the-art diagnostic and staging facilities

Insufficient medical facilities and shortage of doctors plague most government hospitals, resulting in delay in diagnosis, staging and treatment of lung cancer. In one study, 21% of potentially curable lung cancer patients became incurable while waiting for treatment.46 However, systematic reviews reveal only a limited association between survival and delay.47,48 Nonetheless, delay is a psychological burden for the individual patient, and it has been proven that there is a correlation between the length of waiting times and the extent of psychological stress.49 In addition, in countries with a high prevalence of tuberculosis, lung cancer may be wrongly treated as tuberculosis, leading to a delay in diagnosis.50,51

The slow progress of organ-specific subspecialization in developing countries is another cause of the poor results of cancer care. An analysis by Grilli et al. showed that specialized cancer care is associated with a reduction in mortality.52 A multidisciplinary team of specialists who care for a significant number of patients on a regular basis is a necessity for optimal lung cancer care53 and is now a standard part of management of thoracic malignancies in the United Kingdom,54 United States,55 Canada56 and Australia.57–59 Such a multidisciplinary team which ideally should include pulmonologists, thoracic surgeons, medical oncologists, radiation oncologists, pathologists, radiologists, nuclear medicine specialists, palliative care physicians as well as nurses and pharmacists, however, is not uniformly available.57,58

The pulmonologist plays a vital role in the multidisciplinary approach to lung cancer60 and is responsible for the initial diagnosis and staging. The pulmonologist may also be involved in prescribing chemotherapy and performing palliative airway stenting and endobronchial laser therapy.60,61 Initial referrals to non-respiratory physicians are one of the causes of delay.48 Even in developed and resource-rich countries, timeliness of care can be vastly different between the public and private hospitals.62 A qualitative study of timely care in lung cancer in Veterans Affairs settings in the United States of America identified multiple barriers, including inadequate staffing, limited availability of imaging equipment and operating room time, suboptimal coordination of care within and between facilities, institutional inertia and patient non-compliance.63 Consultation with a low patient volume lung cancer specialist or a non-lung cancer specialist is one of the important factors associated with failure to receive cancer-specific therapy.64 Specialist care has been associated with greater access to curative treatment and significantly better survival.64,65 Specialists who see fewer lung cancer patients per year are less likely to be aware of the benefits of non-surgical treatment and to offer such treatment.67,68 Compared to low-volume or non-multidisciplinary centres, high-volume centres and multidisciplinary teams provide more complete staging resulting in improved survival.69

In the Asia-Pacific region, there are wide variations in standards of care and access to quality cancer care plus the imbalanced geographic distribution of specialists and well-equipped cancer centres. Public funded tertiary care cancer hospitals are a rarity in resource-limited countries.69 The few specialized lung cancer centres only cater for a small fraction of lung cancer patients. To increase access to specialized care by more patients there is a need for streamlining referrals and the establishment of hospital networks.70

Religious and cultural beliefs

Cancer fatalism and traditional medicine can be a challenge to mainstream lung cancer management. In low- and middle-income countries, awareness of the importance of early detection is low, and the stigma associated with lung cancer and the financial barriers of poverty prevent many people from seeking care at earlier stages. In Asian countries, the investigation of lung cancer is sometimes hampered by religious and cultural beliefs that prevent or delay seeking and undergoing investigation by mainstream healthcare facilities and promote seeking treatment...
of alternative or traditional treatment. Traditional Chinese herbal medicines are widely used alone or in combination with chemotherapy to treat malignancies including lung cancer in many parts of Asia. In many Asia-Pacific countries, a highly established tradition of medical pluralism exists where doctors, traditional Chinese medicine practitioners and shamans are readily available and patients move freely between modern and traditional medicinal system, or use both systems simultaneously.

Religious sentiment may also play a role in the patients’ decision not to seek medical care as most religions here consider death as the will of God. Cancer fatalism is a barrier to cancer evaluation and treatment with the belief that death is inevitable with the diagnosis of cancer. Cultural beliefs that disturbing the tumour may accelerate the spread of cancer may be one the reason for refusing staging procedures. Even the poorest sector of the society may be reluctant to use free governmental health facilities because of religious or cultural beliefs. Furthermore, the stigma of lung cancer with it being thought of as an avoidable smoking-related cancer somehow deter patients from seeking medical attention because of a feeling of guilt and shame in adding to the workload of an overly stretched public healthcare service.

The median survival of NSCLC patients who accept cancer-specific therapy is significantly longer compared to those who opt out of cancer-specific treatment. A systematic review and meta-analysis of seven cohort studies (4418 patients) and 15 randomized controlled trials (1031 patients) showed that NSCLC patients without active treatment have a pooled mean survival of 7.15 months.

Strategies to overcome the challenges of lung cancer staging in the Asia-Pacific region

Although there are many challenges and barriers to optimal cancer care in resource-poor countries, these can be overcome by utilizing measures that are evidence-based, scientifically sound, resource-level specific, economically feasible, culturally appropriate, pragmatic and reflect good clinical practice. The World Health Organisation has recommended the development of guidelines that are resource-level appropriate for the management of all major cancers. Implementation of guideline recommendations must be tailored to the local setting. In some countries or institutions in the same country, certain tests or procedures may not be available. The situation can be substantially improved by a reorganization of existing human resources and facilities. National and local initiatives such as strategic planning, training of healthcare workers, facilitating access to diagnostic and staging services, and public education can help overcome some of the challenges of implementing advances in lung cancer staging in resource-constrained settings. Several middle-income countries have included cancer care in national health insurance coverage for people living in poverty. These strategies can reduce costs, increase access to health services, and strengthen health systems to meet the challenge of cancer and other diseases. The Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries composed of leaders from the global health and cancer care communities was formed in 2009 with the intention to propose, implement and evaluate strategies to advance this agenda leveraging on the lessons learned from previous initiatives which address diseases such as AIDS and tuberculosis.

Having in place national cancer registries would help to provide essential data for the development of healthcare policies and infrastructure for cancer management and influence the funding authorities to prioritize lung cancer care. Assembling a local team of specialists as well as critically reviewing the major guideline recommendations and the local strengths and challenges are needed. This allows the development of a locally adapted system of care that can significantly streamline the process of care and ensure that patients are receiving thoughtful care to the highest degree possible in that setting. Even if a test is available, one cannot assume that the results in every clinical setting match those of the published literature because the findings cannot be generalized to all healthcare settings due to differing healthcare organization and funding structure.

Instead of functioning in isolation, cancer facilities in low- and medium-income countries should forge links with established centres in high-income countries, thereby benefiting from professional and technical support as well as knowledge transfer and exchange of healthcare professionals.

A concerted effort is needed from the global health community with the participation of local governments and primary healthcare networks to expand cancer care including diagnostic services with strategies that are appropriate to the health systems of resource-constrained countries, accessible to patients with low incomes and integrated into national health insurance systems. Even in extremely resource-poor settings, making use of local clinicians and community health workers, supported by remote consultations with specialists, effective cancer care can be delivered. However, despite success with pilot projects, scale-up of the programmes may face challenges of public funding constraints.

While integrated PET/CT is recommended for more precise staging and is useful for confirmation of the presumed extrathoracic stage in patients with intermediate stages of lung cancer, particularly in the case of a solitary site of metastasis or with lesions that are indeterminate on other scans, its role is limited in patients with strong clinical signs of metastatic disease. In advanced disease, staging should be limited to those examinations with impact on symptom control.

Innovative health insurance schemes that are able to address the weakness and deficiencies in healthcare financing of the individual countries are badly needed. According to the statistics by China’s Ministry of Health, the national public health insurance coverage has increased sharply in recent years from less than 30% in 2003 to almost 100% in recent years following healthcare reforms. For example, the
number of PET/CT facilities in mainland China has increased substantially in recent times.\textsuperscript{42}

Education of the public is crucial for raising awareness of the growing burden of lung cancer and to dispel misconceptions about cancer. A greater awareness of the symptoms of lung cancer among the public and health professionals in primary and secondary care will result in prompt investigation for the disease. Education of governments and health ministries will enable better-informed decisions on lung cancer management. More research is required to study the reasons why patients opt out of modern-day cancer-specific care. It is possible that many of the reasons for declining medical care are unjustifiable and irrational, and appropriate counselling may prevent this.

Control of tobacco smoking remains the key strategy in reducing the number of new cases of lung cancer and eventually the lung-cancer burden. The most effective approach is by reducing smoking rates through public health policy and behaviour interventions. On the individual patient level, smoking cessation must be emphasized at every clinical encounter. Regional respiratory societies such as the Asian Pacific Society of Respirology should work with national respiratory societies to influence healthcare policy makers to push for acceptable uniform standards of care across countries in the region and in the case of developing countries, minimum standards of care. Countrywide research in cost-effective delivery of optimal care for lung cancer including staging within the various healthcare systems should be encouraged.

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