

Estimating the Global Burden of Asbestos-related Diseases Using YPLL

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World Health Assembly Resolution 58.22 from 2005 on cancer prevention and control urged Member States to pay special attention to cancers for which avoidable exposure is a factor, particularly exposure to chemicals at the workplace and the environment. Asbestos is one of the most important occupational carcinogens causing about half of the deaths from occupational cancer (1;2). Furthermore, the Thirteenth Session of the Joint ILO/WHO Committee on Occupational Health in 2003 recommended that special attention should be paid to the elimination of asbestos-related diseases (3).

The term "asbestos" designates a group of naturally occurring fibrous serpentine or amphibole minerals with current or historical commercial usefulness due to their extraordinary tensile strength, poor heat conduction, and relative resistance to chemical attack. The principal varieties of asbestos are chrysotile, a serpentine material, and crocidolite, amosite, anthophyllite, tremolite and actinolite, which are amphiboles (4).

Exposure to asbestos causes a range of diseases, such as lung cancer, mesothelioma, and asbestosis (fibrosis of the lungs), as well as pleural plaques, thickening and effusions (5;6). There is also evidence that it causes laryngeal and possibly some other cancers (7).

Exposures to asbestos and its impact on public health are substantial

Exposure to asbestos occurs through inhalation of fibres primarily from contaminated air in the working environment, as well as from ambient air in the vicinity of point sources, or indoor air in housing and buildings containing friable asbestos materials. The highest levels of exposure occur during repackaging of asbestos containers, mixing with other raw materials and dry cutting of asbestos-containing products with abrasive tools. Exposure can also occur during installation and use of asbestos-containing products and maintenance of vehicles. Friable chrysotile and/or amphibole-containing materials are still in place in many buildings and continue to give rise to exposure to both chrysotile and amphiboles during maintenance, alteration, removal and demolition (5).

Currently about 125 million people in the world are exposed to asbestos at the workplace (1). According to global estimates at least 90,000 people die each year from asbestos-related lung cancer, mesothelioma and asbestosis resulting from occupational exposures (1;2;8). In addition, it is believed that several thousands of deaths can be attributed to other asbestos-related diseases as well as to non-occupational exposures to asbestos. The burden of asbestos-related diseases is still rising, even in countries that have banned the use of asbestos in the early 1990s. Because of the long latency periods attached to the diseases in question, stopping the use of asbestos now will only result in a decrease in the number of asbestos-related deaths after a number of decades.

All types of asbestos cause cancer in humans

Asbestos (actinolite, amosite, anthophyllite, chrysotile, crocidolite and tremolite) has been classified by the International Agency for Research on Cancer as being carcinogenic to humans (9). Exposure to

Key Document for Global Direction

- All types of asbestos cause cancer in humans
- Asbestos, one of most important occupational carcinogens, causes $\frac{1}{2}$ of occupational cancer deaths
- No threshold identified for carcinogenic risk of chrysotile
- Most efficient way to eliminate ARDs is to stop using all types of asbestos

Unequivocal, although some premises are challenged by pro-asbestos parties

September 2006¹

Updates on IARC (WHO) Evaluation of Asbestos

Special Report: Policy

A review of human carcinogens—Part C: metals, arsenic, dusts, and fibres

In March, 2009, 22 scientists from eight countries met at the International Agency for Research on Cancer (IARC) to reassess the carcinogenicity of metals, arsenic, dusts, and fibres previously classified as "carcinogenic to humans" (Group 1) and to identify additional factors and mechanisms of carcinogenesis (Table). These statements will be published in part C of Volume 100 of the IARC Monographs.

Inhalation is the primary route of exposure to arsenic in the workplace and happens in industries such as non-ferrous smelting, arsenic production, wood preservation, glass production, and production and application of arsenic-based pesticides, and electronics. Non-occupational exposure to arsenic is mainly through food, except in areas with high levels of arsenic in the drinking water—Tawan, Bangladesh, West Bengal (India), northern Chile, and Cordoba Province (Argentina). Epidemiological studies have shown that exposure to arsenic through inhalation or drinking water

causes cancer of the lung, skin, and urinary bladder. Evidence suggests an association between exposure to arsenic in drinking water and the development of kidney or several other sites, however, various factors prevent a conclusion. Analytical studies have provided only limited information to support an association with kidney cancer, cases of liver cancer can be difficult to identify or greater than are high-risk for hepatitis B, and data on prostate cancer and arsenic exposure are not consistent between countries. Overall, the Working Group classified arsenic and inorganic arsenic compounds as "carcinogenic to humans" (Group 1). The organic arsenicals monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are the active ingredients of some herbicides and are metabolized to inorganic arsenic. On the basis of sufficient evidence of cancer caused by DMA in experimental animals and because MMA is extensively metabolized to DMA, both compounds are classified as "possibly carcinogenic

to humans" (Group 2B). Antimony and other organo-arsenic compounds that are not metabolized to inorganic arsenic are classified as "Group 3". The Working Group reaffirmed the classification of leadfumes and its compounds, cadmium and its compounds, chromium (VI) compounds, and nickel compounds as "carcinogenic to humans" (Group 1). Studies included a complete occupational exposure to a metal and its compounds, making it impossible to separately assess their carcinogenicity.

Globaly, an estimated 120 million people are still exposed to asbestos in the workplace. Although asbestos has been banned or well restricted in the industrialized world, it is still common in parts of Asia, South America, and the former Soviet Union. Naturally occurring sources of asbestos, its use in brake linings, and deterioration of asbestos-containing products all contribute to environmental exposure worldwide. Exposure may also come from fibres carried home on the clothing of asbestos workers.

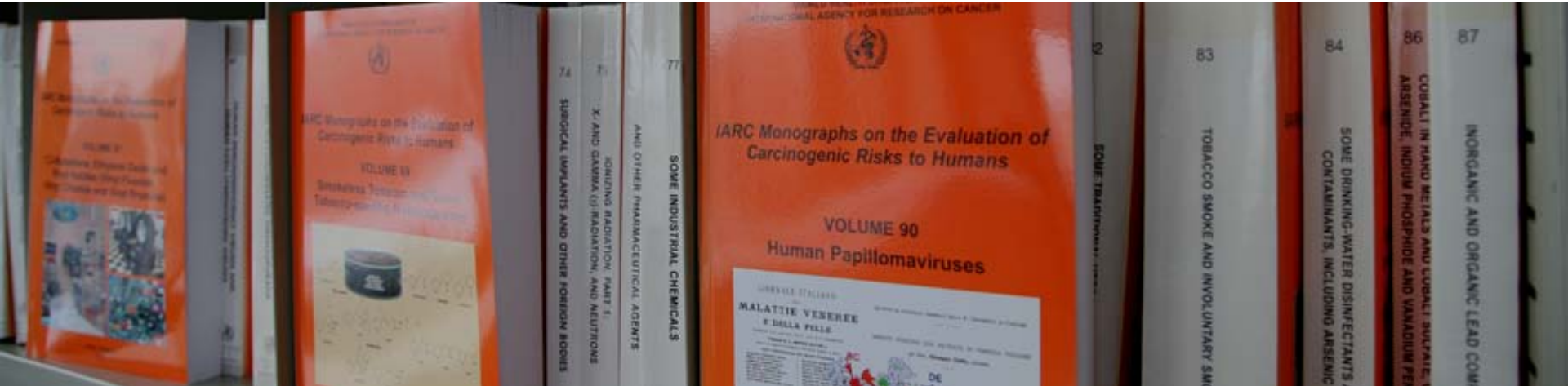


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Group 1 agents	Group 2 agents (possible carcinogens)	Group 2B agents (possibly carcinogenic to humans)	Group 3 agents (not classifiable as to their carcinogenicity)	Group 4 agents (not classifiable as to their carcinogenicity)
Asbestos (chrysotile, amosite, crocidolite)	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Bladder cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Esophageal cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Liver cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Lung cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Prostate cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Stomach cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol
Uterine cancer	Long-term, heavy smoking	Asbestos (tremolite, actinolite)	Alcohol	Alcohol

- “Although potency of differences with respect to **LC** or **mesothelioma** for fibres of various types and dimensions are debated, the fundamental conclusion is that —all forms of asbestos are ‘carcinogenic to humans’ (Group 1)”
- Cancers of **larynx** and **ovary** (sufficient evidence)
- Cancers of **colorectum**, **stomach** and **pharynx** (limited evidence)

Straif K et al, WHO IARC Monograph Working Group. Lancet Oncol 2009, 10:453-4.



Volume 100 just published September, 2012; PDF version also available

Methods 1/2- Database & Formula

- WHO Mortality Database, updated 09 Jul 2012
- Life tables for WHO Member States
- WHO Statistical Information System and USCB Database

- **Years of Potential Life Lost (YPLL)**

$$YPLL = \sum_{i=1}^k D_{g_i} \times LE_{g_i}$$

D_{g_i} : the number of deaths at age group g_i , LE_{g_i} : life expectancy at age group g_i .

- **Annual average of YPLL**

$$\sum_{i=1}^N \frac{YPLL_i}{NY_i}$$

$YPLL_i$: the YPLL of the country i , NY_i : the number of the report years of the country i .

- **Average Years of Potential Life Lost (AYPLL)** [For each decedent]

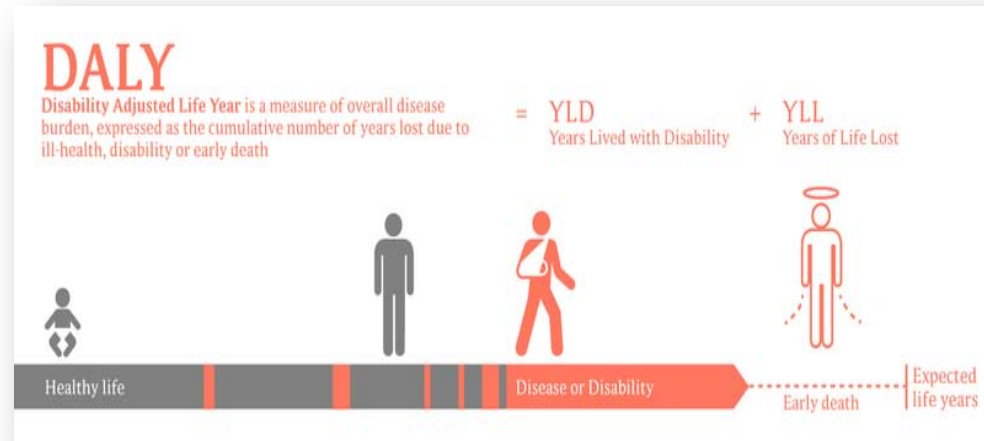
$$AYPLL = YPLL / \text{Number of deaths}$$

DALY = YPLL + Years Lost due to Disability (YLD)*

*Number of incident cases x Average duration of case until death x disability weight

Methods

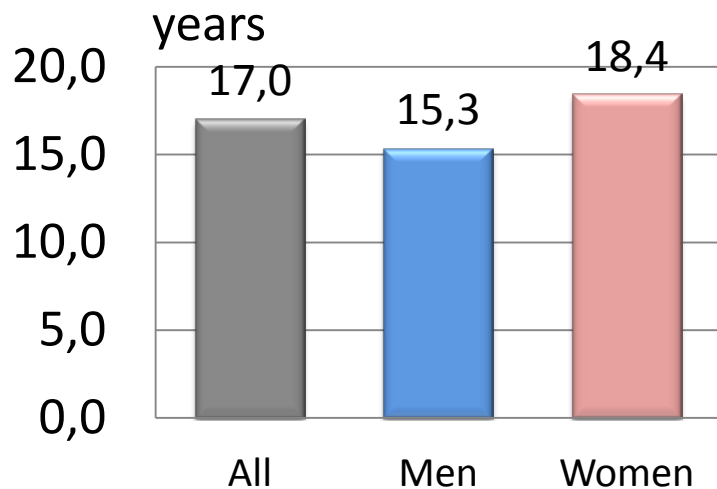
2/2



	Scenario	Incidence*	Duration (yr)	Disability weight
Mesothelioma (C45)	-	number of deaths x 1.5	1	1
Asbestosis (J61)	Case 1	number of deaths x 4	30	1
	Case 2		40	

*Number of incident cases = underlying causes of deaths + associated causes of deaths. 2/3 of incident cases with mesothelioma and ¼ of incident cases with asbestosis were underlying causes of deaths (Anne-Helen Harding, 2010)

AYPLL of Mesothelioma by Gender



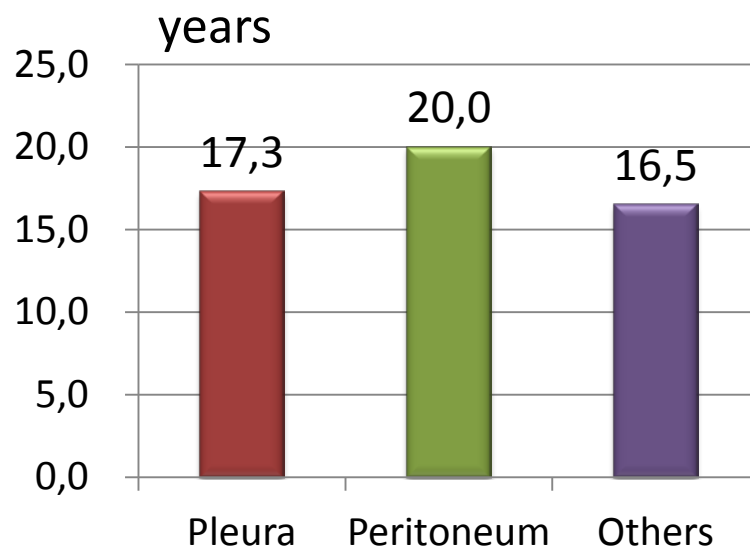
- 17.0 years of potential life is lost
- Women lose 3.1 more years
- YPLL impact more on women (women otherwise live longer)

	All	Men	Women
Total N deaths (%)	128,015 (100.0)	100,143 (78.2)	27,871 (21.8)
Annual mean N deaths	11,884	9,283	2,623
Mean age at death	69.2	69.2	68.9
Total YPLL [person-years] (%)	2,175,857 (100.0)	1,532,793 (75.0)	512,139 (25.0)
Annual mean YPLL	200,799	141,316	48,048

Based on analysis of data in WHO Mortality Database during 1994-2010

AYPLL of Mesothelioma by Anatomical Site

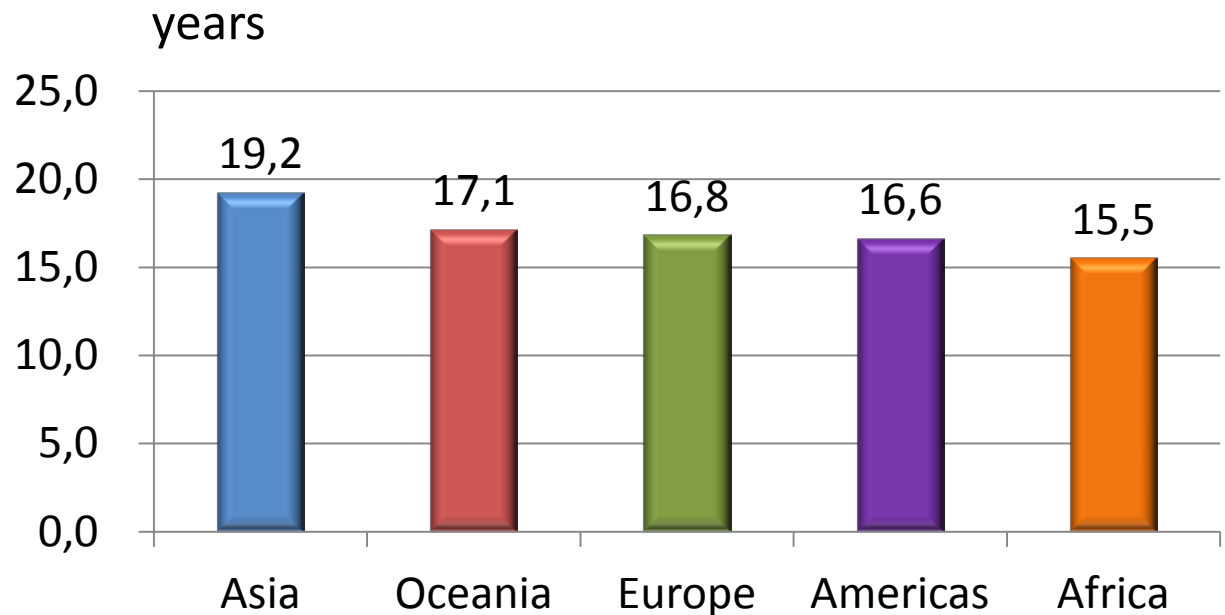
- Majority is classified into “others” but likely overlaps with pleura
- **Peritoneal** type dies younger and incurs higher AYPLL by about **3 years**



Total N deaths	52,759	5,592	69,664
(%)	(41.2)	(4.4)	(54.4)
Annual mean N deaths	4,935	525	6,504
Mean age at death	69.3	65.9	69.3
Total YPLL [person-years]	911,145	111,879	1152,833
(%)	(41.9)	(5.1)	(53.0)
Annual mean YPLL	84,592	10,563	107,151

Based on analysis of data in WHO Mortality Database during 1994-2010

AYPLL of Mesothelioma by Continent

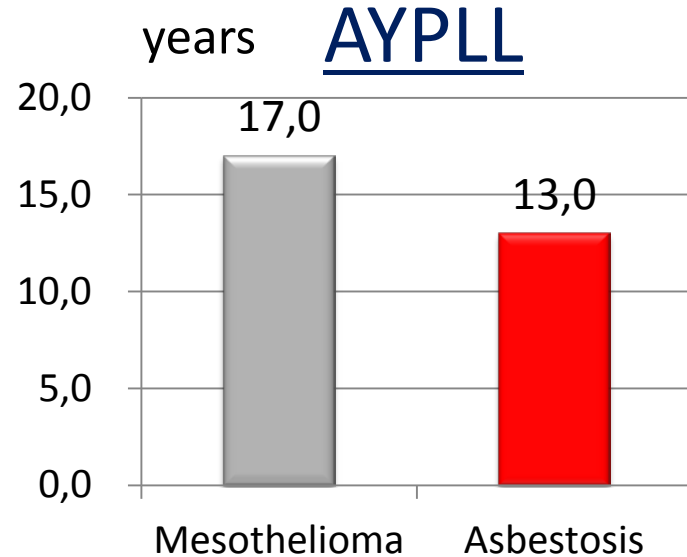


Total N deaths (%, sum 100%)	14,619 (11.4)	4,421 (3.5)	71,162 (55.6)	35,121 (27.4)	2,692 (2.1)
Annual mean N deaths	941	545	6,828	3,374	197
Mean age at death	68.4	69.8	69.4	69.3	63.4
Total YPLL [person-years] (%, sum 100%)	280,855 (12.9)	75,653 (3.5)	1,194,750 (54.9)	582,937 (26.8)	41,662 (1.9)
Annual mean YPLL	18,142	9,342	114,881	55,383	3,051

Based on analysis of data in WHO Mortality Database during 1994-2010

Mesothelioma vs. Asbestosis

- Asbestosis deaths average **73.4 years**, *i.e.*, 4.2 years older than mesothelioma
- For asbestosis, **13.0 years of potential life** is lost, *i.e.*, 4.0 yr shorter than mesothelioma

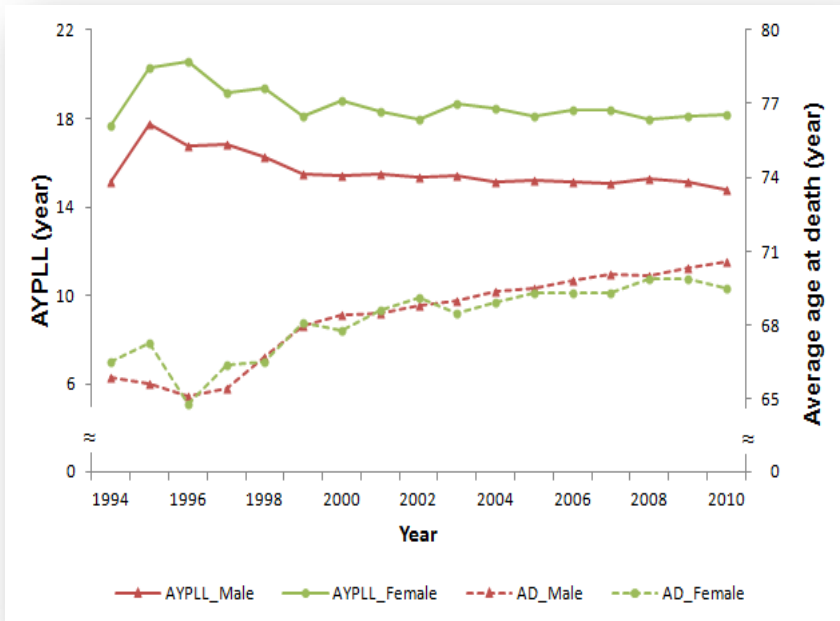


	Mesothelioma	Asbestosis	M/A Ratio
Total N deaths	128,015	13,885	9 : 1
Annual mean N deaths	11,884	1,320	
Mean age at death (yr)	69.2	73.4	NA
YPLL (person-yr)	2,175,857	180,522	12 : 1
Annual mean YPLL	200,799	17,128	

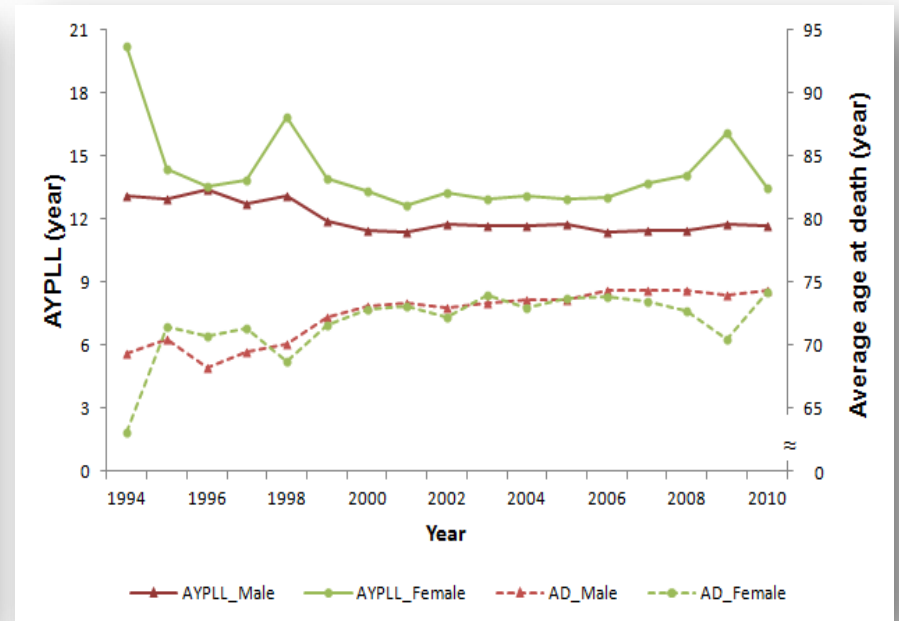
Based on analysis of data in WHO Mortality Database during 1994-2010

AYPLL of Asbestos-Related Deaths

Time-Trend



Mesothelioma (C45, ICD10)



Asbestosis (J61, ICD10)

Age-at-Death, Mesothelioma

	Earlier	Now	Future
Industrialized	Young	Old	Older
Industrializing	None	Young	Old
World	*	*	*

*at each point in time, the combined effect is observed

Discussion

Initial cases are diagnosed (die, *i.e.*, mesothelioma) at young ages.
As more cases accrue, cases are diagnosed (die *i.e.*, mesothelioma) at old ages.

From YPLL to DALY

By analyzing the WHO Mortality Database...

- For mesothelioma with **11,884** annual deaths, we estimate annual incidence to be **17,826** and further estimate DALY as **218,625** [155,241 M, 51,983 F] (cf Study by Driscoll : 564,000 [356,000 M, 207,000 F])
- For asbestosis with **1,320** annual deaths, we estimate annual incidence to be **5,280** and further estimate DALY as **158,400** or **211,200** (cf Study by Driscoll: 376,000)
- Our values are reasonably close to, but about 40-60% smaller than, the WHO-endorsed values; Our M/F ratio is closer to conventional knowledge

Conclusion

- Calculation of YPLL and AYPLL is straightforward and obtainable from existing data
- These indicators provide a quantitative aspect of the global burden of ARDs
- They may have further potential to allow improved comparisons across regions and timelines

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Future studies

- Plot time-trend of asbestosis (precursor; may rise and fall earlier) and mesothelioma (follower) together: x-axis time.
- Perhaps it can be used for prediction!?
- Think of asbestosis and mesothelioma together (combined indicator?)

Annual N of reported deaths (cases)

Rank	Mesothelioma			Asbestosis		
	Country	Value	%	Country	Value	%
1	USA	2,444	20.6	USA	529	40.8
2	UK	1,826	15.4	UK	132	10.2
3	Italy	1,281	10.8	Germany	119	9.2
4	Germany	1,131	9.6	France	99	7.6
5	France	852	7.2	South Africa	67	5.1

Age-adjusted MR (deaths per million per year)

Rank	Mesothelioma			Asbestosis		
	Country	Value	%	Country	Value	%
1	Iceland	24.6	NA	Malta	6.3	NA
2	Bahrain	20.5	NA	Slovenia	2.8	NA
3	Malta	18.8	NA	South Africa	2.43	NA
4	UK	18.3	NA	Finland	2.39	NA
5	Australia	16.5	NA	New Zealand	2.2	NA

Annual YPLL (person-years)

Rank	Mesothelioma			Asbestosis		
	Country	Value	%	Country	Value	%
1	USA	37,438	18.7	USA	6,401	38.3
2	UK	29,107	14.6	Germany	1,684	10.1
3	Italy	21,988	11.0	UK	1,637	9.9
4	Germany	18,592	9.3	France	1,344	8.0
5	Japan	16,287	8.1	South Africa	880	5.3

AYPLL (years)

Rank	Mesothelioma			Asbestosis		
	Country	Value	%	Country	Value	%
1	Egypt	26.3	NA	Egypt	21.5	NA
2	Colombia	24.5	NA	Mexico	18.6	NA
3	Cuba	23.6	NA	Brazil	17.2	NA
4	Ecuador	22.0	NA	Slovakia	16.6	NA
5	Philippines	21.9	NA	Croatia	16.1	NA