

Signal Refinement

Or – What next?

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Motivating Example

In a self-controlled case series looking at diagnosis codes associated with doctor visits in 138,000 1-year olds, visits bearing the ICD9 3-digit code

785 symptoms involving cardiovascular system

were in excess in weeks 2, 3, 4 and 5 following a specific immunization.

This is a signal.

What do we do?

Option 1 – Get a lot of data quickly

- ❑ Redo analyses at ICD 5-digit code level
- ❑ Stratify analyses by location, child history
- ❑ Profile all the cases, looking for a story
- ❑ Call your friends with databases to find if they see the same thing

This is signal amplification.

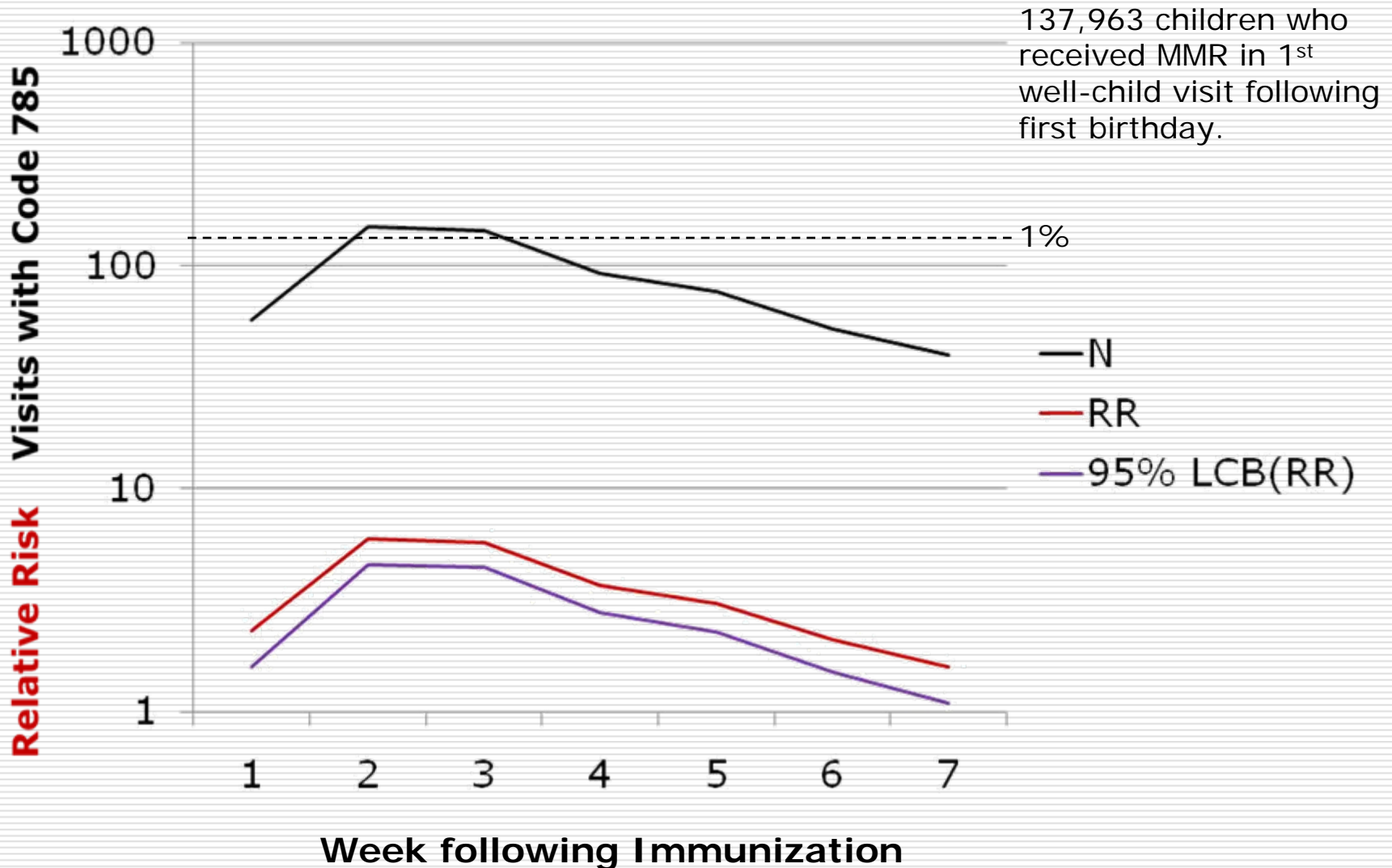
- ❑ You may find truth, or you may have spawned a whole pond full of red herrings
- ❑ In particular, replicating the same signal in a different database tells you almost nothing.

Option 2 – A. Describe content

The words in a label for a code often connote a clinical picture prematurely. Check operationally what could have gone into your signal.

- 785.0 Tachycardia, unspecified
- 785.1 Palpitations
- 785.2 Undiagnosed cardiac murmurs
- 785.3 Other abnormal heart sounds
- 785.4 Gangrene
- 785.5 Shock without mention of trauma
- 785.6 Enlargement of lymph nodes
- 785.9 Other symptoms involving cardiovascular system

Option 2 – B. Describe timing



Option 2 – C. Testable predictions

- Palpitations or tachycardia
 - Most codes: 785.0 Tachycardia; 785.1 Palpitations
 - As a genuine vaccine effect
 - Would have been noted in randomized trials
 - Not seen following nonvaccine visits
 - In association with fever adenopathy, rash
 - Occur more frequently in children with fever, rash
- New murmur heard on examination, with follow-up visits

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 - Later visits with cardiologist; diagnostic procedures
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The means for discriminating more specific hypotheses lie in the original data and other readily accessible information.

Steps to Signal Refinement

- A. Describe the content of the signal
- B. Describe the timing of the signal
- C. Formulate hypotheses that would give rise to signal
 - 1. Direct effect
 - 2. Surveillance artifact
 - 3. Confounding
- D. Look for testable predictions of the hypotheses in original data and readily accessible files
 - 1. Refinements of the code
 - 2. Other services that would follow
 - 3. Other, medically related codes
 - 4. Observations in trials
- E. Test each of the candidate hypotheses against predictions, sharpen those that remain.

Thank You

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