Title: Testing a Microsimulation Model of Pediatric Pneumonia with Data from India

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1. Study Purpose and Rationale

Pneumonia is an acute illness affecting the lungs that can be caused by infectious (bacteria, viruses, parasites) and non-infectious agents. The WHO defines clinical pneumonia as an acute episode of cough or difficulty breathing associated with an increased respiratory rate. [1] Clinical pneumonia is the leading single cause of mortality worldwide in children under 5-years-old, accounting for close to 2 million deaths each year. The vast majority of cases occur in the developing world. There has been significant effort in recent years to address this problem in the hopes of achieving the 4th Millennium Development Goal (MDG): "reduce by two thirds, between 1990 and 2015, the under-five mortality rate." [2,3]

Multiple trials from across the globe have isolated the major independent risk factors associated with the development of pneumonia, including: under-nutrition, lack of exclusive breast feeding, indoor air pollution, parental smoking, low birth weight, crowding and lack of immunization. Some of these risk factors such as malnutrition, along with community case management with antibiotics have been shown to affect the mortality from pneumonia. Based on these data we generated a microsimulation model that follows a birth cohort for 5 years and can estimate both the incidence of and death from pneumonia in a given population with a given risk factor profile. This model preliminarily proved effective using data from Nigeria, where there are an estimated 204,000 deaths per year due to pneumonia. [4-6]

Most cases of pediatric pneumonia worldwide are believed to occur in India. India also has the highest estimated number of childhood deaths due to clinical pneumonia. [4] It is therefore important to validate our model in India. Various funding organizations will then be able to use our model to determine the most cost-effective pneumonia-fighting interventions to implement and scale up. Furthermore because our model is at the micro or individual level, it will elucidate which interventions should target specific sub-populations.

2. Study Design and Statistical Procedures

a) Model Inputs

We will use representative individual child and household data from Demographic and Health Surveys for India - Individual Recode for the years 2005-2006 (DHS-V, National Family Health Survey 3) to generate model subjects and their risk factor constructs. Specifically, we isolate the following variables in the data set: malnutrition, low birth weight, non-exclusive breastfeeding, indoor air pollution, crowding, environmental tobacco exposure, and community case management with antibiotics. We assume all subjects lack Haemophilus influenzae Type b (Hib) and pneumococcal (PCV) immunizations as these are not routinely administered in India. Using STATA, we will set all variables to be binary, coded as 0 or 1, based on pre-determined definitions in the model (e.g. low birth weight defined as less than 2500g, malnutrition defined as weight-for-age z-score < -2, non-exclusive breast feeding defined as 5 or fever months of breast feeding, indoor air pollution defined as predominant cooking fuel is charcoal, firewood/straw, and/or dung, etc). We will use a logistic regression in STATA to estimate any missing data points. We will then generalize the individual subject data to the published annual number of births in India for the year 2006. [7]

b) Expected Incidence of Pneumonia

The precise magnitude of pneumonia in India is not known; there are no nation-wide studies or systematic reviews addressing this issue. A study by Rudan et al suggests an incidence of 0.37 episodes per child-year [4], though these data are calculated using model parameters similar to those described above and some experts suggest that the estimates are based on out-dated data. A few small scale studies have published data on pneumonia incidence [8-12] ranging from 0.03-0.52 episodes per child-year. In the absence of more robust data we will assume the incidence calculated by Rudan et al for the purpose of validating our model.

c) Expected Mortality from Pneumonia

The Registrar General of India surveyed 1.1 million nationally representative deaths in India from 2001-3 and, by methods previously described by The Million Death Study Collaborators, computed the cause-specific mortality rate in India. Pneumonia mortality rate was determined to be 13.5 per 1000 live births, with total estimated deaths from pneumonia 366,000 (CI: 348,000-390,000) from ages 1- to 59-months-old. All-cause mortality was determined to be 85.8 per 1000 live births, with total estimated deaths 2,345,000 from ages 1- to 59-months-old. [13]

d) Model Outputs

Our model will generate an incidence of pneumonia for the above described birth cohort over a 5 year period (from ages 1- to 59-months-old). Our model will further generate a pneumonia specific mortality and an overall mortality for the above described birth cohort over a 5 year period (from ages 1- to 59-months-old). From these outputs we will compute pneumonia incidence per child-year and pneumonia along with all-cause mortality rates per 1000 live births. We will compare these results with the predicted values and deem our model to accurate if these values agree within a 10% margin, where $\frac{actual\_value}{predicted\_value} = [0.90 - 1.10]$.

3. Study Procedures

Not applicable.

4. Study Drugs or Devices

Not applicable.

5. Study Questionnaires

The Demographic and Health Surveys V (DHS-V) Household Questionnaire is a 33-page document that collects household data, i.e. data relevant to all members of a household on a variety of health and socioeconomic topics. Data relevant to this study include: number of household members, environmental tobacco exposure, and type of cooking fuel.

The DHS-V Women's Questionnaire is an extensive 63-page document that collects a data on a wide variety of topics related to a woman's social, medical, and reproductive histories. Data relevant to this study include: reproductive behavior, postpartum care, breastfeeding and nutrition, children's health.

6. Study Subjects

Data was used from National Family Health Survey (NFHS-3) for the years 2005-6. The methods by which these data were collected have been previously described [14]. In brief, target sample sizes were calculated for ever-married women in the reproductive ages of 15- to 49-years-old since many of the key data sampled pertain to this population. The target sample sizes for each state were based on 2001 census populations. Some adjustments were made to account for slum-non-slum urban populations. A uniform sampling design was adopted in all states that randomly selected the rural and urban subjects from census data based on their proportion in the state's population. Urban populations were further subdivided into slum and non-slum populations. A total of 116,652 households were selected, of which 109,041 were interviewed (97.7% response rate). A total of 131,596 eligible women were selected, of which 124,385 were interviewed (94.5% response rate). [14]

These samples were representative of the India's total population. Informed consent was obtained for all subjects prior to the administration of the questionnaire. All data was de-identified before being released for the purposes of our model calculations. [14]

7. Recruitment

No new subjects will be recruited for this protocol.

8. Confidentiality of Study Data

Data made available to the investigators by the Demographic and Health Surveys for India - Individual Recode for the years 2005-2006 (DHS-V, National Family Health Survey 3) has been de-identified.

9. Potential Risks

There are no potential risks associated with this study; all subject data has previously been collected and de-identified.

10. Potential Benefits

There will be no direct benefit to patients, but results from this study could ultimately lead to interventions at the population level that will lower the incidence and rates of childhood mortality from pneumonia.

11. Alternatives

Not applicable.

12. References

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