JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Comorbidity

ACTIVITY 2

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Comorbidity Study Aims

Goal: To determine the role of multiple infections, namely diarrhea, pneumonia, malaria, and measles, and undernutrition on severe disease and mortality among children < 5

The primary aims of this study are:

1. To estimate the overall prevalence of comorbidity, both simultaneous and sequential, among children less than 5 years of age;
2. To quantify the potential increased risk of comorbid infections on:
   - severe morbidity including hospitalizations; and
   - all cause and cause specific mortality
3. To identify a common risk factors (biological and social) predisposing children to multiple simultaneous or sequential infectious diseases.

Search for Data Sets

- Initial call for studies went out to all CHERG colleagues, JHSPH investigators, MERG, and international investigators
  - JHU cohorts need additional follow-up (initially prioritized searching outside investigators and finding data sets unaware of)
- Goal to start with 1 or 2 in-house data sets to familiarize ourselves with types of data and begin analytic approach
- Call an investigators group of lead investigators to further direct analysis

Opportunities for Analysis of Published Datasets

Inclusion Criteria:

- Large scale cohort studies conducted in the past 15 years
- Representative (i.e. non-specialized) populations of < 5s
- At least weekly community-based morbidity surveillance for ≥ 12 mo
- Indicators associated with diarrhea and ALRI (counted RR), axillary temperature, slide confirmed malaria (in malaria endemic areas)
- Socioeconomic, behavioral, and environmental indicators

Outcomes:

- Severe morbidity: hospitalizations, referral to a health facility, prevalence of chronic illness.
- Mortality: standardized VA collected in same study population/area
  - Emphasized that this is ideal but not mandatory

Nepal Micronutrient Supplementation Trial [Data Set #1]

Methods and Preliminary Results

Initial Analysis Designed to Better Understand:

- What is the best way to quantify comorbidity?
- Is the relationship between diseases at a given time separate from their relationship across time?
- How can infectious diseases be better understood by considering their interactions?

Analysis 1: Correlation of Infections

- Co-occurrence beyond chance can be represented by estimating correlation.
- Fenn et al, 2005:
  - modeled the joint risk of diseases in pairs, including diarrhea and pneumonia, for a range of severities.
  - estimated correlation of illnesses increased with increasing disease severity.
- Similarly, we used a bivariate probit analysis to model the probability of acute lower respiratory infection (ALRI) and diarrhea.

Correlation Model

- This model quantifies the correlation (scale from -1 to 1) of ALRI and Diarrhea.
  - – 1: ALRI and Diarrhea never coincide, or protective.
  - 0: ALRI and Diarrhea sometime coincide, but only by chance.
  - 1: ALRI and Diarrhea always coincide, or predictive.
- Adjusted for SES using principle component analysis, scaled baseline MUAC, and age.
  - Covariates are highly significant in predicting ALRI and diarrhea individually
  - But, effect on correlation is marginal

Analysis 1b: Correlated vs. Conditional

- Joint or correlated risks can also be represented as conditional risks.
- Results from bivariate probit model were used to predict ALRI weekly prevalence in two groups:
  - Child-weeks with diarrhea.
  - Child-weeks without diarrhea ($\geq$ 4 loose stools/24hrs)

Analysis 2: ALRI and Diarrhea History

- We modeled the probability of ALRI among groups with different diarrhea 28-day prevalence rates leading up to an ALRI episode (Schmidt et al. 2009)
  - Risk group defined by the number of days with diarrhea in previous 28 days.
- Using a time-to-event analysis (Prentice et al. 1981), the probability of ALRI by diarrhea prevalence in the last 28 days was predicted.

Analysis 2: Conditional Risk Continued

- Modeling of conditional risk allows for risk estimates depending on varying length of preceding diarrhea episode.
  - Risk ratios for Nepal:
    - 1 day more of Diarrhea: 1.019 (1.001 – 1.037)
    - 5 days more of Diarrhea: 1.098 (1.003 – 1.201)
    - 10 days more of Diarrhea: 1.205 (1.006 – 1.443)

Next Steps and Timeline

- Fall 2011
  - Finalize analyses quantifying the role of comorbidity as a part of routine infection among children under 5 years of age.
  - Submit for publication
  - Make final results available on CHERG website after publication

- Spring 2012
  - Develop analysis of comorbidity as a risk factor for mortality and severe infection for children under 5 years of age.
  - Develop manuscript to present the results and submit for publication
  - Make final results available on CHERG website after publication