An international perspective on mesothelioma registries

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DISCLOSURES

I have no actual or potential conflict of interest in relation to this presentation
Mesothelioma Registries Worldwide
Aims:

- Data collected on lung cancer and MPM since 2005
- Commissioned and funded by the Mesothelioma UK charity to maintain and enhance the profile of mesothelioma and set new standards; allow organizations to measure and demonstrate improvement over time
- Create an infrastructure for data collection for mesothelioma

Linkage between different national registries

Information Collected:

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Cancer Diagnosis</th>
<th>Asbestos Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Gender</td>
<td>Stage/ year of diagnosis</td>
<td>Occupational exposure</td>
</tr>
<tr>
<td></td>
<td>Pathological confirmation</td>
<td>Year of exposure</td>
</tr>
<tr>
<td></td>
<td>Cancer treatment</td>
<td>Occupational history</td>
</tr>
<tr>
<td></td>
<td>Survival</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Performance status</td>
<td></td>
</tr>
</tbody>
</table>

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United Kingdom - National Lung Cancer Audit; National Mesothelioma Audit

Strengths:

- Linkage with different national datasets
- Information on treatment and performance status
- Includes malignant peritoneal mesothelioma

Limitations:

- No national coverage
- High percentage of missing data including stage, pathological conformation
- Passive monitoring system
- No exposure information other than occupation

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ITALY - NATIONAL REGISTER OF MALIGNANT MESOTHELIOMAS (RENAM)

- Started in 1993 at the Institute for the Occupational Safety and Prevention (IPESL) for worker compensation purposes

**Aims:**
- Estimate the incidence of malignant mesothelioma in Italy and define the modalities of past asbestos exposure
- Identify underestimated (or unknown) sources of environmental asbestos exposure

**Information Collected:**

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Cancer Diagnosis</th>
<th>Asbestos Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>Tumor site</td>
<td>Occupational history</td>
</tr>
<tr>
<td>Gender</td>
<td>Date of diagnosis</td>
<td>Family members exposed</td>
</tr>
<tr>
<td>Place of residence</td>
<td>Tumor type</td>
<td>Residential history</td>
</tr>
<tr>
<td></td>
<td>Pathology report</td>
<td>Lifestyle habits</td>
</tr>
<tr>
<td></td>
<td>Cytology with markers</td>
<td></td>
</tr>
</tbody>
</table>

**Italy - National Register of Malignant Mesotheliomas (ReNaM)**

**Strengths:**
- Coverage of ~99% of cases
- Nationwide with regional centers for active and passive data collection
- Information collected is shared back with the Cancer Registry
- Includes pathology report and cytology with markers
- Review of Death Index to include missing, deceased patients
- Direct patient interview (~ 47%) vs family interview (~ 46%)
- Data on family members exposure

**Limitations:**
- Missing treatment information
- Limited information when questionnaire is collected via family of deceased patients
- No tissue bank

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FRANCE - FRENCH NATIONAL MESOTHELIOMA SURVEILLANCE PROGRAM (PNSM)

- Started in 1998 to evaluate the compensation process (Asbestos Victims Compensation Fund since 2002)

**Aims:**
- Estimate the incidence of mesothelioma in France and its trend over time
- Study asbestos and other exposures, especially occupational
- 21 departments representing 18 million people (~30% of the population)

**Information Collected:**

<table>
<thead>
<tr>
<th>Demographic Data</th>
<th>Cancer Diagnosis</th>
<th>Cancer Death</th>
<th>Asbestos Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Diagnostic confirmation</td>
<td>Mortality from National Death Statistics Office</td>
<td>Job history</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>Asbestos exposure: source, start date, duration</td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
<td>Personal and family medical history</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>Compensation</td>
</tr>
</tbody>
</table>

http://invs.santepubliquefrance.fr/fr/Dossiers-thematiques/Travail-et-sante/Mesotheliomes/Programme-national-de-surveillance-des-mesotheliomes

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FRANCE - FRENCH NATIONAL MESOTHELIOMA SURVEILLANCE PROGRAM (PNSM)

Strengths:

• Trained investigator collects data from patient (~79%), or family member after death (~ 21%)

• Detailed list of exposures including job and tasks performed, technical training

• Responses analyzed by experts to semi-quantify exposure

• Standardized procedure to confirm pathological diagnosis by national group of mesothelioma experts

• Cases are interviewed even before pathological confirmation

Limitations:

• No nation-wide coverage

• No continuous linkage with the National Death Statistics Office

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http://invs.santepubliquefrance.fr/fr/Dossiers-thematiques/Travail-et-sante/Mesotheliomes/Programme-national-de-surveillance-des-mesotheliomes
**AUSTRALIA - AUSTRALIAN MESOTHELIOMA REGISTRY (AMR)**

**Aims:**
- Monitor all new cases of mesothelioma in Australia diagnosed from July 1\textsuperscript{st}, 2010
- Clarify relationship between asbestos exposure and mesothelioma, identify other exposures that may be associated with mesothelioma
- Inform the development of community education, awareness and prevention strategies
- Linked annually to the National Death Index

*Mandated reporting of all cancer cases to the registry*

**Information Collected:**

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<th>Asbestos Exposure</th>
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<tbody>
<tr>
<td>Cancer Registry</td>
<td>Date of Diagnosis</td>
<td>Death Date</td>
<td>Residential history</td>
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<tr>
<td>Sex</td>
<td>Age at Diagnosis</td>
<td>Death Cause</td>
<td>School history</td>
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<td>Country of birth</td>
<td>Topography Code</td>
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<td>Occupational history</td>
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<tr>
<td>Indigenous status</td>
<td>Morphology Code</td>
<td></td>
<td>Family history</td>
</tr>
<tr>
<td>Date of Birth</td>
<td>Best Method of Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Laterality</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[https://www.mesothelioma-australia.com/home/](https://www.mesothelioma-australia.com/home/)

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Strengths:

• Not necessary to obtain consent from the patient before making initial contact

• Comprehensive information about potential asbestos exposure (all residences, schools, occupations)

• Researchers can apply to obtain information

• Automatic opt-in to contact patients if doctor does not respond within 3-4 weeks

Limitations:

• Could miss exposure interview information from the sickest patients

• No treatment information

• Potentially burdensome for patients (postal questionnaire and a phone interview)

• Participation in surveys is low (~20%), no option to interview family

https://www.mesothelioma-australia.com/home/
SOUTH KOREA - KOREAN MESOTHELIOMA SURVEILLANCE SYSTEM

Aims:

• Established in 2001
• Examine trends in mesothelioma incidence
• Identify histories of asbestos exposure
• Organized by the Korea Occupational Safety and Health Agency

Pathology-centered

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<tr>
<td>Age</td>
<td>Date of Diagnosis</td>
<td>Occupational history</td>
</tr>
<tr>
<td>Gender</td>
<td>Diagnosis method</td>
<td>Take home exposure</td>
</tr>
<tr>
<td>Place of residence</td>
<td>Histologic subtype</td>
<td>Residency history</td>
</tr>
<tr>
<td>Urban/rural status</td>
<td>Occurrence site</td>
<td>Environmental exposure</td>
</tr>
</tbody>
</table>


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**South Korea - Korean Mesothelioma Surveillance System**

**Strengths:**

- Includes information about spousal occupation and exposure and environmental exposure
- Only pathologically confirmed cases are counted
- Worksite visit attempted, if applicable
- Families were interviewed to obtain additional information (with patient consent), if necessary
- Interviews completed for ~40% of cases

**Limitations:**

- No linkage to death data
- May miss cases that are not pathologically confirmed
- No information on treatment
- Based on voluntary reporting of pathologists


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• **Turkey**- Turkey National Mesothelioma Surveillance and Environmental Asbestos Exposure Control Program (TUNMES-EAECPP)

• **Japan**- prospective registry database of patients with MPM, maintained by the Joint Committee of Lung Cancer Registry (JJCLCR)

• **Germany**- Deutschen Mesotheliomregister (German Mesothelioma Registry)

• **Belgium**- Belgian Mesothelioma Registry (BMR)

• **South Africa**- Asbestos Relief Trust Compensation Database

• **Sweden, Norway, Finland, Denmark** - Cancer registry linked to other occupational databases
Mesothelioma in the United States

Approximately 3,000 new cases each year

Age-Adjusted Incidence Rates (per 100,000 persons) 2000-2015

Overall
Male
Female

SEVERAL UNANSWERED QUESTIONS

• Incidence is plateauing but not decreasing

• Mortality has not substantially changed over time

• Geographic areas with an increase in number of cases, the reason is unknown

A system to capture cases in “real time” is needed
AVAILABLE DATA SETS in the US

**SEER**: SEER is supported by the National Cancer Institute, and collects data from population-based cancer registries covering ~34% of the US population. Any person living in a SEER registry area when their cancer is reported is included.

**SEER-MEDICARE**: reflect the linkage of two large population-based sources of data that provide detailed information about Medicare beneficiaries with cancer.

**SPARCS**: comprehensive all payer data reporting system established in 1979 as a cooperation between healthcare industry and government. SPARCS currently collects patient level detail on patient characteristics, diagnoses and treatments, services, and charges for each hospital inpatient stay and outpatient visit.

**NCDB**: a joint project between the American College of Surgeons and the American Cancer Society, and is sourced from hospital registry data collected in >1500 Commission on Cancer -accredited facilities.
Existing Datasets – Strengths and Limitations

SEER
- Country wide (but <30%)
- Population based
- Includes long-term outcomes
- Generalizable (all payers system)
- Large amount of data
- Very detailed on hospital procedures and events
- Captures ~70% of cancer diagnoses
- Includes long- and short term-outcomes
- Some insurance/comorbidity information

SEER- Medicare
- Detailed treatments, combined with cancer information
- Inpatient and outpatient treatments
- Comorbidities and clinical hx

SPARCS
- Lack subsequent treatments
- Limited chemotherapy information
- No insurance status before 2007
- No info on hospital where treated
- Sparse exposure data
- No comorbidities
- No cancer info (stage, histology…)
- No follow-up data, only inpatient events
- No exposure data

NCDB
- Only patients > 65 years
- Only Medicare, cannot study other insurances
- Limited to geographic regions of SEER
- Little variability in race/ethnicity
- No exposure data
- No information on subsequent treatments
- Limited facility information
- Inclusion is based on hospital characteristics, not population based
- Capture of cases is less comprehensive in minority groups
What is currently missing in US databases?

- Hard to get details on type of surgical treatment (codes are not mesothelioma specific)
- No information on asbestos exposure (occupational and residential)
- No information on other exposures
- No data on quality of life before/after treatment
- No opportunity to interview patients
SEX DIFFERENCES IN SURVIVAL (NCDB)

It is reported that females have better survival than males. Reasons are still unclear.

Compare survival between females and males, assess what factors contribute to better survival in females.

**SELECTION CRITERIA**
DEMOGRAPHIC AND CLINICAL FACTORS ASSOCIATED WITH SEX (N = 12 759)

Relative Odds in females versus males

- ref: Charlson 0
- ref: Epithelial

Age (years); ref: <50
OVERALL SURVIVAL ACCORDING TO SEX IN (A) PROPENSITY-MATCHED COHORT, (B) <50 YEARS, (C) ≥50 YEARS

After propensity matching within the epithelial group, survival remained significantly better for females compared with males (HR: 0.85, 95% CI: 0.74–0.97).
CONCLUSIONS

- MPM females survive significantly longer than males, independently from other contributing factors
- Within the epithelial group, we confirmed the survival advantage of females
- Males and females equally received surgery or radiotherapy, females received chemotherapy less frequently

STRENGTHS:
- Study on > 12,000 cases
- Allowed to stratify for many important covariates (age, histology…).
- Allowed propensity matching

LIMITATIONS:
- No biological information on the tumor (mutations, germline polymorphisms….)
- Missing data
SHORT TERM OUTCOMES AFTER SURGERY (SPARCS)

In-patient records with MPM diagnosis (ICD-9: 163) (n= 3826)

Records with at least EPP (ICD-9: 325, 3250, 3259), P/D (ICD-9: 345, 3451, 3452), pleurodesis (ICD-9: 3492), chemotherapy (9925), or radiotherapy (ICD-9: 9921, 9222, 9223, 9224, 9225, 9226, 9227, 9228, 9229) (n=1697)

Excluded (n=2129):
- No MPM treatment (n=2123)
- No patient ID (n=6)

Patients with MPM treatment (n=1495)

Excluded (n=202)
- Surgery not first treatment in patients with multiple treatments (n=202)

Excluded (n=956)
- No surgical treatment, only other MPM treatments (n=887)
- Surgical treatment + other MPM treatment in same year (n=69)

Patients treated with only surgery (n=539)
- EPP (n=235)
- P/D (n=304)

AIM: Compare postoperative mortality, morbidity, and 30-day mortality after Extra Pleural Pneumonectomy (EPP) and Pleurectomy/Decortication (P/D)

Journal of Surgical Oncology, 118: 7, 1178-1187
EPP patients were younger
• significantly more likely to be white
• privately insured
• admitted for an elective procedure than P/D patients
MORTALITY AND COMPLICATIONS, EPP vs. P/D

Journal of Surgical Oncology, 118: 7, 1178-1187
Conclusions

• Tendency towards higher in-hospital mortality for EPP vs P/D
• Supraventricular arrhythmia as postoperative complication significantly higher after EPP vs P/D
• Increased chance of death after EPP compared with P/D over the first 30 days after surgery

LIMITATIONS:
• No stage, histology or use of antiarrhythmic drugs before surgery
• No long terms follow-up
<table>
<thead>
<tr>
<th>Information of Interest</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical/Demographic</strong></td>
<td>• Cancer characteristics • Pathology and cytology • Treatment</td>
</tr>
<tr>
<td></td>
<td>(type of surgery) • Date of diagnosis • Performance status</td>
</tr>
<tr>
<td></td>
<td>• Linkage with data from family/spouses • Linkage to NDI</td>
</tr>
<tr>
<td><strong>Behavior/Exposure</strong></td>
<td>• Occupational exposure • Residential exposure • Spousal</td>
</tr>
<tr>
<td></td>
<td>exposures • Smoking history • Reproductive history (women)</td>
</tr>
<tr>
<td></td>
<td>• Geographic Region • Country of birth • Family History</td>
</tr>
<tr>
<td><strong>Quality of Life</strong></td>
<td>• Interview timing with treatment • Pain • SF 12/36</td>
</tr>
<tr>
<td></td>
<td>• Help with daily living • Home Care • Functional Limitations</td>
</tr>
<tr>
<td><strong>Tumor Biology</strong></td>
<td>• Genetic markers • Tumor tissue</td>
</tr>
<tr>
<td></td>
<td>• Normal tissue • Blood</td>
</tr>
</tbody>
</table>
Possible model of a mesothelioma registry

Individual reporting (Patients/Family)

Healthcare institutions and professionals diagnosing

Surgeons and Pathologists:

Epidemiologic Hub: IRB, Consent, Questionnaire, Interviews, SOP, quality control Feedback and changes

Pathologic Hub: Case confirmation, pathology, cytology, genetic and other

Cancer registry

Merge data identify duplicates Confirm cases

Follow up
Periodic data linkage with: SPARC, AMR, Insurance database,

EPIDEMIOLOGIC DATABASE

TISSUE BANK

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CHARACTERISTICS OF A MESOTHELIOMA REGISTRY

• As “real time” as possible
• Capture maximum number of cases
• Clear SOP and standardized method of data collection
• Centralized quality control system
• Simplify the consent process
• Ability to interview patients for additional information
• Ability to link with other relevant datasets
  (cancer registry, pathology report, tissue bank, NDI, EMR)
• Consistent with other countries’ registries
  (if we want to pool data)
• Flexible and able to add/modify modules upon request
  (if we want to expand the research questions)
• Able to quickly connect patients to clinical trials
THANKS!

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