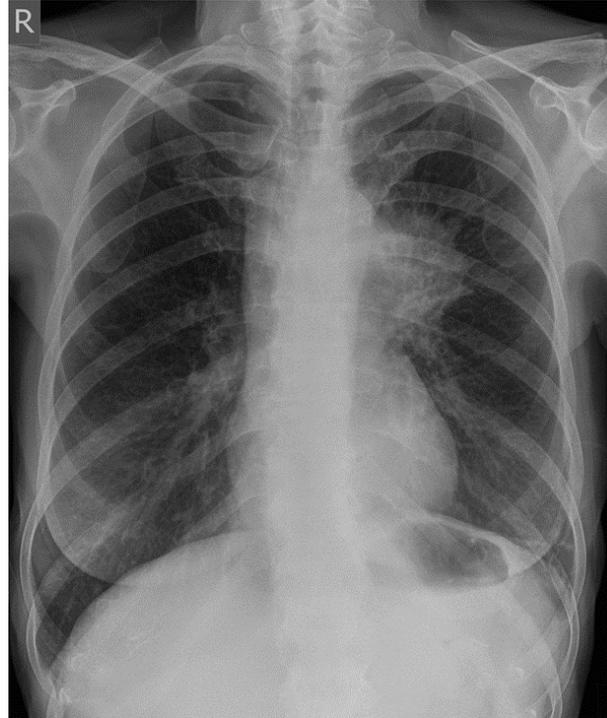


Cancers of the lung.



Christopher Whitty
Gresham College 2020.

We are steadily winning the war against most cancers.
In this talk we enter a bleaker world.

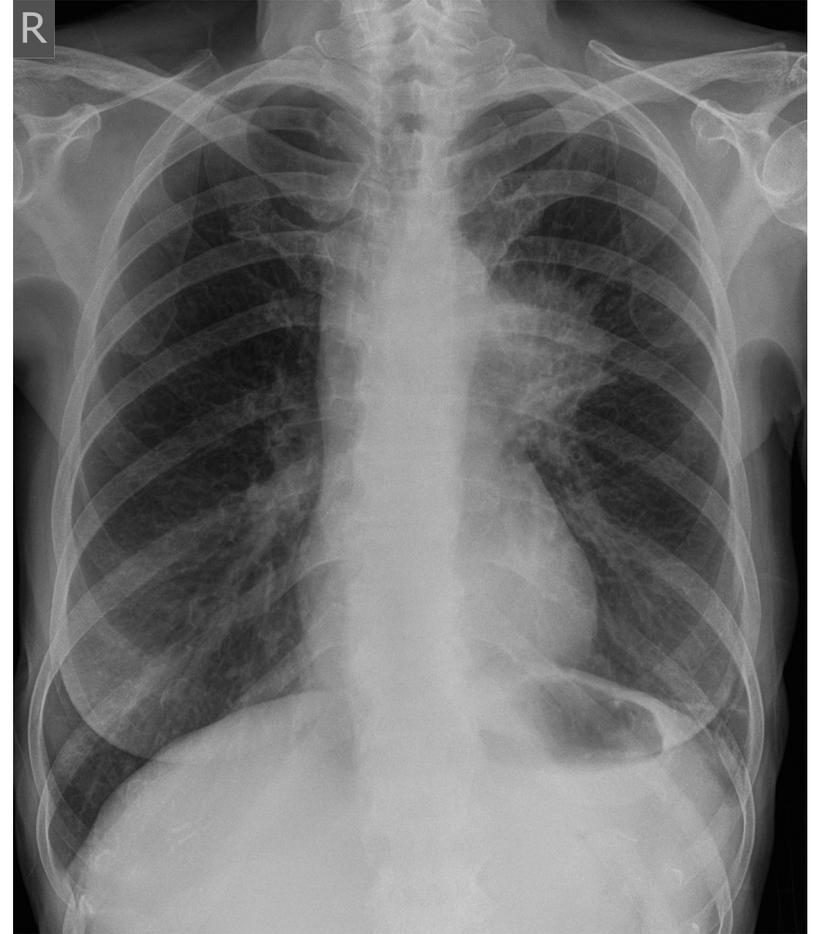
- The commonest cause of cancer deaths in the UK.
- Most diagnosed with lung cancer today will be dead within a year.
- The remarkable progress we have seen in treating other cancers slower in lung cancers.
- The great majority because a wealthy industry has pushed highly addictive products they know will kill their customers onto them at an early age.
- Others are the by-product of air pollution and industry.



Vincent Van Gogh

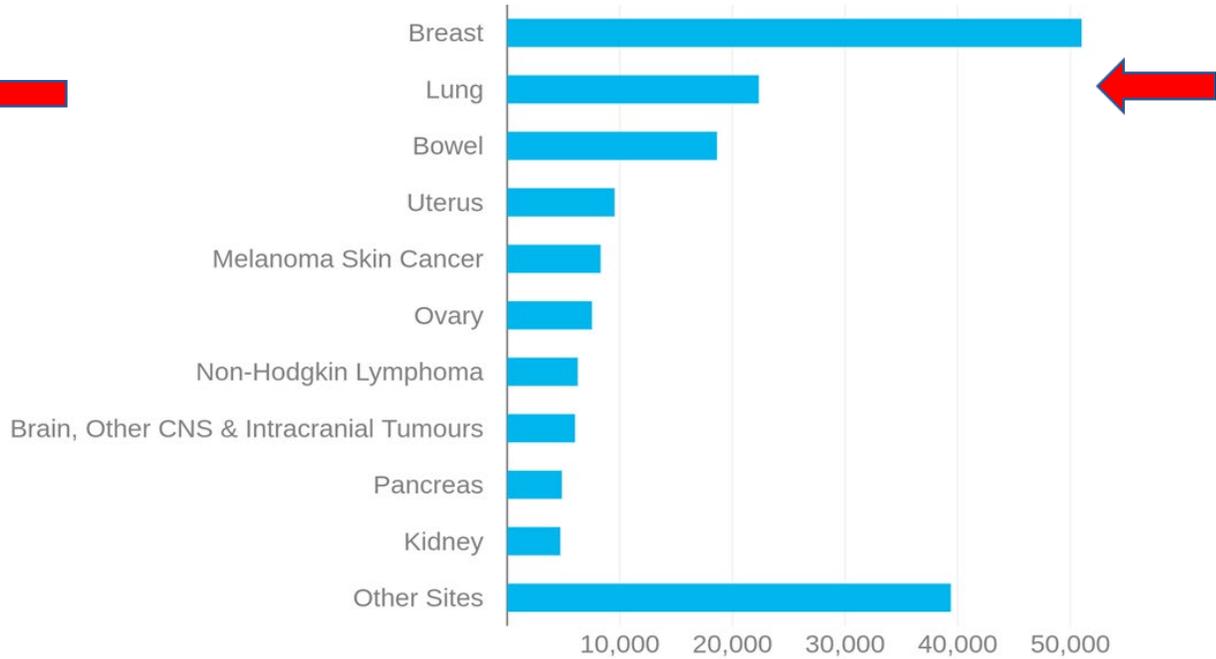
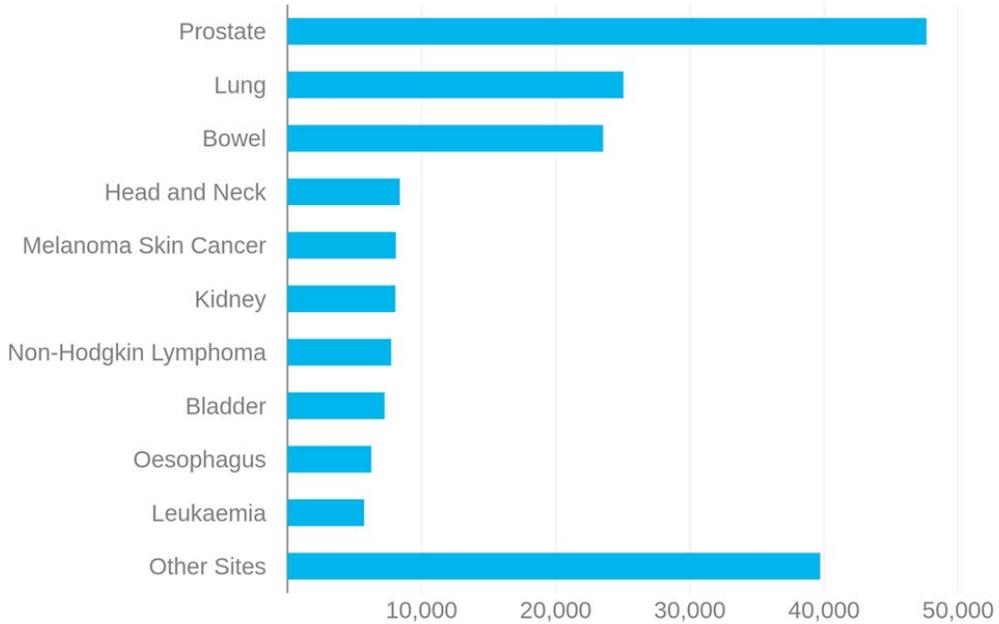
There is progress.

- In higher income countries smoking is declining, slowly.
- Substantial improvements in treating some (rarer) types of lung cancer.
- Earlier diagnosis would be transformative.
- The field of immunotherapy holds considerable promise.
- The asbestos epidemic, which drives mesothelioma, probably peaks this year.



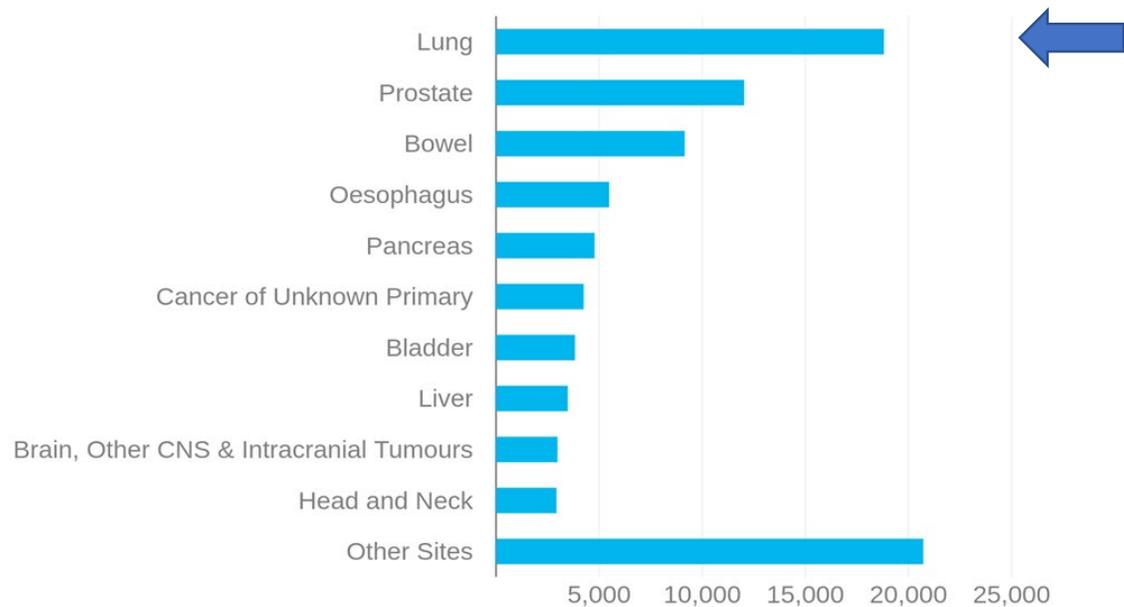
Ian Bickle, Radiopaedia.org

Second most common cancer in men (L) and women (R) in UK. CRUK.

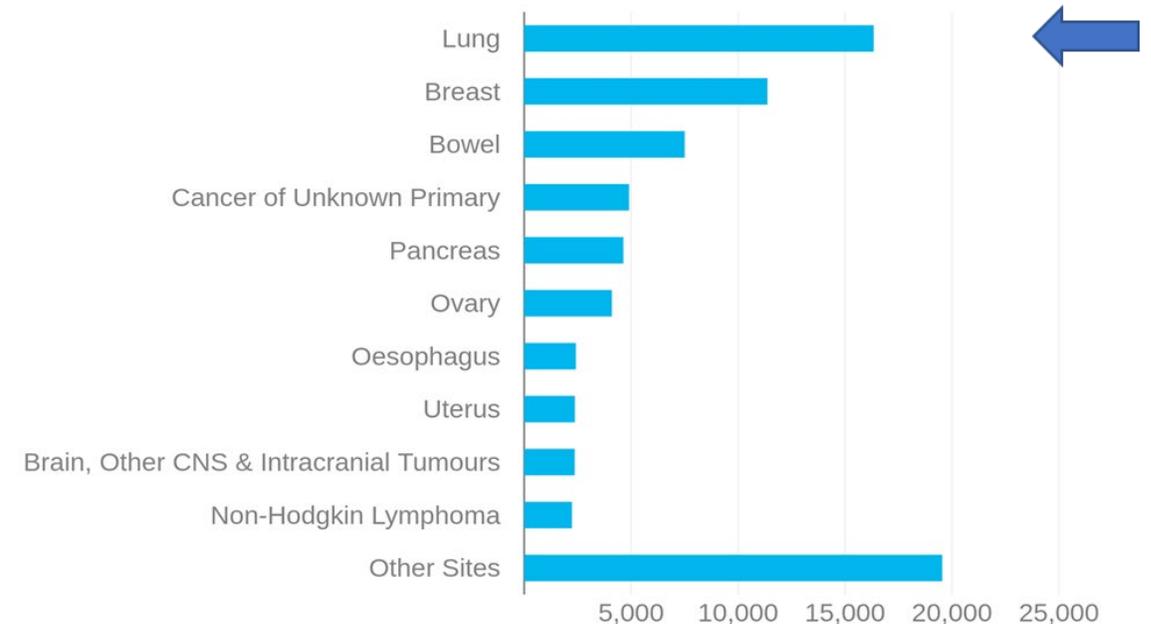


Lung cancers are the most important in terms of mortality.
Around a fifth of all cancer deaths in the UK are lung cancer.

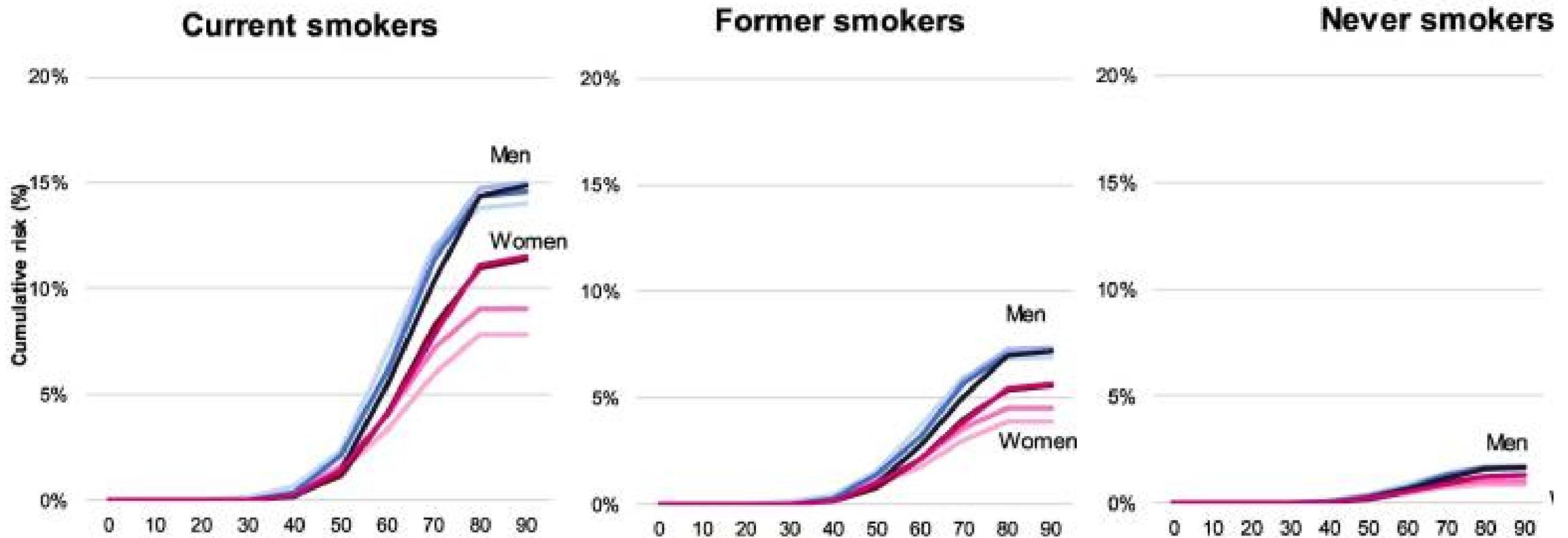
Men: 18,810 UK in 2017



Women: 16,338 in UK, 2017

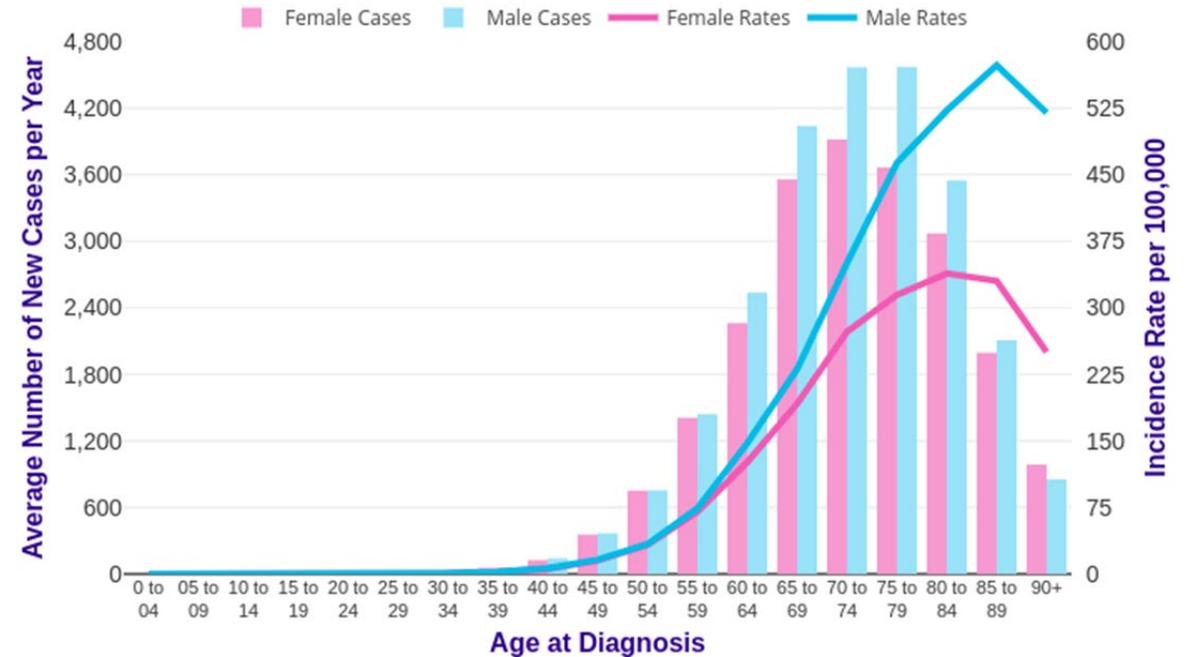


Cumulative lifetime risk around 15% for male smokers, <2% for non-smokers. (Swiss data from C. Bruder et al 2018).



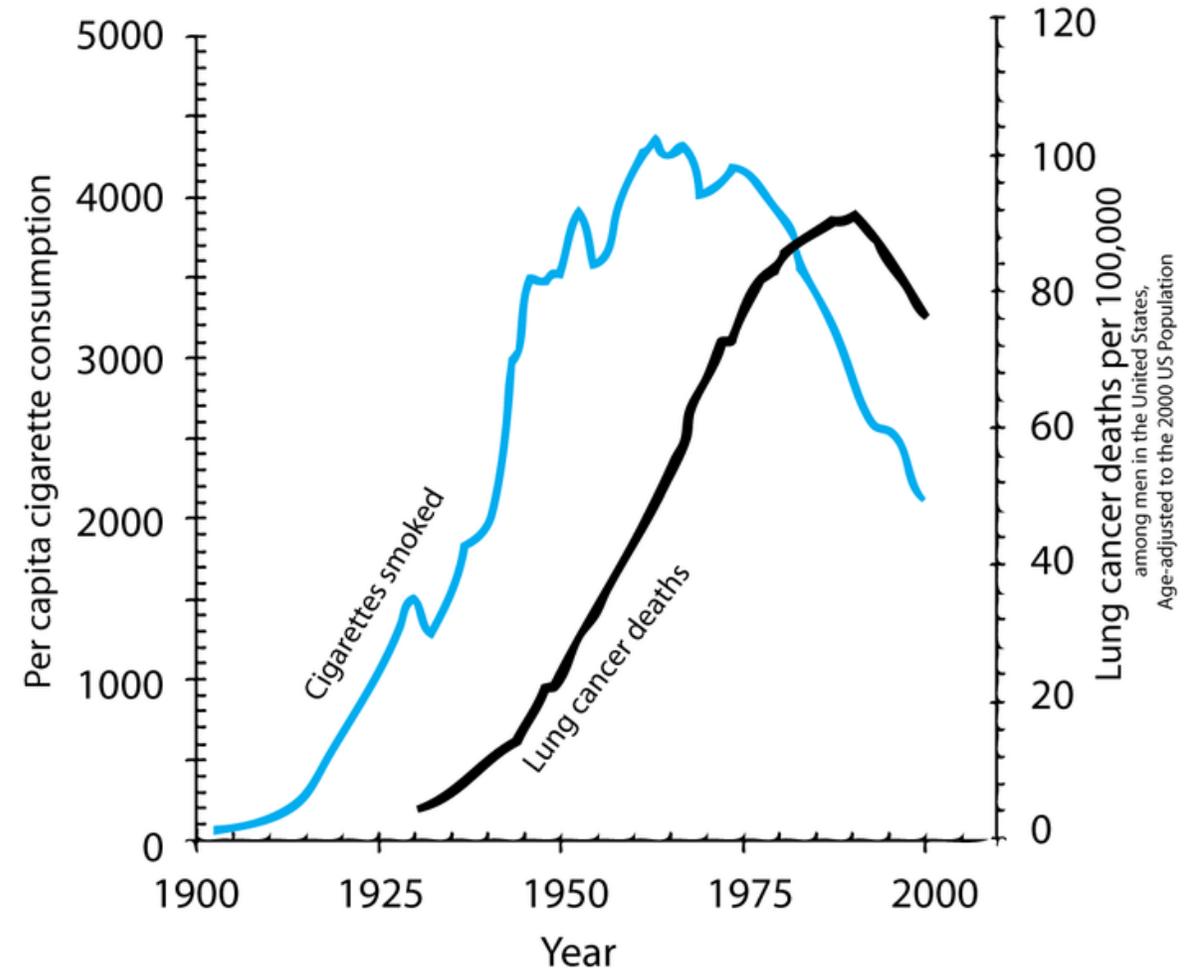
UK age profile.

- After smoking, the major risk factor is age.
- Lung cancer is not a single entity; there are several types.
- Association with smoking and age profile different.



The epidemiological evidence.

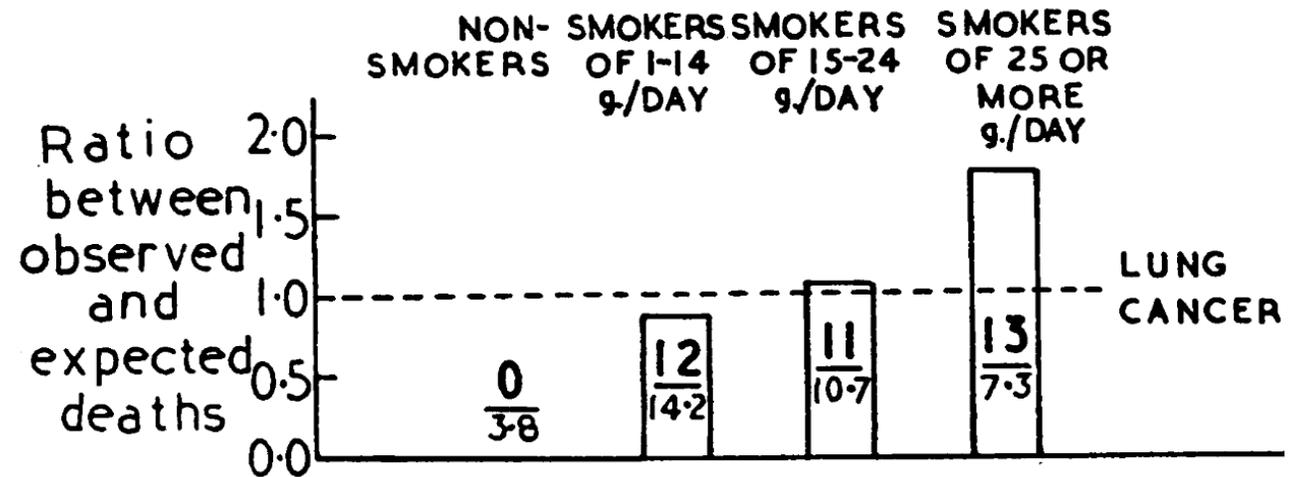
- Simplest data correlated smoking and cancer rates in the population.
- Case-control studies from the 1930s onward compared patients suffering from lung cancer (case) with those without (control).
- Much higher rates of smoking in the cancer cases.



US data.

Cohort studies.

- The most convincing evidence was from cohort studies.
- The British doctors study followed 34,439 male doctors from 1951.
- Within 4 years lung cancer rates much higher in heavier smokers.

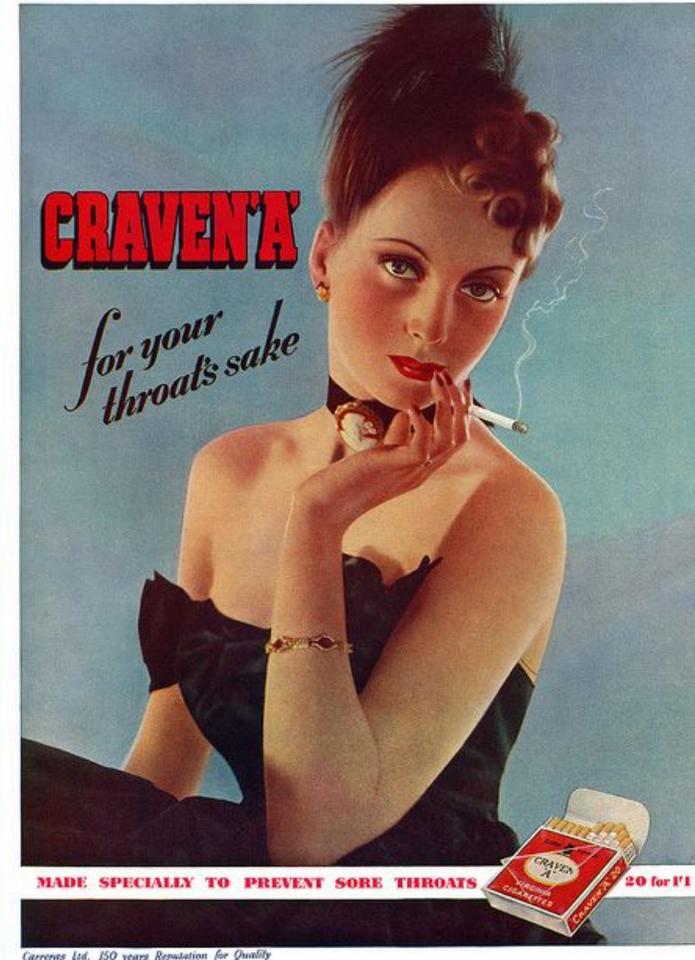


Doll & Bradford Hill BMJ 1954

Unsurprisingly heavier smoking = more cancer.

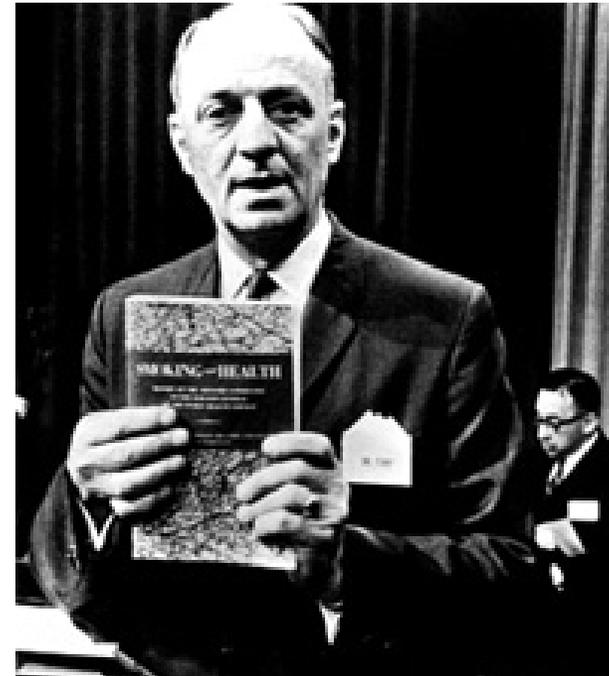
- The initial data have held up.
- For lung cancer in women, one meta-analysis estimates:
 - 1-9 cig/day RR 1.4
 - 10-19 cig/day RR 3.3
 - 20+ cig/day RR 24

S. Gandini et al 2007



It took a long time to convince the medical profession, let alone the public.

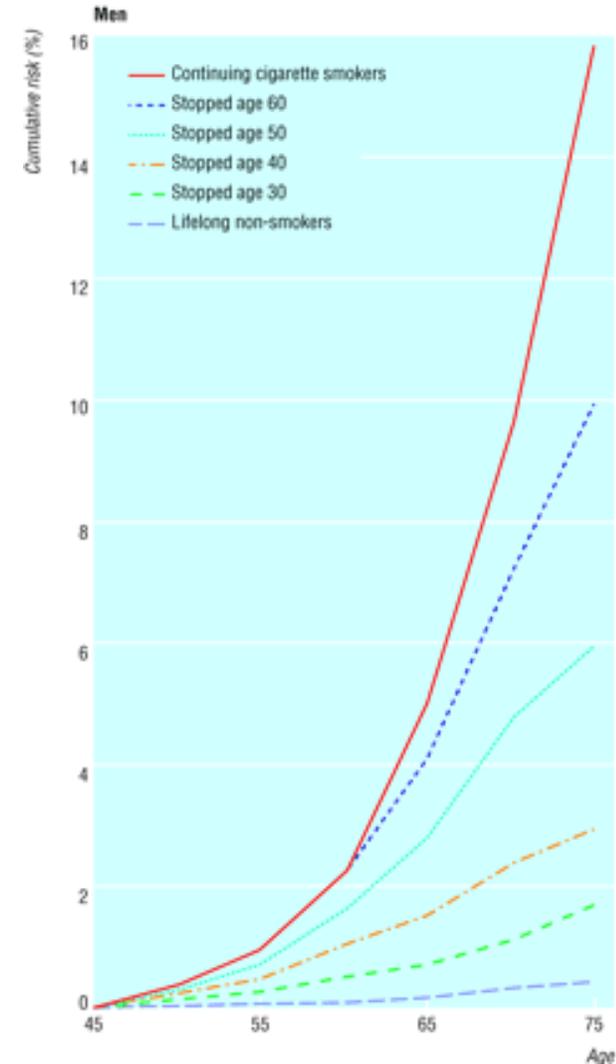
- A 1960 poll organised by the American Cancer Society: only 1/3rd of US doctors agreed cigarette smoking should be considered 'a major cause of lung cancer'.
- Most of the tobacco industry tried to make sure the science was labelled 'speculative' long after its own scientists privately agreed the link was causal.



Dr. Luther Terry, US Surgeon-General and his Report '*Smoking and Health*' 1964

Stopping smoking reduces risk. Effect of stopping smoking on lung cancer rates at age 75. *Data from Peto et al BMJ 2000.*

- For men who stopped at ages 60, 50, 40, and 30 the cumulative risks of lung cancer by age 75 were 10%, 6%, 3%, and 2%.
- 16% in current smokers at that stage.
- For lifelong non-smokers 0.2% for men and 0.4% for women.



A systematic, collaborative and sustained attack on science.

“Tobacco companies secretly funded “independent” experts to conduct research, publish papers, appear at conferences and lobby WHO’s scientific investigators with the intention of influencing, discrediting or distorting study results.” WHO



- Initial attempts to undermine data showing active smoking caused health problems.
- Then a sustained attempt to undermine data that clearly demonstrated second-hand smoke is harmful.
- And the evidence for banning smoking in public places...plain packaging...and it goes on.

Imperial Tobacco research (1970s).

“Starters no longer disbelieve the dangers of smoking, but **they almost universally assume these risks will not apply to themselves because they will not become addicted.** Once addiction does take place, it becomes necessary for the smoker to make peace with the accepted hazards...

The desire to quit ... often seems to take hold as soon as the recent started admits to himself that he is hooked on smoking. **However, the desire to quit, and actually carrying it out, are two quite different things, as the would-be quitter soon learns.”**

“Believe me, folks, you'll want to read this important new evidence on the effects of smoking. Then you'll say, as I do... **MUCH MILDER CHESTERFIELD IS BEST FOR ME!**”
Arthur Godfrey

NOW...Scientific Evidence on Effects of Smoking!

A MEDICAL SPECIALIST is making regular bi-monthly examinations of a group of people from various walks of life. 45 percent of this group have smoked Chesterfield for an average of over ten years.

After ten months, the medical specialist reports that he observed . . .

no adverse effects on the nose, throat and sinuses of the group from smoking Chesterfield.

MUCH MILDER CHESTERFIELD IS BEST FOR YOU

First and Only Premium Quality Cigarette in Both Regular and King-Size

CONTAINS TOBACCOS OF BETTER QUALITY AND HIGHER PRICE THAN ANY OTHER KING-SIZE CIGARETTE

APRIL 1953 13

The reality is of course rather different.

70% of smokers want to quit. And try.

Never blame individual smokers for lung cancer. They were up against one of the most powerful and wealthy industries in the world.



NHS

The average smoker needs over five thousand cigarettes a year.
Get unhooked. Call 0800 169 0 169 or visit getunhooked.co.uk

SMOKEFREE



WARNING

This is what dying of lung cancer looks like.

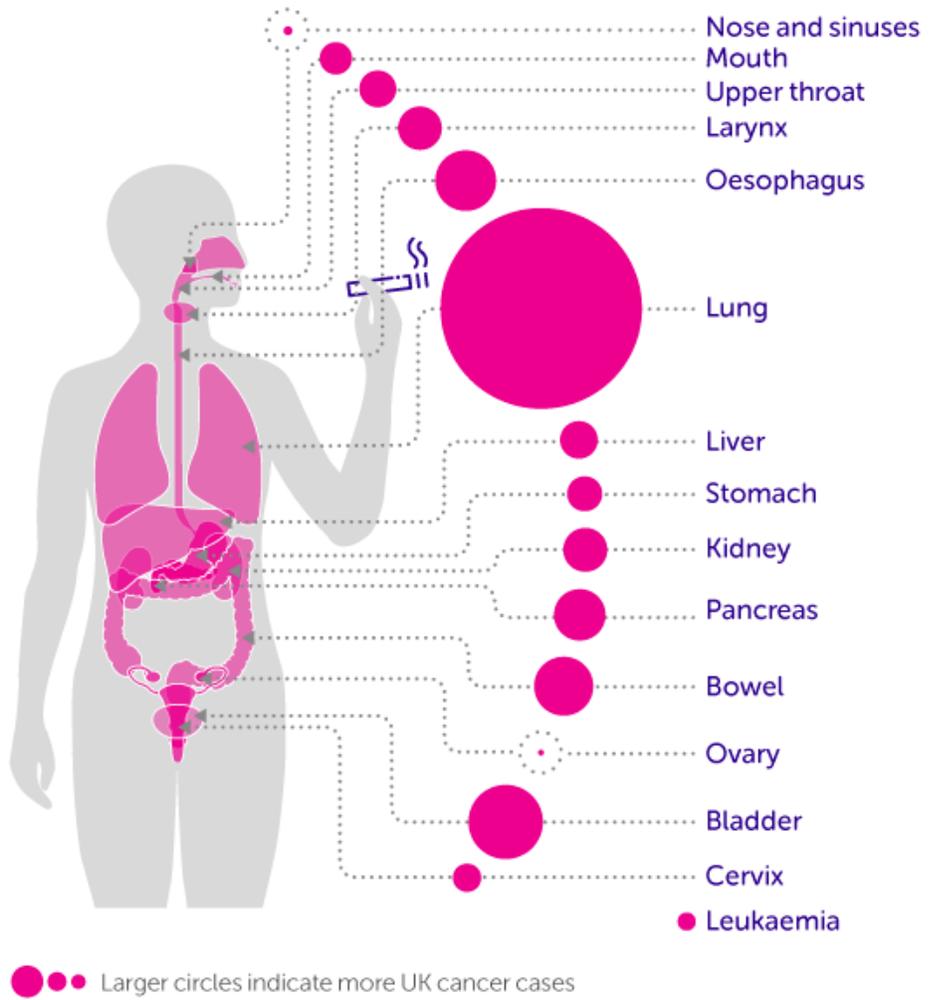
Barb Tarbox died at 42 of lung cancer caused by smoking.

You can quit. We can help.
1-888-888-8888
internet/url.ca

© Greg Southam
© The Edmonton Journal

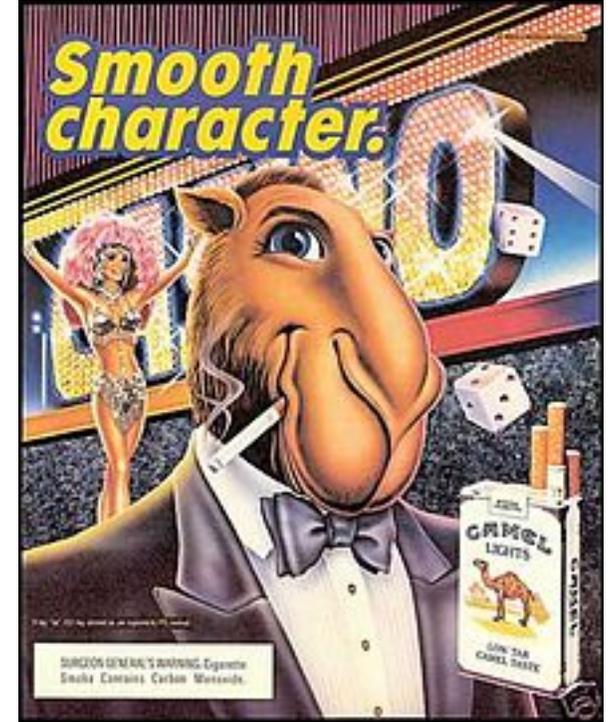
Health Canada

In addition to other major diseases including heart disease, stroke and dementia there are many other cancers.



Targeting children and teenagers was overt, then covert.

- “School days are here. And that means BIG TOBACCO BUSINESS for somebody. Lets get it.” R.J Reynolds 1927 internal memo.
- Big push to target teens from the 1970s. “The base of our business is the high school student”. Lorillard memo 1978.
- Consistent pattern of claiming to deplore child and teenage smoking, whilst undermining measures to curb it.
- An example: the industry positioned itself as a partner with UNICEF on youth smoking prevention initiatives as a way to avoid meaningful tobacco control measures that could save children’s lives.



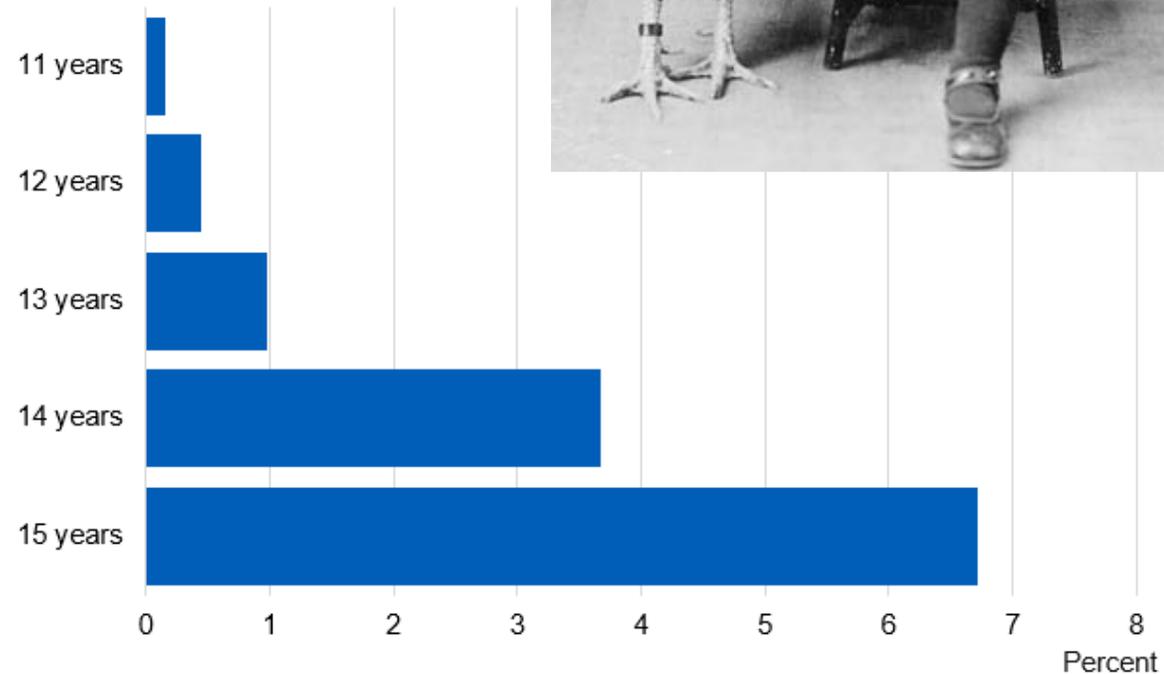
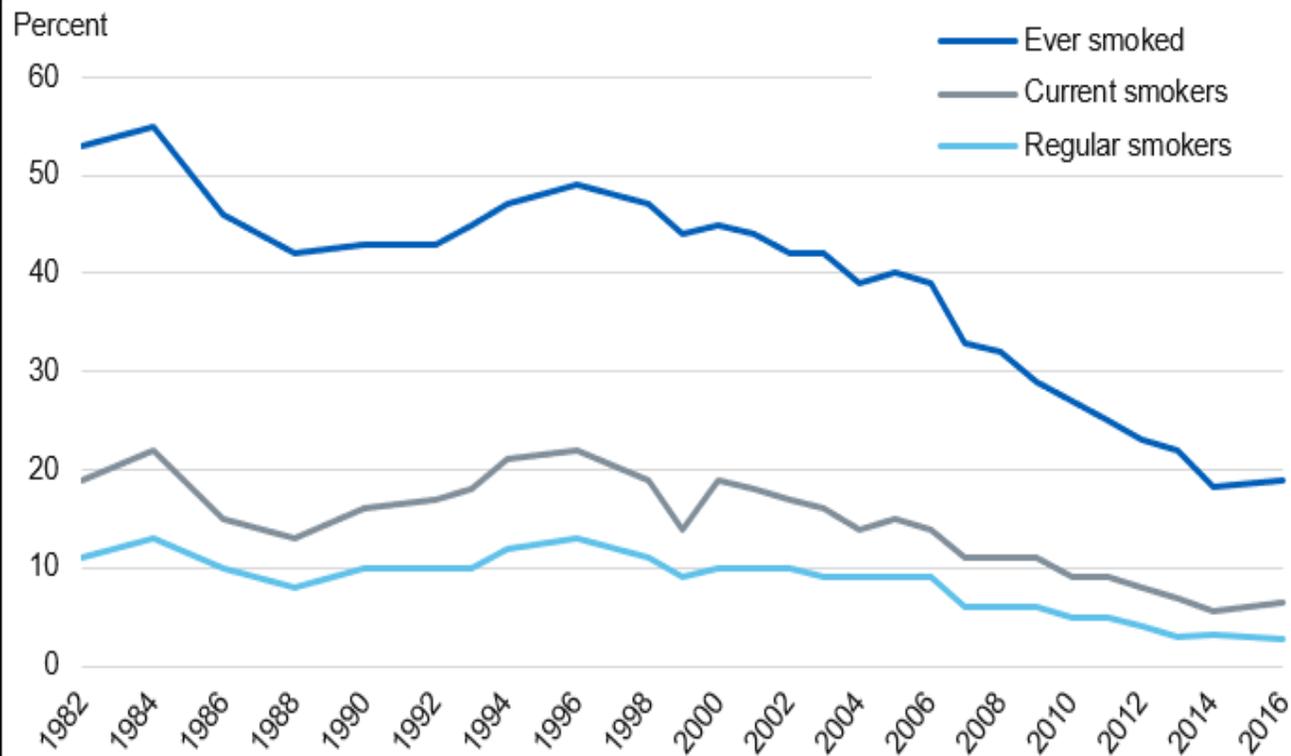
Joe Camel ad. Moved from 1% to 32.8% of underage market. Started 1988, stopped 1997.

'We never target children'

Regular smoking by age 11-15 years (R), and school children over time (L).

74% pupils say it would be very difficult to give up.

NHS Digital data 2019, England.



Cigarette companies make their profit from the most deprived.

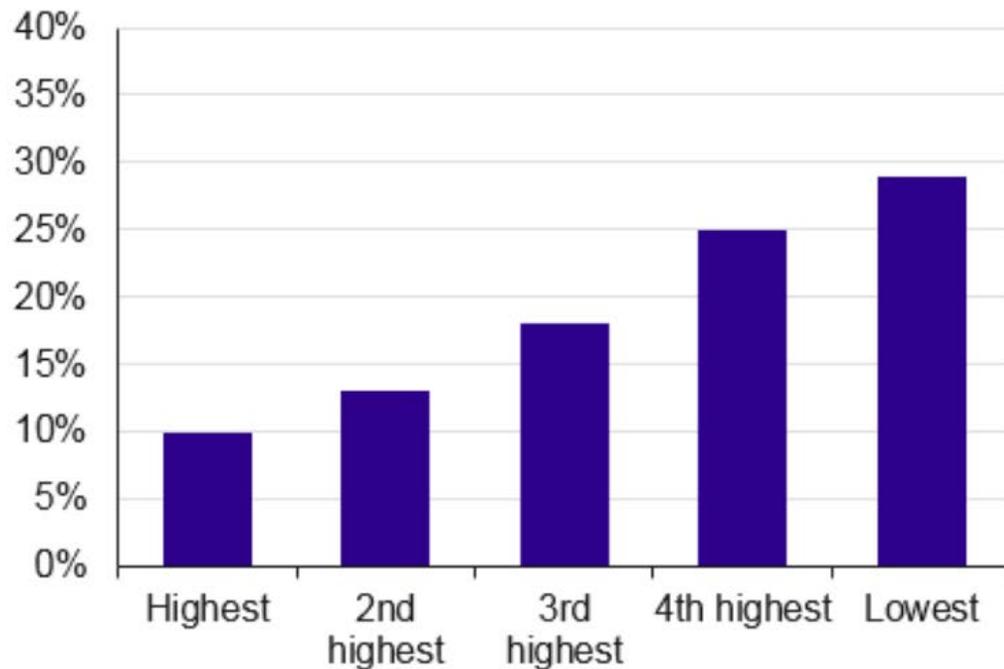
Unemployed are almost 2x as likely to smoke as those in work.

Annual income <£10,000 2x rate of those with >£40,000.

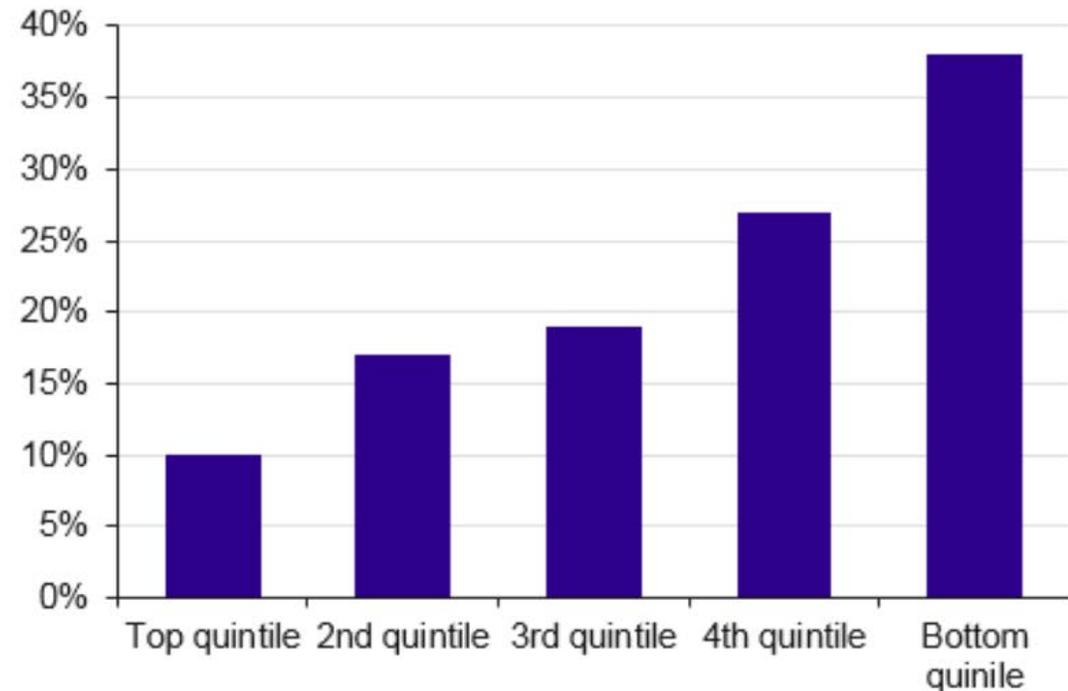
Smoking prevalence among adults with a serious mental illness 2.5x.

Smoking by equivalised household income. England and Scotland.

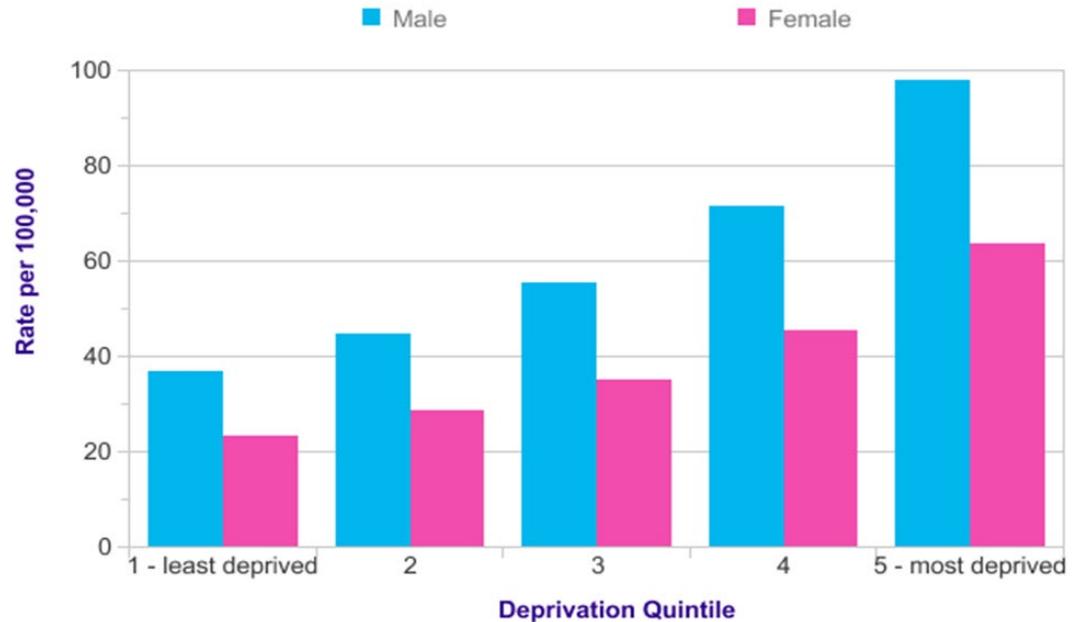
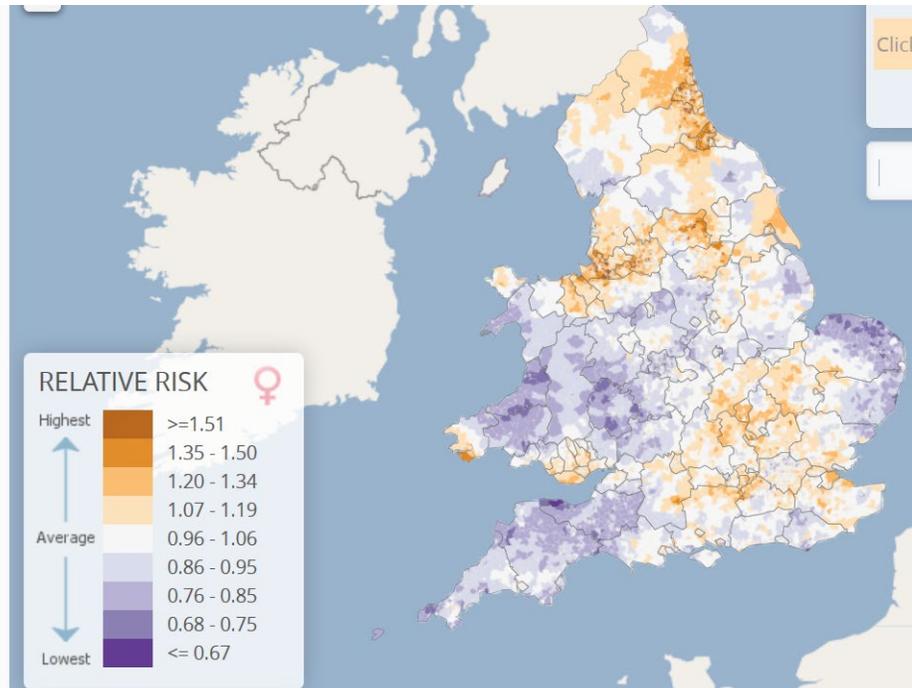
England 2015 (HSE)



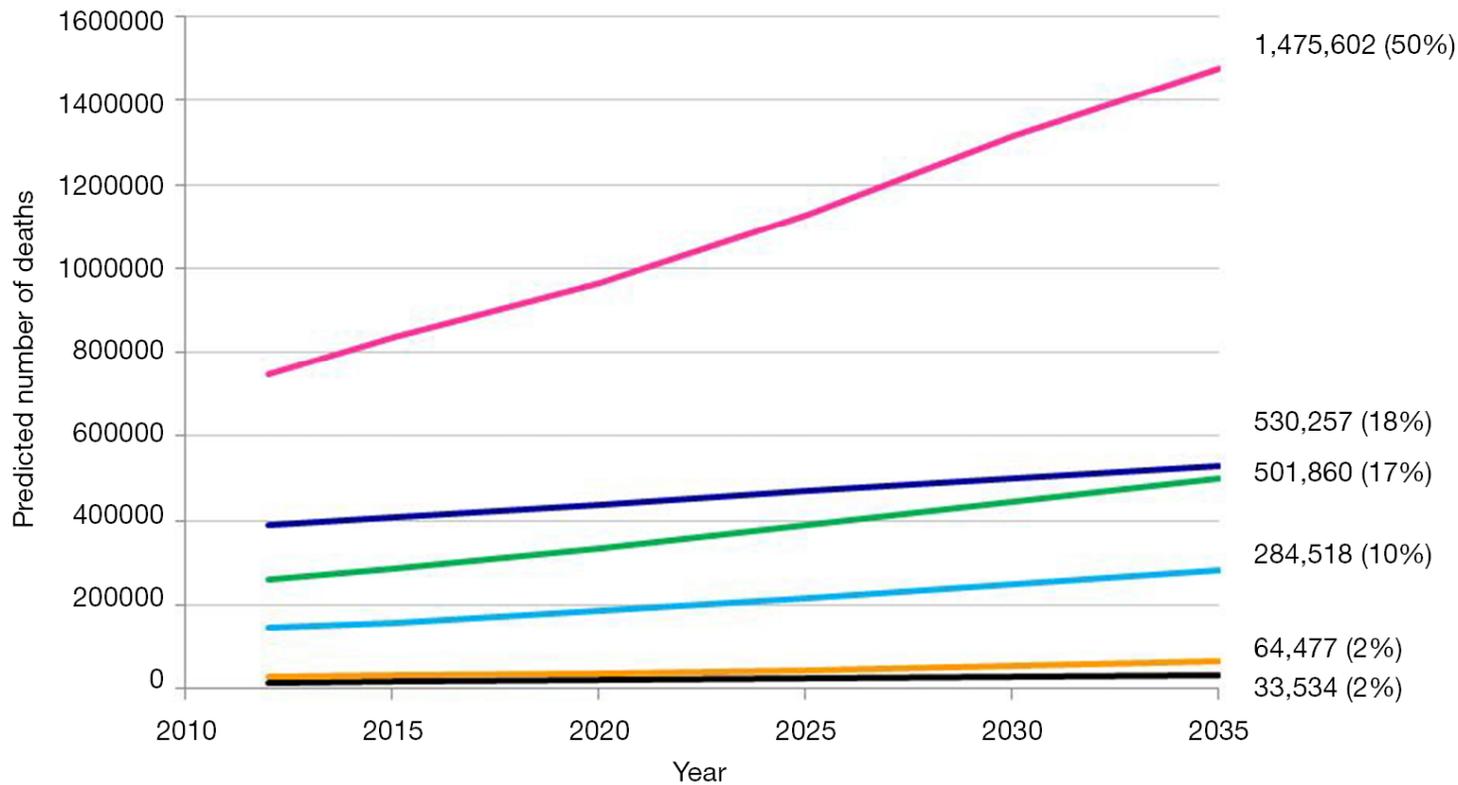
Scotland, 2016 (SHeS)



Lung cancer is very heavily weighted towards deprivation.
That is where the cigarette industry make their profits.



Only a minority of cigarettes now in **high-income countries**.
 300M smokers in China alone. Projected lung cancer deaths to 2035 (L),
 current smoking prevalence (R).



- Africa region (AFRO)
- East Mediterranean region (EMRO)
- South-East Asia region (SEARO)
- Americas region (PAHO)
- Europe region (EURO)
- Western Pacific region (WPRO)



- Super-Regions**
- Central Europe, Eastern Europe, and Central Asia
 - High-income
 - Latin America and Caribbean
 - North Africa and Middle East
 - South Asia
 - Southeast Asia, East Asia, and Oceania
 - Sub-Saharan Africa

The cigarette industry is in rude financial health.

- “We are on track for one of our best financial performances for many years.” British American Tobacco 2019.
- Data from BAT 2018 Annual Report. 708bn cigarettes (+3.3%) 189m vaping units.
- The UK High Court accepts that the net economic costs of tobacco use to society estimated at about £13.7bn p.a. whilst the industry pay approximately £10bn in taxes p.a.
- The profit for BAT is 3x the combined investment in the MRC, NIHR, Wellcome in **all** medical research into **any** disease.

Group cigarette (and tobacco heating products – THP) volume

708bn
+3.3% (-3.5% representative[†])

2017: +3.2% (2.6% organic[†])
2016: +0.2% (-0.8% organic[†])

Group market share of Key Markets

+40 bps

2017: +40 bps
2016: +50 bps

Strategic Cigarette and THP volume

451bn
+17.9% (+5.8% representative[†])



2017: +17.9% (+7.6% organic[†])
2016: +7.5%

Oral (snus (no pouches)

3.9bn
+93% (+10.5% representative[†])



2017: +117% (+32% organic[†])
2016: +9%

Vapour (units)

189m
+100% (+35% representative[†])



2017: +120%
2016: +832%

Revenue (£m)

£24,492m
+25.2%



Definition: Revenue recognised, net of duty, excise and other taxes.

In 2018, revenue includes £17,257 million of revenue from the Strategic Portfolio, an increase of 49% on 2017 (on a reported and representative basis).

Change in adjusted² revenue at constant rates¹ (%)

+33.4%



Definition: Change in revenue before the impact of adjusting items and the impact of fluctuations in foreign exchange rates.

Change in adjusted² revenue from the Strategic Portfolio at constant rates¹ (%)

+56.1%



Definition: Change in revenue from the strategic portfolio before the impact of adjusting items and the impact of fluctuations in foreign exchange rates.

This measure was introduced in 2018, with no comparators provided.

Changes in 2018

In 2018, the Group introduced a new measure called 'adjusted revenue growth from the Strategic Portfolio' as part of the continual assessment of the Group's short- and long-term delivery of the strategic vision. This measure replaced the GDB and Key Strategic Brands volume growth metric as a key performance indicator in connection with the Group's compensation plans. This Strategic Portfolio reflects the focus of the Group's investment activity and includes the 'Strategic Combustible Brands' being Kent, Dunhill, Lucky Strike, Pall Mall, Rothmans, Camel (US), Newport (US) and Natural American Spirit (US) and our potentially reduced-risk products portfolio, which comprises our THP, vapour, modern oral and traditional oral

Profit from operations (£m)

£9,313m
+45.2%



Definition: Profit for the year before the impact of net finance costs/income, share of post-tax results of associates and joint ventures and taxation on ordinary activities.

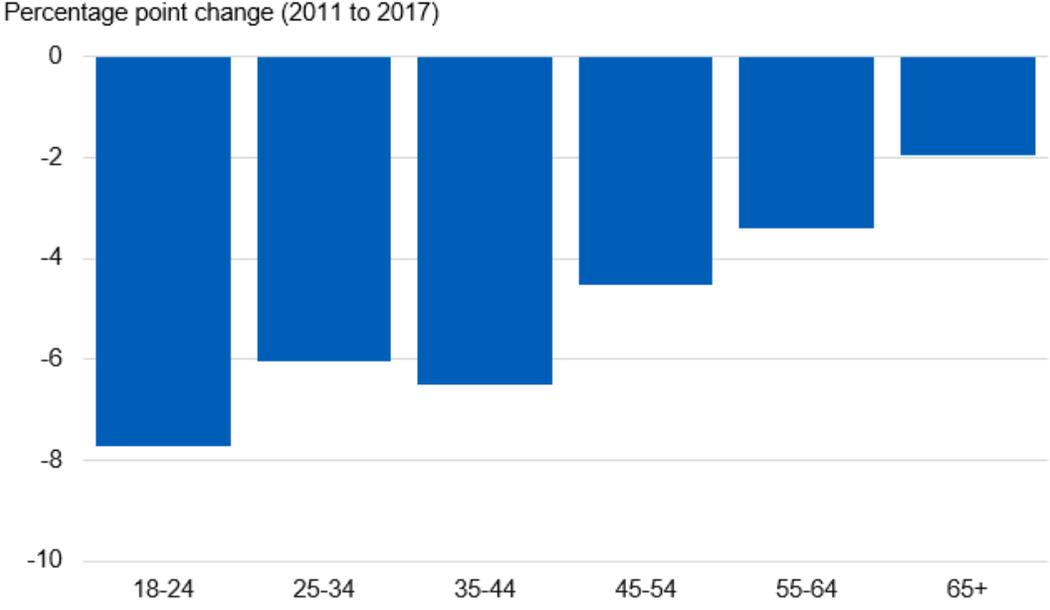
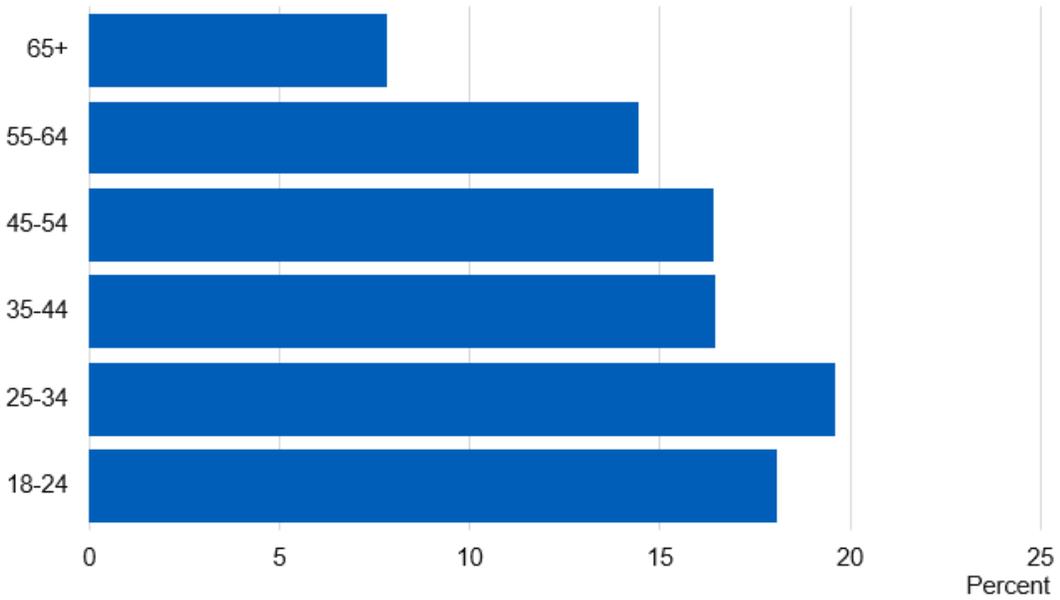
Change in adjusted² profit from operations at constant rates¹ (%)

+37.8%



Definition: Change in profit from operations before the impact of adjusting items and the impact of fluctuations in foreign exchange rates.

Smoking prevalence in England by age, and change in agegroup 2011-2017. *NHS Digital.*



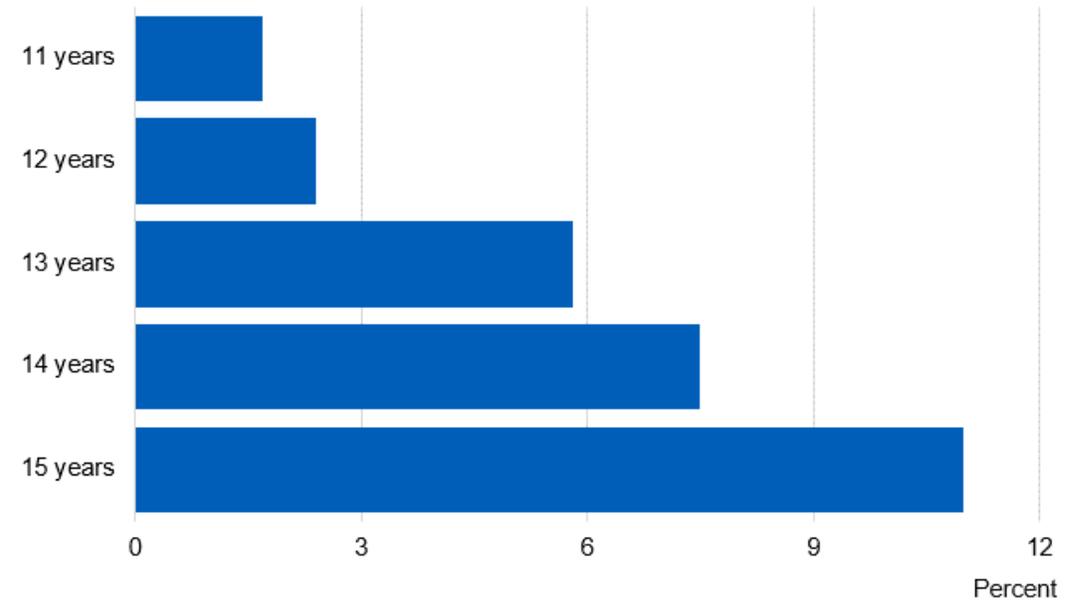
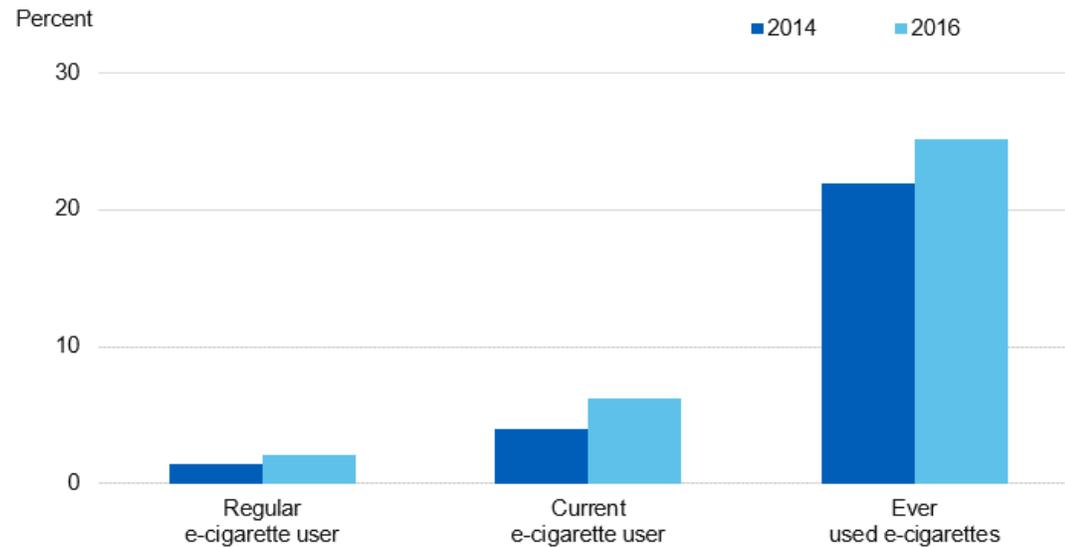
E-cigarettes / vaping. Definitely better than smoking (despite some headlines).

- This is however not a high bar, because smoking is so harmful in so many ways.
- A recent trial in NHS patients who wanted to quit (Hajek et al NEJM 2019).
- The 1-year abstinence rate was 18.0% in the e-cigarette group, 9.9% in the nicotine-replacement group.
- NOT harmless however.
- So if you smoke, switch to vaping. But if you don't smoke don't vape.
- A ? over long-term risks of flavours.



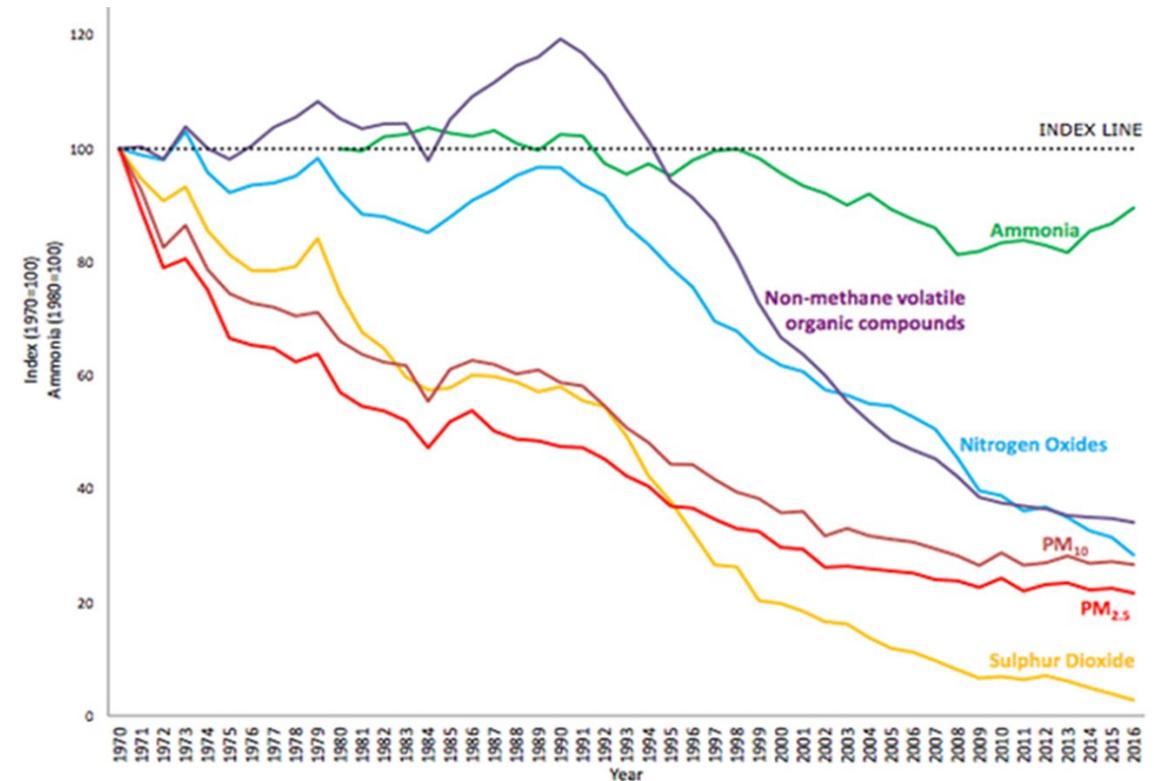
E-cigarette use in children is creeping up in UK, from a low base. 6% overall, but above this in 15 year-olds. 1 in 4 in the USA.

If an e-cigarette brand is increasing in children we will assume the company is marketing to them, and act accordingly.



Indoor and outdoor air pollution and radon gas as risk factors for lung cancer (dwarfed by smoking).

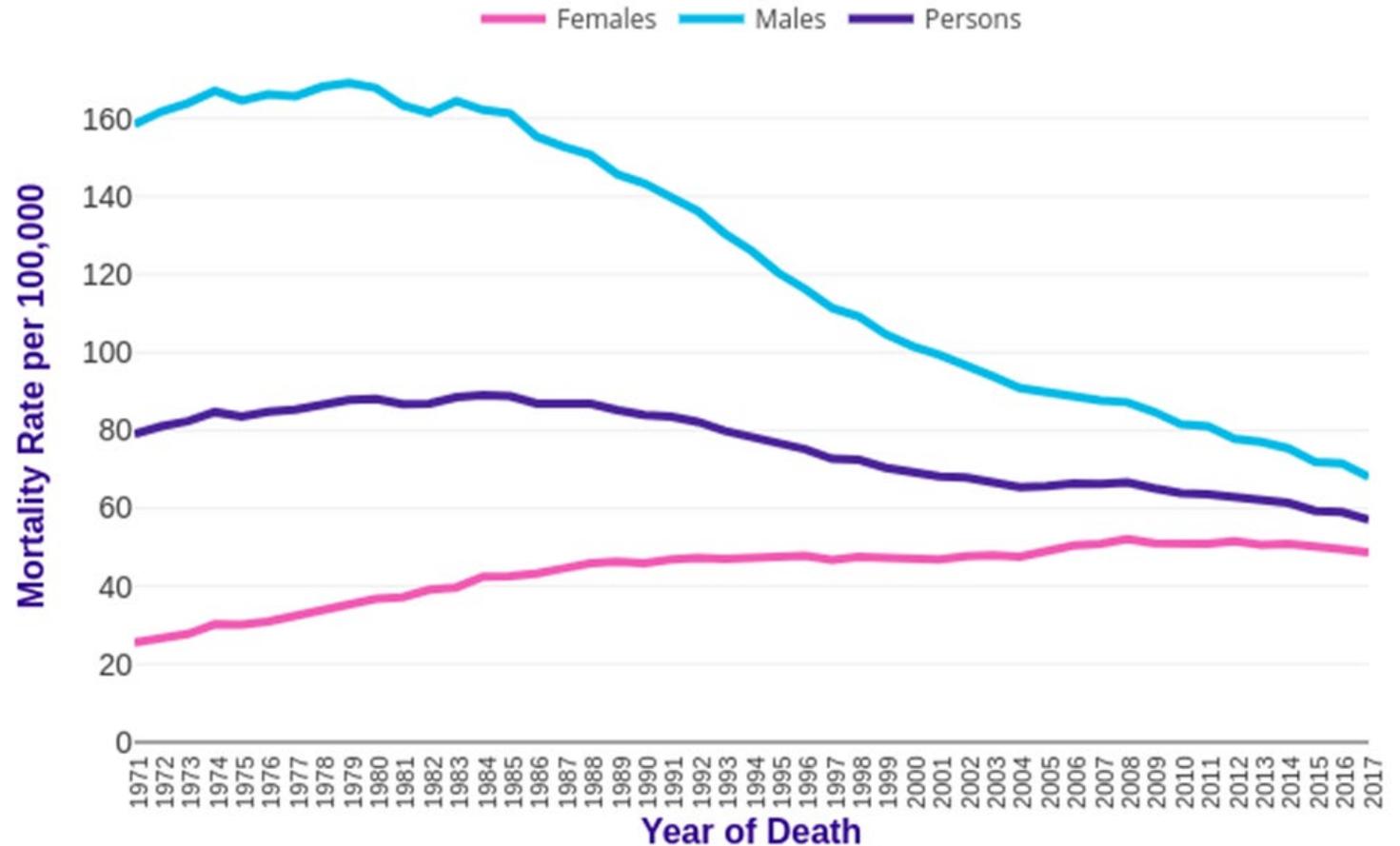
- International Agency for Research on Cancer (IARC) confirmed pollution epidemiological link 2013.
- About 1 in 10 lung cancer cases in the UK currently estimated to be caused by exposure to air pollution.
- Mainly particulate matter PM2.5 and possibly PM10.
- Indoor air pollution- biggest risk secondhand cigarette smoke.
- Radon gas a natural (but small) risk.



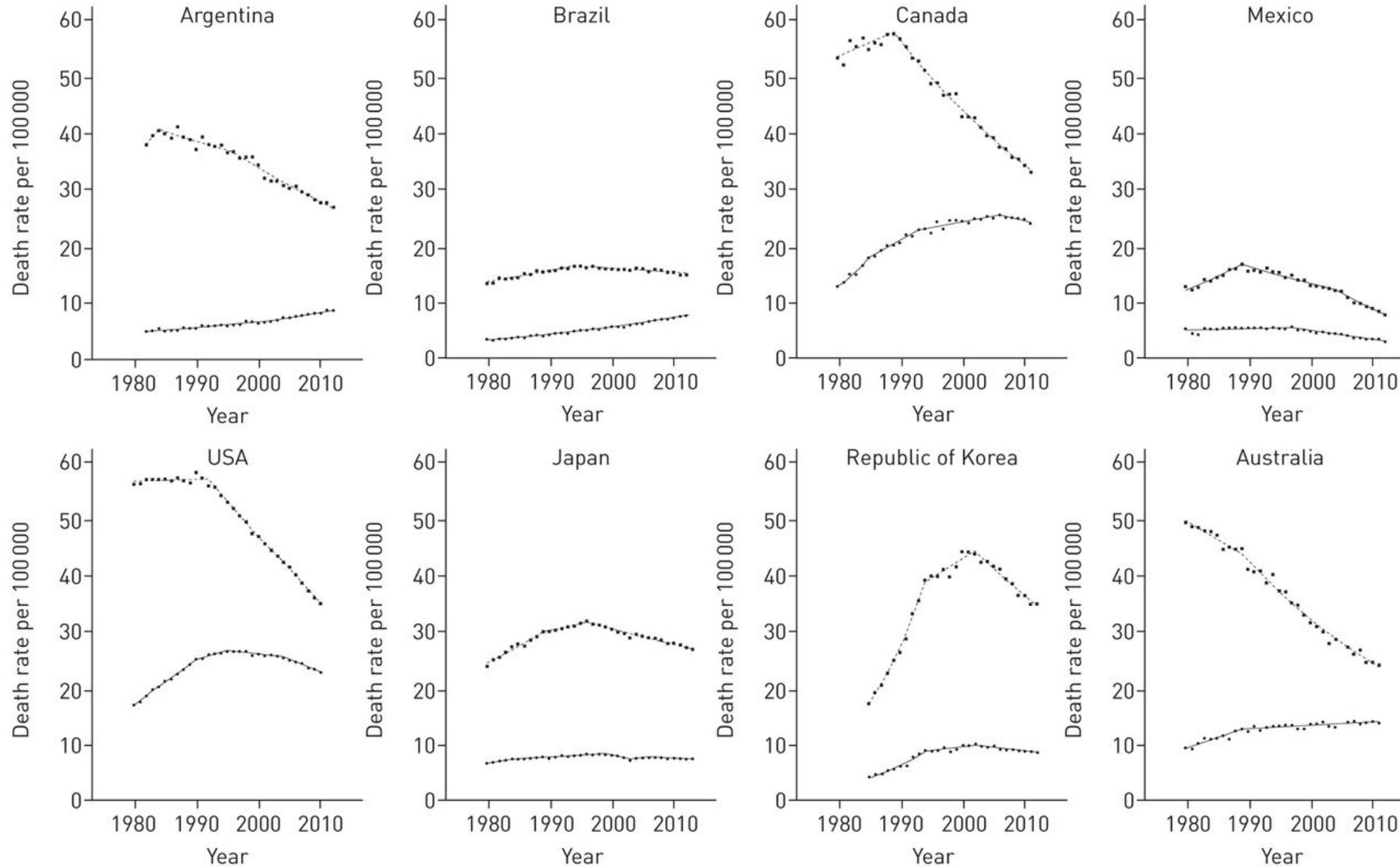
DEFRA/ONS 2018. Data from 1970.

There is roughly a 30 year timelag between reductions in smoking and reductions in lung cancer. Mortality 1970-2017, UK.

- Smoking peaked in the 1950s in men and in the 1970s in women.
- Later peak due to aggressive marketing aimed at women.



Different patterns globally depending on smoking culture.



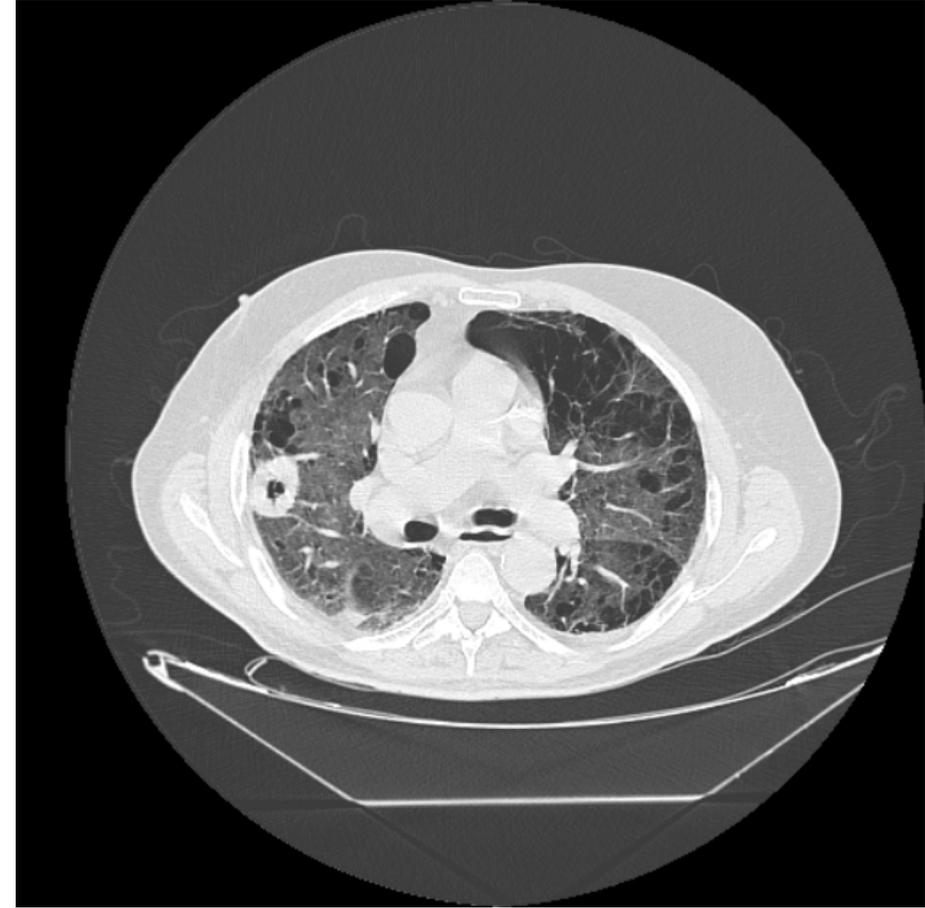
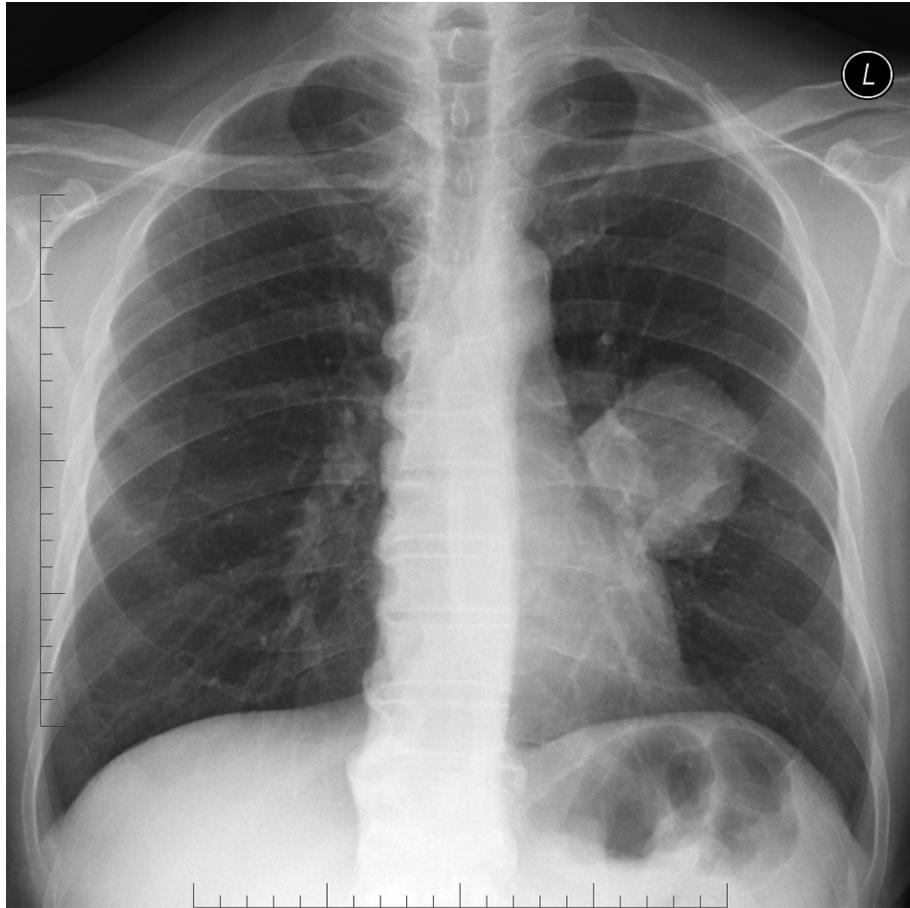
Malhotra J et al 2016

Symptoms and signs of lung cancer.

- Unfortunately minimal in early cancer.
- Once start include:
Persistent cough.
Cough with blood.
New shortness of breath.
Fatigue, weight loss.
Shoulder or chest pain.
Most people with these symptoms NOT cancer.



Initial diagnostic tests usually chest X-ray and/or CT.



Likely to have bronchoscopy and biopsy, and staging CT/MRI.
If a better approach biopsy may be through the skin or chest wall.



Stage, grade and type of lung cancers.

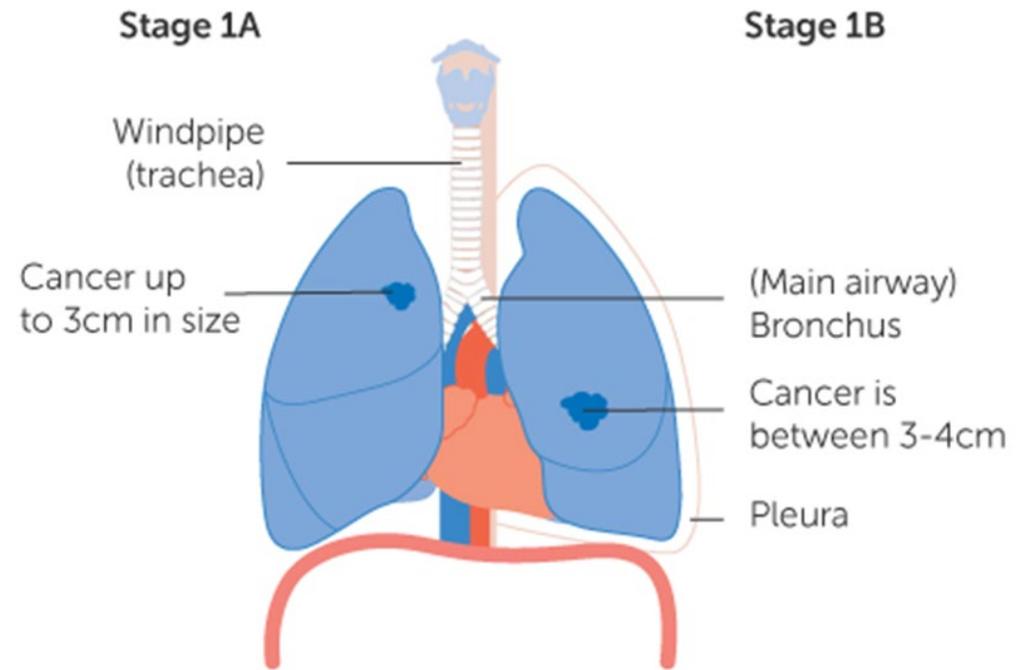
Stage: size and degree of spread.

Generally Stage 1-4.

Grade: appearance of the cells.

The more different from normal cells the higher the grade.

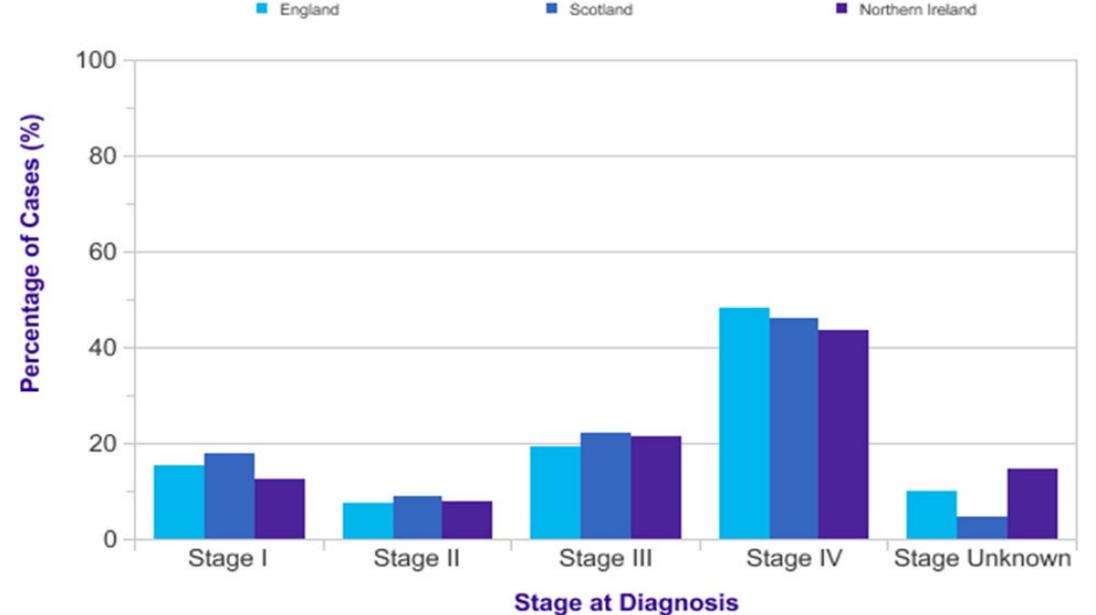
Type: Several types in the lung, from the cell they arise from.



CRUK

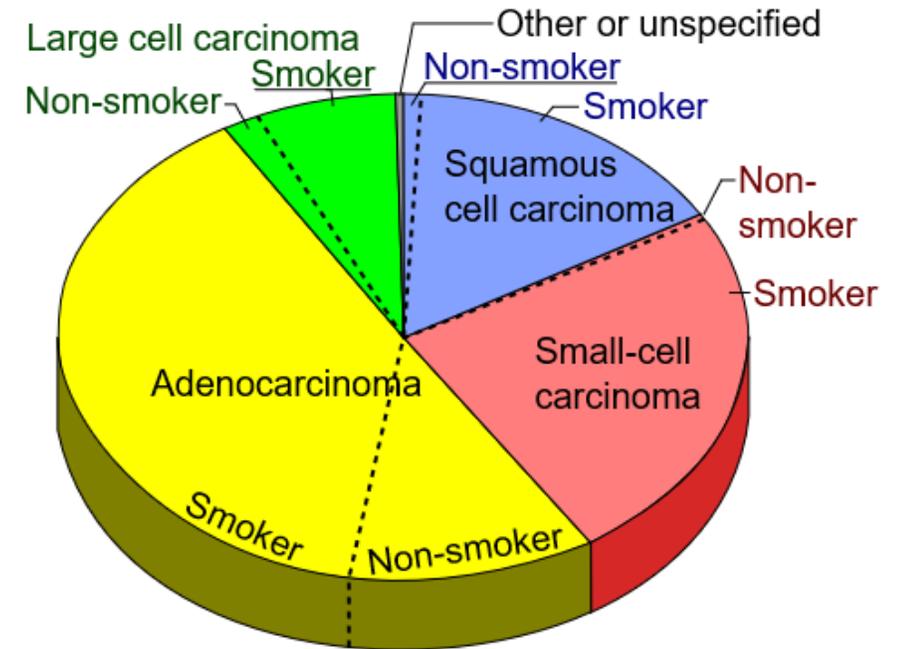
Lung cancer mainly diagnosed in late stages.

- Symptoms are usually non-existent, or non-specific until spread.
- Stage 2 smaller or v local spread.
- Stage 4: cancer both lungs, or local or general spread.
- Should we screen heavy smokers for lung cancer with CT scans?



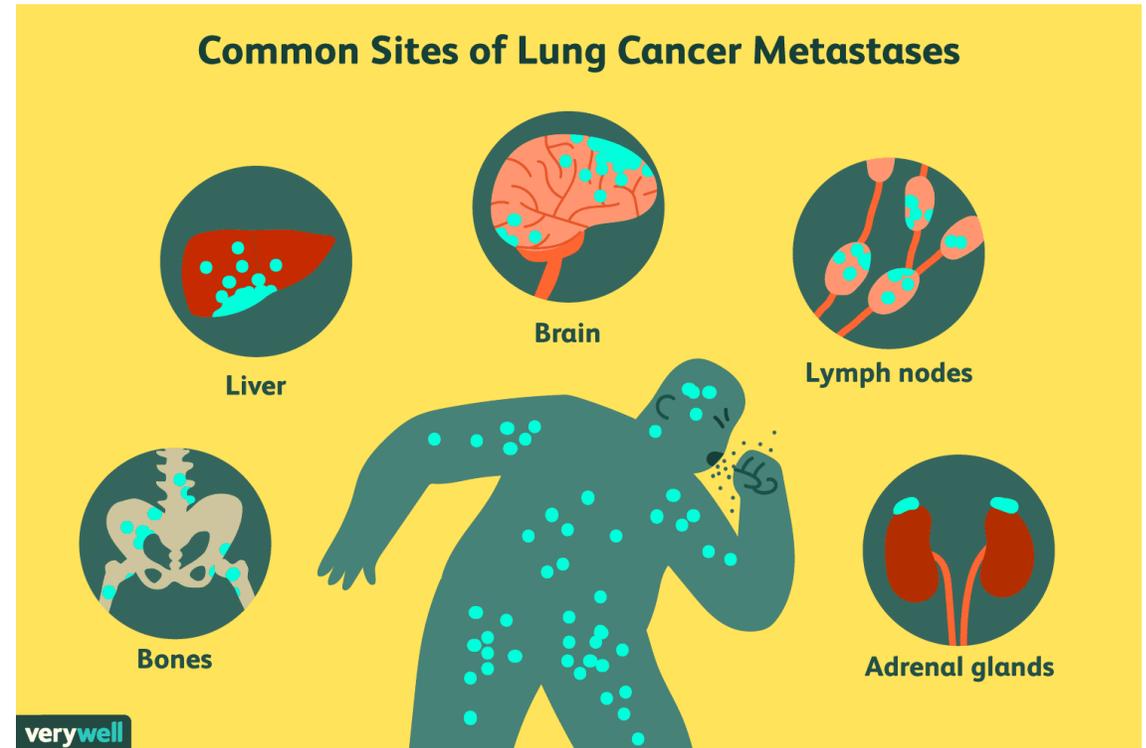
Type of lung cancer: small cell and non-small cell.

- **Small cell lung cancer** (SCLC). Around 12%, almost all smoking.
- **Non small cell lung cancer** (NSCLC), currently mainly treated the same way:
 - *Adenocarcinoma* most common type, starts in the mucus making gland cells of airways.
 - *Squamous cell cancer* develops in the flat cells that cover the surface of your airways.
 - *Large cell carcinoma*.



Common locations for lung cancer spread.

- Local lymph nodes.
 - Liver.
 - Bone.
 - Adrenal glands.
-
- Brain. Spread to brain is particularly common in small cell carcinoma.



5-year survival in USA. American Cancer Society.

In the US more people die of lung cancer than breast, prostate and colon combined.

	Non-small cell carcinoma	Small-cell carcinoma
Localized	61%	27%
Regional	35%	16%
Distant	6%	3%
Overall.	24%	6%

Surgery.

- Usually remains the best treatment for localised non-small cell lung cancer.
- Continues to develop.
- In last 3 weeks NHS had first 'keyhole' surgery for Stage 4 cancer.

THE Sun WS | FABULOUS | MONEY | TECH | TRAVEL | MOTORS | DEAR DEID

LUNG & SHORT OF IT NHS medics become first in world to remove cancer patient's lung using special keyhole surgery

Daniel Hammond
27 Jan 2020, 0:01 | Updated: 27 Jan 2020, 8:02

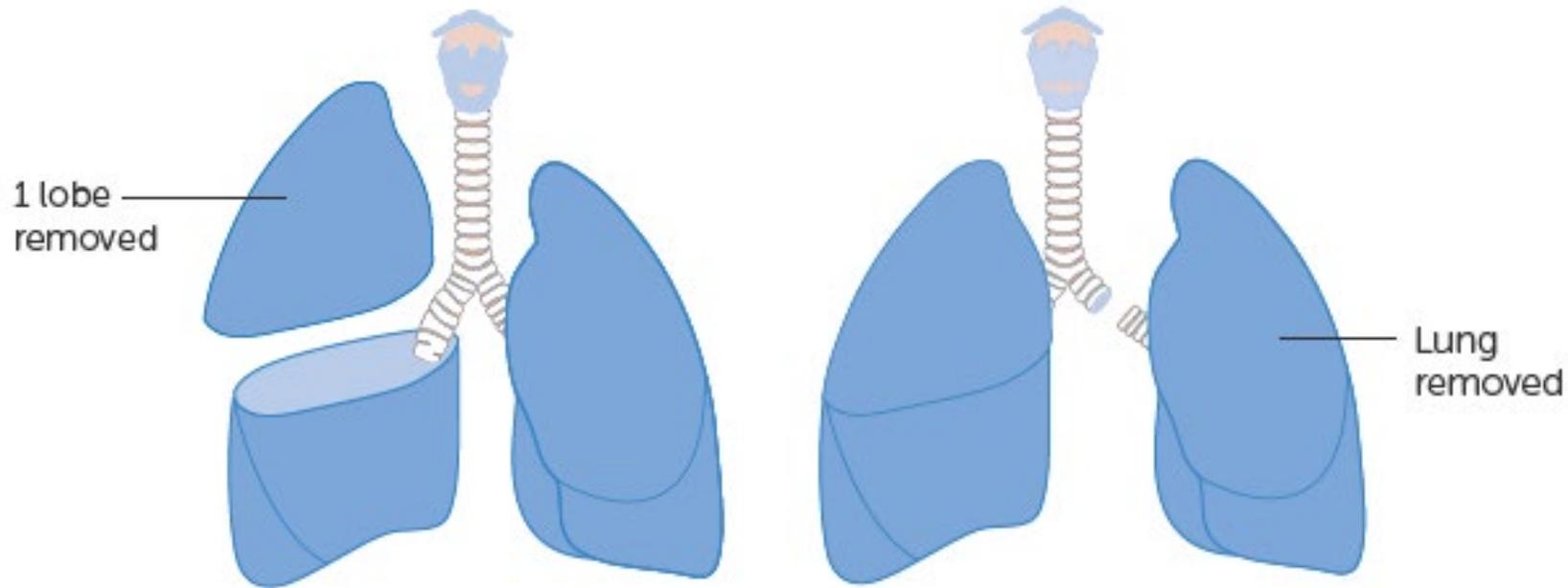
[Twitter](#) [Facebook](#) [5 Comments](#)

NHS medics have become the first in the world to remove a cancer patient's lung using special keyhole surgery.

Raymond Page, 74, was diagnosed with the most advanced form of the disease, stage 4, after a scan found two tumours.



Depending on the site might have one lobe removed, or a whole lung.



Percentage surgery for lung cancer *(CRUK England data)*

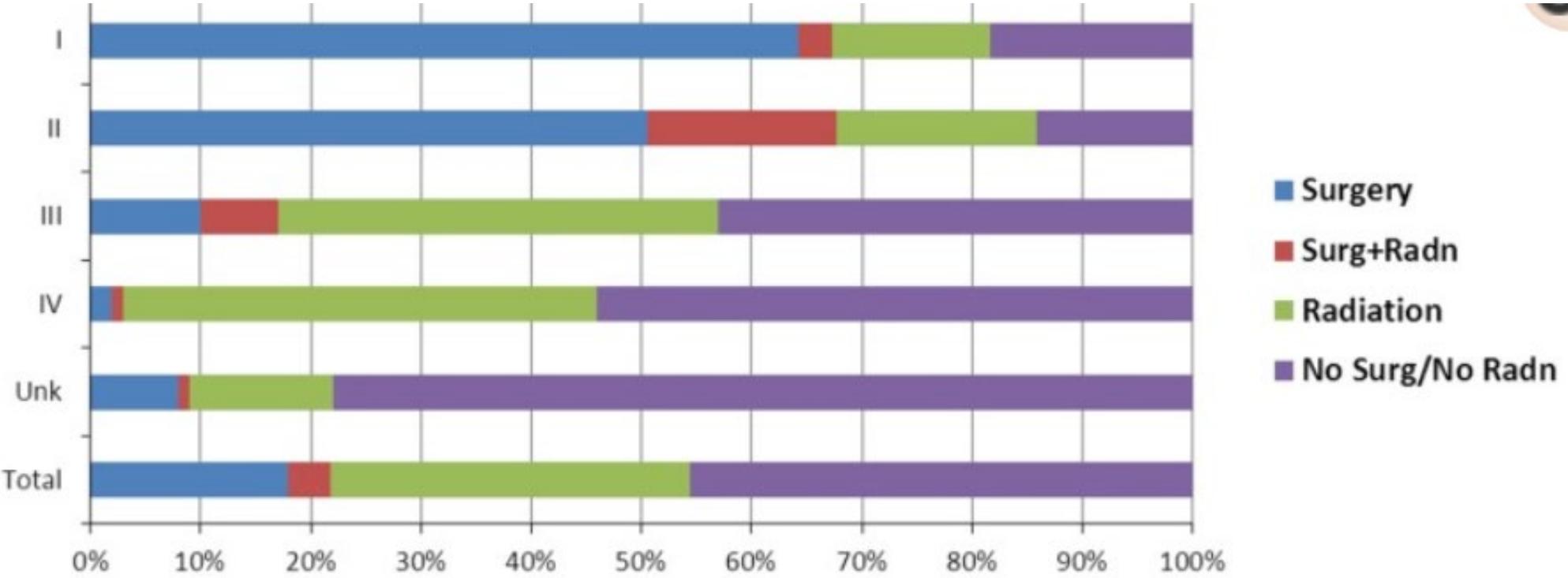
Stage at diagnosis	Patients with SCLC	Patients with NSCLC
All stages combined	2%	15.6%
Stage 1	37.3%	53.4%
Stage 2	15.2%	46.7%
Stage 3	1.6%	11.1%
Stage 4	0.1%	1.5%

Radiotherapy.

- In *non-small cell cancer* may have if not fit enough for surgery.
- Or after surgery, or with chemotherapy to aid treatment.
- In *small cell cancer* in early disease with chemotherapy.
- In *small cell cancer* prophylactic cranial irradiation (brain).
- To control symptoms (palliative).
- External beam, or occasionally stereotactic, radiotherapy treatment.



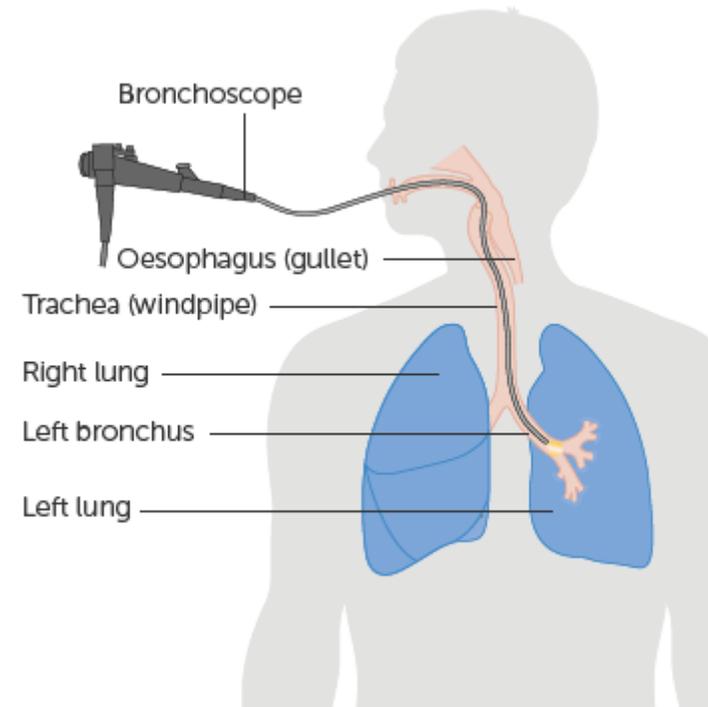
The relative mix of surgery and radiotherapy for non-small cell lung cancer. USA data on 288,670 patients. *Cheng M et al 2019*



Other ways of destroying lung cancer cells locally. Generally to reduce symptoms.

May be via CT guidance or
bronchoscopy.

- Radiotherapy ablation.
- Microwave ablation.
- Laser therapy.
- Diathermy.
- Photodynamic therapy (PDT).



Chemotherapy in lung cancer.

The majority of small cell lung cancer, minority of NSCLC.

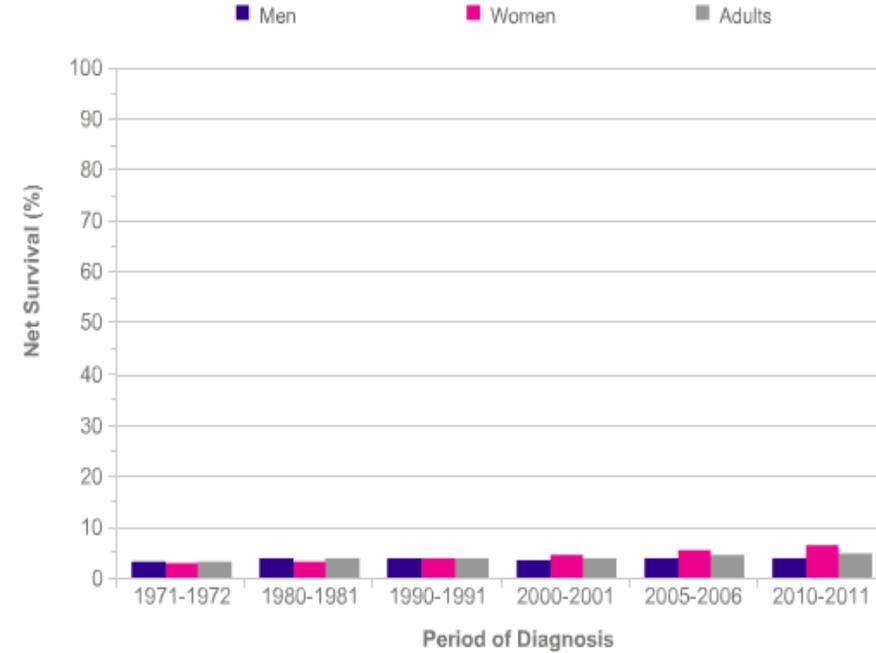
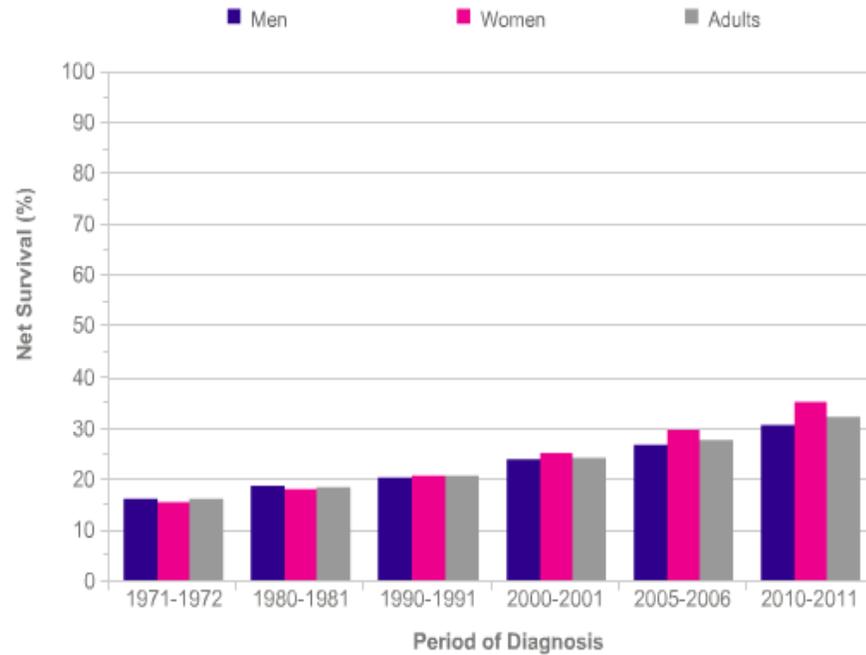
- Cytotoxic drugs- kill cells which are dividing.
- Normal cells recover much better than cancer cells.
- Have significant, although in most cases temporary, side effects.
- Many are many decades old. Origins include plants, bacteria, mustard gas.



Percentage of patients receiving chemotherapy as part of primary lung cancer treatment *(CRUK, England data)*.

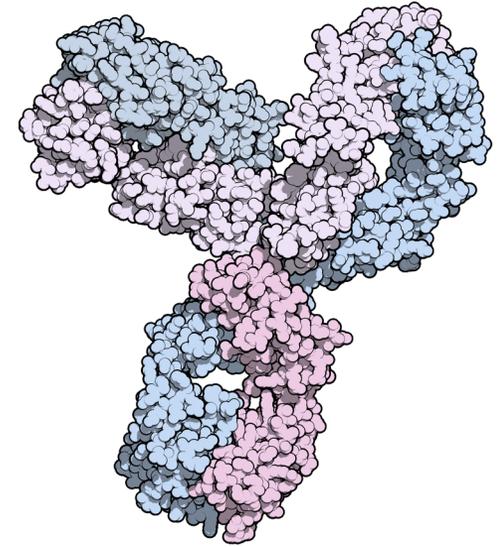
Stage at diagnosis	Patients with SCLC	Patients with NSCLC
All stages combined	67.7%	25.2%
Stage 1	55.7%	5.6%
Stage 2	77.5%	28.9%
Stage 3	81%	41.8%
Stage 4	65.1%	29.7%

Lung cancer, 1 year (L, 32%) and 10 year (5%) survival. *CRUK*



Advances in drug treatment of lung cancer.

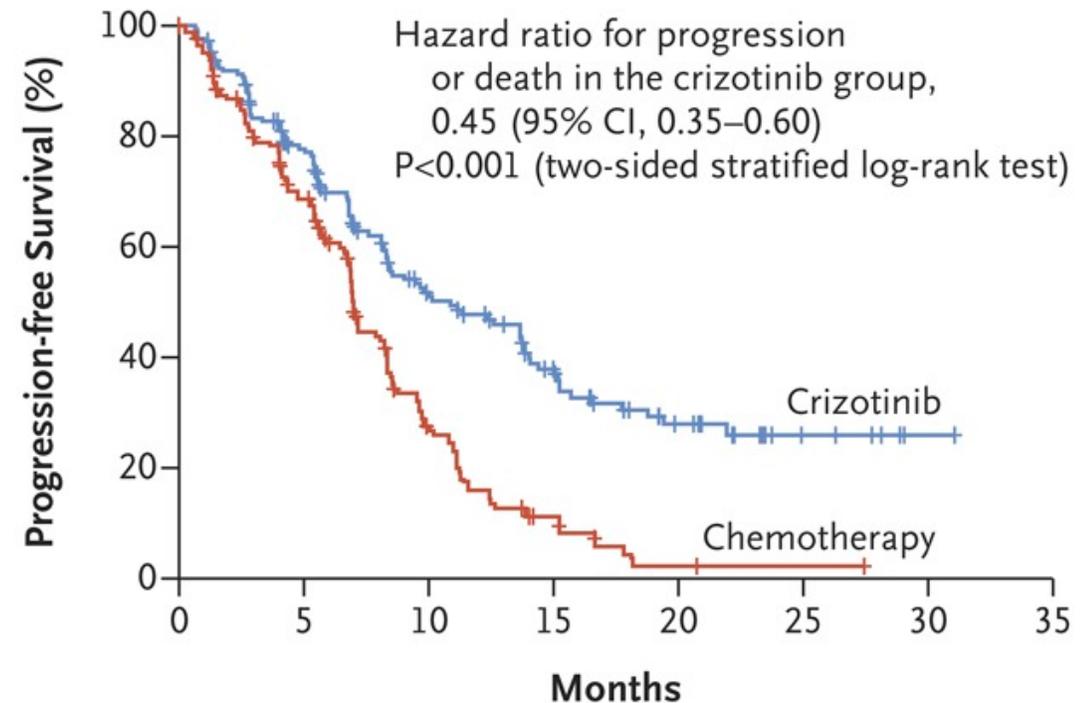
- Targeted therapy: drugs which interfere with the functioning of lung cancer cells.
- Immunotherapy: drugs (or possibly vaccines) which use the immune system to fight lung cancer.
- Currently for quite a restricted range of situations, but likely to expand.



Pembrolizumab (Keytruda, Wiki)

ALK+ non-small cell lung cancer.

- Anaplastic lymphoma kinase (ALK) mutation. This makes abnormal protein that can make cancer cells grow.
- 3-5%. Typically younger (50-60) and non- or light smokers.
- ALK inhibitor such as **crizotinib** or **alectinib** first-line treatment better than chemotherapy for advanced disease.
- Several new inhibitors developed. Brain penetration important.
- As resistance develops move from one ALK inhibitor to another.

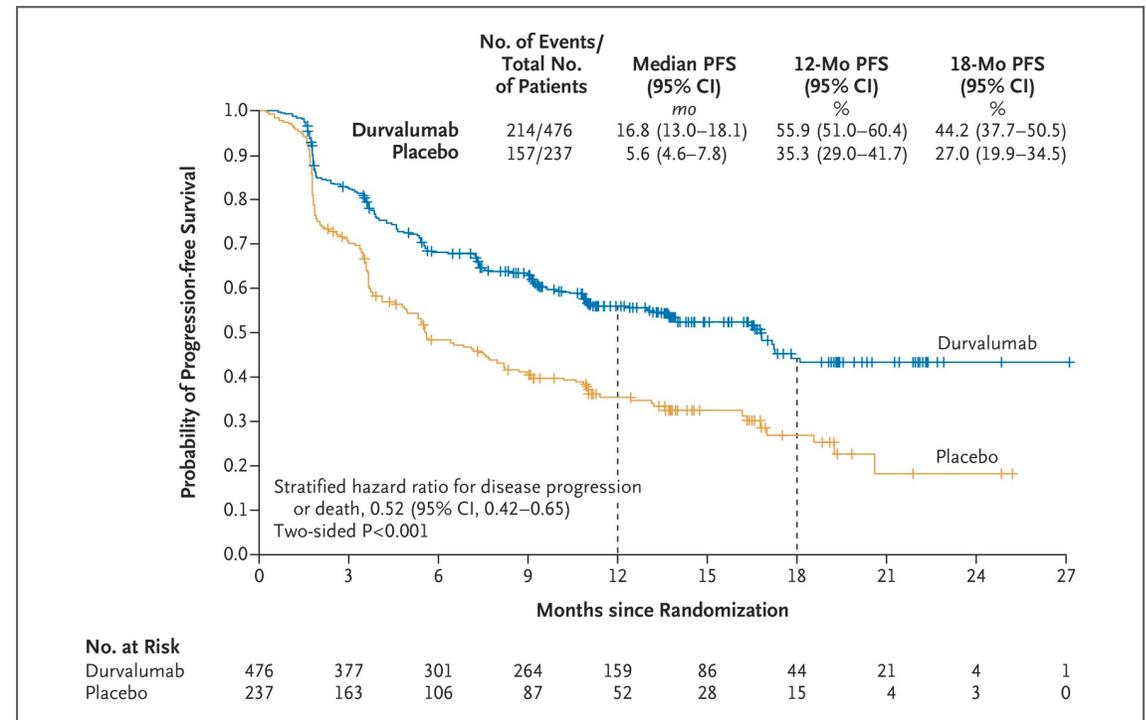


Progression-free survival v chemotherapy advanced disease.

Solomon et al 2014 NEJM. 1st generation.

An example of immunotherapy in advanced lung cancer.

- Durvalumab: a human IgG1 monoclonal antibody that blocks programmed death ligand 1 (PD-L1) binding.
- Allows T cells to recognise and kill tumor cells.
- NICE approved 2019 for people with advanced non small cell lung cancer who can't have surgery if positive for PD-L1.



Antonia S et al NEJM 2017

Of the occupational exposures that cause most cancer in the UK most lead to lung cancer and mesothelioma.

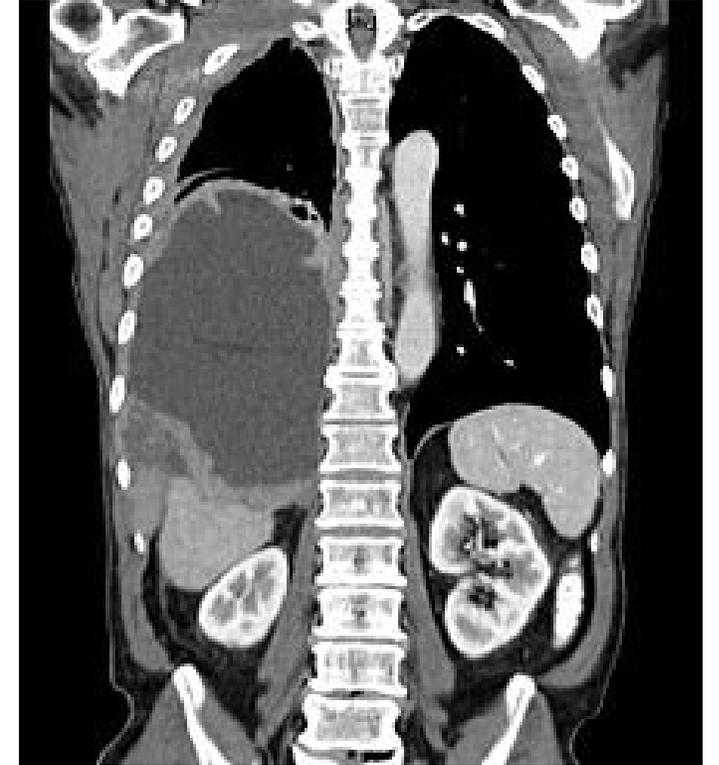
- Asbestos: 4000 pa.
- Silica 800.
- Diesel exhaust 650.
- Mineral oils 550.
- Paint 350.
- TCCD 230
- Radon 180.



Stanley Spencer. *Shipbuilders on the Clyde* (detail, 1946). IWM

Mesothelioma.

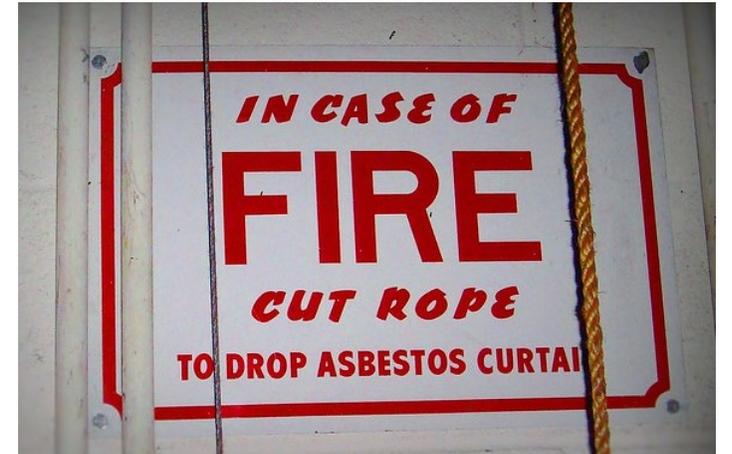
- An almost entirely preventable cancer.
- 94% of risk related to exposure to asbestos, almost all occupational.
- In 1955 Doll showed asbestos link with lung cancer; in 1960s link with mesothelioma clearly demonstrated in South Africa.
- “It would be ludicrous to outlaw this valuable and often irreplaceable material in all circumstances (as) asbestos can save more lives than it can possibly endanger.” *The Lancet* 1967



Mesothelioma
pleural effusion.
Wiki Commons.

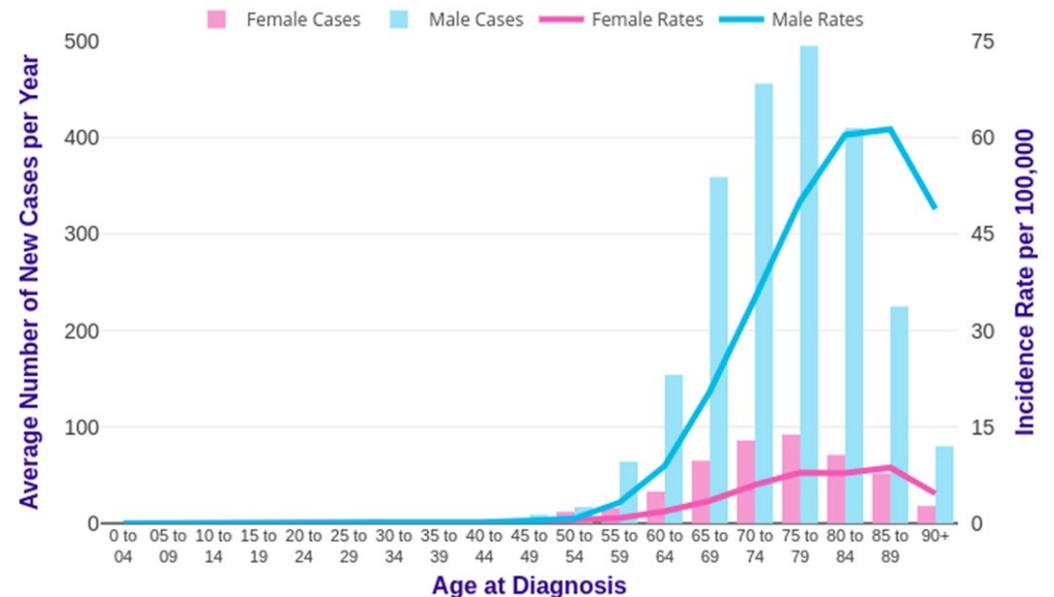
Asbestos was everywhere.

- Shipbuilding
- Heat insulation
- Cement and tiles
- Electrical insulation
- Safety curtains and blankets
- Ropes, brake pads
- Artificial snow
- Schools, kitchens, ironing boards, sheds...
- At 1973 peak, UK asbestos imports around 190,000 tonnes a year; by 1997, the amount had fallen to 4820 tonnes, banned in 1999.



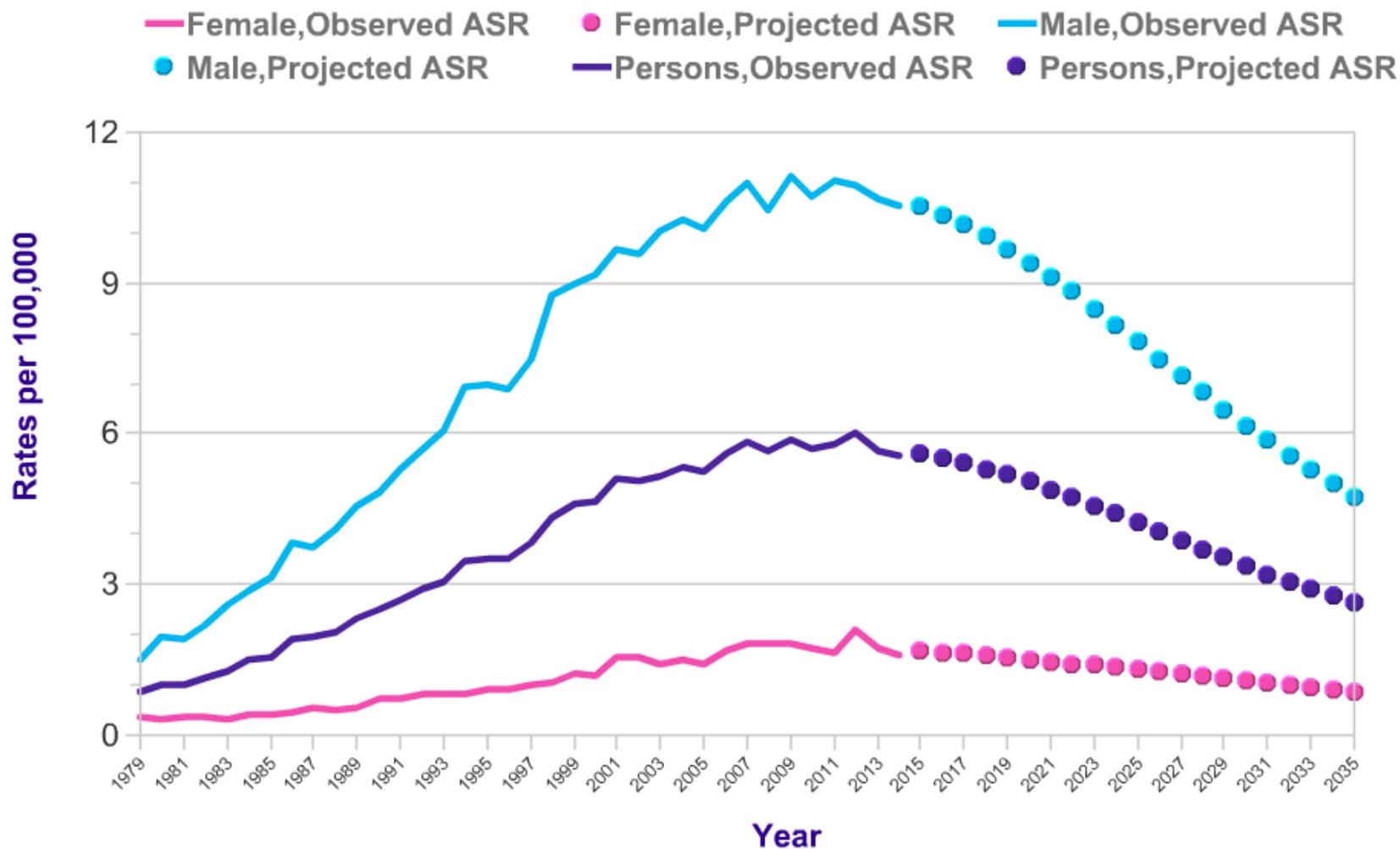
Although rare, mesothelioma has poor longer term survival.
Usually diagnosed in later stages.

- Around 2700 cases a year.
- Mesothelioma mortality rates increased by 887% since the early 1970s.
- 59% of patients diagnosed at Stage 1 survived their disease for at least one year, 30% of patients diagnosed at Stage 4.
- Five-year survival in men ranges from 13% in 15-49 year-olds to 4% in 80-99 year-olds in England.



Observed and projected mesothelioma incidence, UK. Rose rapidly, peak 2020, projected to fall by over 50% by 2035.

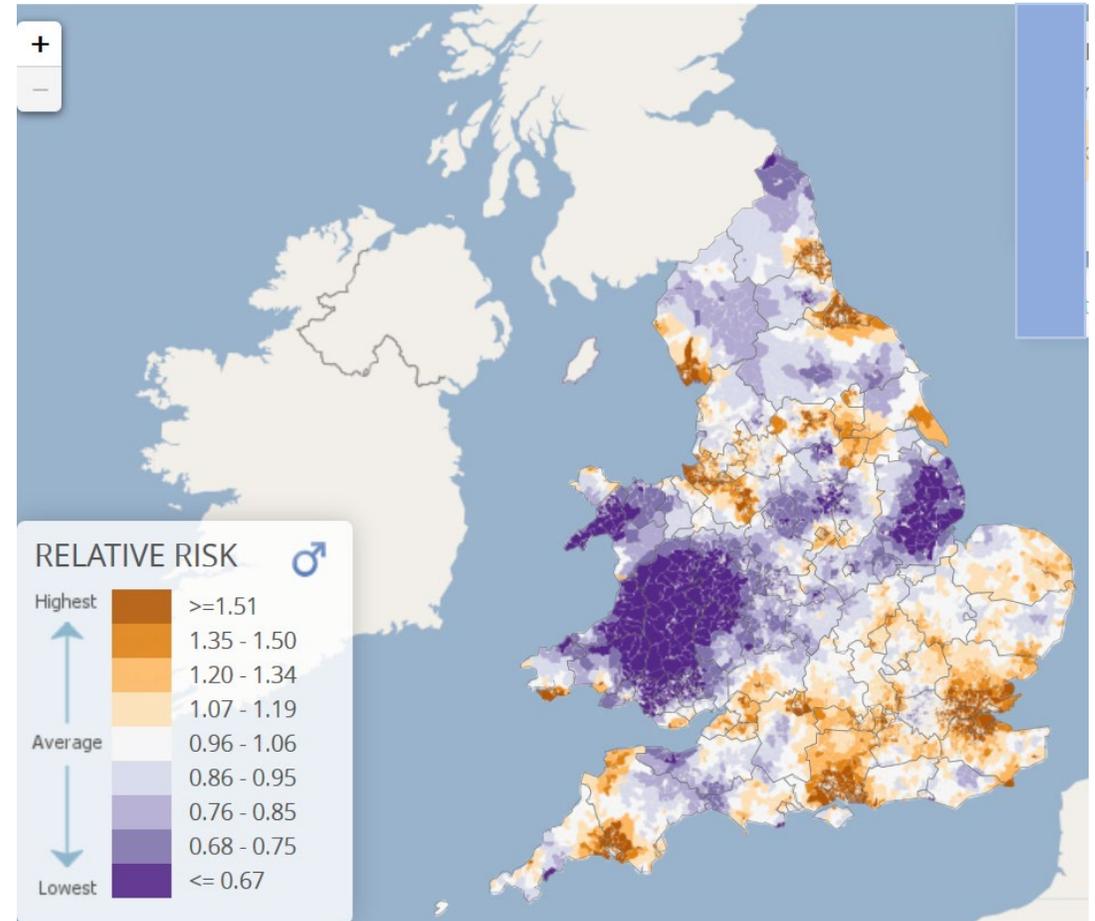
(CRUK)



Mesothelioma heavily concentrated in males and in specific areas.

- Former shipbuilding areas.
- Construction / demolition workers.
- Smoking a co-factor.

- Partners of asbestos workers also at higher risk.



Mesothelioma in men. Small area health statistics unit.

Lung cancer and mesothelioma.

- Lung cancer is, and will remain for many years, the leading cause of cancer mortality.
- The great majority due to smoking; it is a profit-driven cancer, using deliberate early addiction.
- Smoking is falling, and so will lung cancer.
- A minority is due to air pollution and occupation, also mostly preventable.
- Earlier diagnosis is essential.
- Treatment is improving.
- Asbestos is the leading occupational cause of cancer-mesothelioma and lung cancer.



Vincent Van Gogh