SOUTH EAST INSTITUTE OF PUBLIC HEALTH
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DIRECTORATE OF PUBLIC HEALTH MEDICINE

CANCER PROGRAMMES

BLUEPRINT OF SERVICES FOR LUNG CANCER

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BLUEPRINT FOR LUNG CANCER INTERVENTIONS AND SERVICES

INTRODUCTION.

Primary lung cancer is the commonest malignant disease in the developed world, and is the most prevalent form of cancer among men over 65 years. It continues to rise in those aged over 75 years. Mortality from lung cancer is increasing in women. The condition still has a short clinical course and a poor prognosis. The literature is in agreement about the effectivness of preventing lung cancer incidence by targeting smoking behaviour, particularly in preventing young people taking up smoking. There is further consensus about the lack of a population screening method which can be recommended, and the desirability of detecting non-small cell lung cancer early enough for surgical intervention. The effectiveness of treatment for advanced disease is less marked, and it is of concern that many people who present with lung cancer are unsuitable for surgical intervention. The role of palliative care is critical in this condition and this care should be introduced early in the interaction between the patient and the services.

This document is presented in three sections:

i. A summary of interventions available with a classification of effectivness, and a flow chart of the progress of patients with this condition through the health services
ii. Models of good practice in health services drawn from national and international guidance on the topic
iii. Supporting information on the interventions available with references .

The classification of the evidence is drawn from the model used by the Canadian Task Force on Periodic Health Examinations. [1]

Quality of evidence	**Strength of recommendations**
I- Evidence from at least one properly randomised controlled trial	A- There is good evidence to support the recommendation/intervention
II-Evidence obtained from well designed trials without randomisation, or with confounding factors not adequately accounted for	B- There is fair evidence to support the recommendation
III-Evidence obtained from well designed epidemiological studies	C- There is poor evidence to support the recommendation
IV-Evidence from comparisons, observational studies or opinions of respected authorities	D- There is fair evidence to exclude this intervention from practice
	E- There is good evidence to exclude this intervention from practice

[1]Canadian Task Force on Periodic Health Examinations. Community Medicine Society Journal 1979;121:1193-1254.

1. SUMMARY OF INTERVENTIONS

INTERVENTION	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
PREVENTION		
iv. Smoking cessation programmes: reduction in starting smoking		
Provision of health education materials for children is potentially highly effective initially	B	II
Provision of advice via the mass media are potentially highly effective	B	II
Community campaigns to reduce smoking(all ages) are potentially effective	B	II
v. Smoking cessation programmes: support for quitting		
Advice from GP/primary care team leads to quitting smoking in a proportion of their patients	B	II
Workplace smoking policies with support is moderately effective in reducing risk	B	I
Advice from a nurse in antenatal clinic is moderately effective in reducing risk	C	II
Nicotine chewing gum is moderately effective in reducing risk	C/B	I
Provision of group support leads to risk reduction in a small proportion of participants	C	II

INTERVENTION	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
PREVENTION		
vi. Environmental risk factors		
Reduction of exposure to tobacco from passive smoking protects against lung cancer	A	II
Reduction in air pollution exposure(coal and tar fumes; nickel, zinc, benzpyrene) will not in itself reduce incidence	C	III/IV
vii. Reduced risk of lung cancer follows reduction in occupational exposure to:		
Asbestos	A	II
Radioactivity	B	III
Metal workers	B	III
Arsenicals	B	III
Inorganic lead	B	III
viii. Dietary factors		
Increase intake of b-carotene containing foods	B/C	III
ix. Chemoprevention		
Compounds with tumour preventive properties are promising but still experimental	C	?
x. Identification by genetic markers of at-risk groups is still experimental	C	?

INTERVENTIO	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
EARLY DETECTION		
xi. Screening by sputum cytological examination is not recommened at population level	E	I
xii. Screening by chest radiography is not recommended at population level	D	I
DIAGNOSIS		
xiii. Diagnostic procedures available include:		
(1)Fibreoptic bronchoscopy and TNM staging of the tumour	A	II/III
(2)Routine lung function tests	A	III
(3)CT scanning of the chest and upper abdomen	B	I
(4)Liver function tests	B	II
(5)Mediatinoscopy	B	II
(6)Thoracotomy	B	II
(7)MRI scanning of the chest and upper abdomen	B/C	I
(8)Bone scanning and skeletal radiology	C	II
(9)Bone marrow aspiration	C/B	II
(10)CT scanning of the brain and other sites(e.g. adrenal glands)	C/B	II
(11)Tomography of the chest	D	II
(12)Genetic diagnosis with flow cytometry	E	?
A diagnosis of lung cancer requires (1 - 2) preferably enhanced by (3-4). (5) is considered important in patients selected for surgery, and (6) should only be undertaken if necessary after (1-5) have failed to define the staging adequately. (7) is not recommended over (3). (8-10) are additional tests which can be useful in selected patients if used as a 'road map' (11-12) are not recommended as they are either superceded, or still in development(12).		

INTERVENTION	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
TREATMENT		
xiv. *Non-Small Cell Lung Cancers(NSCLC): early disease(Stage I and II)*		
Surgery(lobectomy the minimal procedure) provides the best chance of cure. Highly dependent on patient selection.	A	II
Pre-operative radiotherapy not recommended	E	I
Adjuvant radiotherapy following curative surgery may reduce local recurrence rate; no proven survival benefit	C	II
Pre-operative chemotherapy may reduce the recurrence rate, no unequivocally proven survival benefit	C/D	II
Adjuvant chemotherapy following surgery not standard therapy, but may reduce distant recurrence; survival data inconclusive.	B/C	II
Photodynamic therapy in tumours of < 1cm provides promising results. Use is experimental.	C	?
xv. *NSCLC: late disease (Stage III and IV)*		
Radiotherapy alone has a modest one-year survival of 40%; 20% @ 2 years and 5 %at five years	A	I
Single agent chemotherapies show low response rates and no survival advantage.	D	I
Combination chemotherapy, including mitomycin, cisplatin, ifosamide, paclitaxel and vinca alkaloids prolong survival as compared with no care, but the value of chemtherapy is still questioned in advanced disease, and should only be used in clinical trials	A/B	I
Combination chemtherapy and radiotherapy has been shown to have a potential benefit of 2-7% .	B	I

INTERVENTION	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
TREATMENT		
xvi. *Small Cell Lung Cancer(SCLC).*		
Combination chemotherapy including combinations of cyclophosphamide, etoposide, methotrexate, nitrosuears, vinca alkaloids, cisplatin and anthracyclines have led to improved outcomes in trials The emphasis is on more intense but smaller numbers of doses.	A	II
Autologous bone marrow transplant is not of proven survival benefit as a support therapy to more intense chemotherapy regimens.	C/D	IV
Combination chemo and radiotherapy have been shown to have a reduction in relative mortality of 14% over chemotherapy alone. This translates into a 5% benefit in survival at 3 years.	A	I
The place of radical radiotherapy in the long term outcome of SCLC is unclear. It is most effective in local disease and recurrence of local disease.	B	I
xvii. Other forms of treatment for NSCLC and SCLC		
(1)Prophylactic cranial irradiation: of limited value, toxic, and of no proven benefit in survival	C	I
(2)Colony stimulating factors: still experimental	C	?
(3)Somatostatin and analogues: role has still to be established	C	?
(4)Immunotherapy(BCG, levimasole, C parvum): not of proven benefit	C	II
(5) Fast neutron therapy: toxic, conflicting results, but not of superior benefit to current therapies	C/D	I
(6)Transfer factor	D	II
(7)Tracheobronchial stents: promising in palliation; no known increase in survival	B	III
xviii. Metastacectomy		
Treatment remains controversial	C	II

	INTERVENTION	LEVEL OF STRENGTH	RECOMMENDATION QUALITY
AFTERCARE			
xix.	Palliative radiotherapy for patients with loco-regional disease in NSCLC relieves troublesome obstructive symptoms. There is no survival benefit in active treatment unless symptoms are present	A	I
xx.	Palliative chemotherapy in NSCLC is associated with toxicity and it's value is questionable.	C/D	I
xxi.	Clincial evidence of brain and painful bone metastases in SCLC are alleviated by radiotherapy	B	II
xxii.	Population based terminal care is required @ 1-2 home care nurses per 250,000 population, particularly those patients with severe pain	B	III & IV
xxiii.	Specialist palliative services should be available locally to support hospital, hospice, home and primary health care services	B	III & IV
xxiv.	12.5 hospital beds per 250,000 population is recommended for patients with specific inpatient needs	B	IV

TYPICAL PATTERNS OF TREATMENT FOR LUNG CANCER

The numbers are estimates of the expected numbers in a population of 700,000 (figures in parentheses are percentages of total cases).

679 males
(70% of total cases)

294 females
(30% of total cases)

973 cases

827 NSCLC
(85%)

146 SCLC
(15%)

248 (maximum) suitable for surgery
(30%)

Mortality of 5% for pneumonectomy and
2% for lobectomy. Persons over 70 years
tolerate surgery poorly.
50% survival @ Stage I at 5 years
40% survival @ stage II at 5 years

Overall, histological types vary.
Likelihood of survival @ 5 years
from 37% to 27%

48 with limited disease
(33%)

Chemotherapy, 7 (15%) alive at 2 years if
limited disease
Combination chemo-and radiotherapy has
indicated 3 year survival of 2(5%)

579 (70%) not suitable for surgery:

Palliative radiotherapy
Combination chemotherapy (intial response of up to 60%);
effects on survival unproven
Specialist palliative services with median survival of 8.5 months

98(66%) with extensive disease

Chemotherapy for 49(50%), with combination
chemo-and radiotherapy for 29(30%).
Specialist palliative services with median survival of 9 months
Survival of 5 months without treatment

MODELS OF GOOD PRACTICE

The following documents provided guidance for the principles of good practice, with a special emphasis on purchasing.

Standing Medical Advisory Committee. The Management of Lung Cancer: Current Clinical Practices. London: HMSO, 1994.
Sanderson H, Mountney L, Harris J. Cancer of the Lung. In: Epidemiologically Based Needs Assessment, Vol 1. Oxfrod University Press, 1994.,
Saunders C. Hospice and Palliative Care. An interdisciplinary approach. London: Edward Arnold, 1990.
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Department of Health and the Welsh Office. A Policy Framework for Commissioning Cancer Services. London: Department of Health, 1995.
The Association of Cancer Physicians. Review of the Pattern of Cancer Services in England and Wales. London: ACP, 1994.
The Royal Marsden NHS Trust.Purchasing and Providing Cancer Services: A Guide to Good Practice.
Younger T. Lung Cancer: Profile of the Evidence. South Thames Regional Health Authority, 1995.

DESCRIPTION
Specific Guidelines for Lung Cancer 1. The most effective way of reducing the incidence of lung cancer is through methods of preventing tobacco smoking, targeted at the young. 2. The aim of clinical management of lung cancer is to achieve a good quality life for the patient for as long as possible. This includes services which provide good symptom control and palliative care. Too often, effective care is measured in terms of survival or tumour response to the exclusion of quality of life. 3. Lung cancer demands the closest integration of health and social care. The role of the general practitioner and the primary care team is important at all stages of the disease. 4. Early detection of symptoms by general practitioners, and speedy referral, ideally within one week contributes to the clinical management of the disease. 5. There should be pre-referral access by general practitioners to X-ray services, and access to specialist and experienced medical staff for the diagnosis and subsequent management of the disease. 6. A report on the X-ray results should be available to the GP within one week. An outpatient appointment to a specialist within two weeks should be regarded as appropriate practice. Wherever possible, bronchoscopy should be done within one week of the clinic appointment and pathology results should be available wthin one week of this.

DESCRIPTION
Specific Guidelines 7. The appropriate specialists are usually a chest physician, oncologist and thoracic surgeon, with access to radiotherapy services. There should be evidence of collaborative care between these specialists, and clear locally agreed guidelines identifying which group of doctors have major clinical responsibility at different stages of care. 8. All principal clinical support services should be available on site including expert histopathology services. 9. Doctors and nurses working in primary care should be kept promptly up to date with the patient's progress, and joint educational activities for general practitioners, hospital doctors and nurses should be developed locally. 10. Patients and their carers/families should be told of the diagnosis early on, with adequate information about the consequences of the disease, and it's management. 11. If preliminary investigations suggest that a patient is potentially curable by surgery, he or she should be referred to a thoracic surgeon. There is evidence that considerably more cases may be suitable for such treatment. 12. There should be co-ordinated nursing services for patients with lung cancer, with care supervised and provided by the appropriate clinical nurse specialist. 13. Clinical trials are of importance in lung cancer management and wherever possible patients who wish to consider active treatment at later stages of the condition should be referred to a specialist actively engaged in such trials. Data should also be regularly collected for clinical audit. 14. Palliative care should include patient rated quality of life assessments. Good symptom control is integral to lung cancer management and should aim for psychological , physical and functional well being. 15. Good communication, adequacy of information and continuity of care are all essential components of clinical practice in this condition. 16. There are opportunities to improve the organisation and co-ordination of services within and across sectors. Activity, costs and outcomes need to be assessed more accurately through audit, review and evaluation.

3. BACKGROUND INFORMATION ON THE EFICACY OF INTERVENTIONS

INTERVENTION	LEVEL OF RECOMMENDATION		REFERENCES
	STRENGTH	QUALITY	
I. SMOKING CESSATION PROGRAMMES			
Health education materials for children produce initially good results but these are hard to sustain. The impact is high, as many children receive the messages. The HEA has shown that mass media materials can lead to a quitting rate of 5% at one year; other series have shown quitting rates of up to 11%.	B	II	1,2 1,3
Community campaigns are potentially highly effective, leading to quitting rates of up to 15%.	B	II	1,4
Advice from the GP and primary care team is known to lead to 5% quitting rates, although the optimal circumstances have to prevail with the service provider and the patient.	B	II	1,5
Workplace initiatives have a moderate effect, and programmes are confined mainly to larger employers	B	II	1,6
Nicotene chewing gum and advice from nurses are moderately effective, with a limited target audience.	C/B	I	1,7-9
Group support has led to 20% quitting rates, but is difficult to sustain	C	II	10
II. ENVIRONMENTAL RISK FACTORS			
Over 20 epidemiological studies have investigated passive smoking and concluded that there is an increased risk in the range of 10-50% of getting lung cancer from exposure. Recent overviews have raised some doubt about the causal nature.	A	II	11-13
There is not a causal link established between air pollution and lung cancer and research is needed to quantify the individual and population effects of air pollution	C	III/IV	14,15

INTERVENTION	LEVEL OF RECOMMENDATION		REFERENCES
	STRENGTH	QUALITY	
III. OCCUPATIONAL EXPOSURE Although causing only a small proportion of cancers, the IARC has identified over 200 agents as carcinogenic. In the UK, the majority of cases relate to asbestos and lung cancer. A recent meta-analysis has found an excess risk of several cancers including lung, in people exposed to inorganic lead, but the studies have not taken account of confounding factors.	A B	II II	16-18 19
IV. DIETARY INFLUENCES The risk of lung cancer is 2.0 times higher among smokers who eat foods low in b-carotene than among those who eat foods high in b-carotene. There is fair evidence to support an increase in b-carotene intake. There is no evidence to support effectiveness of physician counselling in including dietary changes.	B/C C	III III	20-4
V. CHEMOPREVENTION The administration of agents to block or reverse carcinogenesis is being investigated in ongoing trials. The National Cancer Institute in the USA has funded research on 14 compounds that may inhibit tumour development. This is still at an experimental stage.	C C	? ?	25-6. 27
VI. IDENTIFICATION BY GENETIC MARKERS OF AT-RISK GROUPS Research on dominant oncogens and tumour supressor genes is still under way with prospective studies. These initiatives are still at the experimental stage			

INTERVENTION	LEVEL OF RECOMMENDATION		REFERENCES
	STRENGTH	QUALITY	
VII. EARLY DETECTION			
Frequent cytologic examination of the sputum does not significantly change detection and mortality rates. There is good evidence to exclude from periodic health examinations of asymptomatic people.	E	I	22, 28-30
Frequent screening by chest readiographhy improves detection rates, but not mortality. There is fair evidence to exclude from periodic examinations	D	I	
VIII. DIAGNOSIS			
Flexible fibreoptic bronchoscopy has become the single most useful diagnostic procedure in the diagnosis of endobronchial lung carcinoma. The additional procedure of transbronchial needle aspiration has been found to be valid for diagnosing malignancy in the mediastinum and micrometastases.	A	II/III	31-32
Several prospective trials have shown the sensitivity and specificity of CT scanning over MRI as a all-round tool for imaging thoracic abnormalities . Both modalities are least accurate when detecting mediastinal lymph nodes.	B	I	33, 34-36
Mediastinoscopy will improve the diagnostic yield, but should be used in selected circumstances of diagnostic difficulty, after redaiological procedures have been undertaken. Thoracotomy can complement mediastinoscopy but has a definite mortality and morbidity.	B B	II II	37-38
Routine assessments of distant metastases, particularly if asymptomatic remains controversial.	C	II	31, 34, 39
Standard tomography has a limited place in assessment and diagnosis.	D	II	40
The contribution of flow-cytometry in evaluation of lung cancer remains disputable.	D/E	?	41

INTERVENTION	LEVEL OF RECOMMENDATION		REFERENCES
	STRENGTH	QUALITY	
IX. TREATMENT *NON-SMALL CELL LUNG CANCERS*			
The five year survival rate for those suitable for surgery is reported as 50-70%. Less than 30% of newly diagnosed cases are suitable for surgery. Tumour stage is more important than histology. Randomised controlled trials have not yet been completed to prove the benefit conclusively. There is some evidence that more people could benefit from surgery than currently receive it. The North American Lung Cancer Study Group has initiated a prospective randomised trial of limited resection V lobectomy . At 2 years, there was a significant increase in local recurrence in the limited resection group. Lobectomy is the minimal procedure recommended.	A A	II I	1,31, 32, 42 43
There is no place for pre-operative radiotherapy outside of clinical trials,as there is No demonstrable survival benefit	E	I	44
Pre-operative chemotherapy has been the focus of Phase II trials recently. Studies are flawed by the lack of an adequate control group. Toxicity rates are significant and survival data are inconclusive	C/D	I	45
Two randomised controlled trials have found a significant decrease in distant metastases from surgery and sequential combination chemotherapy(CAP regimen), but other trial data are inconclusive, and this treatment is not yet considered standard.	C/B	II	46-8
Phase I & II trials in Japan indicate that for cancers < 1cm complete eradication can be achieved in 90% of cases using photodynamic therapy; it is considered a promising curative treatment for early NSCLC. It also enhances responses to radiotherapy	C	?	49

INTERVENTIONS	LEVEL OF	RECOMMEDNATION	REFERENCES
	STRENGTH	QUALITY	
TREATMENT NSCLC cont'd...			
In late disease, a meta-analysis of 11 RCTs has shown that thoracic irradiation in patients receiving chemotherapy for local disease led to an odds of surviving at 2 years of 1.5 over those receiving no radiotherapy. This was associated with treatment related deaths. Seven randomised trials of combination chemotherapy following radiation and best supportive care showed similar results. Trials of concurrent chemo and radiotherapy have led to conflicting results.	A	I	50-52
Meta-analyses have shown that combination chemotherapy, especially with newer agents result in an odds ratio of death of 0.44 as compared with supportive treatment in late disease. Toxicity is considerable. The National Cancer Institute of Canada has indicated that at least some chemotherapy regimens may be less costly than best supportive care	A/B	I	53-54. 55
There is continued debate about the role of radiotherapy alone in advanced disease, and clinical trials are needed to determine its benefit to survival. It has been shown in observational studies to have significant palliative benefits in local obstruction	C	III	56
SMALL CELL LUNG CANCER			
Administration of three or four drugs is required for optimal results in combination chemotherapy, leading to a 60-90% initial response. This, combined with intensified treatment periods have led to treatment related deaths.	A	II	57-60
Hematopoietic growth factors have been disappointing in reducing these deaths, and RCTs are recommended to examine the benefits of this adjuvant treatment.	C/D	IV	61
Meta-analyses of 13 RCTs shows that thoracic irradiation moderately improves survival of patients on chemotherapy for SCLC.	A	I	52, 62-3

INTERVENTIONS	LEVEL OF	RECOMMEDNATION	REFERENCES
	STRENGTH	QUALITY	
TREATMENT *OTHER FORMS OF TREATMENT FOR NSCLC AND SCLC* Prophlyactic cranial irradiation(PCI) may influence long term survival of patientswith limited stage disease, but this is not clearly established. Ten randomised controlled trials have examined the value of PCI and have found no demonstrable survival benefit, although brain recurrences can be reduced, This treatment is not recommended as standard.	C	I	64-6
Granulocyte macrophage colony stimulating fact has been shown to induced increased production of blood cells, which may reduce toxicity of chemotherapy. This treatment is still experimental	C	?	67
Somatostatin and analogues inhibit release of various hormones and may inhibit tumour growth. It is a promising adjuvant therapy in cancer, but as yet of unproven benefit	C	?	68
Trials have shown a slight improvement in disease -free survival for patients treated with immunotherapy, but the trial data are not detailed enought to permit meta-analysis. There is insufficient evidence to justify the use of these treatments.	C	II	69-70
Twenty five RCTs have examined the benefits of fast neutron therapy. None has demonstrated neutrons to be advantageous over photons, nor that the treatment is safe. The National Cancer Institute of the USA has sponsored RCTs which show that in selected patients with inoperable NSCLC, fast neutron therapy may provide therapeutic benefit, but at the cost of severe toxicity.	C/D	I	71-2.
RCTs on transfer factor show conflicting results, and several show no clinical benefit.	D	II	73
Studies using tracheobronchial stents have found them useful in high grade stenosis. Mean duration of stenting was 3.35 months in one study(longest 2.7 years).	B	III	74
Despite much literature, the treatment of pulmonary metastases remains controversial	C	II	75-6

INTERVENTION	LEVEL OF RECOMMENDATION		REFERENCES
	STRENGTH	QUALITY	
AFTERCARE			
Results from the MRC trial of palliative radiotherapy suggest that smaller fractions are as effective in controlling symptoms as larger ones.	A	I	1, 77
Chemotherapy may prolong survival in advanced disease in SCLC for several months, but will lead only to a small reduction in relapse rate. Its role is questioned in advanced NSCLC.	C/D	I	78-80
Population based terminal care and specialist palliative services should be available to support people in home, hospice, hospital and primary care settings	B	IV	1, 81-2

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