Registries: Uses and Limitations

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Purpose

- To discuss the uses and limitations of registry data while emphasizing the evaluation of the quality of these data

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Our Uses

- Incidence and prevalence data (e.g., SEER)
- Demographic information (Census Bureau)
- Answer new research questions

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Our Uses

- Caution must be used when using registries/databases for research
  - Data often not specific enough
  - Subcontracting organization may know more about the database than the contact organization
  - Not all data are easily obtainable

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Our Uses

- Good points:
  - Caveats about data collection
  - Tables “on the fly” for FAQs

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Strengths

- Can provide relatively rapid results
- Allow for ability to gather data early in the life of a product and analyze unusual events for timing of exposure and biological plausibility considerations
- Can provide long-term results
- Can include data from many patients
  - (many patients allows for detection of rare events)

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Strengths

- Can be relatively inexpensive
- Can overcome the deficiency of RCTs; that they overestimate how well something works in the “real world”
- If trends can be ascertained, future needs can be forecast

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Weaknesses

- Miscodings/data entry errors
- Incomplete data
- Observational
- Data Interpretation can be difficult

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Retrospective Registries

- Retrospective registries help identify potential benefits or harms, but do not allow for calculation of event rates
- Retrospective registries are more likely to contain
  - Abnormal/unusual outcomes (though this can also occur in prospective registries)
  - Unusual cases
- Invite retrospective data analysis (“data dredging”)

Voluntary Registries

- Voluntary registries cannot provide incidence data
- Are subject to under-reporting
- Are subject to selective reporting caused by self-selection, media coverage

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Data Entry Errors/Miscodings

- Data entry errors
  - Inexperienced workers may be prone to make errors
  - One audit of the Florida statewide trauma registry found that over 12,000 records contained impossible values for the Glasgow coma scale
  - Errors in transcribing birth dates
  - Errors in transcribing date of diagnosis

Incomplete Data

- Incomplete data:
  - 11% (Major Trauma Outcomes Study database)
  - 18.4% (N.W. England cervical cancer registry)
  - 2.2% (Danish cervical cancer registry)
  - 67% (adverse drug reactions in Sweden)
  - 30-50% of forms not turned in (adverse drug reactions in Britain). Of those turned in, at least 15-20% are incomplete
  - 77.2% of records in Florida statewide trauma registry

Incomplete Data

- In Florida:
  - State rule (HRS 1728) requires that each trauma patient identified by prehospital care providers or emergency department personnel must be the subject of a trauma registry form
  - The data sheet is to be completed on every patient who suffers from injury no matter what the severity of the injury or the destination facility might be

Incomplete Data

- Designated trauma centers are required to have a designated trauma case coordinator, one of whose functions is to collect trauma registry data
- However, of 6 critical items studied, only 6.7% (Level I centers) to 71.3% (non-designated centers) of forms contained them all (Rodenberg, 1996)

Incomplete Data

- Physicians may not see the need to report adverse drug events after treatment has been discontinued
- Patients may discontinue visits to their physician
- Physicians may terminate treatment in sicker patients

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Incomplete Data

- Some physicians refuse (on ethical grounds) to allow patients to be approached (Muir, 1984)
- Cases are often missed due to change of name by divorce or marriage

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Missing and Incomplete Data

- Inconsistent (and sometimes high) rates of missing and incomplete data imply the need for ongoing quality control

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Quality of Registries

- Registries and databases are observational studies
- In an observational study, something other than randomization determines group assignment or exposure
- That registries are observational studies means their quality can be evaluated like the quality of a published observational study

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Quality of Registries

- Quality affects validity of results
- Internal Validity: The connection between treatment and study's results
- External Validity: How well the study results resemble those found in actual clinical practice

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USPSTF System: Levels of Evidence

Level I	Evidence from at least one RCT (includes a systematic review of RCTs)
Level II-1	Evidence from well-designed controlled trials without randomization
Level II-2	Evidence from well-designed cohort or case-control studies
Level II-3	Evidence from multiple time series with or without intervention. Dramatic results from uncontrolled experiments (e.g. penicillin)
Level III	Opinions of respected authorities, descriptive studies, case reports

The AHRQ Key Domains

RCT

- Study Population
- Randomization
- Blinding
- Interventions
- Outcomes
- Statistical Analysis
- Funding or Sponsorship

Observational

- Comparability of Subjects
- Exposure or Intervention
- Outcomes
- Statistical Analysis
- Funding or Sponsorship

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The NHS Key Domains

Non-Randomized Controlled Studies

- Creation of Treatment Groups
- Blinding
- Soundness of Information
- Follow-up
- Analysis: Comparability
- Analysis: Outcome

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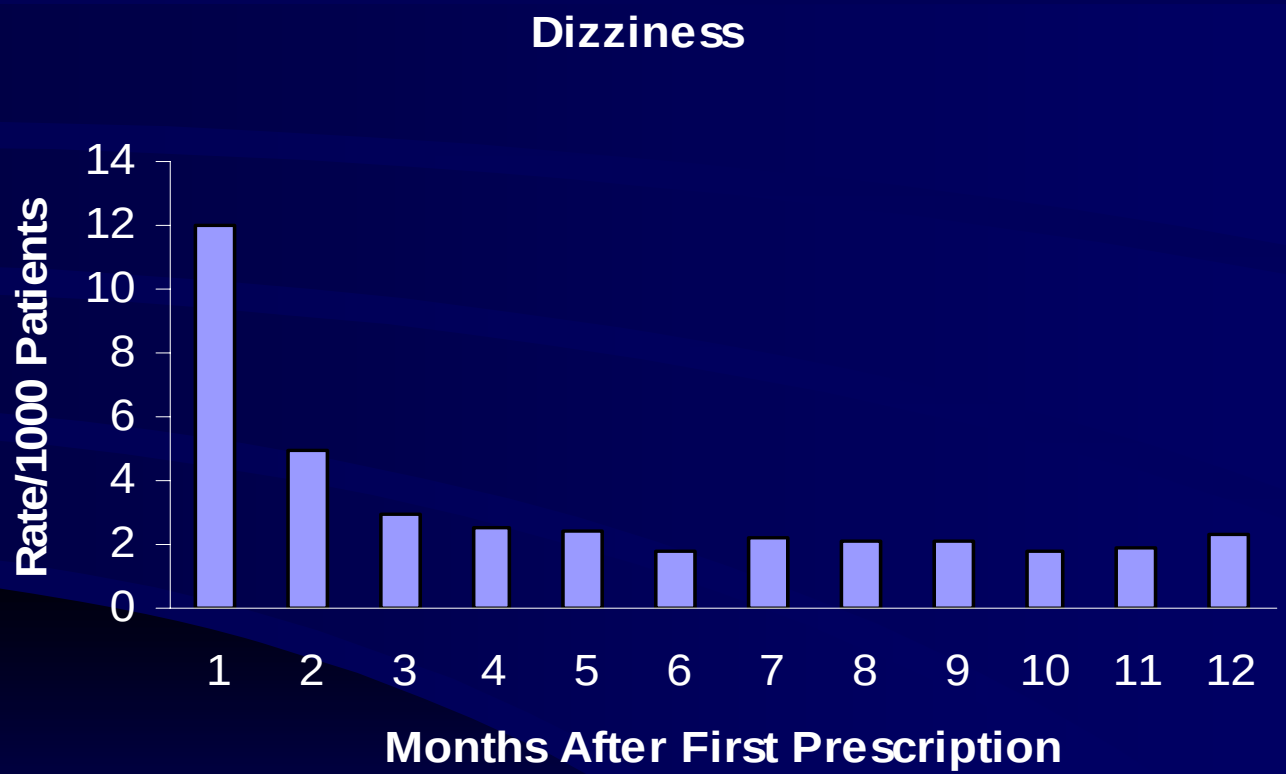
Quality of Registries

- Registries have been used as two types of observational studies:
  - Case series/cohort study in which a single group is followed forward in time to evaluate an outcome of interest

Data Interpretation

- When registries are used as a cohort studies, it is sometimes difficult to tell if an effect is a benefit or a harm

Data Interpretation



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Data Interpretation

- Is this a reduction in dizziness caused by hypertension?
- Are patients susceptible to dizziness caused by the drug ceasing to take it, thus decreasing rates?

Quality of Registries

- Registries have been used as two types of observational studies
  - Non-randomized controlled studies
  - Using registry data involves a comparison, sometimes explicit, other times implicit

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RCTs vs. Observational Studies

- Some studies find that observational studies overestimate the effects of an intervention:
  - Khan et al., 1996
  - Colditz et al., 1989
  - Miller et al., 198
  - Sacks et al., 1982

RCTs vs. Observational Studies

- Other studies find no consistent overestimation an intervention's effects:
  - Concato et al., 2000
  - Benson et al., 2000
  - McKee et al., 1999
  - Britton et al., 1998

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Quality of Registries

- There is no consistent pattern
- The results of a registry can be overestimates or underestimates
- Cancer registries that contain cases without histological verification of cancer might contain some patients without cancer, which would artificially inflate survival rates
- On the other hand, such cases often have advanced disease or receive unsatisfactory care, which would artificially decrease survival rates

Quality of Registries

- Mis-estimation of an effect will often result from difficulties in constructing an appropriate “control group” for a registry

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Quality of Registries

- Inappropriate controls can result when patients receive an intervention determined by:
  - Practice patterns
  - Personal choice
  - Policy decisions
- This can create confounding

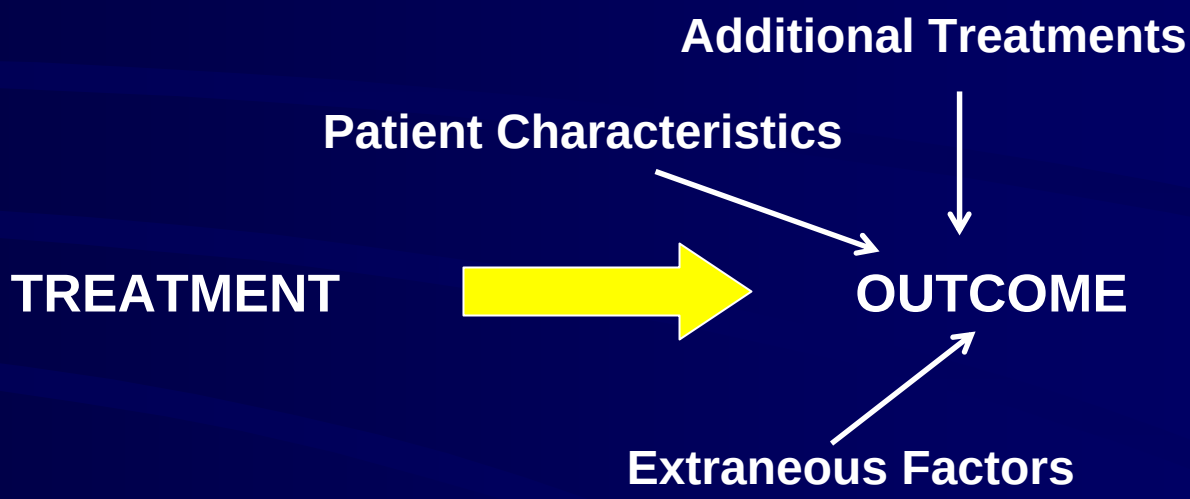
Confounding

- Confounding occurs when:
  - One or more patient characteristics is different between groups AND the characteristic(s) is related to outcome in terms of prognosis or susceptibility
  - Confounding can occur when characteristics differ in terms of the mean or the degree of variation

Confounding

- Confounding occurs when:
  - OR when patients in the two groups are interventions other than the one of interest are unequally given to both groups

Confounding



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Confounding

- Example: The Genentech Inc., in the prospective Phase 4 study of thrombolytics (NRM-1 and NRM-2; essentially a database), those who did not get thrombolytics were at greater risk (e.g., elderly, those with CHF, strokes, diabetes) than those who did get them (Cundiff, 2002).
- Uses of this database to compare outcomes of patients with and without thrombolytics is problematic

Confounding

- Unfortunately, our knowledge of confounders related to patient characteristics is imperfect
- Some characteristics related to outcome are not known
- This is the purpose of randomization

Confounding

- Administrative databases often contain too little information about patient characteristics to allow one to assess and correct for confounding

Confounding

- Confounding can also occur when events unrelated to an intervention affect outcome
  - Example: increased post-AMI survival from the 1960's to the 1990's may have been due to increased public awareness of cardiac symptoms, and higher rates of hospitalization of patients with milder AMI (Cundiff, 2002), and not due to advances in treatment

Validation

- Difficulties with registries can be ameliorated by validation

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Validation

- Validation of the Swedish National Total Hip Arthroplasty Register comprised of:
  - Showing that patient characteristics were similar across years
  - Determining whether there were “missing” patients by examining a randomly selected sample of patients from the Swedish Discharge registry
  - Determining whether physicians and physiotherapists agreed in responses on the Harris Hip Score

Validation

- Validation of the Swedish National Total Hip Arthroplasty Register comprised of:
  - Determine whether multiple measures of health status yielded the same result
  - Compare number of procedures in the THA and Discharge registries
  - Where possible, compare outcomes in these two registries

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Conclusions

- Standardized forms
  - Designing forms can be difficult because one wants easily completed forms and, at the same time, information that is as complete as possible
- Validation
- Ongoing quality control

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Conclusions

- Registries are observational studies
- They provide “alerts”
- Using registry data involves considering the trade-offs between potential benefits and harms

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