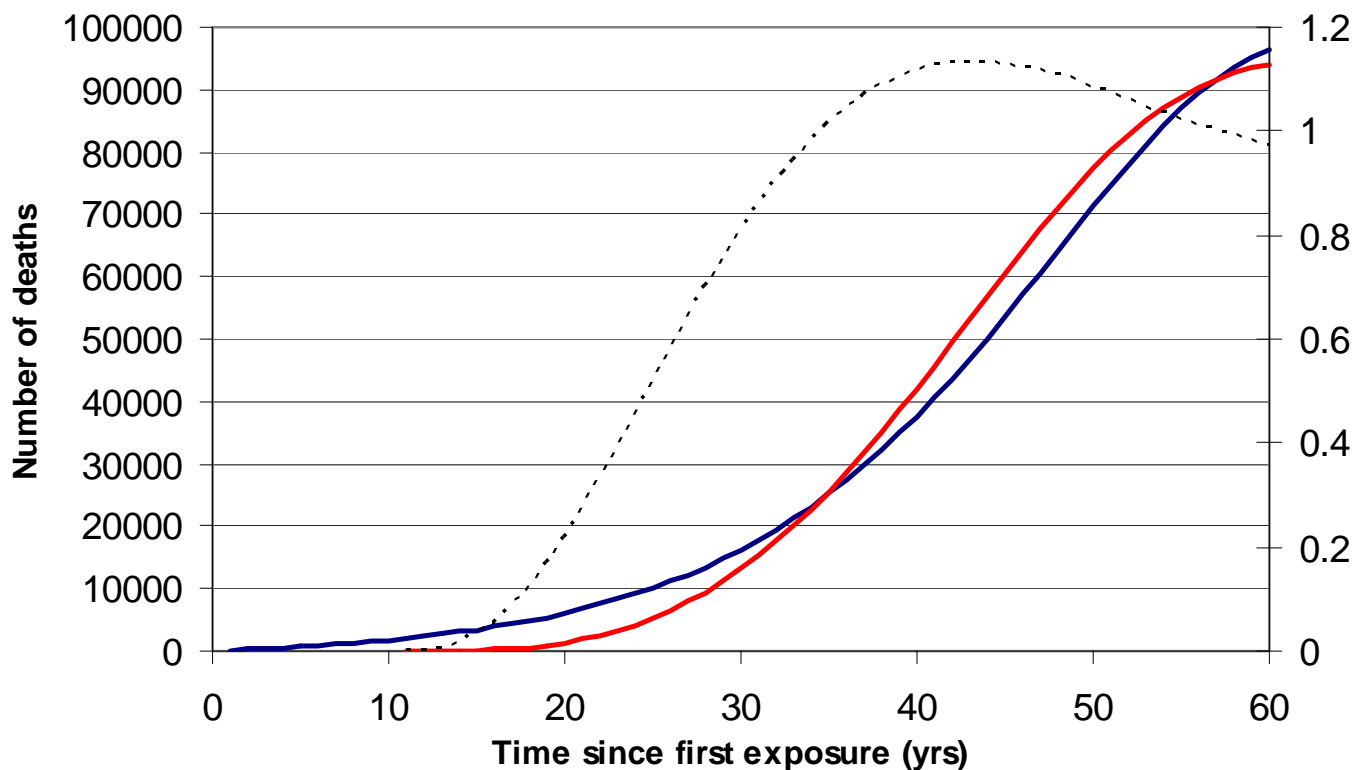


(1) Comparison of studies with different follow-up periods

- Is the absolute potency of amphiboles and relative potency of chrysotile underestimated because of studies with substantially incomplete follow-up?

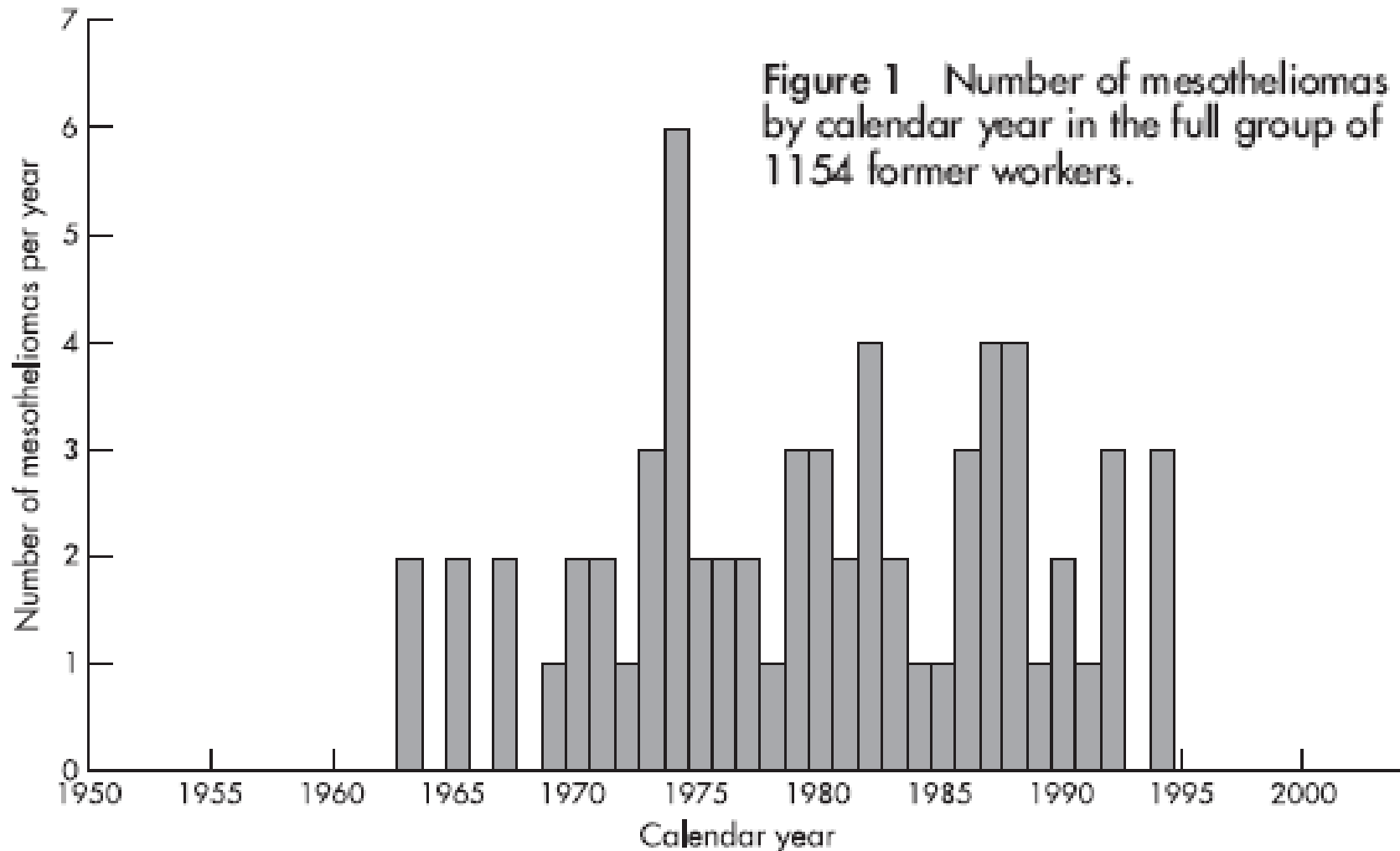
Cumulative expected all cause and cumulative predicted mesothelioma mortality by time since first exposure



- (1) Cumulative expected all cause mortality
- (2) Cumulative predicted mesothelioma mortality
- Ratio (2)/(1)

Cohort	Reference	% survival	Follow up	Expected all cause	Mesotheliomas	% XS (unadjusted)
Wittenoom	Berry91	80	1943-1986	601.8	72	11.96
	Musk..07	63	1943-2000	1589.4	190	11.95
Wittenoom environs	Hansen..98	90	1943-1993	377	31	8.22
	Reid..07	85	1943-2002	578.9	57	9.85
Quebec	Liddell..97	56	<1974	3464.7	6	0.17
		34	<1984	5206.0	21	0.40
		18	<1992	6279.9	38	0.61
Libby (small cohort)	McDonald..86	59	1940-1982	141.0	4	2.84
	McDonald..04	30	1940-1999	224.0	12	5.36
US insulators	Seidman.90	92	1967-72	945.4	35	3.70
		82	1967-79	2140.5	81	3.78
		72	1967-86	3453.5	167	4.84

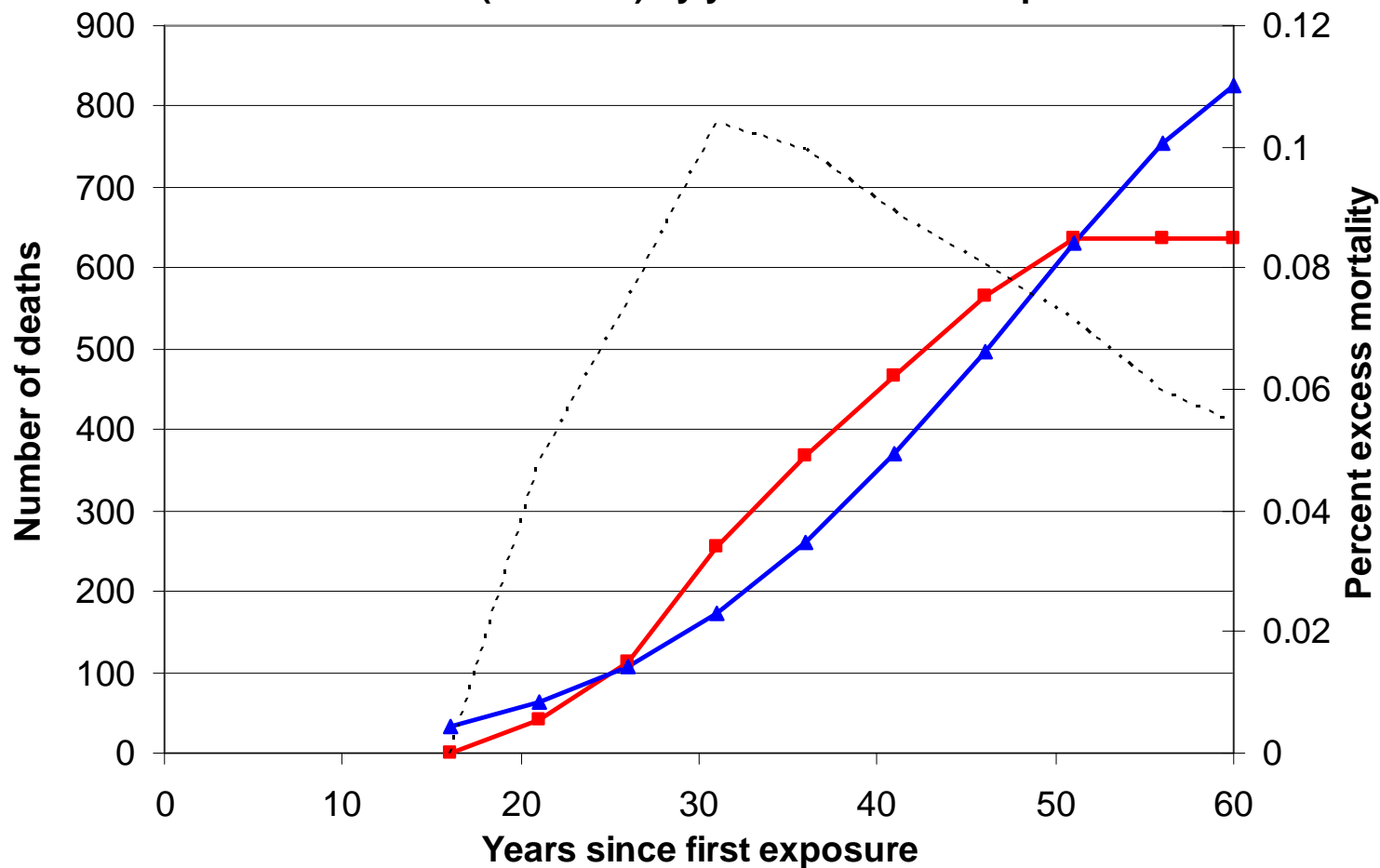
Nottingham gas masks *



* Nottingham Gas Mask

Reference : McDonald C, Harris J, Berry G (2006) Sixty years on: the price of assembling military gas masks in 1940 Occup Environ Med 2006;63:852-855

Cumulative expected all cause mortality and cumulative observed mesothelioma (rescaled) by years since first exposure



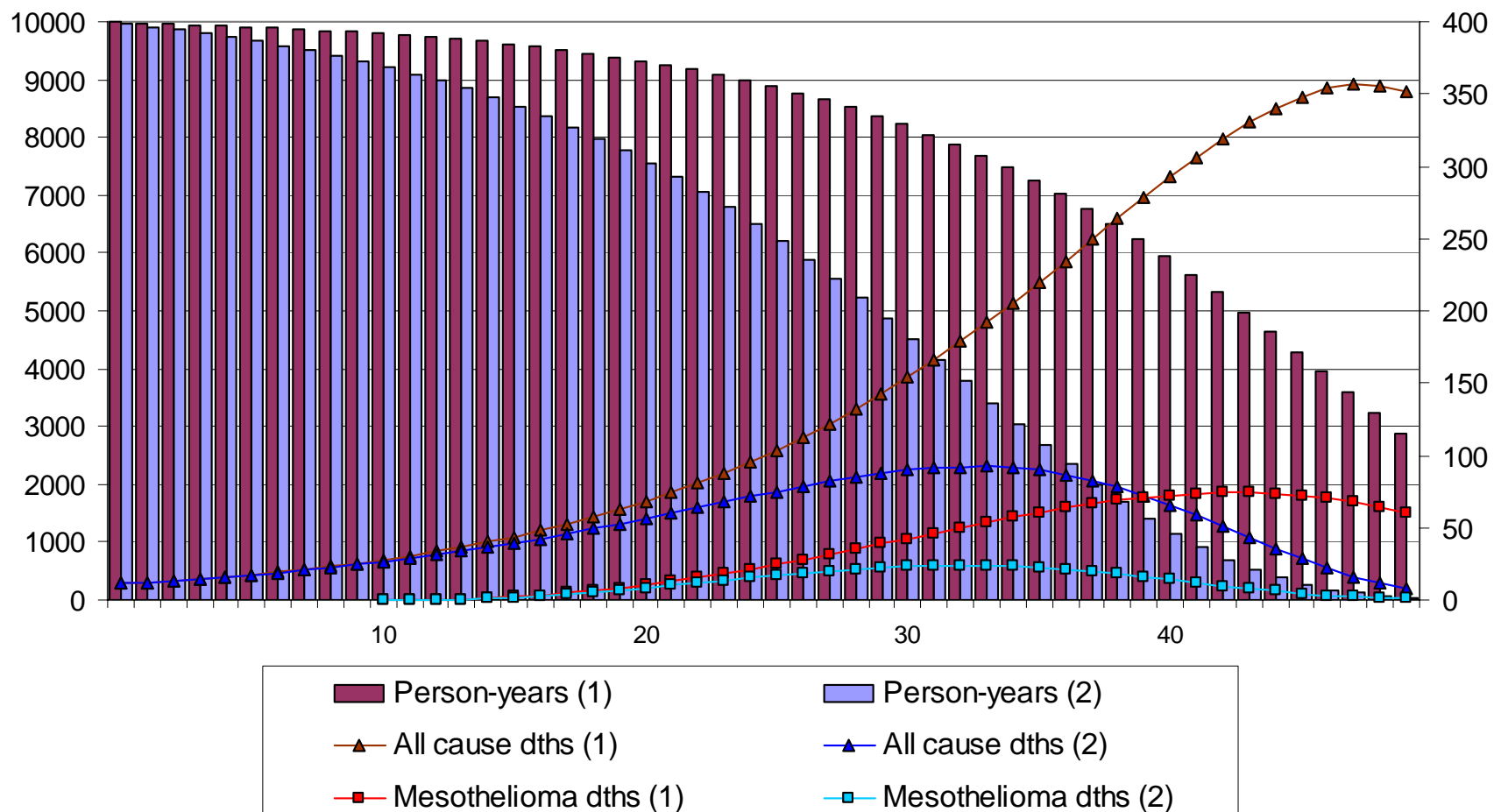
(2) Competing risks

- Does the H&D analysis underestimate the risks due to mesothelioma and lung cancer because of high mortality in cohorts from “competing risks”?

Hypothetical example:

- Cohort of 10,000 men aged 30, heavily exposed to asbestos for 5 years
- Follow up for 50 years until age 80
- If their overall mortality rates are broadly in line with national rates for mid 1970s, what is the ratio of predicted mesothelioma deaths to age 80 to the expected all cause mortality to age 80?
- What if they suffer high mortality from all causes of death such that death rates in the cohort are X times as high as national rates throughout the follow-up period (ie the all-cause $SMR=X$)

Person-years, all cause and mesothelioma deaths by time since first exposure



SMR	Person-years	Observed deaths	Expected deaths (E)	Mesothelioma deaths (M)	M/E
1.0	401940	7124.3	7124.3	1546.1	0.217
2.0	343863	9238.3	4619.1	953.8	0.206
3.0	305848	9817.2	3272.4	640.0	0.196
4.0	278711	9961.1	2490.3	458.9	0.184

(3) Life expectancy

- Are the lifetime risks presented in the H&D analysis underestimates of the risks for those exposed today because of increased life expectancy?

How are the lifetime risks calculated?

- Metric for mesothelioma risk (P_M) is observed mesothelioma deaths as a proportion of total expected all cause mortality as calculated from national deaths rates relevant to the time periods over which the cohorts were observed.
- Thus, strictly speaking, the mesothelioma risk estimate relates to this past pattern of mortality.
- Mid 1970s rates were taken to be broadly typical of average all cause mortality used to calculate expected numbers in cohorts.
- This allows us to estimate lifetime risks for mesothelioma if this pattern of mortality was still relevant.
- The 1970s average male mortality patterns show that 70% of those aged 30 will die between ages 40-80 (the age during which all mesotheliomas are assumed to occur).
- Thus the relevant expected all cause mortality for 100,000 men aged 30 during the period in which they are at risk from mesothelioma is 70,000, and the lifetime risks per 100,000 is thus just $70,000 \times P_M$.
- **Note: if we use a more recent lifetable we will underestimate the risk! This is because there will be fewer deaths in the at risk period (age 40-80) since more will survive to ages 80+.**

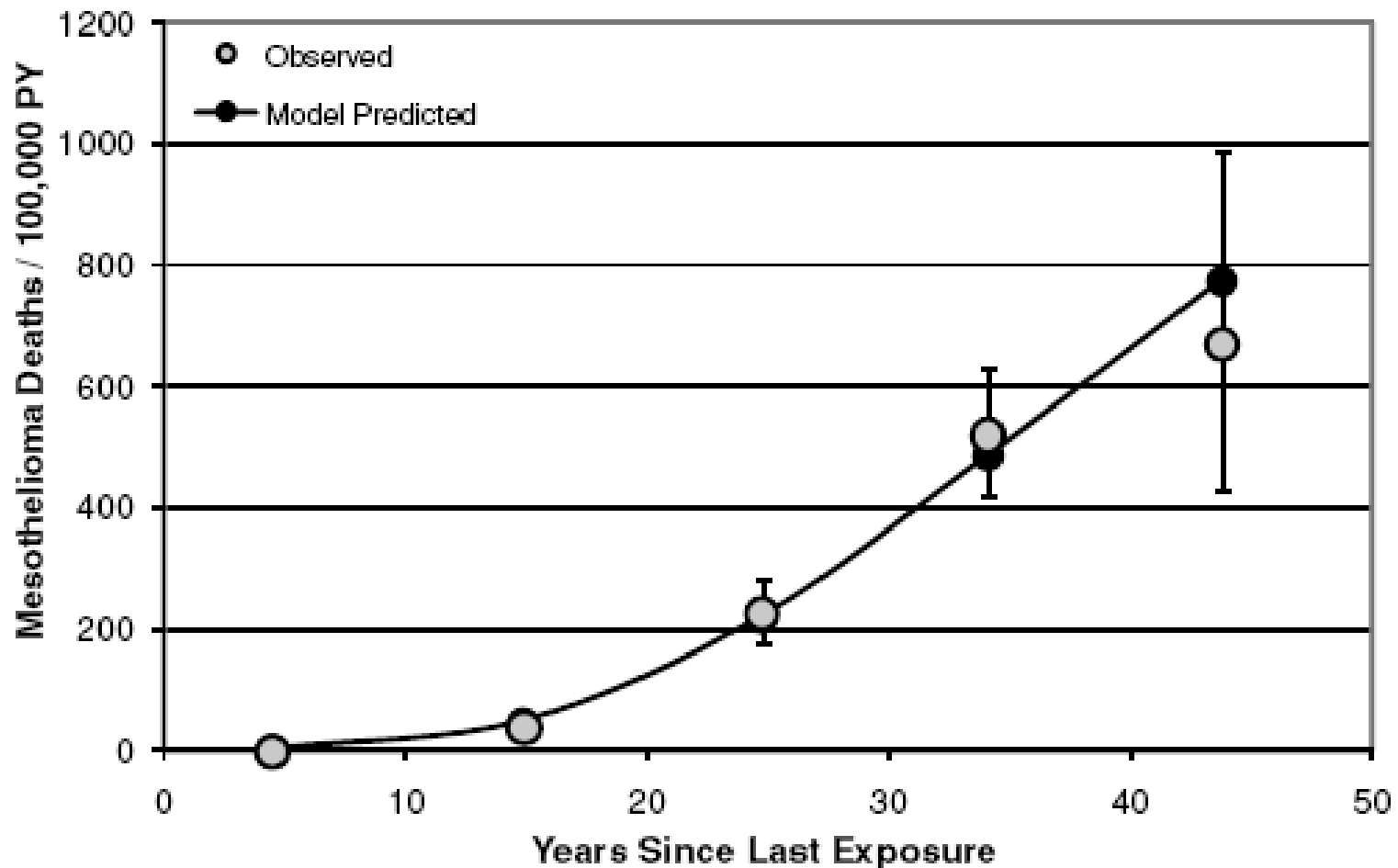
So how should we adjust for increased life expectancy?

- Need to adjust the expected all cause mortality to take account of additional person-years (ie survivors into the 40-80 age group).
- 1000 survivors to age 30 – how many person-years at risk?
 - 1970s average lifetable: 30970
 - 2002-2004 GB lifetable: 33630 (about 8.5% more)
- Thus in order to estimate risks for 30 year old with life-expectancy as predicted by the 2002-04 GB lifetable we should increase our estimate of the expected all cause mortality by about 8.5%

(4) Mesothelioma risk at very long follow up times

- HEI model predicts that risk continue to increase rapidly for all time.
- However, some evidence that this is not the case from various cohorts (some examples to follow).
- Difficult to be precise because of small numbers surviving to very long follow up times.
- Relevance to H&D analysis:
 - Is our assumption that all of the mesothelioma risk is expressed by age 80 a reasonable way of approximating the lifetime risk?
 - If the risk does continue to increase then this would imply that risks due to exposure in childhood could be substantially higher than at, say, age 20.

Wittenoom cohort *

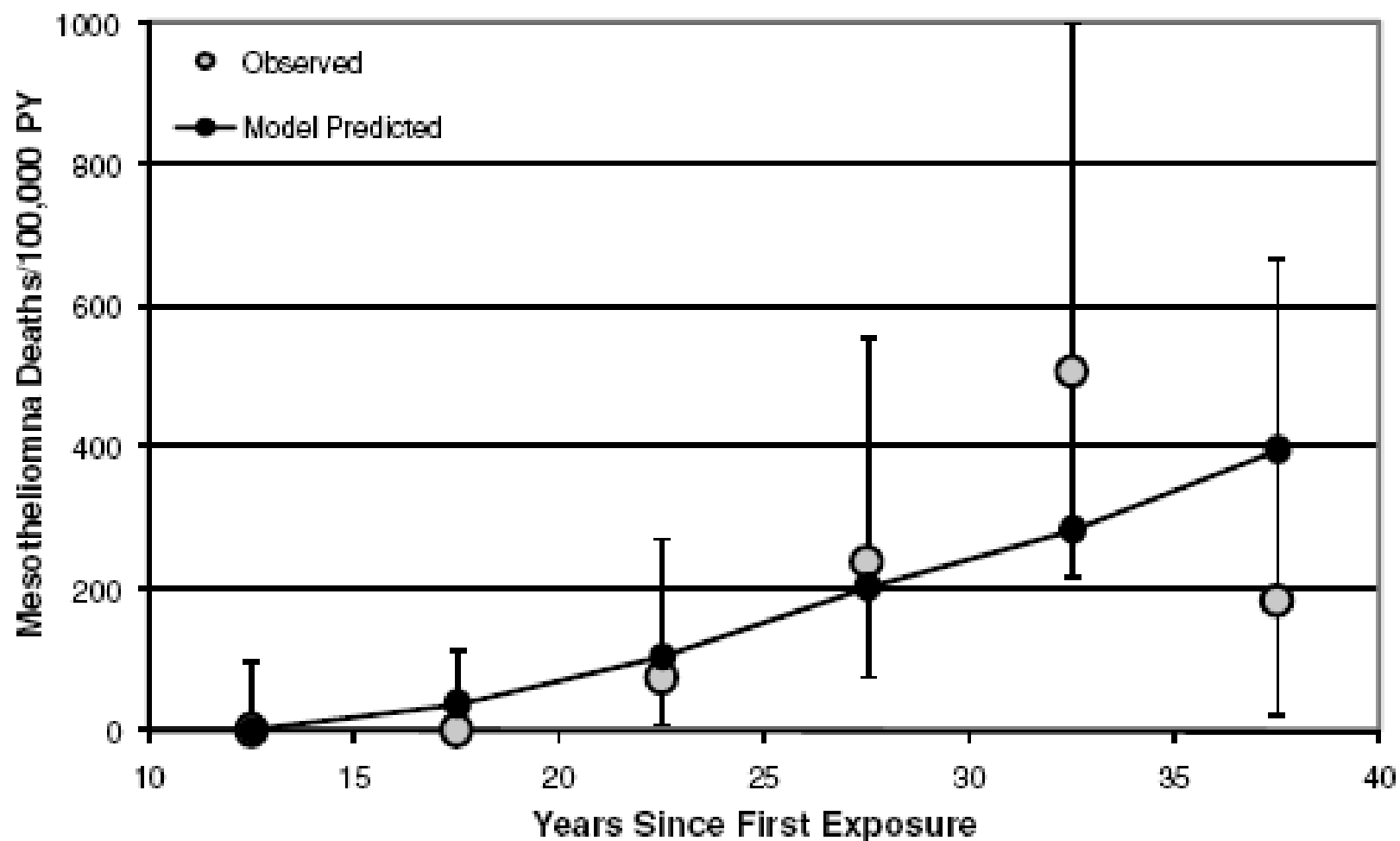


Numbers of mesotheliomas by increasing years after exposure ends are 0, 18, 79, 100, 25.

* Wittenoom cohort

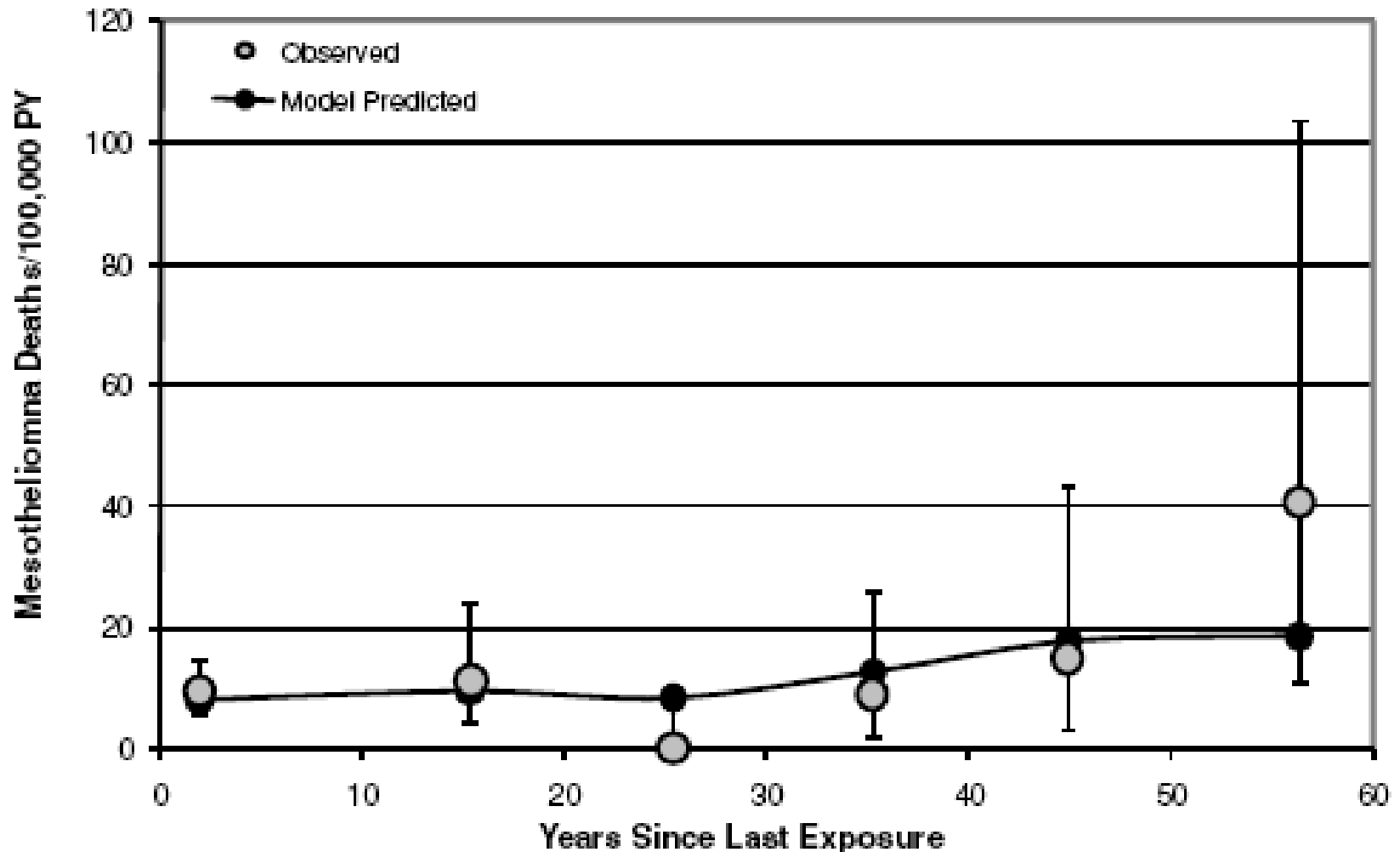
Berman W and Crump K (2008) Update of Potency Factors for Asbestos-Related Lung Cancer and Mesothelioma *Critical Reviews in Toxicology*, 38(S1):1-47

Paterson cohort



Numbers of mesotheliomas by increasing years since first exposure are 0, 0, 2, 5, 8, 2.

Quebec *



Numbers of mesotheliomas by increasing years after exposure ends are 19, 6, 0, 3, 3, 4.

* Quebec

Berman W and Crump K (2008) Update of Potency Factors for Asbestos-Related Lung Cancer and Mesothelioma *Critical Reviews in Toxicology*, 38(S1):1-47

Nottingham gas masks *



Table 3 Mesothelioma and calendar year

Calendar year (years since exposure*)	No. mesotheliomas		Total†		Cohort‡		Person-years‡	Mesothelioma rate‡§
	Total†	Cohort‡	PT	PL	PT	PL		
1956–60 (16)	0	0	0	0	0	0	5134	0
1961–65 (21)	4	3	2	2	1	2	4982	60
1966–70 (26)	5	5	1	4	1	4	4741	105
1971–75 (31)	14	10	4	10	3	7	4341	230
1976–80 (36)	11	8	3	8	2	6	3768	212
1981–85 (41)	10	7	3	7	2	5	3167	221
1986–90 (46)	14	7	2	12	1	6	2582	271
1991–95 (51)	7	5	3	4	2	3	1925	260
1996–00 (56)	0	0	0	0	0	0	1334	0
2001–03 (60)	0	0	0	0	0	0	604	0
Total	65	45	18	47	12	33	32578	138.1

*Average time from midpoint of production period (1940–44) to midpoint of calendar year range.

†Total number in 1154 former workers.

‡In cohort of 1061 workers with known duration of employment.

§Rate per 100 000 person-years at risk.

PT, peritoneal; PL, pleural.

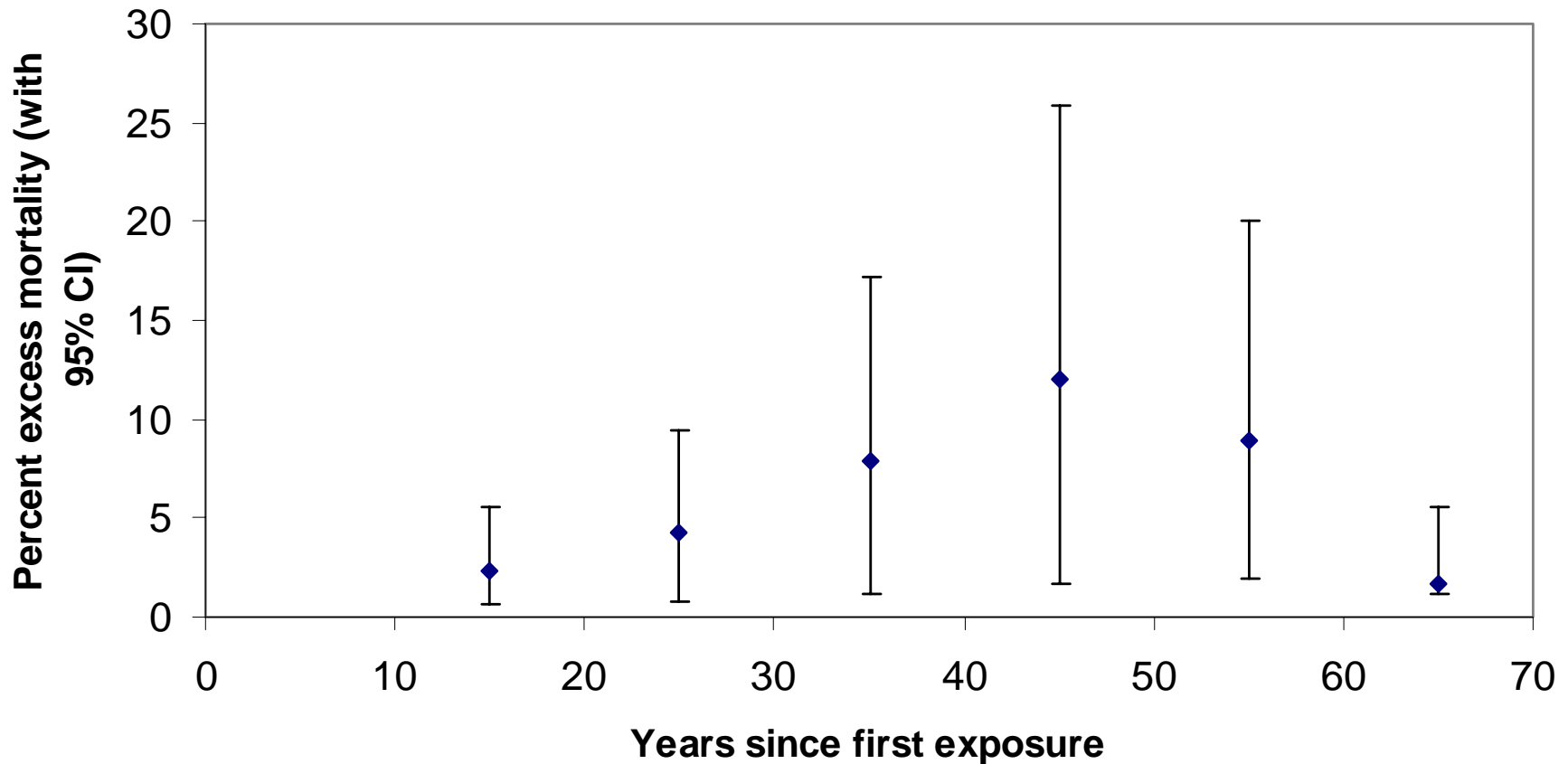
* Nottingham Gas Masks

Reference : McDonald C, Harris J, Berry G (2006) Sixty years on: the price of assembling military gas masks in 1940 Occup Environ Med 2006;63:852-855

GB asbestos workers – follow up to 2005 *



**Mesothelioma as a proportion of all cause expected mortality by
time since first exposure**



GB asbestos workers – follow up to 2005 *

Reference : Harding A and Frost G (2009) The asbestos survey: mortality among asbestos workers 1971-2005 Health and Safety Laboratory MSU/2007/13.