Best practice in early assessment and diagnosis of lung cancer: a rapid review

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This rapid review was brokered by The Sax Institute.

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EXECUTIVE SUMMARY

Background

This review has been carried out to assist the Cancer Institute NSW to better understand the evidence around best practice in early diagnosis and assessment of lung cancer and rapid access service models. The findings from this review will be used to inform a broader program aimed at increasing lung cancer survival by earlier diagnosis and improved access to treatment. Lung cancer is the leading cause of cancer death in Australia. Of those diagnosed with lung cancer, 20% will be alive after one year and only 5% at 10 years. As the population ages, it is likely that the incidence of lung cancer will rise. Many people will also have comorbid conditions which increase the risks and complexity of assessment and diagnosis of lung cancer. Later presentation, complex physical and social circumstances place an increased emphasis on the importance of multidisciplinary teams, shared decision-making and advance care planning.

Intuitively, screening would seem to be the optimal approach for the early identification of lung cancer. Screening programs can be provided at a population level (e.g. systematic, non-symptomatic bowel cancer screening) or opportunistic, based on high risk identification (e.g. targeted high risk screening in lung cancer). Choosing the best approach and timing of screening and subsequent assessment depends on the appraisal of the evidence for relative harms and benefits both to the individual and society. While established population-based programs for breast, cervical and bowel cancer are underway in Australia, evidence does not support such an approach in lung cancer. A tailored approach for screening high risk individuals is described in recent recommendations from the United States National Comprehensive Cancer Network, *Guidelines for Lung Cancer Screening* (2012). These guidelines are based on evidence from a large-scale clinical trial that screening via helical computed tomography can reduce lung cancer mortality. In spite of these recommendations uptake has been slow. Screening and diagnosis is just one part of the picture and subsequent to diagnosis there needs to be broader access to services for lung cancer tumour staging and treatment.

Tobacco smoking is the leading cause of lung cancer, and the time lag of two to three decades between exposure and presentation challenges screening and surveillance models. The stigma and prejudices associated with smoking and lung cancer, and a high comorbidity burden in individuals at high risk, influences help seeking behaviours of the individual and interaction with health care providers. These issues may also alter health professional's threshold for screening and referral for diagnostic tests. Moreover, perceptions of nihilism and futility may influence the referral and practice patterns of some health professionals. Many barriers inhibit patients getting to the appropriate health provider at the correct time. Delay times for diagnostic tests and staging of treatment often accumulate with the result that a critical window of opportunity is missed; qualitative data suggest that the most significant time delays are prior to referral to specialist care and many at the level of the patient. Most patients with symptoms (e.g. haemoptysis) will consult a general practitioner (GP) or other primary care health professional before they are referred for specialist advice. As general practice is the gatekeeper in the Australian health care system, GPs are an important focus for promoting early assessment and diagnosis of all cancers. This is especially the case for lung cancer, where an index of suspicion and appraisal of risk is needed to drive diagnostic testing and appropriate referral. Moreover, reimbursement models for opportunistic screening are more likely to be undertaken at the primary care level. Recent recommendations from Cancer Australia provide guidance under the title of Investigating symptoms of lung cancer: a guide for GPs (2012).

Coordination of care across primary, secondary and tertiary care is always challenging and this is especially pronounced in care for individuals with lung cancer who are commonly in regional, rural and remote areas. Providing care across settings and providers is the focus of the National

Health and Hospital Reform agendas. The socioeconomic differentials and health disparities for individuals living in regional, rural and remote settings underscore the importance of both outreach and in-reach models to improve cancer outcomes. The higher prevalence of lung cancer in areas distal to metropolitan settings is of special consideration and should be a focus of telehealth initiatives and organisation of care in Medicare Locals.

Summary of answers to review questions

1. *Which models that have been designed to facilitate the early assessment and diagnosis of cancer have been evaluated?*

Addressing the burden of lung cancer requires an increased focus on models of lung cancer screening, early assessment and diagnosis, and the tailoring and targeting of health care models for high risk groups, particularly current and ex-smokers. Once there is a high index of suspicion or signs, increasing access to diagnostic and staging services such as positron emission tomography (PET), and computerised tomography (CT) and endobronchial ultrasound (EBUS) is important for diagnosis and tumour staging. These services require expertise and are generally available in specialist centres and part of specialist lung cancer teams, often referred to as multidisciplinary teams (MDTs).

Many guidelines and recommendations endorse referral to the MDTs. Access to lung cancer MDTs, where there is access to equipment, expertise and improved outcomes due to operator volume, appears to be the most promising model to facilitate early assessment and diagnosis. This approach is to gather key professionals to assist in tumour diagnosis, staging and treatment. But to date, the impact of this approach in altering the disease trajectory and patient outcomes are unclear, largely because much of the opportunity to improve outcomes lies at the level of the individual patient in seeking diagnosis. There is also limited high level evidence for MDTs' optimal composition, role and function. Currently, there are limited incentives for participation in MDTs in the private sector. Isolated rapid access assessment and diagnosis models exist, but their success is largely dependent on appropriate diagnostic testing, tumour staging and treatment. Improving access and referral to specialist centres through networks and systematic referral mechanisms are warranted.

2. *What is the evidence for the effectiveness of rapid access assessment and diagnosis service models for cancer in improving patient outcomes?*

Survival is directly related to the time of diagnosis and as presentation is commonly late, rapid access assessment and diagnosis service models for cancer can be successful in improving outcomes from the provider and system perspective through increased expertise in procedural volumes and increased efficiencies in moving through the health care system. Studies have found that a rapid diagnostic system produced reduced wait times from presentation to first treatment, higher overall patient satisfaction, and less follow-up visits to general practitioners when compared with the conventional system. However, other studies have found no association between long treatment delays and worse outcomes in the advanced stages of lung cancer. Strategies addressing patient delay are likely to leverage better improvements in mortality in the longer term.

3. *What is the evidence for the effectiveness of rapid access assessment and diagnosis service models for cancer in improving outcomes from the provider and system perspective?*

A simple and efficient access strategy is considered to be important for improving the health care experience of the patient and the quality of diagnostic care. A centralised point of entry following lung cancer diagnosis is commonly advocated by the United Kingdom, National

Institute for Health and Clinical Excellence, Scottish Intercollegiate Guidelines Network and Ontario guidelines, yet there has been minimal evaluation of this approach on distal outcomes. However, extrapolating from many other clinical conditions centralising approaches of diagnosis and management is likely to provide individuals with access to expertise, diagnostic and management services. Ensuring communication of referral pathways in the health care system is required.

4. What is the evidence for the efficacy of screening for lung cancer in high risk populations?

Although the efficacy of low-dose helical CT screening for lung cancer in high risk populations has been demonstrated, measures of effectiveness and cost-effectiveness are yet to be determined. Optimal methods of lung cancer screening will maximise the detection of early stage cancer, minimise false positives, radiation exposure and costs associated with procedures and investigations. To date this has not been achieved. Only a small number of preliminary cost benefit analyses have been performed in respect to lung cancer screening and many of these have used predictive modelling. Examination of the funding implications of low-dose helical CT screening to the Australian health care system in high risk populations is warranted. Internationally, in spite of guideline recommendations, uptake of low-dose helical CT has been slow. Consideration of the implications of false positives, iatrogenesis and ongoing monitoring will be important considerations in recommending screening recommendations.

Recommendations

- Focus on primary care health professionals and high risk patient populations to increase awareness of risk factors for lung cancer and the importance of early assessment and diagnosis
- There is a need to standardise protocols for low-dose helical CT and other screening, assessment and diagnostic techniques
- Including assessment for lung cancer risk in funded models of health assessment in general practice, such as Aboriginal Health Checks, which are funded by the Medical Benefits Schedule (MBS) may yield benefits. Optimise availability of technical expertise through telehealth initiatives, particularly those that are reimbursed by the MBS
- Promote access to pathways and coordinated referral systems in local health areas, particularly for high risk individuals. This will need to include increased access to expertise in lung cancer, through standardised pathways and telemedicine strategies
- Ensure MDT composition, function and role is optimal to cope with a high proportion of false-positives until such time that the specificity of lung cancer screening can be improved
- Increase emphasis on the importance of timely and appropriate assessment and diagnosis from primary to palliative care services and incorporation of process and outcome measures in health care delivery approaches
- Benchmark and monitor procedural volumes and outcomes for surgical, chemotherapy and radiotherapy. This should be part of quality assurance projects for lung cancer care
- Promote coordination between the public and private sectors and the development of clinical pathways and quality assurance projects (e.g. the National Lung Cancer Audit (LUCADA)) project in the UK to support adherence with guidelines
- Consider modelling and projections for population screening within the context of emerging evidence for CT screening
- Target social marketing for high risk groups and collaborate with government and non-

government organisations to ensure community reach high risk groups, such as Aboriginal and Torres Strait Islanders. Engagement with high risk groups should be undertaken according to culturally competent practices, for example through engaging with the Aboriginal community controlled sector and multicultural community groups and agencies

- Develop implementation strategies to translate evidence into practice rather than rely on uptake of guidelines without targeted interventions.

Conclusions

The epidemiology and presentation of lung cancer represents a different paradigm to other cancers with regard to screening and early detection. There is a need to increase awareness of lung cancer risk factors and the importance of early assessment and diagnosis among health professionals as well as the community. Enabling timely treatment will require engagement of primary care, non-lung specialist medical providers and referral mechanisms that enable triage, assessment and appropriate access to services. Increasing specialisation in the diagnosis and staging of lung cancer means that timely access to specialist centres is critical.

Available data suggests that it is important to reserve screening to patients at risk rather than using a population based approach. There is a need for further research to increase the sensitivity and specificity of screening models. In the meantime, MDTs need to be capable of managing a high number of false-positives. Given the high cost of efficacious screening technologies, there is a need to understand the cost-effectiveness of lung cancer screening on a societal level and the impact of expected and unintended consequences of potential screening models. Providing patients with information about screening models will be important for future implementation.

Targeting and tailoring models of screening for high risk populations is warranted, including Aboriginal and Torres Strait Islanders, those living remote from health care services and those from targeted culturally and linguistically diverse populations. Models based on early/rapid assessment need to be seamlessly linked to definitive diagnostic and treatment services.

1 Introduction

An Evidence Check review is a rapid review of existing evidence tailored to the individual needs of an agency. Evidence Check reviews answer specific policy questions and are presented as a short report in a policy friendly format. Reviewers identify gaps in the evidence but do not undertake new research to fill these gaps.

Review parameters

The review's parameters were defined by the project brief as follows:

- Population: include cancers with a focus on lung cancer
- Early assessment: include medical, physical, functional, psychosocial, and spiritual needs for carers and patients
- Health service models and screening models: include models based on private health sector
- Setting: population and individual models including screening with an emphasis on early assessment and diagnosis.

2 Method

The review proceeded in two stages. At Stage 1, we identified and synthesised existing clinical practice guidelines and reports, epidemiological data and NSW population statistics and health service utilisation. This was intended to provide a context for a synthesis of research evidence for assessment and early diagnosis and service planning tools at Stage 2.

Method used for searching, selecting and synthesising relevant literature

Stage 1: Clinical guidelines, policy documents and data on NSW populations

Eligibility criteria

All current policy documents relating to cancer screening and diagnosis, with an emphasis on lung cancer were included. Policy document were defined as any publically available statement of position, standards or recommendations officially put forward by a government, peak professional body or other authority.

We also included data on health services utilisation and the distribution of culturally and linguistically diverse / non-English speaking background groups and Aboriginal and Torres Strait Islanders in NSW.

Information sources

Policy and information pages of the following key websites were searched for relevant policy documents: CareSearch; Cancer Council, Cancer Australia (and similar bodies in each OECD country); NSW Health / Ministry of Health; Australian Institute of Health and Welfare and the World Health Organisation including GLOBOCAN. Clinical trial registries were consulted in Australia, United States, Canada and the United Kingdom for novel screening and assessment strategies.

Population data, including the distribution of cancers in culturally and linguistically diverse groups and Aboriginal and Torres Strait Islander groups, was sourced from the Australian Bureau of Statistics (ABS), Australian Institute of Health and Welfare and relevant governmental reports. Recommendations for screening and early assessment were also identified from reports.

Synthesis

Recommendations and standards from each national standards policy document were summarised with regard to recommendations for screening, assessment and diagnosis. Analysis was driven by the research question “What are the most effective and efficient models of early assessment and diagnosis of lung cancer?”. As part of this process barriers and facilitators to screening on an individual and population level were considered. Moreover, these considerations were mapped in the context of the Australian health care system and the implications for policy, practice and research.

Stage 2: Published research papers

Eligibility criteria

To be included, studies needed to have been conducted in an Organisation for Economic Co-operation and Development (OECD) country and made publically available in English since 2002. Eligible document types included reports by health services and peak bodies as well as peer-reviewed journal articles and books/book sections. Due to the scope and timing of the review, a focus was on systematic reviews and identification of issues impacting on efficacy and effectiveness.

We also consulted qualitative literature, particularly pertaining to process issues and identification of barriers and enabling factors.

Types of participants and settings

Studies were included if they focused on population screening for cancer and high risk population or opportunistic screening.

Types of intervention

Interventions were identified as to their relevance to each of the research questions and search terms guided by MESH terms. Broadly models of screening interventions were reviewed but a particular reference to lung cancer.

Information sources

Electronic searches

We searched Medline, AMED, CINAHL, the Cochrane Database of Systematic Reviews, Health Technology Assessment Database (Technology Assessments) and CENTRAL from their earliest records. For grey literature, the Care Search, SEER and HealthInsite search engines reviewed relevant online clearinghouses and conducted desktop searching of the internet using Google and Google Scholar search engines. Deep web searching using Mednar was considered useful for the targeting of scientific material unavailable to search engines like Google.

Other sources

We identified data sources, such as government reports and clinical trial registries. The reference lists of all included reviews were searched manually for further relevant articles.

Search

Searches used Medical Subject Headings (MeSH) terms or equivalent as well as keywords relating to cancer screening and early assessment (see Appendix 1 for terms). Consultation with a health librarian was undertaken. In accordance with the Review brief, searches were date-limited to articles published since 2002.

Study selection

Returned articles were imported into Endnote (version X4) and electronically coded by a single researcher against each inclusion using standardised criteria.

Data collection process

Data were extracted by one researcher using proformas and reviewed and discussed within the project team.

Data items

Studies of models identified for Review Question 1 were summarised according to the project brief.

Appraisal of evidence

Evidence was informed by the National Health and Medical Research Council (NHMRC) levels and grades where appropriate.

Notes on the review and nomenclature

Definition of screening

We followed the World Health Organisation's (WHO) definition, adapted by the Australian Health Ministers Advisory Committee, Population Based Screening Framework as follows: "The presumptive identification of unrecognised disease or defects by means of tests, examinations, or other procedures" (p.16).

Definition of high risk

We used the high risk definition from the National Lung Screening Trial (NLST) (older, current or former smokers) which compared two ways of detecting lung cancer: low-dose helical computed tomography (CT) and standard chest X-ray. The NLST, which enrolled more than 53,000 current or former heavy smokers, found that a 20% relative reduction in deaths from lung cancer occurred among participants screened with low-dose helical computed tomography compared with those screened with standard chest x-rays equating to a 0.3 to 0.4% absolute reduction in deaths at about 6.5 years.[1,2-4]

Results from this trial represent the current best evidence in lung cancer screening. This does not rule out the possibility that the optimal definition of high risk will be modified by future data. Moreover, it has been recently stated that it is important to consider that these findings can only be applied to the population in the trial. Data on those at lower risk, e.g. those exposed to second hand smoke are likely to be considered at a lower risk.

Population approach

We have used the criteria of the Australian Health Ministers Advisory Committee, Population Based Screening Framework. According to this definition, "screening is offered systematically to all individuals in the defined target group within a framework of agreed policy, protocols, quality management, monitoring and evaluation by applying a screening test for a disease or risk marker which is considered important and will produce a net benefit that is cost effective and that the community considers acceptable. A screening program begins with identification and invitation of the target population and has a defined end point usually at definitive diagnosis and referral" (p.17). Such an approach will require the mapping of health service delivery and funding models.

Screening test

Again, we have used the Australian Health Ministers Advisory Committee, Population Based Screening Framework definition as "a comparatively simple investigation of anatomy, physiology, biochemistry or pathology that is able to classify people according to their likelihood of having a particular disease or risk marker for a disease" (p.17). Existing screening models in Australia are summarised in Appendix 2.

3 Background and context

Globally, lung cancer is the leading cause of cancer death, accounting for 1.3 million deaths per year.[5] This trend is increasing in the developing world as a consequence of globalisation and increased tobacco usage, particularly in segments of the population and the developing world.

Lung cancer in Australia

In Australia, the burden of lung cancer remains a significant and growing challenge. Lung cancer is the leading cause of death due to cancer and is the second leading cause of all deaths in men and the fifth cause of all deaths amongst women. In women the incidence is increasing internationally[6,7] and in Australia projected to increase by 38% to 4,001 cases by 2011 and in males by 17% to 6,301 cases by 2011. This increase is primarily attributable to increased smoking rates in women.[8,9]

For approximately 80% of people with lung cancer, outcomes are poor because the malignancy has been diagnosed too late a stage.[10,11] Of those diagnosed with lung cancer, only 20% will be alive after one year and only 5% at 10 years.[2,12,13] Although impressive improvements in survival have occurred across many tumour groups, these are less pronounced in lung cancer. The incidence and mortality rates for lung cancer are declining in men yet are increasing rates in women. The higher rates of lung cancer in Indigenous Australians and those from socioeconomically deprived groups remain an important concern for improving health outcomes.[14] Late diagnosis remains an important issue and concern. Prevention and early detection of lung cancer will likely decrease the burden of disease in Australia.[11]

Lung cancer classifications include non-small cell carcinoma, adenocarcinoma, squamous cell carcinoma and large cell carcinoma. These classifications are defined by histological characteristics and are associated with different risk factors and responsiveness to therapy. The Australian Institute of Health and Welfare report provides the most contemporaneous national Australian data (see Appendix 3 for a summary). This report documents that in 2007 in Australia, lung cancer was the fourth most commonly diagnosed cancer in both males and females. The incidence of lung cancer was strongly related to age, with 84% of new lung cancers in men and 80% in women diagnosed in those aged 60 and over.[15]

Between 1982 and 2007 the number of new lung cancers increased markedly in both sexes. The incidence rate of lung cancer has fallen in men by 32% but increased in women by 72%. Lung cancer is the leading cause of cancer deaths for both sexes, accounting for 21% of all cancer deaths in men and 17% in women. The incidence of lung cancer in Australia and state distribution are provided in Table 1 and Table 2.[15]

Table 1: Incidence of lung cancer, Australia, observed for 2007 and extrapolated [(a)] for 2010

Sex	2007			2010	
	Number of cases	Age-standardised rate[(b)]	95% confidence interval	Extrapolated number of cases[(a)]	Extrapolated age-standardised rate[(a, b)]
Males	5,948	57.9	56.5–59.4	6,300	57
Females	3,755	31.3	30.3–32.4	4,200	32

The extrapolations were based on incidence data for 1998 to 2007. The rates were age-standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 population.
Source: AIHW Australian Cancer Database 2007.

Table 2: Incidence of lung cancer by state and territory, Australia, 2003–2007

State or territory[a]	Males			Females		
	Average annual number of cases[b]	ASR[c]	95% CI	Average annual number of cases[b]	ASR[c]	95% CI
New South Wales	1,928	58.5	57.3–59.7	1,162	29.9	29.1–30.7
Victoria	1,453	60.0	58.6–61.4	876	30.0	29.1–30.9
Queensland	1,160	62.6	61.0–64.3	630	30.1	29.1–31.2
Western Australia	551	62.0	59.7–64.4	329	31.8	30.3–33.4
South Australia	487	59.0	56.7–61.4	284	28.4	26.9–29.9
Tasmania	172	67.3	62.9–72.1	108	36.4	33.4–39.7
Australian Capital Territory	52	44.0	38.7–49.8	40	27.2	23.5–31.2
Northern Territory	41	72.0	60.6–84.6	18	33.8	26.3–42.5
Total	5,844	60.2	59.5–60.9	3,448	30.2	29.7–30.6

(a) Relates to the state or territory of usual residence
(b) Numbers may not sum to the total due to rounding
(c) The rates were age-standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 population. The rates are based on the total number of cases over the 5 years from 2003–2007.

Source: AIHW Australian Cancer Database 2007.

Lung cancer in NSW

Lung cancer accounts for 8.9% of all cancer diagnoses and 20.2% of cancer deaths. See Figure 1 for aged standardised rates for incidence and deaths in men and women from 1972–2008

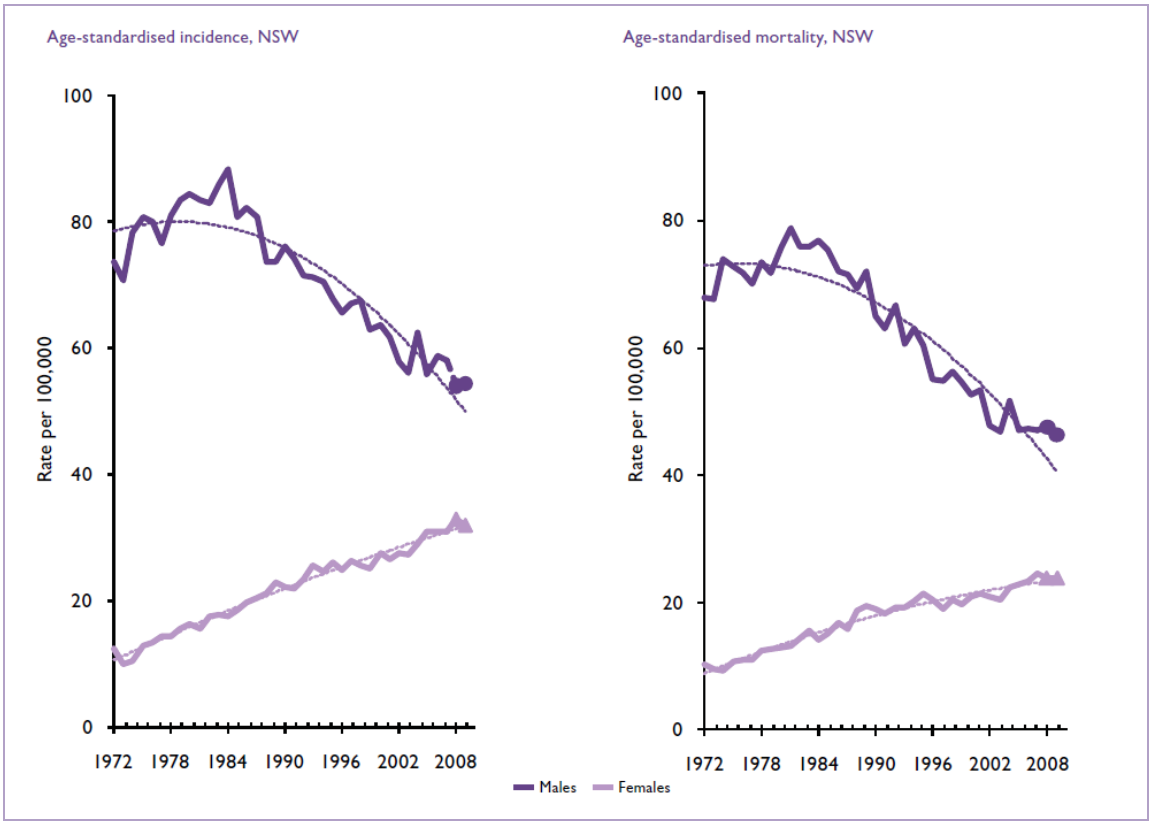

Figure 1. Age-standardised incidence rates and age-standardised death rates of lung cancer in men and women in NSW 1972–2008
SOURCE: Cancer Institute NSW, 2012.

Aboriginal and Torres Strait Islanders

Health outcomes of Aboriginal and Torres Strait Islander people show disadvantage relative to other Australians across many conditions.[1516,17,18] Aboriginal people are more likely to live in remote areas of Australia and have a younger age distribution relative to non-Indigenous people, with a median age of 21 years compared with 37 years for the non-Indigenous population and most importantly have a higher smoking prevalence and exposure to environmental factors.[14]

Between 2003 and 2007, lung cancer was the most commonly diagnosed cancer in Indigenous men (average of 42 cases per year) and the second most commonly diagnosed cancer in Indigenous women (average of 29 cases per year). The age-standardised incidence rate of lung cancer was significantly higher for Indigenous than non-Indigenous Australians. Specifically, Indigenous men were 1.7 times as likely to be diagnosed with lung cancer as non-Indigenous men and Indigenous women were 1.6 times as likely to be diagnosed with lung cancer as non-Indigenous women.[15,19, 20,14]

Lung cancer is the most common cancer among Aboriginal people and they are 2.5 times more likely to die within five years of a cancer diagnosis than non-Aboriginal people.[15,21,14] While the high mortality rate can be linked to higher incidence, spiritual and cultural beliefs, barriers to diagnosis, management and treatment such as distance, low socioeconomic status and language contribute to lower access to treatment.[14,19,22]

Overall, the literature shows clear disparities in diagnosis and treatment across a number of measures and aspects. Aboriginal people were less likely to receive delayed or incomplete treatment, had lower admission rates and an overall later diagnosis of lung cancer. Aboriginal people were also less likely to use private medical services, to be recommended for curative treatment and to take up treatment interstate. Furthermore, there is generally low participation in cancer screening programs by Aboriginal people.[14,23,24,25]

In international studies, cancer patient navigation programs have been shown to increase access to and utilisation of cancer care for poor and underserved individuals. Navigators work with patients on a range of tasks across the cancer care continuum (education and outreach, screening, diagnosis and staging, treatment, survivorship, and end-of-life). This approach focuses on making cancer services understandable, available, accessible, affordable, appropriate, and accountable.[26,27,28] These individuals are commonly community health workers.[14]

Rural and remote populations

Rural and remote living has a well-documented negative correlation to access and outcomes for patients diagnosed with lung cancer[29,15] with lung cancer being said to be the fifth highest burden of disease.[30] Therefore it is important to consider these factors in screening and early identification.[31]

Lung cancer is the third highest avoidable mortality, with rates found to be higher in rural versus metropolitan areas, and highest in remote Local Government Areas. Pre-diagnosis barriers include: knowledge of risk; health seeking behaviours; and high rates of comorbidities.[11] Recommendations for improved rural/remote access and health knowledge include: increased dissemination of cancer prevention knowledge and practices to improve patient knowledge of risk; encouragement of positive health seeking behaviours; and decreasing delays in seeking the advice of a health professional.[11] A recent study has shown that although lung cancer screening tests are not currently recommended for asymptomatic patients, primary care physicians order these including chest X-rays, CTs and sputum cytology.[32]

Post-diagnosis barriers include: distance to 'local' GP[11,33,34,35-37]; limitations to treatment options due to late stage diagnosis and/or comorbidity[35-37]; socio-economic status (SES) and/or private health insurance status[30]; distance to care[38]; longer waiting times[39]; poor coordination of follow-up processes with specialists[11,40,38] impacting patient treatment intensity and compliance[41]; shortages of healthcare providers available rurally[33,34]; currency of treatments and facilities[41,42]; and limited access to psychological/bereavement services.[43]

With only 18.4, 13.4, 4.7 outer-regional, remote, and very remote allied professionals, respectively, per 10,000 capita[44], increased numbers of rural/remote health professionals is recognised as necessary to improve services to lung cancer rural/remote patients; the availability of a MDT is suggested to be most beneficial for improved patient outcomes.[38] Another suggested technique aimed at overcoming distance, socioeconomic differentials, health professional shortages, and (to some extent) late diagnosis barriers is telemedicine.[45] In Japan a mobile unit consisting of a van with a spiral CT machine and various telecommunications equipment has undertaken mass screenings of 19,117 individuals. This screening resulted in the identification of 75 cases of early lung cancers.[46]

Culturally and linguistically diverse groups

The 'healthy immigrant effect' often results in lower incidence of cancer in migrant groups. Yet in lung cancer there appears to be a reverse trend. From 2003 to 2007, the highest age-standardised incidence rates of lung cancer in men were for those born in North-Western Europe (69 per 100,000) and the United Kingdom and Ireland (67 per 100,000). These rates were significantly higher than that for Australian-born men (58 per 100,000). Men born in Southern and Central Asia had a relatively low lung cancer incidence rate (31 per 100,000), as did males born in Sub-Saharan Africa (35 per 100,000); these rates were significantly lower than the rate for Australian-born males. These data may reflect smoking behaviours in these groups underscoring a cultural and gender lens in appraising risk factors and health seeking behaviours.[15,21]

Women living in Australia, who were born in the United Kingdom and Ireland (41 per 100,000) and in New Zealand (37 per 100,000), had higher age-standardised incidence rates of lung cancer than women born in Australia (29 per 100,000). The lowest age-standardised rate was for females who were born in Southern and Central Asia (17 per 100,000) and this rate was significantly lower than that for females born in Australia.[15,21]

The cultural diversity and pluralism of Australian society underscores the importance of introducing culturally competent programs for health promotion and health screening.[47,48]

Low socioeconomic status

Between 2003 and 2007, mortality rates were higher for Aboriginal and Torres Strait Islander people, people living in remote areas and those living in the lowest socioeconomic status areas. The rate of death for men in the lowest socioeconomic status areas in Australia was 1.5 times the rate for men living in the highest socioeconomic status areas. The differential between the lowest and the highest socioeconomic status areas was lower for women. The increased incidence of lung cancer can be explained by differences in smoking as well as health seeking behaviours and access to health care services. Many of these are associated with socioeconomic factors. These factors are to be considered in developing appropriate screening strategies, particularly given costs associated with CT scanning and PET scans for early diagnosis.[11]

Challenges in the early assessment, diagnosis and management of lung cancer include:

- An absence of a cost-effective, valid and reliable screening test for lung cancer with demonstrated efficacy and effectiveness in the Australian health care system.[49-51] Although low-dose helical CT screening is proposed there is no definitive population based modelling but a study is underway in Queensland[52]
- The strong association of smoking with lung cancer and associated stigma, shame and potentially prejudicial treatment[49,53]
- Late presentation with signs of lung cancer, a high symptom burden and the need to increase community awareness[54,55]
- The strong association of comorbid conditions with lung cancer, particularly chronic obstructive pulmonary disease and coronary heart disease, requiring coordination between service providers and increasing individual risk.[56,57] This may influence the initial diagnosis and also influence health care outcomes
- A view of therapeutic nihilism among some clinicians - that is, that treatment is futile[58,53]
- Perceptions of fatalism among patients[59]
- The low prevalence of lung cancer in general practice (relative to practice volume) may limit knowledge of local services and referral pathways[32,60]
- Limited access to or awareness of MDTs, specialist services and low levels of evidence to drive health service models[11,40,61]
- Lack of integration and coordination across data management systems[11]
- Delays in coordinating assessment, diagnosis, staging and treatment leading to delays in treatment.[12,13] Lack of coordination of treatment across public and private sectors[11]
- Lower public awareness of treatment of lung cancer compared with other tumour groups and the potential of 'survivorship'[62,63]
- Multiple professional groups required for ensuring optimal outcomes for lung cancer (e.g. general practice, surgery, respiratory medicine, medical oncology, radiation oncology, and radiology) require coordination and communication[64,65]
- The cultural diversity of Australia and high rates of smoking in some population groups means targeted culturally sensitive health information and prognostic information is likely to be required. [48,66-68] Age, socioeconomic considerations such as income and transportation barriers contribute to lower guideline adherence[65,11,40]
- Individuals with breast cancer are more likely to receive treatment than those with colon, rectal or lung cancer suggesting sociocultural factors influencing care patterns[69]
- The poor prognosis of lung cancer emphasises the need for integrated and supportive care strategies.[70,71]

Internationally, in addition to advances in biomedical treatment, many of the improvements in lung cancer care have resulted from increasing awareness, developing clinical guidelines and implementation strategies and the fostering of clinical leadership, networks and resources. Issues in coordination and communication relating to clinical care in Australia are not unique to lung cancer and are being addressed in national health reform initiatives.[72 73]

With the exception of isolated research studies[74], there is no consistent information on percentage of Australian patients with histologically confirmed lung cancer that were offered or

received active treatment. Incorporating such an approach into existing data management systems may leverage benefits and inform strategies for screening and early diagnosis.[75,76]

4 Screening Strategies

Approaches

Determining individuals at high risk

Identifying individuals at risk of lung cancer is important for screening and timely diagnosis and is critical for health service planning, delivery and monitoring of health outcomes. Existing models have only modest capabilities to classify persons at risk. Prospective data from 70,962 control subjects in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) were used in two models: general population (model 1) and for a sub cohort of ever-smokers (N = 38,254) (model 2). [77] Both models included age, socioeconomic status (education), body mass index, family history of lung cancer, chronic obstructive pulmonary disease, recent chest x-ray, smoking status (never, former, or current), pack-years smoked, and smoking duration.

The PLCO lung cancer risk models demonstrated discrimination and calibration. During follow-up (median 9.2 years) of the control arm subjects, 1040 lung cancers occurred. During follow-up of the external validation sample (median 3.0 years), 213 lung cancers occurred. In the external validation sample, models 1 and 2 had area under the curves of 0.841 and 0.784, respectively. These models had high discrimination in women, men, whites, and non-whites.[77] Moreover, SES data in NSW identifies areas for target and focus in developing programs.[31] These foci could consider SES status, environmental exposure, rurality, ethnicity and Indigenous status and should be considered in risk assessment models that extend beyond biomedical characteristics alone.

Lung cancer screening tests

A review[78] of screening in lung cancer provided ten criteria for an effective screening model, principles of a screening test, and findings from studies evaluating specific procedures. At that time, the authors concluded there was insufficient evidence to differentiate between the efficacy of common procedures, namely low-dose helical computed tomography (CT), sputum cytology and chest radiography. Recent data has challenged this evidence base.

The Early Lung Cancer Action Project (ELCAP) identified that low-dose helical CT can identify nodules as small as 2-3mm, potentially three times as many small lung nodules as a standard chest radiograph.[79] This study was not designed to assess whether screening via CT reduced overall mortality. ELCAP data also contain inconsistencies that need to be addressed if they are to inform guidelines.[80,81]

More recently, a National Cancer Institute (NCI)-sponsored RCT National Lung Cancer Screening Trial (NLST) was halted after low-dose helical CT was found to reduce lung cancer mortality by 20% and all-cause mortality by 7% when 3 annual low-dose helical CT scans were performed in heavy (≥ 30 pack-years) current or former (within 15 years) smokers between 55 and 75 years of age.[4] On average over the three rounds of screening exams, 24.2% of the low-dose helical CT screens were positive and 6.9% of the chest X-rays were positive. False positives were similar across arms: 96.4% of low-dose helical CT tests and 94.5% of the chest X-ray exams. In both arms of the trial, the majority of positive screens led to additional tests. Adverse events from the actual screening examinations were few and relatively minor.[4]

Additional studies based on the complete NLST data set are ongoing and will include reports on cost-effectiveness of low-dose helical CT as well as the ability to use the data to develop models that may help indicate whether other groups of smokers, such as light smokers or younger smokers, would benefit from screening with low-dose helical CT. Other modelling studies are

expected to examine the optimal frequency and duration of screening. A recent actuarial analysis using NLST data has shown a potential commercial insurance benefit in the high-risk US population ages 50–64 years. Assuming current commercial reimbursement rates for treatment, these investigators suggest that screening would cost about $1 per insured member per month in 2012 dollars. The cost per life-year saved would be below $19,000, an amount that compares favourably with screening for cervical, breast, and colorectal cancers.[82] This would require a model considering dimensions such as in Figure 2 below.

The NLST has informed advice on setting up a lung cancer screening program published in 2012 in the Journal of the National Comprehensive Cancer Network (NCCN), which recommends that screening focus on individuals identified as high risk using the NLST criteria (see Table 3).[83] The guideline notes that important differences exist between current cancer screening strategies and those for lung cancer screening. First, the rate of false-positives for lung cancer screening is higher than for breast, colon, or prostate cancer screening, leading to further testing in a high percentage of patients to determine the likelihood of cancer. Nearly 25% of all CT scans in NLST showed false-positive results, meaning that on follow-up 1 in 4 observed abnormalities turned out not to be cancer. In addition to suffering unnecessary anxiety, these patients underwent some kind of additional diagnostic procedure. Second, because screening for lung cancer should be offered to high-risk individuals and not to the general population, this places considerable emphasis on identifying individuals at high risk for lung cancer according to NLST criteria. Flow diagrams from the NCCN guideline are available free of charge at NCCN.org.

Table 3: Eligibility Criteria for the National Lung Screening Trial

Age	55–74 years, with no signs of symptoms of lung cancer
Smoking history	Active or former smoker with a 30 pack-year history (A pack-year is the equivalent of 1 pack of cigarettes per day per year. One pack per day for 30 years or two packs per day for 15 years would both be 30 pack-years)
Active smoker	If active smoker, should also be vigorously urged to enter a smoking cessation program
Former smoker	If former smoker, must have quit within 15 years
General health exclusions	Metallic implants or devices in the chest or back Requirement for home oxygen supplementation Prior history of lung cancer or other lung cancer symptoms

Developments since the NLST have highlighted several new testing techniques, including measurement of volatile organic compounds in exhaled breath, an airway epithelial gene expression biomarker, and serum sampling for antibodies to tumour-associated antigens, that are currently being evaluated and may prove useful as part of a screening algorithm for lung cancer.[84]

The PLCO Cancer Screening Trial is an ongoing randomised controlled trial that involves 154,901 participants aged 55 through 74 years. Of these, 77,445 were assigned to annual screenings and 77,456 to usual care at one of ten screening centres across the United States between November 1993 and July 2001. Lung cancer screening in the intervention group involved annual posteroanterior view chest radiograph for 4 years. Diagnostic follow-up of positive screening results was determined by participants and their health care practitioners. Participants in the usual care group were offered no interventions and received their usual medical care. Annual questionnaires are mailed to participants requesting information on dietary issues and health care utilisation. All diagnosed cancers, deaths, and causes of death were ascertained through the earlier of 13 years of follow-up or until December 31, 2009.[85,86]

Screening adherence was 86.6% at baseline and 79% to 84% at years 1 through 3; the rate of screening use in the usual care group was 11%. Cumulative lung cancer incidence rates through 13 years of follow-up were 20.1 per 10,000 person-years in the intervention group and 19.2 per 10,000 person-years in the usual care group (rate ratio [RR], 1.05; 95% CI, 0.98–1.12). A total of 1,213 lung cancer deaths were observed in the intervention group compared with 1,230 in usual care group through 13 years (mortality RR, 0.99; 95% CI, 0.87–1.22). Stage and histology were similar between the two groups. The RR of mortality for the subset of participants eligible for the NLST, over the same 6-year follow-up period, was 0.94 (95% CI, 0.81–1.10).[87]

The conclusion was that annual screening with chest radiograph did not reduce lung cancer mortality compared with usual care. Mortality from lung cancer was the primary outcome. Secondary outcomes included lung cancer incidence, complications associated with diagnostic procedures, and all-cause mortality.[87] A summary of other findings to date is presented in Table 5. However, it is important to emphasise that a conclusion on the effectiveness of screening must await final PLCO results, which are anticipated at the end of 2015. These recommendations will then need to be applied to a population screening model as described in Figure 3. A summary of lung cancer screening tests is provided in Appendix 4**.**

Table 4. Summary of published PLCO findings to date

Outcome	Finding
Risk factors for lung cancer	A predictive model that included age, socioeconomic status (education), body mass index, family history of lung cancer, chronic obstructive pulmonary disease, recent chest x-ray, smoking status (never, former, or current), pack-years smoked, and smoking duration demonstrated high discrimination and calibration in the general population[77] No effect was found for consumption of meat, meat cooking preferences, meat mutagens or heme iron[88]
Proportion of lung cancers detected at early stage	A higher proportion of chest radiograph screen-detected lung cancers were early stage compared with control[87,89,90]

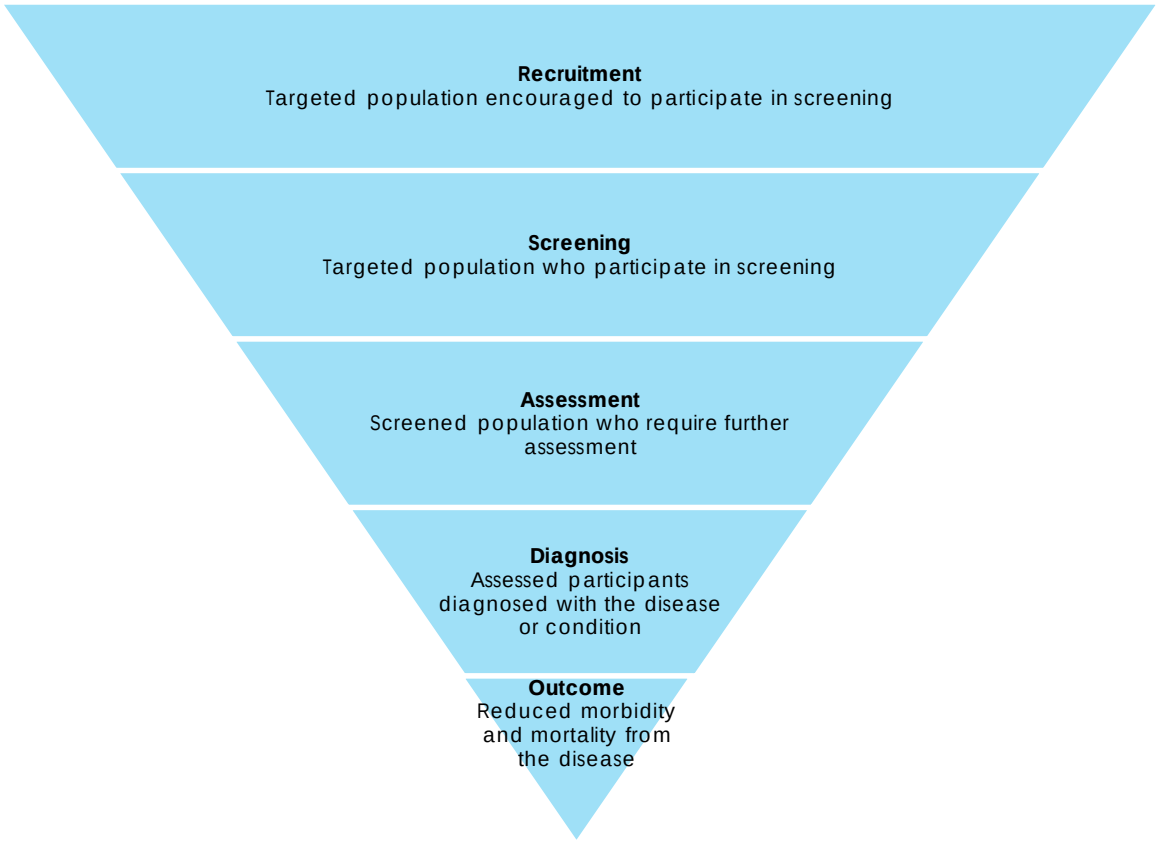

Figure 2: Defined target population

SOURCE: Population Based Screening Framework
ISBN: 1-74186-778-9; Online ISBN: 1-74186-779-7 p3.

5 Specific review questions

Question One

Which models that have been designed to facilitate the early assessment and diagnosis of cancer have been evaluated?

The majority of delays in care are related to patient factors. Increasing evidence has demonstrated that the establishment of multidisciplinary teams (MDTs) has streamlined care for many tumour groups and allowed individual teams to discuss cancer patients' management within a wider body of technical and clinical expertise. The nomenclature for this approach varies and in some instances these have been named as Rapid Outpatient Diagnostic Clinics.[91] In the United Kingdom (UK), the Cancer Network's quality assurance team assesses the MDTs to ensure that standards are maintained.[92] Though MDTs are likely to improve quality and consistency of care for patients with lung cancer, the effects on overall survival rates and costs are less certain. The majority of patients have advanced incurable disease at presentation, underscoring a need for an integrated approach to care for high risk individuals. A systematic review has summarised available evidence (Appendix 5 and existing guidelines in Appendix 6).[93]

In spite of recommendations regarding best practices and the increased emphasis on lung cancer care, variations in care patterns are evident from diagnosis to treatment.[11] A New Zealand study undertaking a retrospective review of the clinical records of 80 patients referred to a secondary care respiratory service and diagnosed with primary lung cancer in 2004. Eighty-five percent of inpatient referrals and 48.5% of outpatient referrals were for advanced stage lung cancers. The median interval from receipt of outpatient referral to first chest physician assessment was 18 days, with median interval from the first chest physician assessment to bronchoscopy of 17 days and for staging CT chest of 16 days. For patients requiring a CT-guided percutaneous needle aspiration for diagnosis, there was a further median delay of 37 days after the initial CT scan. The median interval from the date of receipt of initial outpatient referral to diagnosis was 38 days, but for early stage lung cancers it was 54 days. The median interval to diagnosis for inpatient admissions was 6 days after the first respiratory assessment. These time windows are likely not to be unusual based upon a Cancer Australia review and are an issue of key concern. These management delays are like to be compounded where individuals are required to travel to specialty centres.[94]

As in many clinical conditions, operator volume and access to expertise is associated with improved health outcomes. Ensuring expertise and access to dedicated positron emission tomography (PET) and gamma-camera PET.

Most guidelines support an MDT model for early assessment and diagnosis of lung cancer as follows:

- MDTs are commonly situated in academic medical centres in urban settings[11,40,95]
- MDTs have been found to increase patient access to best evidence based practice, thus improving patient management and survival rates in select populations.[96] MDT also provides for improved access to timely treatment in patient care and greater exposure to clinical trials.[97] Furthermore, MDTs promote team support and peer education.[96] The inclusion of most appropriate and best available specialists allows for improved staging[98] and disease management [99]
- MDTs, when organised effectively, can streamline processes, minimise duplicate investigations enable individual provider burdens to be decreased with potential for improvements to cost effectiveness[100]

- Decision-making within the MDT and between professional and discipline groups requires further investigation, as when investigated in the UK, team discussion wasn't found to impact accuracy of individual clinician's prognostic predictions.[101] The initial patient journey has been shown to be improved by the involvement of MDTs in a Scottish study.[102] The use of a 'results clinic' was also found to be useful. Where patients received their results 1–2 weeks after first being seen by a respiratory consultant. This allowed for a preliminary management plan to be developed and discussion of either further investigations or treatment options available. It was found that concern reflected by the MDT specialists often encouraged patients to agree to the further testing required. In this study –8 MDT meetings evaluated over a 2 month period, 60 patients with lung cancer were discussed. Twenty three (38.5%) of these had a histological diagnosis, with 19 non-small cell lung cancer and 4 small cell lung cancer. Thirty seven (61.5%) were clinically/radiologically suspected of having lung cancer at the time of their first discussion and many underwent further investigation to obtain a histological diagnosis. In this clinic recommendations for further investigations to arrive at a histological diagnosis, 2 were referred for mediastinoscopy and 3 were referred for Video Assisted Thoracoscopic Surgery (VATS). One was referred directly for Positron Emission Tomography scanning (PET). Twenty eight patients (46.7%) were referred for one or more forms of anti-cancer treatment (surgery, chemotherapy and/or radiotherapy). Eight patients (13.3%) were referred for chemotherapy. Radiotherapy was recommended for 15 patients (25%) which included 12 palliative cases, 2 high dose palliative cases and one emergency treatment. Two patients were referred for lung resection (lobectomy) and 3 for VATS biopsy and pleurodesis. Five patients were referred for palliative care (active symptom control) only[102]
- Risks include gaps in MDT formation and lack of care coordination, all affecting the patients' quality of care.[103] These risks highlight the need for further investigation specific to Australian delivery of lung cancer care at a national and state level, and the development of guidelines on the patient journey and required inclusions in an MDT
- Composition (number and type of health professionals) and governance (monitoring of outcomes) of MDTs need to be monitored and subject to clinical governance.[95,104]

Health system organisation

Inferior treatment[33,34,39] as a consequence of limited access to services suggests rural locations would benefit most from the availability of a MDT.[44] Telemedicine and telehealth overcome rural/remote disadvantage where facilities to access this service would be available.[105,106] Rural patients may benefit from their primary carer becoming their palliative care giver, in relation to continuity of care and rural cultural awareness.[11] Recently introduced remuneration strategies through the MBS show promise but would likely need to be integrated in models of care with exemplars, pragmatic considerations and medico-legal and privacy issues.[107] Examples include the Practice Incentives Program (PIP) aimed at supporting general practice activities that encourage continuing improvements, quality care, enhance capacity, and improve access and health outcomes for patients and the Practice Nurse Incentive Program (PNIP) commenced on 1 January 2012 and provides incentive payments to practices to support an expanded and enhanced role for nurses working in general practice.[108] Using these fund approaches to screening, monitoring and recall for individuals of high risk of lung cancer show promise.

Living beyond urban settings and in rural and remote areas is well documented in the literature as being detrimental to the access and outcomes of patients diagnosed with lung cancer. The awareness of risk has been identified as lower in rural/remote areas, with recommendations to improve dissemination of cancer prevention knowledge and practices. Delays in seeking the advice of a health professional are exacerbated by symptoms being easily attributed to other non-serious issues, particularly in the case of lung cancer where symptoms are difficult to associate only to this disease. In high risk groups, access to health care services can be an issue.[11,14,40]

Patient characteristics and funding

Currently, risk assessment models for lung cancer focus on smoking and other physiological risk factors. Considering other dimensions, such as rurality, socioeconomic status and ethnicity require consideration in developing models of risk.[11] The costs of private diagnostic services are likely a high barrier to individuals, even those with symptoms suggestive of lung cancer.[17] Moreover, professional issues and gate keeping behaviours may alter the capacity of individuals to reach appropriate settings for diagnosis and treatment.[17]

Question Two

What is the evidence for the effectiveness of rapid access assessment and diagnosis service models for cancer in improving patient outcomes?

There is limited high level evidence for rapid access and diagnosis service models as few of these have been subject to the scrutiny of randomised controlled trials. Often these have developed organically to meet local needs. However, integral to most of these models are: (1) Refined referral processes; (2) Timely access to diagnostic services and treatment; (3) Access to clinical expertise; and (4) Improved coordination through a complex and challenging health care system.[17,109,110] Many of the studies to date use before and after models for evaluation. These studies are summarised in Appendix 5 and are commonly embraced under the term of MDTs.

Key patient outcomes include: number of people diagnosed with early stage disease; number of people with early stage disease who receive curative surgery and/or treatment wait times; five year (and longer) survival rates; and quality of life. The composition of MDTs varies across studies but most commonly includes thoracic surgery, medical oncology, respiratory physicians, radiotherapy nursing and allied health.

Question Three

What is the evidence for the effectiveness of rapid access assessment and diagnosis service models for cancer in improving outcomes from the provider and system perspective?

The complexity of cancer management requires a range of expertise from a range of medical, technical, nursing and allied health teams. This expertise can range from diagnosis,[111] curative treatment and symptomatic care.[112] Multidisciplinary team meetings are also known as tumour boards, multidisciplinary cancer conferences, multidisciplinary case reviews, or multidisciplinary clinics, in different health care systems and generally comprise these rapid access models.[112,113-115,116] In a retrospective, comparative, non-randomised, interventional cohort study of 14,358 patients diagnosed with symptomatic invasive breast cancer between 1990 and 2000, residing in health board areas in the west of Scotland there was an improvement in survival.[117] Similarly improved outcomes have been demonstrated in colorectal cancer[118] and head and neck cancer patients.[119]

The rapid assessment dimension has been classified as the 'front end' of the MDT.[120] Core characteristics of rapid assessment and diagnosis service models have the following characteristics:

- A range of surgeons, pathologists, oncologists, radiologists, and specialist nurses specific to the tumour group

- Access to specialised and appropriate diagnostic tests and expertise in interpretation
- Adherence to evidence based guidelines
- Meet regularly and formally to discuss results and agree on adjuvant treatment for individual patients
- Undertake audited clinical activity and reported results at regular intervals
- Facilitate referral and transition through the health care system
- A range of studies have identified the needs of patients with advanced cancer and compared with other groups there has been less attention compared with those in the curative phase.[121,122,123] A study from Krishnasamy demonstrated that patients have needs for: (1) The pathway to confirmation of diagnosis (2) Communication of diagnosis, treatment options and prognosis (3) Provision of coordinated, family-oriented care (4) Support away from acute services.[124] MDTs that are configured to support shared decision making and provide psychosocial support can assist in meeting these needs. However, achieving the benefits of MDTs is dependent on access and variability in quality has been documented
- Although many clinical guidelines for lung cancer recommend access to a MDT to facilitate timely and appropriate diagnosis and treatment.[100,51,125] A systematic review by Coory and colleagues shows limited evidence linking lung cancer MDTs with improved survival. There was heterogeneity in the trials limiting meta-analysis.[126] In spite of this a recent review undertaken by Cancer Australia recognised that key opinion leaders provided such an approach and were able to illustrate examples of improved access.[17] Systems and processes that improve efficiencies across care settings, such as clinical pathways demonstrate some potential.[127] From the perspective of the provider, MDTs increase capacity to debate and discuss diagnostic and therapeutic approaches as well as increasing efficiencies
- To date there is sparse data on cost-effectiveness of MDTs, largely due to the absence of randomised controlled clinical trials.[127] In respect of identifying barriers and enablers, data from a Cancer Australia report has identified lack of remuneration, private- public sector considerations as a barrier
- Although isolated studies investigating lung cancer care have been undertaken in Australia these are predominately in academic medical centres and have not undertaken a population based approach and largely focused on those with symptoms. Table 5 provides a summary of the barriers and enablers to early diagnosis, assessment and management.

Table 5: Barriers and enablers of the successful models include:

	Barriers[128,101,115,129,80,130–133]	**Enablers**[112,113,128,26,115,116,134–140]
Provider and health care system	• Distance of patient from referral centre • Delays in diagnostic testing • Cost of diagnostic tests • Limited access for PET and EBUS • Therapeutic nihilism • Cultural barriers to care • Ambiguity in medico legal liability • Access to cardiothoracic expertise • Variation in determining prognosis • Physician's inability to provide a service (e.g. chemotherapy) • Physician referral patterns	• Integrated clinical networks and referral mechanisms • Proficient laboratory staff for pathology services and tumour typing • Access to thoracic surgery • Access to clinical expertise and volume performance • Evidence based guidelines • Access to specialised diagnostic and staging procedures e.g. PET scanning EBUS • Access to social services and psychosocial support • Access to support to manage complex comorbidities • Facilitation of shared decision making • Teamwork • The use of a "navigator" in Indigenous and marginalised groups

	Barriers[128,101,115,129,80,130–133]	Enablers[112,113,128,26,115,116,134–140]
		• Patient centred approaches • Comprehensive physical, social and psychological assessment

Invariably increased recognition of need in one sector of the health care system (e.g. screening in high risk patients) is going to lead to an increased demand in another (access to PET scanning). This is why the National Bowel Screening Program is being rolled out slowly, to allow for the adaptation of services, such as colonoscopy to accommodate increased demand.
In the United Kingdom, The National Lung Cancer Audit (LUCADA) was developed to improve the quality and outcomes of services for patients with lung cancer in response to lower outcomes compared with other Western countries. After five years the audit is capturing approximately 100% of the expected number of incident cases across hospitals in England, Wales, Scotland, Northern Ireland and Jersey. Measures of process and outcome have improved over the audit period. These measures include the histological confirmation rate (64–76%), the proportion of patients discussed in a multidisciplinary team meeting (78–94%), and the proportion of patients having anti-cancer treatment (43-–9%), surgical resection (9–14%) and small cell lung cancer chemotherapy (58–66%). Variations between hospitals which cannot be accounted for by differences in case mix have been identified by this review.[54,141] Issues in access, physician and patient characteristics, likely contribute to these variations.[40,17]

Question Four

What is the evidence for the efficacy of screening for lung cancer in high risk populations?

Although screening trials for lung cancer have been identified, these have been minimally extrapolated from clinical trials to usual care. Currently, most screening is opportunistic and not linked to standardised registries and monitoring. Ambiguity and uncertainty regarding the value of screening for lung cancer has resulted in conflicting recommendations and confusion in populations at risk. 'High risk populations' would include both individuals at increased risk e.g. smokers as well as Indigenous and ethnic groups with a higher incidence of lung cancer.

The National Cancer Institute (NCI)-sponsored RCT National Lung Cancer Screening Trial (NLST) was halted after low-dose helical CT was found to reduce lung cancer mortality by 20% and all-cause mortality by 7% when three annual low-dose helical CT scans were performed in heavy (≥ 30 pack-years) current or former (within 15 years) smokers between 55 and 75 years of age.[4] A 20% decrease in the relative risk of dying of lung cancer translated to an approximately 0.4% reduction in lung cancer mortality (from 1.7 % in the chest x-ray group to 1.3 % in the CT scan group) after about 6.5 years of follow-up. This translates to a 0.3 to 0.4% absolute reduction in deaths at about 6.5 years.

A recent commentary of the NCI in the US describe a '*cautious pace of adoption'* of lung cancer recommendations in spite of the landmark findings of the NLST trial.[1]

Although low-dose helical CT shows promise, cost effectiveness has not been determined. Evaluation within the context of the Australian health care system is warranted. There is currently a study in Queensland underway to address this issue.[52] The Veterans Health Administration's (VHA) National Center for Health Promotion and Disease Prevention in the US is planning to conduct a lung cancer screening pilot program, based on the NLST findings, at six to eight VHA medical centres starting early next year. This trial is to assess pragmatic issues in recommendations of the NLST Trial.[1] Consideration of the implications of false positives, iatrogenesis and ongoing monitoring will be important considerations in recommending screening recommendations.

The study of cancer epigenetics in the last decade has radically altered our views in cancer pathogenesis, providing new insights in biomarker development for risk assessment, early detection and therapeutic stratification. DNA methylation and miRNAs have rapidly emerged as potential biomarkers in body fluids showing promise to assist the clinical management of lung cancer. For example, methylation of certain genes has been detected in samples from the upper aerodigestive tract epithelium of cancer-free heavy smokers. Such techniques show promise but require further investigation.[142,143]

Targeting high risk populations will require collaboration with Local Health Districts, the Aboriginal Community Controlled Sector Organisations and Medicare Locals.[11,14,83] Based on this review, an adaptation to include sociodemographic characteristics as well as biomedical risks in risk assessment tools will ensure targeting appropriate populations. Access to reimbursement for LDCT technology and monitoring of quality is important to consider in the development of future models. Arenberg and Kazerooni (2012) in a recent article caution that although the recent recommendations of LDCT technology are exciting, they are an important first step and should be considered within the broader concept of society and the health care system.[83] The controversy surrounding screening for prostate cancer is an important lesson in pausing and planning and considering benefits, risks as well as unintended consequences.[144,145]

6 Conclusion

This review has summarised what is known about the best practices of cancer screening and early diagnosis and provides summarises issues in considering lung cancer screening services on a population (high risk groups) and those with a high index of suspicion (opportunistic). Based on available data it is important to reserve screening to patients at highest risk. In parallel, there needs to be MDTs capable of managing the high number of false-positive findings. In addition there is the need for further research of biomarkers and risk models for lung cancer to increase the sensitivity and specificity of screening models. Perhaps more importantly there is a need to understand the cost-effectiveness of lung cancer screening on a societal level and the impact of expected and unintended consequences of potential screening models.

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APPENDICES

Appendix 1. Search terms

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND early[All Fields] AND ("Assessment"[Journal] OR "assessment"[All Fields])

906 reviewed – 52 included

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND rapid[All Fields] AND ("Assessment"[Journal] OR "assessment"[All Fields])

102 abstracts review – 2 included

(("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields])
(("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("interdisciplinary studies"[MeSH Terms] OR ("interdisciplinary"[All Fields] AND "studies"[All Fields]) OR "interdisciplinary studies"[All Fields] OR "multidisciplinary"[All Fields]) AND team[All Fields]) AND ("2002/10/18"[PDat] : "2012/10/14"[PDat])

132: 46 reviewed – 6 included

RCTs- 6 results- one SR (including one RCT), otherwise trial protocols (Coory et al – key article)
("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "diagnosis"[MeSH Terms]) AND ("2002/10/18"[PDat] : "2012/10/14"[PDat] AND "humans"[MeSH Terms] AND Randomized Controlled Trial[ptyp])57642

1297 titles reviewed – 26 relevant to scope of review

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "diagnosis"[MeSH Terms]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("2002/10/18"[PDat] : "2012/10/14"[PDat] AND "humans"[MeSH Terms] AND systematic[sb] AND English[lang])

862 titles reviewed relevant to the review – 73 items selected

General practice

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "diagnosis"[MeSH Terms]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("general practitioners"[MeSH Terms] OR ("general"[All Fields] AND "practitioners"[All Fields]) OR "general practitioners"[All Fields]) AND ("2002/10/18"[PDat] : "2012/10/14"[PDat] AND "humans"[MeSH Terms] AND English[lang])

30 titles reviewed – 17 retained

Lung cancer and Australia

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] AND "cancer"[All Fields]) OR "lung cancer"[All Fields]) AND ("australia"[MeSH Terms] OR "australia"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "diagnosis"[MeSH Terms]) AND ("2002/10/18"[PDat] : "2012/10/14"[PDat] AND "humans"[MeSH Terms] AND English[lang])

633 titles reviewed – 43 retained

Lung Cancer and Indigenous

("lung neoplasms"[MeSH Terms] OR ("lung"[All Fields] AND "neoplasms"[All Fields]) OR "lung neoplasms"[All Fields] OR ("lung"[All Fields] ("lung neoplasms"[MeSH Terms] OR #"lung"[All Fields] AND "neoplasms"[All Fields]# OR "lung neoplasms"[All Fields] OR #"lung"[All Fields] AND "cancer"[All Fields]# OR "lung cancer"[All Fields]) AND #Aboriginal[All Fields] AND Australians[All Fields]#

3 titles identified

Appendix 2. Summary of screening programs

Tumour Group	Guideline	Health professional driven	Targeted population	Cost to consumer	Cost effectiveness studies	Screening tool/ Gold standard	Mortality benefit from population screening
Breast	✓	✓	✓	x	✓	Mammography	✓
Bowel	✓	✓	✓	x	✓	Faecal occult screening	✓
Ovarian	✓	✓	X	✓	Pending	Ca125 & TVA	X
Lung	✓	✓	X	X	Pending	LSCT	?
Prostate	✓	✓	X	✓	?	PSA, DRE	X
Cervical	✓	✓		✓	✓	Pap smear	✓
Skin Melanoma	✓	✓		✓	?	Examination Biopsy	X

PSA= prostate-specific antigen; DRE=digital rectal exam; LSCT= low-dose helical CT screening

Population screening is where a test is offered to all individuals in a target group, usually defined by age, as part of an organised program. The Screening Subcommittee of the Australian Population Health Development Principal Committee (APHDPC) has developed *a* Population Based Screening Framework (PBSF) to provide guidance to decision makers when assessing potential screening programs in Australia. This framework adheres to the World Health Organisation recommendations. There are three national population-based screening programs in Australia: BreastScreen Australia, the National Cervical Screening Program, and the National Bowel Cancer Screening Program. These are briefly summarised below. The PBSF recommends:

> *The screening program will provide more benefit than harm to the people being screened.*
>
> *The condition should:*
> - *Be an important health problem*
> - *Have a recognisable latent or early symptomatic stage.*
>
> *The test should:*
> - *Be able to find the early stages of the disease (be highly sensitive)*
> - *Be very accurate in finding the early stages of disease (be highly specific)*
> - *Be able to provide consistent results from the test (be validated)*
> - *Be safe*
> - *Find most disease present at the time of the screening test (have a relatively high positive predictive value)*

- *Be normal when there is no disease present (have a relatively high negative predictive value*

- *Be acceptable to the target population including important subgroups such as target participants who are from culturally and linguistically diverse backgrounds, Aboriginal and Torres Strait Islander people, people from disadvantaged groups, and people with a disability.*

Systems should be in place for evidence based follow-up assessment of all people with a positive screening test regardless of rurality, ethnicity, socio-economic status or disadvantage status.

Treatment should be effective, available, easily accessible and acceptable to all patients with the recognised disease or condition.

Bowel cancer screening

Bowel cancer is one of the most common forms of cancer in Australia, and around 80 Australians die each week from this cancer. Bowel cancer can be treated successfully if detected in its early stages, but currently less than 40% of bowel cancers are detected early. Currently, the Australian Government runs the National Bowel Cancer Screening Program, by inviting around one million Australians each year (who are permanent residents have a Medicare or Gold Department of Veterans Affairs card) who are turning 50, 55 and 65 years of age between 1 January 2011 and 31 December 2014 to participate in the Program. The Program is being phased in gradually to help ensure that health services, such as colonoscopy and treatment services, are able to meet any increased demand. This is consistent with the introduction of other screening programs, such as the National Cervical Screening Program, which was also phased in over a number of years.

See National Bowel Screening Program
http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/bowel-about

Breast cancer screening

Mammographic screening can substantially reduce deaths from breast cancer.

In June 1990 the ministers responsible for health in all states and territories joined the Commonwealth in agreeing to jointly fund a national mammography screening program. The National Program for the Early Detection of Breast Cancer, now known as BreastScreen Australia, was established by the Commonwealth and the states and territories in 1991 and is now recognised as one of the most comprehensive population-based screening programs in the world. BreastScreen Australia is targeted specifically at well women without symptoms aged 50–69 years, although women aged 40–49 and 70 years and older are able to attend for screening.

At present, BreastScreen Australia operates in over 500 locations nationwide, via fixed, relocatable and mobile screening units. Screening has increased significantly since commencement of BreastScreen Australia in 1991, with a total of 1,641,316 women screened across Australia in 2007–2008. Of these women, 1,273,403 (78%) were in the screening program target age group of 50–69 years. The program's aim is to achieve a participation rate of 70% among women aged 50–69 years. At present the program is screening 54.9% of women in this age group.

"In the context of the national program, 'screening' refers to population-based screening, of apparently well women in the target age group, for breast cancer. Screening mammography is

carried out in an organised and systematic manner to detect unsuspected cancer at an early stage so that early treatment can reduce illness and death from breast cancer. This population based approach is distinctly different from the use of mammography to investigate symptoms in an individual woman, which is a diagnostic procedure. "
See Breast Screen Australia
http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/breastscreen-about

Cervical cancer screening

The National Cervical Screening Program is a joint program of the Australian and state and territory governments administered through Australian Health Ministers Advisory Council. In 1988, the Australian Health Ministers' Advisory Council established the Cervical Cancer Screening Evaluation Steering Committee to examine cervical screening. In light of their findings, the Committee recommended health authorities establish an organised approach to screening which would provide better protection against cervical cancer. In 1991, the Organised Approach to Preventing Cancer of the Cervix was established as a joint initiative of the Australian and state and territory governments. In 1995 it was renamed the National Cervical Screening Program. The National Cervical Screening Program aims to reduce morbidity and deaths from cervical cancer, in a cost-effective manner through an organised approach to cervical screening. The program encourages women in the target population to have regular Pap smears. The program promotes routine screening with Pap smears every two years for women between the ages of 18 (or two years after first sexual intercourse, whichever is later) and 69 years.

The program includes: implementation and monitoring of adherence to a nationally agreed screening policy; establishment of cervical screening registers in each state and territory; and development and enhancement of other quality management strategies across the screening pathway.

The cervical screening pathway involves the following steps:

- Encouraging all eligible women to enter and remain in the screening program
- Ensuring optimal quality of Pap smears by adequate training of Pap smear takers
- Ensuring optimal quality of Pap smear reading through a quality assurance program for laboratories
- Ensuring appropriate follow-up of abnormal Pap smears through management guidelines
- Providing an efficient system for notifying results to women by Pap smear providers
- Providing recall and reminder systems to ensure adequate follow-up of women with screen-detected abnormalities and
- Maintaining women's participation in the program by encouraging providers to set-up reminder systems, and developing cervical screening registers and national cancer data.

See National Cervical Screening Program
http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/cervical-about

Skin Cancer

Currently there are no population based screening approaches for skin cancer. The Screening Subcommittee of the Australian Population Health Development Principal Committee has endorsed the Cancer Council Australia's position statement on Screening and early detection of

skin cancer developed in consultation with the Australasian College of Dermatologists. This statement recommends that general practitioners:

- *Develop surveillance programs for patients at high risk*
- *Assess patients who are concerned and develop appropriate management programs depending on their level or risk and*
- *Who identify risk factors for skin cancer in patients presenting for other reasons to inform patients about sun protection measures and offer them an opportunity for a full body examination and an appropriate management plan (i.e. case finding with follow-up).*

Prostate Cancer

Almost 3,000 Australian men die from prostate cancer each year and the incidence and prevalence will increase as Australia's population ages. Early detection and management of prostate cancer is a complex issue. In addition, unlike cancers of the bowel, breast and cervix, there is in population-based screening for prostate cancer.

See recommendations for prostate screening
http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/449D837448F6BA03CA25752700062313/$File/joint%20prostate%20screening%20statement.pdf

Ovarian cancer

Ongoing ovarian cancer screening trials are investigating the efficacy of a two-step screening strategy using currently available blood and imaging tests [CA125 and transvaginal sonography (TVS).[146] To date there is no national screening program.

Appendix 3. Summary of lung cancer incidence in Australia (Australian Institute of Health and Welfare Report)

In 2007:

- 9,703 lung cancers (5,948 in males and 3,755 in females) were diagnosed
- Lung cancer was the fourth most commonly diagnosed cancer in both males and females (excluding basal and squamous cell carcinoma of the skin)
- The age-standardised incidence rate was 58 per 100,000 for males and 31 per 100,000 for females
- 84% of lung cancers in males and 80% in females occurred in the age range of 60 years and over
- The risk of being diagnosed with lung cancer by the age of 85 years was 1 in 12 for males and 1 in 23 for females.

Between 1982 and 2007:

- The incidence rate of lung cancer decreased by 32% in males (from 85 to 58 per 100,000) and increased by 72% in females (from 18 to 31 per 100,000).

In the 5 years from 2003 to 2007:

- The incidence rate of lung cancer was higher for Indigenous than for non-Indigenous people
- The incidence rate for males was highest in the Northern Territory (72 per 100,000) and lowest in the Australian Capital Territory (44 per 100,000), while the rate for females was highest in Tasmania (36 per 100,000) and lowest in the Australian Capital Territory (27 per 100,000)
- The incidence rate for males tended to increase with remoteness, while there was little variation in the rate for females by remoteness
- The incidence rate of decreased with improving socioeconomic status for both males and females.

Appendix 4. Summary of lung cancer incidence in Australia

The majority of costs for lung cancer management are related to hospitalisation. The funding for lung cancer comprised 5.8% of the expenditure for all cancers and 0.4% of expenditure for all diseases. In 2004–05, four-fifths (79%) of the health expenditure on lung cancer was for hospital admitted patient services ($131 million). Another 18% ($30 million) was spent on out-of-hospital medical services and 3% ($5 million) on prescription pharmaceuticals. The proportion of health care expenditure that consisted of hospital admitted patient services was higher for lung cancer compared with all cancers and all diseases—that is, it equalled 79% of health care expenditure on lung cancer compared with 70% for all cancers and 54% for all diseases. This may reflect symptom burden or a lack of access to community based services. In contrast, the proportion of health care expenditure on prescription pharmaceuticals was lower for lung cancer (3%) compared with all cancers (8%) and all diseases (18%).

Expenditure by health-care sector and disease, Australia, 2004–05

Health-care sector	Lung cancer		All cancers[a]		All diseases	
	$ (million)	Per cent	$ (million)	Per cent	$ (million)	Per cent
Hospital admitted patient services[b]	131	78.9	2,007	69.8	24,221	54.4
Out-of-hospital medical expenses	30	18.1	417	14.5	11,900	26.7
Prescription pharmaceuticals	5	3.0	231	8.0	8,144	18.3
Cancer screening	. .	. .	222	7.7	222	0.5
Total allocated expenditure[c]	**166**	**100.0**	**2,876**	**100.0**	**44,486**	**100.0**

(a) Includes cancers coded in the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10) as C00–C97. Does not include cancers coded as D45, D46, D47.1 and D47.3.

(b) Expenditure for hospital admitted patient services for lung cancer pertains to those hospitalisations for which the principal diagnosis was lung cancer (ICD-10 code of C33–C34). It does not pertain to hospitalisations for which lung cancer was an additional diagnosis, with the principal diagnosis related specifically to the type of cancer treatment or care received

(c) Values may not sum to the total due to rounding.

Source: AIHW Disease Expenditure Database.

Appendix 5. Summary of systematic reviews of lung cancer screening, assessment and early diagnosis

Review	Focus
Bach et al.[81]	To review the available data on the early detection of lung cancer, with a focus on three technologies: chest x-ray (CXR), sputum cytology, and low-dose CT (LDCT) scanning.
Betchel and Petty[147]	Types of screening procedures available for lung cancer, their cost, and the approaches and timing that are most beneficial to the public as a whole.
Bepler et al.[148]	A systematic review and lessons learned from early lung cancer detection trials using low-dose computed tomography (LDCT) of the chest.
Black et al.[149]	The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews.
Goulart et al.[4]	Lung cancer screening with low-dose computed tomography: costs, national expenditures, and cost-effectiveness.
Mulshine et al.[150]	Considerations in developing successful, population-based molecular screening and prevention of lung cancer.
Silvestri, Alberg & Ravenel[78]	The changing epidemiology of lung cancer with a focus on screening.
Arenberg & Kazerooni [83]	Best practices of lung cancer screening and provides suggestions for the proper structure for institutions considering offering lung cancer screening services.

Appendix 6. Summary of effects on outcomes of multidisciplinary teams (MDTs) for people with lung cancer

Summary of results for survival: comparative studies

Author(s)	Study design	Results	Adjustment for potential confounders
Murray et al. (2)	Randomised controlled trial	No statistically significant difference in 2-year survival between groups (p = 0.7), 33% of patients in the MD team group survived compared to 40% in the non-MD team group	Baseline comparisons of age, gender, type of lung cancer, performance status and stage were done, but numbers were too small to make an assessment of whether there were any imbalances, although none of the comparisons were statistically significant. No adjustment of these variables in analysis of outcomes
Price et al. (3) (abstract)	Before-and-after study	1-year survival increased from 18.3% to 23.5% after the introduction of MD teams and site specialisation (p = 0.049)	Gender and stage were considered. No formal adjustment for these variables, although there was no difference between study groups, according to the author
Martin-Ucar et al. (4)	Before-and-after study	1- and 5-year post-operative survival was similar before-(63% and 31%) and-after (62% and 32%) the establishment of MD meetings and the appointment of a specialist thoracic surgeon; median survival for stage I NSCLC was also similar in the two groups (46 months, 95% CI: 31—61 for pre-MD group and 46 months, 95% CI: 22—70 for post-MD group)	Not clear whether age was considered a confounder or an outcome; other outcomes were not adjusted for pre- and post-intervention age differences; stage was similar pre- and post-intervention, but was adjusted for in the survival analysis
Dillman and Chico (5)	Before-and-after study	After the opening of the affiliated facility and weekly multidisciplinary conferences there was an increase in: 5-year observed survival from 16% to 19% (p = 0.012); median observed survival from 11 months to 13 months; relative 5-year survival (overall): 4% (p = 0.032). None of the differences by stage were statistically significant (local: p = 0.66; regional: p = 0.45; distant: p = 0.51); historical and contemporary extramural comparisons (Hoag Hospital cohorts with SEER) showed a 6% and 9% increase, respectively in relative 5-year survival	Age, gender, race, stage were considered; significant differences by stage of disease; data for the other variables were not provided separately for lung cancer; no formal statistical adjustment for these variables in the observed survival analysis; statistical adjustment for age, gender and race in the relative survival analysis (extramural comparisons); relative 5-year survival analysis stratified by stage for historical intramural comparisons
Forrest et al. (6)	Before-and-after study	3.2 months improvement in median survival after the introduction of multidisciplinary team from 3.4 (2.4—4.1) to 6.6 (3.7—9.5) months, p < 0.001; on follow-up, 116/117 patients	Age, gender, deprivation index and stage were considered. No formal statistical adjustment for these variables, although there was no difference in age, gender

Author(s)	Study design	Results	Adjustment for potential confounders
		diagnosed in 1997 had died compared with 116/126 diagnosed in 2001 (p = 0.011)	and deprivation index between groups; there was a ''stage drift'' towards more advanced disease, so this could account for the improvement in survival

Summary of results for other reported outcomes: comparative studies

Author(s)	Study design	Results
Murray et al. (2)	Randomised controlled trial	Statistical significant difference in time from presentation to first treatment (p = 0.0025); 4 weeks difference: 3 weeks for MD group vs. 7 weeks non-MD group; no difference in time from diagnosis to radical treatment (p value not reported); percentage of patients receiving radical treatment: 43% MD group vs. 33% non-MD group (p > 0.05); percentage of patients receiving chemotherapy: 66% MD group vs. 37% non-MD group (p = 0.03); satisfaction with care: trend towards better satisfaction in the MD group for organisation of investigations (p = 0.07), personal experience of care (p = 0.09); number of visits to GPs: 164 MD group vs. 88 non-MD (p = 0.002); also significant for patients with positive diagnosis 95 vs. 66 (p = 0.02)
Price et al. (3) (abstract)	Before-and-after study	Statistical significant increase in radical radiotherapy from 3% to 12%, p = 0.004 following the introduction of MD teams and site specialization; fractionation of palliative thoracic radiotherapy to thorax decreased significantly from 65% to 55% (p < 0.0001)
Bowen et al. (7) (letter)	Before-and- after study	Resection rates for NSCLC increased from 4.7% to 27% in favour of the MD group
Davison et al. (8)	Before-and-after study	30% increase in the resection rate after the establishment of telemedicine multidisciplinary meetings (from 14.7 to 19 resections per year)
Martin-Ucar et al. (4)	Before-and-after study	After the appointment of thoracic surgeon and multidisciplinary meetings there was an increase in: surgical resection rates from 12.2% to 23.4% MD group (p = 0.001); resection older than 75 years: 4% vs. 18% (p = 0.02); ratio of lobectomy to pneumonectomy: 0.7 vs. 2.4 (p < 0.001); en-block chest wall resections, bronchoplasty and VATS lobectomy were performed only in the MD group; accounted for 14% of the total number of resections; in-hospital mortality did not change: 5.5% vs. 7.7% (p > 0.05)
Forrest et al. (6)	Before—after study	After the introduction of MD team; chemotherapy treatment increased from 7% to 23% (p < 0.001); palliative care decreased from 58% to 44% (p = 0.045); percentage of patients who were formally staged increased from 70% to 81% (p = 0.035)
Seek and Hogle (9)	Before—after study	Average number of days from diagnosis to treatment decreased following the establishment of multidisciplinary lung cancer clinic (MLCC) from: 29.3% to 18.76 days; 92% of patients started treatment within 14 days; 48% increase in the number of patients with lung cancer seen and treated in MLCC; patients satisfied with care provided at the MLCC (data not available)

1. Coory M, Gkolia P, Yang IA, Bowman RV et al. Systematic review of multidisciplinary teams in the management of lung cancer. Lung Cancer. [Review]. 2008; 60(1):14–21.

2. Murray PV, O'Brien MER, Sayer R. The pathway study: results of a pilot feasibility study in patients suspected of having lung carcinoma investigated in a conventional chest clinic setting compared to a centralised two-stop pathway. Lung Cancer. 2003; 42(3):283–290

3. Price A, Kerr G, Gregor A, Ironside J et al. The impact of multidisciplinary teams and site specialisation on the use of radiotherapy in elderly people with non-small cell lung cancer (NSCLC). Radiother Oncol 2002;64(Suppl. 1):80.

4. Martin-Ucar AE, Waller DA, Atkins JL et al. The beneficial effects of specialist thoracic surgery on the resection rate for non-small-cell lung cancer. Lung Cancer 2004; 46(2):227–32.
5. Dillman RO, Chico SD. Cancer patient survival improvement is correlated with the opening of a community cancer center: comparisons with intramural and extramural benchmarks. J Oncol Pract. 2005: 1(3):84–92.
6. Forrest LM, McMillan DC, McArdle CS et al. Evaluation of the impact of a multidisciplinary team, in a single centre, on treatment and survival in patients with inoperable non-small-cell lung cancer. Br J Cancer 2005; 93(9):977.
7. Bowen EF, Anderson JR, Roddie ME. Improving surgical resection rates in lung cancer without a two stop service. Thorax. 2003; 58(4):368.
8. Davison AG, Eraut CD, Haque AS et al. Telemedicine for multidisciplinary lung cancer meetings. J Telemed Telecare 2004; 10(3):140–143.
9. Seek A, Hogle WP. Modeling a better way: navigating the healthcare system for patients with lung cancer. Clin J Oncol Nurs 2007; 11(1):81–85.

Appendix 7. Existing clinical guidelines

Guidance Material	Organisation	Country	Year	URL
Lung cancer screening	National Comprehensive Cancer Network	United States	2012	https://subscriptions.nccn.org/gl_login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf
Palliative thoracic radiotherapy in lung cancer: an evidence-based clinical practice guideline	American Society for Radiation Oncology	United States	2011	http://download.journals.elsevierhealth.com/pdfs/journals/1879-8500/PIIS1879850011000919.pdf
Non-small cell lung cancer stage IV	Alberta Health Services, Cancer Care	Canada	2011	http://www.albertahealthservices.ca/hp/if-hp-cancer-guide-lu004-nsclc-stage4.pdf
Clinical practice guideline update on chemotherapy for stage IV non–small-cell lung cancer	American Society of Clinical Oncology (ASCO)	United States	2011	http://www.asco.org/ASCOv2/Practice+%26+Guidelines/Guidelines/Clinical+Practice+Guidelines/Lung+Cancer/American+Society+of+Clinical+Oncology+Clinical+Practice+Guideline+Update+on+Chemotherapy+for+Stage+IV+Non-Small+Cell+Lung+Cancer
NCCN Clinical Practice Guidelines in Oncology for Lung Cancer Screening	National Comprehensive Cancer Network (NCCN)	United States	2011	https://subscriptions.nccn.org/gl_login.aspx?ReturnURL=http://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf
Lung cancer. The diagnosis and treatment of lung cancer	National Institute for Health and Clinical Excellence (NICE)	United Kingdon	2011	http://www.nice.org.uk/nicemedia/live/13465/54202/54202.pdf
Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer	National Institute for Health and Clinical Excellence (NICE)	United Kingdon	2010	http://www.nice.org.uk/nicemedia/live/13058/49880/49880.pdf
Pemetrexed for the maintenance treatment of non-small-cell lung cancer.	National Institute for Health and Clinical Excellence (NICE)	United Kingdom	2010	http://www.nice.org.uk/nicemedia/live/13028/49355/49355.pdf
First Line Systemic Chemotherapy in the Treatment of Advanced Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2010	http://www.ncbi.nlm.nih.gov/pubmed/20101151
Non-small-cell lung cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up	European Society for Medical Oncology (ESMO)	Europe	2009	http://annonc.oxfordjournals.org/content/20/suppl_4/iv68.full.pdf+html
Small-cell lung cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up	European Society for Medical Oncology (ESMO)	Europe	2009	http://annonc.oxfordjournals.org/content/21/suppl_5/v120.full.pdf+html
Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181)	National Institute for Health and Clinical Excellence (NICE)	United Kingdom	2009	http://www.nice.org.uk/nicemedia/live/12243/45501/45501.pdf

Guidance Material	Organisation	Country	Year	URL
American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non-Small Cell Lung Cancer	American Society of Clinical Oncology	United States	2009	http://www.asco.org/ASCO/Downloads/Cancer%20Policy%20and%20Clinical%20Affairs/Clinical%20Affairs%20(derivative%20products)/NSCLC/NSCLC%20Unabridged%2011.16.09.pdf
Lung Cancer 2009 Treatment Guidelines	Providence Health & Services, Portland, Oregan	United States	2012	http://oregon.providence.org/ptkattachments/ProprietaryHealthArticle/2012%20Lung%20Cancer%20Treatment%20Guidelines.pdf
NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer	National Comprehensive Cancer Network (NCCN)	United States	2009	http://www.medscape.com/viewarticle/714976
Control of pain in adults with cancer (106)	Scottish Intercollegiate Guidelines Network (SIGN)	United Kingdom	2008	http://www.sign.ac.uk/pdf/SIGN106.pdf
Erlotinib for the treatment of non-small-cell lung cancer	National Institute for Health and Clinical Excellence (NICE)	United Kingdom	2008	http://www.nice.org.uk/nicemedia/pdf/TA162Guidance.pdf
ACR Appropriateness Criteria nonsurgical treatment for non-small-cell lung cancer: poor performance status or palliative intent	American College of Radiology	United States	2008	http://guideline.gov/content.aspx?id=37925&search=brachytherapy+
Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants	American Society of Clinical Oncology	United States	2008	http://jco.ascopubs.org/content/27/1/127.full.pdf
Guidelines for Treatment of Cancer: Non-small cell lung cancer	National Comprehensive Cancer Network (NCCN)	United States	2008	http://misc.medscape.com/images/586/420/nscl.pdf
18-Fluorodeoxyglucose Positron Emission Tomography in the Diagnosis and Staging of Lung Cancer	Cancer Care Ontario	Canada	2007	http://guidelines.gov/content.aspx?id=12137
Postoperative Adjuvant Chemotherapy in Completely Resected Non-Small Cell Lung Cancer: Guidance for Nurses	Cancer Care Ontario	Canada	2007	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14164
Standards, options and recommendations (SOR) for the perioperative treatment of patients with resectable non-small cell lung cancer	French National Federation of Cancer Centers (FNCLCC)	France	2007	http://www.ncbi.nlm.nih.gov/pubmed/18033192
Standards, Options and Recommendations (SOR) for the perioperative treatment of operable patients with resectable non-small cell lung cancer	French National Federation of Cancer Centers (FNCLCC)	France	2007	http://www.ncbi.nlm.nih.gov/pubmed/18033192
Pemetrexed for the treatment of non-small-cell lung cancer (TA124)	National Institute for Health and Clinical Excellence (NICE)	United Kingdom	2007	http://www.nice.org.uk/nicemedia/live/11823/36170/36170.pdf

Guidance Material	Organisation	Country	Year	URL
Bronchial intraepithelial neoplasia/early central airways lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://sinaipulmonary.org/wp-content/uploads/2010/09/Bronchial-Intraepitheal-Neoplasia.pdf
Bronchioloalveolar lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://sinaipulmonary.org/wp-content/uploads/2010/09/BAC.pdf
Chronic cough due to lung tumours: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://pneumonologia.gr/articlefiles/Paliative%20Care%20in%20Lung%20CAncer.pdf
Complementary therapies and integrative oncology in lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675873&PDFSource=13
Diagnostic surgical pathology in lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/data/Journals/CHEST/22061/zcb10907000078.pdf
Evaluation of patients with pulmonary nodules: when is it lung cancer?: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675824&PDFSource=13
Follow-up and surveillance of the lung cancer patient following curative-intent therapy: ACCP evidence-based clinical practice guideline (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675876&PDFSource=13
Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675828&PDFSource=13
Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidenced-based clinical practice guidelines	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675831&PDFSource=13
Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675844&PDFSource=13
Lung cancer chemoprevention: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675813&PDFSource=13
Management of small cell lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675870&PDFSource=13

Guidance Material	Organisation	Country	Year	URL
Palliative care consultation, quality-of-life measurements, and bereavement for end-of-life care in patients with lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675884&PDFSource=13
Palliative Care in Lung Cancer	American College of Chest Physicians (ACCP)	United states	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675879&PDFSource=13
Screening for lung cancer: ACCP evidence-based clinical practice guidelines	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675816&PDFSource=13
Special treatment issues in lung cancer: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675861&PDFSource=13
The non-invasive staging of non-small cell lung cancer: ACCP evidenced-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675836&PDFSource=13
The physiologic evaluation of patients with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675833&PDFSource=13
Treatment of non-small cell lung cancer stage I and stage II: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675849&PDFSource=13
Treatment of non-small cell lung cancer stage IV: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675857&PDFSource=13
Treatment of non-small cell lung cancer, stage IIIB: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675854&PDFSource=13
Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines (2nd Ed)	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675852&PDFSource=13
Chemotherapy for Relapsed Small Cell Lung Cancer	Cancer Care Ontario	Canada	2006	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14196
Management of Unresected Stage III Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2006	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14206
Postoperative Adjuvant Chemotherapy, with or without Radiotherapy, in Completely Resected Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2006	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14162
Second line or Subsequent Systemic Therapy for Recurrent or Progressive Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2006	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34349

Guidance Material	Organisation	Country	Year	URL
Use of the Epidermal Growth Factor Receptor Inhibitors, Gefitinib (Iressa) and Erlotinib (Tarceva), in the Treatment of Non-small Cell Lung Cancer	Cancer Care Ontario	Canada	2006	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14214
ACR Appropriateness Criteria induction and adjuvant therapy for N2 non-small-cell lung cancer	American College of Radiology	United States	2006	http://www.acr.org/~/media/9149F6C2E9274024910BC65BE16429BC.pdf
ACR Appropriateness Criteria nonsurgical, aggressive therapy for non-small-cell lung cancer	American College of Radiology	United States	2006	http://www.acr.org/~/media/ACR/Documents/AppCriteria/Oncology/NonsurgicalTreatmentForNSCLCPoorPerformanceStatusOrPalliativeIntent.pdf
ACR Appropriateness Criteria postoperative adjuvant therapy in non-small-cell lung cancer	American College of Radiology	United States	2006	http://www.acr.org/~/media/ACR/Documents/AppCriteria/Oncology/PostoperativeAdjuvantTherapyNSCLC.pdf
Assessment and Management of Lung Cancer Evidence based guidelines: A guide for General Practice	Cancer Council of Australia	Australia	2005	http://www.cancer.org.au/content/pdf/HealthProfessionals/ClinicalGuidelines/lungguidelinesforGPs.pdf
Postoperative Adjuvant Radiation Therapy in Stage II or IIIA Completely Resected Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2005	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14158
The Role of High Dose Rate Brachytherapy in the Palliation of Patients with Non-small Cell Lung Cancer	Cancer Care Ontario	Canada	2005	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14192
The Role of Photodynamic Therapy (PDT) in Patients with Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2005	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14188
Management of patients with lung cancer. A national clinical guideline	Scottish Intercollegiate Guidelines Network	Scotland	2005	http://www.sign.ac.uk/pdf/sign80.pdf
Lung Cancer :The diagnosis and treatment of lung cancer	National Institute for Health and Clinical Excellence (NICE)	United Kingdom	2005	http://www.nice.org.uk/nicemedia/live/13465/54199/54199.pdf
Referral guidelines for suspected cancer in adults and children	National Collaborating Centre for Primary Care	United Kingdom	2005	http://www.nice.org.uk/nicemedia/pdf/cg027niceguideline.pdf
Clinical Practice Guidelines for the Prevention, Diagnosis and Management of Lung Cancer	Cancer Council of Australia	Australia	2004	http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp97.pdf
Smoking Cessation: Guidelines for Australian General Practice	Cancer Council of Australia	Australia	2004	http://www.quitsa.org.au/cms_resources/documents/AustralianGeneralPracticeGuidelineHandbook.pdf
Prophylactic Cranial Irradiation in Small Cell Lung Cancer	Cancer Care Ontario	Canada	2003	https://www.cancercare.on.ca/common/pages/UserFile.aspx?serverId=6&path=/File%20Database/CCO%20Files/PEBC/pebc7-13-2f.pdf

Guidance Material	Organisation	Country	Year	URL
The Role of Combination Chemotherapy in the Initial Management of Limited-Stage Small-Cell Lung Cancer	Cancer Care Ontario	Canada	2003	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14174
The Role of Thoracic Radiotherapy as an Adjunct to Standard Chemotherapy in Limited-Stage Small Cell Lung Cancer	Cancer Care Ontario	Canada	2003	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14178
Diagnosis and Management of Lung Cancer: ACCP Evidence-Based Clinical Practice Guidelines	American College of Chest Physicians (ACCP)	United States	2007	http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3675887&PDFSource=13
Altered Fractionation of Radical Radiation Therapy in the Management of Unresectable Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2002	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=14170
Use of Preoperative Chemotherapy with or without Postoperative Radiotherapy in Technically Resectable Stage IIIA Non-Small Cell Lung Cancer	Cancer Care Ontario	Canada	2002	https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34359