Internship Training

at

THE INCLEN TRUST INTERNATIONAL

Topic of dissertation:

Cost of hospitalization of Indian children aged 0 to 59 months due to pneumonia and diarrhea in March 2019: A subgroup meta-analysis

by

Shivansh Verma

Enrolment No. PG/17/060

Under the guidance of

Dr Pradeep K Panda

Post Graduate Diploma in Hospital and Health Management

2017-19

International Institute of Health Management

Research New Delhi

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TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Shivansh Verma** a student of Post Graduate Diploma in Hospital and Health Management (PGDHM) from International Institute of Health Management Research, New Delhi has undergone internship training at **The INCLEN Executive Office (IEO) of The INCLEN Trust International** from **6th February 2019 to 19th June 2019**.

The Candidate has successfully carried out the study designated to him during internship training and his/her approach to the study has been sincere, scientific and analytical. The Internship is in fulfillment of the course requirements.

I wish him all success in all his future endeavors.

PK Panda

Dr Pradeep K Panda
Dean, Academics and Student Affairs

IIHMR, New Delhi

PK Panda

Mentor Name :
Dr Pradeep K Panda

IIHMR, New Delhi

Certificate of Approval

The following dissertation titled **"Cost of hospitalization due to diarrhea and pneumonia in Indian children aged 0 to 59 months in the time period 2000-2019"** at **"The INCLEN Trust International"**is hereby approved as a certified study in management carried out andpresented in a manner satisfactorily to warrant its acceptance as a prerequisite for the award of **Post Graduate Diploma in Health and Hospital Management** for which it has been submitted.It is understood that by this approval the undersigned do not necessarily endorse or approve any statement made, opinion expressed or conclusion drawn therein but approve the dissertation only for the purpose it is submitted.

Dissertation Examination Committee for evaluation of dissertation.

Name	Signature
Dr Pradeep Panda	PK Panda
Dr. P. L. Joshi	
Dr. Manish Priyadarshi	

Certificate from Dissertation Advisory Committee

This is to certify that **Mr. Shivansh Verma,** a graduate student of the **Post-Graduate Diploma in Hospital and Health Management** has worked under our guidance and supervision. He is submitting this dissertation titled **"Cost of hospitalization in Indian children aged 0 to 59 months due to pneumonia and diarrhea: A subgroup meta-analysis"** at **INCLEN Executive Office (IEO)** of **The INCLEN Trust International** in partial fulfillment of the requirements for the award of the **Post-Graduate Diploma in Hospital and Health Management.**

This dissertation has the requisite standard and to the best of our knowledge no part of it has been reproduced from any other dissertation, monograph, report or book.

P K Panda

Dr. Pradeep Panda

Professor of Health Economics

Dean of Academics and Student Affairs

International Institute of Health Management Research - Delhi

Abhishek

Dr. Abhishek Agarwal

Program Officer

INSPIRE Project

The INCLEN Trust International

INTERNATIONAL INSTITUTE OF HEALTH MANAGEMENT RESEARCH, NEW DELHI

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled **"Cost of hospitalization in Indian children aged 0 to 59 months due to pneumonia and diarrhea: A subgroup meta-analysis"** and submitted by **Shivansh Verma** with Enrollment Number **PG/17/060** under the supervision of **Dr. Pradeep Panda** for the award of Post Graduate Diploma in Hospital and Health Management (**PGDHM**) of the International Institute of Health Management Research Delhi (**IIHMR-Delhi**) carried out during the period from **6th February 2019 to 19th June 2019** embodies my original work and has not been formed on the basis of any degree, diploma, associate-ship, fellowship, titles in this or any other Institute or other similar institution of higher learning.

Signature

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RESEARCH AND TRAINING FOR IMPROVING
EQUITY, EFFICIENCY AND QUALITY IN HEALTH CARE

FEEDBACK FORM

Name : **Shivansh Verma**

Dissertation Organisation : **The INCLEN Trust International**

Topic of Dissertation : **"Cost of hospitalization in Indian children aged 0 to 59 months due to pneumonia and diarrhea: A subgroup meta-analysis"**

Attendance : --- out of --- days (including working Sundays and overtime as part of leave management system)

Objectives achieved :

He has done a systematic review on the economic evaluation of a cost of treatment of a case of pneumonia and diarrhea.

Deliverables :

Protocol finalization and tool development.

Dr. Abhishek Agarwal (Program Officer-INSPIRE Project)

Signature of the Officer-in-Charge/ Organisation Mentor (Dissertation)

Date: 19-6-2019

Place: New Delhi

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Strengths :

He is hard working, goes in depth to understand the subject. He is dedicated to work, sincere. He has a sound knowledge of technology and eager to learn new things. Communication skills are his strength.

Suggestions for Improvement :

He need to accomplish tasks assigned in time and consisely. Should learn to present his thoughts and knowledge in consise way.

Suggestions for Institute (course curriculum, industry interaction, placement, alumni) :

He should be directed and need guidance to be an asset to work in the field of health economics.

Dr. Abhishek Agarwal (Program Officer-INSPIRE Project)

Signature of the Officer-in-Charge/ Organisation Mentor (Dissertation)

Date: 19-6-2019

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Ref: INCLEN-IEO Delhi/Corres2019/HR - Misc.-48 **Date: 18th June 2018**

Internship Certificate

This is to certify that **Mr. Shivansh Sharma**, pursuing **Post Graduate Diploma in 'Hospital and Health Management (PGDHM)"**, a student of International Institute of Health Management Research, Delhi is doing internship at **"The INCLEN Trust International"** from 6th February, 2019 to 30th June, 2019. He is doing his internship under the guidance of **Dr. Abhishek Agarwal**.

During his internship, he is involved in a project titled **"Indian Network for Streptococcus Pneumoniae and PCV Impact Research".** He is involved in reviewing literature, protocol and tool development under the above-mentioned project.

We have found him to be a self starter who is motivated, duty bound and hard working. He is working sincerely on his assignment and his performance is satisfactory.

This certificate is being issued to him for submitting his final dissertation.

For The INCLEN Trust International

THE INCLEN TRUST INTERNATIONAL NEW DELHI

Brig. V. K. Panday (Retd.)
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CERTIFICATE ON PLAGIARISM CHECK

Name of Student (in block letter)	Dr./Mr./Ms.: SHIVANSH VERMA		
Enrollment/Roll No.	PG/17/060	Batch Year	2017 – 19
Course Specialization (Choose one)	Hospital Management	Health Management ✓	Healthcare IT
Name of Guide/Supervisor	Dr./ Prof.: PRADEEP PANDA		
Title of the Dissertation/Summer Assignment	Cost of hospitalization in Indian children aged 0 to 59 months due to diarrhea pneumonia and diarrhea : A subgroup meta-analysis.		
Plagiarism detect software used	"TURNITIN"		
Similar contents acceptable (%)	Up to **20** Percent as per policy		
Total words and % of similar contents Identified	13 %		
Date of validation (DD/MM/YYYY)	19/06/2019		

Guide/Supervisor
Name: Dr. PRADEEP PANDA
Signature: PKPanda

Student
Name: SHIVANSH VERMA
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Ongoing Dissertation Internship from The INCLEN Trust International

The certificate is awarded to

Mr. Shivansh Verma

In recognition of having successfully completed his thesis on

"Cost of hospitalization in Indian children aged 0 to 59 months due to pneumonia and diarrhea: A subgroup meta-analysis"

As part of his **Internship** in **INSPIRE** (Indian Network for Streptococcus Pneumoniae and PCV Impact Research) **Project**

At the INCLEN Executive Office (**IEO**) of **The INCLEN Trust International,**

From : 6th February 2019 to 30th June 2019

He comes across as a committed, sincere & diligent person who has a strong drive & zeal for learning.

We wish him/her all the best for future endeavors.

THE INCLEN TRUST INTERNATIONAL NEW DELHI

18 Jun 2019

Dr. Abhishek Agarwal (Program Officer-INSPIRE Project)
Training & Development

Brig. V. K. Panday (Retd.)
Chief Operations Officer
The INCLEN Trust International

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I would like to express my deep gratitude and thank Prof. Pradeep Panda who provided me with a direction every time I got lost in this research journey. Prof. Panda is Dean of Academics and Professor of Health Economics at the International Institute of Health Management Research.

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I would like to thank Mrs. Vaishali Deshmukh for helping me with research methodology issues. She is a Senior Program Officer at The INCLEN Trust International.

I would like to thank Dr. Cristina Garcia for helping me develop capacity to search electronic databases better. Dr. Garcia is an Assistant Scientist at Johns Hopkins University, Baltimore, USA.

There are many other people who I would like to thank at INCLEN Executive Office (IEO) who helped me with this research. Some of them are Dr. Archisman Mohapatra (Deputy Director at INCLEN), Dr. Abhishek Wahi (Research Officer at INCLEN), Mrs Neha Gupta (Program Officer at INCLEN), Mr. Deepak Singh (Librarian at INCLEN), and Mrs. Shipra Joshi Kapila (former INCLEN employee).

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Chapter 1: Introduction and Background

1.1) abbreviations used in this thesis

1) ARI = Acute Respiratory Infection

2) LRI = Lower Respiratory Infection

3) URI = Upper Respiratory Infection

4) COI = Cost Of Illness

5) a.k.a. = Also Known As

6) DMC = Direct Medical Cost

7) DNMC = Direct Non Medical Cost

8) IC = Indirect Cost

9) TDCHHEP = Total Direct Cost to Household from Hospitalisation from an Episode of Pneumonia.

10) TDCHHED = Total Direct Cost to Household from Hospitalisation from an Episode of Diarrhea.

11) SDG = Sustainable Development Goals

12) AIDS = Acquired Immuno-Deficiency Syndrome

13) IEC = Information Education Communication

14) BCC = Behaviour Change Communication

15) NGO = Non-Governmental Organisation

16) INR = Indian National Rupee

17) USD = United States Dollar

1.2) General definitions (as a pre-requisite for understanding this thesis)

1.2.1) **Pneumonia :** Pneumonia has been defined by a medical dictionary as "infection of the lung that can be caused by nearly any class of organism known to cause human infections. These include bacteria, amoebae, viruses, fungi and parasites." [3]

1.2.2) **Diarrhoea :** An increased liquidity or decreased consistency of faeces, such as running stool. Fecal consistency is related to the ratio of water-holding capacity of insoluble solids to total water, rather than the amount of water present. Diarrhea is not hyperdefecation or increased fecal weight. [4]

1.2.3) **Cost of illness :** A measurement of economic burden placed on society because of a disease or illness. Cost of illness is determined by the following equation: direct costs (DC) + indirect costs (IC) + intangible costs = cost of illness (COI). [24]

Most COI studies focus on a single disease (e.g., cancer), condition (e.g., brain injury) or class of health problems (e.g., accidents). But several studies have sought to calculate the overall cost of illness in a geographical region using a standardized method across all diseases. (47)

1.2.4) **Direct medical cost (DMC) :** Costs related to the provision of medical care, including the screening, prevention, diagnosis, and treatment of diseases. Direct costs include costs for emergency room visits, hospital inpatient visits, hospital outpatient visits, nursing home care, (prescription and over-the-counter) medications/treatments, and treatment by medical professionals. [24]

1.2.5) **Direct non-medical cost (DNMC) :** Costs related to the illness borne by the patient that do not involve treatment. Examples of direct non-medical costs are transportation or

lodging in order to access the healthcare system and childcare while obtaining medical treatment. Household expenses such as home modifications because of a medical condition are also contained in the category of direct non-medical costs. [24]

1.2.6) **Indirect cost (IC)** : Costs of illness related to loss in productivity by the individual

who is ill and by family members who care for that individual. Two components of indirect costs are morbidity and mortality costs. Morbidity costs are those costs associated with a loss in productivity, and mortality costs are calculated using the present value of future earnings lost. [24]

1.2.7) **Total Direct Cost** = (Direct Medical Cost) + (Direct Non-Medical Cost)

1.3) Definitions used in this thesis (for arriving at results)

1.3.1) **Total Direct Cost to Household from Hospitalisation due to an Episode of Pneumonia/Diarrhea (TDCHHEP / TDCHHED)** = (DMC for pneumonia treatment) + (DNMC for pneumonia treatment)

1.3.2) **Direct Medical Cost for pneumonia / diarrhea treatment** = DMC = medical cost of treating diarrhoea/pneumonia = (hospital bed cost for the duration of stay) + (cost of medicines) + (cost of diagnostic facilities) + (cost of medical human resources) + (cost of other ancilliary hospital services)

Definitions of ancilliary hospital services are based on those provided in URL: http://www.ancillarymedsolutions.com/what-are-ancillary-services-in-health-care

1.3.3) <u>Direct Non-Medical Cost for Pneumonia / Diarrhea treatment</u> = DNMC = (cost of transport from home to hospital) + (cost of transport from hospital to home) + (cost of food for the family including the child over and above average food bill for duration of illness) + (cost of stay for parents / guardians)

1.4) Why Diarrhoea and Pneumonia ?

Lower respiratory infections (LRIs) were responsible for 17.9 % deaths among under 5 children in India in the Year 2017, the second largest killer of children [2]

16.62 % of total DALYs among children under 5 years of age for the year 2017 in India were attributable to LRIs, meaning LRIs are the second biggest cause of DALYs. [2]

In a study analysing the burden of LRI in 195 countries and presenting country-wise disaggregated data , at least 81.3 % of LRI deaths in India in 2015 were in fact pneumonia deaths from 4 causative agents - Pneumococcus (58.7 %), Haemophilus influenza type B (14·9 %), Respiratory syncytial virus (6·0 %) and Influenza (1·7 %). [13]

So Pneumonia appears to be one of the most important diseases among the LRIs leading to DALYs in India in the 2015. The hypothesis can be made that Pneumonia must be a major cause of DALYs in 2019 also.

Similarly diarrhoea was responsible for the deaths of 9.9 % under 5 children in the year 2017 in India, making it the 3rd largest killer of children under 5 years [2].

9.36 % of total DALY's among children under 5 years of age for year 2017 in India were attributable to diarrhoeal diseases. This means diarrheal diseases were the third biggest cause of DALYs. [2]

The most appalling part of these pneumonia and diarrhea deaths is that they are vaccine preventable. "Addition of vaccines against pneumonia (pneumococcal conjugate, *Haemophilus influenzae* type B) and diarrhoeal diseases (rotavirus) to outreach home-based immunization programmes would reduce child deaths" [14]

1.5) Enough epidemiological data but not enough economic data ?

After doing literature review it was realised that there is enough epidemiological data but not enough economic data on burden of pneumonia and diarrhea.

However nowadays policies are built using both epidemiological and economic data. [15]

Usually policies are made using a scoring system with 5 domains - Magnitude, Severity, Vulnerability to intervention, Cost-effectiveness and Political expediency. [15]

Each possible health problem is assigned a score on each of these domains from 1 to 4 (with one value out of 1,2,3,4 being assigned). The minimum and maximum total scores possible are of 5 and 20 respectively. [15]

Moazzam Ali has given “ARI and diarrhoeal disease in under 5 children” a score of 15/20 such that it tops the chart. Other health problems listed are “maternal mortality”, “high fertility”, “pulmonary tuberculosis” and “HIV/AIDS”. [15]

Magnitude, severity and vulnerability to intervention may be epidemiological variables but one must not forget that cost-effectiveness is an economic variable and political expediency is a political one.

Also cost description estimates (the kind that has been found out in this study) are helpful for deriving cost-effectiveness estimates. In other words future researchers, policymakers and policy researchers can use this study to build a better and more robust study.

1.6) Why studying only children under 5 years of age and not all age groups ?

There are broadly two age groups of individuals that are most likely to get hospitalized in India. They are children and elderly **[16]**. More specifically children under 5 years of age and adults over 50 years of age as can be seen in figure 3 of this study **[16]**.

Hospitalisations due to diarrhoea and pneumonia are expected to form a large proportion of total hospitalisation among children of ages under five years. **[1], [2]**

The United Nations Sustainable Development Goal 3 (good health and well being) has certain targets that are especially for children under 5 years of age :

Target 3.2 : By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births [17].

Target 3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases [17].

Clearly these and a lot of other targets within the SDGs aim at providing preventive healthcare measures among children under 5 years of age. Preventive healthcare interventions include specific protection in the form of vaccines, or general protective measures such as effective handwashing.

1.7) Use of these results for advocacy purposes

However, no preventive healthcare intervention is going to work (despite their documented evidence) if the beneficiaries do not realize their importance.

There is a lot of IEC and BCC by the state government and NGO's, with regard to clinical benefits of vaccines, however not that much IEC and BCC with regard to economic benefits of vaccines.

IEC and BCC messages that contain both the clinical as well as economic elements are going to be more successful as compared to the ones with only clinical component. The out of pocket cost of vaccination borne by a household is INR 0 in many states of India

like Himachal Pradesh, Uttar Pradesh, Bihar, Madhya Pradesh and Rajasthan. [18] [19] [20]

It will soon be expanded to other parts of India, if the state governments of these states decide to do so.

“The pneumococcal conjugate vaccine (PCV) that India will introduce provides protection against more than 2/3 of all the disease-causing strains.” [21]. “It protects infants and young children against disease caused by the bacterium Streptococcus pneumoniae.” [22]

“Rotavirus Vaccine” are also provided for free in select states of India.

In order for us to assist beneficiaries realize the importance of getting vaccinated for Streptococcus pneumoniae and Rotavirus, we need to tell parents the costs they are likely to incur in the future, if the children contract these illness from these pathogens. We also need to tell them that they will not have to worry about incurring such costs if they get their children vaccinated and that too free of cost.

CHAPTER 2: Literature Review

Studies that helped in framing the methodology:

The purpose of exploring secondary research studies was to identify which methodology to follow.

Some relevant secondary research studies that helped in the refinement of the methodology have been described in the subsequent paragraphs.

Lili Wang et al [23] have done a systematic review of cost of illness studies. This is one type of cost description study that aims to put a monetary value on a disease for a given number of people within a defined geographic region. It may be based on historic data or it may even be probabilistic.

A lot of studies that are included in my meta-analysis are cost of illness studies. Page 8 of Katherine Anderson's dissertation [24] is a great starting point for understanding the philosophy, behind cost of illness studies.

A little bit of retrospective snowball referencing from this dissertation will take us all the way back to a seminal monograph written by economist Dorothy Rice in 1966 [25]. She hoped to streamline the methodology of cost of illness studies in this monograph. And she was fantastically successful because a lot of future studies replicated her methodology.

From the literature search on cost of illness studies, the conclusion is that cost of illness studies try to capture four kinds of costs - direct medical costs, direct non-medical costs, indirect costs and intangible costs. [24] [25]

The method to estimate each of these costs is pretty concrete, however there is still room for subjectivity, with regards to indirect costs and intangible costs. **[24] [25]**

There is significant debate regarding the usefulness of cost of illness studies. With some critics of questioning their validity and their inherent flaws of circularity and bias **[26]**

Others however say that cost of illness studies is useful for priority setting and policy-making **[31]**

None of the studies reviewed took into consideration all four types of costs. *Not a single study* I could not find any study that took into consideration "intangible costs."

Another significant study is a systematic review of cost of management of severe pneumonia in children aged 0 to 59 months **[27]**.

This study can be replicated for pneumonia and diarrhoea for India with an aim to identify cost for a particular year by conducting a similar meta-analysis. To be a little more poetic, if my research is a ship then this study was the guiding lighthouse. The methodology followed by them helped me frame my own.

CHAPTER 3: Methodology

(3.1) Objectives

Objective 1: To estimate cost of an episode of community acquired diarrhea requiring hospital treatment for a child aged 0 to 59 months for March 2019 in India by multiplying the costs of studies using cost of illness methodology similar to that defined by Katherine Anderson in her thesis [24] by an inflation factor and get a meta-analysis table similar to that in Appendix 4 spreadsheets.

Objective 2: To estimate cost of an episode of community acquired pneumonia requiring hospital treatment for child aged 0 to 59 months for March 2019 in India by multiplying the costs of studies using cost of illness methodology similar to that defined by Katherine Anderson in her thesis [24] by an inflation factor and get a meta-analysis table similar to that in Appendix 4 spreadsheets.

Objective 3: To perform subgroup meta-analysis on completed meta analysis tables of diarrhea and pneumonia and subsequently prepare a three by two table with the following axes :

1st axis : type of hospital (government, non-profit and for-profit) … 3 columns or 3 rows

2nd axis : type of disease (diarrhea, pneumonia) … 2 rows or 2 columns

(3.2) Method of conducting research :

This was a secondary research using grounded theory approach to identify the economic burden of diarrhoea and pneumonia in Indian children under the age of 5 years. [28]

The data that we collected was in the form of studies from PubMed. It is assumed that it is one of the most comprehensive free electronic databases of research articles out there. Also it was assumed that it will have sufficient number of cost of illness studies and other similar genres of studies for pneumonia and diarrhoea even after restricting to the 0 to 59 months age group and other attributes included in the search strategy along the lines of inclusion and exclusion criteria. (oral communication from Dr. Pradeep Panda, Dean of Academics at International Institute of Health Management Research Delhi, 2019).

Multiple searches were used to retrieve articles. Each search string entered into PubMed retrieved a certain number of articles. All articles screened using subjective judgement at title stage. Those that made it were abstract-screened, based on inclusion criteria mentioned in appendix 1A and subsequently full-text screened as per inclusion criteria in 1B.

We developed a search strategy incorporating the following:

1) Mesh terms
2) keywords (mostly searched in “All Fields”)
3) boolean operators.

For a sample search string see appendix 2. Search strings like the one shown in Appendix 2 were saved in a Microsoft word file (.docx) as well as in Google Docs

format. Later search strategies were combined into a final search string using the "OR" boolean operator to include as many studies as possible for initial screening.

A theoretical model for improving my searching:

For each of the variables below the subscript i will be used to denote the serial number of the search performed. Eg (i = 1) for first search, (i = 2) for second search and so on.

Let NUM_i be number of studies retrieved by ith search.

Let $POSNUM_i$ = number of studies that meet the inclusion criteria for abstract-screening out of all the studies retrieved by the ith search.

Let me define PR_i = Positivity Rate of the ith search = $(POSNUM_i) / (NUM_i)$

Quality of search = $QOS_i = a*(NUM_i) + b*(PR_i)$

It was decided that it is more important to have good PR_i and less of a concern to have a higher (NUM_i).

What were the factors that lead to an improvement in search quality?

There were two primary contributors to improvements in search strategy

A) Learning by doing: With exposure to more and more articles, there was clear idea about what kind of research, will have more of an impact for my organisation in particular and the scientific community, in general.

This lead to the discovery of many keywords and MeSH terms, that were added to the final search strategy.

B) Help from Dr. Cristina Garcia: There were several telephonic and email-based conversations with Dr. Cristina Garcia, who is an assistant scientist at Johns Hopkins Bloomberg School of Public Health. She greatly helped in accelerating the improvement in search strategy.

Research design:

The research aimed to dig out literature along the lines of "cost of hospitalisation due to pneumonia and diarrhoea in Indian children aged 0 to 59 months."

It was decided to not to consider all the studies that met the full text inclusion criteria as there was way too much heterogeneity in the pool of studies from which data was extracted. In other words there were diverse methodologies being followed.

Why time period 1st January 2000 to 31st March 2019 was chosen? :

As per several telephonic and email-based conversations with Dr. Cristina Garcia it was decided that this was a large enough time-frame to get some studies along the lines decided. It is important to remember that India does not have many cost of illness studies that meet my inclusion criteria, as was discovered by us in preliminary literature

reviews. In order to get meaningful meta-synthesized summary estimates, it was decided that a large time frame be used as inclusion criteria.

A 9 step process was followed for this research :

Step 1 : Title screening

This was subjective. If the title looked relevant then the abstract was read. I tried to lean on the side of over-inclusion than under-inclusion, i.e. we followed a lenient and easy to pass subjective inclusion criteria at this stage.

Step 2 : Abstract screening

For those studies whose title looked relevant, the abstract was screened. Studies were rejected/selected using "inclusion criteria for abstract screening" given in the appendix 1A.

Step 3 : Full text screening

For those studies that met all "abstract inclusion criteria", the full texts were located and screened using "inclusion criteria for full text screening" given in appendix 1B.

Step 4 : Data extraction protocol followed:

For studies that met the full text inclusion criteria data extraction was carried out.

Studies were listed in a random order and each study was given a study code (same as serial number).

Data extraction template was designed prior to actual data extraction as shown in first row of google sheets titled “cost of pneumonia master datasheet” and “cost of diarrhoea_diarrhea master datasheet” in appendix 3. These serve as variables for populating this datasheet, i.e. each column can be considered as a qualitative variable. After this each full text study was read and the columns were filled for each of the above mentioned datasheets.

These data sheets were the starting point for meta-analysis (see next step for more details).

Please note : you can find online links to these data sheets in Appendix 3.

Step 5 : Preparing meta-analysis spreadsheets, the first steps

The datasheets obtained in the previous study were screened for the presence of key characteristics given in Appendix 5. If the key characteristics were missing then they were excluded from the meta-analysis.

All studies with the key characteristics of Appendix 5 were listed sequentially and given new study codes (same as serial numbers).

Step 6 : Preparing meta-analysis spreadsheets, splitting studies if possible

These studies were then screened for availability of data dis-aggregated by type of hospital funding (government, non-profit or for-profit). If dis-aggregated data was present then the study was split into parts as required.

e.g. : If a multi-site cost of illness study on diarrhea had one site as a government hospital and another site as a non-profit hospital with study code 4 (same as serial number) then the study

was split into 2 parts, in a way creating 2 studies with study codes 4.1 and 4.2 such that they will be meta-analysed as if they were 2 separate studies.

This can be better appreciated by having a look at Appendix 4, which contains online links to spreadsheets that contain the detailed process followed by me untill this point.

Step 7) Filling data for sub-studies if required

In case a study was split into multiple parts the sample size for each of the parts was located by reading the full text again. This was then entered into the "meta-analysis" spreadsheet under the column titled "sample size" of the appropriate work-book.

E.g. : In the meta-analysis workbook for diarrhea, The study with code 1 had to be split into 3 parts, namely government hospital study arm, non-profit hospital study arm and for-profit hospital study arm. We then read the full text to enter data into each sub-study row in the worksheet titled "meta-analysis" of the workbook titled "(D8_COD_DM-S)_(Draft 8_Cost Of Diarrhea_Diarrhoea Meta-Synthesis)".

Step 8 : Converting cost data to March 2019 United States Dollars

Procedure 8.1 : Followed if cost data in study is presented in USD

Start point : cost data tagged to USD for data collection period of study.

End Point : cost data tagged to March 2019 United States Dollar

Procedure followed to reach end point from start point :

Use the website below to convert a USD value from the past to a USD Value in the present. https://www.inflationtool.com/indian-rupee?amount=66&year1=2009&month1=1&year2=2019&month2=3&subject=Total

For example USD 66 in January 2009 is equivalent to USD 137.8 in March 2019.

All figures were converted to March 2019 for the cost data to become meta-analysable.

Procedure 8.2 : Followed if cost data in study is presented in INR (no USD value present)

Start point : cost data tagged to INR for data collection period of study.

End Point : cost data tagged to March 2019 United States Dollars.

Procedure followed to get to end point from start point :

1) Go to the website mentioned below [29] which presents daily exchange rates (Number of INR per USD) for any year that you choose from 2005 to 2019 : https://www.poundsterlinglive.com/bank-of-england-spot/historical-spot-exchange-rates/usd/USD-to-INR-2005

2) copy and paste the relevant exchange rate data. For example there was a study in which cost data was collected from November 2008 to February 2009. So data needs to pasted into a google sheet or excel workbook from 1st November 2008 to 27th February 2009.

By the way all the cost data periods for the studies that met full text inclusion criteria can be gotten by following below diagram :

Appendix 4 → Go to meta-synthesis worksheet → column titled “Time period of cost data collection” (for both pneumonia and diarrhea data sheets)

3) Make data ready for algebraic treatment by using find and replace function. Find “1 USD = ” and replace with blanks. Then find “ INR” and replace with blanks. convert all cells into currency format.

4) use “average function” to get mean exchange rate for the cost data collection period. It was decided to use mean rather than median as mean is capable of further algebraic treatment [30].

5) paste the average exchange rate into your meta-synthesis worksheet in the column titled “mean exchange rate during cost data collection period (number of INR per USD).”

6) divide the “TDCHHEP/TDCHHED in INR during study data collection period” by “mean exchange rate …” to get “TDCHHEP/TDCHHED in USD during study data collection period”

7) now follow “procedure 8.1”

Step 9 : Using statistical formulae to arrive at summary estimates

The statistical formulae used are available in the work-books whose online links are provided in Appendix 4.

These statistical formulae helped us arrive at the final results that are presented in the next section.

Chapter 4: Results

If a child under five years of age was hospitalized for **pneumonia** in **March 2019**, the **total direct cost** to **household** was likely to be **USD 14.26**, **USD 164.35** and **USD 192.77** for **government, non-profit** and **for-profit** hospitals **respectively**.

Total direct cost to an Indian **household** if one of its child below 5 years was hospitalized for **diarrhea** in **March 2019** was likely to be **USD 6.61**, **USD 124.12** and **USD 198.46** for **government, non-profit** and **for-profit hospitals respectively**.

These 2 paragraphs can be summarised in Table 1 given below :

Table 1 (summary estimates table) : Units for all numerical figures is March 2019 USD

Type of Disease / Category of Hospital	Diarrhea	Pneumonia
Government	6.61	14.26
Non-Profit	124.12	164.35
For-Profit	198.46	192.77

Chapter 5: Discussion

This was an exploratory study estimating cost of hospitalization for treating children aged 0 to 59 months due to diarrhoea or pneumonia in India for the time period March 2019. To the best of my knowledge no such study has been conducted before.

Different studies use different names for variables that are otherwise trying to capture the same type of cost. E.g. some studies call cost of treating pneumonia/diarrhoea as direct medical cost. Others call it medical direct cost. Therefore in order to make the variables comparable across studies they have been recoded them as “DMC” or “direct medical cost” as well as “DNMC” or “direct non medical cost”. Note that even if not explicitly mentioned in the full-texts of these studies, it is evident that these studies have been inspired from Rice’s seminal work of 1966 [25].

Please note that these are variables from the household perspective.

Most studies followed a simplified version of Rice’s original equation. That is most studies followed:

TDCHHED/TDCHHEP = DMC + DNMC + IC

where indirect cost (IC) was lost wages among all the caregivers of the household who could not work due to episode of illness in the young child.

However since IC was not considered in all studies, therefore it was not included for calculation of meta-analysed summary estimates.

Mathematical model to explain the heterogeneity in studies with Rice's 1966 methodology [25] as reference (a semi-quantitative model to explain heterogeniety in meta-anlysed studies):

Let conditions 1, 2 and 3 be defined by logical variables C_1^i , C_2^i and C_3^i respectively with values "true", "false" and "NA" where i stands for the serial number of study such that first study in worksheet titled "meta-analysis" in any given workbook (diarrhea or pneumonia), such that i has a value of 1 for first study, 2 for second study and so on.

Condition 1 (defined by variable C_1^i) : There exists a difference in nomenclature of variables used in meta-analysed cost of illness studies and nomenclature of variables used by me (which was heavily derived from the original cost of illness framework given by Dorothy Rice in her seminal monograph of 1966). The variable C_1^i has no regard for whether the definitions used are different or not. It is only bothered about nomenclature.

Observation : Condition 1 was true for some studies and false for other studies.

Condition 2 (defined by variable C_2^i) : The variables used in the meta-analysed cost-of-illness studies were defined in a manner similar to the way I defined them at the beginning of my thesis. The value of C_2^i is determined irrespective of the nomenclature given by the authors to the variables. That is a variable may be given a different name than the name given by me but has the same definition as me.

Observation : It was true for some studies that gave a detailed breakdown of the sub-variables contained within the main variables DMC and DNMC. However there were other studies in which the sub-variables were either vaguely defined, or not defined at all. This resulted in some of the values of $C_2^{\mathbf{i}}$ being indeterminate.

Factors causing heterogeneity in the pool of studies that were meta-analysed (A qualitative approach for describing heterogeneity in meta-analysed studies) :

There were some studies in Appendix 3 where the definitions of variables were rather vaguely defined. Often times leaving room for doubt as to how they were estimated. When the definitions were vague there was no way to say whether they were defined along the lines of Rice's 1966 model or not. In these cases it created confusion of whether or not to meta-analyse these studies. However it was decided to take the risk and go ahead with the meta-analysis.

Summing the above observations for qualitative and semi-quantitative methods to describe heterogeneity, most studies were inherently following a simplified version of rice's original cost of illness model but were giving variables some other names and not the names which Rice had given. Some times definitions were vague in the meta-analysed studies, meaning we should be careful while interpreting the findings.

Chapter 6: Conclusion

Total direct cost to the households seeking care in government hospitals was the lowest and the for-profit hospitals was the highest. If total direct cost to household is considered as a proxy to their out of pocket expenditure, then we can say that for-profit hospitals entail the highest out of pocket expenditure and government hospitals entail the lowest out of pocket expenditure.

Chapter 7: References

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Summary: an idea about qualitative reviews

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Appendix 1A:

Inclusion criteria for screening of abstracts

Inclusion criteria (Inclusion required 1 and 2. Also required atleast one of 3 or 4.):

1) Data for patients of age 0-59 months may be present in the full text.

2) Data for Indian patients may be there in the full text

3) Data for cost of average length of stay at hospital maybe present in full text with respect to severe diarrhoea or severe pneumonia.

4) “Cost of illness” is in the title, abstract, keyword or MeSH terms along with simultaneous presense of “pneumonia” and/or “diarrhea/diarrhoea” in the title, abstract, keyword or MeSH terms. Due regard be given to synonyms and PubMed controlled vocabulary (MeSH).

Appendix 1B:

Inclusion criteria for screening of full texts

Inclusion required ALL of the following:

1) Age: 0-59 months

2) Patients are residents of India

3) Are being treated or have already been treated for diarrhoea or pneumonia in hospital.

4) Community acquired diarrhoea or pneumonia

5) Empirical cost data presented.

Appendix 2

(Sample search string developed during the process of research) :

("Pneumonia"[All Fields] OR "diarrhoea"[All Fields] OR "diarrhea"[All Fields] OR "pneumonia"[Mesh] OR "diarrhea"[Mesh]) AND ("Infant"[MeSH Terms] OR "Infant, Newborn"[MeSH Terms] OR "child"[MeSH Terms] OR "Child, Preschool"[MeSH Terms] OR "Minors"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR "Young Adult"[MeSH Terms] OR "infant"[All Fields] OR "infants"[All Fields] OR "neonate"[All Fields] OR "neonates"[All Fields] OR "neonatal"[All Fields] OR "newborn"[All Fields] OR "newborns"[All Fields] OR "new-born"[All Fields] OR "new-borns"[All Fields] OR "baby"[All Fields] OR "babies"[All Fields] OR "child"[All Fields] OR "children"[All Fields] OR "youth"[All Fields] OR "youths"[All Fields] OR "young people"[All Fields] OR "childhood"[All Fields] OR "toddler"[All Fields] OR "toddlers"[All Fields] OR "kid"[All Fields] OR "kids"[All Fields] OR "young patient"[All Fields] OR "young patients"[All Fields] OR "boy"[All Fields] OR "boys"[All Fields] OR "girl"[All Fields] OR "girls"[All Fields] OR "young age"[All Fields] OR "pediatric"[All Fields] OR "pre-schooler"[All Fields] OR "preschooler"[All Fields] OR "under 5"[All Fields] OR "under five"[All Fields] OR "under-fives"[All Fields] OR "less than five"[All Fields]) AND ("Economics"[Mesh] OR "Economics"[all fields] OR "Economic"[all fields] OR “costs and cost analysis”[mesh] OR “pricing”[all fields] OR “cost of illness”[mesh] OR “Costs”[all fields] OR “cost”[all fields] OR “Burden of Illness”[all fields] OR “Illness Burden”[all fields] OR “Illness Burdens”[all fields] OR “cost-benefit analysis”[MeSH] OR “Cost-Benefit Analysis”[all fields] OR “Cost-Benefit Analyses”[all fields] OR “Cost-Benefit Data”[all fields] OR “hospital costs”[mesh] OR “cost control”[mesh] OR “drug costs”[mesh] OR “economic value of

life”[mesh] OR “economic value of life”[all fields] OR “health care costs”[mesh] OR “Cost Measure”[all fields] OR “Cost Measures”[all fields] OR “cost of illness”[all fields] OR “Illness Cost”[all fields] OR “Illness Costs”[all fields] OR “Cost of Disease”[all fields] OR “Costs of Disease”[all fields] OR “Sickness Cost”[all fields] OR “Disease Costs”[all fields] OR “Disease Cost”[all fields] OR “Cost of Sickness”[all fields] OR “Cost Benefit”[all fields] OR “Benefits and Costs”[all fields] OR “Costs and Benefits”[all fields] OR “hospital costs”[all fields] OR “hospital cost”[all fields] OR “cost control”[all fields] OR “cost controls”[all fields] OR “cost containment”[all fields] OR “cost containments”[all fields] OR “drug costs”[all fields] OR “drug cost”[all fields] OR “health care costs”[all fields] OR “health care cost”[all fields] OR “Healthcare Cost”[all fields] OR “Healthcare Costs”[all fields] OR “Medical Care Costs”[all fields] OR “Medical Care Cost”[all fields] OR “Treatment Cost”[All Fields] OR “Treatment Costs”[All Fields] OR “Medical Care Cost”[All Fields] OR “Medical Care Costs”[All Fields] OR “health cost”[all fields] OR “health costs”[all fields]) AND ("India"[Mesh] OR “India”[All Fields])

Appendix 3

Data extraction template along with extracted data :

→ You will need an internet connection to access the online links given below :

→ To access the **diarrhea** file please use the link :

https://docs.google.com/spreadsheets/d/1z68Nn-jy2ReTl9amx-Xc6ZFpTheWsb0R9NqdwRlqgU8/edit?usp=sharing

→ To access the **pneumonia** file please use the link :

https://drive.google.com/file/d/1m917a7s789d1lXguNqJE5vjNURhl4SH9/view?usp=sharing

Appendix 4

Meta-analysis template along with calculations :

→ You will need an internet connection to access the online links given below :

→ To access the file for **diarrhea** please use the link :

https://drive.google.com/file/d/1QRS92ag-XOVXq5RIWpUF08_2MXM04jJW/view?usp=sharing

→ To access the file for **pneumonia** please use the link :

https://drive.google.com/file/d/13NE-k-Yke0T_FX1Emfizgy_0W3TCwnch/view?usp=sharing

Appendix 5

Key characteristics used to select/reject studies for meta-analysis

Selection required ALL of the following characteristics :

1) presence of numerical value of TDCHHEP / TDCHHED (for pneumonia and diarrhea meta-analyses respectively).
2) definitions of variables “DMC”, “DNMC” and “TDCHHEP / TDCHHED” were roughly the same as defined by me.