

Avoidable causes of cancer

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How many 'environmental' cancers could be prevented?

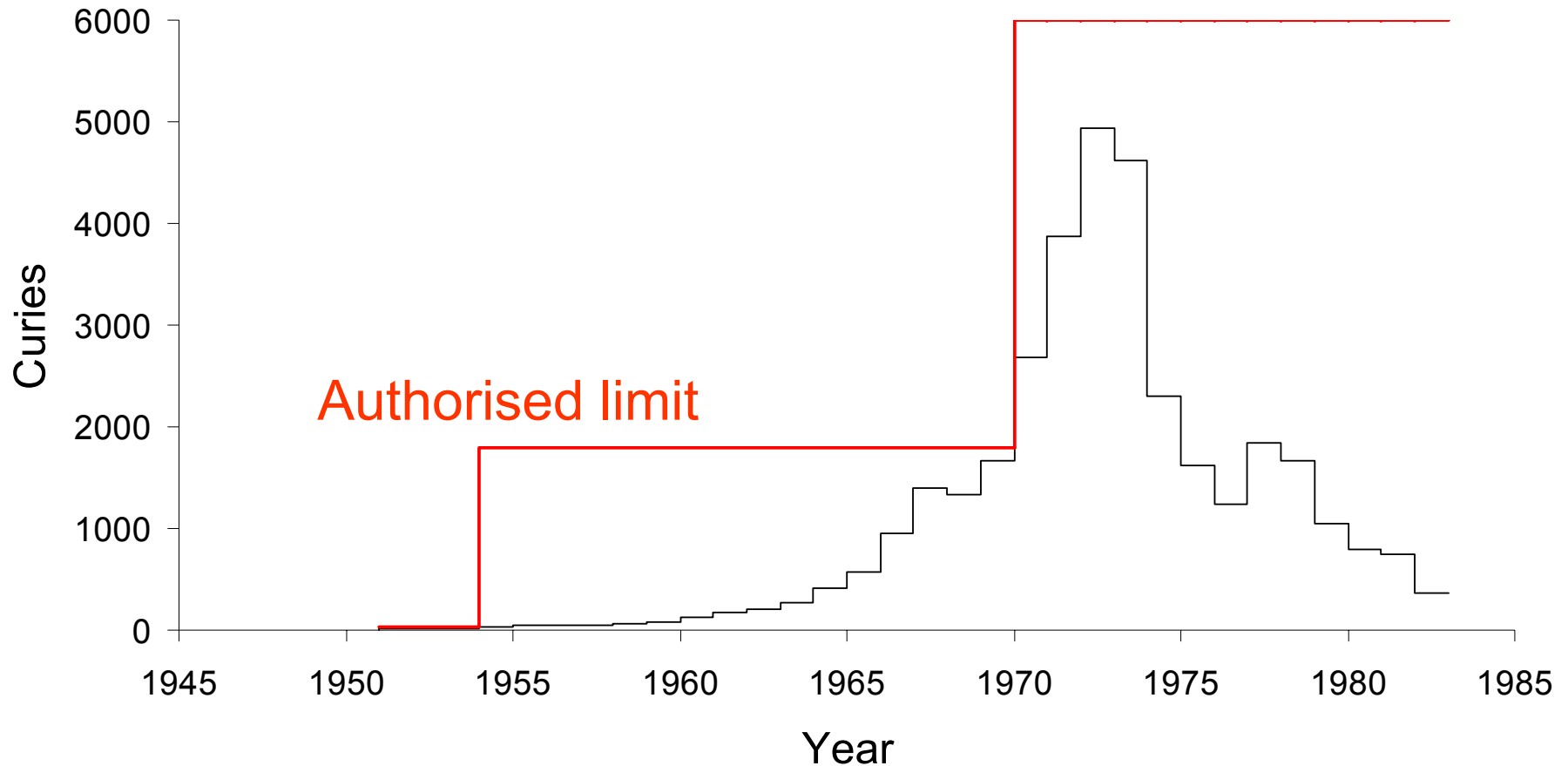
1. Current cancer rates or current exposures?
2. Separate analyses for smokers and non-smokers
3. What is 'environmental'? HPV causes cervical cancer and breast-feeding prevents breast cancer
4. Protection of susceptible subgroups (RB1 etc)

Percentage of US cancer deaths that would be avoided by eliminating known risks

Peto (2001) Nature 411: 390

Cause	Current smokers	Non-smokers
Smoking	60	-
Known infections	2	5
Alcohol	0.4	1
Sunlight	0.4	1
Air pollution	0.4	1
Occupation	0.4	1
Lack of exercise	0.4	1
Toxic chemicals	?	?
Overweight (BMI>25kg m ²)	4	10
Other dietary factors	4 - 12?	10 - 30?
Presently unavoidable	About a quarter	At least half

Sellafield – Radioactive alpha discharges to the sea and authorised limits



The example of asbestos

Most Western countries (not Canada)

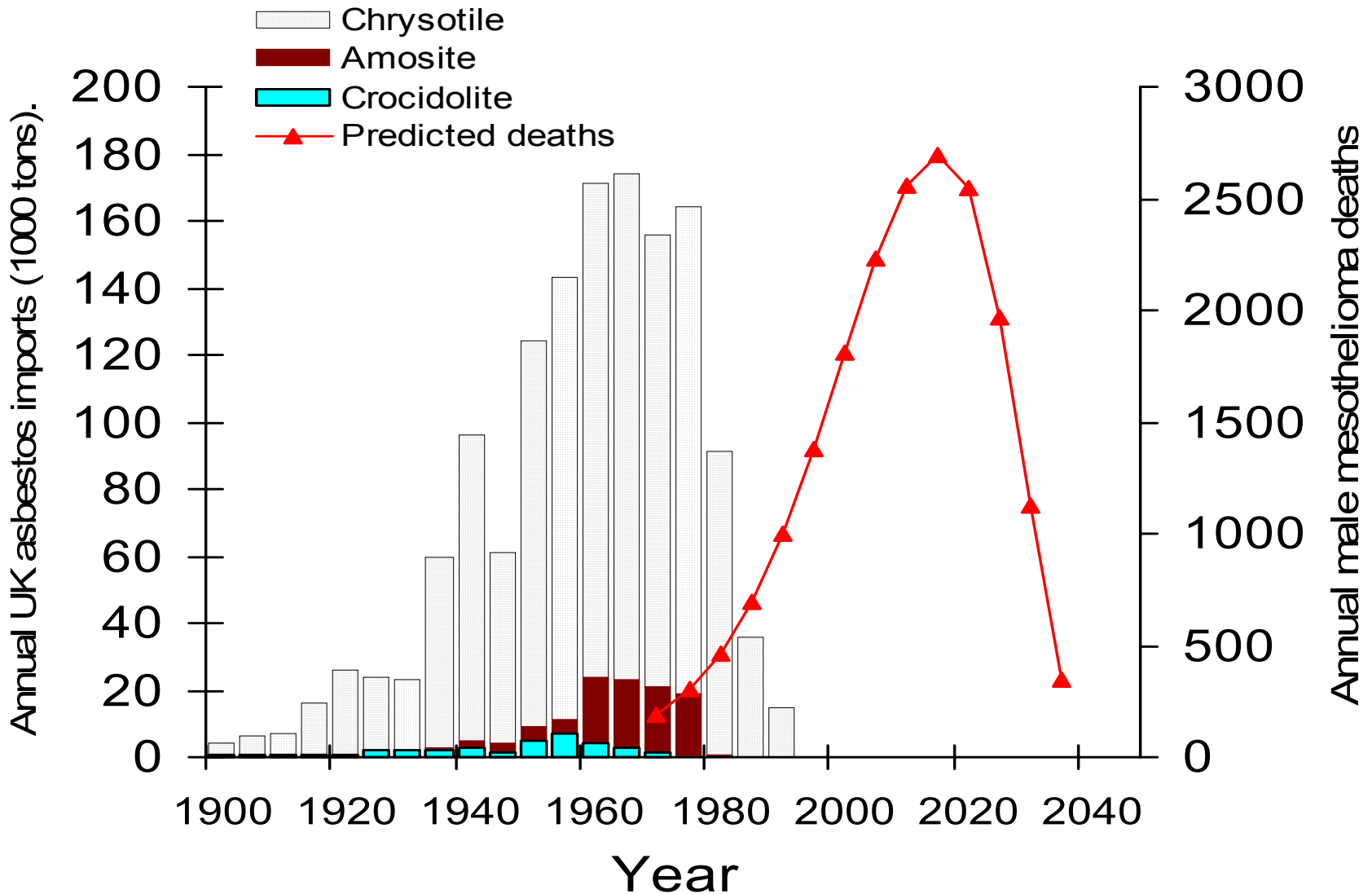
Most or all asbestos products are now banned.

Mesothelioma rates are still rising in old age, but are level or falling at younger ages in countries that have stopped using asbestos products.

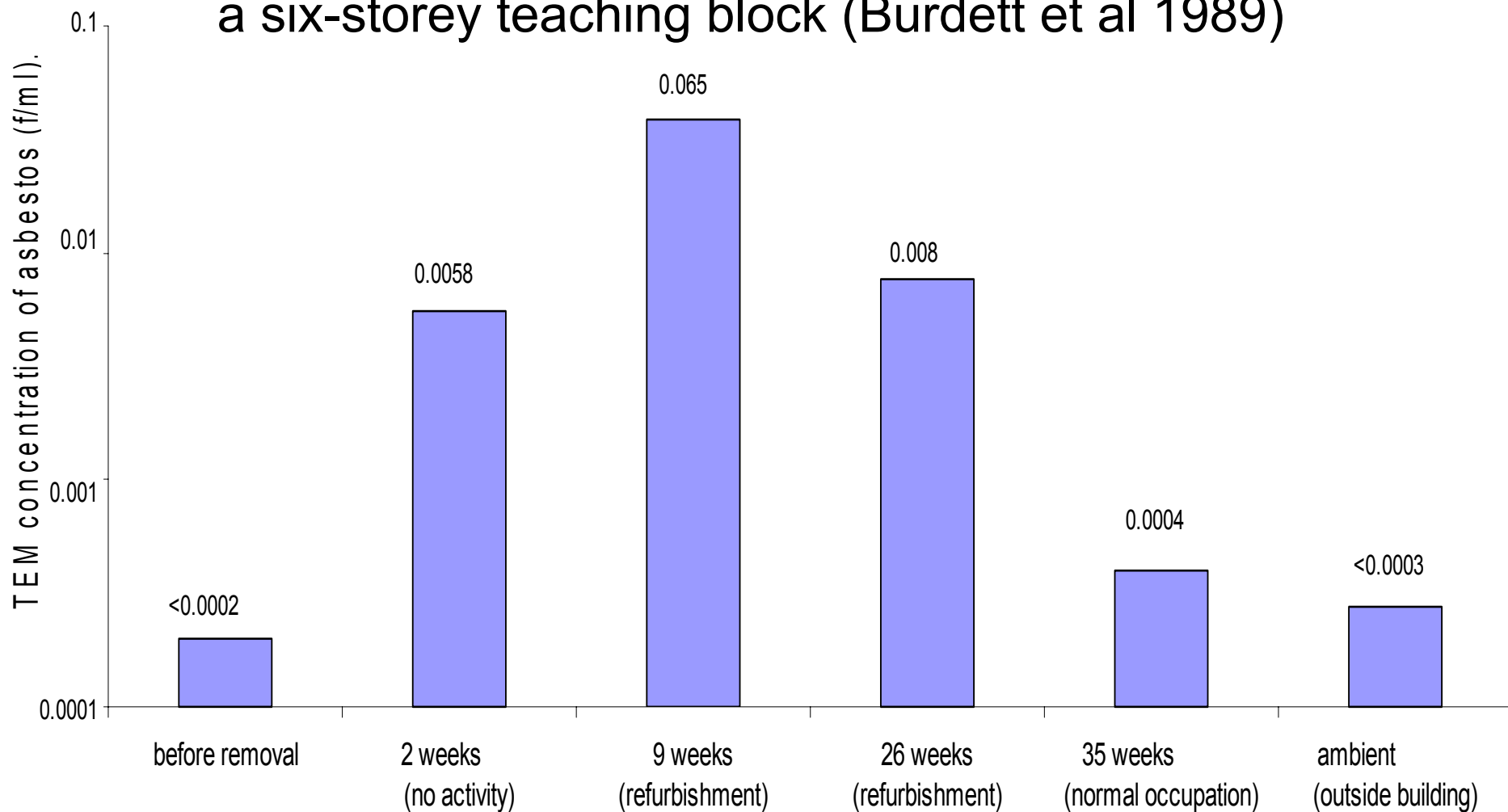
Rest of the world

Asbestos use is continuing and in some cases increasing. Leading consumers include Russia, India and most other Asian countries except Japan.

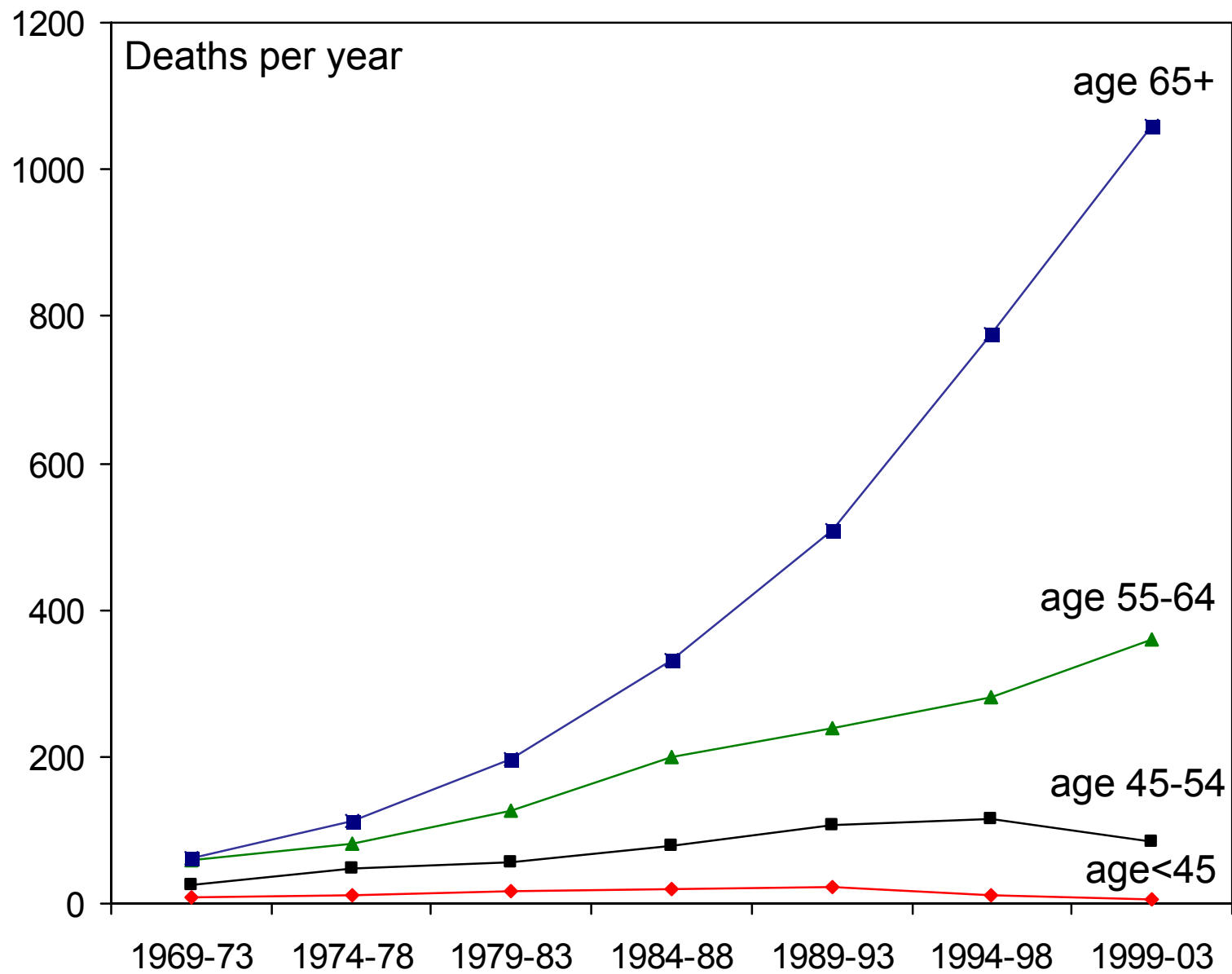
UK asbestos imports & predicted mesothelioma deaths in men born before 1953



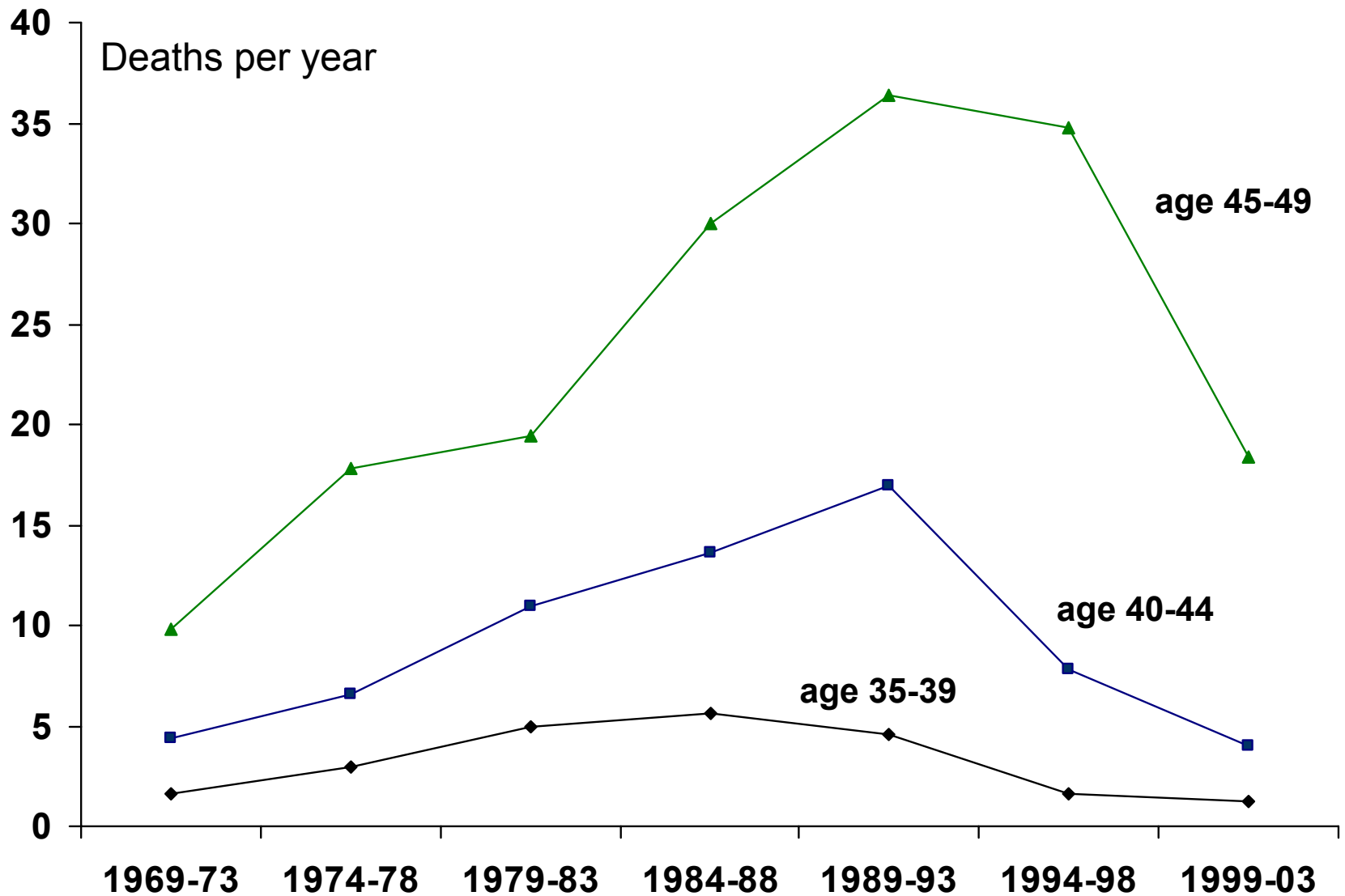
Average TEM concentrations of asbestos fibres >5µm long before, during and after an asbestos removal programme from a six-storey teaching block (Burdett et al 1989)



British male mesothelioma deaths since 1969



British male mesothelioma deaths below age 50 since 1969



Current cancer rates due to past occupational and environmental exposures, and future cancers due to current exposure levels

Cancer deaths in Britain in 2004 caused by asbestos:
1,500 of the 1,700 male mesothelioma deaths
(plus 100 of the 300 mesothelioma deaths in women)
2,000 – 4,000 lung cancers?
Total ~ 5% of all cancer deaths in men

How many deaths in 2150 will be caused by asbestos exposure in 2007?

British case-control study of 513 male mesotheliomas diagnosed 2000-2005 and 1112 population controls

Exposure category	Odds ratio	Percent of population	Lifetime risk
Any asbestos at work <1980	13.4	47%	1.1%
(Carpenters	~60	1%	6.0%)
Lived with asbestos worker	2.7	12%	0.2%
Lived < 1 mile from source	3.2	2%	0.3%
Any other industrial work	1.7	24%	0.1%
All other men	1.0	14%	0.1%
<hr/>			
All British men born 1940-49		100%	*0.6%

*Predicted cumulative risk to age 90 in British men born 1940-49

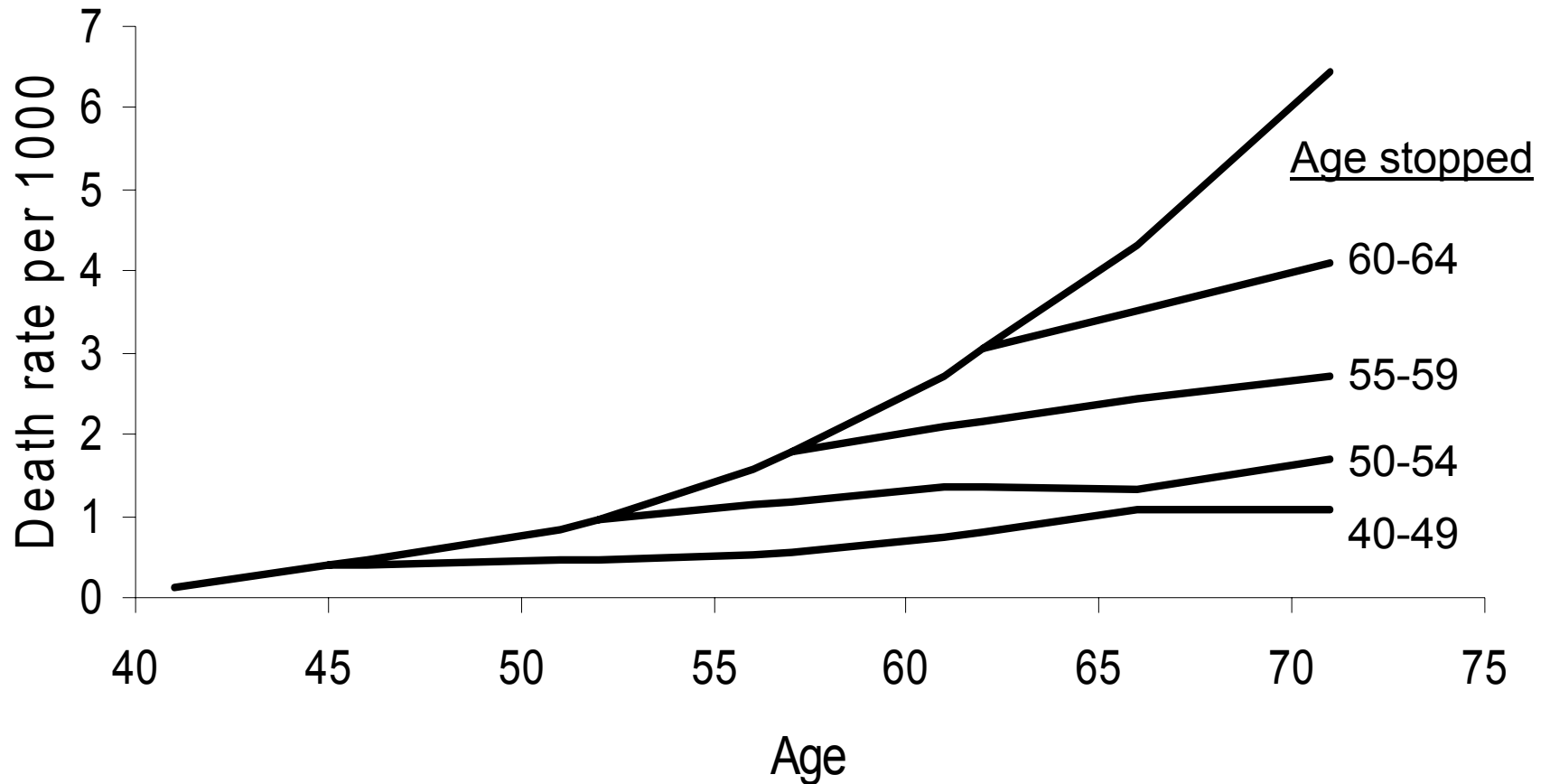
Interaction between smoking and other carcinogens

North American insulation workers: lung cancer mortality in smokers and non-smokers

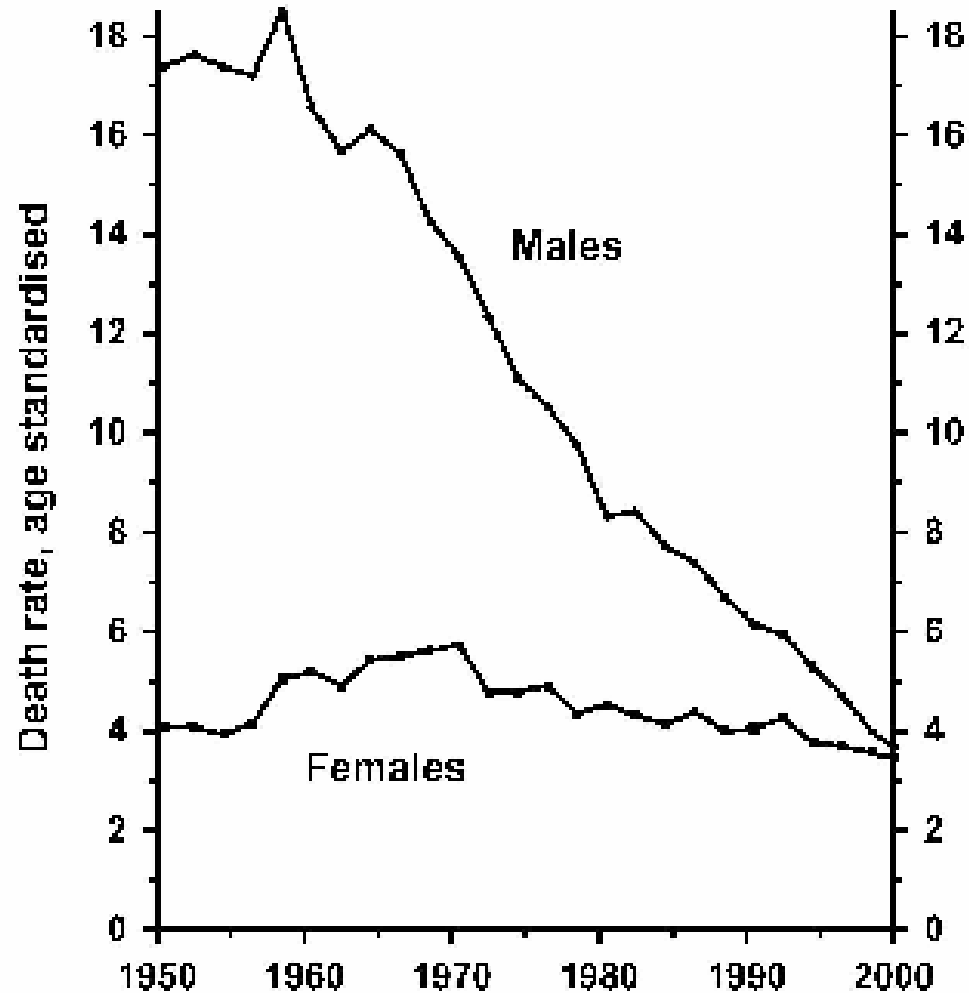
	Observed	Expected*	Obs/Exp*
Smokers first exposed to asbestos before age 25	211	32.7	6.5
Smokers first exposed to asbestos after age 25	237	48.1	4.9
Non-smoking insulation workers	5	1.04	4.8

*Expected numbers are based on smoking-specific population rates

Lung cancer mortality in continuing smokers and ex-smokers. Halpern et al (1993) JNCI 85, 457



UK lung cancer mortality at ages 35-44 since 1950



Does chrysotile cause mesothelioma?

“At present day levels of exposure to commercial chrysotile, whether or not contaminated with tremolite, the risk must be vanishingly small”

JC & AD McDonald 1997

“Exposure to chrysotile probably remains the leading cause of mesothelioma in the world in view of the far wider use of this material than of other types of asbestos.....The proposition of putting more asbestos into the environment.....is foolhardy”

MR Cullen 1998

Pooled mortality from 7 cohort studies of male
chrysotile workers
(Health Effects Institute, 1991)

Lung cancer deaths: 448 observed, 309 expected
Excess = 139 deaths

Mesothelioma: 15 deaths

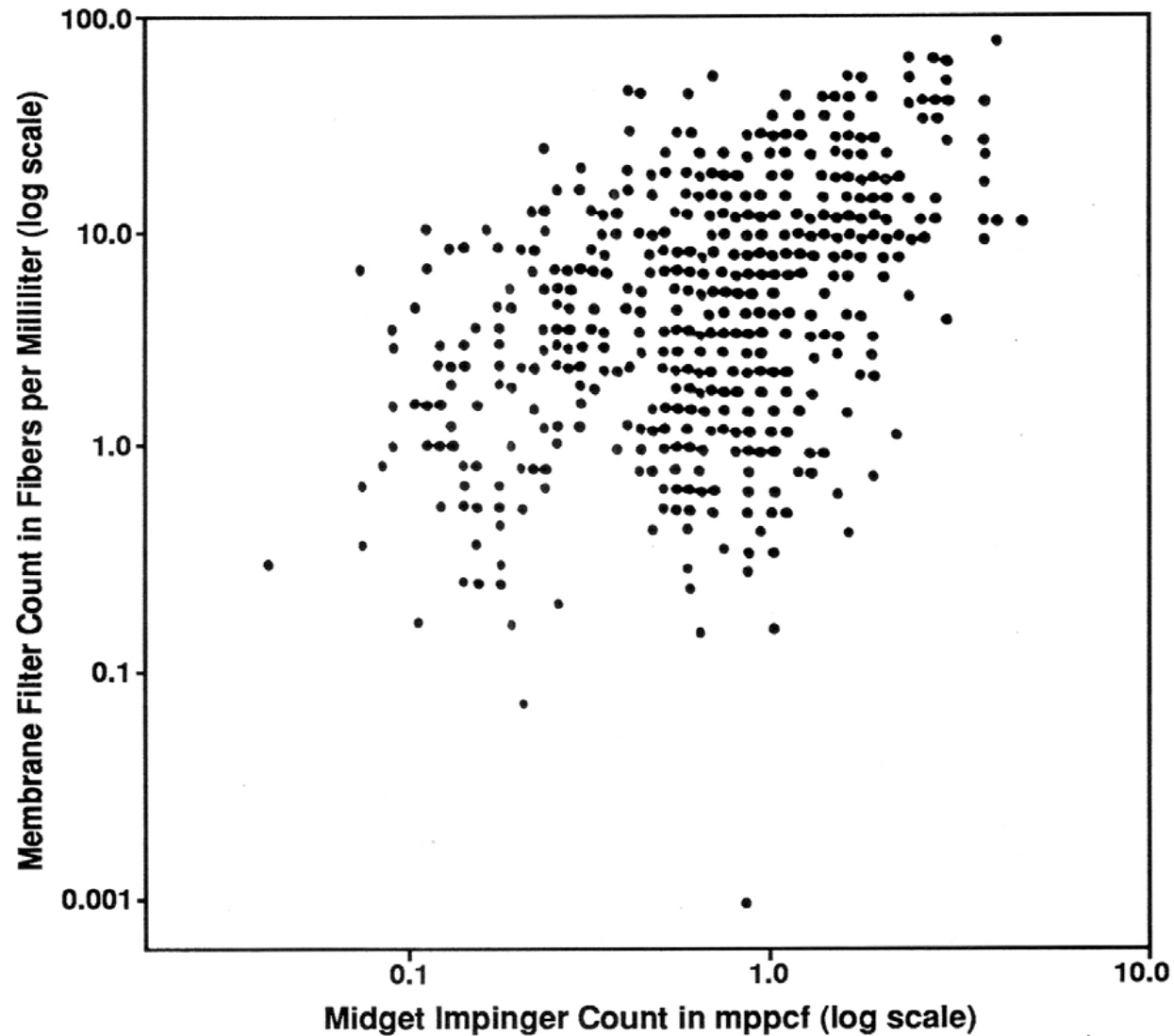
Can we predict the effect of current exposure levels from historical dose-response data?

Lung cancer deaths in Quebec chrysotile miners and millers

McDonald et al., 1980. Br J Ind Med 37: 11-24

Duration (years)	Exposure level			
	Low/Medium ~ 5 mppcf		High/Very high ~ 40 mppcf	
	Deaths	SMR	Deaths	SMR
< 1	31	1.1	16	0.8
1 – 4	18	0.8	11	0.8
5 – 19	27	1.3	23	1.5
> 20	48	1.2	56	2.4

Quebec chrysotile mines and mills: parallel particle and fibre counts in the early 1970s



How many 'environmental' cancers could be prevented?

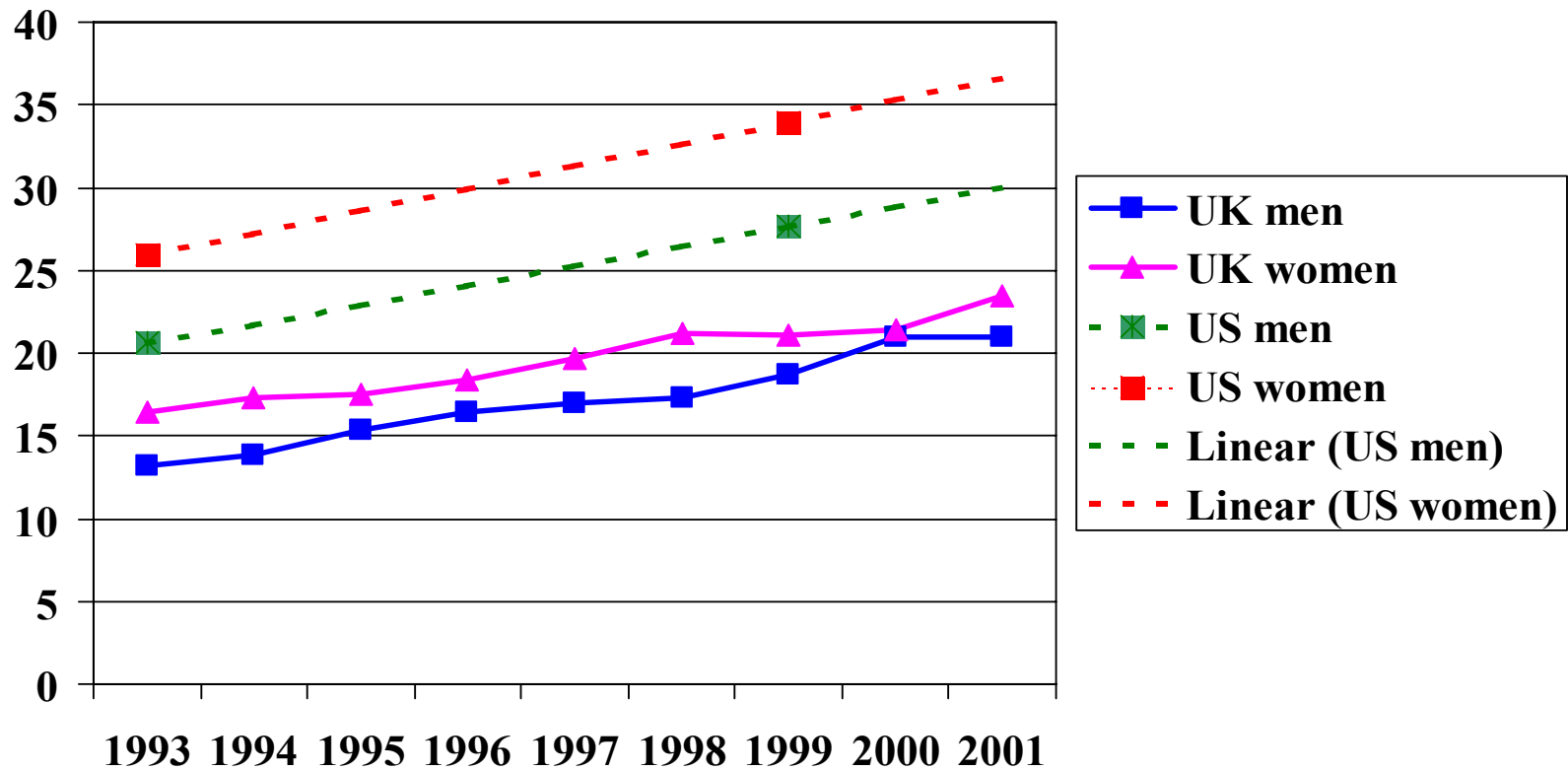
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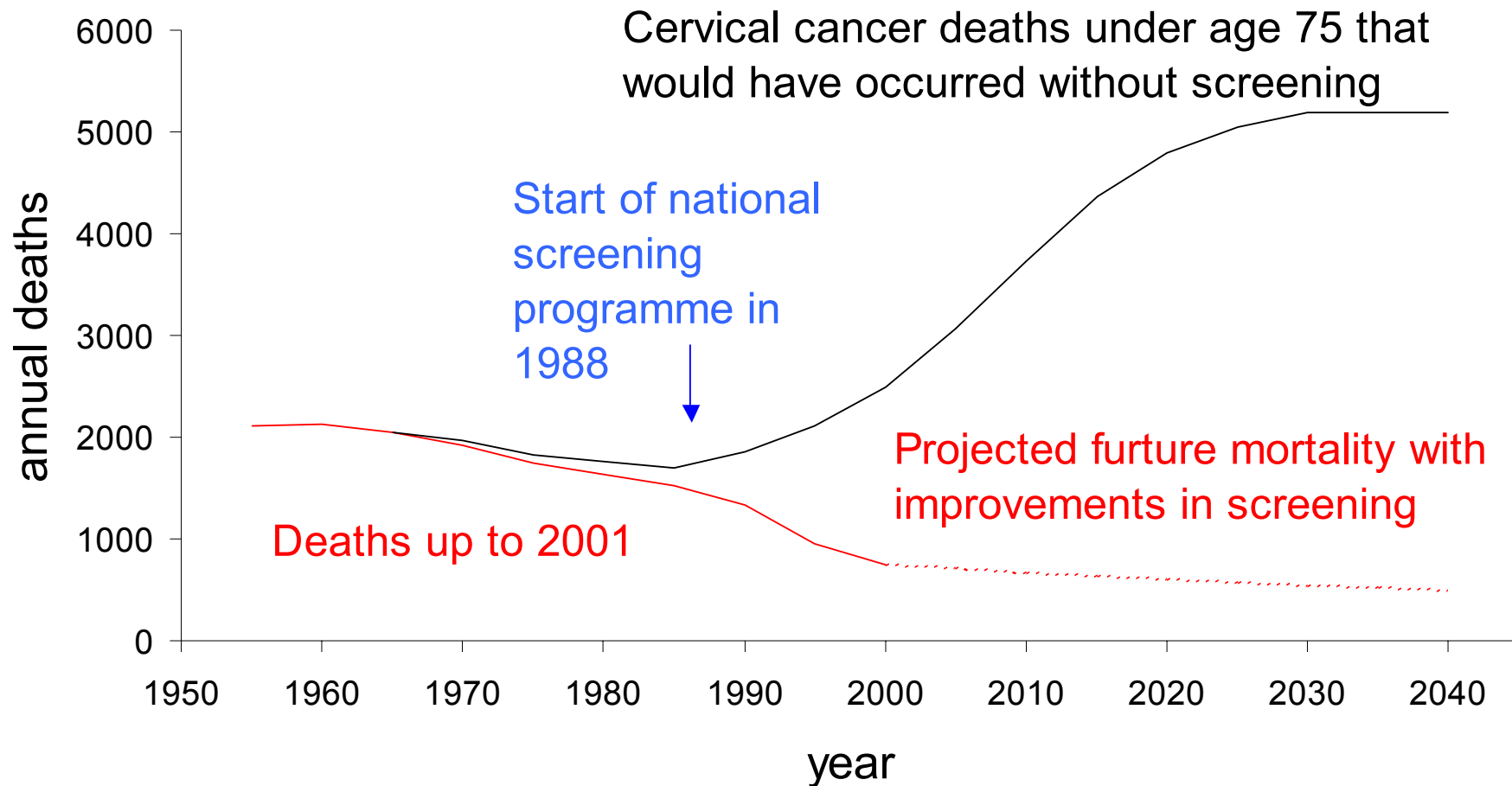
Peto (2001) Nature 411: 390

Cause	Current smokers	Non-smokers
Smoking	60	-
Known infections	2	5
Alcohol	0.4	1
Sunlight	0.4	1
Air pollution	0.4	1
Occupation	0.4	1
Lack of exercise	0.4	1
Toxic chemicals	?	?
Overweight (BMI>25kg m ²)	4	10
Other dietary factors	4 - 12?	10 - 30?
Presently unavoidable	About a quarter	At least half

Prevalence of obesity in men and women 1993-2001 (data from Health Survey for England)

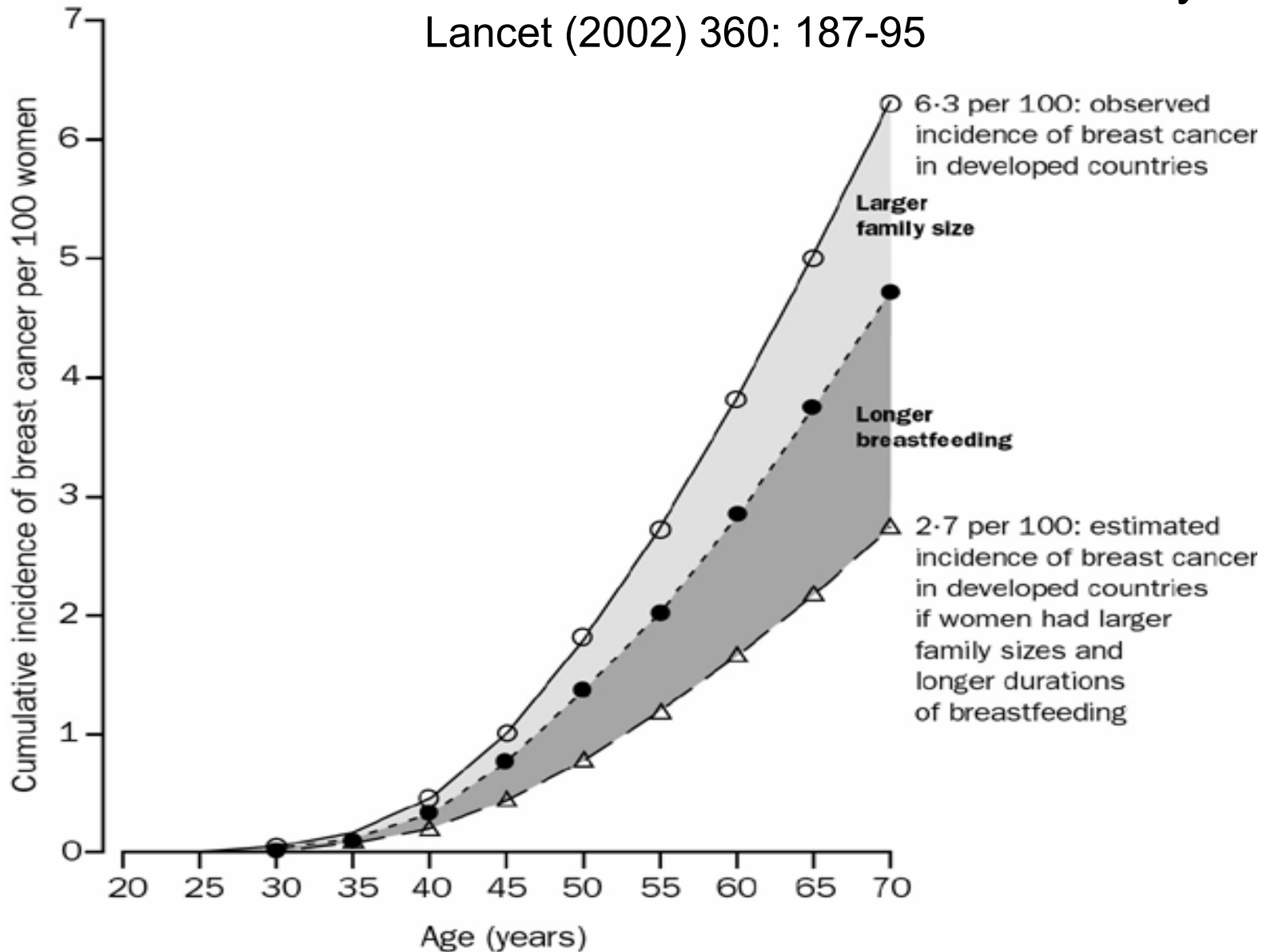


Reduction in British cervical cancer mortality due to screening



Predicted reduction in Western breast cancer rates if women had 6 or 7 children and breastfed each child for 2 years

Lancet (2002) 360: 187-95



The inhaled particles study (TIPS)

Aim:

- To determine current asbestos lung burdens in builders and other workers who started work after asbestos installation had ceased in Britain

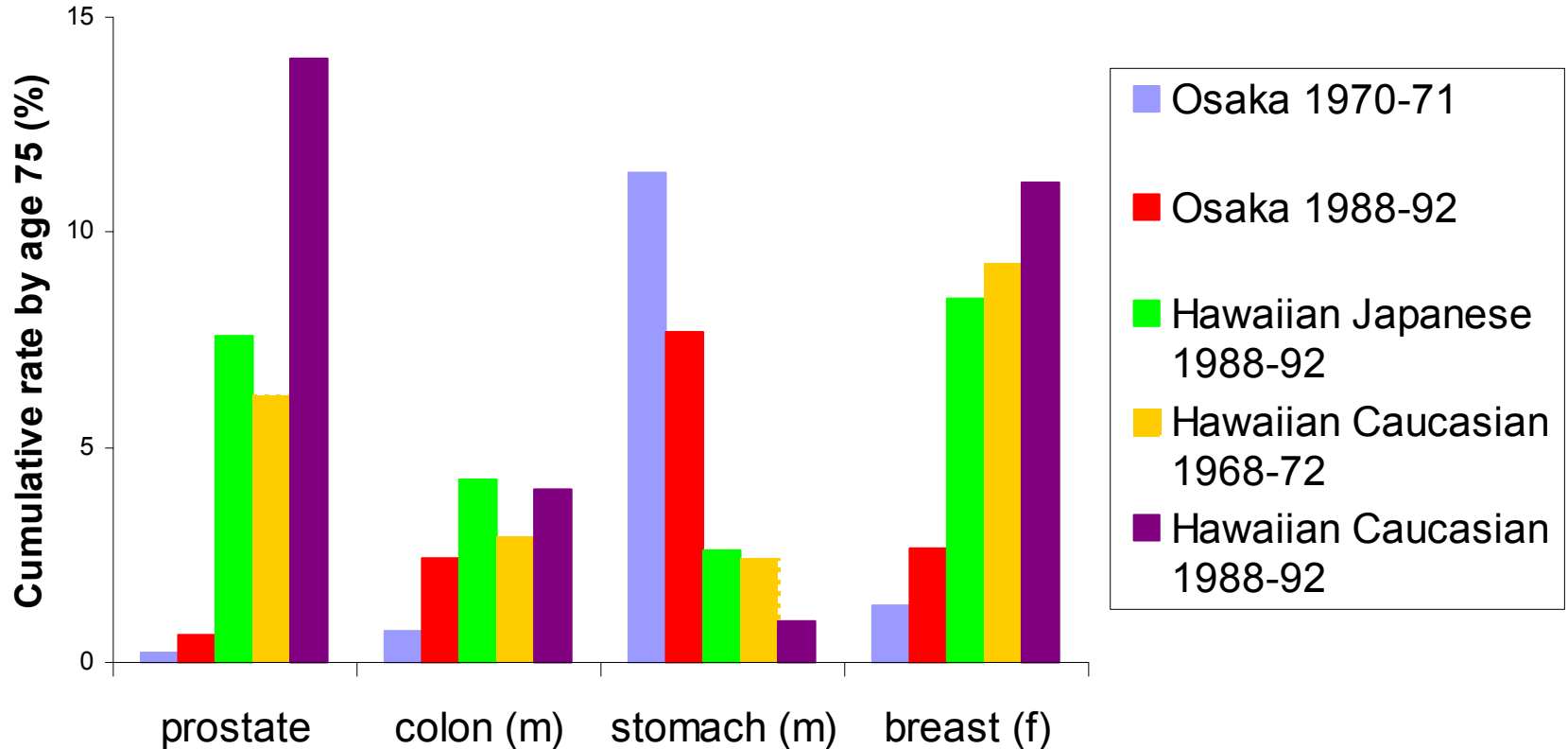
Study Plan:

- Asbestos fibre count on samples from apex of lung from pneumothorax patients aged 18-60
- Occupational and residential history
- 500 patients from Guy's and St Thomas's

CANCER RESEARCH UK



Cancer rates in migrants become similar to those in the local population



Conclusion:

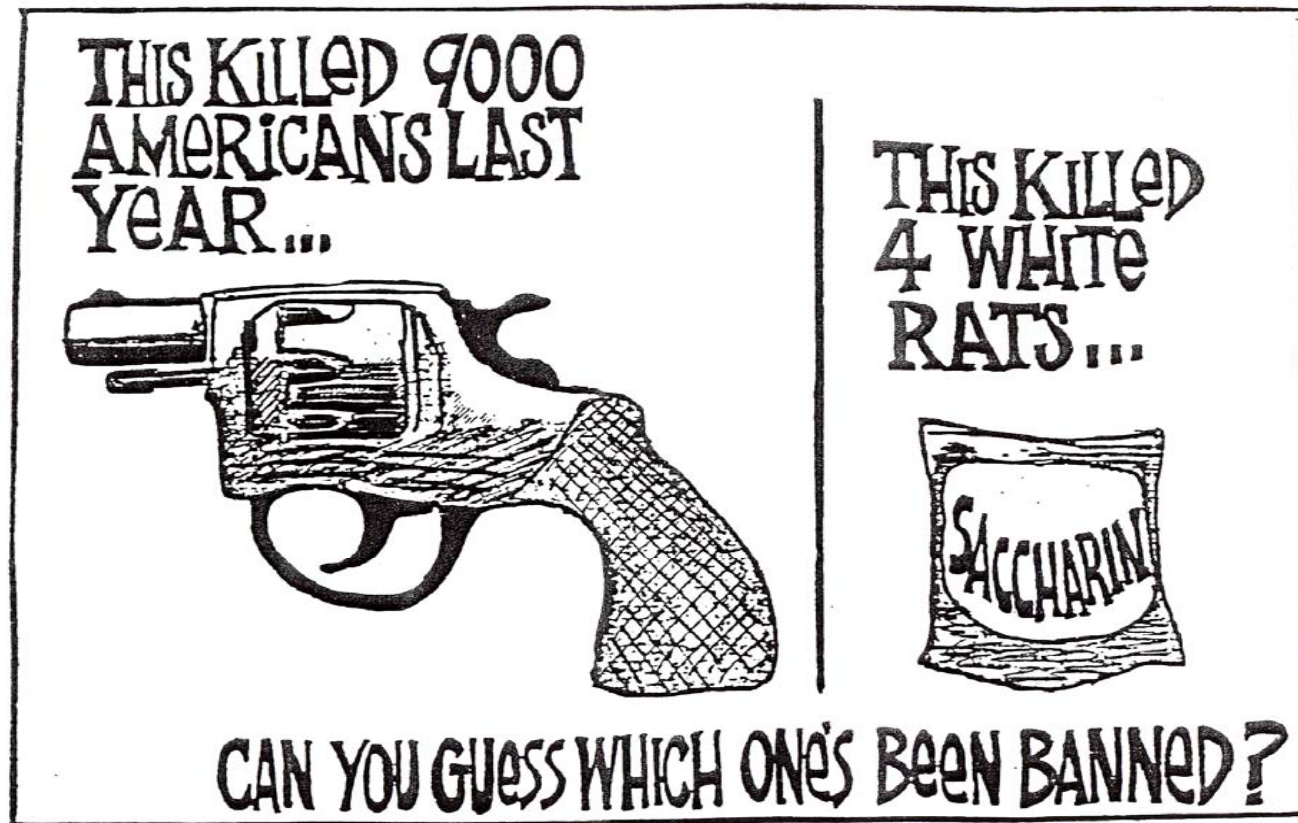
Cancer rates in migrants show that most human cancer is 'environmental' – it is avoidable by a suitable lifestyle.

Non sequitur:

Most human cancer is caused by carcinogens in the environment.

‘There is a gradually developing myth, partly promoted by those who derive a psychopathological delight in spreading alarm, that most human cancer is the result of an exposure to chemicals in the environment.’

John Barnes (1974) Essays in Toxicology 5: 5-15.



Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50 302 women with breast cancer and 96 973 women without the disease

Collaborative Group on Hormonal Factors in Breast Cancer
Lancet (2002) 360:187-195

Reduction in risk:

3.0% per year for earlier age at first birth

7.0% per birth

4.3% per year of breastfeeding

Richard Doll's view of historical exposure data

‘When so much work has been done in collecting and analysing measures of ambient pollution, we hesitate to suggest that the results are insufficiently reliable to justify making any quantitative extrapolation from past experience to the effects of current exposures. Nevertheless, this may in fact be the case and we may have to be satisfied with qualitative conclusions based on knowledge of the direction in which progress has been made and epidemiological observations of the effects of qualitatively different types of exposure.’

Effects on health of exposure to asbestos
(Doll & Peto, HSC Report 1985)

Cancer mortality and body-mass index in American men

(Calle et al. 2003. NEJM 348: 1625-38)

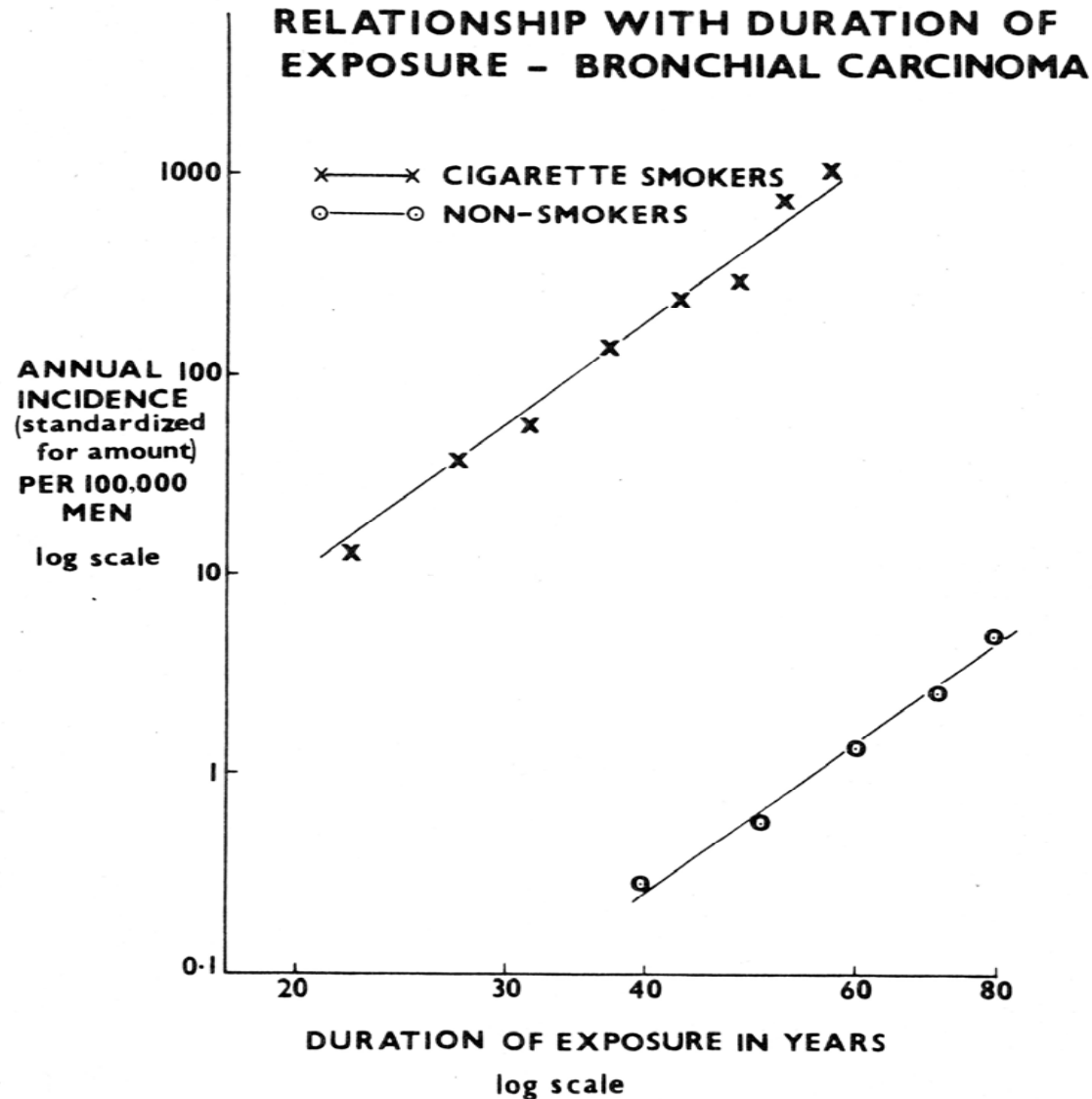
	Body-mass index (kg/sq m)			
	18.5-24.9	25.0-29.9	30.0-34.9	>35.0
Colorectal	1.0	1.2	1.5	1.8
Pancreas	1.0	1.1	1.4	1.5
Kidney	1.0	1.2	1.4	1.7
Liver	1.0	1.1	1.9	4.5
Oesophagus	1.0	1.8	1.9	
NH lymph.	1.0	1.1	1.6	1.5
Myeloma	1.0	1.2	1.4	1.7
Leukaemia	1.0	1.1	1.4	1.7
Prostate	1.0	1.1	1.2	1.3
All cancers in non-smokers	1.0	1.1	1.4	1.3

Cancer mortality and body-mass index in American women

(Calle et al. 2003. NEJM 348: 1625-38)

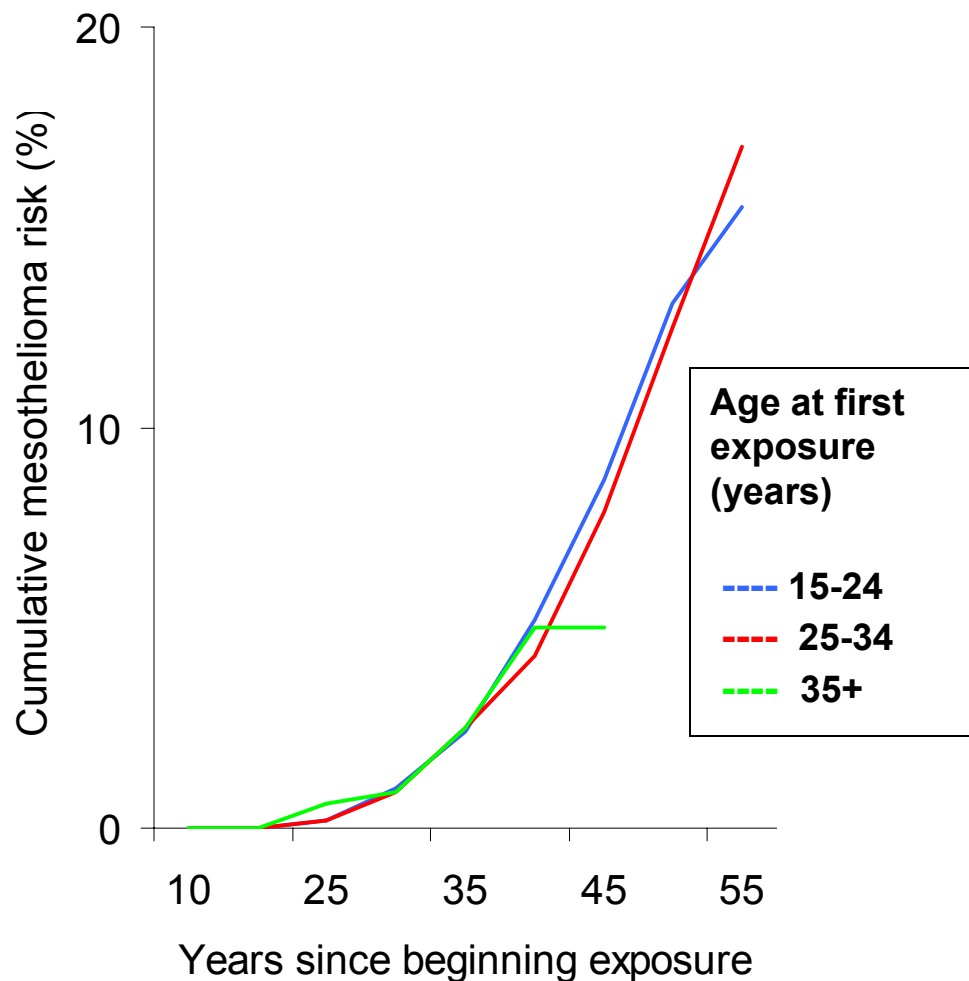
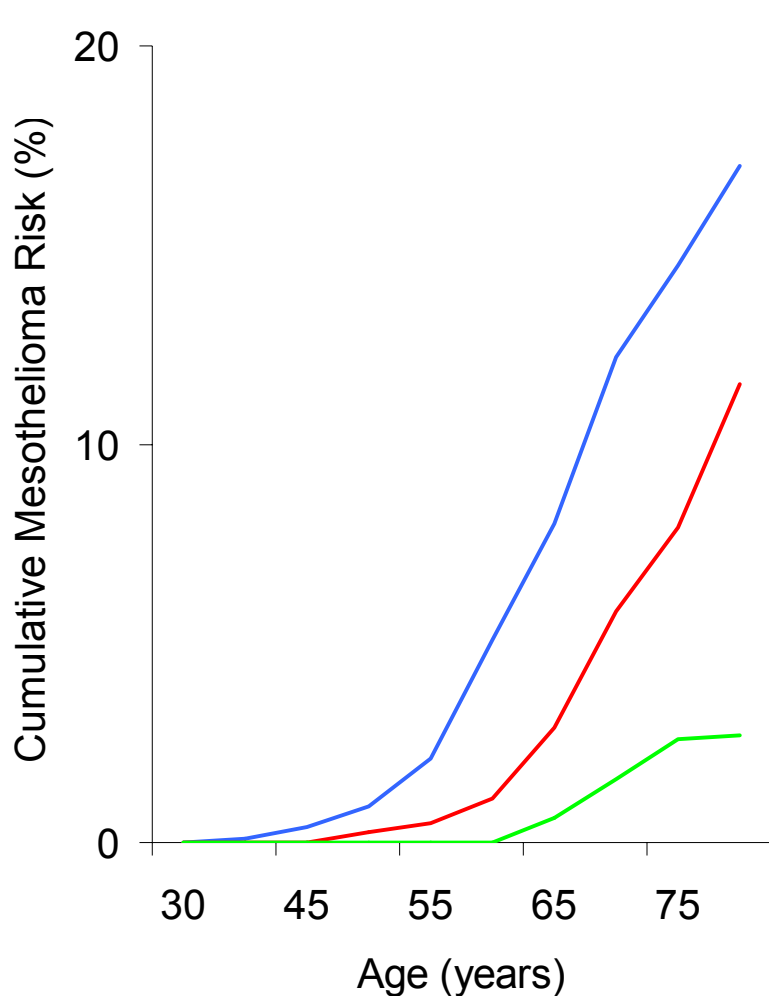
	Body-mass index (kg/sq m)				
	18.5-24.9	25.0-29.9	30.0-34.9	35.0-39.9	>40
Breast	1.0	1.3	1.6	1.7	2.1
Uterus	1.0	1.5	2.5	2.8	6.3
Cervix	1.0	1.4	1.2	3.2	
Ovary	1.0	1.2	1.2	1.5	
Colorectal	1.0	1.1	1.3	1.4	1.5
Pancreas	1.0	1.1	1.3	1.4	2.8
Kidney	1.0	1.3	1.7	1.7	4.8
Liver	1.0	1.0	1.4	1.7	
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Myeloma	1.0	1.1	1.5	1.4	
All cancers in non-smokers	1.0	1.1	1.3	1.4	1.9

Lung cancer incidence in non-smokers is proportional to the fourth power of age. In smokers it is proportional to the fourth power of duration of smoking, independent of age. (Doll 1978: Cancer Research 38: 3573-83)



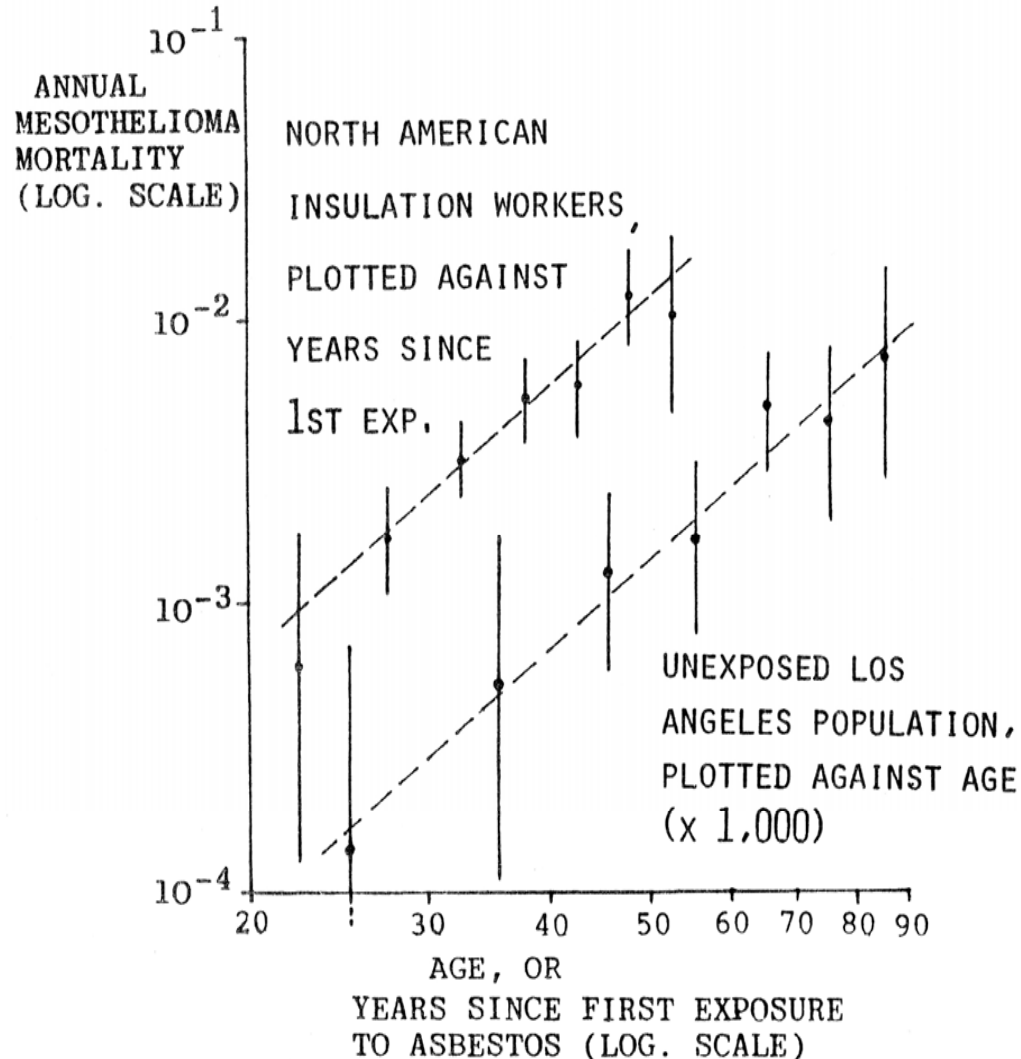
Mesothelioma mortality in North American insulation workers is independent of age

(Peto et al 1982: Br J Cancer 45: 124-135)



Mesothelioma incidence is proportional to the third power of time since first asbestos exposure, independent of age. In unexposed people it is proportional to the third power of age.

(Peto et al 1982: Br J Cancer 45: 124-135)



Dose-response models: predicted increase in cancer incidence at age T caused by one year of asbestos exposure at a level of F fibres/ml at age A
(Peto 1978: Lancet i 484-489)

Lung cancer:

Increase in smoking-specific relative risk is proportional to F , irrespective of ages A and T .

Mesothelioma:

Increase in incidence is proportional to F multiplied by the second or third power of latency ($T - A$).

SV-40 and mesothelioma

International SV-40 Working Group (2001)

Cancer Epidemiology, Biomarkers and Prevention. 10: 523-532

- Replicate samples from 25 fresh frozen mesothelioma samples and 25 controls were analysed in nine laboratories
- None was reproducibly positive for SV-40 DNA by PCR
- The previously reported association may have been entirely due to contamination

What is the risk at 1 fibre/ml?

‘The results [may be] insufficiently reliable to justify making any quantitative extrapolation from past experience to the effects of current exposures.....’

We may have to be satisfied with qualitative conclusions based on knowledge of the direction in which progress has been made and epidemiological observations of the effects of qualitatively different types of exposure.’

Effects on health of exposure to asbestos

(Doll & Peto, HSC Report 1985)

Lung cancer and mesothelioma deaths in Rochdale asbestos textile workers

(about 10 fibres/ml: 95% chrysotile, 5% crocidolite)

Year first employed	Duration (years)	Lung cancer Deaths	Lung cancer SMR	Mesothelioma Deaths	Mesothelioma SMR
Pre-1923	Over 20	13	8.2	2	-
1933-73	Over 20	28	1.7	5	19.1
	10-19	39	1.7	5	13.2
	1-9	47	1.0	2	2.4
	Under 1	83	1.1	7	3.4

Effects of chrysotile alone

Lung cancer

3 to 10 fold excess after prolonged heavy exposure.

20-fold variation in risk at the same nominal fibre level.

Low risk after less than 10 years of exposure.

Mesothelioma

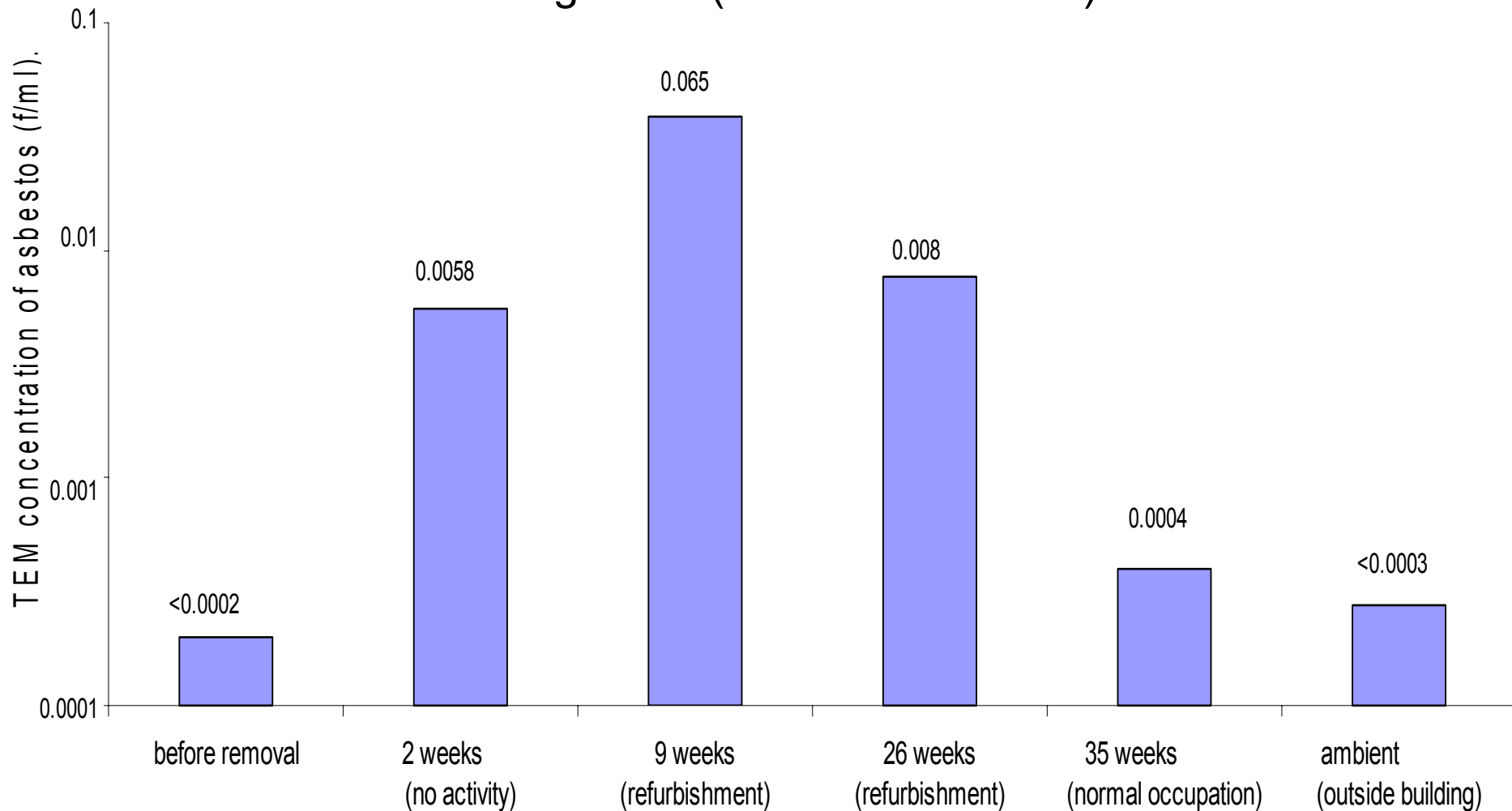
Low risk.

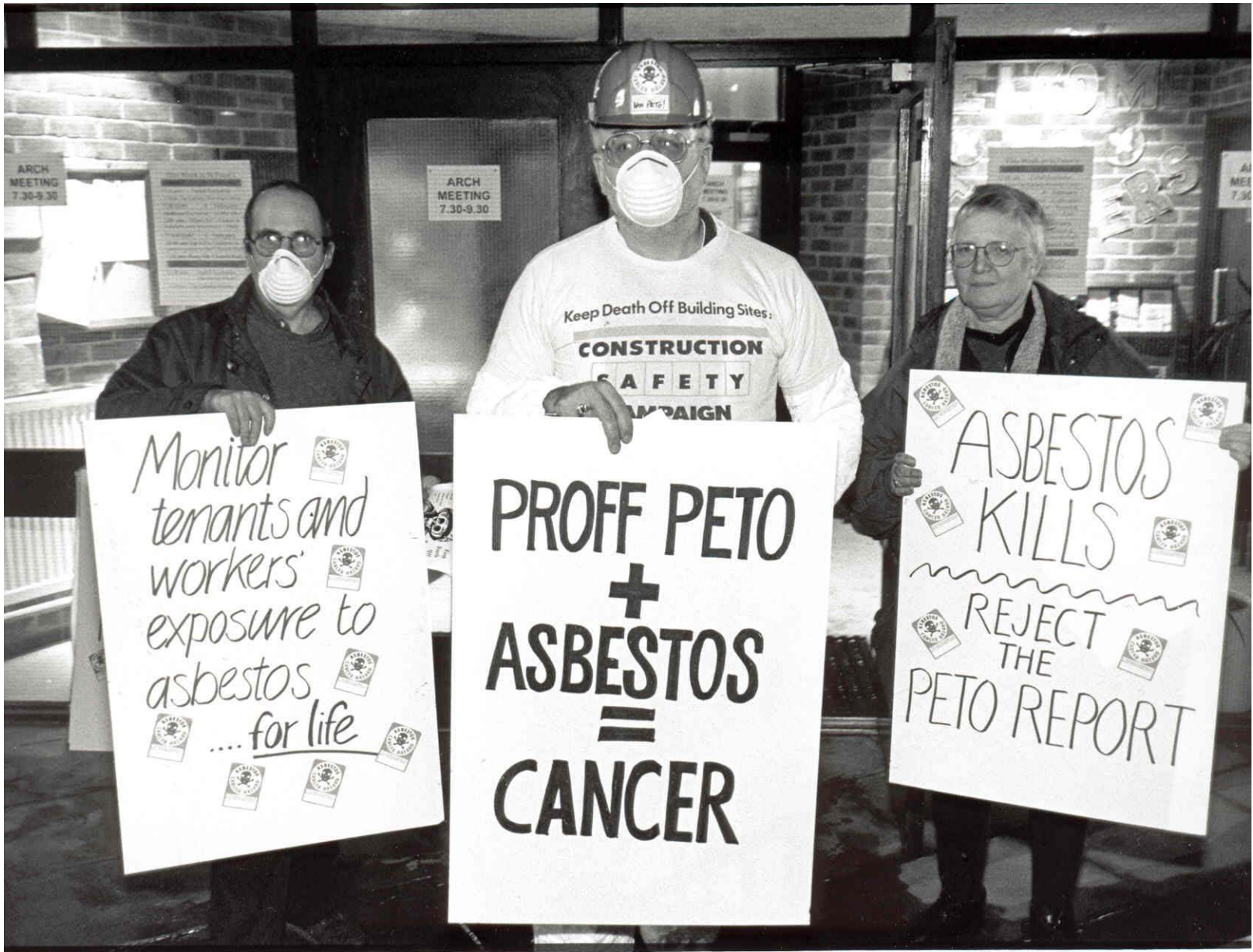
1980 – the asbestos panic

By the end of the 1970s asbestos exposure was fairly well regulated in most factories, but uncontrolled use of amosite (brown) asbestos cement board had continued in construction.

Environmental exposure was negligible, but after 1980 widespread public concern led to removal from schools and public buildings, and asbestos use virtually ceased.

Average TEM concentrations of asbestos fibres >5µm long before, during and after an asbestos removal programme from a six-storey teaching block (Burdett et al 1989)





Monitor
tenants and
workers'
exposure to
asbestos
.... for life

Keep Death Off Building Sites
**CONSTRUCTION
SAFETY
CAMPAIGN**

**PROFF PETO
+
ASBESTOS
=
CANCER**

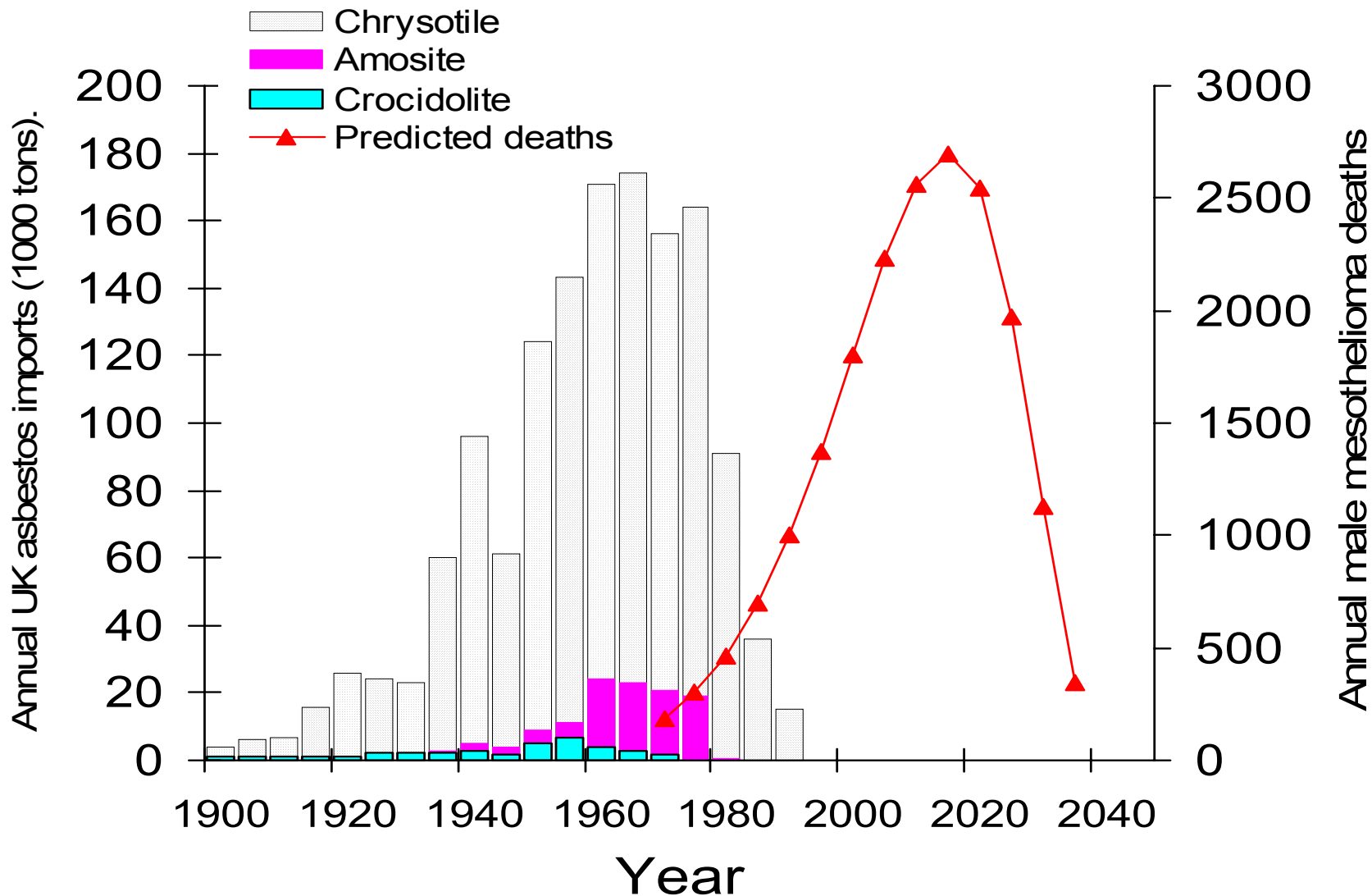
**ASBESTOS
KILLS**
~~~~~  
**REJECT  
THE  
PETO REPORT**

1995 - the mesothelioma  
epidemic



# UK asbestos imports and predicted mesothelioma deaths in men born before 1953

Peto et al 1995: Lancet 345: 535-39



# HSE Asbestos Workers Mortality Survey

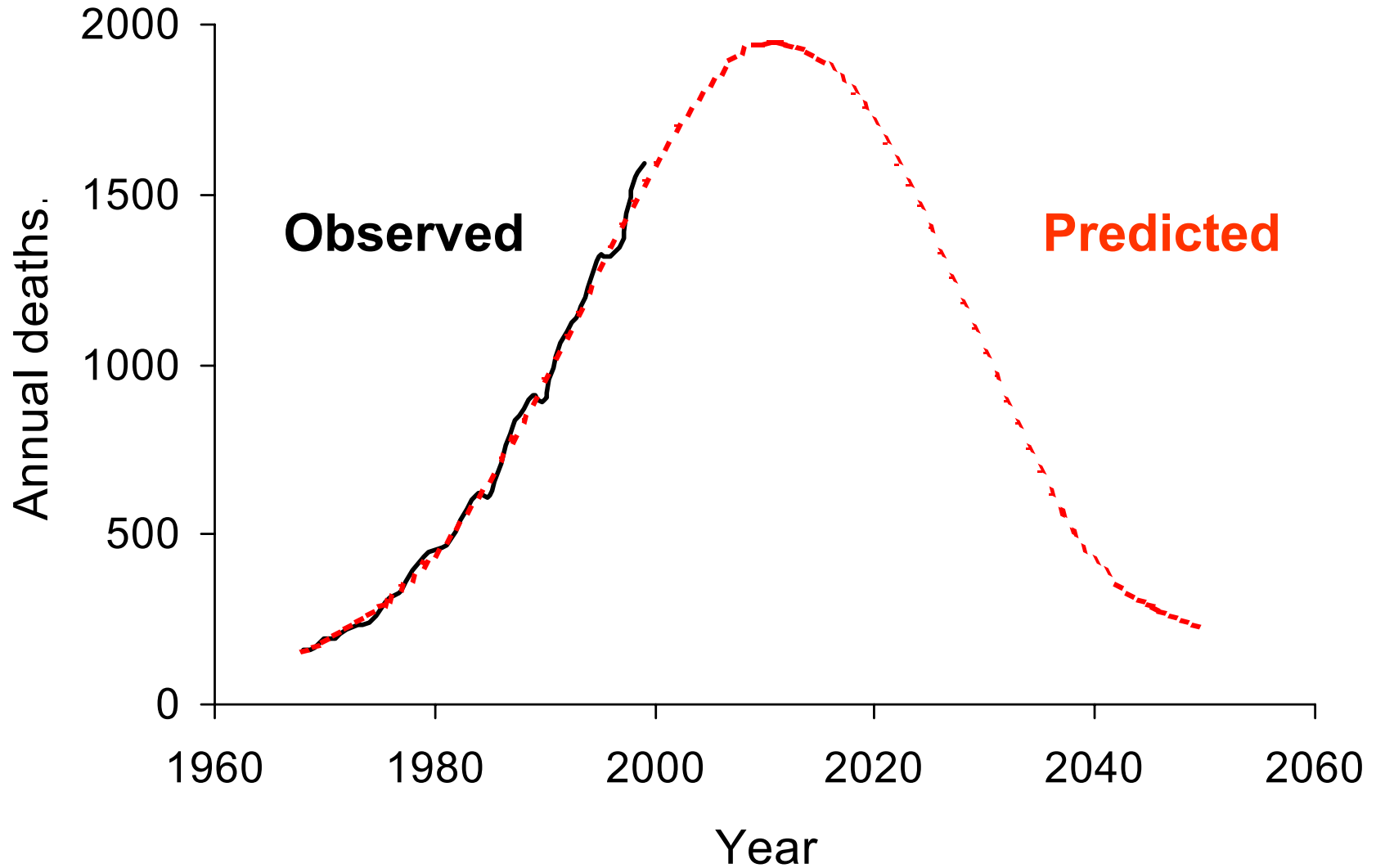
Mortality 1971-91 of workers covered by the 1969 Asbestos Regulations

(Hutchings, Jones and Hodgson: Decennial Supplement, OPCS 1995)

| Industry                            | Lung Cancer |              |              | Meso       | Asbestosis |
|-------------------------------------|-------------|--------------|--------------|------------|------------|
|                                     | Obs         | Exp          | O-E          |            |            |
| Textile manufacture                 | 58          | 44.6         | 13.4         | 11         | 5          |
| Asbestos cement manufacture         | 95          | 87.7         | 7.3          | 19         | 15         |
| Asbestos/rubber/bitumen manufacture | 156         | 110.1        | 45.9         | 20         | 5          |
| Asbestos board/paper manufacture    | 35          | 23.4         | 11.6         | 4          | 2          |
| Garment manufacture                 | 3           | 2.5          | 6.5          | 0          | 2          |
| Insulation/plaster manufacture      | 7           | 3.5          | 3.5          | 0          | 1          |
| Maintenance in manufacture          | 69          | 66.2         | 2.8          | 18         | 4          |
| Asbestos removal                    | 14          | 15.8         | -1.8         | 12         | 1          |
| Shipbuilding                        | 50          | 47.3         | 2.7          | 17         | 6          |
| Construction                        | 12          | 8.9          | 3.1          | 6          | 6          |
| Insulation                          | 169         | 64.0         | 105.0        | 67         | 47         |
| <b>Total</b>                        | <b>668</b>  | <b>474.0</b> | <b>194.0</b> | <b>170</b> | <b>88</b>  |

# Mesothelioma deaths in Britain and predicted numbers based on new HSE model

Hodgson et al (2005) Br J Cancer 92: 587-93



# The expected burden of mesothelioma in Britain

Hodgson et al (2005) Br J Cancer 92: 587-93

- Mesothelioma mortality in Britain has increased by a factor of 12 since 1968
- There are now 1,900 mesothelioma deaths per year
- The annual total will increase to about 2,200 within 5 or 10 years and will remain above 1,500 until about 2025

## Mesothelioma mortality in British men

|                                  | PMR | Percent of all deaths<br>in 2003 at age 40-79 |
|----------------------------------|-----|-----------------------------------------------|
| All men:                         | 100 | 0.9%                                          |
| Construction: Plumbers           | 413 | 3.6%                                          |
| Carpenters                       | 388 | 3.3%                                          |
| Electricians                     | 279 | 2.4%                                          |
| Manufacture: Metal plate workers | 503 | 4.3%                                          |
| Vehicle body makers              | 526 | 4.5%                                          |
| Low risk: Farmers                | 26  | 0.2%                                          |
| Doctors                          | 28  | 0.2%                                          |
| Motor mechanics                  | 48  | 0.4%                                          |

# The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure

Hodgson & Darnton (2000) *Ann. Occup. Hyg.* 44:565-601

“At exposure levels seen in occupational cohorts it is concluded that the exposure specific risk of mesothelioma.....is broadly in the ratio 1:100:500 for chrysotile, amosite and crocidolite respectively.”

# The future

What is the current risk to construction workers from existing asbestos in British buildings?

# The future – the developing world

## World asbestos production

|      |                |
|------|----------------|
| 1975 | 5 million tons |
| 1991 | 4 million tons |
| 2001 | 2 million tons |

Asbestos regulation and consumption in Asia  
 Takahashi and Karjalainen IJOEH (2003)

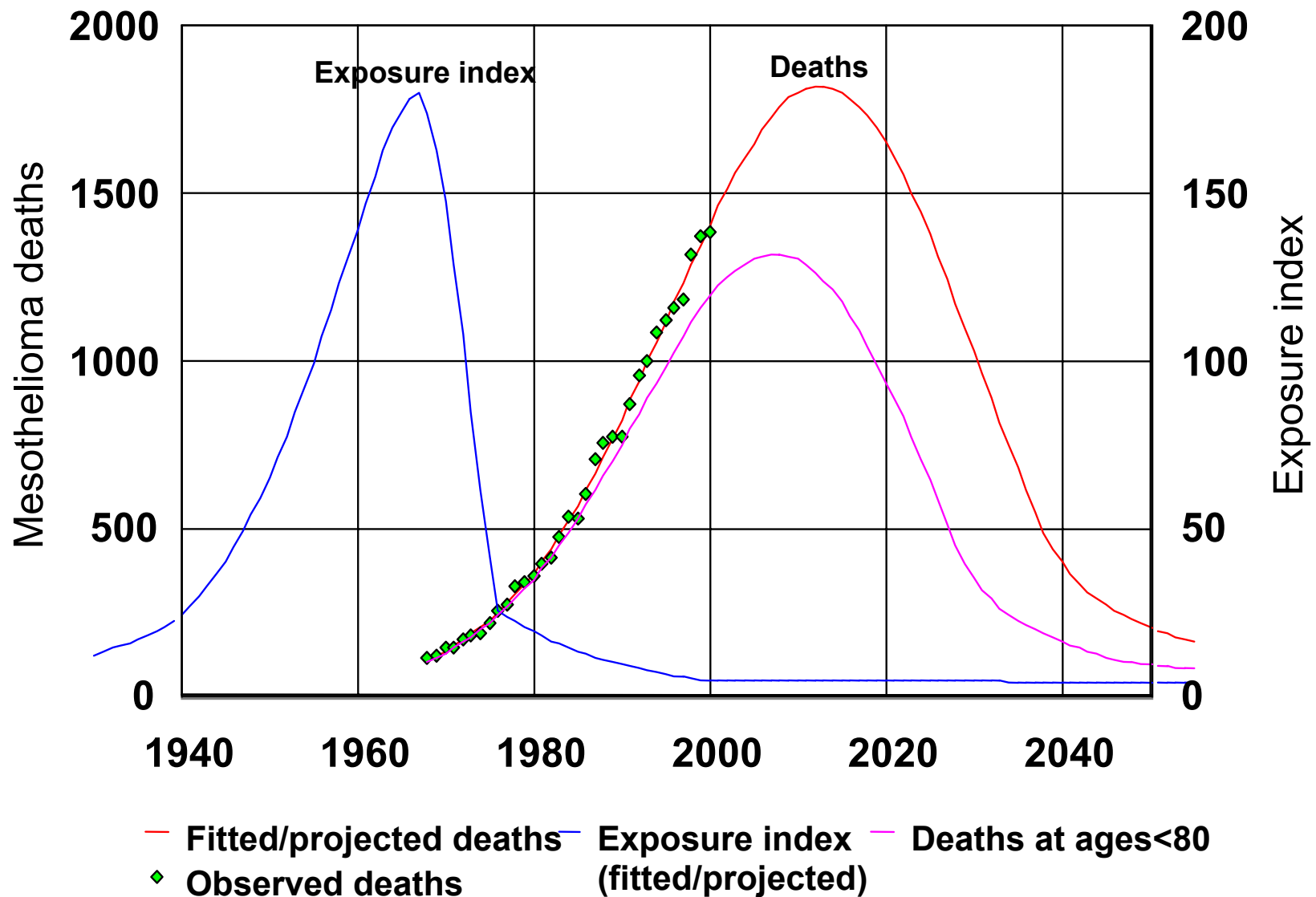
|             | Imports (\$M) | Ban  |       |       | Trend |
|-------------|---------------|------|-------|-------|-------|
|             |               | blue | brown | white |       |
| China       | 1,275         | yes  | no    | no    | up    |
| Indonesia   | 211           | ?    | ?     | no    | up    |
| Korea       | 42            | yes  | yes   | no    | down  |
| Malaysia    | 23            | yes  | no    | no    | flat  |
| Philippines | 76            | yes  | yes   | no    | up    |
| Taiwan      | 22            | yes  | yes   | no    | down  |
| Thailand    | 62            | yes  | yes   | no    | up    |
| Vietnam     | 78            | no   | no    | no    | up    |

# The future in Britain

- 30,000 mesothelioma deaths already and a further 60,000 by 2050
- About 250,000 in Western Europe by 2035

# Projected British male mesothelioma deaths – all deaths (red) and deaths below age 80 (purple)

Hodgson et al (2005) Br J Cancer 92: 587-93



## UK Situation Report on Chrysotile 2002

John Bridle (Asbestos Cement Product Producers Association)

‘We have increased publicity and with Chris Booker’s help in the Sunday Telegraph have now got the European MEPs asking questions..’

## Conclusions

1. All use of amphiboles is unacceptably dangerous.
2. The hazards of chrysotile mining and manufacture can be greatly reduced, and the risk from environmental exposure is probably negligible. The major risk results from widespread exposure to users, which can never be controlled.

## Conclusions

3. Continued use of chrysotile in asbestos cement and friction products would not cause an epidemic of mesothelioma in future generations as large as those seen in Britain and Australia, but the risk to workers who have already been exposed to blue or brown asbestos might be considerably increased by continued exposure to chrysotile. Chrysotile products might also cause a substantial lung cancer risk, at least until smoking has been greatly reduced in the developing world.

## Conclusions

4. Cheap substitutes are already available, and a worldwide asbestos ban should be implemented as rapidly as possible.

## Percentage of cancers associated with specific causes

| Cause      | Entire Population | Current-smokers (40%) | Former-smokers (30%)<br>(N=300,000) | Never-smokers (30%)<br>(N=200,000) |
|------------|-------------------|-----------------------|-------------------------------------|------------------------------------|
| Smoking    | 39%               | 60%                   | 30%                                 | 0%                                 |
| Infections | 13%               | 8%                    | 13%                                 | 20%                                |
| Alcohol    | 3.6%              | 5%                    | 3%                                  | 1%                                 |
| Radon      | 1.1%              | 2%                    | 1.1%                                | 0.2%                               |