Epidemiology Panel Discussion: Postmarketing Safety Review in CDER

Paul J. Seligman, M.D., M.P.H.

Director

Office of Pharmacoepidemiology and Statistical Science

Background: Premarket

- Randomized clinical trials are the basis for most approved drugs' indications
  - These trials are typically powered and designed around efficacy, rather than safety endpoints
  - Safety assessment frequently *post hoc*

Background: Premarket

- **Guidance for Industry**
  - **Premarketing Risk Assessment**
    - Considerations for Developing a Premarketing Safety Database
      - *size*
      - *long-term controlled safety studies*
      - *diversity*
      - *dose effects*
      - *unanticipated interactions*
      - *developing comparative safety data*

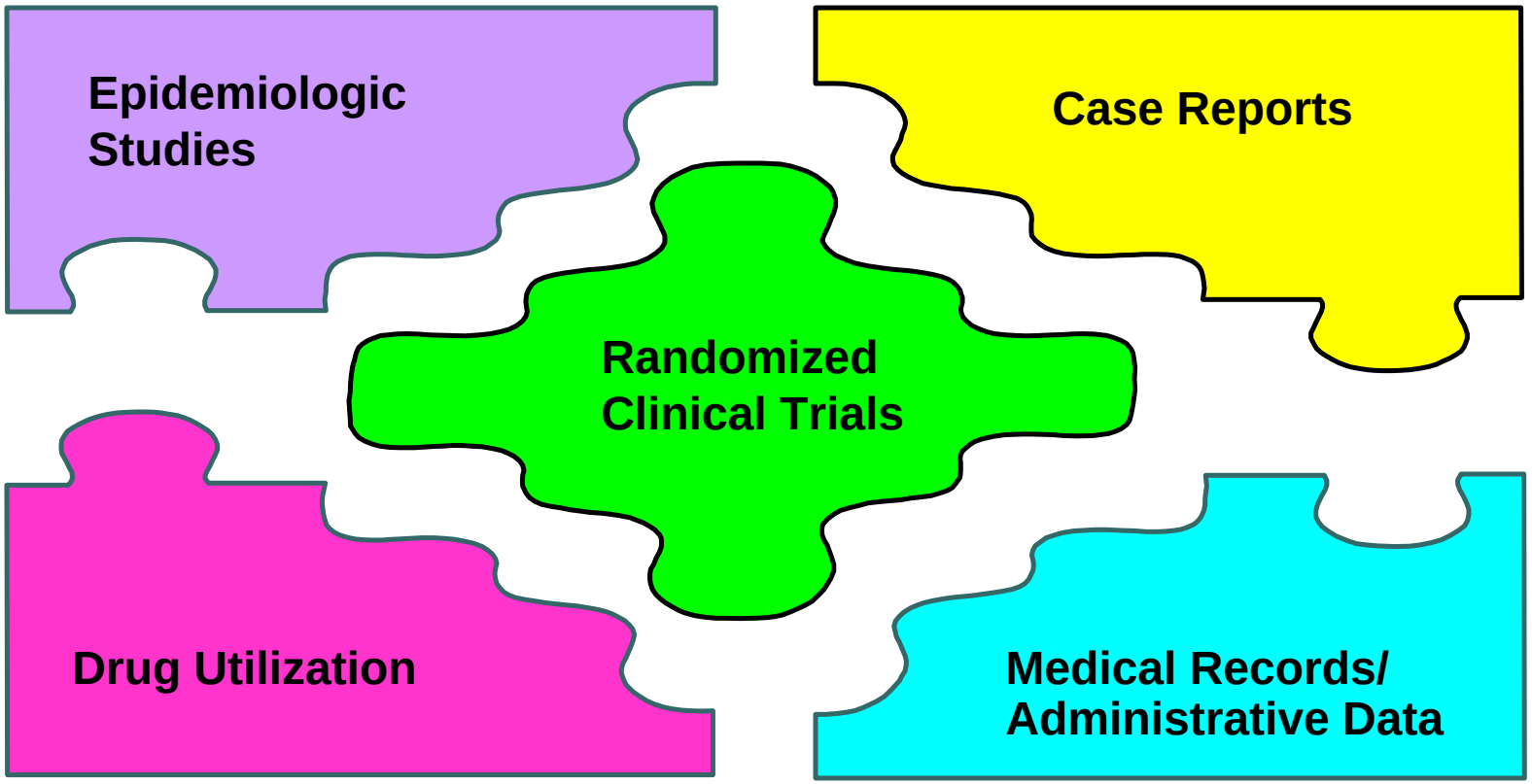
Background: Premarket

- Frequently, the nature and extent of safety signals identified early in development cannot be fully characterized prior to approval
  - Randomized clinical trials (RCTs) may not be large enough to detect rare events
  - The trial environment can fail to account for “real world” use:
    - Comorbid illnesses
    - Concomitant medications

Background: Postmarket

- Guidance for Industry
  - Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment
    - Identifying & describing safety signals
      - case reports/case series
    - Investigating signals through observational studies
    - Interpreting safety signals
    - Developing a pharmacovigilance plan

All Data Sources Are Valuable



Conclusions

- All data have relative strengths and weaknesses
  - RCTs: poor external validity, expensive to conduct, difficult to recruit subjects, BUT strong internal validity
  - Observational studies: poor internal validity, BUT easier to conduct, good external validity
- **The kind of data we use depends on the nature of the question and what's available**