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

UNITED KINGDOM - NATIONAL LUNG CANCER AUDIT NLCA; NATIONAL MESOTHELIOMA AUDIT; NATIONAL CANCER REGISTRATION AND ANALYSIS SERVICE (NCRAS)

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:

Demographic Data	Cancer Diagnosis	Asbestos Exposure
• Age • Gender	• Stage/ year of diagnosis • Pathological confirmation • Cancer treatment • Survival • Performance status	• Occupational exposure • Year of exposure • Occupational history

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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:

Demographic Data	Cancer Diagnosis	Asbestos Exposure
• Age at diagnosis • Gender • Place of residence	• Tumor site • Date of diagnosis • Tumor type • Pathology report • Cytology with markers	• Occupational history • Family members exposed • Residential history • Lifestyle habits

Marinaccio A, et al. Epidemiology of malignant mesothelioma in Italy: surveillance systems, territorial clusters and occupations involved. J Thorac Dis. 2018; 10 (2) S221-S227

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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https://www.inail.it/cs/internet/attivita/ricerca-e-tecnologia/area-salute-sul-lavoro/sorveglianza-epidemiologica-negli-ambienti-di-lavoro-e-di-vita/renam.html

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:

Demographic Data	Cancer Diagnosis	Cancer Death	Asbestos Exposure
• Age • Gender • Place of residence • Education	• Diagnostic confirmation	• Mortality from National Death Statistics Office	• Job history • Asbestos exposure: source, start date, duration • Personal and family medical history • Compensation

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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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AUSTRALIA - AUSTRALIAN MESOTHELIOMA REGISTRY (AMR)

Aims:

- Monitor all new cases of mesothelioma in Australia diagnosed from July 1st, 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:

Demographic Data	Cancer Diagnosis	Cancer Death	Asbestos Exposure
• Cancer Registry • Sex • Country of birth • Indigenous status • Date of Birth	• Date of Diagnosis • Age at Diagnosis • Topography Code • Morphology Code • Best Method of Diagnosis • Laterality	• Death Date • Death Cause	• Residential history • School history • Occupational history • Family history

https://www.mesothelioma-australia.com/home/

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Australia - Australian Mesothelioma Registry (AMR)

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/

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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

Information Collected:

Demographic Data	Cancer Diagnosis	Asbestos Exposure
• Age • Gender • Place of residence • Urban/rural status	• Date of Diagnosis • Diagnosis method • Histologic subtype • Occurrence site	• Occupational history • Take home exposure • Residency history • Environmental exposure

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Jung SH et al. A decade of malignant mesothelioma surveillance in Korea. American Journal of Industrial Medicine. 2012; 55:869-875

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

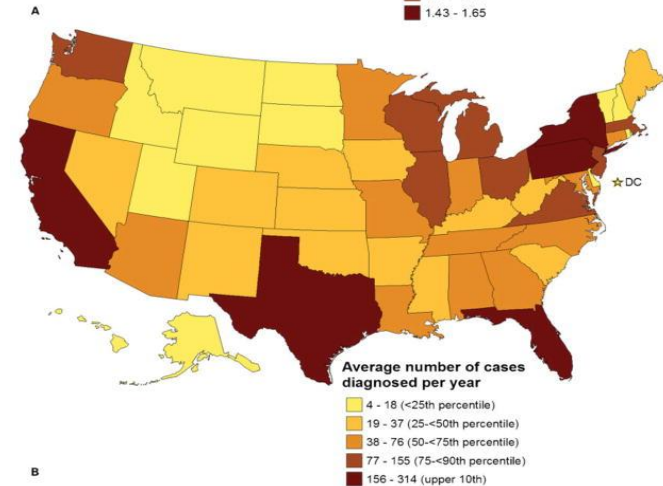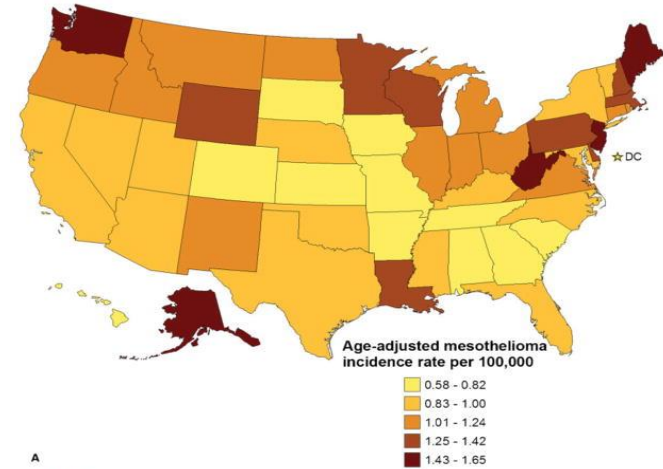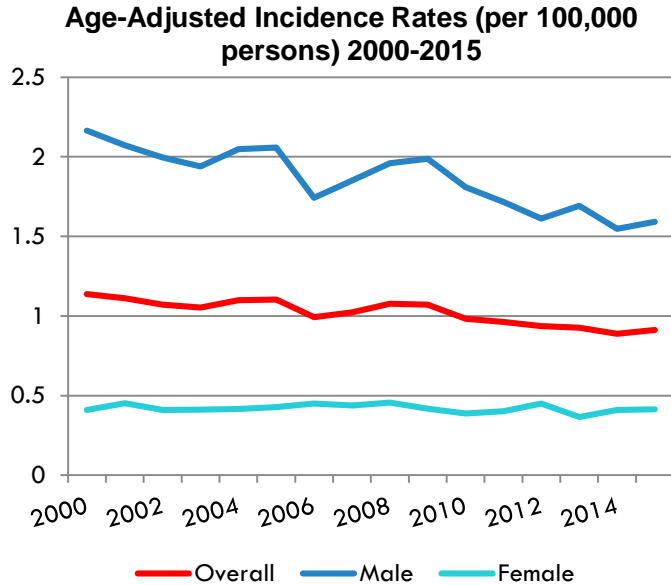- Based on voluntary reporting of pathologists

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Jung SH et al. A decade of malignant mesothelioma surveillance in Korea. American Journal of Industrial Medicine. 2012; 55:869-875

Other Mesothelioma Registries Worldwide

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

- **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

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Mesothelioma in the United States

Approximately 3,000 new cases each year

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

Legend: Overall, Male, Female

Age-adjusted mesothelioma incidence rate per 100,000
- 0.58 - 0.82
- 0.83 - 1.00
- 1.01 - 1.24
- 1.25 - 1.42
- 1.43 - 1.65

A

Average number of cases diagnosed per year
- 4 - 18 (<25th percentile)
- 19 - 37 (25-<50th percentile)
- 38 - 76 (50-<75th percentile)
- 77 - 155 (75-<90th percentile)
- 156 - 314 (upper 10th)

B

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.
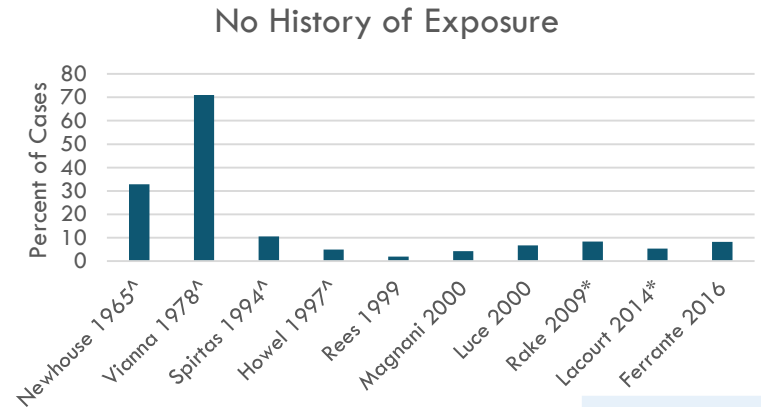
Existing Datasets – Strengths and Limitations

SEER

- Country wide (but <30%)
- Population based
- Includes long-term outcomes

- Lack subsequent treatments
- Limited chemotherapy information
- No insurance status before 2007
- No info on hospital where treated
- Sparse exposure data
- No comorbidities

SPARCS

- Generalizable (all payers system)
- Large amount of data
- Very detailed on hospital procedures and events

- No cancer info (stage, histology…)
- No follow-up data, only inpatient events
- No exposure data

SEER- Medicare

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

- Only patients > 65 years
- Only Medicare, cannot study other insurances
- Limited to geographic regions of SEER
- Little variability in race/ethnicity
- No exposure data

NCDB

- Captures ~70% of cancer diagnoses
- Includes long- and short term-outcomes
- Some insurance/comorbidity information

- 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

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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

Review of case-control studies on pleural mesothelioma and non-occupational exposure to asbestos

No History of Exposure

Percent of Cases (y-axis: 0, 10, 20, 30, 40, 50, 60, 70, 80)

Categories: Newhouse 1965^, Vianna 1978^, Spirtas 1994^, Howel 1997^, Rees 1999, Magnani 2000, Luce 2000, Rake 2009*, Lacourt 2014*, Ferrante 2016

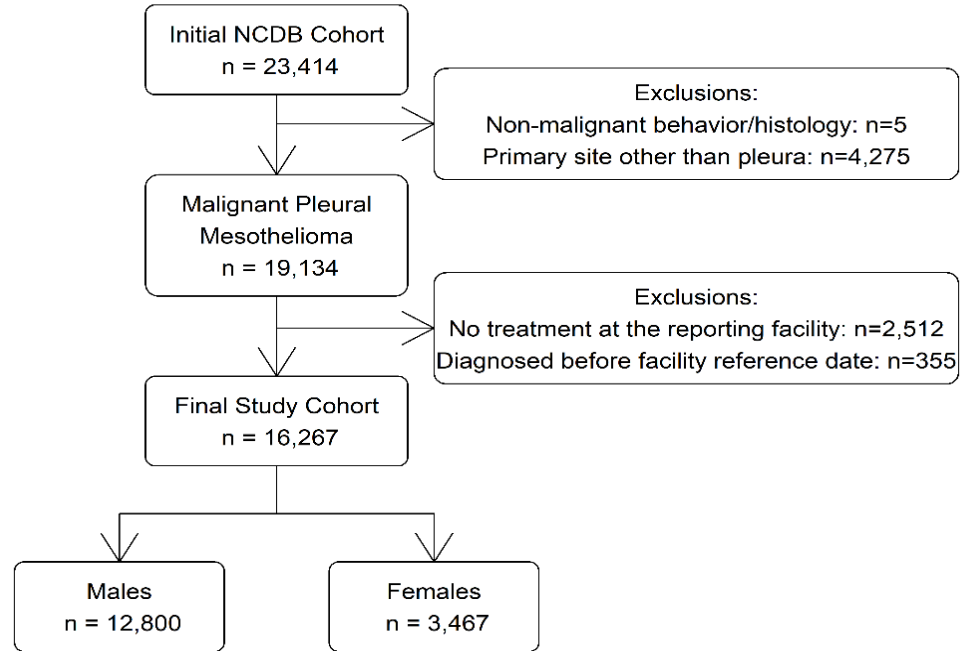^ retrospective, death certificates
*survivors only
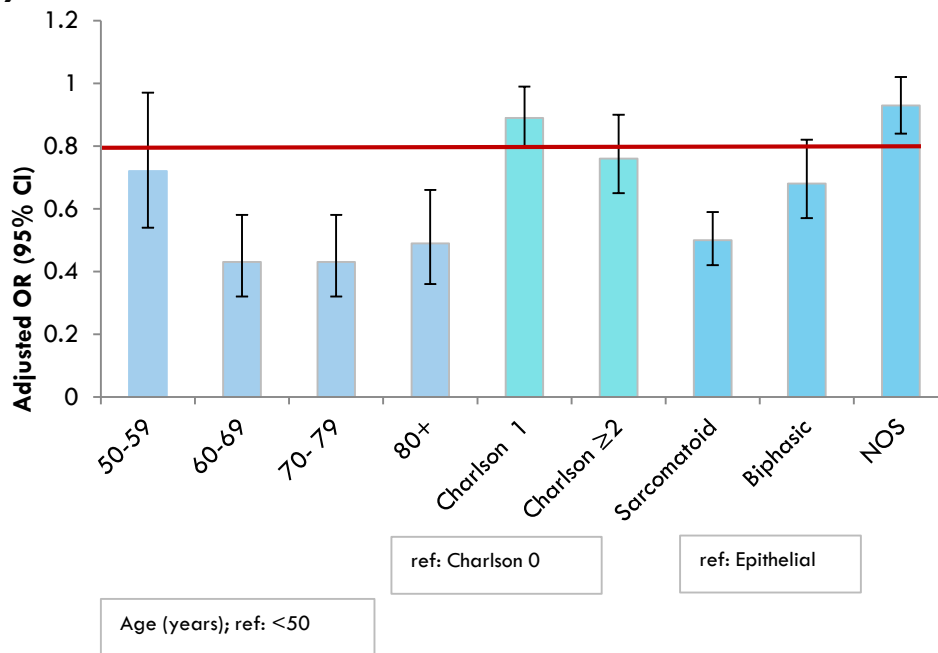
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SEX DIFFERENCES IN SURVIVAL (NCDB)

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

Initial NCDB Cohort
n = 23,414

Exclusions:
Non-malignant behavior/histology: n=5
Primary site other than pleura: n=4,275

Malignant Pleural Mesothelioma
n = 19,134

Exclusions:
No treatment at the reporting facility: n=2,512
Diagnosed before facility reference date: n=355

Final Study Cohort
n = 16,267

Males
n = 12,800

Females
n = 3,467

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

Relative Odds in females versus males

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OVERALL SURVIVAL ACCORDING TO SEX IN (A) PROPENSITY-MATCHED COHORT, (B) <50 YEARS, (C) ≥50 YEARS
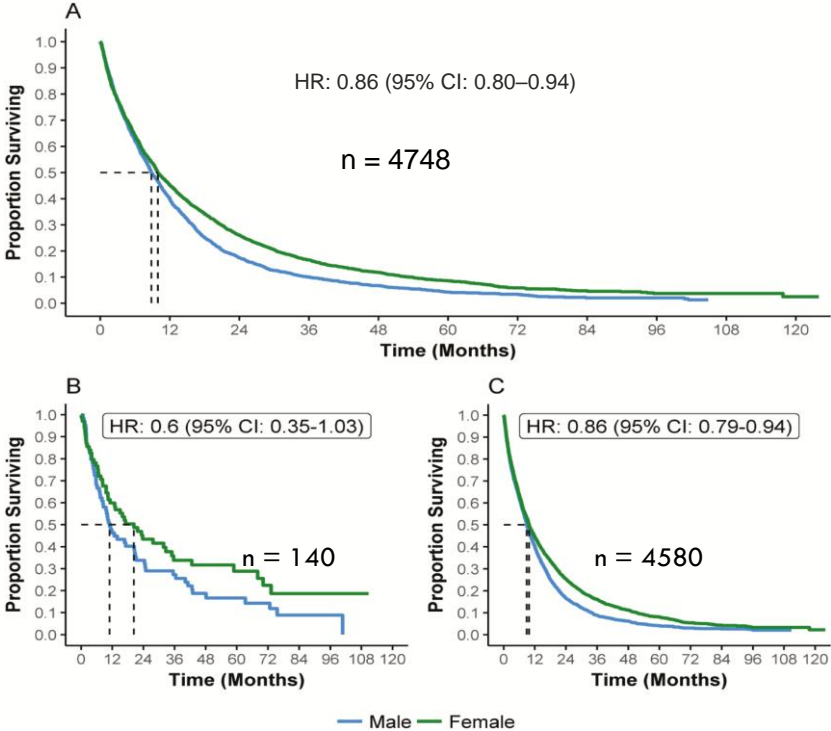
After propensity matching within the epithelial group, survival remained significantly better for females compared with males (HR: 0.85, 95% CI: 0.74–0.97).

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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
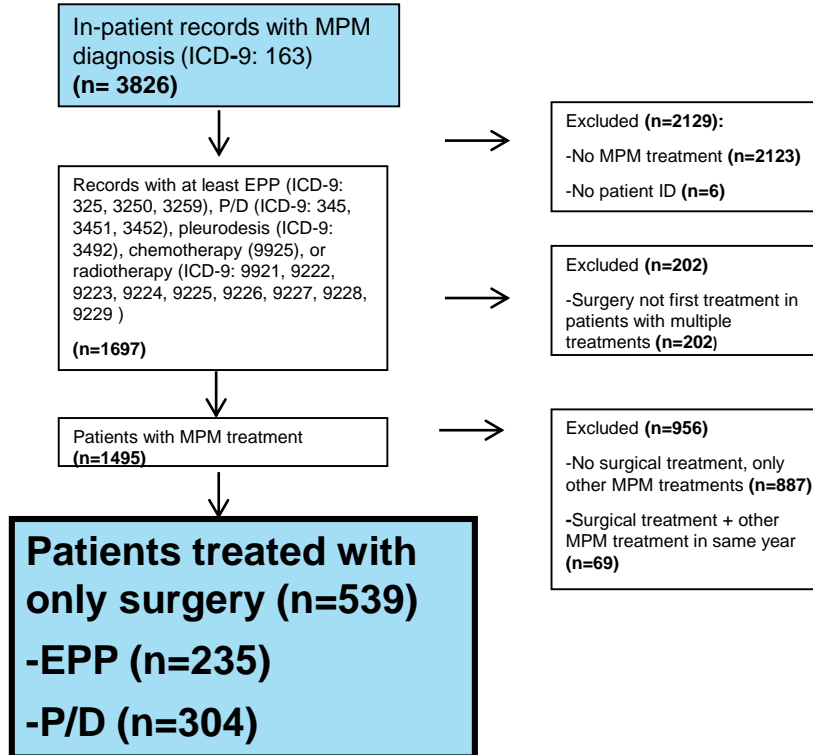
STRENGHTS:

➤Study on > 12,000 cases

➤Allowed to stratify for many important covariates (age, histology…).
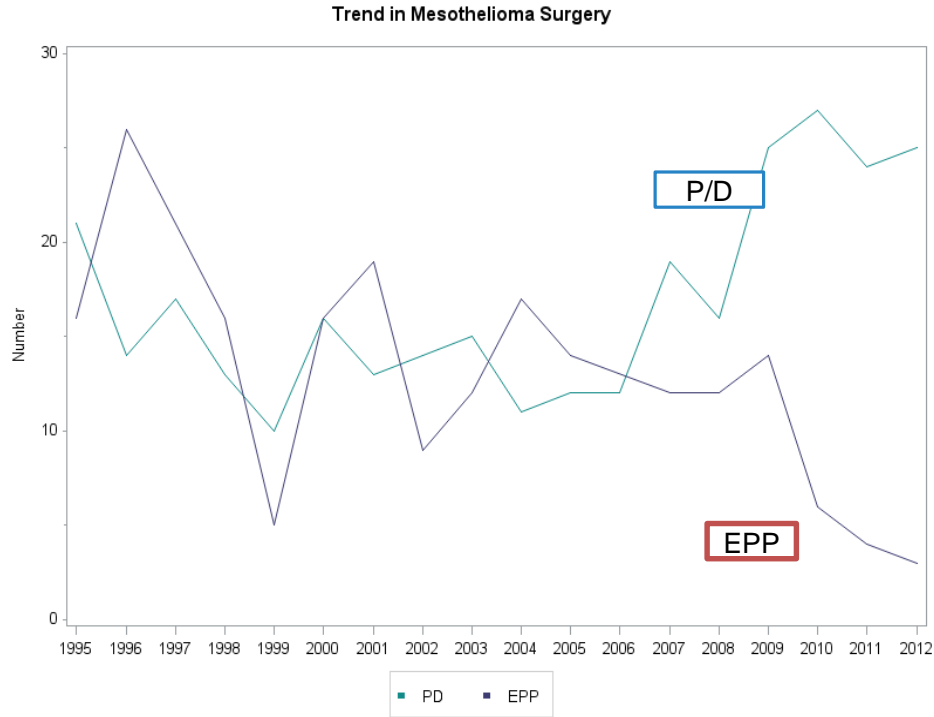
➤Allowed propensity matching

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)**

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

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

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

Patients with MPM treatment **(n=1495)**

→ 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)

Trend analysis, type of mesothelioma surgery

Trend in Mesothelioma Surgery

- 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
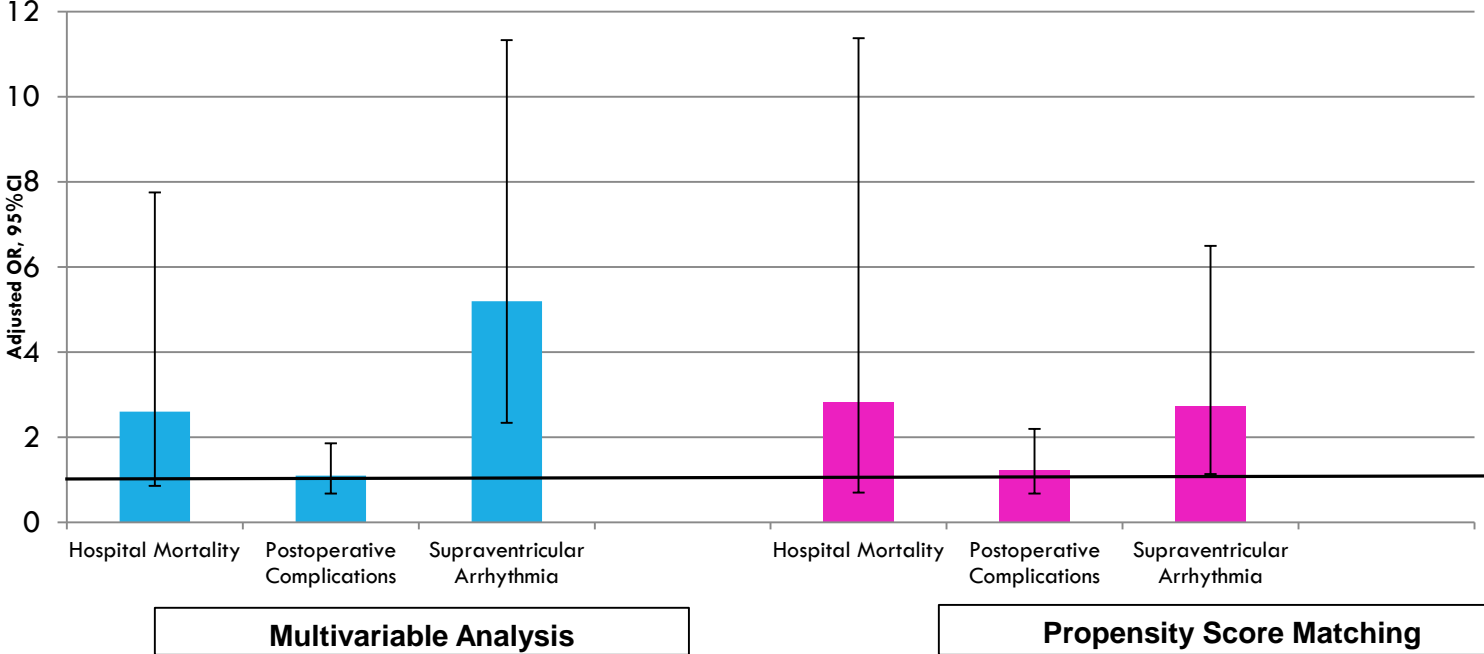
Conclusions

- 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

Information of Interest

Clinical/Demographic		
	• Cancer characteristics	• Performance status
	• Pathology and cytology	• Linkage with data from family/spouses
	• Treatment (type of surgery)	
	• Date of diagnosis	• Linkage to NDI

Behavior/Exposure		
	• Occupational exposure	• Reproductive history (women)
	• Residential exposure	• Geographic Region
	• Spousal exposures	• Country of birth
	• Smoking history	• Family History

Quality of Life		
	• Interview timing with treatment	• Help with daily living
	• Pain	• Home Care
	• SF 12/36	• Functional Limitations

Tumor Biology		
	• Genetic markers	• Normal tissue
	• Tumor tissue	• Blood

Possible model of a mesothelioma registry

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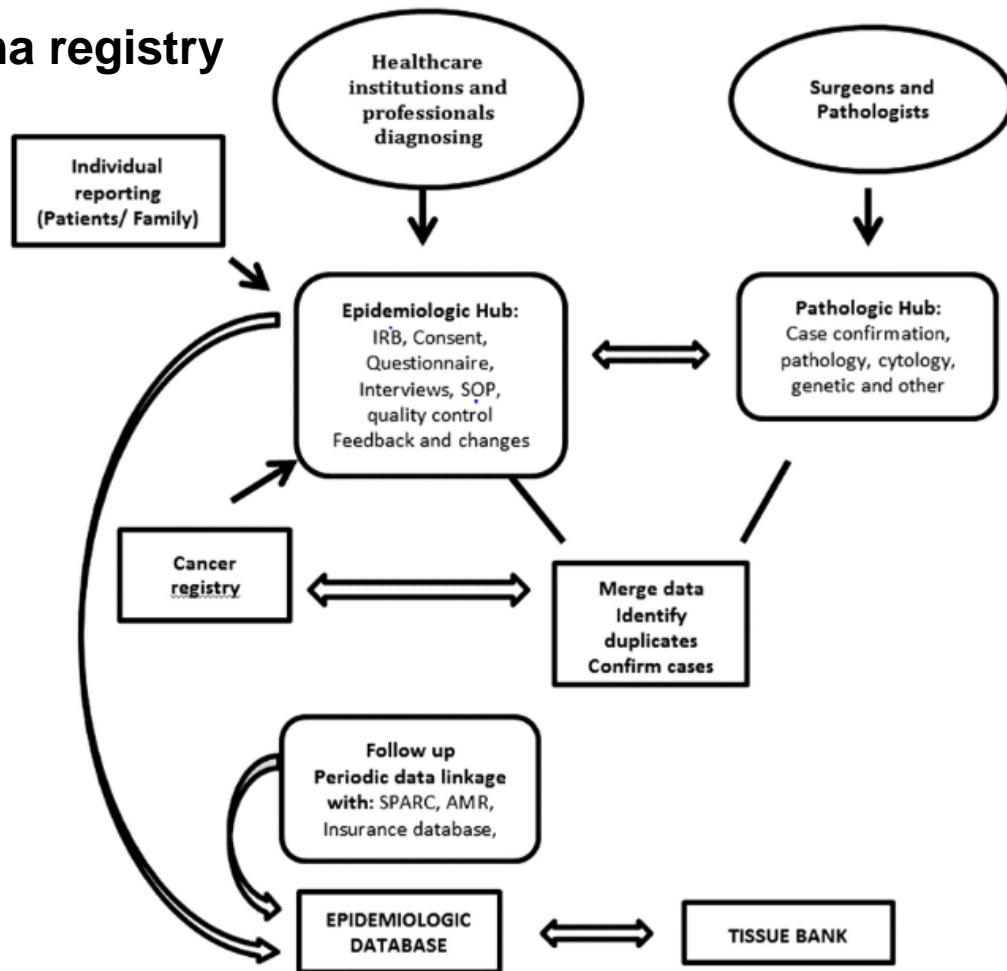
CHARACTERISTICS OF A MESOTHELIOMA REGISTRY

- 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

CASES IDENTIFICATION

↓

INFORMATION COLLECTION

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UTILIZATION AND GROWTH
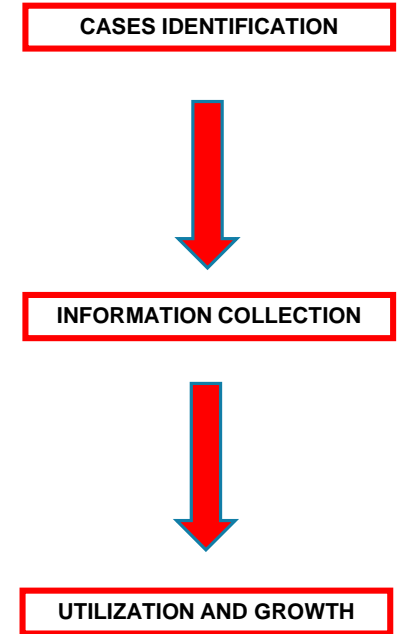
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