

LAD CASE STUDY

Burden of Proof: The Hib Vaccine in Bangladesh

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LAD

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Introduction

Bangladesh has a population of 157 million people compressed into a land area roughly the size of Greece. Traditionally an agrarian society based around the Bay of Bengal, the country has rapidly urbanized. The capital city, Dhaka, is a dense metropolis containing approximately 20 million people. Dhaka was built on a wetland region and constant rains saturate the ground, causing the streets to fill with muddy torrents.

Bangladesh is a relatively new state that came into existence in the early 1970s. From the 18th century, the area that is now Bangladesh was part of a colonial region of the British Empire called Bengal. This region was constructed by packaging Bangladesh together with several Indian states, including West Bengal and Assam. British rule continued in the region until immediately following WWII when the Bangladeshi people had a decision to make. The country could push for unification with its geographically closest neighbor, India, or it could try its luck with nascent Pakistan that was being born from the divided British Indian province. Primarily due to religious similarities, (Bangladesh was predominately Muslim in the 1940s and this number has increased to around 90 percent in the 2000s), Bangladesh chose to join Pakistan despite the fact that this new non-contiguous territory would be separated by over 1,000 miles of sovereign Indian land. After joining West Pakistan, Bangladesh become known as East Pakistan. During this period, observers noted drily that only three things held Pakistan together: Islam, the English language, and Pakistan International Airlines... and the airline was the strongest of the three links.¹

Bangladesh has been a troubled, fragile democracy since independence that has been interrupted by three separate military coups. The country has focused its foreign policy attention

Lucas Beard conducted interviews and prepared this case under the supervision of Francis Fukuyama of Stanford University. This case was developed solely as a basis for class discussion. It is not intended to serve as a historical record, a source of primary data, or an illustration of effective or ineffective management

on involvement with multilateral organizations by sending large numbers of troops to serve as U.N. Peacekeepers. The first Prime Minister of Bangladesh even explicitly envisioned the country becoming the “Switzerland of the East” by following that European country’s example of global integration and non-involvement in major international conflicts.²

In 2007, Bangladesh is a dynamic, growing economy bolstered by a massive population and a growing textile and agricultural sector.³ The country mainly relies on the service sector, agriculture (dominated by rice farming), and garment manufacturing. Despite positive growth, Bangladesh is very vulnerable to climate change, hurricanes, and flooding that have derailed growth before. Additionally, political instability has hurt the economy and remains a point of contention for the government and labor organizations. Due to the increasing use of a strike technique known as *hartals*¹, disgruntled political actors have been able to successfully stymie production, and this year, industrial growth of 6.9 percent had dropped from 2006 (8.4 percent) due to labor turmoil in Bangladesh that disrupted shipments.

In the face of this growing, but uncertain, economy, Dr. MD Tajul Bari, the head of the National Expanded Program on Immunization (EPI) in Bangladesh was considering a new vaccine rollout. Dr. Bari’s organization, the EPI, was first launched in 1979 with the goal of providing a unified list of supplements and vaccines to all Bangladeshi citizens. The EPI would add vaccinations to its list it was convinced the vaccine was cost effective, the disease had a significant presence in the country, and the need for the vaccine apparent. The measure of proof that the EPI requires is called the disease burden in the vaccination community—the impact of a disease such as Hib on the population over time. Disease burden can also be defined as the gap between a population's actual health status and a reference status that would exist if the disease were not present.⁴

For example, the tetanus toxoid vaccine was added to EPI’s list in 1993 and the Hepatitis B vaccine in 2003 once the EPI concluded that disease burden of Hep B and tetanus was

¹ A *hartal* is a widespread political protest that is aimed at disrupting political, commercial, and residential life. These strikes are popular forms of civil disobedience often instigated by the political party in opposition to the ruling party.

sufficiently large.⁵ Dr. Bari must decide whether he should support the plan to add the Haemophilus influenza type B (Hib) vaccine to the EPI list and administer this vaccine to all newborn Bangladeshis.

Dr. Bari is a lifelong public health expert with over a decade of experience working with vaccines and infectious diseases. He dresses in traditional academic attire with a large button down shirt draped over his slight frame that billows when the room fans blow in his direction. A clutter of papers, pens, and journals are strewn across his desk, and this highlights the fact that his computer has been relegated to small side table across the room. Dr. Bari is not only the head of the EPI, but also a member of the influential Inter-agency Coordination Committee, National Committee for Immunization Practice, and Science and Technical Sub-Committee, groups that decide vaccination policy in Bangladesh. In these capacities, he is responsible not only for deploying the vaccines but also helping decide which vaccines the country should prioritize. The Science and Technical Sub-Committee (STSC) is the first hurdle a vaccine must pass on the road to universal rollout. The STSC is responsible for determining if a disease actually exists in Bangladesh and whether the disease burden is significant enough to take action.

As a member of the STSC, which includes members of the EPI and other scientific community leaders, Dr. Bari has recently heard Dr. Samir Saha's proposal regarding the Hib vaccine at the group's meeting. Dr. Saha, the presenter, is a well-known microbiologist who possesses the rare talent of being able to bridge the gap between politics and scientific research. Dr. Bari now has to decide whether he should endorse Dr. Saha's vaccine proposal and help add the Hib vaccine to the EPI.

Dr. Bari knows that the GAVI Alliance, a public-private partnership between the Gates Foundation, vaccine providers, and international health organizations, would be able to initially fund the majority of the project, but after that trial period, Bangladesh would have to fund the vaccine program by itself. While the GAVI Alliance application would have to wait until Bangladesh was sure it wanted to add the Hib vaccine to the national vaccination list, informal

communications with the Alliance have produced promising signals regarding the funding options.

Whereas Dr. Bari is generally supportive of vaccination programs, he also must consider the long-term budgetary constraints of the Hib vaccine and weigh these costs versus the other public health issues that require his attention and government funding. Additionally, several studies conducted in Africa and Asia indicated a risk that the Hib vaccine, as a portion of the five-part pentavalent vaccine, could cause serious adverse effects among the inoculated. Dr. Bari must also consider how the Hib disease burden stacks up against these safety concerns.

Public Health in Bangladesh

Public health in Bangladesh has improved drastically over the last thirty years. An integral part of this success story has been the development of a universal vaccination program, the national Immunization Policy, while other contributors to these health improvements can be attributed to increased spending on healthcare, limiting the damage from natural disasters, and more technology and expertise transfers from developed countries. Additionally, Bangladesh's citizens have benefited from economic growth, improved nutrition, and better physical infrastructure.

The life expectancy in Bangladesh hovered below 50 years old in 1960. While other low-middle income countries saw rapid increases in life expectancy during the 1960s and 1970s, Bangladesh, due its specific situation as a separate province of Pakistan, actually saw a decline during this period. Following independence in 1971, life expectancy in Bangladesh increased rapidly, now surpassing the average expectancy of low-middle income countries. See Appendix A for more information on life expectancy over time in Bangladesh.

Currently, in 2007, infant mortality rates are 46 per 1,000 live births, which places the country behind its neighbor Cambodia (45) and just ahead of Myanmar (48).⁶ Bangladesh has been making significant progress on the World Bank's Millennium Development Goal 4 target,

which is to reduce deaths of children under five-years of age by two-thirds from 1990-2015. This goal, along with the other Millennium Development Goals established by the World Bank, are important to Dr. Bari and other in the Bangladeshi public health community.

Despite these important strides, Bangladeshi children still face many health-related challenges. The country has one of the highest incidences of child malnourishment (over 40 percent, depending on the metric) and premature births can often constitute a death sentence with the poor state of neonatal care.⁷ A national UNICEF study found in 2005 that the top four leading causes of death for infants were preterm birth, pneumonia, birth asphyxia, and diarrhea.⁸ Just as Bangladesh tax revenues are tied to agricultural production, so too does children's nourishment rely on good rice crop harvests. Frequent, yet unpredictable natural disasters have affected rice production, reduced food security, and hurt infant health, particularly in the countryside.

Increased spending on healthcare and more focus on public health has contributed to some of the child health successes. From 1998 to 2012 total healthcare expenditures (THE) in Bangladesh have increased 77 percent in nominal terms and the ratio of THE to the country's total GDP increased from 2.6 percent to 3.3 percent, a 27 percent boost.⁹ See Appendix B for more information on healthcare spending in Bangladesh. These expenditures increased to both public and private sector sources, and included programs such as immunizations, early childhood healthcare, and community insurance schemes. The majority of the health care budget in Bangladesh is spent on clinical services. As the economy grew, it became prudent to invest some of these earnings into healthcare, but as political unrest and natural disasters affected GDP growth outlooks, additional public health spending could prove costly for Bangladesh.

The history of immunization in Bangladesh has helped drive widespread improvements in Bangladesh's public health. Immunization, through the Immunization Policy and the EPI, has been called "one of Bangladesh's greatest public health success stories," and reportedly prevented approximately 2 million deaths from 1987-2000.¹⁰ The government has a history of working with foreign donors to successfully deploy a universal vaccine. With GAVI Alliance

support, Bangladesh was able to introduce the Hepatitis-B vaccine in a phased manner starting in 2003 with near universal coverage achieved in 2005. This rollout is considered early for low-income countries (India began phased Hepatitis-B distribution in 2007).¹¹ During this phased rollout of the Hepatitis-B vaccine, the GAVI Alliance also included funding for field and community health worker training. Due to these vaccination-related successes, there exists strong political will from both major political parties to implement further vaccine public health programs.¹² Since joining the EPI, Dr. Bari has overseen the successful launch of several vaccine programs through partnerships with foreign governments and multilateral organizations.

The Hib Vaccine

The *H. influenzae* bacterium is a member of the Pasteurellaceae family that generally lives in the mucosal areas in the respiratory tract of mammals. *H. influenzae* will sit in the rear of an individual's throat and, for the majority of those infected, will not produce any adverse reactions. *H. influenzae* has six distinct strains that are identified with letters a-f; type b is the most strain that causes most serious illness in people.¹³ The bacteria is referred to as an opportunistic pathogen, and these organisms only become pathogenic following an exogenous stressor inflicted on their host (such as disease, wound, medication, prior infection, immunodeficiency, and aging).⁴ While for most people, the presence of Hib does not have any adverse effects, in individuals with lowered immune systems, including children aged 5 and younger, the bacteria can cause illness including life threatening meningitis and pneumonia. To the public health community, one of the most notable features of Hib disease is its age-dependent nature. Hib disease is not common beyond 5 years of age. Thus, Hib vaccine needs to be administered to infants to be effective.

Hib exists only in humans, and is transmitted through the air by respiratory droplets from individuals carrying Hib bacteria. Hib was universally distributed throughout inhabited areas in the world, and prior to the successful rollout of Hib vaccines, the bacterium was the leading

cause of bacterial meningitis and other invasive bacterial disease among young children. Approximately one in 200 children developed an invasive Hib disease.¹⁴

The diagram below illustrates the disease cycle of Hib. Starting from the left, the bacteria infects the child; the child then has a chance of getting an invasive disease, including meningitis (teal); the symptoms spiral away from the disease; and the detection method for each disease hovers above the disease (blue). The complicated web of symptoms and diseases demonstrates just how difficult it is for public health professionals to know whether Hib is the underlying problem behind a number of childhood illnesses.

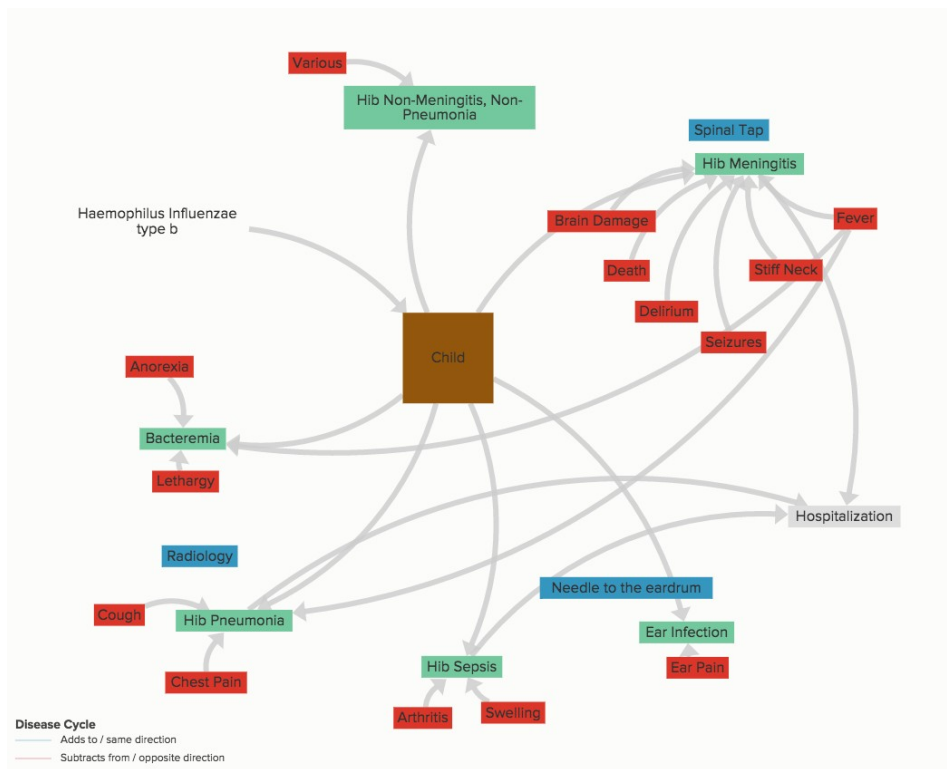


Figure 1 - Disease Cycle. Figure: Compiled by the author

Once the bacteria infects the child, depending on the specific conditions, this infection can lead to a variety of other diseases ranging from meningitis (most severe) to an ear infection. Infection is usually asymptomatic; however, the invasive disease can be life threatening and involve different invasive disease syndromes. Of the serious diseases commonly caused by Hib infection, the most common is pneumonia (58 percent). Please see Appendix C for more

information on the frequency that these illnesses occur in children who have been infected with Hib.

History of Hib Vaccine

Haemophilus influenzae type B, despite its name, is not related to the influenza virus, which is responsible for the common cold. Hib was originally found in a group of patients during an influenza outbreak in 1892, and scientists mistakenly believed that Hib was causing the flu-like symptoms. While this is incorrect (Hib is a bacteria while influenza is a virus), Hib has maintained its original name.

Hib was first fought with a polyribosylribitol phosphate (PRP) bactericidal vaccine in the 1970s. This vaccine was only approved for use in children aged 18-24 months, and was not effective when administered to children younger than 18 months old. This PRP vaccine was not a widespread success due to the fact that it wasn't suitable for the youngest age group, which included children bearing most of the disease burden.

In 1987, a new vaccine was developed that was effective even in young children. This vaccine piggybacked on the PRP vaccine by chemically conjugating the vaccine to carrier proteins, thereby producing a more robust immune response. The new vaccine, named the Hib conjugate vaccine, is remarkably effective, and is the vaccine being considered for rollout in Bangladesh. The conjugate vaccine not only has the ability to stop infectious diseases, it also affects Hib colonization which hinders the spread of the bacteria. After exposure to the Hib conjugate vaccine, individuals no longer carry a dormant version of the bacteria, and this reduces the risk of spreading the bacteria to others.

Until the 1980s, Hib was the leading cause of a variety of illnesses, including meningitis, sepsis, and other life threatening bacterial infections in infants and young children even in developed countries, such as the United States. Following successful field trials, this vaccine was

rapidly deployed in developed countries. In the United States, the vaccine caused cases of invasive Hib infections to drop from approximately 20,000 to 29 per year. This eradication of the Hib disease in industrialized areas has been characterized by the *Journal of Clinical Infectious Diseases* as "arguably the major success story in pediatrics in the last 2 decades." Yet, it would take many years to achieve this same success in the developing world.

Since the 2000s, the GAVI Alliance and WHO advocated for the use of a pentavalent vaccine format that combined five common vaccinations into one immunization due to a combination of cost savings, easier distribution and supply chain issues, and increased coverage. The pentavalent format combines individual vaccines for Hib, hepatitis B, diphtheria, pertussis, and tetanus into a single package.¹⁵⁶ Despite the positive aspects of using a combined vaccine, potential health problems accompanied the deployment of a vaccine. Troubleshooting health problems from a combined vaccine can be much more difficult than for a singular vaccine due to the difficulty of pinpointing which vaccine among the five was responsible. By combining all five vaccines into one immunization and administering this in a new country, public health officials limit the amount of individualized testing that would be possible with single vaccinations.

History of Hib in Bangladesh

The most significant published work on Hib's disease burden in Bangladesh was Dr. Saha's examination of children with meningitis starting in the 1990s. Dr. Saha is a trained microbiologist and the head of the microbiology department at Dhaka's Shishu Hospital (children's hospital). Children came to that hospital with a variety of illnesses and maladies, however, Dr. Saha, who was keeping meticulous records of H. Influenzae cases, became convinced that the bacterium was responsible for more children's deaths than anyone imagined. Yet, many Bangladeshi health professionals did not believe agree. There had been no published evidence of the infection and no reason for clinicians to identify Hib as the cause of meningitis and pneumonia cases or other childhood maladies. While the developed world had long before

began to administer the relatively expensive Hib pentavalent, developing countries, such as Bangladesh, had not been convinced of Hib's disease burden, and chose not to pursue the vaccine.

Dr. Saha began his laboratory-based studies of Hib in 1987 with a longitudinal research project that identified 852 cases of meningitis at his hospital from 1987 - 1994. Due to his microbiology training and attention to detail, he was able to determine through lumbar punctures that 47 percent of the cases involved a strain of H. Influenza. Further analysis showed that 98 percent of these strains were of the type b variety, which led Saha to begin realizing the massive disease burden that Hib was having on the Bangladeshi infant population. This longitudinal study was a great start to establishing the proof necessary to understand Hib's disease burden, but Dr. Saha knew that it wouldn't be enough to convince all of the policymakers.

In 1997, Dr. Saha published his findings in the *Annals of Tropical Paediatrics*, concluding that this research “strongly supports the need for a large-scale Hib vaccination for young children. However, such nationwide intervention will probably need to be based on a prospective and population-based surveillance of H. influenzae infections.”¹⁶ Saha knew at this early stage that the political community would need more proof of a Hib problem than just one study at one hospital. He began to gather additional information through a follow-up case-control study. A case-control study, common in medical research, assigns a group of individuals to a control group (unchanged conditions) and a case group (a group of people who are inoculated with the Hib conjugate vaccine). Dr. Saha would then use this information to determine the efficacy of the Hib vaccine.¹⁷

This case-control study was much larger and required coordination between several hospitals, including the Centre for Child and Adolescent Health at the International Centre for Diarrheal Disease Research, Bangladesh (“ICDDR,B”), where Dr. Shams El Arifeen was the director of the Child Health Program. Dr. El Arifeen was an influential public health expert who had experience working with international public health organizations.

Dr. Saha and Dr. El Arifeen studied a birth cohort of 68,000 children in Dhaka. Health centers in the city were randomly assigned to vaccinate with vaccine #1, which included the diphtheria, pertussis, and tetanus vaccines or vaccine #2, which had vaccines for Hib, diphtheria, pertussis, and tetanus. Vaccination started in June 2000 and continued until November 2001. These health centers were located throughout the city, some in the slums and some in the richer neighborhoods, but none were outside of Dhaka. The researchers discovered that those children who had received the Hib vaccination were 34-44 percent less likely to get X-ray proven pneumonia and 71-83 percent less likely to get bacterial meningitis. These two diseases were seen as the most severe Hib impacts, and this study appeared to show that Hib in Bangladesh had a significant and demonstrable disease burden and could be prevented using a Hib conjugate vaccine. The case-control study was published in 2007 in the widely read *Pediatric Infectious Disease Journal*.¹⁸

Both the original longitudinal study and the subsequent case-control research had convinced Dr. Saha and Dr. El Arifeen that Hib's disease burden was sufficient to warrant a universal vaccine in Bangladesh. Dr. Saha knew that getting policy made was not only a matter of presenting academic research to a subcommittee, but it was also about connecting to the political sphere in a more personal way. He was known in the community for his clout among the members of the Bangladeshi bureaucracy and his ability to match public policy initiatives with emerging public health research. As policymakers in Bangladesh have to continually manage scarce resources to bring about maximum impacts, Dr. Saha knew that he would have to prove the disease burden beyond facts and figures. To this end he enlisted the help of the influential Bangladesh Pediatric Association (BPA). With the support of clinicians, he believed that in his presentations to Dr. Bari and the subcommittee, he could place a face to the research statistics. As a member of the BPA, Dr. Saha was able to present his findings first to the organization before bringing the evidence to the EPI and Dr. Bari.

The Case for Universal Hib Vaccine Deployment in Bangladesh

Dr. Saha's presentation to Dr. Bari and the Technical Subcommittee focused on establishing a sufficient evidence of disease burden so that the Hib conjugate vaccine would become part of Bangladesh's National EPI. Dr. Bari knew that understanding the disease burden of any health problem could be difficult. Particularly in developing countries, discovering the cause of death can be problematic, as technicians do not often have access to good lab equipment or funding to run a full spectrum of post-mortem tests. Hib as the underlying cause of death is especially difficult to determine because its effects (meningitis, pneumonia, etc.) can also be caused by other infections. Hib is just one of many causes of meningitis and other ailments, and these diseases themselves may be hard to spot. Other than a complicated lab test to confirm, the traditional symptoms and signs of acute meningitis may be absent in very young populations, which can make accurate diagnosis, let alone understanding disease burden, extremely difficult.¹⁹ While Dr. Bari was impressed with Dr. Saha's research and the support he had garnered from the BPA, he still had questions regarding the disease burden outside of the capital city, as well as what the opportunity cost would be for pursuing the Hib vaccine as opposed to focusing public health efforts on nutrition or prenatal care. The 2015 World Bank Millennium Development Goal deadline loomed large, and to accomplish a two-thirds reduction in infant mortality, Dr. Bari knew they needed an important intervention.

Bangladesh has the infrastructure to accommodate an additional universal vaccine rollout. The majority of children aged 1-2 have access to immunization services, and approximately 84 percent of all children in that age group have been vaccinated (although not with any form of Hib vaccine).²⁰ An additional vaccination could easily be tagged onto the existing vaccination schedule and immediately reach at least 84 percent of Bangladeshi infants. Adequate training and provisions for cold storage, prerequisites for GAVI Alliance funding, had already been demonstrated during the earlier Hepatitis B vaccine partnership. Dr. Bari knew that the country had the capacity to rollout the Hib vaccine with the EPI infrastructure.

The universal nature of a full vaccine rollout in Bangladesh can also be seen as a way of addressing poverty and inequality, Saha had argued. The Health Economics Unit of the Ministry of Health and Family Welfare claimed that additional spending on universal healthcare projects represents a redistribution of resources towards the poor. Despite these claims, there is evidence that in Bangladesh, members of poor communities are unlikely to use hospital-based services, and instead prefer home or neighborhood care.²¹ Understanding and accounting for these distribution difficulties would affect the cost of any universal vaccine rollout that looked to address poverty and inequality.

From an international donor perspective, the World Health Organization, World Bank, and GAVI Alliance were all generally very supportive of mandatory Hib vaccination programs. WHO released a position paper in November 2006 that described the significant disease burden of Hib in developing countries and recommended that governments include the Hib conjugate vaccine in their national immunization programs. The organization noted that laboratory confirmation of Hib can be very difficult and that hospital estimates of the disease burden “consistently underestimate the total burden of the Hib disease.” The report also mentioned that as a consequence of routine childhood vaccination programs in developed countries, the disease has been eliminated from those countries. Finally, WHO warned that the “lack of local surveillance data should not delay the introduction of these vaccines.”²²

Funding the Vaccine

The GAVI Alliance is a key player in helping developing countries to make choices on immunizations and on funding inoculation programs. GAVI is a public-private joint venture founded by a Gates Foundation grant that includes international health organization partners, including UNICEF and WHO, as well as large pharmaceutical companies like Sanofi Pharma and Serum Institute of India Ltd. The GAVI Alliance works by partnering with local government ministries to provide information, education, and financing for vaccination programs. In 2000, the GAVI Alliance began supporting Hib vaccine programs in eligible countries (Bangladesh

among them). In 2005, the GAVI Alliance earmarked \$37 million in funding to set up the Hib Initiative explicitly to expedite the use of the Hib vaccination to prevent childhood meningitis and pneumonia in developing countries.²³ To be GAVI-eligible, a country's GNI per capita in 2003 must be less than \$1,000. Bangladesh easily met this requirement. See Appendix E for more information on GAVI-eligibility and Bangladesh's GNI per capital.

In order to receive support for a new vaccine from the GAVI Alliance, Bangladesh would be obligated to finance a portion of the cost. In 2007, Bangladesh is classified as a "Poorest State,"²⁴ allowing it to pay just \$0.20 per dose for the first vaccine. For more information on GAVI Alliance co-funding prices, please see Appendix H. This co-financing pricing scheme will be valid from 2007 until 2010, at which point the GAVI Alliance would review their finances for the 2011-2015 period. A GAVI Alliance statement, published with US AID in 2007, advised GAVI-eligible countries to prepare for "expected increase in co-payments in 2010."²⁵ Therefore, a country that agrees to GAVI Alliance support in 2007 would be obligated to shoulder the higher price starting in 2010 without knowing how much higher those prices might be. The GAVI Alliance anticipates that most countries would be responsible for paying the market rates for the vaccine by no later than 2015.

The 2009 birth cohort (the estimated year of Hib vaccine rollout, assuming approval by the Government of Bangladesh and GAVI Alliance) is anticipated to include 4.03 million newborns. With the initial co-financing (\$0.20 per dose), plus additional healthcare support, deployment, and monitoring costs, Bangladesh would expect to pay approximately \$3 million for the Hib vaccine. Currently, Bangladesh spends approximately 3.3 percent of its total GDP (total GDP \$79.61 billion) on healthcare costs, but \$32,026,000 in 2007 on its current immunization plan that deploys nine vaccines and supplements across the country. This represents a fraction of a percent of total government revenues (\$5.6 billion government revenue in 2007). The expected \$3 million Hib vaccine burden would represent approximately 9 percent of the total annual vaccination budget.²⁶ Despite these high costs, Dr. Steve Luby, a public health expert at Stanford University, claimed that "Bangladesh was already paying for a three-part vaccine [that did not

include the Hib vaccine]. However, with GAVI alliance support, the new pentavaccine would be cheaper. More for less.”²⁷

The GAVI Alliance expected that Bangladesh would begin paying full market rates for the vaccine by 2015. The GAVI Alliance funding was anticipated to give Bangladesh a breathing space during which time vaccine cost was expected to drop so that Bangladesh could afford to immunize without assistance. In 2007, the Hib pentavalent vaccine was \$3.20. Bangladesh expected this price to drop to \$2.90 by the time all of the applications were approved in 2008. The total annual cost for the vaccine would then be $\$2.90 \times 4.03 \text{ million} = \$12,000,186$. Of this \$12 million, the GAVI Alliance would cover 79 percent with Bangladesh funding 21 percent. During this period of GAVI Alliance support, Bangladesh projected that Hib vaccine costs would drop further, from \$2.90 in 2007 to \$2.65 in 2009 with additional price decreases expected. For more pricing information and the anticipated pricing schedule, please see Appendix G.

The Case Against Hib Vaccination

There were many reasons why the Hib vaccine did not have a widespread roll out in developing countries and Dr. Bari wanted to understand why not. Many developing countries that decided against deploying the Hib vaccine did so for the following reasons: lack of data on burden of disease or vaccine impact; inadequate vaccine supply; upfront and long-term vaccine costs; emerging evidence that the pentavalent vaccine caused harm to patients; and more attractive alternative uses of public health money.²⁸

First, although Dr. Saha was convinced that Hib was a clear and present danger for Bangladeshi children, Dr. Bari knew that view was not universal. Dr. Saha had some evidence of Hib infections in the Dhaka Shishu hospital and its surroundings but had not conducted a single study outside of the capital city of Dhaka. These two studies (one published in 1997 and the other in 2007) had not been not replicated outside of Dr. Saha’s labs and he remains the only researcher to build any significant evidence on Hib in Bangladesh. To make policy decisions for

the entire country through a large-scale mechanism such as the EPI, Dr. Bari wanted to be sure that Hib was a widespread, universal problem that needed a universal solution. Additionally, despite WHO's statements that one nation could rely on data from other countries to understand Hib's disease burden, it was difficult to see how knowledge of a disease in Ethiopia could inform on-the-ground decisions in Bangladesh. Additionally, many public health officials believed there was less Hib disease in Asia. Dr. Bari knew of a 1998 study in Indonesia found that the Hib incidence rates were unknown in Indonesia, and consequently the Hib vaccine was not included in the routine vaccine schedule.²⁹

Second, as worldwide demand for Hib vaccines increased, especially from countries with large populations such as Bangladesh, there were concerns that global supplies would prove inadequate. This was especially true in developing countries where the users might not be able to afford the full cost of the vaccine. International companies, such as Novartis, typically do not sell large quantities of their vaccines to developing countries, citing the need to cover their research and development, and manufacturing costs. This meant that developing countries in need of a vaccine would have to rely on NGO partners, like the GAVI Alliance, to convince Novartis and others to manufacture/license vaccines to poorer countries.³⁰ The two supply bottlenecks at the manufacturing level and at the advocacy and lobbying level complicate a quick, universal Hib rollout.

Third, the GAVI Alliance's funding requirements raised questions about the vaccine program's long-term sustainability. While the Alliance and the Hib Initiative agreed to co-fund the initial Hib vaccine rollout, after this initial period, Bangladesh would need to pay for the vaccinations through other channels. Locking a country into long-term funding obligations at a time when natural disasters and political turmoil abounded involved risk. The GAVI Alliance offer felt like it might be a good short-term option, but it could have costly long-term funding consequences.

Furthermore, despite successful program collaborations in the past, Dr. Bari understood the concerns that Bangladesh was delegating public health choices to members of the

international aid community. For example, once Bangladesh contracted with the GAVI Alliance funding for the Hib vaccine, any decision to switch from a pentavalent variety to a single vaccine container, would have to be “updated, reviewed, and endorsed” by the Interagency Coordinating Committee (ICC) and then submitted to the GAVI Secretariat for approval.³¹ Increasing the level of bureaucracy (already considered a problem in Bangladesh) by adding a foreign decision making apparatus could potentially create an unwieldy public health structure in Bangladesh.

Dr. Bari also considered the fact that Dr. Shams’ organization, ICCDR,B, is known in the public health community as primarily dedicated to fighting cholera. Due to Dr. Shams’ key involvement in the second disease burden research study, Dr. Bari was reminded that ICCDR,B is still housed in the medical facility known as “Cholera Hospital.” Since cholera was a disease that could be effectively fought with vaccines, some public health observers have viewed ICCDR,B as an organization that regards vaccines as the solution to most problems, even if that is not the optimal means of treatment.³²

Additionally, Dr. Bari knew that the health community would be concerned about the potential negative health impacts of using the pentavalent vaccine that the GAVI Alliance prefers. That vaccine was initially rolled out in Sri Lanka in a pilot with the expectation it would be used more broadly in Asian countries in 2007. However, early reports linked the vaccine, manufactured by Crucell (the same pharmaceutical company interested in making Bangladesh’s vaccine), to serious injuries and deaths, which prompted the administration to suspend the vaccine program.³³

Hib Vaccine Introductions Abroad

While most developed countries have already mandated Hib vaccines as part of their national immunization plans, the uptake in developing countries has been much slower. In 2004, only 13 of 75 (17 percent) developing countries that were GAVI-eligible had rolled out a national Hib immunization program.³⁴ Of these 13 countries, eight are in Africa, including a

successful, decade-long program in Gambia, and five are in the Americas; no Asian countries have introduced a universal Hib vaccine.³⁵ Two important reasons may explain this lag. First, the developing countries saw no clear proof of Hib's disease burden. Second, some governments worried about the relative cost of the vaccination program. The Hib vaccine is not cheap, and especially when the vaccine was first being developed, it was out of reach for many low-middle income countries.

India is a relatively analogous country to Bangladesh in terms of culture, public health, location, and infrastructure. Adjacent to one another, the two countries have large, dense populations with limited resources and similar development metrics. An early Hib disease burden study performed in India from 1993 to 1997 found that while Hib in India was a “prominent preventable cause of death... additional prospective studies are needed to better define the clinical and economic burdens of preventable Hib disease in India and Asia and to define its incidence in the population.” A further community health investigation in India, conducted between 1997 and 1999, found a Hib meningitis incidence of just 0.007 percent, which led the WHO coordinator of India's EPI to claim that the Hib vaccine could not be recommended for routine use in India due to the lack of proven disease burden.³⁶ Microbiologists were aware that Hib is a very difficult organism to culture, and there exists a strong potential for false negatives when examining patients for Hib.

In 2006, the Indian government had planned to support a multisite Hib vaccine probe study, but stopped planning for this vaccine at the same time that WHO recommended global use of the vaccine.³⁷ Compared to Bangladesh, which sees collaboration with multinational NGOs and international organizations as a lynchpin of its foreign policy, India has a strong history of generating and using local evidence to inform decision-making and not relying as much on foreign assistance. Currently, India has some Hib vaccine coverage through private clinics, but no publicly funded, universal programs.

The Vaccine Decision-Making Structure in Bangladesh

The process for deploying a vaccine in Bangladesh is highly bureaucratic involving a series of three nested committees. Once the first committee endorses a vaccine proposal, then the proposal moves up the ladder and must be presented to the second committee, etc. Only when all three relevant committees have greenlighted use of the vaccine does the application process for outside funding begin. Many different stakeholders are represented in these committees and several members sit on all three committees, including Dr. Bari. The following timeline shows how a vaccine would be approved for distribution in Bangladesh with GAVI Alliance funding.

1. Dr. Saha Begins Research into Hib
2. Academic Publication Illustrates Disease Burden
3. **Science and Technical Sub-Committee (STSC) Reviews Disease Burden Information**
4. **STSC Forwards Recommendation to Inter-agency Coordination Committee (ICC)**
5. **ICC Approves the Recommendation and Forwards to National Committee for Immunization Practice (NCIP)**
6. **NCIP Approves the Recommendation and Applies for GAVI Alliance Funding**
7. GAVI Alliance Revises Vaccine Application and Sends Back to NCIP
8. NCIP Includes MoHFW in Revision Process and Re-submits Application to GAVI Alliance
9. GAVI Alliance Approves Application and Vaccine is Introduced³⁸

BOLD: Committees where Dr. Bari is a member

In general, the STSC assesses the viability of the proposal (whether Bangladesh has the capacity to rollout the vaccine), determines if there is sufficient disease burden, and provides the primary point of contact for the scientists. Dr. Saha presented to the STSC, and this was the first

hurdle. The STSC submits the proposal to the ICC, which is primarily a policy committee comprised of numerous non-health members, including the Ministry of Finance. After approval, the ICC will forward the application to the NCIP. The NCIP is in charge of deciding which vaccine should be rolled out and assessing the opportunity cost of supporting one vaccine over another. For more information on the healthcare decision making structure in Bangladesh, please see Appendix F.

Even though the NCIP is nominally above ICC, which itself is above the EPI, public health practitioners knew that most of the important decisions were made at the EPI level. The EPI is more of an administrative body and not a formal part of the vaccine application process, but the EPI's decisions held significant sway with both the ICC and NCIP. Once the EPI and the head of the organization, Dr. Bari, were convinced of the Hib disease burden, there was an expectation that the vaccine program would be approved by the higher-level, more generalist bureaucratic bodies.

Due to the fact that Bangladesh is a GAVI-eligible country and that the Ministry of Health and Family Welfare has authority over its own budget (and not the Ministry of Finance), once the public health community was convinced of the need for a Hib vaccine, approval to fund the vaccine program would likely follow.

Bangladesh's Political and Civil Servant Background

In Bangladesh, the political and civil service structures affect the deployment of public health programs. Because public health decisions are made by a combination of elected policymakers and unelected civil servants, the structures behind these two groups also influence public health choices.

Bangladesh is a unitary government where political and economic power is highly centralized in Dhaka. Compared to India, where federalism has enshrined powerful autonomy with regional states, Bangladesh's individual divisions (the major administrative unit) outside of Dhaka do not have a strong influence on policy. Practically, this means that once policymakers within Dhaka make a decision regarding public health it will be implemented in all the outside divisions. The division encompassing Dhaka comprises over 30 percent of the country's total population. This centralized approach to thinking in the capital city influences academia, international organizations, and research, as well as policy. When Dr. Saha analyzed Hib's disease burden in Bangladesh, he only focused on Dhaka.

Corruption in Public Service in Bangladesh

Bangladesh is considered one of the most corrupt countries in the world. One estimate places the losses due to corruption at \$1.5 billion annually. This corruption, defined as the abuse of public power for private gains, affects all levels of the Bangladeshi civil service from lowly tax collectors to elected officials. Despite rules outlined in the Government Servants (Conduct) Rules, 1979, prohibiting accepting "gifts" and other sources of corruption, the country continues to operate under a system where getting things done in government requires greasing the wheels. According to Transparency International's 2007 survey, 66.7 percent of Bangladeshi citizens have experienced corruption within the preceding 12 months.

The hiring and appointment process for filling civil service positions in Bangladesh is heavily influenced by nepotism, clientalism, and outright corruption. Members of the international public health community have noted that their Bangladeshi counterparts will often temporarily purchase their position. The position is then resold to a new Bangladeshi civil service member after approximately one year. The civil servants who hold the decision making power of appointing and hiring therefore see these positions as assets from which they can extract favors and payments. In addition to the fact that corruption undermines meritocracy in the Bangladeshi civil service, it also has produced high turnover in key positions. The revolving cast

of public health officials erodes programming continuity and complicates efforts of donors and government officials to identify and nurture talent. On the other hand, rapid turnover within the public health space means that ambitious officials must move quickly to accomplish anything meaningful during their short tenures at each position.

Corruption in Bangladesh's civil sector also affects its willingness to partner with international organizations. Pay for civil servants is comparatively low compared to that for private sector NGO jobs. Even elite officials in Bangladesh may earn 4x - 6x less than their private sector counterparts. As a result, partnerships with international organizations like GAVI Alliance and WHO expose government employees to large sums of money and Bangladeshi public health officials have observed that low-level corruption is quite common.

During the 2003-2005 Hepatitis-B vaccine distribution period, the GAVI Alliance paid for field training of public health workers. According to knowledgeable academics, these training sessions were known sources of petty corruption. The trainers would reportedly request funding for 12 or 13 trainees when only 9-10 participated with the trainers pocketing the extra funding.. In Bangladesh, these types of petty corruption were common and expected in any large-scale public health initiative.³⁹ These small payments, nominally illegal in Bangladesh, may incentivize the adoption of public health partnerships with international organizations.

The Current Political Situation

Bangladesh is currently in a state of political crisis. A caretaker government backed by the military has controlled the government since 2006 with a new elections expected in 2007. After Bangladesh's independence from Pakistan in 1971, contentious elections have been common with intense rivalries among the major parties: the Awami League, the Bangladesh National Party (BNP), and the Jatiya Party. That tension is the source of recurrent conflict, violence, imprisonment, and public discord. When the planned national election was cancelled in late 2006 due, in part, to the discovery of 12 million fake names on the voter roll and

continued street battles between political partisans, the *BBC* reported that “the ceaseless bickering and violent confrontations have meant that the Bangladeshi economy – already fragile – is coming under further pressure.”⁴⁰ Dr. Bari understandably worries that this might not be the best time to raise concerns about vaccinations and long-term payment plans.

Conclusion

After hearing Dr. Saha’s presentation advocating for the inclusion of the pentavalent Hib vaccine, Dr. Bari now must decide whether to support adding the Hib vaccine to the National Immunization Policy. Among Dr. Bari’s considerations are whether the disease burden of Hib is large enough (and widespread enough) to warrant a nationwide intervention, if the pentavalent vaccine is safe enough for use, and if the GAVI Alliances funding partnership will benefit the country in the long-term. For a poor country such as Bangladesh, there is a significant opportunity cost with any public health choice, and Dr. Bari is concerned that if they put time and energy behind the Hib vaccination, other needs, including nutrition and reproductive health, may fall through the cracks. Furthermore, Dr. Bari wonders if the policymaking direction for public health issues should be set by outside NGOs and not internally. With the final meeting of the STSC fast approaching, Dr. Bari must weigh these varied factors and present his recommendation to the subcommittee.

Appendix A – Life Expectancy

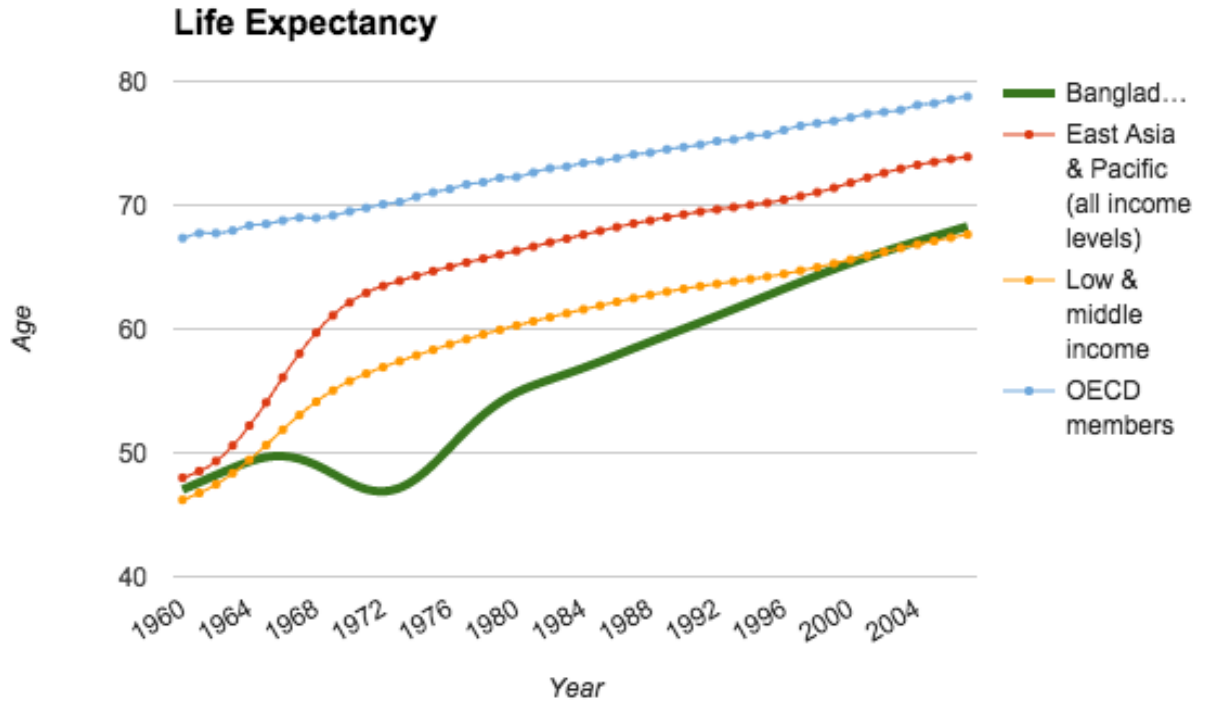


Figure 2 - Life Expectancy in Bangladesh, Data: WHO, Figure: Compiled by the author

Appendix B – Total Healthcare Expenditure

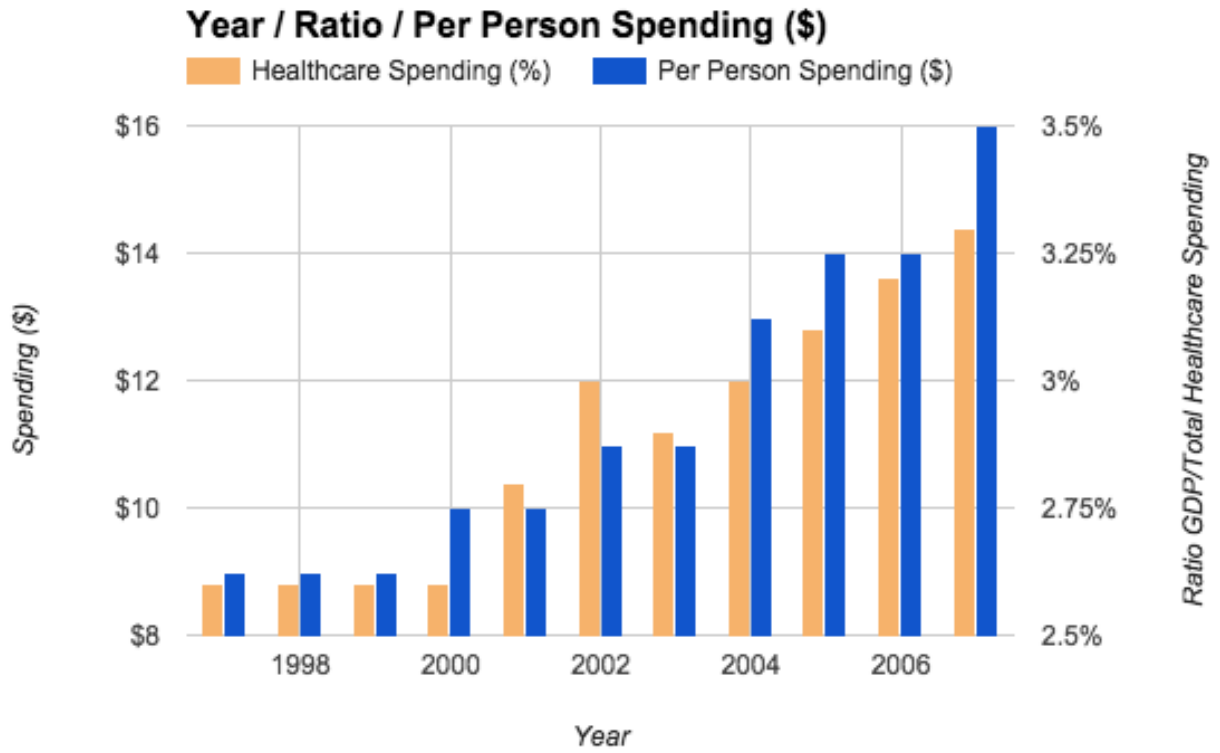


Figure 3 - Total Healthcare Expenditures, Data: WHO. Figure: Compiled by the author

Appendix C – Hib Disease Frequency

Type and Frequency of Hib Disease	
Disease	Frequency
Pneumonia	58%
Bacteremia	31%
Meningitis	7%
Hib Non-Meningitis, Non-Pneumonia	4%

Figure 4 - Hib Diseases...Source? Data?

Appendix D – GAVI Eligibility

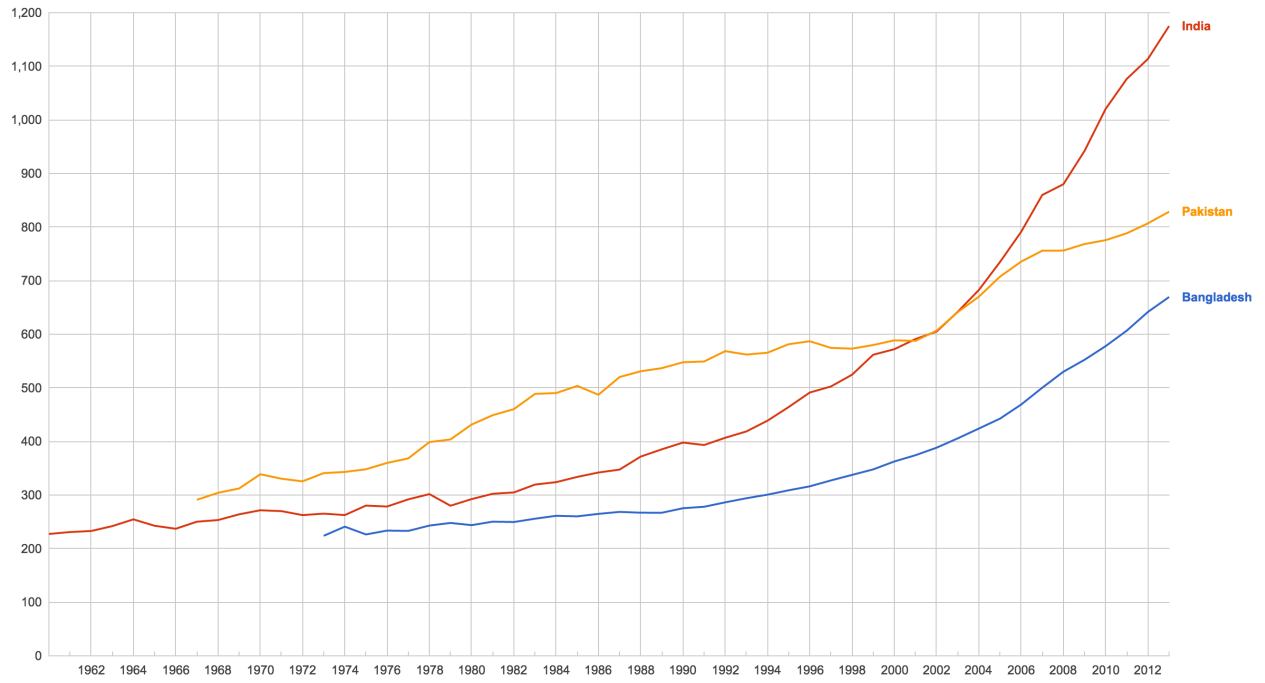
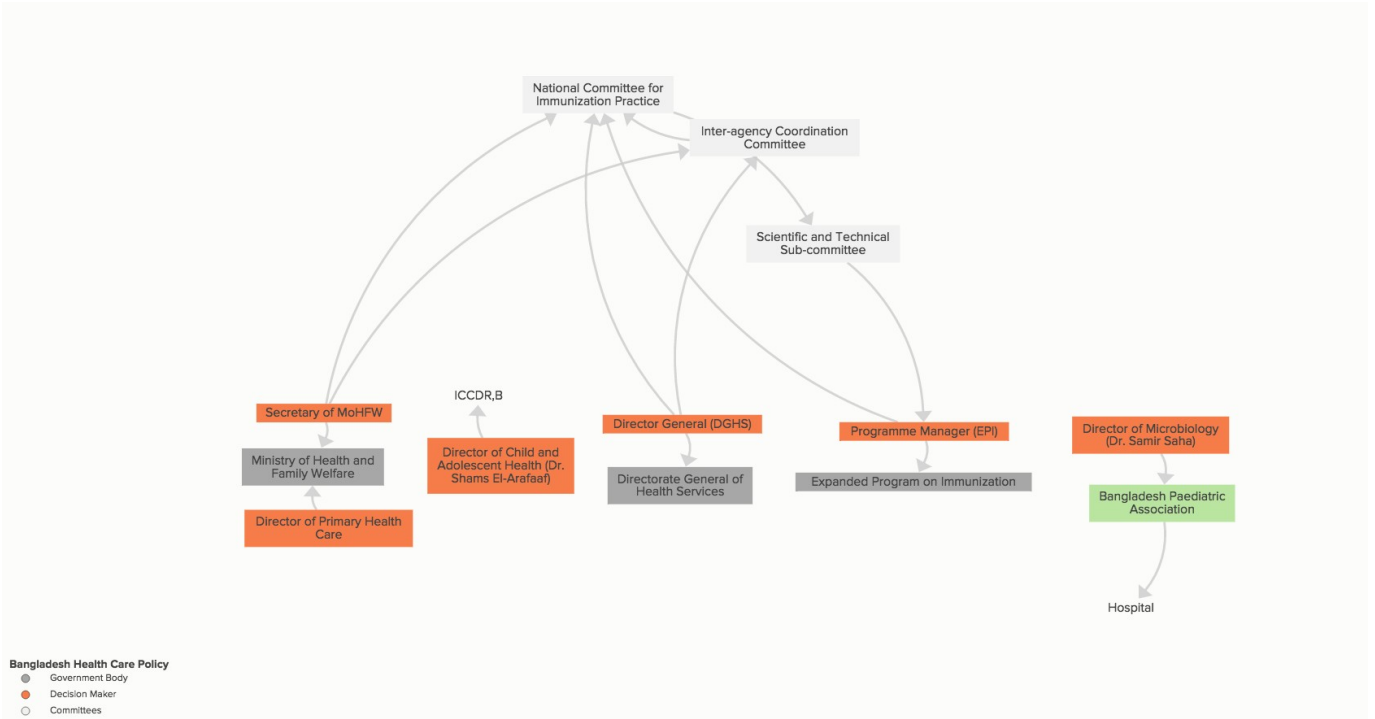


Figure 5 - Bangladesh GNI per Capita. Data: World Bank. Figure: Compiled by the author

Appendix E – Decision Making Structures I



Appendix F – Decision Making Structures II

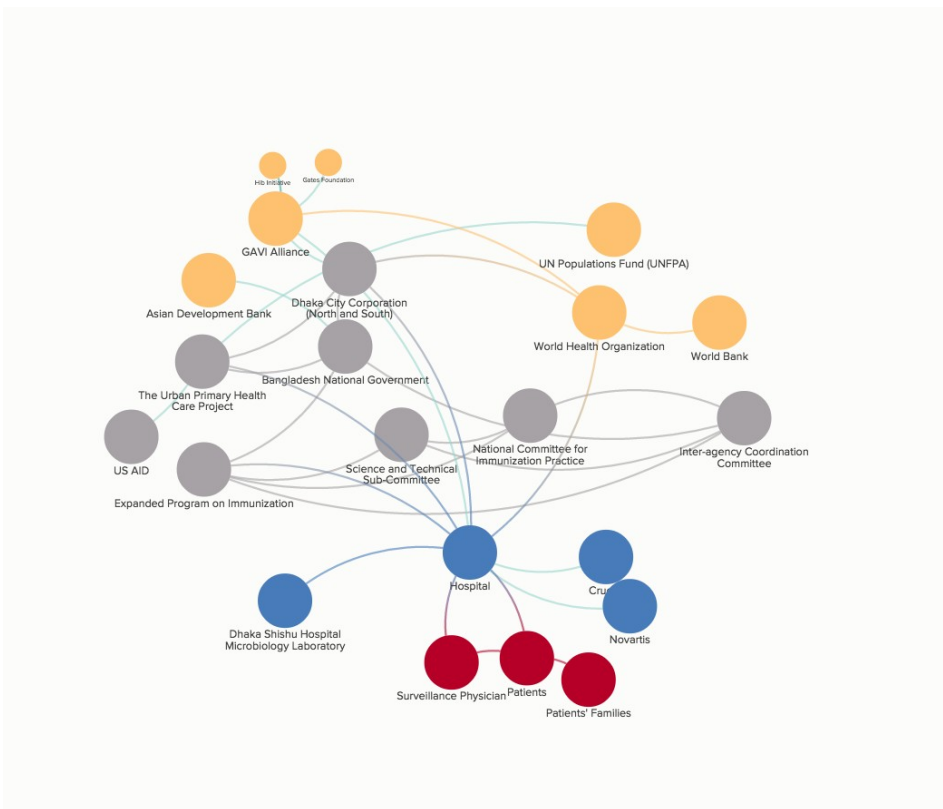


Figure 6 - Stakeholder System. Figure: Compiled by the author

Appendix G – Hib Vaccine Pricing

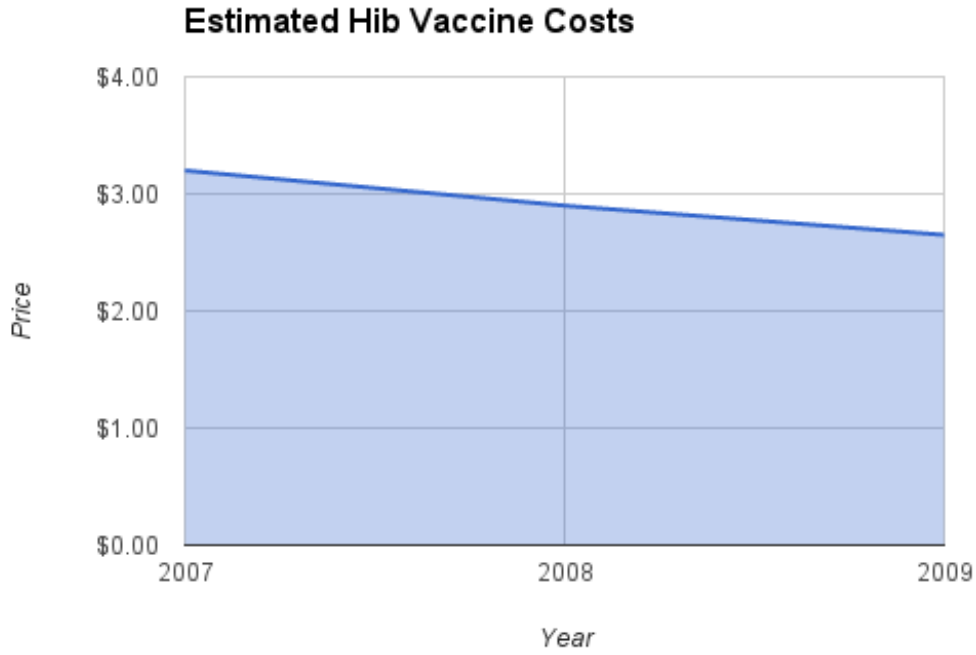


Figure 7 - Estimates Hib Vaccine Costs. Data: Bangladesh Government 2007. Figure: Compiled by the author

Appendix H – GAVI Alliance Pricing

Vaccine	Fragile States	Poorest States	Intermediate States	Least Poor States
1st Vaccine	\$0.10	\$0.20	\$0.30	\$0.30
Additional Vaccines	\$0.15	\$0.15	\$0.15	\$0.15
Subject to 15% annual increase				

Figure 8 GAVI Alliance Co-Funding Table. Data: GAVI Alliance, 2007. Figure: Compiled by the author

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