

の精度は不明である（後述）。環境ばく露の実態（人口中のばく露者の割合）については、ほとんどわからないのが現状と言える。

成人男性の 20-40%が何らかの石綿ばく露の可能性のある職業に従事したとする報告がある(Anonymous 1997; Goldberg et al. 2000)。国や地域など、大きな集団での石綿ばく露者の割合については、以下の因子が推定を困難にしている。

- 1) 環境ばく露を測定ないし推定した結果をばく露者の割合に外挿する試みが皆無
- 2) 女性の石綿ばく露者に関して推定は、ほとんど皆無
- 3) 職業ばく露集団におけるばく露レベル・ばく露量は労働衛生目的で実施されているが(日本で言えば作業環境測定) その結果は、一部の疫学研究に利用されることはあっても、ばく露者の割合の推定に利用するという試みが皆無

この点については、次のように考察できる。国や地域など、大きな集団での石綿ばく露者の割合について評価しようとする、上述のように、集団間で大きな格差があると考えられるが、少なくとも国や時期に依存する面がある。これまでの科学研究の中には、石綿の「消費量」と「消費量の推移」がある程度、当該集団の「ばく露の実態」を反映する一指標であるという考えに依拠して実施され研究報告がある。この中には実態を記述するための報告的論文(Harington and McGlashan 1998; LaDou 2004)と下記の生態学的関連を評価した論文(Nurminen et al. 2003; Takahashi et al. 1999; Tossavainen 2004)が含まれる。

生態学研究などで国段階の消費量をばく露指標とする場合がある。なお、生態学的関連によって因果関係は論じられず、記述疫学研究の一種とみなすべきである。国段階の石綿消費量の定義については、米国地質学調査において消費量＝生産量＋輸入量－輸出量という定義が採用されている(Virta 2003)。この値を当該国の同時点の人口で除することで、国民一人当たり石綿消費量という指標が求まる。

#### Q4-2. 把握困難な点は何か

##### A4-2.

職業性の石綿ばく露についても個人の詳細なばく露歴を正確に記述することは多大な困難を伴う。最大の理由は、数十年前の記憶に頼らざるを得ないことや、石綿へのばく露程度は様々で、例えば石綿として認識されずに使用/接触/周辺ばく露していた状況があり得ること、職業歴自体の同定の困難さの上に職業一ばく露関連の多様性の問題などを挙げるができる。Takahashiらは職歴に基づくばく露指標と（生物学的に疾病要因となる）肺内線維量の関係について評価しており(Case et al. 1994; Takahashi et al. 1994)、関連する論文カテゴリーが存在する。居住歴などの環境性の石綿ばく露についてはなおさら記述が困難となる。

現在、関連するテーマについて、平成 18-20 年度文部科学省萌芽研究「石綿ばく露診断支援システムの構築」（課題番号 18659190）において検討を進めている。

#### Q4-3. 利用可能なデータベース・情報源について

##### A4-3.

今回、利用したデータベースは米国地質学調査(United States Geological Survey, USGS)のが調査研究向けの Special Publications として発行している”Worldwide Asbestos Supply and Consumption Trends from 1900 to 2000 (OF-03-083)”である。USGS のウェブサイト <http://minerals.usgs.gov/minerals/pubs/commodity/asbestos/>

から無料でダウンロード可能である。

今回、利用していないが、Market Research 社がウェブ上で石綿関連の商用調査向けのデータベースとして発行している”The World Market for Asbestos: A 2005 Global Trade Perspective”が存在する。検討に値するが1年分で850米ドルと高価な上、調査研究向けに必要な過去分が2003年までしか遡ることができないため、現時点では未入手である。ウェブサイトから有料でダウンロードをする仕組みをとっている。 <http://www.marketresearch.com/>

#### 5. 上記以外の疫学的知見の整理

##### Q5-1. 生態学的関連を評価した知見

##### A5-1.

一人当たり石綿消費量が国など規模の大きい集団のばく露レベルを反映する代替指標として妥当性があるなら、その限りにおいて、一人当たり石綿消費量と石綿関連疾患の統計値を用いて両者の間の生態学的関連を評価できる。これまでの知見(Nurminen et al. 2003; Takahashi et al. 1999; Tossavainen 2004)は全中皮腫に限られているが、いずれにおいても一定の合理的結果が得られている。生態学的関連としては地域相関(Takahashi et al. 1999; Tossavainen 2004)および時系列相関(Nurminen et al. 2003)があるが、いずれにおいても有意の関連があるとする知見である。

#### 4. 諸外国における石綿関連疾患リスクの評価に関する疫学的研究

##### 4-1. 新たに創出された知見

##### 4-1-1. 関連情報 (資料②③④)

「諸外国における石綿ばく露と健康障害発症リスク」という課題について、様々な角度から検討を加えようとする際、国段階の情報として、活用できる主要な関連情報としては、(1)各国別・年代別の石綿消費や使用実態に関連する情報、と(2)各国別・性別・年代別・疾病別の石綿関連疾患のリスクに関連する情報を挙げることができる。

(1)については、さらに、(a)石綿の使用実態そのものに関する定量的情報、と(b)当該石綿使用実態の基盤を与え、または背景となる各国・年代別の法律制度的な使用方針、産業需要、用途等の定性的情報に分類できる。これらは、いずれも石綿の種類別に情報が整理できることが望ましい。(2)については、さらに、(a)罹患数・率の情報、(b)死亡数・率の情報、

(c)当該石綿関連疾患のリスクの基盤を与え、または背景となる各国・年代別の疾病の診断・治療・報告・登録・補償に関連する情報に分類できる。これらは、いずれも石綿関連疾患の種類別に情報が整理できることが望ましい。理論的には、(1)と(2)をつなぐものは、要因(石綿)と結果(石綿関連疾患)を結びつける疫学的関係(臨床医学的關係を含む)ということになるが、その関係は本来的には医学・生物学的に規定される関係であるから、国段階で集めるべき情報とは異なる。

すなわち、国段階で必要な関連情報は以下の表のように整理できる。

表. 「諸外国における石綿ばく露と健康障害発症リスク」の検討に必要な国段階の基本的情報

(1)石綿消費や使用実態に関する情報(各国別・年代別)

(a)石綿の使用実態そのものに関する定量的情報

- ・石綿の消費量(生産・輸入・消費・輸出)、国民1人当たり消費量など
- ・石綿種類別が望ましい
- ・産業や業種別が望ましい

(b)当該石綿使用実態の基盤を与え、または背景となる定性的情報(各国・年代別)

- ・石綿の法制度的な使用方針
- ・産業需要
- ・石綿用途

(2)石綿関連疾患のリスクに関する情報(各国別・性別・年代別・年齢階級別・疾病別)

(a)罹患数・率の定量的情報

(b)死亡数・率の定量的情報

(c)当該石綿関連疾患のリスクの基盤を与え、または背景となる定性的情報

- ・石綿関連疾患の診断・治療
- ・石綿関連疾患の報告・登録(例 中皮腫登録制度、がん登録制度等)
- ・石綿関連疾患の補償(例 公的補償制度、訴訟制度/実態)

表のうち、実際に収集可能なデータは著しく限られている。国際比較可能なデータが学術論文に掲載されることが少ない上に、国段階のいわゆるマクロデータを集めたDBの形で情報が存在するものはほとんどない。石綿関連疾患のグローバルな流行が懸念されるようになった最近になってようやくこの種の情報の必要性が認識され始めた段階といってもよい。

(1)(a)についてはQ4-3に記述した米国地質学調査のDBが存在する。本研究では、最新情報を加えて統合DBに登録した。

(2)(b)についてはQ3-4に記述したWHO Mortality DBが存在する。最新情報を加えて統合DBに登録した。

文献情報が限られる中で、研究者間のネットワークを最大限活用して国段階の情報を集める目的で、上記内容の中核部分を網羅し、かつ回答しやすいアンケートを設計した。アンケートを主任研究者らが出席した学会やメール等で配布し、協力を求めた（資料③アンケート票参照）。その結果、従来知られていなかった国単位の石綿使用実態や石綿関連疾患の報告数がまとまるなど、一定の成果を収めた（資料③アンケート票集計結果参照；石綿関連疾患については資料②死亡数も参照）が、さらにアンケート内容の改善や配布先を増やす努力をはじめ、情報収集の努力を継続する必要がある。

#### 4-1-2. 学術論文（資料①）

論文タイトル：「石綿関連疾患と歴史的石綿使用量の生態学的関連：グローバルな解析」

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受理雑誌：Lancet

##### 《論文要旨 Summary》

【背景】石綿関連疾患(asbestos-related diseases; ARDs)の世界的流行に対する懸念が増大している。そこで我々は国段階におけるARD（全中皮腫、胸膜および腹膜中皮腫、石綿肺症）の死亡率と歴史的石綿使用量の間の生態学的関連を評価した。

【方法】データの利用可能なすべての国について、2000-2004年における各ARDの性別・年齢調整死亡率（百万人口・年当たり）と1960-1969年の平均国民一人当たり石綿使用量（国民一人・年当たりキロ数）を算出した。次に、各国人口の規模で重みづけをした上で、歴史的石綿使用量をARDの最近の死亡率に回帰させた。

【結果】全中皮腫では男女ともに歴史的石綿使用量が同死亡率に対して極めて有意な予測因子となった。すなわち男性では調整  $R^2=0.74$ ,  $p<0.001$  かつ単位石綿使用量当たり2.4倍のリスク上昇を、女性では調整  $R^2=0.58$ ,  $p<0.001$  かつ単位石綿使用量当たり1.6倍のリスク上昇を認めた。さらに、男性の胸膜中皮腫 ( $R^2=0.29$ ,  $p=0.002$ , 1.8倍のリスク上昇)、男女の腹膜中皮腫（男性で  $R^2=0.54$ ,  $p<0.001$ , 2.2倍のリスク上昇、女性で  $R^2=0.35$ ,  $p<0.001$ , 1.4倍のリスク上昇）、男性の石綿肺症 ( $R^2=0.79$ ,  $p<0.001$ , 2.7倍のリスク上昇）で同様の傾向を認めた。回帰式の切片はいずれも原点に近かった。

【解釈】生態学的研究の制約下で、ARDと歴史的石綿使用量の間には明瞭で合理的な関係が示された。その関係は男女の全中皮腫と男性の石綿肺症で顕著であった。

#### 4-2. 今後の課題

今回、石綿関連データベースの基盤を構築し、そこから得られたデータを利用することで、諸外国における歴史的石綿使用量と中皮腫と石綿肺症を含む石綿関連疾患の死亡率の間の生態学的関連を評価することができた。すなわち、「諸外国の実態」を基本データとするグローバルな解析を行い、原著論文として新規知見を創出することができた。同論文は医学雑誌の

中でも最高水準のインパクトを持つ *Lancet* 誌に受理され、印刷予定である。本論文の発展形としては、グローバルな解析手法にグローバリゼーションや経済発展段階等の社会科学的見地も加えて検討を深める予定である。

「諸外国における石綿ばく露と健康障害発症リスクに関する調査研究」を標題とする厚生労働科学研究としての実施は平成 17 年度の単年度研究として終了するが、既存かつ新たに報告される膨大な知見を完全に捕捉し、活用範囲を広げるためには、データベースの維持更新を図り知見を積み増しながら、大局的見地から批判的総説を加える必要がある。これらの継続すべき課題については既に採択されている平成 18-20 年度厚生労働科学研究「石綿ばく露による健康障害発症リスクに関する疫学調査の開発研究」（主任研究者高橋謙）の中においても鋭意取り組む予定である。

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資料① 平成 17 年度研究成果としての学術論文

**Ecological relation between asbestos-related diseases and historical asbestos consumption: a global analysis. *Lancet* 2006, in press.**

[日本語訳 石綿関連疾患と歴史的石綿使用量との生態学的関連：グローバルな解析]

# **Ecological relation between asbestos-related diseases and historical asbestos consumption: a global analysis**

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Running Title: Global asbestos-related diseases

## Summary

**Background** There is growing concern regarding a global epidemic of asbestos-related diseases (ARDs). We assessed the ecological relation between national mortality rates of ARDs (all, pleural and peritoneal mesothelioma, and asbestosis) and historical consumption level of asbestos.

**Methods** Age-adjusted average mortality rates (cases per million population per year) of each ARD during 2000–2004 and average per capita asbestos consumption (kg per capita per year) during 1960–1969 were calculated across the fullest range of countries with available data, differentiating for sex. Historical asbestos consumption was regressed on recent ARD mortality, weighted by the size of sex-specific national populations.

**Findings** Historical asbestos consumption was a highly significant predictor of mortality for all mesothelioma in both sexes (adjusted  $R^2=0.74$ ,  $p<0.001$ , 2.4-fold mortality increase was predicted per unit consumption increase for males;  $R^2=0.58$ ,  $p<0.001$ , 1.6-fold for females), male pleural mesothelioma ( $R^2=0.29$ ,  $p=0.002$ , 1.8-fold), peritoneal mesothelioma in both sexes ( $R^2=0.54$ ,  $p<0.001$ , 2.2-fold for males;  $R^2=0.35$ ,  $p<0.001$ , 1.4-fold for females), and male asbestosis ( $R^2=0.79$ ,  $p<0.001$ , 2.7-fold). Linear regression lines consistently had intercepts near zero.

**Interpretation** Within the constraints of an ecological study, clear and plausible relations were shown to exist between mortality of the studied ARDs and historical asbestos consumption, markedly for all mesothelioma in both sexes and male asbestosis.

**Keywords:** Asbestos; World Health; Environment and Public Health; Occupational

Exposure; Occupational Diseases; Mesothelioma; Asbestosis

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## Introduction

There is widespread concern regarding the possibility of a global epidemic of asbestos-related diseases (ARDs). The milestone serial research on ARDs by Selikoff and colleagues urged such caution as early as the 1960s.<sup>1,2</sup> More recently, the work by Peto is of seminal importance. Based on birth-cohort modeling, Peto predicted a drastic increase in future mesothelioma deaths in Britain<sup>3</sup> and Europe.<sup>4</sup> Follow-up investigations showed close agreement between projected and observed numbers on the one hand and tapering<sup>5</sup>/deceleration<sup>6</sup> of the mesothelioma epidemic on the other. Lately, statistical projections of mesothelioma have expanded to include a host of countries,<sup>7-10</sup> and suggested substantial increases in the respective countries.

The *current* global impact of ARDs has also been estimated: the annual number of asbestos-related cancer deaths in workers may reach 100 000–140 000.<sup>11</sup> 5–7% of lung cancer cases may be attributed to occupational asbestos exposure<sup>11,12</sup> although estimates for lung cancer would vary also with tobacco consumption. The International Expert Meeting on Asbestos, Asbestosis and Cancer of 1997, in discussing the “global asbestos epidemic,” agreed that every year, 20 000 asbestos-induced lung cancer and 10 000 mesothelioma cases occur in West Europe, North America, Japan and Australia.<sup>13</sup> The International Labour Organization (ILO) and the World Health Organization (WHO) jointly communicated that elimination of ARDs is a priority area for collaboration. Currently ILO is expressing a high level of concern about an ongoing and evolving epidemic of ARDs giving due regard to the long latency period required for disease manifestation.<sup>14</sup> Recently, ILO adopted a resolution to promote a global asbestos ban.<sup>15</sup>

The global spread of *exposure* to asbestos is far more difficult to grasp, primarily because quantified measurement data are limited. A rough estimate is that 20–40% of adult men held jobs that may have entailed asbestos exposure.<sup>13,16</sup> However, attempts to estimate the proportion of

the exposed in populations are generally hampered by a lack of reliable estimates for women, the extent of environmental exposure, or even levels of exposure in the occupationally exposed population. A wide disparity in exposure status of populations is likely, but this should be contingent at least upon the country and timeframe concerned. As such the volume of asbestos consumption and its chronological trend have been used for characterization of various populations. By virtue of these indices, it is suggested that the center of asbestos consumption is shifting towards developing countries.<sup>11,17</sup>

An ARD is a health effect on individuals related to past exposure to asbestos, mostly but not exclusively by occupations. When the experience is aggregated in populations, it should manifest as a global ARD epidemic. To the extent that *per capita* consumption volume can be treated as a surrogate for the exposure level of a population, ecological relations can be evaluated against statistical rates of ARDs. Preliminary investigations have been made for mesothelioma and have produced plausible findings,<sup>12,18,19</sup> albeit limited by the scope of available data. Exploring the ecological relation for national populations can be improved by incorporating the fullest range of available information on ARDs and by using refined methodologies. We precluded lung cancer from the analysis because of its apparent causal link with smoking and lack of reliable comparable data to adjust for this. The objective of the present study is thus to explore on a global basis the ecological relation between national rates of ARD-induced mortality and historical asbestos consumption.

## **Methods**

The ARDs evaluated were all mesothelioma, pleural mesothelioma (C45·0, International Classification of Diseases, 10th Revision or ICD-10), peritoneal mesothelioma (C45·1, ICD-10),

and asbestosis (J61, ICD-10). All mesothelioma was defined as follows: mesothelioma (C45, ICD-10) as an independent category and/or composite of all or any of its subcategories, i.e., pleural (C45·0), peritoneal (C45·1), pericardial (C45·2), other sites (C45·7), and unspecified (C45·9), as reported by the respective countries. The annual number of deaths during 2000–2004 for each ARD by sex and 5-year age category was obtained from the WHO Mortality Database.<sup>20</sup> National population data were obtained from WHO,<sup>20</sup> the United States Census Bureau (USCB),<sup>21</sup> and the United Nations (UN),<sup>22</sup> prioritized for use in this order. For each country, sex- and age-specific mortality rates (cases per million (M) population per year) were calculated by dividing the number of sex-specific deaths during 2000–2004 by the size of the corresponding sex-specific national populations, and then age-standardized to the World Standard Population published in 1966.<sup>23</sup> These rates were then averaged for the same period.

Historical asbestos consumption rate was defined as annual average *per capita* asbestos consumption (kilograms or kg per capita per year) for the period 1960–1969 (i.e., the average of data for 1960 and 1970, the two years for which data are available for this period). For each country, the volume in number of *tons* for asbestos production, import and export was extracted from the United States Geological Survey (USGS) Report.<sup>24</sup> The definition of consumption followed the conventional definition of (production + import – export)<sup>24</sup> and was divided by the national population of the corresponding period. The period of asbestos consumption (1960–1969) was chosen *a priori* to allow for a sufficient time lag of about 30–40 years between this and the annual average ARD mortality rates of 2000–2004. This was deemed reasonable because mesothelioma is known to have latency periods of approximately 40 years. Although variable latency periods have been reported for asbestosis morbidity, we postulated the same latency period in asbestosis patients accounting for the additional period required from incidence

to death.

There was a maximum of 33 countries with both consumption and mortality data available for analyses. These countries consumed 63% of the world's consumption level during 1960–1969 and accounted for nearly one-fourth (22%) of the world population in 2000–2004, comprising 84%, 74%, and 48% of the population in the Americas, Oceania, and Europe (but only 8% and 5% in Africa and Asia), respectively.

For each ARD, linear regression analyses were conducted separately for each sex, with age-adjusted mortality rates of each ARD as the dependent variable and historical asbestos consumption as the independent variable. The national mortality rates were log-transformed to comply with the assumptions underlying the random errors in the regression model. Parameters in the regression model were estimated by the least-square method, weighted by the size of sex-specific national populations of 2000–2004. All statistical procedures were performed using SAS V8.02 (SAS Institute Inc., Cary, NC, USA). Graphs were drawn using SigmaPlot V9.01 (Systat Software Inc., Richmond, CA, USA). A p-value less than 0.05 was considered statistically significant in this study. This research was supported in part by a Grant-in-Aid for “Research of Asbestos in the World” from the Ministry of Health, Labor and Welfare of Japan.

## **Results**

The figure shows the scatter plot of national data for each ARD (the sex with the higher adjusted  $R^2$  value was chosen for presentation in the panel, i.e., males), in which a clear positive linear relation between historical asbestos consumption and log-transformed ARD mortality rate was demonstrated. The sex-specific association of each ARD is expressed as a linear regression model in the table, with the parameters (intercept  $B_0$  and slope  $B_1$ ) and adjusted  $R^2$  values.

Strong linear relations are apparent for all mesothelioma in both sexes, male asbestosis and peritoneal mesothelioma.

Panel A shows the relation for all mesothelioma in males, where a higher asbestos consumption clearly corresponded to a higher log-transformed mortality rate. As the table shows, historical asbestos consumption was a highly significant positive predictor of all mesothelioma mortality rate with an adjusted  $R^2$  value of 0.74 in males ( $p < 0.001$ ). In females, asbestos consumption was a highly significant positive predictor of all mesothelioma mortality rate with an adjusted  $R^2$  value of 0.58 ( $p < 0.001$ ). The slope ( $B_1$ ) of the regression lines indicated that, for an increment in asbestos consumption of 1 kg per capita in the entire population, males had a 2.4-fold ( $10^{0.382 \times 1}$ ) increase and females a 1.6-fold ( $10^{0.208 \times 1}$ ) increase in mesothelioma mortality rate. The intercepts ( $B_0$ ) were small at  $10^{-0.135} = 0.73$  (95% CI=0.47–1.14) for males and  $10^{-0.326} = 0.47$  (95% CI=0.33–0.67) for females. The mortality rate predicted for the mean consumption value (1.67 kg per capita) was 3.18 (95% CI=2.55–3.82) and 1.05 (95% CI=0.56–1.54) (per M population per yr) in males and females, respectively. Thus the male/female mortality rate ratio was 3.0.

Historical asbestos consumption was a significant positive predictor of pleural mesothelioma rate in males (Panel B,  $R^2 = 0.29$ ,  $p = 0.002$ ,  $B_0 = 10^{-0.408} = 0.39$  (95% CI=0.18–0.87)). The slope indicated a 1.8-fold ( $10^{0.257 \times 1}$ ) increase in male pleural mesothelioma mortality rate per incremental asbestos consumption in the entire population. By contrast, the relation was not statistically significant ( $p = 0.107$ ) in females.

The relations for peritoneal mesothelioma mortality rate were positive and statistically significant for both sexes (Panel C,  $R^2 = 0.54$ ,  $p < 0.001$ ,  $B_0 = 10^{-1.475} = 0.03$  (95% CI=0.02–0.07) for males and  $R^2 = 0.35$ ,  $p < 0.001$ ,  $B_0 = 10^{-1.190} = 0.06$  (95% CI=0.04–0.10) for females). The slope

indicated a 2.2-fold ( $10^{0.333 \times 1}$ ) and a 1.4-fold ( $10^{0.132 \times 1}$ ) increase in peritoneal mesothelioma mortality rate in males and females, respectively, per incremental asbestos consumption in the entire population. The mortality rate predicted for the mean consumption value (1.67 kg per capita) was 0.12 (95% CI=-0.72-0.96) and 0.11 (95% CI=-0.40-0.61) (per M population per yr) in males and females, respectively. Thus the male/female mortality rate ratio was 1.1.

The relation for asbestosis mortality rate was positive and statistically significant in males and yielded the highest adjusted  $R^2$  among all studied ARDs (Panel D,  $R^2=0.79$ ,  $p<0.001$ ,  $B_0=10^{-1.255}=0.06$  (95% CI=0.03-0.09)). The slope indicated a 2.7-fold ( $10^{0.439 \times 1}$ ) increase in male asbestosis mortality rate per incremental asbestos consumption in the entire population. By contrast, the relation was not statistically significant in females.

## Discussion

We found that recent national mortality rates of ARDs were highly related to historical asbestos consumption rates of 1960–1969. The ecological relations were consistently positive for all ARDs in males. In females positive ecological relations were found for all and peritoneal mesothelioma but not for pleural mesothelioma or asbestosis. The relations were particularly strong for male asbestosis ( $R^2=0.79$ ), male all mesothelioma ( $R^2=0.74$ ), female all mesothelioma ( $R^2=0.58$ ) and male peritoneal mesothelioma ( $R^2=0.54$ ). For these diseases, mortality rates increased 2.7, 2.4, 1.6 and 2.2-fold, respectively, per incremental asbestos consumption.

For all studied ARDs, the increase in mortality rate per incremental increase of asbestos consumption was higher in males than females. In males, the highest increase was for asbestosis at 2.7-fold and lowest for pleural mesothelioma at 1.8-fold. In females, increases in mortality rates were generally lower, with the highest increase occurring for all mesothelioma at 1.6-fold

and lowest for asbestosis at 1·1-fold (this model was not significant, NS). Although the positive correlation in females was more apparent for all mesothelioma than pleural mesothelioma, this may be related to the fact that pleural mesothelioma was relatively fewer, and some countries lacked data for the specific subcategories of mesothelioma. But it should also be considered that the level of statistical significance for the positive relation was close to marginal ( $p=0\cdot107$ ). This problem could also have occurred in males.

For all mesothelioma, the male/female rate ratio of 3·0 for the predicted dependent value was within, but closer to the lower boundary, of the reported range of 2 to 10,<sup>25,26</sup> although the male/female distribution of exposure differs by population. The male/female rate ratios for pleural and peritoneal mesothelioma were 3·7 (the regression model for females was NS) and 1·1 (the regression model for both sexes was significant), respectively, which were similar to previously reported values of 5 and 2.<sup>27</sup> The male/female rate ratio for asbestosis was 8·1. There are no reports with which to compare our results, but the results are within plausible range.

Although our findings cannot be extrapolated beyond the data range, the regression lines had intercepts close to zero for all ARDs. This suggests that minimal historical asbestos consumption is predictive of minimal mortality rates for ARDs.

A demonstration of the ecological relation between lung cancer and historical asbestos consumption, as it pertains to national rates, would provide leads to estimating the attributable fraction of lung cancer to asbestos exposure in the general population. The issue on asbestos-induced lung cancer has been under-appreciated<sup>28</sup> as current scientific knowledge is restricted to asbestos-induced lung cancer/mesothelioma ratios (i.e., ratio of excess cases of lung cancer and of cases of mesothelioma) reported by epidemiological studies of occupationally exposed populations, ranging from 1–2 to 30–40 with 2 as the most cited figure.<sup>29–32</sup> No