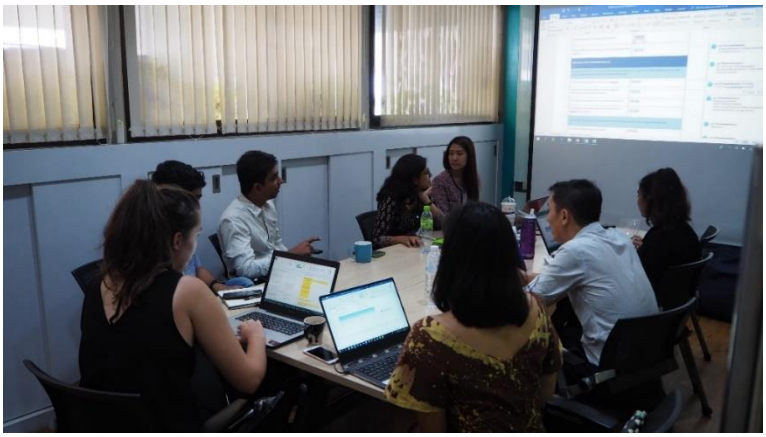

CHRISTIAN MEDICAL COLLEGE (CMC) VELLORE RESEARCH INTERNSHIP TO THE HEALTH INTERVENTION AND TECHNOLOGY ASSESSMENT PROGRAM (HITAP)

11th to 18th October, 2018

Reported by Health Intervention and Technology Assessment Program

Acronyms and Abbreviations

ANC	Absolute Neutrophil Count
CBA	Cost Benefit Analysis
CEA	Cost Effective Analysis
CMA	Cost Minimization Analysis
CMC Vellore	Christian Medical College, Vellore
CUA	Cost Utility Analysis
DHR	Department of Health Research, Ministry of Health and Family Welfare, Government of India
ESRD	End-Stage Renal Disease
GHCC	Global Health Costing Consortium
HD	Hemodialysis
HITAP	The Health Intervention and Technology Assessment Program
HTA	Health Technology Assessment
ICER	Incremental Cost Effective Ratio
iDSI	International Decision Support Initiative
IHPP	International Health Policy Program
LY	Life Years
MoH&FW	Ministry of Health and Family Welfare, Government of India
MoPH	Ministry of Public Health
NMB	Net Monitory Benefit
NHSRC	National Health Systems Resource Centre
PD	Peritoneal Dialysis
PGIMER	Post-Graduate Institute of Medical Education and Research
QALY	Quality Adjusted Life Years
RRT	Renal Replacement Therapy
UCBP	Universal Coverage Benefits Package
UCS	Universal Coverage Scheme
UHC	Universal Health Coverage
WHO	World Health Organization

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Executive Summary

This report aims to describe the study visit of researchers at Christian Medical College (CMC) Vellore who are undertaking cost of illness studies on enteric fever and rotavirus vaccines in India at the Health Intervention and Technology Assessment Program (HITAP). HITAP, known regionally for supporting health technology assessment (HTA) and economic evaluations, was requested by CMC Vellore for an internship program at HITAP. After discussions, HITAP organized a week-long internship for three research scientists from CMC Vellore. The internship focused on familiarizing the researchers with HITAP, the role of HTA in the Thai health system, principles and best practices for conducting costing studies using the Global Health Cost Consortium (GHCC) reference case, and methods of conducting economic evaluations and modelling of health economics. Through the internship, the researchers were able to identify areas for further work and develop a plan for their studies and potential for economic evaluations, including areas of support from HITAP and future collaborations between the two institutions.

Introduction

Background

Despite India making strides to improve health indicators, public expenditure on health remains low, with high out-of-pocket expenses and broad variation in health provisions and health outcomes across the country. Over the years, there has been growing pressure from citizens to increase access to quality health services. With the recent announcement of the Government's commitment to achieving Universal Health Coverage (UHC), the Ayushman Bharat program, there is a momentum for investing in healthcare. As with any country, India is dealing with limited resources to provide this universal care; now, more than ever, the need for evidence-informed policies to meet the healthcare needs of the second most populous country in the world is of high importance. To address this issue, the mandate for Health Technology Assessment (HTA) was placed at the Department of Health Research (DHR), Ministry of Health and Family Welfare (MoH&FW), Government of India.

A survey conducted on the role of HTA in India included identifying potential users and generators of HTA as well as the challenges for the development of HTA in India showed a shortage of technical capacity and infrastructure for HTA (Dabak et al, 2018). Hence, it is ever more important that health research institutions gain support to ramp up their efforts to provide high quality data and research.

Over the past seven years, HITAP has collaborated with partners in India such as DHR, World Health Organization (WHO), the Post-Graduate Institute of Medical Education and Research (PGIMER), and the National Health Systems Resource Centre (NHSRC) on HTA. Through various engagements, HITAP and other HTA partners such as Imperial College London and other partners under the International Decision Support Initiative (iDSI) have shared knowledge, raised awareness, and contributed to building India's HTA capacity. Examples of such efforts include hosting delegates from various institutions, organizations, and ministry offices to learn about Thailand's HTA processes, insurance schemes, UHC, HITAP's role in assessing various health technologies and programs, as well as providing technical support for HTA studies in India. With the growing appetite for HTA in India, there will be more opportunities for sharing experiences and lessons learned with each other as well as other countries.

Collaboration with CMC Vellore

The Wellcome Trust Research Laboratory at the Christian Medical College (CMC) Vellore, India, requested HITAP to host its researchers for a research internship. The researchers are undertaking cost of illness studies on enteric fever and rotavirus vaccine implementation in India. The internship program is structured as a series of visits to HITAP over a period of several months over the course of their studies. This report describes the first visit from 11th to 18th October 2018 attended by Dr. Nayana Nair, a medical doctor who is currently in the 2nd year of her PhD program, Dr. Jacob John a Public Health professor and physician in Maternal and Child Health, and Dr. Prasanna Samuel who has a background in Biostatistics and is currently working on collecting costing data from four urban based primary health care settings.

Topics on the components and approaches used for costing were prioritized to meet their needs. The internship involved a combination of presentations, exercises, and discussions which allowed them not

only to learn from HITAP, but also apply concepts and techniques to their studies, ask clarifying questions, and raise specific issues related to their work. Throughout the internship program, HITAP will continue to provide feedback and advice on various aspects of their studies, share resources, and support them to prepare their studies as parts of full-scale economic evaluations. HITAP in turn will learn from the application of the methods in different state contexts as well as have an increased understanding of how HTA and its tools can be useful throughout India

Objectives of the internship

This initial visit was organized into two parts according to the objectives of the visit. The first part of the visit was structured as a training to introduce the researchers to the Thai context and the principles of HTA. The second part of the visit aimed to introduce HTA, economic evaluations, and costing of health interventions for use in the two studies. The agenda for the visit is provided in Appendix 1.

Introduction to HTA and its role in supporting UHC in Thailand

During the first two days, the researchers were familiarized with UHC in Thailand (see summary ion Appendix 2), the role of HTA in supporting evidence-informed decision making, and HITAP's contribution to HTA in Thailand. Technical aspects of conducting an HTA were also covered, introducing the concepts of costing, measurement of health outcomes as well as conducting a health economic evaluation.

Economic evaluations are studies that consider both the comparative costs associated with two or more health care interventions, and the comparative clinical effects, measured either in clinical units, health preferences, or monetary benefit. There are essentially five main types of economic evaluation methods: costing study, cost-minimization analysis (CMA), cost-benefit analysis (CBA), cost effectiveness analysis (CEA), and cost utility analysis (CUA). Each of these methods produces a specific outcome and results. Therefore, when determining the type of economic evaluation method to use, it is important to think about the interventions under study, what the purpose of the study is, and who will be impacted by the results of the study. In Thailand, the HITAP, a research unit within the MoPH was established in 2006/7 and a year after the first national HTA guidelines were published. In 2009, HTA was used to inform a comprehensive health package. The governance structures that support the use of HTA include several stakeholder groups including various boards, committees, HTA agencies, and working groups. However, for HTA to take root there were Champions who were the backbone for gaining support and ensuring continuity of the work.

During the internship, the researchers were asked to complete a take home exercise based on an economic evaluation of End-Stage Renal Disease (ESRD) that was used to inform decision making in Thailand. The study was commissioned by the Thai UCS manager, the National Health Security Office. The two comparators were the following renal replacement therapy (RRT) options: "Peritoneal Dialysis (PD) first" and "Hemodialysis (HD) first" versus standard treatment. Results of the study showed that both strategies were cost ineffective at the threshold value of 160,000 Thai baht, but a PD first option was found to be relatively more cost effective than an HD first option. In October 2007, PD first policy was included in the UCS Benefits Package (UCBP). The number of patients with access to dialysis increased and patients were expected to survive for at least 5-10 years (as compared to 3-6 months pre-RRT

introduction) due to access to treatment. For the exercise, HITAP divided the work into 4 parts, with each building into the next. Part 1 included calculating statistical parameters, part 2 involved constructing the Markov Model, part 3 required applying probabilistic modeling, and part 4 entailed producing the outputs and results.

Learning about costing

Rotavirus Vaccine Costing Study

Dr. Nayana Nair is conducting a costing study of ROTAVAC vaccine for rotavirus/acute gastroenteritis, which has been administered nationally to 70% of the population under 5 years of age. The study design is a prospective cost analysis study to estimate the cost per episode of diarrhea. The costing study aims to calculate the total cost of outpatient and inpatient hospital visits for acute gastroenteritis in 11 sites across India where the rotavirus vaccine has been introduced. The sites selected include both private and public hospitals at all levels of care; primary, secondary, and tertiary. She has developed two survey forms that have been used to collect data from the patients at point of care and to collect information on further complications and other expenses incurred post hospital visit (one month). She used convenience-based sampling to collect information from patients.

Typhoid Vaccine Costing Study

Dr. Jacob John and Dr. Prasanna Samuel are conducting national sentinel surveillance for hospital visits for enteric/typhoid fever. This national surveillance study has three components that aim to: 1) determine the burden of typhoid; 2) understand the consequences of typhoid through surveillance cost in primary health care settings (clinical severity and antimicrobial resistance); and, 3) assess the impact of interventions on the disease and transmission. For this study, the data was collected from the largest hospital that serves the most people in the community. To determine the dominant hospital in each community, the researchers conducted a health care utilization survey at the household level that asked questions related to health seeking behavior and preferred provider. Currently, research is being undertaken to understand the first two components. Questionnaires are administered by health providers to collect clinical and cost data. A costing study on outpatient visits and inpatient hospitalizations in

secondary and tertiary hospitals due to typhoid in rural and urban India is being developed to understand its financial burden on households.

For more information on the details of the costing study characteristics, see Appendix 4. For both the studies the goal is to conduct an economic evaluation after the costing studies have been completed. The costing component described above will be a key input to the larger economic evaluation. However, the exact details of the methodology have not been determined.

Using the Global Health Costing Case (GHCC) Reference

To further guide their research, the HITAP team and interns reviewed the GHCC Reference for Estimating the Costs of Global Health Services and Interventions developed by global experts and academics with support from the Bill and Melinda Gates Foundation (BMGF). “The GHCC reference case ensures the process of cost estimation is clearly conveyed and reflects best practices, so that the users of the cost data can interpret the findings properly and assess their quality (accuracy, precision, generalizability, and consistency)” (Vassall et al, 2017). The reference case outlines principles, methods, and reporting standards to follow from the inception through to the end of a costing study and includes accompanying tools that the interns completed together with HITAP colleagues (see Box 1 on Costing Tips and Tricks for some of the items discussed).

Box 1

Costing Tips and Tricks

- **Shadow pricing:** for informal care and housewives, researchers can use the costs of hired help with specific tasks, e.g. cooking, cleaning, and childcare, or the cost of hiring a maid for the day. One can also look at the average income from the national survey; however, knowing the unemployment rate will give an indication of the extent or potential impact of informal services, e.g. 40% of people in the country are unemployed and/or housewives, etc.

- **Valuing productivity**: the **human-capital method** measures the potential value of production loss due to an employee's illness, disability, early retirement, and presenteeism or reduced productivity level at work, though it fails to consider the possibility of their replacement. The **human friction cost approach** measures the actual value of production lost due to illness and assumes that the absent employee can be replaced. However, this is conditionally valid; for example, with death, the post parity cost is high in the beginning and then declines as the person is replaced.

- **Above service delivery costs:** often overlooked, examples include cold chain and procurement, monitoring and evaluation, training, and hospital accreditation costs.

- **Supporting charges:** these are additional programs like initiatives, new guidelines, new interventions, etc. that come with providing care.

- **Willingness vs ability to pay**: in the surveys, researchers must ensure the correct questions are asked to distinguish between willingness and ability to pay. In the survey study, researchers should give the patient a scenario of an instance when a reference price is not available in the market. Using HIV vaccine as an example, the researcher may ask their respondents, "if you needed to pay in the next three months for this vaccine, where would you get the funds from?" They should be able to state reasonable sources of money, such as borrowing from family, selling assets, etc. to show that they are able to pay.

- **Avoiding ambiguities in the survey form:** for the survey tool for collecting costing data from patients, researchers need to ensure the timescales are logical and applicable. For instance, when asking about the cost of school fees, they may ask on a biannual or annual basis, but when asking about groceries, they may ask on a weekly or monthly basis. Researchers need to think about the user's ability to provide information as accurately as possible and reduce ambiguity by blocking out (or removing) information that do not apply.

- **Accounting for donations and in-kind contributions:** first, show how significant the amount is, and then attribute these as facility level costs.

Source: Reference Case for Global Health Costing (Vassal et al 2017)

Recommendations and Next Steps

Both studies have data on the cost of health care collected from the patient perspective as well as data for the societal perspective. Now, the interns will train hospital staff to collect costing data from the health providers' perspective. Key costs for the researchers to consider during data collection include: calculating labour costs and including "relaxation/down time," accounting for above service delivery costs of materials or infrastructure provided by the ministry/departments, costing the physical space of the room and land used, using a top down approach to get the unit cost for the disease, and to collect cost from secondary and tertiary providers it may be easier to use activity based costing. Overall, the provider perspective costing needs to be comprehensive (e.g. include depreciation). There are several approaches that can be applied, but the approach taken is determined by the aim of the overall costing study.

Because diarrhoea is one of the most common ailments for which care is provided in the primary health system in India, this study can be more ambitious. A more comprehensive study on primary care (capital, labour, and materials for the whole facility costed for one year) can serve as the baseline for many studies and potential policy decisions in the future. Disease characteristics for no more than 10 high-burden disease groups, e.g. the no. of cases of diarrhoea, respiratory tract infection, unknown fever, and other, select ailments can also be tracked; costs per unit can be allocated to each ailment. Selective or purposive sampling can be done for 10 cases of each of these ailment/disease groups, tracking the costs of capital, labour, materials, absolute neutrophil count (ANC) for each or other lab tests, with the final goal of having a unit cost for each illness.

Reflections on the internship experience

At the end of the internship a final recap and review session was held and during this time we asked sought verbal feedback from the researchers. Below are a few thoughts from Nayana Nair and Prasanna Samuel.

"It was very interesting to see how economic evaluation is applied here. I'm very thankful for this opportunity and would like to keep these interactions active. Your inputs were very helpful." -- Nayana Nair

"Now I can say that I have a fundamental understanding of HTA. It is one thing to read or learn from lecture, but these interactions are beneficial. I see the effort needed for this work and have an appreciation and value for the activities being done in the health care settings. I need to observe [economic evaluation] in the real-world setting." -- Prasanna Samuel

Continued Engagements Between CMC Vellore and HITAP

In the next several months, HITAP aims to keep the interaction active with CMC Vellore. HITAP has agreed to provide suggestions and inputs on their technical difficulties in collecting cost data and conducting future HTA or economic evaluation efforts. Dr. Yot Teerawattananon will be an informal reviewer for any protocols, preliminary reports, and manuscripts that are produced. Below are the outputs/documents that CMC researchers will share with HITAP:

- Revised patient perspective costing protocols with a summary of the revisions (with justifications)
- A research protocol for economic evaluation
- A protocol for health system costing
- A report for out-of-pocket data collection study
- A questionnaire for a future study on dengue
- The final reports and manuscripts of the studies
- A summary of this visit

Over the coming year, it is possible that the CMC Vellore researchers will come back to HITAP for internships on other areas such as conducting economic evaluations. Through the internship, there may be a possibility for HITAP to visit CMC Vellore in the future to learn more about the capacity of HTA and economic evaluations there and possibly advocate for further investments in this field.

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Appendices

Appendix 1: Agenda

Title: Research Internship Agenda
Conducting Cost-effectiveness Analyses (CEA)

Dates: 11th-19th October 2018
Note: 15 October, 2018 is an official holiday.
Location: Meeting Room 3, HITAP, Ministry of Public Health, Thailand

Schedule:

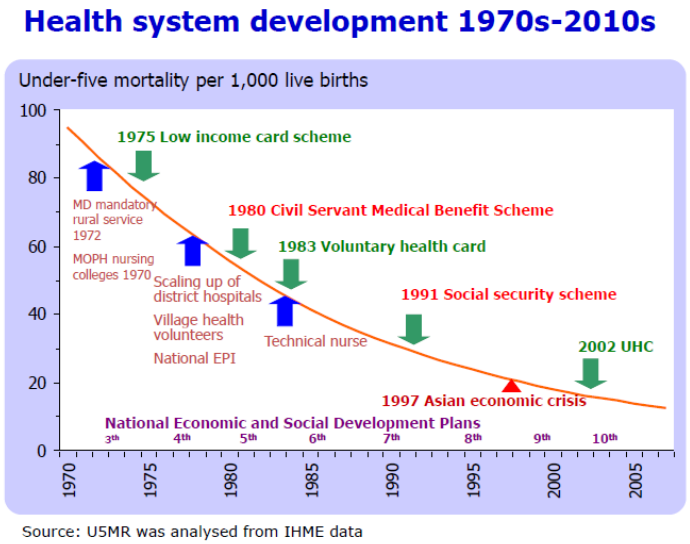
Time	Session	Description	Person (s) Responsible
11th October, 2018			
09:00 – 09:30	Welcome and Scope of the internship	• Introductions • Define the overall objectives of the internship • Timeline and work plan • Required outputs	Avnee Patel
09:30 – 12:00	Healthcare System in Thailand	• Design and implementation of universal health coverage in Thailand	Mrs. Netnapis Suchonwanich
Lunch			
13:00 - 14:00	Overview of HITAP	• Overview of organization and structure • Role in supporting HTA in Thailand	Saudamini Dabak
14:00 – 15:00	Overview of HITAP's International Work	• Country work • Regional and global work	Rachel Archer
15:00 -- 16:00	Overview of HTA Process in Thailand	• Role of HTA in supporting evidence-informed decision making	Manushi Sharma
16:00 – 16:30	Reflect and share comments	• Colleagues reflect, share thoughts and ask questions • Discuss deliverables from internship	CMC Vellore
12th October, 2018			
09:00 – 09:30	Recap	• Summary of activities from previous day	CMC Vellore
09:30 – 10:45	Introduction to economic evaluations	• Concepts and practices for conducting economic evaluations	Alia Gonzales Luz
10:45 – 12:00	Useful resources for conducting economic evaluations	• Overview of resources eg medical databases, guidelines, costing database, GEAR, etc.	Alia Gonzales Luz

Time	Session	Description	Person (s) Responsible
Lunch			
13:00 – 14:00	Costing healthcare	• Concepts and approaches • Using case studies from Thailand	Sarayuth Khuntha
14:00 - 15:00	Measuring health outcomes	• Concepts and approaches	Phorntida Hadnorntun
15:00 – 16:00	Health economic modelling	• Overview of Decision Tree and Markov models	Pritaporn Kingkaew
16:00 – 17:00	Introduction to take-home exercises	• Exercises on economic evaluations using case study of evaluation of End-stage renal disease (ESRD) in Thailand	Avnee Patel and Evelyn Thsehla
16th October, 2018			
08:00 – 8:30	Introductions and recap	• Review of previous days	Dr. Yot Teerawattananon
8:30 – 10:00	Take-home exercises. Dr Yot present on costing. Discussion of presentation and specific issues from their work	• Present on progress with exercise	CMC Vellore/ Dr. Yot Teerawattananon, Alia Gonzales Luz
10:00 – 11:00	Study on enteric fever and rotavirus	• Present on design of study, type of costs, methodology for costing data collection • Plan for further data collection or analysis	CMC Vellore
11:00 – 12:00	Discussion	• Discussion on presentation	Dr. Yot Teerawattananon, Alia Gonzales Luz
Lunch			
13:00 – 14:00	Go over GHCC reference case and do exercises together	• Overview of reference case	Avnee Patel and Alia Gonzales Luz
14:00 – 15:00	Discussion	• Discussion on presentation	Alia Gonzales Luz, Rachel Archer, Avnee Patel
15:00- 15:30	End-of-day check-in	• Summarize and discuss progress, ask questions	CMC Vellore, Avnee Patel
17th October, 2018			
9:00 – 9:30	Recap from previous day	• Summarize work from previous day	Dr. Yot Teerawattananon
9:30 – 12:00	Review additional costs to be identified and valuation approach	• As per discussion previous day	CMC Vellore, Dr. Yot Teerawattananon, Avnee Patel
Lunch			
13:00 – 14:30	Develop a plan for additional data collection	• As per discussion previous day	CMC Vellore, Dr. Yot Teerawattananon, Avnee Patel

Time	Session	Description	Person (s) Responsible
14:30 – 4:30	Self study	• Time for the team to reflect and conduct research	Support from Avnee Patel
18th October, 2018			
9:00 – 9:15	Recap from previous day, and	• Summarize work from previous day	All
9:00 – 12:00	Nayana present her preliminary findings Discuss current materials/tools for data collection.	• Nayana present • Everyone discuss data collection issues and review survey	Dr. Yot Teerawattananon Waranya Rattanavipapong, Avnee Patel
Lunch			
13:00 – 14:30	Review materials/tools for data collection	• As per discussion previous day	Dr. Yot Teerawattananon Waranya Rattanavipapong, Rachel Archer, Avnee Patel
14:30 – 16:30	Review take home exercises from the weekend	• Dr. Yot explains the exercise in detail	Dr. Yot
16:30 - 17:00	End-of-day recap	• Summarize and discuss progress, areas for further research	Dr. Yot Teerawattananon
19th October, 2018			
9:15 – 12:00	Prepare analysis plan	• As per discussion previous day	CMC Vellore
Lunch			
13:00 – 17:00	Discussion and questions Next steps	• Present on data collection and analysis • Plan for activities for studies and next visit for internship	Dr. Yot Teerawattananon, with attendance from others

Appendix 2: Development of UHC in Thailand

To show the interns the importance of their studies as potential evidence for policy, the UHC system in Thailand, how HTA is conducted and applied, and the role HITAP has played in institutionalizing HTA was discussed. Properly launching the UHC system was a journey that started in the early 1970's; like all journeys, there was a beginning, middle, and end (launch of UHC with continued improvements). Therefore, in order to explain how UHC developed in Thailand, the interns were taken back in time to the beginning when the initial pieces were being placed, the middle when the system was developing with necessary processes, policies, infrastructure, human resources, and institutions, to the end when the UHC scheme was formally started. After the launch of the scheme, further developments and adjustments were undertaken, with the UHC system evolving and growing to meet the population's needs.



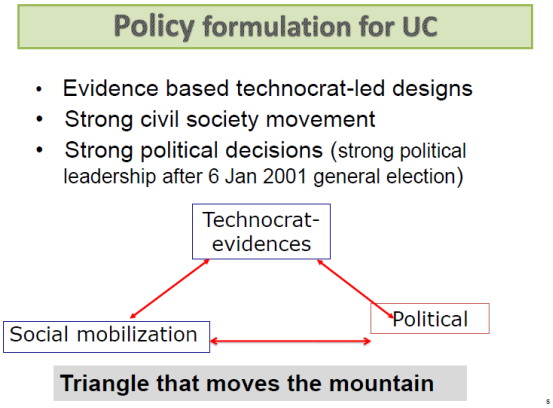
Source: U5MR was analysed from IHME data

Beginning: Three decades ago, in 1972, the Thai government launched the mandatory rural service that required every graduating medical doctor to work for three years in a rural setting. There were also investments made by the Ministry of Public Health (MoPH) to increase the number of nurses by developing nursing colleges. In the early 1980's, the rural health development program was launched to ensure that people in all areas of the country could access health care (Thaiprayoon & Wibulpolprasert, 2017). During this time, the country was in a financial crisis; despite this, the government put a freeze on all investments for urban hospitals and re-directed the funds to build rural hospitals and health centers. Huge efforts were put into training one million "village health volunteers." This rural development programme laid down a foundation for the future of UHC (Thaiprayoon & Wibulpolprasert, 2017).

***Middle*:** There were fundamental investments and structures put in place before the launch of the UHC scheme in January 2002. These investments included addressing gaps in the healthcare sector such as: lack of infrastructure/facilities, workforce development and shortage, health management information systems, and quality issues. Further, the government increased efforts for public involvement with matched support from non-government sectors. In March 2001, civic groups joined forces to collect 50,000 signatures for a new bill on National Health Security to be submitted to Parliament. The success of this bill earned them seats in the special parliamentary commission (Thaiprayoon & Wibulpolprasert,

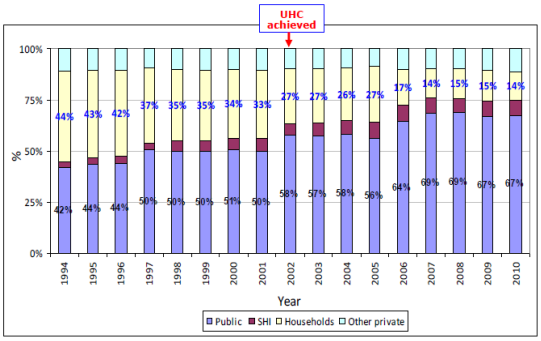
2017). In 2001, the International Healthy Policy Program (IHPP) was established to strengthen capacity for knowledge generation and management. In the same year, the general election provided a window of opportunity to introduce the Universal Coverage Scheme (UCS) reform.
Later, in 2006, HITAP was formed to conduct HTA and economic evaluation for new high-cost health care and technologies (Thaiprayoon & Wibulpolprasert, 2017).

End, Launch of UHC: Strong political leadership and decision-making on strengthening and providing health care for all was the foundation for the launch of the UCS. Qualified health professionals and experts called "champions" in health economics and research promoted and appealed to the government. Additionally, influential civil society organizations and public support provided an added pressure to improve and expand services. Collectively, the three powers – political, social, and intellectual – constitute the "Triangle that Moves the Mountain," (presentation by Mrs. Netnapis Suchonwanich) which has been essential towards achieving an acceptable consensus on UCS policies and processes.



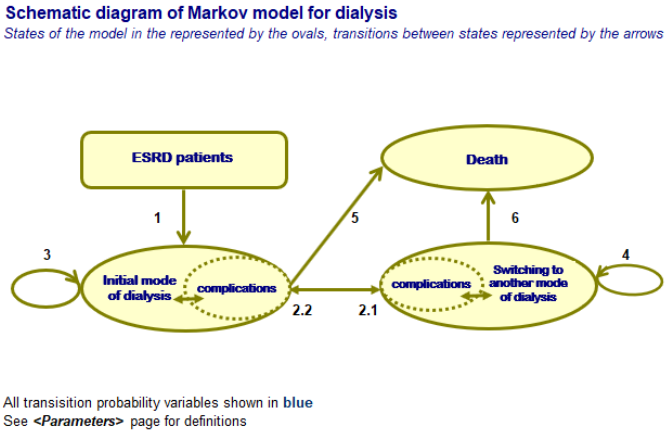
After the launch of the UHC scheme, notable milestones and key successes were seen. For example, the percentage of people who were uninsured decreased from 24.1% in 1997 to 3.2% in 2002. In 1987, 38% of outpatient visits were at regional primary health centers; however, in 2010, this increased to 54%. This shows an overall increase in primary health care utilization. Other successes include reduction in out-of-pocket health expenses and impoverishment from health spending and an increase in consumer and provider satisfaction (Thaiprayoon & Wibulpolprasert, 2017).

Outcome: reduction in out of pocket payment



Appendix 3: The take home exercises are divided into three parts

Part 1: Calculating statistics/parameters (using data previously collected) such as survival analysis of dialysis cohort, transition probabilities, costs (direct & indirect medical and non-medical costs) utilities (Life Years [LY] and Quality-Adjusted Life Years [QALY]), and discounting of costs and outcomes.
Part 2: Constructing the Markov Model. The Markov model is used when there is continuous risk over a period and when important events may occur more than once. The model assumes that a patient will always be in one of a finite number of discrete health states and the event is a transmission between the health states (Sonnenberg, Beck, 2009). Through development of this model researchers will calculate an Incremental Cost-Effectiveness Ratio (ICER) which is calculated by cost/QALY.



Part 3: Probabilistic modelling using the Monte Carlo simulation which is run 1,000 times using random values to get an average from the distribution.
Part 4: The outputs and results

- ICER
- Cost effectiveness acceptability curve is a method of providing a measure on the uncertainty in estimating cost-effectiveness surrounding a choice (Fenwick, Marshall, R. Levy, Nichol, 2006).

The net monetary benefit (NMB) value describes the value of an intervention in monetary terms when a willingness to pay threshold has been identified to gain a unit of health benefit, such as the QALY. An incremental net monetary benefit can be used to measure the difference in benefits between alternative interventions. A positive incremental NMB indicates that the intervention is cost effective compared to the alternative with a given willingness to pay threshold (https://www.yhec.co.uk, 2016).

Appendix 4: Costing of Illness: Study characteristics

Characteristics	National sentinel surveillance for enteric fever study (typhoid fever)	Rotavirus vaccine impact study (Acute gastroenteritis)
Objective	To estimate the total costs for hospitalizations due to typhoid in six secondary care hospitals situated in smaller towns of rural India and in eight tertiary care hospitals in urban India.	To determine the total costs of outpatient and inpatient hospital visits to hospitals for acute gastroenteritis in 11 sites across India.
Study design	Hospital based prospective surveys to estimate costs are conducted in parallel with the ongoing surveillance of typhoid fever in these settings	This costing study is nested within the ongoing surveillance to estimate the effectiveness of ROTAVAC vaccine under conditions of routine use in India.
Study population	Patients who are hospitalized with culture confirmed typhoid fever are eligible to participate in the costing study	Children less than five years of age presenting to the surveillance sites for the treatment of acute diarrhea in the previous 7 days are eligible to participate in the costing study.
Cost components	Direct costs (out-of-pocket expenses) to patients and families due to inpatient care associated with typhoid fever (hospital stay, consultation, procedures and diagnostic tests, medications, devices and services, etc.,.); Indirect costs due to reduced productivity (lost wages)	Direct costs to patients and families due to inpatient and outpatient care; and productivity costs
Main outcome	Costs per episode of hospitalization;	Costs per episode of hospitalization; costs per outpatient visit
Source of data	Family caregivers	Family caregivers
Overall goal	To estimate total costs of illness and to determine whether vaccination will be a cost-effective intervention.	