

# Vaccine Safety Datalink (VSD)

## Overview

**Immunization Safety Branch  
National Immunization Program**

# Institute of Medicine (IOM) Reports on Vaccine Safety

- **"Many gaps and limitations" in current knowledge + research capacity:**
  - **Infrastructure for vaccine safety surveillance inadequate**
  - **Needed: Population laboratory under active surveillance**

# Vaccine Safety Studies: Pre-Licensure

- Laboratory
- Animals
- Humans
  - Phases I: gross toxicity (N: ~ 10)
  - Phase II: dosing range/ reactogenicity (N: 10-100)
  - Phase III: efficacy (+ preliminary safety) (N: 1000-10,000)
  - Advantages:
    - Close, detailed follow-up
    - Randomized, placebo-controls => causality assessment easy
  - Disadvantage:
    - Poorly detected reactions: rare, delayed onset, subpopulations
    - No standard case definition for "safety"

# Vaccine Safety Studies: Post-Licensure

- Traditional tools
  - passive surveillance (spontaneous reporting system)
  - ad hoc controlled epidemiologic studies
- New tools
  - Phase IV trials "linked" to licensure of new vaccine
    - Large-Linked Database (LLDB) in HMO population
    - N ~10,000
  - pre-organized LLDB's (Vaccine Safety Datalink)
    - ongoing safety monitoring
    - controlled epidemiologic studies

# Vaccine Safety Datalink

- Collaboration between CDC and managed care organizations (since 1991)
- Powerful, cost-effective resource for the ongoing evaluation of vaccine safety
- Planned vaccine safety studies and timely investigations of safety concerns

# Advantages of HMOs for Health Research

- Identifiable (large) population
  - incidence rates and attributable risks
- Computerized data bases
- Cost data
- Integrated systems
- Infrastructure

# Vaccine Safety Datalink

- Population under “active surveillance”
  - 8 HMOs
  - >7 million members
- Large-linked databases
  - Exposure (vaccination)
  - Outcome (ER, OPD, hosp, lab)
  - Covariates (birth, death certificates)
- Scientifically rigorous hypothesis testing

# VSD DATA LINKAGES

**Vaccination Records**  
(Vaccine type, Date of Vaccination, Manufacturer, Lot #, Injection Site)

**Health Outcomes**  
(Hospitalizations, ER visits, Outpatient visits)

**Patient Characteristics**  
(Birth Certificates, Census Data)

**VSD Linked Analysis Database**



# VSD Analytic Approach

- Screening analyses (automated data)
  - preliminary assessment of vaccine-outcome associations
- In-depth studies (chart reviews, interviews)
  - validate outcomes (and dates)
  - verify vaccination history (and dates)
  - additional risk factor or clinical information

# VSD SELECTED FINDINGS

(from over 50 publications)

- **Diabetes**: did not find a risk after Hib or HBV vaccine
- **Multiple Sclerosis or Optic Neuritis**: did not detect a risk after HBV vaccine
- **Intussusception**: noted increased risk in Days 3 – 7 after rotavirus vaccine
- **Seizures**: detected an association with vaccination (MMR and DTP) and febrile seizure but no association with long term seizure disorders

# More Selected Findings from VSD Studies

- **Chronic arthropathy**: No increased risk among women receiving rubella vaccine
- **Aseptic meningitis**: No increased risk after Jeryl-Lynn mumps vaccine (in U.S. MMR)
- **Safety of second MMR**: Risk of clinical events after vaccination greater at 10-12 than at 4-6 years of age

# **A Case-Control Study of MMR and Other Measles-Containing Vaccines and Inflammatory Bowel Disease.**

Study Question:

Is vaccination with MMR or other MCV associated with increased risk for Crohn's disease or ulcerative colitis?

- Case-Control study

- Eligible population:

  - Born between 1958 and 1989

  - Enrolled from 6 months of age or younger

- Medical record review of diagnoses of either Crohn's disease or ulcerative colitis: (ICD-9 codes 555.\* and 556.\*)

- Databases:

  - Hospitalizations (all four sites)

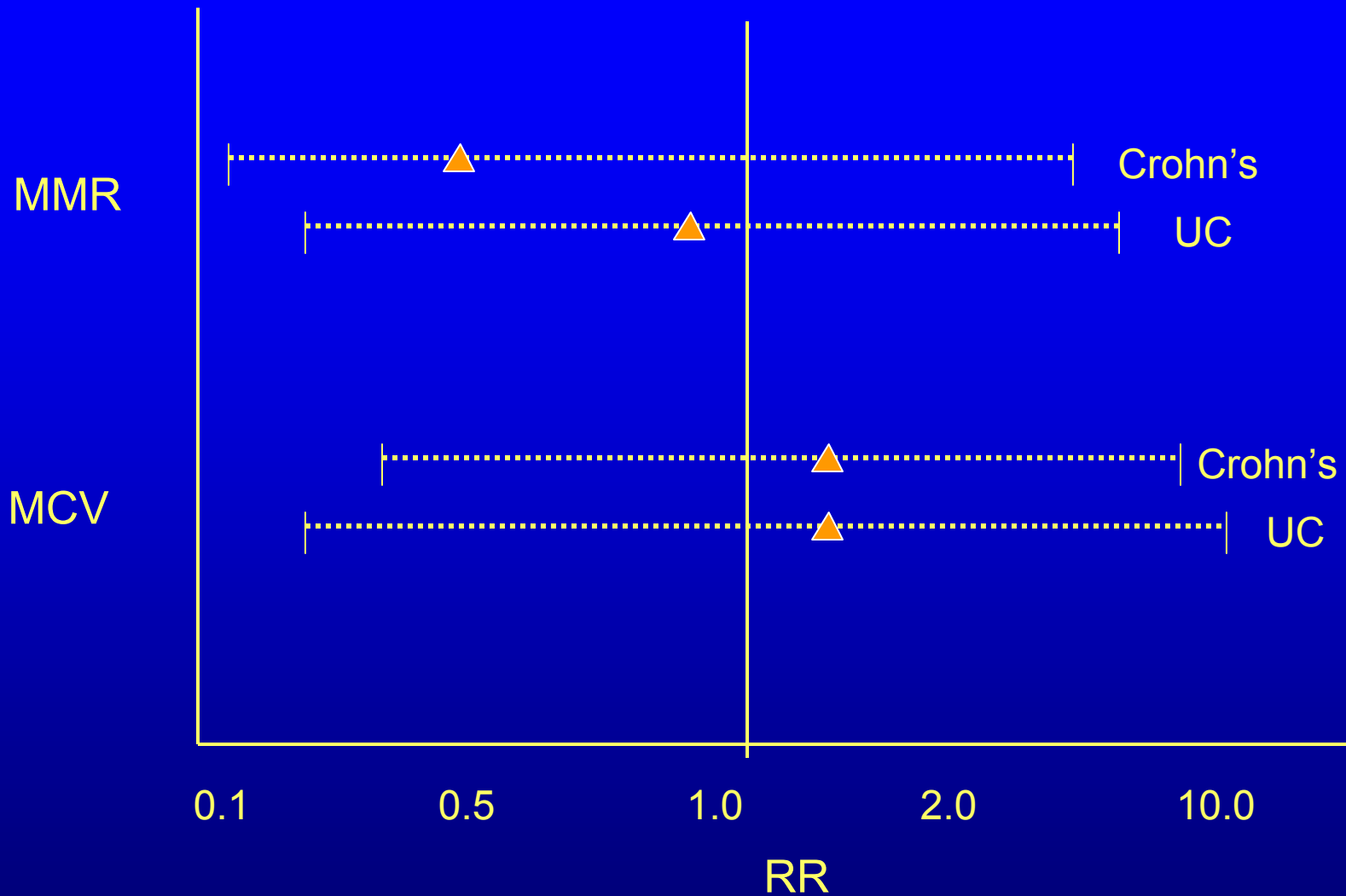
  - Outpatient/Emergency dept visits (three sites)

## Exposure measurement:

- Medical record review of lifetime vaccination history

## Analysis:

- Up to 5 controls matched by HMO, gender and birth year
- Conditional logistic regression
  - accounting for matching/enrollment criteria
  - adjusted for race



\*Adjusted for race, HMO, gender, and birth year

# Research in VSD: Conclusions

- Managed care is the dominant health care delivery system in the U.S.
- VSD provides ability to perform for population-based research: unbiased; generalizable
- Immunization research in VSD allows timely and efficient monitoring of vaccine safety



# VSD Future Directions: Integrating Genomics to Study High-Risk Individuals

- Candidate gene approach: Rheumatoid arthritis and hepatitis B vaccine
- Candidate gene & gene pathway approach: Myocarditis and smallpox vaccination