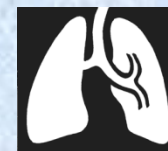


Lung cancer

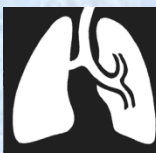
Prof. MUDr. Miloslav Marel, CSc.

Pulm. Dept. of the 2nd Medical
Faculty of Charles University, Prague-
Motol



What is Lung Cancer?

- An estimated 219,440 people diagnosed in the United States in 2009
- The leading cause of cancer death among men and women
- Begins when cells in the lung grow out of control and form a tumor
- There are two main types of lung cancer: non-small cell and small cell



Lung Cancer

Global situation in the world

- **The leading cause of cancer death in both women and men in USA, Canada and China**
- **997 000 death in men and 333 000 death in women in the world in 2000**
- **An increase of adenocarcinoma**
- **12,3 % of all malignant tumors , 30% of cancer related death**



Lung Cancer

Global situation in the world

European Union

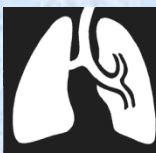
29% of cancer death in men

9% in women

The highest incidence in the world

New Orleans 105/100 000 in men

New Zealand 73/100 000 in women



Incidence and mortality

C34 - ZN průdušky - bronchu a plicí, muži

Časový vývoj, Počet případů na 100 000 osob

Rok	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995
Incidence	99.31	94.53	96.81	99.2	101.91	100.28	100.44	101.07	97.99	96.18	99.18	96.2	96.3	95.54	98.45	94.53	94.68	96.98	95
Mortalita	52.59	78.45	82.84	90.09	90.58	91.51	94.37	92.3	89.86	92.02	90.07	88.73	88.73	89.69	89.64	89.65	86.93	85.57	89.48

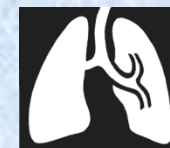
Rok	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Incidence	102.22	95.16	95.78	94.29	93.77	91.22	92.64	93.66	95.68	93.82	91.14	94.07	92.52	88.71	91.48	87.85	87.35	86.1	83.03	82.31
Mortalita	88.1	88.99	85.71	87.65	86.41	83.35	83.69	81.32	83.23	80.14	79.69	80.58	79.97	78.67	78.03	77.14	74.85	74.1	73.13	69.75

C34 - ZN průdušky - bronchu a plicí, ženy

Časový vývoj, Počet případů na 100 000 osob

Rok	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995
Incidence	9.48	9.93	9.79	10.88	11.66	11.55	12.28	12.86	12.87	13.12	14.3	14.38	16.18	15.36	18.06	17.91	18.24	21.58	21.41
Mortalita	5.49	7.6	7.85	9.04	9.66	10.35	10.89	11.32	11.41	12.01	12.76	12.28	14.21	13.97	15.74	15.69	15.73	17.76	18.68

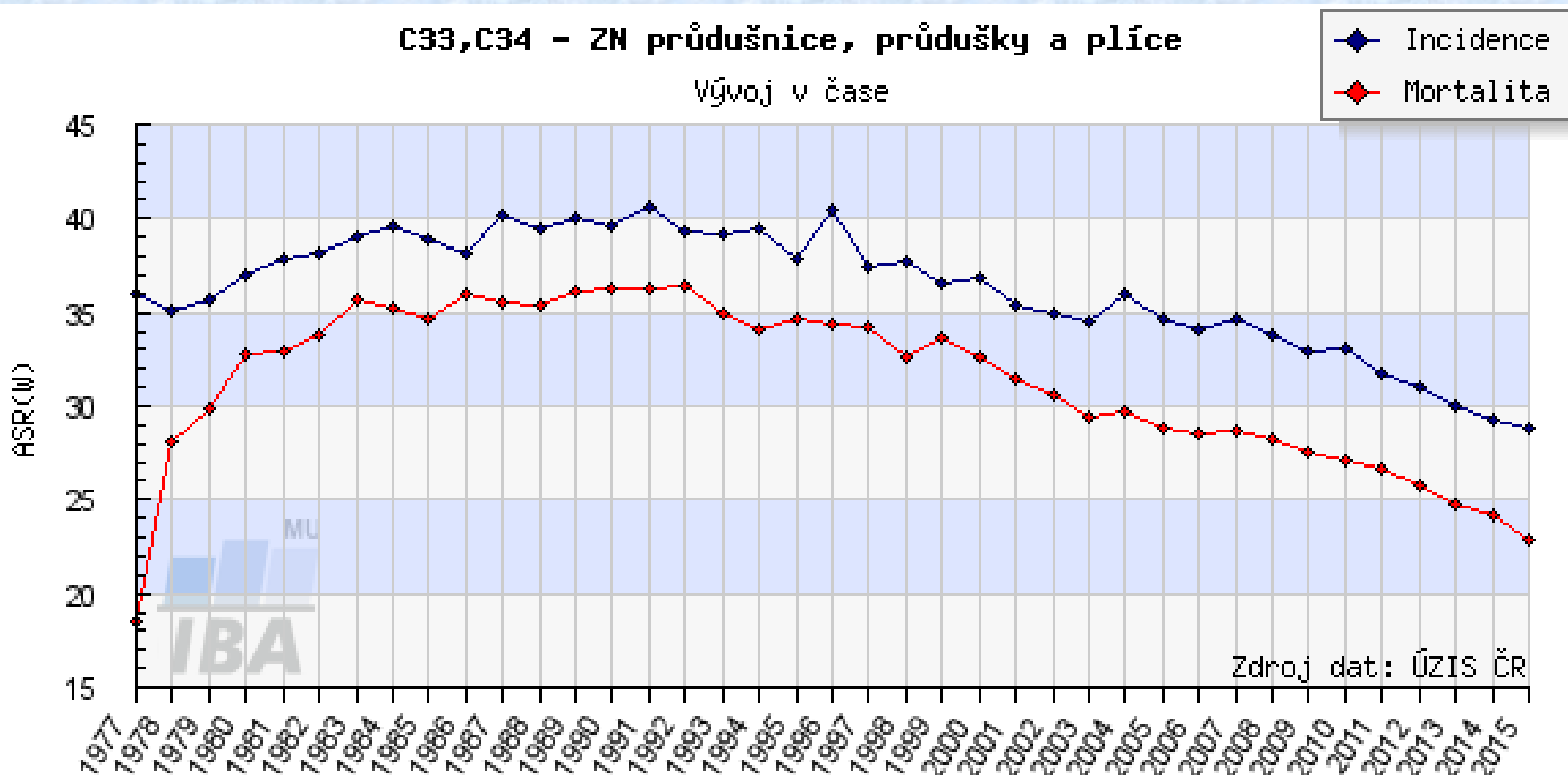
Rok	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Incidence	22.9	22.09	24.57	24.19	26.93	27.55	27.12	27.06	30.43	31.34	32.11	34.2	34.87	36.38	36.11	38.59	38.11	38.38	39.96	41.25
Mortalita	19.56	19.16	20.24	22.25	22.07	23.66	22.73	23.2	23.63	24.99	26.23	27.19	28.23	28.76	28.43	30.9	31.92	30.83	31.46	31.98



Lung cancer in the Czech republic

C33,C34 - ZN průdušnice, průdušky a plíce

Vývoj v čase

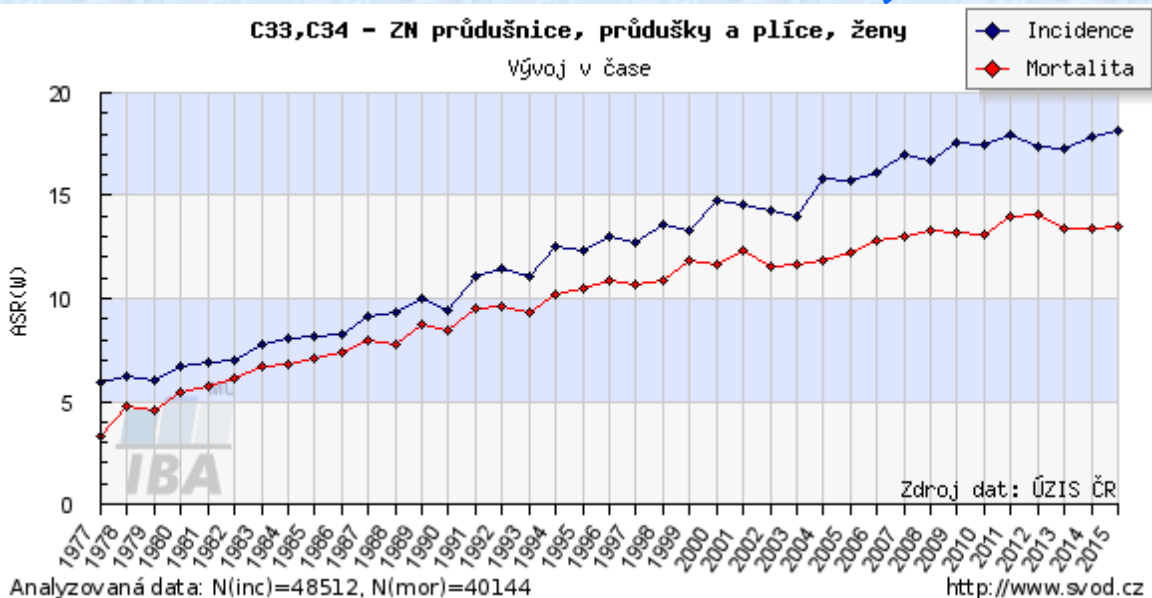


Zdroj dat: ÚZIS ČR

Analyzovaná data: N(inc)=236217, N(mor)=206414

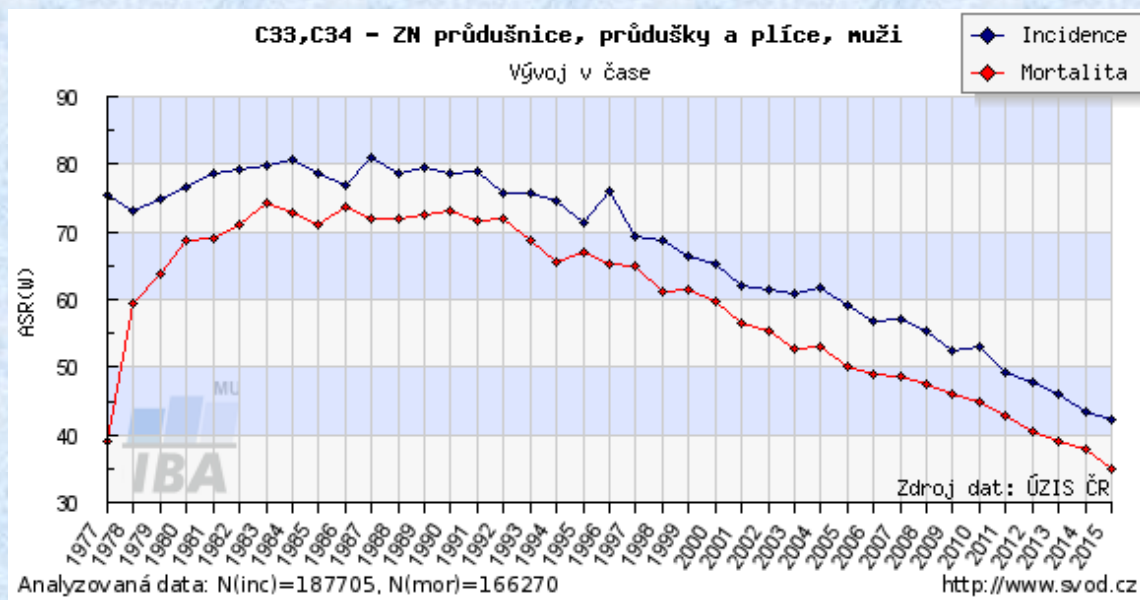
<http://www.sv.od.cz>

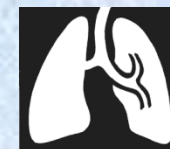
Incidence and mortality , LC, 1977-2015 men, women



82/100 000

41/100 000

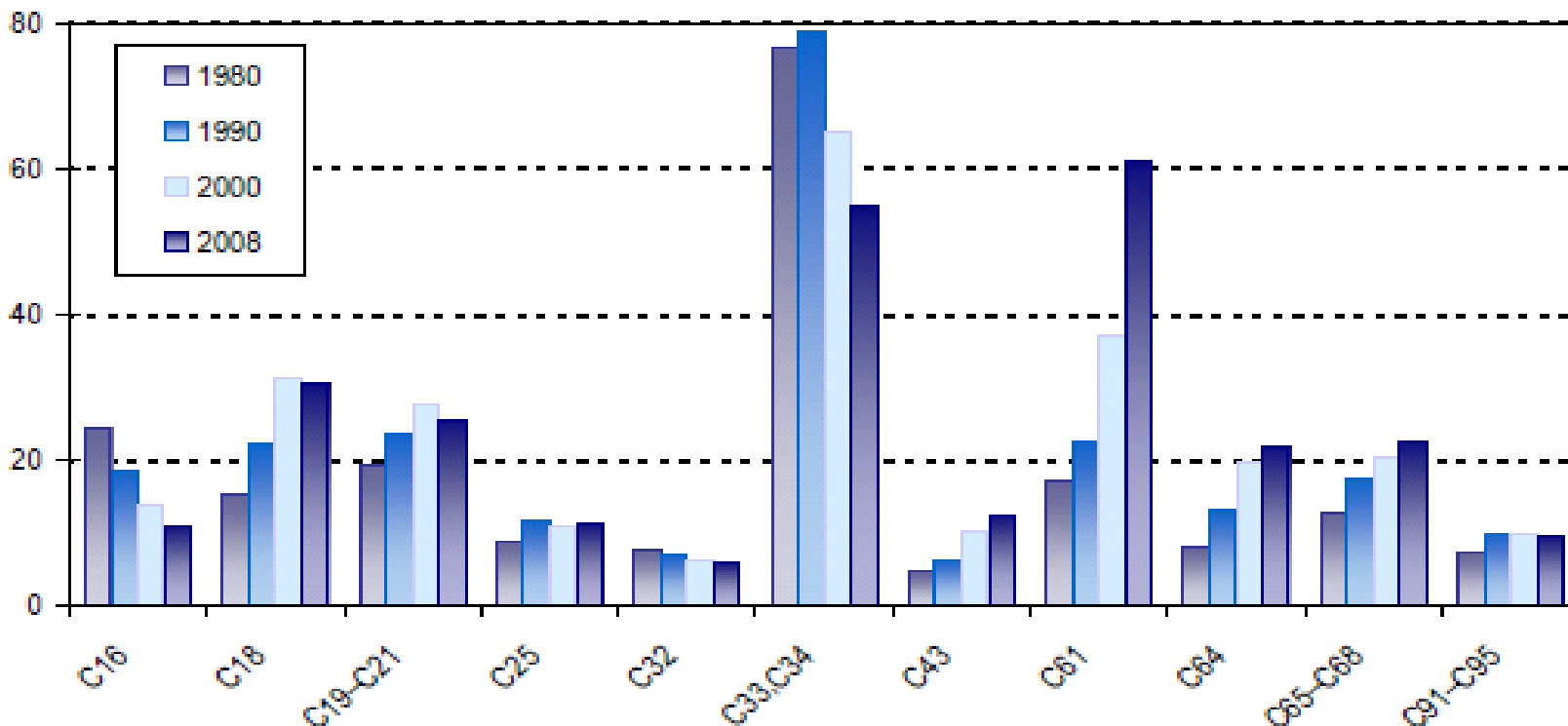




Evolution of incidence in tumors in men

Vývoj incidence novotvarů - vybrané diagnózy - muži
Trend of cancer incidence - selected diagnoses - males

světový standard na 100 000 / world standard per 100 000



C16-žaludek

C19-21 rektosigma

C32hrtan

C33-34 plíce

C61prostata

C67 měchýř

C91-95 hemoblastosy

C18- colon

C25 slinivka

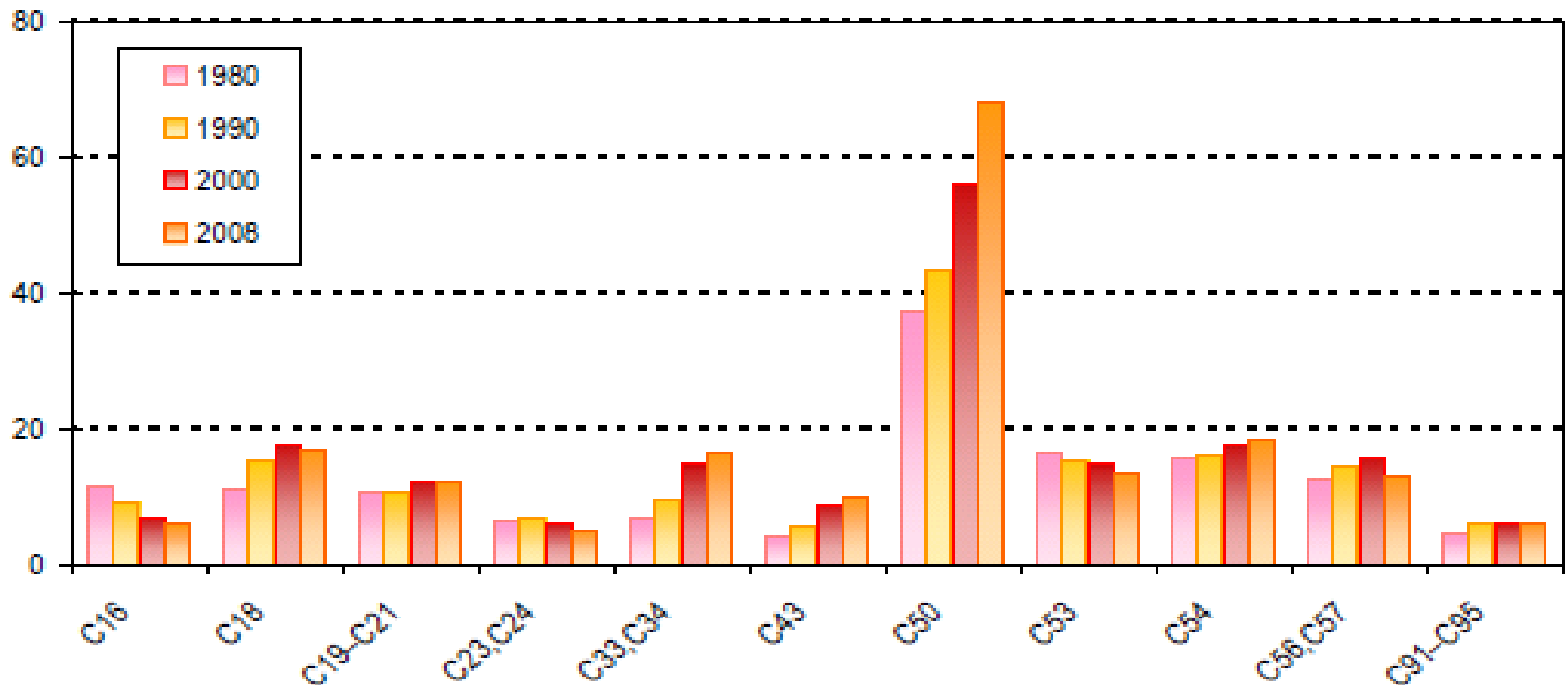
C43 melanom

C64-68- ledviny

Evolution of incidence of tumors in women

Vývoj incidence novotvarů - vybrané diagnózy - ženy
Trend of cancer incidence - selected diagnoses - females

světový standard na 100 000 / world standard per 100 000



C16-žaludek

C19-21 rektosigma

C33-34 plíce

C50 prs C53cervix.

C56-7 ovariů C91-95 hemoblastosy

C18- colon

C23-4 žlučník

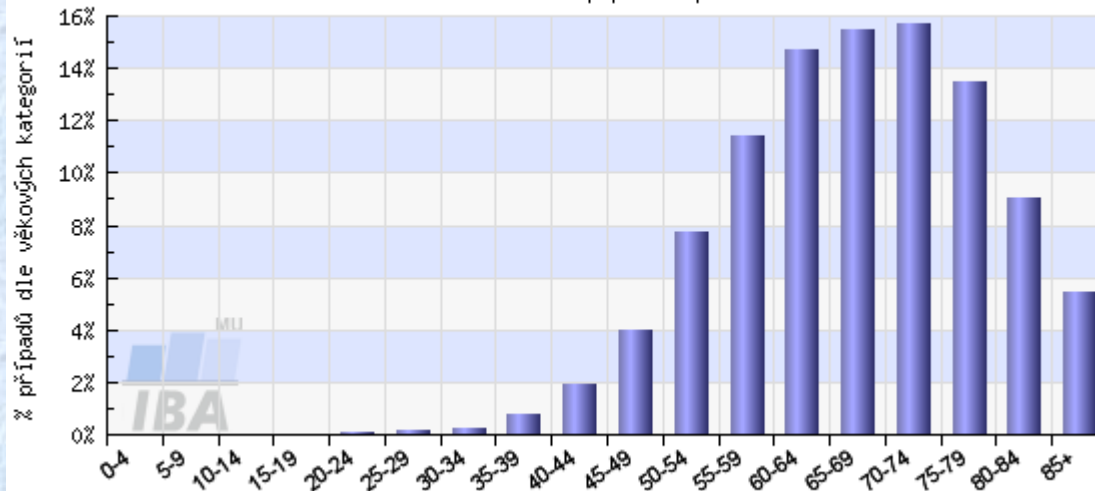
C43 melanom

C54 tělo dělohy

Age of patients at the time of diagnosis

C33,C34 - ZN průdušnice, průdušky a plíce - Incidence, ženy

věková struktura populace pacientů



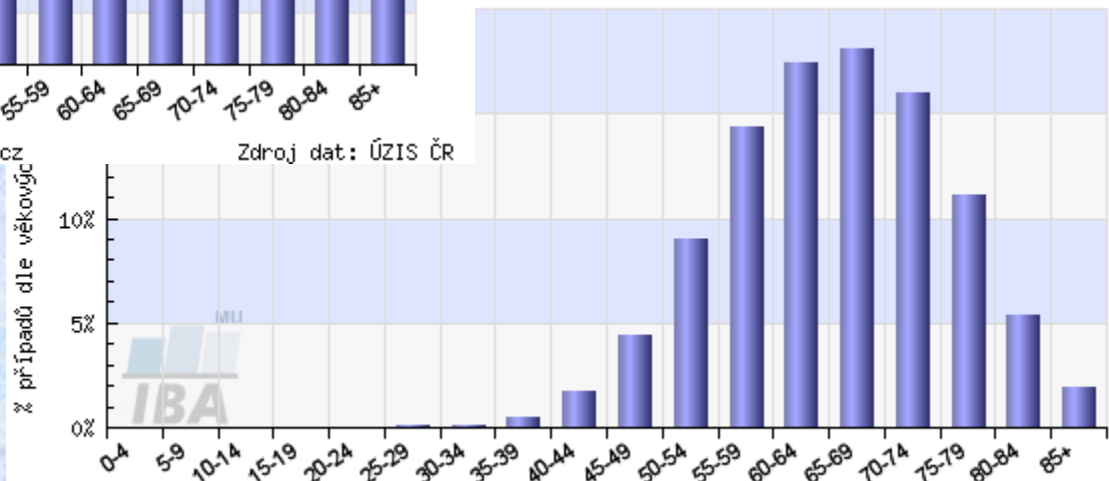
Analyzovaná data: N=39992

<http://www.svod.cz>

Zdroj dat: ÚZIS ČR

C33,C34 - ZN průdušnice, průdušky a plíce - Incidence, muži

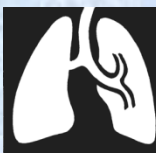
věková struktura populace pacientů



Analyzovaná data: N=170071

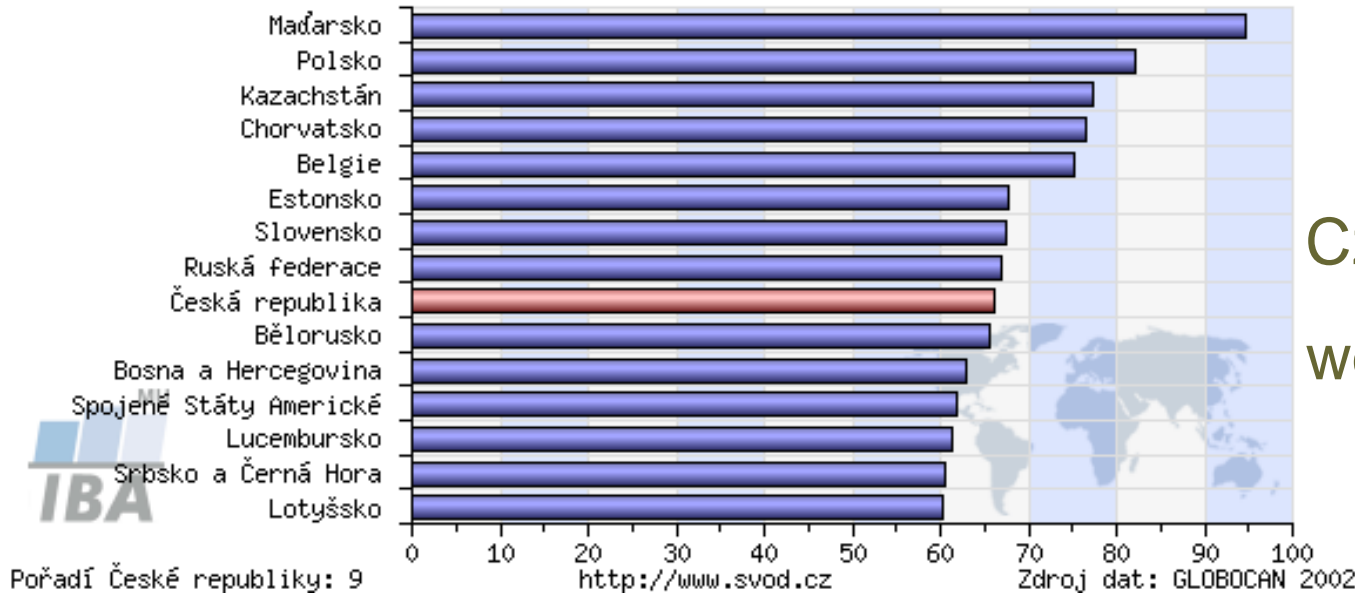
<http://www.svod.cz>

Zdroj dat: ÚZIS ČR



C33,C34 - Průdušnice, průdušky a plíce, muži

srovnání incidence v ČR s ostatními zeměmi světa, ASR - světový standard

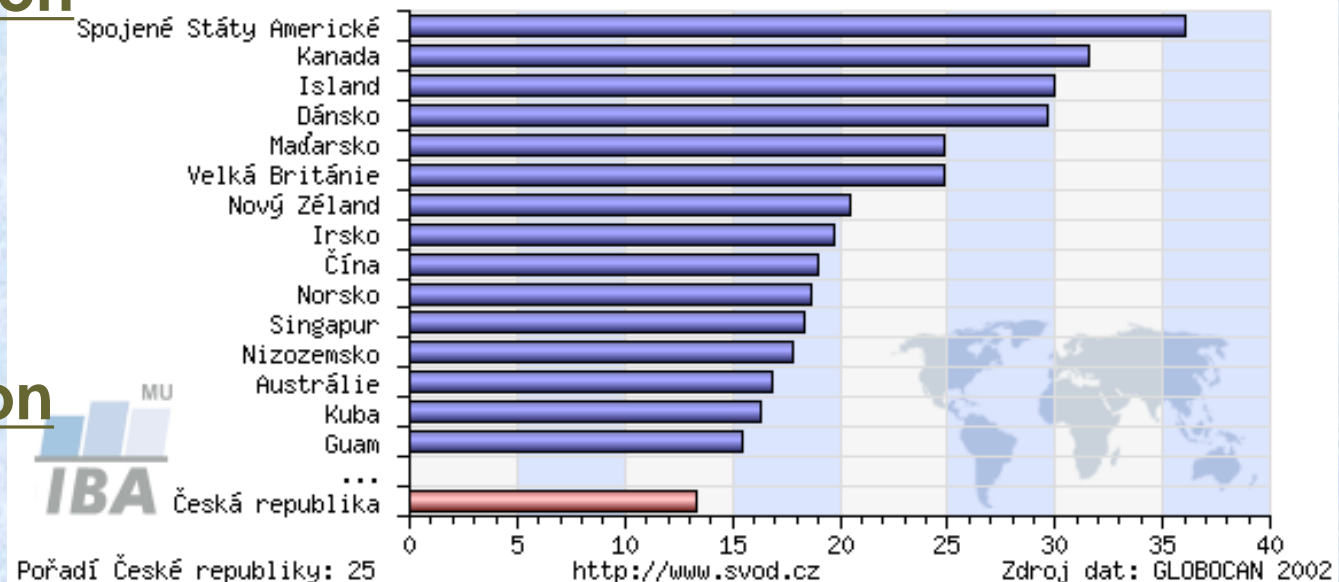


Czech republic and world

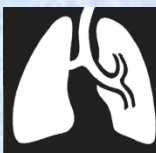
2015 13. position

C33,C34 - Průdušnice, průdušky a plíce, ženy

srovnání incidence v ČR s ostatními zeměmi světa, ASR - světový standard

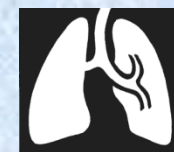


2015 24. position



Incidence of lung cancer according age groups

	2003	%	2008	%
• Men - 49 years	191	4,2	119	3
50-59	1106	24,1	979	22
60-69	1525	33,2	1821	38
70-79	1382	30,1	1287	27
older	386	8,4	480	10
• Women - 49 let:	92	6,6	63	3
50-59	301	21,7	355	20
60-69	347	25	591	32
70-79	470	33,9	491	27
older	177	12,8	327	18

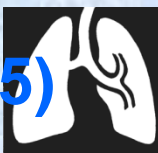


Incidence of LC in regions in CR to 100 000 inhabitants (2005)

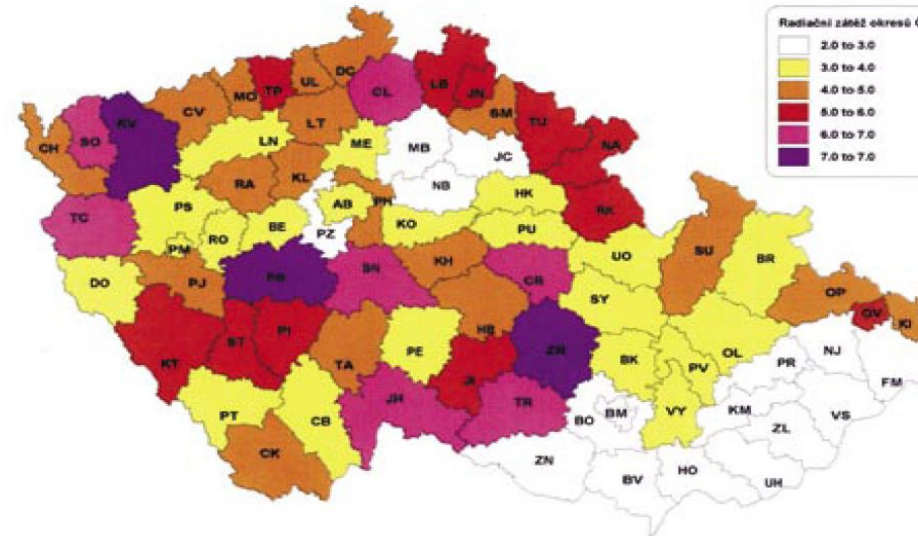
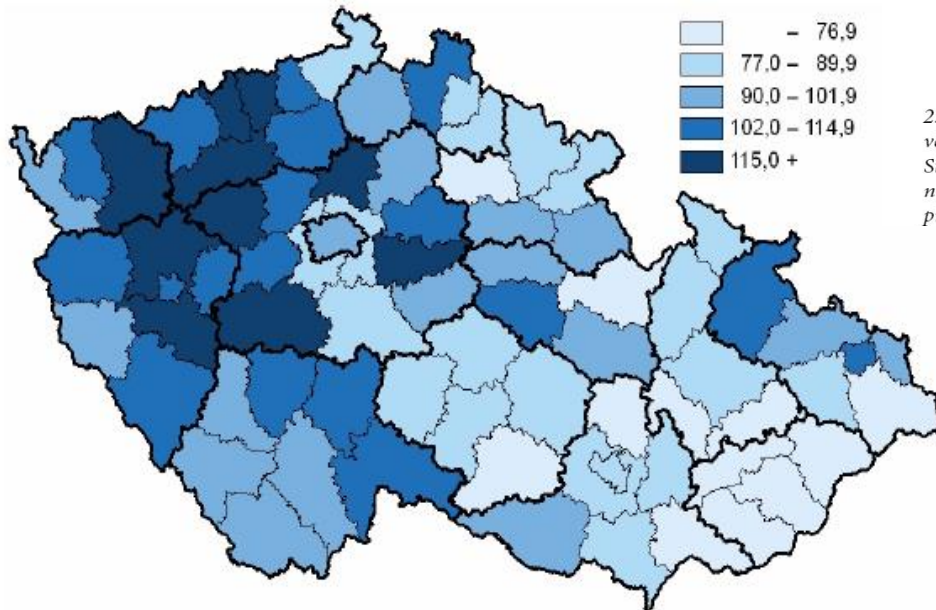
region	men n/100 000	women n/100 000
• Praha	95	49
• Středočeský kraj	100	35
• Jihočeský kraj	98	29
• Plzeňský kraj	109	34
• Karlovarský kraj	105	51
• Ústecký kraj	117	42
• Liberec	93	40
• Hradec Králové	85	20
• Pardubice	96	26
• Vysočina	92	17
• Jihomoravský kraj	77	24
• Olomoucký kraj	79	24
• Zlín	62	13
• Moravskoslezský	92	24



Incidence of lung cancer to 100 000 men (2001 - 2005) and the maps of CR with radioactive risk



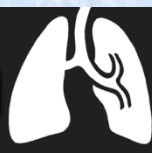
Incidence ZN průdušky, průdušnice a plíce na 100 000 mužů
(průměr 2001–2005)
*Incidence of MN of trachea, bronchus and lung per 100 000 males
(average 2001–2005)*



2. Klasifikace území České republiky podle radioaktivního rizika. Mapa vyjadřuje jakou pozornost je věnovat řešení radonové problematiky v jednotlivých správních územních jednotkách (bývalých okresech). Stupnice znamená radiační zátěž (od 2,0 – nejmenší, do 7,0 největší). Větší pozornost radonové problematice je nutno věnovat některým regionům Čech (Karlovarsko, Příbramsko) a západní Moravy, což je způsobeno přítomností magmatitů a ložisek uranových rud.



Evolution of mortality on LC in CR



	Men abs. numb	women abs. numb	Men n/100000	women n/100000
1940	426	134	12,1	3,7
1960	3145	386	66,8	7,8
1980	5100	638	101,8	12,0
2000	4480	1246	89,6	23,6
2004	4346	1343	87,4	25,7
2008	3928	1483	76,8	27,9



- **Standardized mortality to diag. C33,C34 to 100 000 women in CR and abroad**

• Country	2000	2001	2002	2003	2004	2005
• Austria	17	16	18	17	18	17
• Czech Republic	18	19	18	19	19	19
• Finland	12	12	12	13	12	13
• Hungary	30	30	32	33	33	31
• Ireland	29	25	26	27	28	28
• Lithuania	8	9	7	9	8	8
• Norway	23	24	23	24	25	26
• Poland	18	19	20	20	19	21
• Romania	11	11	11	12	11	12
• Russian F.	9	9	9	8	8	8
• Ukraine	8	8	7	7	7	7

- **Standardized mortality to diag. C33,C34 to 100 000 men in CR and abroad**

• Country	2000	2001	2002	2003	2004	2005
• Austria	54	54	55	53	51	50
• Czech Republic	90	86	84	81	82	77
• Finland	52	51	49	48	46	46
• Hungary	115	114	112	115	114	103
• Ireland	59	56	54	56	53	50
• Lithuania	78	81	80	79	76	74
• Norway	45	46	49	47	46	44
• Poland	99	100	101	97	96	95
• Romania	65	65	66	65	65	68
• Russian F.	87	84	82	80	78	77
• Ukraine	72	69	67	64	63	61



**Standardized mortality to diag. C33,C34 to 100 000 inhabitants in CR and abroad
(UZIS 2008)**

Country	2000	2001	2002	2003	2004	2005
Austria	33	32	33	32	32	31
Czech Republic	49	48	46	45	46	44
Finland	28	28	27	27	26	27
Hungary	65	65	65	66	66	61
Ireland	42	39	38	40	39	38
Lithuania	35	37	35	36	35	34
<u>Norway</u>	<u>33</u>	<u>33</u>	<u>34</u>	<u>34</u>	<u>34</u>	<u>34</u>
Poland	52	52	53	52	51	51
Romania	36	36	36	36	36	37
Russian Federation	39	37	36	35	35	34
Ukraine	33	32	31	30	29	28

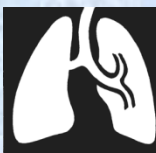
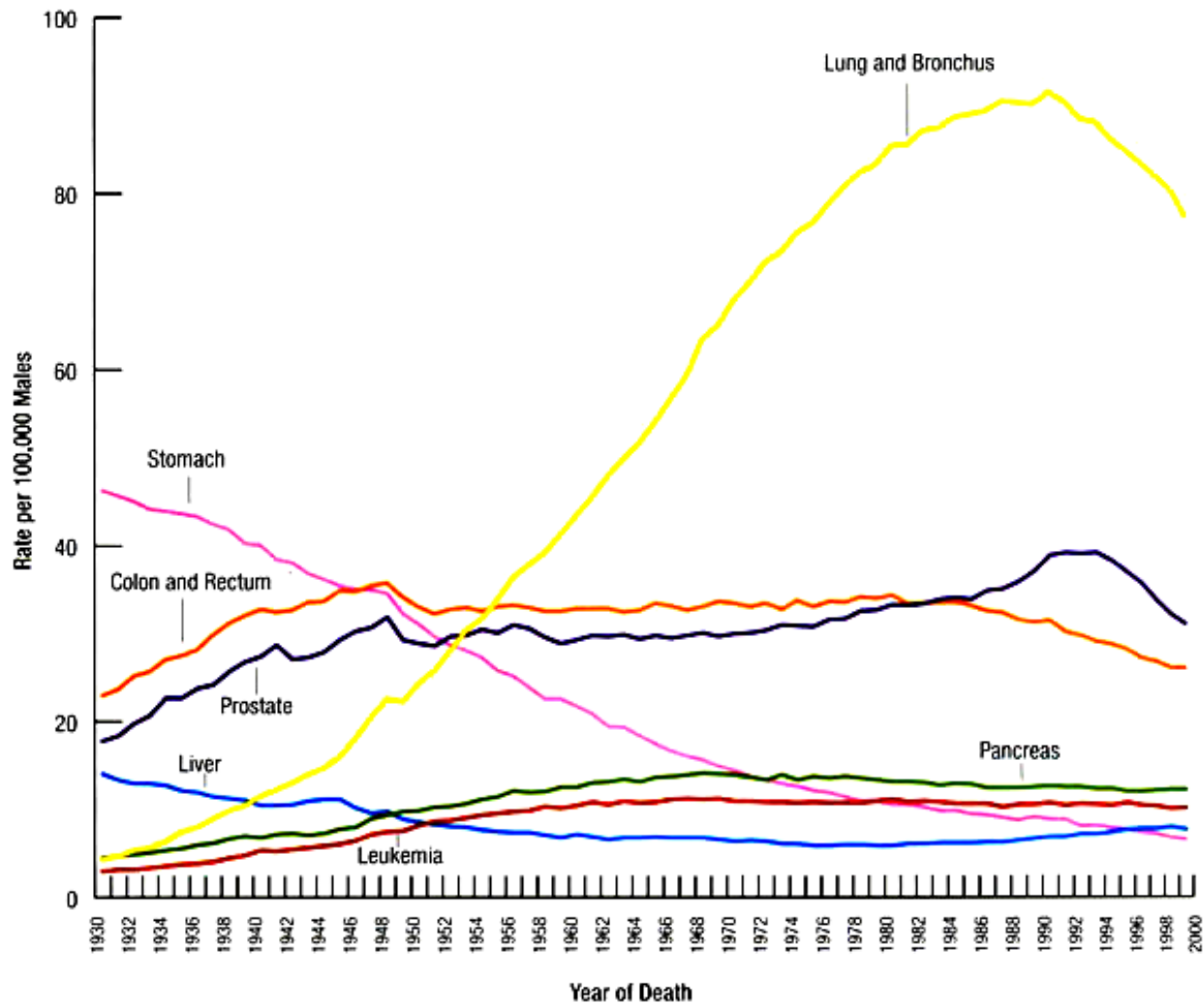


FIGURE 4

Annual Age-adjusted Cancer Death Rates* Among Males for Selected Cancer Types, US, 1930 to 1999



*Rates are age adjusted to the 2000 US standard population.

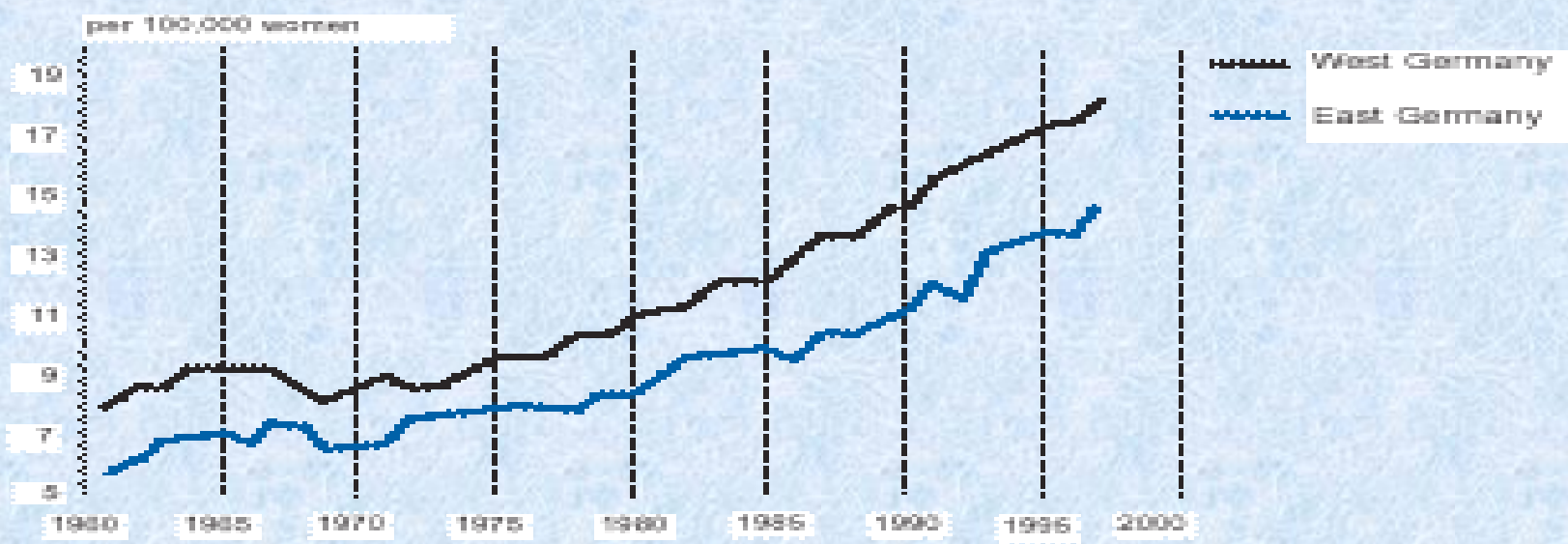
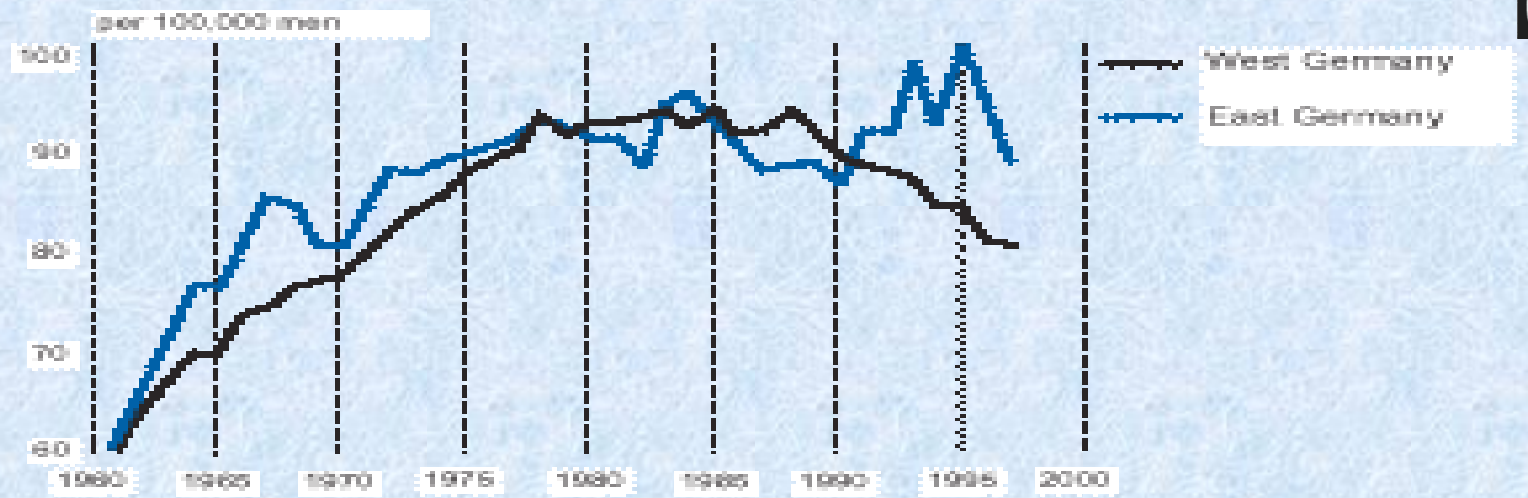
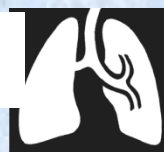
Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the lung and bronchus and colon and rectum are affected by these coding changes.

Source: US Mortality Public Use Data Tapes, 1960 to 1999, US Mortality Volumes 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

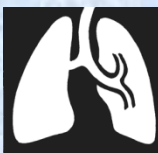


Figure 1

Age-standardized mortality rates of lung cancer in men and women^{1,2}

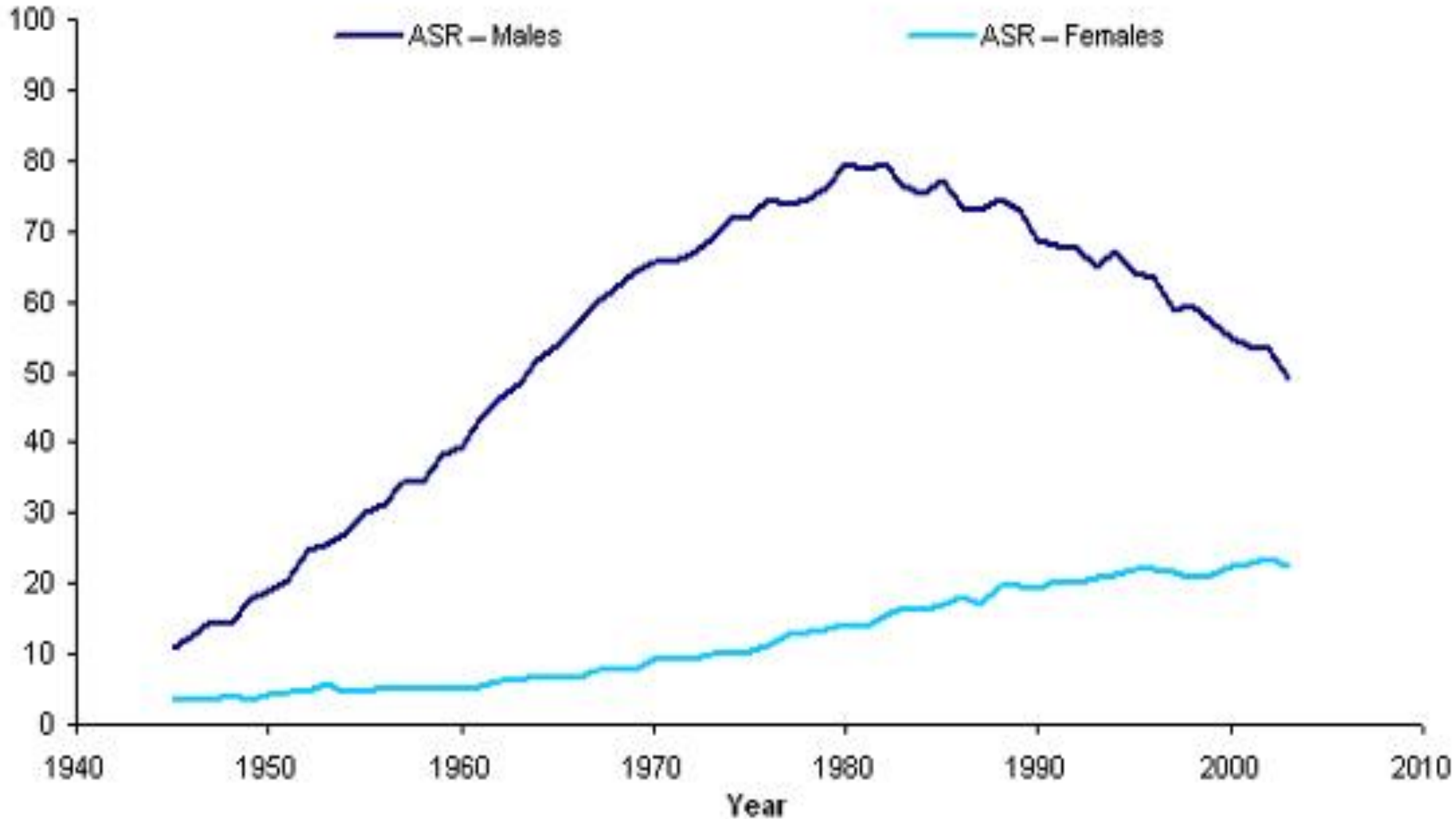


Standard population: Germany 1989 (West and East Germany)



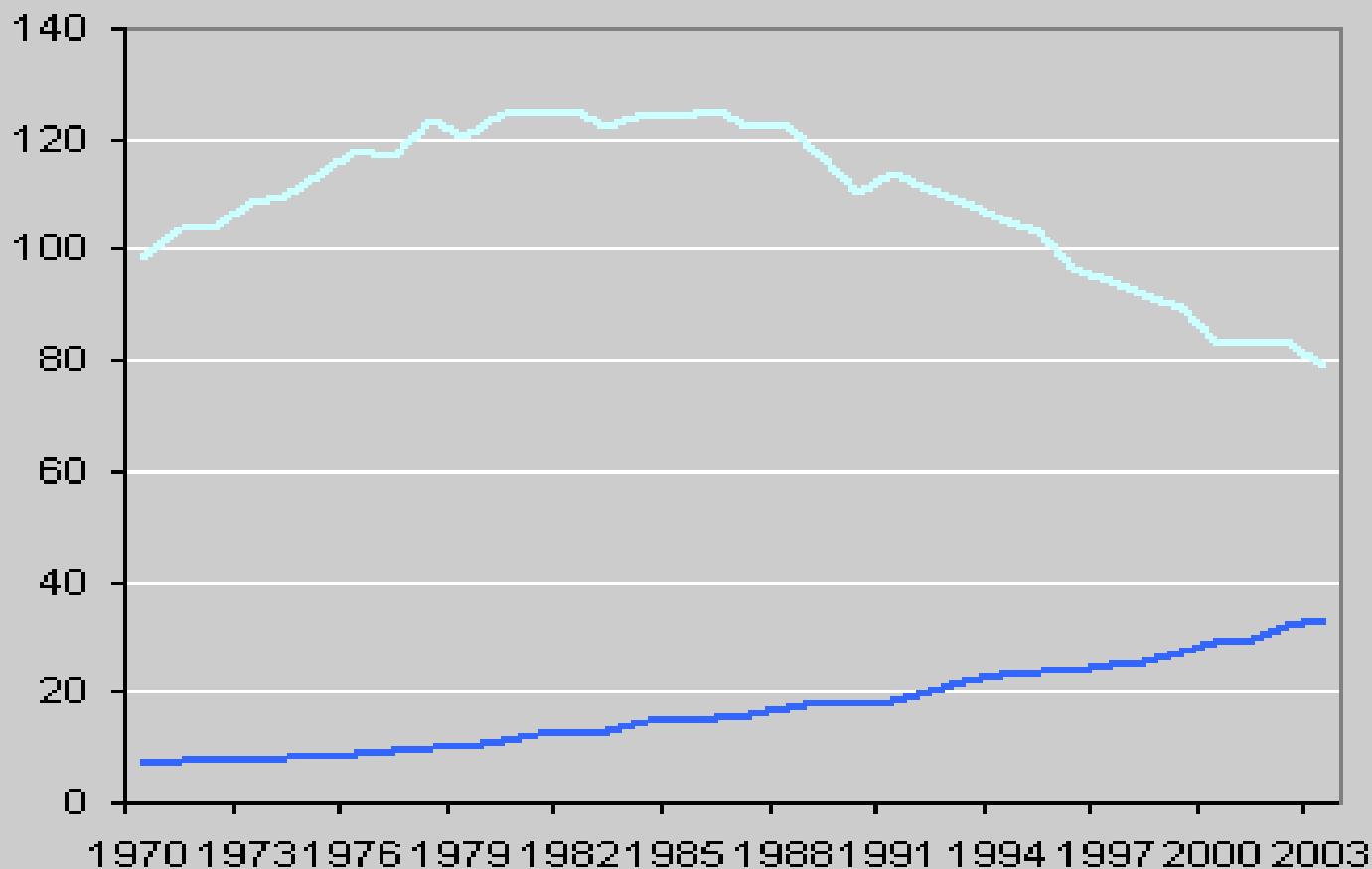
Mortality on LC in Australia

Per 100,000





Mortality in Netherlandes to 100 000 inhabitants

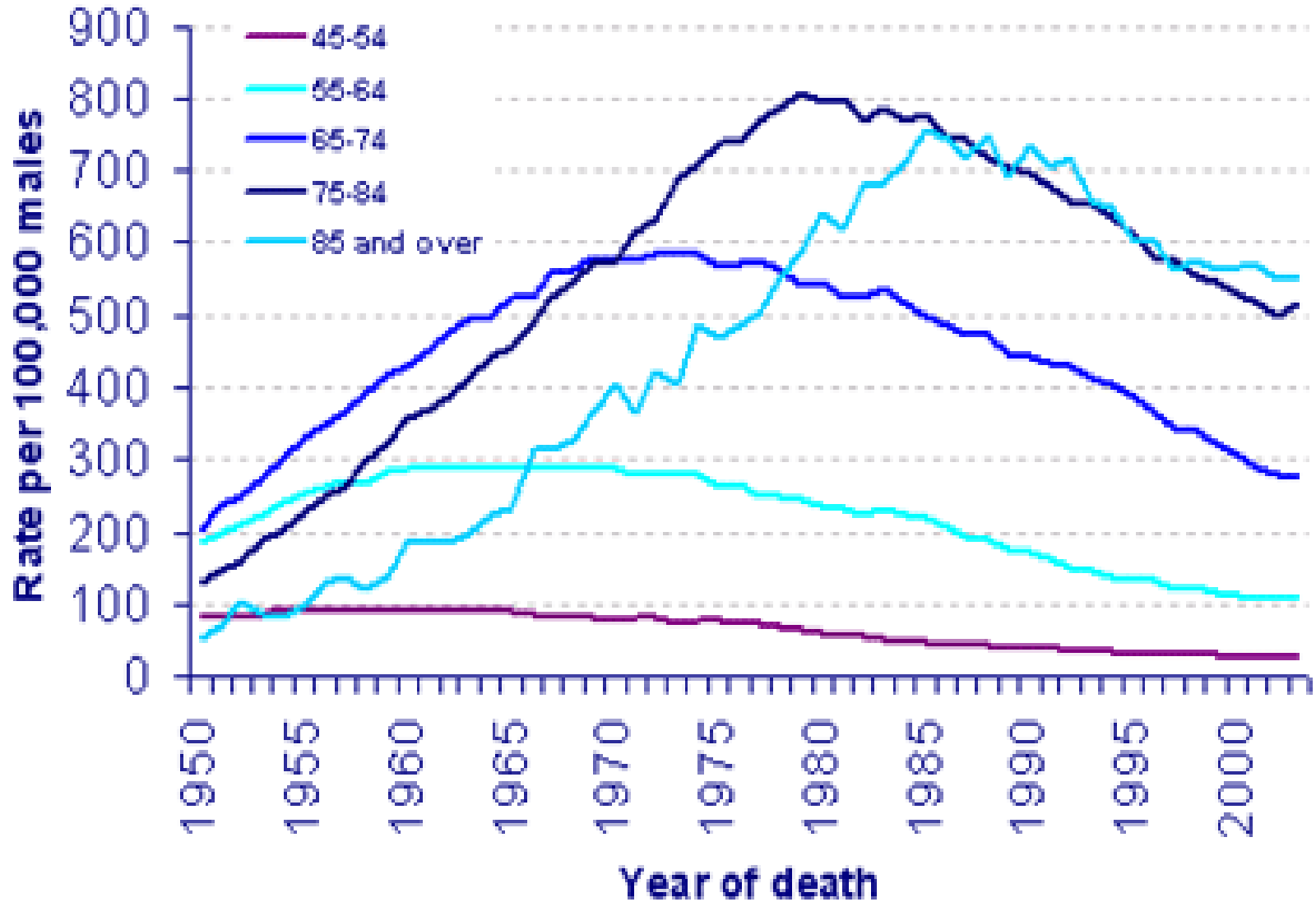


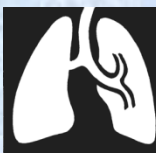
Source: CBS

— Men — Women

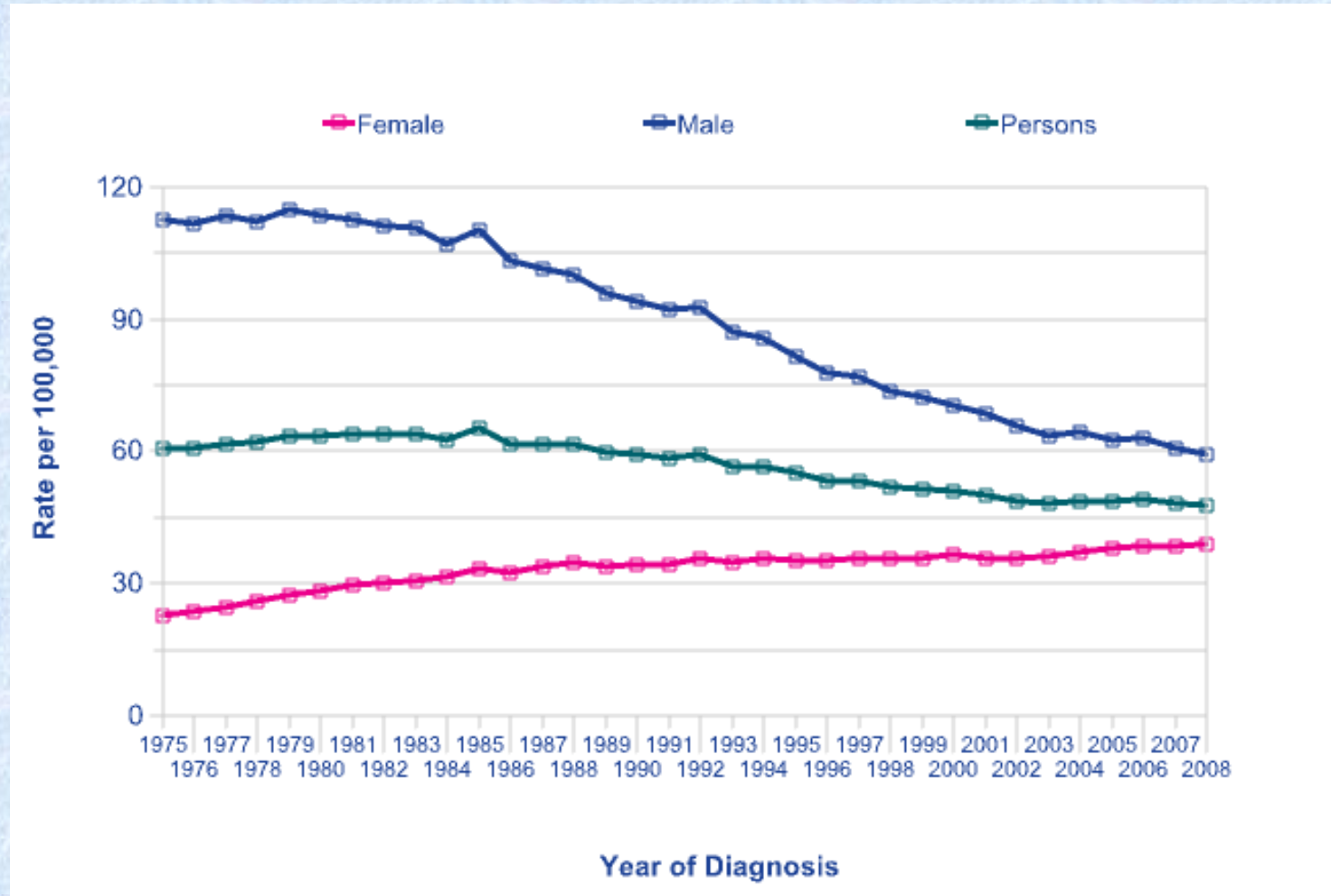


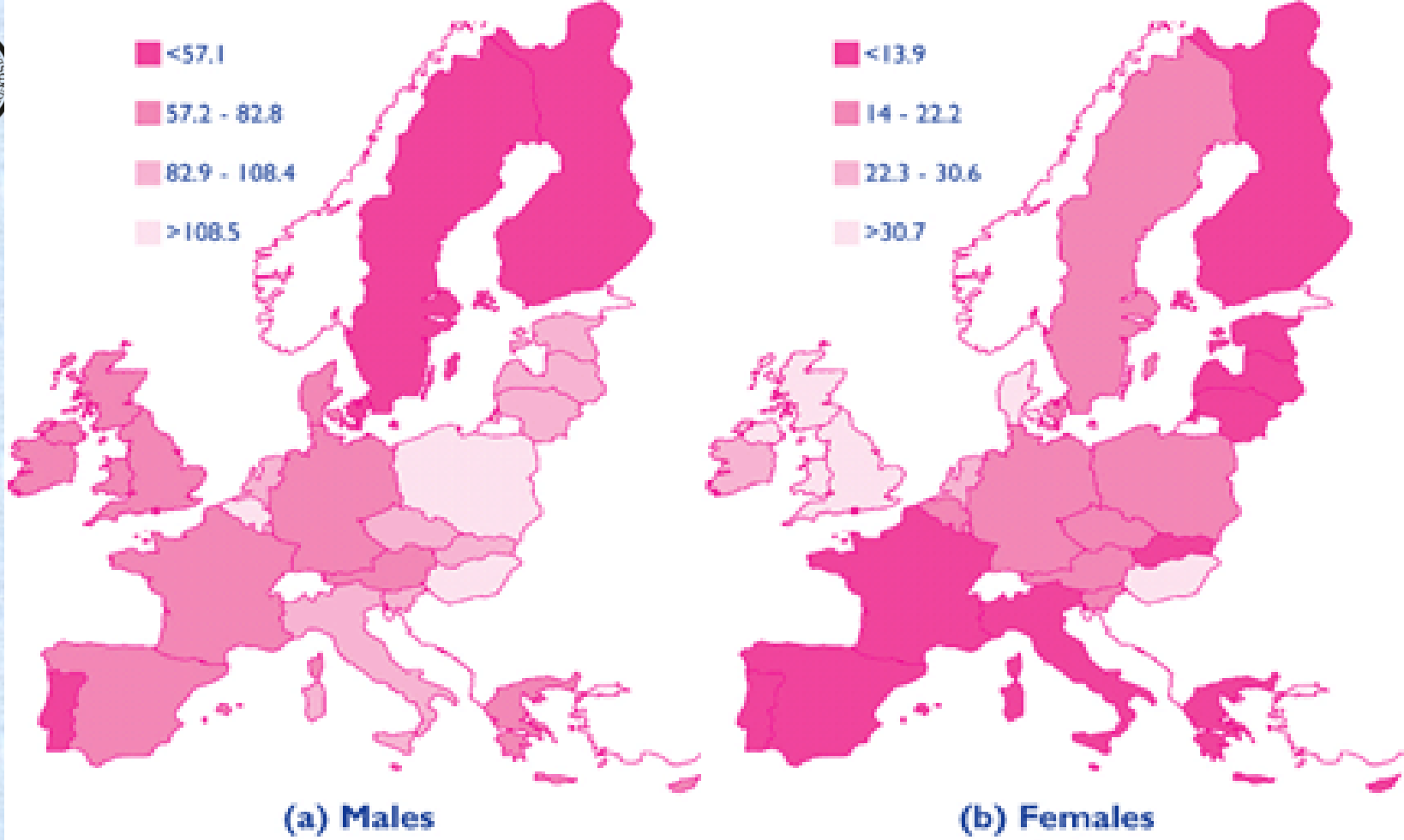
Figure 2.3: Age-specific mortality of lung cancer, males, England and Wales, 1950-2003





Lung Cancer (C33-34), European Age-Standardised Incidence Rates, Great



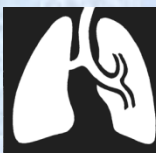


Lung cancer is the 3th most frequent TU diagnosed in EU

year 2000: 243,600 newly diagnosed cases of LC

Ratio men to women 4:1.

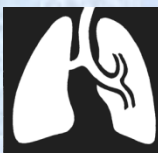
**Highest incidence for men is in Hungary, Poland and Belgium
for women in Denmark, Hungary and UK**



Lung Cancer

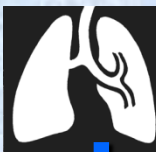
Situation in the Czech Republic

- 5411 deaths in 2008 (80 deaths of TB), 5536 in 2005, 2015 5 200 deaths
- Incidence in men 91,8/100 000, in women 34,5/100 000 in 2005
- **Stable figures in men, linear increase in women**
- Leading cause of cancer death in men, 4. in women (breast, uterus-ovarium, colon)
- Change in the ratio men : women from 17/1 (in 1970) to 3/1 (in 2008)



What are the Risk Factors for Lung Cancer?

- Tobacco and secondhand smoke
- Asbestos
- Radon
- Most people who develop lung cancer today have either stopped smoking years earlier or have never smoked

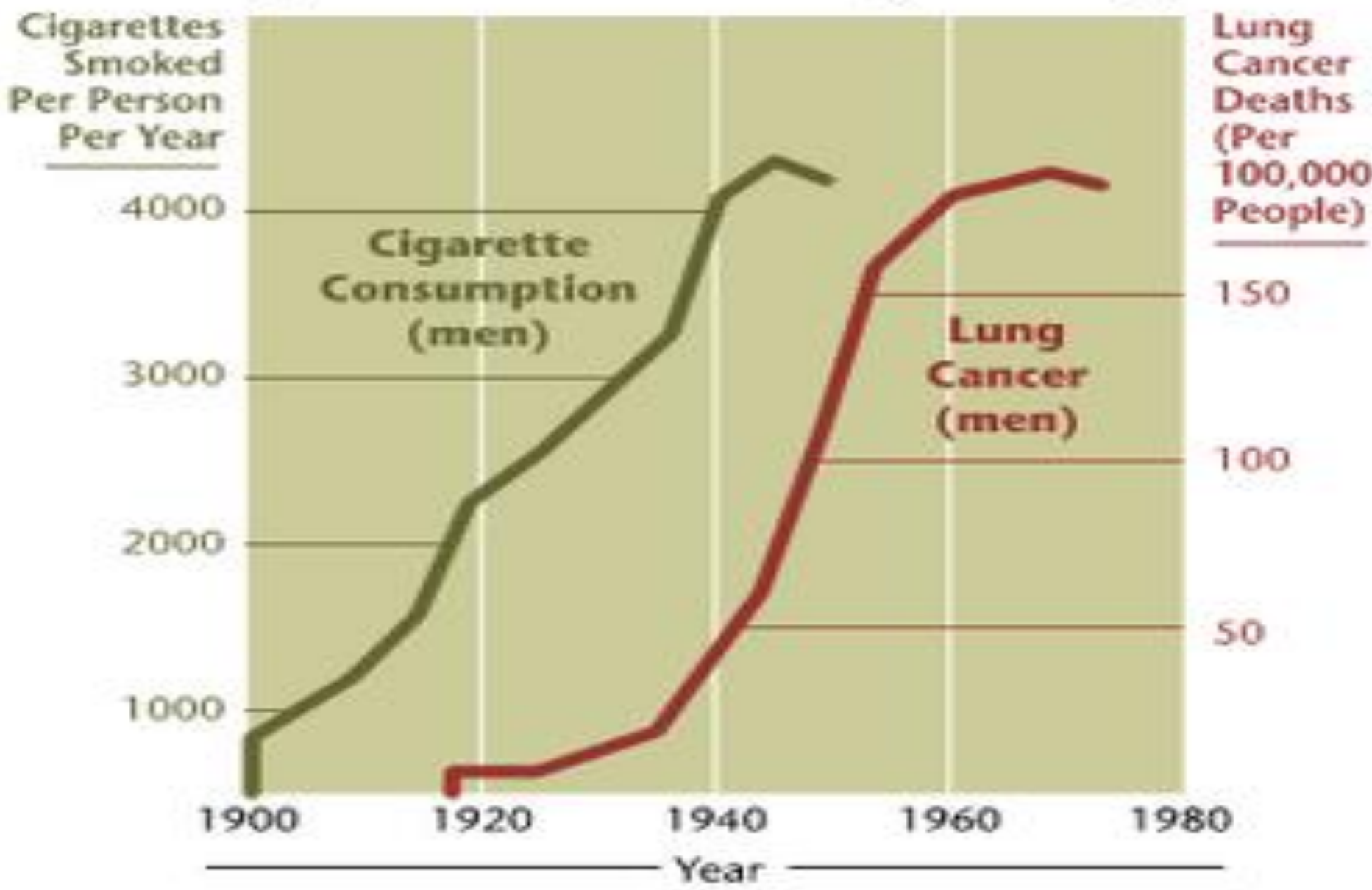


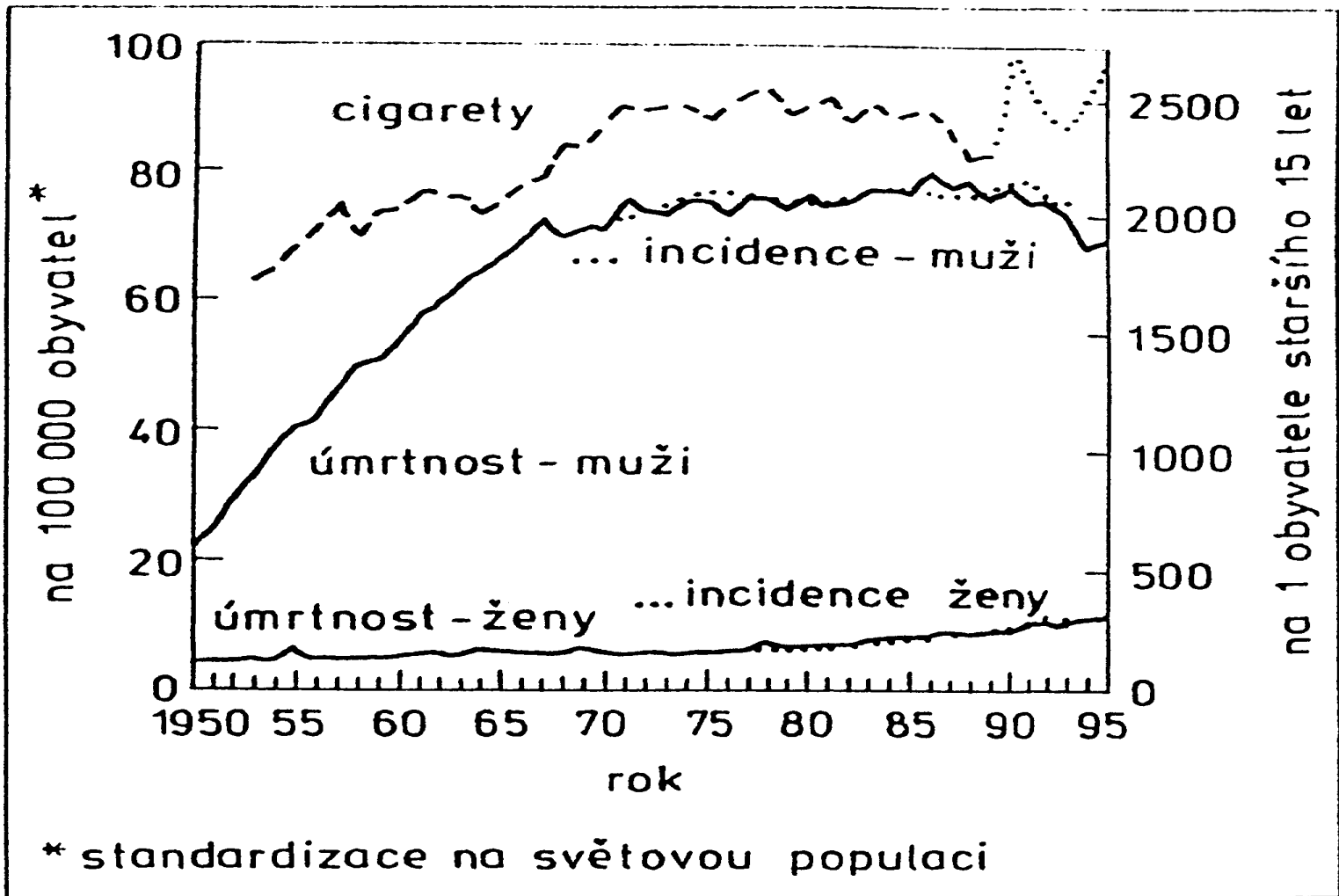
Lung cancer epidemic = Smoking epidemic

- LC incidence follows the smoking incidence with the latency of 20-30 years
- USA smokers in 1965 - 42%, in 1995 - 25% (men)
- WHO in 1998 47% men and 12% women are smokers in the world
- Smoking related LC - 83-94% in men, 57-80% in women



20-Year Lag Time Between Smoking and Lung Cancer

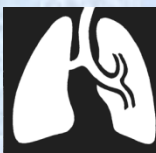




Standardizovaná úmrtnost (1950-95) a incidence nových onemocnění (1970-93) plicní rakovinou (na 100 000), podle pohlaví, a počet prodaných cigaret na 1 obyvatele ve věku 15 a více let (1953-95) v České republice




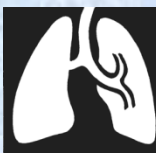
Smoking and other risk factors



- Smoking caused lung cancer in 94% men and 52% women (*Kubík et al: Cancer, 1995, 7, 2452-60*)
- CR: 40 % men and 25 % women in the age 30 - 60 years are smokers (*UZIS ČR 2004*)
- 10 – 18 % of smokers will suffer from lung cancer
- coincidence with chronic lung diseases
- genetic predisposition
- cumulative effect of risks !!



Morfo Epid. Ca		1985	90	97	98-00	02	01-3	2005	04-7 
Aden ca	ČR	55 %	52 %	51 %		51 %		49%	
	FN M				49 %		37 %		
	I.TRN Brno ČB								29% 50% 59%
Small ca	ČR	13 %	17 %	19 %		20 %		23%	30%?
	FN M				26%		34 %		
	I.TRN Brno ČB								28% 19% 14%
Nedif - ca	ČR	23 %	23 %	23 %		22 %		23%	
	FN M				18 %		18 %		
	I.TRN Brno ČB								24% 27% 23%
Aden ca	ČR	9 %	8 %	7 %		7 %		5%	
	FN M				7 %		11 %		
	I.TRN Brno ČB								19% 4% 4%

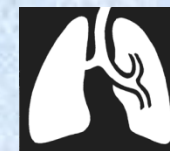


Diagnostic and therapy in men

			2008
• Histology verification	ČR		78%
	highest	JM	87%
	lowest	PAR	63%
• up to 2 weeks diagnosed			69 %
• over 6 weeks			8 %
• I. TNM	12,4%		10%
• II. TNM	7,4%	2005 -2008	7%
• III. TNM	28,1%	→	28%
• IV. TNM	52,1%		55%
• Surgical th.	11,4%... 11,1%		
	most in	PAR	14,5%
• RT	23,9.....22,8%		
• CHT	35,3%....39,5%		
• not treated	41,1%.....37,6%		



Diagnostic and therapy-women



2008

73%

histology verification ČR

highest

OLO

86,9%

lowest

HK

60%

up to 2 weeks diagnosed

67%

over 6 weeks

11%

I. TNM

13,2%

12%

II. TNM

6,1%

2005-8

7%

III. TNM

26,9%

25%

IV. TNM

53,8%

56%

Surgical th

13,2%...13,1%

most in

JHM

16,8%

RT

20,7%

CHT

32,3%....36,3%

not treated

44,8%....39,1%



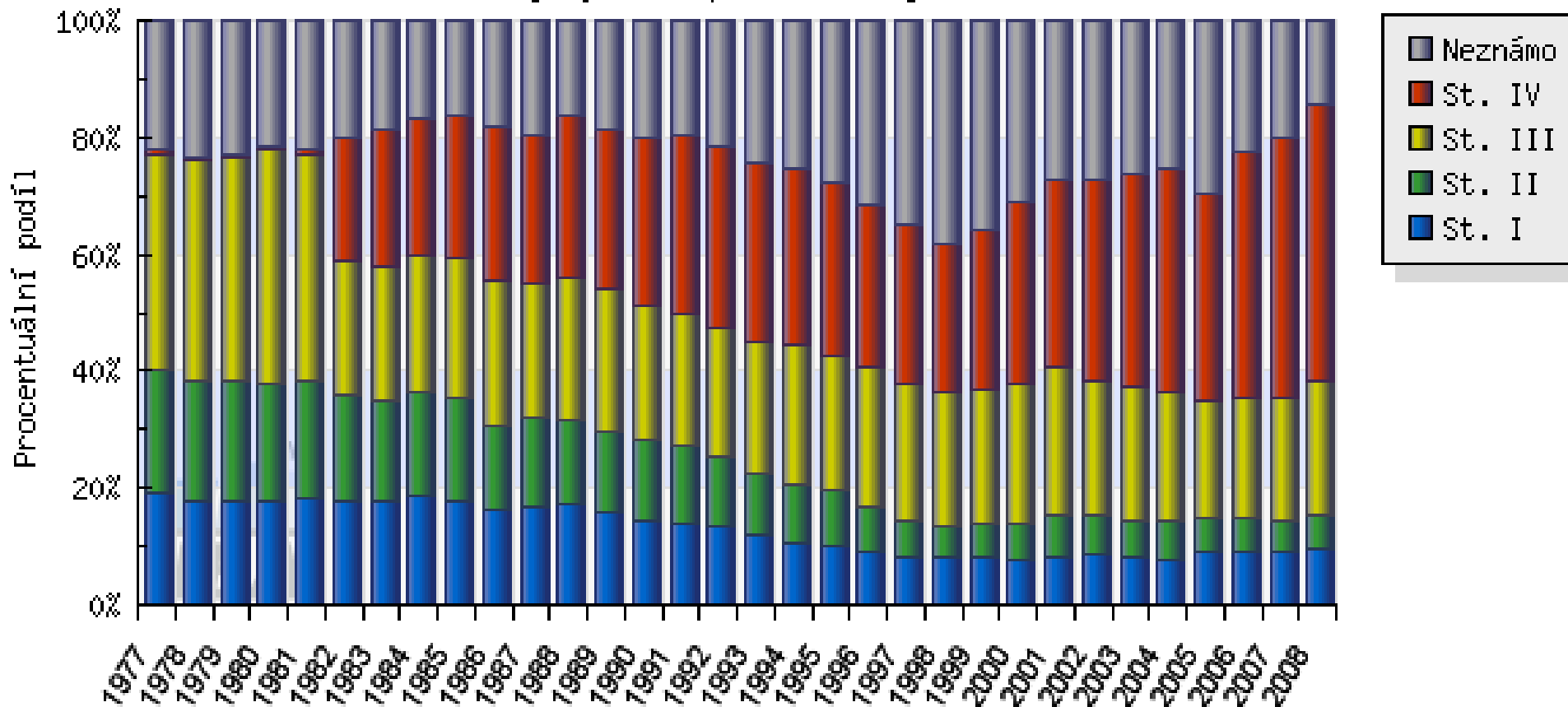
Patients with LC in TNM stages I a II and the types of therapy in CR 1980 - 2005

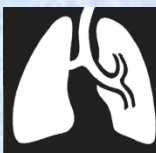
	1980	1996	2008
TNM I a II	39 % m, 28 % w	24 %	17% m, 19 % w
Resection of TU	7,0 %	8,3 %	11,1 % m, 13,1%
radioterapy (RT)	26 %	21 %	22 %
chemoterapye (CHT)	18 %	22 %	38 %
<i>abs. number of pts, = 100 %</i>	<i>n = 5606</i>	<i>n= 6346</i>	<i>n= 6236</i>

Clinical stadium

C34 - ZN průdušky - bronchu a plíce

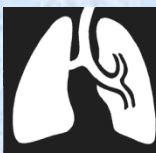
vývoj zastoupení klinických stadií





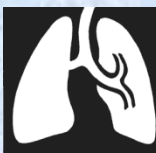
5 year survival of diagnosed in the 1980 - 84 and 1999 - 2003

	1980-84	99-2003
Men in I. and II. st. TNM	8,5%	28 %
in III. a IV. st.	1,7%	4 %
all stages	4,4%	<u>8,3%</u> (10,2%)
• Women all stages	7,9%	<u>10,3,%</u> (12,3%)
• EU 5year survival:	men 10%	women 11%
• USA „ „ :	men 12%	women 17%



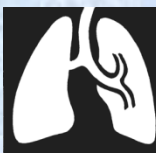
Epidemiological conclusions

- decreasing incidence of LC in men, plateau point of incidence of women is nearing...hopefully
- problems - high incidence of LC in men
 - late diagnostics
 - operability only 11,4% in men and 13,2 in women
 - in 2008 6528 new cases , died 5411 !!
 - number of „ NO therapy“ didnt change in the past 20 years
- positive data
 - we did not reached the highest EU incidence in women
 - increased 5 year survival
 - higher level of verification of LC
 - lower late diagnosed pts over 6 weeks



Patogenezis, pathology

- Ciliated cells fade away – multiplication of basal cells – hyperplasy and metaplasia of multilayer epidermoid epithel – loss of polarity – atypical nuclei - abnormal mitózes – dysplasia mild, moderate, severe - proliferation of the cells - ca in situ
- field cancerization x progenitor cell
- reversibility of changes
- histology
 - Small cell ca – agresive, frequent metastases
 - spindle cells - metastases later, typical cauliflower shape - karfiol
 - adenocarcinoma - gland type, cave metastases and periferal leasionsbronchioalveolar ca
 - nedifferentiated – large cells ca



Pathology- 2

- Development of cancer in the mucosa up to 15 years
- doubling time
- death - 1 kg tumor mass

	doubling time	years to diagnosis	to death
• Small cell ca	29 days	2,8	3,2
squamous ca	88 days	8,4	9,6
adenoca	161 days	15,4	17,6

- central, peripheral

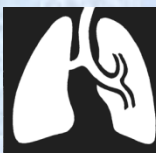
Metastases to - liver, suprarenal glands, bone, brain

- Direct invasion
- lymphatics
- hematogenous



Symptoms of lung cancer

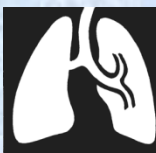
- **cough** 75%
- **weight loss** 68%
- **dyspnoe** 60%
- **haemoptysis** 20-35%
- **bone pain, clubbing** 25%
- **fever** 15-20%
- **Vena cava syndrome** 4%
- **recurrent laryngeal palsy** 5%
- **Fatigue, chest pain**



Paraneoplastic syndrome

Endocrine syndromes

- **Cushing's sy (ACTH) 2-7%, SCLC 30-50%,**
- **Nonmetastatic hypercalcemia - squamous ca 15%**
- **Inappropriate antidiuretic hormone in SCLC , hyponatremia, urine osmolarity over 500 mOsm.kg⁻¹**
- **Gynecomastia (HCG)**
- **Arthralgia .. pseudoreumatism**



Paraneoplastic syndrome

Neurological syndrome

- Symptoms peripheral neuropathy, encephalomyelitis
- Lambert Eaton myasthenic syndrome

Cutaneous

- Erythema gyratum repens, acanthosis nigrans

Haematological

- microcytic anemia in 20%, haemostatic disturbance

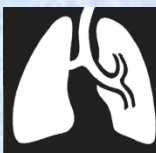
Clubbing

Anorexia, nausea, vomiting



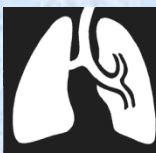
How is Lung Cancer Diagnosed?

- Because almost all patients will have a tumor in the lung, a chest x-ray or CT scan of the chest is performed
- The diagnosis must be confirmed with a biopsy or cytology
- The location(s) of all sites of cancer is determined by additional CT scans, PET (positron emission tomography) scans, and MRI (magnetic resonance imaging)
- It is important to find out if cancer started in the lung or somewhere else in the body. Cancer arising in other parts of the body can spread to the lung as well- metastases



Diagnosis of lung cancer

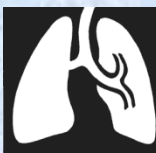
- **screening method does not exist... (??)**
- **passive approach – waiting for symptoms**
- **personal history and physical examination, performance status**
- **pulmonary function tests- air flow limitation-Risk factor**
- **sputum cytology, chest X ray, chest CT scan**
- **bronchoscopy (TBNA, brush, forceps biopsy....), cytology, histology**
- **autofluorescence, EBUS**
- **transparietal fine needle lung biopsy**
- **PET, bone scan, mediastinoscopy (?)**
- **thoracoscopy**
- **operability ???**



Staging of lung cancer

prognosis
therapy

NSCLC – SCLC

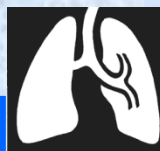


The rules for TNM staging

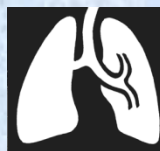
- T- tumor T0,T1-4,
- N - lymphonodes N0, N1-3
- M – metastases M0, M1
- clinical cTNM vs pathological pTNM (based on surgical and pathological examination)
- cTNM – therapeutical options, pTNM - prognosis
- According established T-, N-, M- are tumors divided to the stages. The stage should be fixed in the documentation and should not to be changed



Bronchogenic carcinoma-TNM

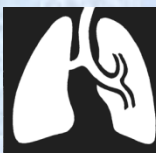


- TX- malignant cells in sputum but no X-ray and bronchoscopical findings
- T0- no evidence of lung cancer
- Tis - ca in situ
- T1 < 3 cm, not in the main bronchus
- T2 > 3 cm, involving main bronchus, > 2 cm distal to the carina, visceral pleura, atelectasis or pneumonia in part of the lung (T2 also if the size is ≤ 3 cm if any non-size-based descriptor were present)



Bronchogenic carcinoma-TNM

- T3 - chest wall, diaphragm, main bronchus < 2 cm from carina but without involvement of it, mediastinal pleura, atelectasis, pneumonia in the entire lung
- T4 – any size with invading to the mediastinum, heart, great vessels, trachea or satellite tumor/s in the same lobe, malignant pleural or pericardial effusion

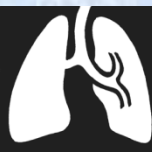


Changes in classification T and M since 2011

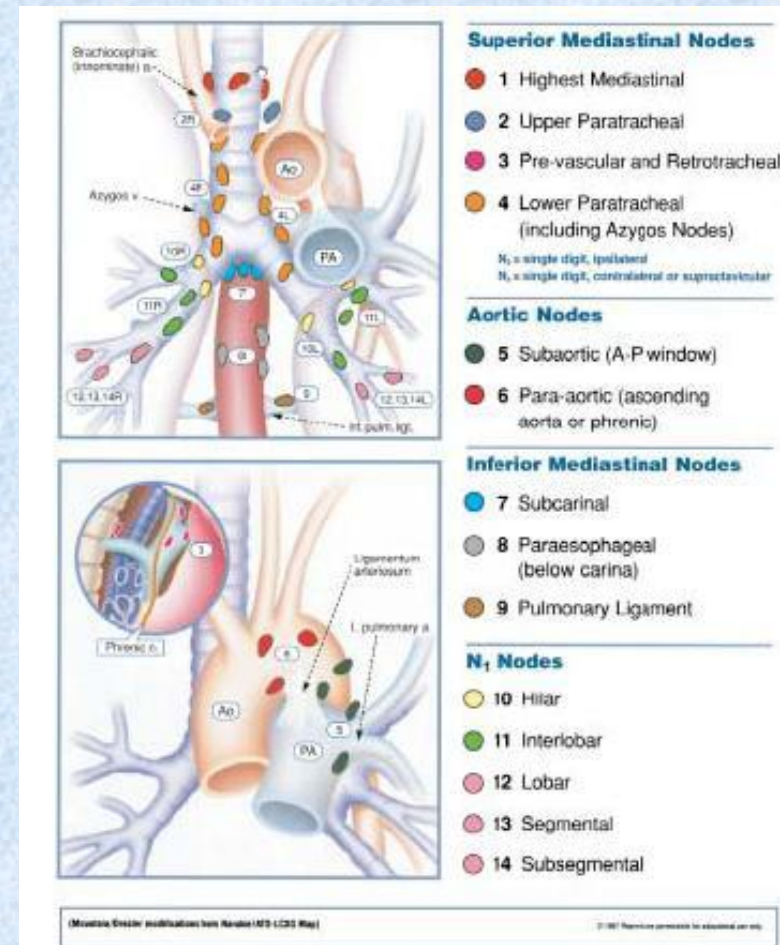
- T1 ---- T1a ≤ 2 cm and T1b ≥ 2 cm,
- T2 ---- T2a 3-5 cm, T2b ≥ 5 a ≤ 7 cm, T2 ≥ 7 cm will be T3
- T2 may be in main bronchi >2 cm from carina, invading visceral pleura, may be partly atelectasis
- T3 >7 cm; involve chest wall, diafragma, pericard mediastinal pleura, in the main bronchi <2 cm from carina, full atelectázis, **separat nodul/s in the same lobe (earlier T4)**
- T4 invading mediastinum, heart, great vessels, carina, trachea, oesophagus, vertebrae;
separát tumor nodules in ipsilateral lobus (earlier M1)
- N clasification –no change
- M1a separát tumor nodule in contralateral lobus; **pleural nodules or malignant pleural or pericardial effusion (earlier T4)**
- M1b distant metastases

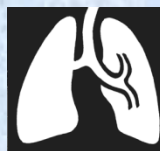


Bronchogenic carcinoma-TNM



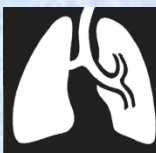
- NX – N cannot be assessed
- N0 – No regional lymph node metastasis
- N1 – ipsilateral peribronchial, intrapulmonary, hilar (code 10-14) also infiltrated directly by tumor
- N2 – ipsilateral mediastinal and/or subcarinal (code 1-9)
- N3 – contralateral mediastinal, hilar, ipsi/ contralateral scalene or supraclavicular (contralateral 1-10)





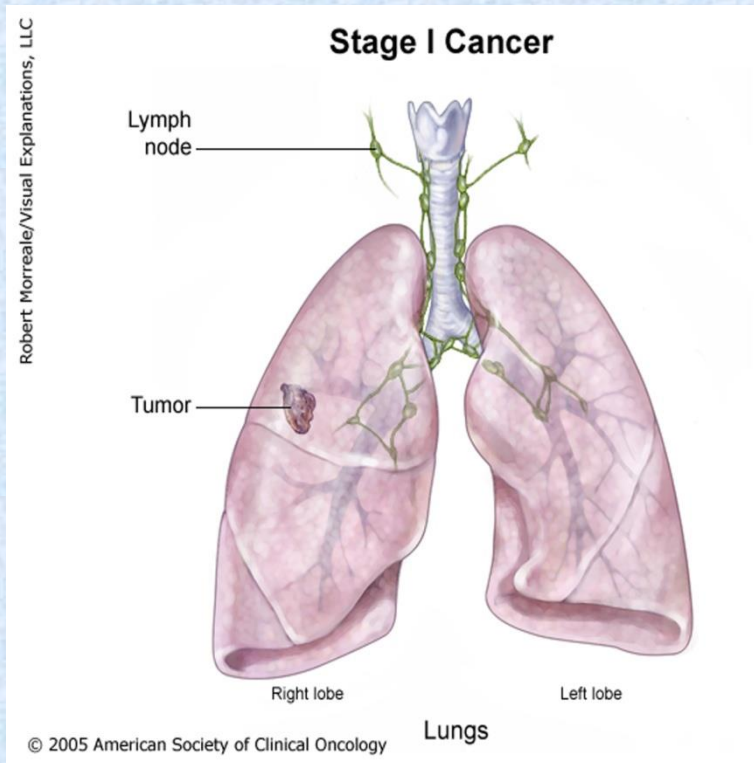
Bronchogenic carcinoma-TNM

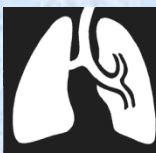
- MX - M cannot be assessed
- M0 – no distant metastasis
- M1 – distant metastasis or other tumor nodule in other ipsi/contralateral lobes



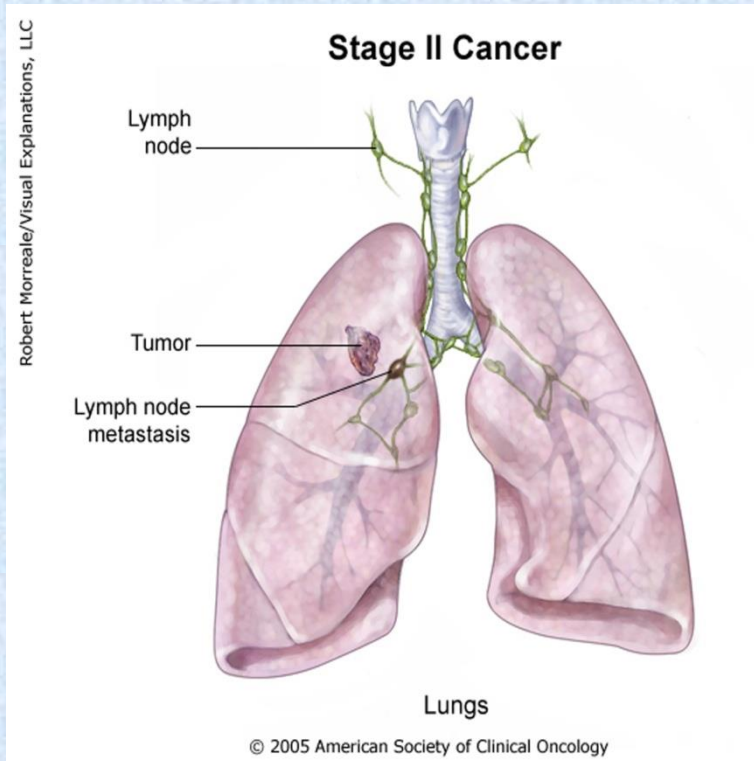
Stage I Non-Small Cell Lung Cancer

- Cancer is found only in the lung
- Surgical removal recommended
- Radiation therapy and/or chemotherapy may also be used

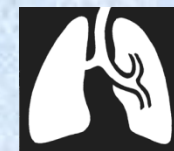




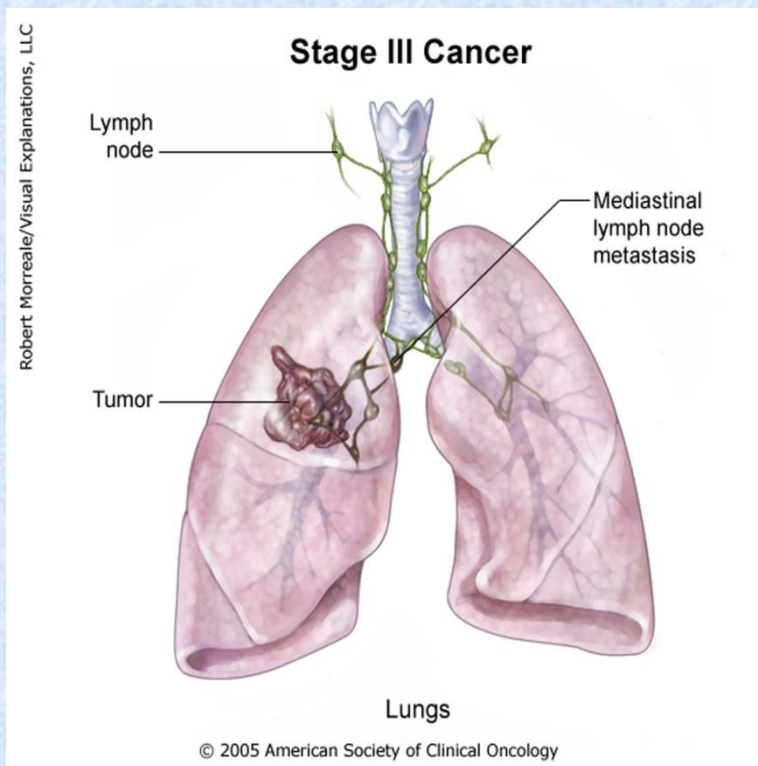
Stage II Non-Small Cell Lung Cancer



- The cancer has spread to lymph nodes in the lung
- Treatment is surgery to remove the tumor and nearby lymph nodes
- Chemotherapy recommended; radiation therapy sometimes given after chemotherapy



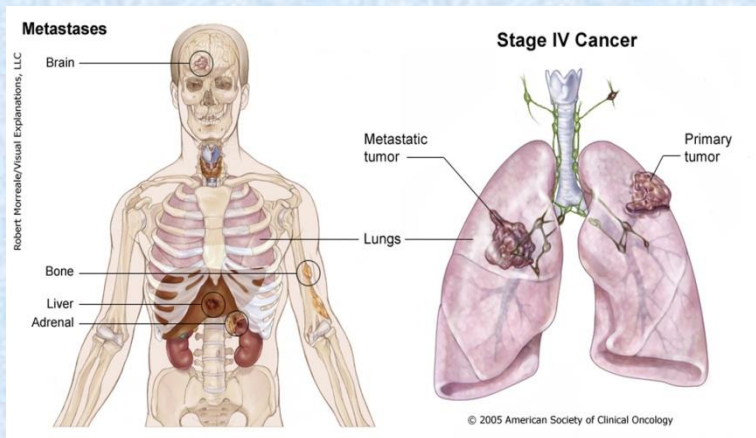
Stage III Non-Small Cell Lung Cancer



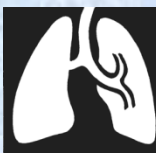
- The cancer has spread to the lymph nodes located in the center of the chest, outside the lung
- Stage IIIA cancer has spread to lymph nodes in the chest, on the same side where the cancer originated
- Stage IIIB cancer has spread to lymph nodes on the opposite side of the chest, under the collarbone, or the pleura (lining of the chest cavity)
- Surgery or radiation therapy with chemotherapy recommended for stage IIIA
- Chemotherapy and sometimes radiation therapy recommended for stage IIIB



Stage IV Non-Small Cell Lung Cancer

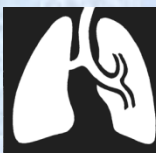


- The cancer has spread to different lobes of the lung or to other organs, such as the brain, bones, and liver
- Stage IV non-small cell lung cancer is treated with chemotherapy
- More information can be found in the *What to Know: ASCO's Guideline on Advanced Lung Cancer*



Other characteristic of tumors

- G- histopathological grading
GX not assessed
G1 well differentiated
G2 middle grade of differentiation
G3 poorly differentiated
G4 non differentiated
- *Resection of tumor under 2 cm in 160 pts with stage I TNM. In every pts were checked clinicopathological features : sex, age, smoking habits, CEA, and histopathological grade.*
- *Results: pts with poorly differentiated carcinomas showed significantly unfavorable survival $p < 0,001$ compared with pts with well-moderately differentiated carcinomas. Kobayashi N et al: J Thorac Oncol 2007, September,2(9):808-12*
- R- residual tumor after treatment
RX residual tumor not evaluated
R0 without residual tumor
R1 microscopic residue of tumor
R2 macroscopic residue of tumor

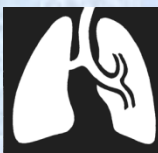


Lung Cancer Staging

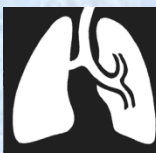
- Staging is a way of describing a cancer, such as the size of a tumor and if or where it has spread
- Staging is the most important tool doctors have to determine a patient's prognosis
- The type of treatment a person receives depends on the stage of the cancer
- Staging may be different for non-small cell lung cancer and small cell lung cancer
- Recurrent cancer is cancer that comes back after treatment



Small Cell Lung Cancer: All Stages

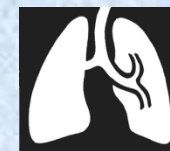


- Classified as limited stage (confined to one area of the chest) or extensive stage (not confined to one area of the chest)
- Patients with limited stage small cell lung cancer are best treated with simultaneous radiation therapy and chemotherapy
- Patients with extensive stage small cell lung cancer are treated with chemotherapy
- In patients whose tumors have shrunk after chemotherapy, preventive radiation therapy to the head cuts the risk that the cancer will spread to the brain and extends patients' lives



Small cell lung cancer

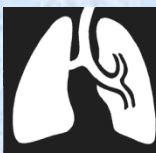
- TNM classification may be useful for SCLC too ! *Shepherd FA et al, J Thorac Oncol, 2007,1067-77*
- Veterans Administration Lung Cancer Group (VALG)+ IASLC:
- Limited disease – one hemithorax:
 - with/without ipsi- and/or contralateral N or supraclavicular lymphonodes
 - with/without ipsilateral pleural effusion regardless malignant or paramalignant (TNM IA-IIIB)
- Extensive disease - more extensive than described above (TNM IV)



Survival according TNM stages

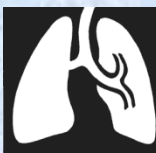
Mountain, 1997, Naruke 1988

cTNM	n	5 year surv. %	pTNM	n	5 year surv. %
cIA	687	61 65	pIA	511	67 76
cIB	1189	38 42	pIB	549	57 57
cIIA	29	34	pIIA	76	55
cIIB	357	24	pIIB	375	39
cIIIA	511	13	pIIIA	399	23
cIIIB	1030	5			
cIV	1427	1			



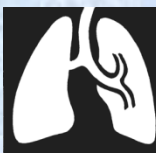
Differential diagnosis

- **metastatic disease**
- **other tumors – Hodgkin l., mesothelioma, thymoma**
- **benign tumors**
- **pleural effusion**
- **nontumorous masses**
 - tuberculoma**
 - pneumonia – lung absces**
 - sarcoidosis**
 - aspergiloma**
 - pulmonary emboli**



Screening ???

- 3 USA and 1 Czechoslovak study
chest X ray + sputum cytology
no effect on mortality
- biomarkers ?
- molecular genetics ?
- high risk population ?
- low dose spiral CT ?



Screening ???

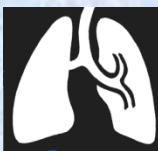
low dose spiral CT ?

Sone 0,48 % LC cases in screened group

Jett 1,5 %

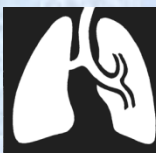
Henschke 2,7%

80-90% operability of screened cases



Lung Cancer and Early Detection

- No tests are recommended for screening the general population today but after NLCST may it be low dose spiral CT
- A low-dose helical computerized tomography (CT or CAT) scan is currently being studied for this purpose

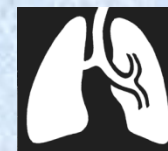


National Lung Cancer Screening Trial

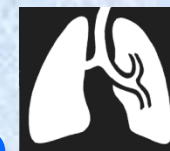
- The National Lung Screening Trial (NLST) compared two ways of detecting lung cancer: low-dose helical computed tomography (CT) and standard chest X-ray. Both chest X-rays and low-dose helical CT scans have been used to find lung cancer early, but the effects of these screening techniques on lung cancer mortality rates had not been determined.
- NLST enrolled 53,454 current or former heavy smokers from 33 sites and coordinating centers across the United States. Age 55-74 years
- On June 29, 2011, the primary results were published online in the New England Journal of Medicine and appeared in the print issue on August 4, 2011. These findings reveal that participants who received low-dose helical CT scans had a **20.0 percent lower risk of dying** from lung cancer than participants who received standard chest X-rays.
- This finding was highly significant from a statistical viewpoint
- non-contrast helical diagnostic CT of the lung is \$300
- no lung cancer mortality benefit for those who got chest X-rays.
- Reimbursement for screening CT scans is not provided by most insurance carriers.
- Up today not general recommendation for screening in the world.. But it may be and must wait



NLCST

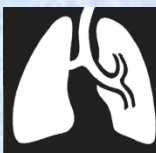


- On average, over all three screening rounds, 24.2 percent of the low-dose helical CTs were positive and 6.9 percent of the chest X-rays were positive and led to a diagnostic evaluation. Among people who had multiple annual screens (up to three screens) 39.1 percent had at least one positive screen in the CT arm and 16.0 percent had at least one positive screen in the chest X-ray arm. Diagnostic evaluation most frequently consisted of further imaging, and invasive procedures were rare.
- 96.4 percent of the low-dose helical CT tests and 94.5 percent of the chest X-ray exams were false-positive
- FP was confirmed noninvasively by the lack of change in the finding on follow-up CTs.



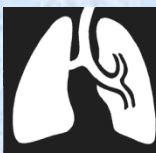
How is Lung Cancer Treated?

- Treatment depends on the stage and type of lung cancer
- Surgery
- Radiation therapy
- Chemotherapy (options include a combination of drugs)
- Targeted therapy
- Lung cancer is usually treated with a combination of therapies



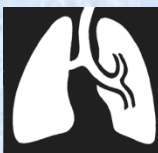
Therapy in Nonsmall cell LC

- I st TNM – surgery (or RT in inoperability)
- II st. TNM – surgery (or CHT/RT in inoperability)
- III A TNM – surgery, or neoadjuvant CHT 2-3 cycles gemcitabin-cis platina followed by surgery or RT/CHT
- Adjuvant CHT in resected IB-IIIA
- N2 found at surgery – adjuvant RT
- III B TNM – concomitant CHT(navelbin - platina)/RT , or only paliative RT
- IV st TNM wrong status – symptomatic therapy, good status CHT (gemcitabin a carboplat.) or paliative RT



Therapy in Small Cell Lung Cancer

- Limited disease: good general condition - CHT (cis platin + etoposide) and concomitant normo/hyperfractionated radiotherapy (RT) from 1.cycle 45-55Gy
- I stage surgery and adj CHT,
- LD SCLC wrong general status, polymorbidity, sequence CHT- 4-6 cycles/RT up to 60 Gy
- Extensive diseases – 6x CHT (etoposid-carboplatin)
- Relaps till 3 months - other CHT (gemcitabin, taxany, ifosf. , topotecan aj.)
- Relaps over 3 months the same CHT as in 1.line

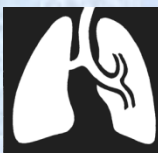


Cancer Treatment: Surgery

- The tumor and the nearby lymph nodes in the chest are typically removed to offer the best chance for cure
- For non-small cell lung cancer, a lobectomy (removal of the entire lobe where the tumor is located), has shown to be most effective
- Surgery may not be possible in some patients



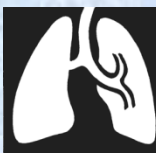
Cancer Treatment: Adjuvant Therapy



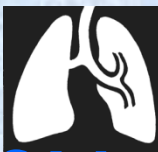
- Treatment given after surgery to lower the risk of the cancer returning
- May include chemotherapy, radiation therapy, and targeted therapy
- More information may be found in the *What to Know: ASCO's Guideline on Adjuvant Treatment for Lung Cancer*



Cancer Treatment: Radiation Therapy



- The use of high-energy x-rays to destroy cancer cells
- Side effects include fatigue, malaise (feeling unwell), loss of appetite, and skin irritation at the treatment site
- Radiation pneumonitis is the irritation and inflammation of the lung; occurs in 15% of patients
- It is important that the radiation treatments avoid the healthy parts of the lung

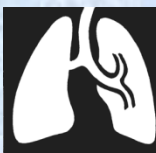


Cancer Treatment: Chemotherapy

- Use of drugs to kill cancer cells
- A combination of medications is often used
- May be prescribed before or after surgery, or before, during, or after radiation therapy
- Can improve survival and lessen lung cancer symptoms in all patients, even those with widespread lung cancer



Cancer Treatment: Targeted Therapy



- Treats lung cancer by stopping the action of abnormal proteins that cause cells to grow and divide out of control
- Bevacizumab (Avastin) prevents the formation of new blood vessels, which help feed the growth and spread of a tumor; given with chemotherapy
- Erlotinib (Tarceva) approved for locally advanced and metastatic non-small cell lung cancer
- Cetuximab (Erbix) (*monoclonal AB IgG1, which bind to receptor of epidermal growth factor (EGFR). Cetuximab is highly specific with higher affinity to this receptor than - epidermal growth factor (EGF) and transforming growth factor alfa (TGF-alfa)*) may be given with chemotherapy in situations where bevacizumab may be unsafe



Thank you
for your
attention

