A Review on Dengue Epidemiology: Transmission Dynamics, Socioeconomic Impacts, and Public Health Strategies: South Asia and Bangladesh

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Declaration

It is hereby declared that :

1. The thesis submitted is our own original work while completing a degree at BRAC University.

2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.

3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.

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Approval

We hereby declare that the thesis entitled ***"A Review on Dengue Epidemiology: Transmission Dynamics, Socioeconomic Impacts, and Public Health Strategies: South Asia and Bangladesh"*** is from the Student's own work and effort, and all other sources of information used have been Acknowledged. This Thesis has been submitted with our approval.

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Ethics Statement

This study is solely a review of published literature, and it does not involve any primary data from animal or human participants. For this reason, both informed consent and ethical approval are not required.

This study's data was only used for research and instruction. The facts were not manufactured or made up, and the findings and conclusions were presented in an understandable manner.

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Abstract

Dengue fever is among the most important mosquito-transmitted viral illnesses and remains an important public health problem in the tropics and subtropics. Dengue has become an emerging disease in South Asia with Bangladesh becoming one of the countries with a high incidence of the disease in recent decades, which is attributed to rapid urbanization, climate change, population growth, poor vector control, and high mobility within the population. This increase in the incidence and severity of outbreaks has led to increased disease burden, both health and socio-economic, and therefore highlighted the need for a comprehensive approach to prevention and control. This review will explain the epidemiology, transmission, socioeconomic impacts, and public health strategies related to dengue, in a comprehensive manner and specifically for the South Asian context and Bangladesh. It compiles scientific literature and reports to consider the changing epidemiological characteristics of dengue, the role of the virus vector Aedes aegypti and Aedes albopictus, and the effects of environmental, climate, and demographic conditions on disease transmission. The review also provides a summary of the clinical manifestations, diagnostic procedures, contemporary therapy, and recent advances in dengue vaccine development.

Dengue also brings high economic and social costs, including healthcare expenses, loss of productivity, and strain on healthcare systems. The repeated epidemics in Bangladesh have underscored the need to enhance surveillance, vector control, and community awareness. The review addresses existing public health tools such as integrated vector management, environmental control, health education, and novel public health tools, including 'Wolbachia' based mosquito control and vaccination tools. It also highlights the key areas of concern for dengue prevention, such as insecticide resistance, climate variations, and lack of public health resources. Finally, coordinated, evidence-based, and sustainable public health interventions are needed for effective dengue control. Further strengthening of surveillance needs, increasing community engagement, encouraging regional group action, and implementing innovative new vector control and vaccination programmes are crucial to lessen the burden of dengue in South Asia, especially in Bangladesh.

Keywords: Dengue, Bangladesh, South Asia, Transmission Dynamics, Aedes, Vector Control, Public Health Strategies, Socioeconomic Impact.

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Chapter - 1
Introduction

1.1. Global Burden and Epidemiology of Dengue

Dengue fever is one of the most important mosquito-borne viral diseases and is an important public health issue in the tropics and subtropics. Dengue is the fastest-growing arboviral disease in the world, with an estimated 3.9 billion people worldwide exposed to its risk of infection in over 120 countries (Hossain et al., 2023a). Dengue was recognized as one of the WHO's 10 most dangerous diseases in the world, which is an increase of 30-fold over the last 50 years. Dengue virus is transmitted mostly by Aedes aegypti and Aedes albopictus mosquitoes, and is composed of four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). Dengue can manifest as a clinical spectrum from asymptomatic infection to severe dengue causing plasma leakage, haemorrhage and impaired function of organs, which is life-threatening (Rathore et al., 2020).

Until 1970, only nine countries had reported severe dengue epidemics. By 2023, there are over 120 countries endemic for the disease in Asia, the Americas, Africa and the Pacific (Hossain et al., 2023a). It is estimated that 100-400 million infections will occur each year, with approximately 96 million causing clinical illness. The economic costs are significant at USD 8 to 9 billion annually globally, consisting of direct and indirect costs. As of October 2023, the Americas region reported the highest number of cases for 2023 (more than 3.7 million) and deaths (more than 1,700), with more than 4.5 million cases and over 4,000 deaths reported from 80 countries and territories around the world throughout the year. Cases of Dengue transmission have also been reported in European countries, including Italy, France and Spain, in people who had not traveled to any place outside Europe. This growth has been facilitated by various converging trends: urbanization, globalisation, climate change (expansion of the geographical range of Aedes mosquitoes and of vectors carrying the disease into new regions) and continued weakness of vector control programmes.

Dengue virus is an approximately 11-kilobase, single-stranded, positive-sense RNA virus, member of the genus Flavivirus, family Flaviviridae. One serotype infection provides lifelong homotypic immunity, but heterotypic immunity that lasts only for about two to six months, with cross-reactive antibodies possibly enhancing antibody-dependent enhancement (ADE) during reinfection with another serotype, which makes vaccine design difficult. The lifelong immunity assumption has been further shaken by recent studies which found that immunities against dengue can wane and then strengthen again over time, leading to a return of the

debate on cyclical nature of outbreaks. Advances in prevention and treatment measures are also being made, such as a large study evaluating the vaccine candidate, TV003, in over 16,000 people that showed about 80 per cent efficacy in preventing symptoms, current development of the antiviral compound, JNJ-1802, and the use of Wolbachia-infected mosquitoes to reduce Dengue's vector competence.

1.2. Regional Epidemiological Shift: Asia-Pacific and South Asia

There is no even spread of dengue in endemic areas. Asia-Pacific has about 70% of dengue burden, and severe disease and deaths are disproportionately distributed between the South and South-East Asia. In this area the epidemiology of the disease has changed from episodic epidemics during the 1980s to hyperendemicity in the 2010s and 2020s, with all four serotypes of the disease co-circulating and large epidemics occurring every 2-5 years. Such a hyperendemic pattern leads to the likelihood of secondary heterotypic infections, which are associated with a 15-80 times increased risk for severe dengue relative to primary infections.

Dengue is a major cause of febrile illness following international travel from tropical areas and transmission in autochthonous form has been reported in southern Europe, the southern USA, and northern Australia. The spread of Aedes albopictus into temperate zones may mean the possibility of dengue transmission in non-endemic areas. There was a worldwide increase, with more than 6.5 million cases reported to WHO in 2023-24, the largest number reported in one year ever, and outbreaks in Bangladesh, Brazil, Burkina Faso and Peru were above record levels.

1.3. South Asia: A Hyperendemic Hotspot

South Asia is a hyperendemic corridor for dengue with all four serotypes circulating across countries. The high population density, the porous borders, the increasing urbanization and climate seasonality in the region due to monsoon seasons, combined with fast, largely unplanned urbanization, lead to conditions that allow for the year-round transmission of diseases and synchronous epidemic waves (Ganeshkumar et al., 2018). With about 1.9 billion people, or one-quarter of the world's population, the region is home to eight countries, each of which has seen the dengue burden escalate over the last decade.

The Southwest monsoon (June – September) controls the climate with warm humid conditions and an abundance of standing-water breeding sites which contribute to the spread of the Ae. population. The urbanization rate in South Asia is more than 2.5 per cent per year and is heavily skewed towards informal settlements where water, sanitation and waste management is inadequate. The health systems in the region are characterized by financial constraints, with limited public-sector capacity for clinical management, diagnosis and surveillance and heavy reliance on out-of-pocket financing, accompanied by low per-capita expenditure on health. Dengue also carries considerable socio-economic burden, such as healthcare costs, loss of productivity, burden on health systems and increased amounts of travel to, from and across borders for trade, working and family visits allows new serotypes to be introduced and spread.

1.4. Bangladesh: The Epicenter of Regional Dengue Burden

In this regional setting, Bangladesh has experienced a very dramatic epidemiological shift and now has one of the highest disease burden rates in the last several decades, due to its effects of rapid urbanization, population mobility, poor vector control, population growth, and climate change. After the first recorded outbreak in 2000 (causing some 5,500 hospitalizations; 93 deaths), the country advanced to more or less regular epidemic cycles, and the virus has reached a hyperendemic status. The 2019 outbreak was the first to surpass 100,000 cases and 164 deaths, and was the final to achieve hyperendemicity. This outbreak of 2023 broke all previous records of the ever highest outbreaks in the history of the country, involving more than 300,000 cases and over 1,500 deaths, the case fatality rate being the highest ever recorded in the country (Mahmud et al., 2023; Sarker et al., 2024). Bangladesh is one of the most dengue affected country in the world on per capita basis due to co-circulation of all four serotypes, geographical expansion of disease transmission from Dhaka to nationwide and more virulent genotypes of dengue virus.

Located in the Ganges-Brahmaputra-Meghna delta, Bangladesh is a low-lying area prone to flooding and has a lot of standing water. It has a high population density of more than 1,200 people per km² that is one of the highest in the world. The expansion of the cities has been faster than the infrastructure development, notably in Dhaka city, has led to water storage practices, neglect of solid waste management and high level of informal settlements conducive to Aedes breeding. Multiple epidemics have highlighted the importance of

strengthening surveillance, vector control and community awareness, whilst the health system still has challenges in achieving year-round vector control and in response to hospital surges during outbreaks.

1.5. Rationale, Aim, and Scope of the Review

A Review on Dengue Epidemiology: Transmission Dynamics, Socio-economic Impacts and Public Health Strategies: South Asia and Bangladesh is organized into four dimensions of analysis of the dengue challenge, namely, disease magnitude, ecological vulnerability, health-system capacity, and policy readiness. It reviews the scientific literature and reports on the evolution of the epidemiological profile of dengue, role of vectors Aedes aegypti and Aedes albopictus, and impact of environmental, climate and demographic factors on transmission. It also outlines clinical signs, diagnostic techniques, current treatment methods and recent innovations in vaccine development, and systemic public health strategies such as integrated vector management, environmental control, health education, and new technologies like Wolbachia-based mosquito control, as well as important issues like insecticide resistance, climate changes, and limited public health resources.

The aim of the review is to provide a synthesis of the transmission dynamics, epidemiological trends and socio-economic impacts of the disease across South Asia with a particular focus on the evidence from Bangladesh, and to identify actionable priorities for coordinated, evidence-based and sustainable public health interventions such as enhanced surveillance, community engagement, regional cooperation, and innovative vector control and vaccination programmes. It is a structured narrative review of peer-reviewed research articles published between 2016–2026 using PubMed, Scopus, Web of Science and Google Scholar databases and is designed to provide information to researchers, clinicians and policy makers in order to reduce the burden of dengue in one of the most affected regions of the world (Tambo et al., 2016; Mutsuddy et al., 2019).

Chapter - 2
Methodology

2.1. Review Design

The paper focuses on the epidemiology of dengue, the mechanisms of its transmission, the socioeconomic effects and public health measures against dengue in the context of South Asia, especially in the case of Bangladesh. Given the multidisciplinary nature of the subject, the epidemiology, entomology, clinical medicine, health economics and policy, and the diverse study designs of the included studies that were not easily amenable to a meta-analysis, a narrative review format was selected. This method is aligned with the narrative review style used in the health sciences and is flexible enough to allow for thematic synthesis while simultaneously adapting to the new information of outbreaks, such as the unprecedented 2023 epidemic in Bangladesh.

2.2. Search Strategy and Sources

Literature was searched from PubMed, Scopus, Web of Science, and Google Scholar for general indexing of literature and Bangladesh Journals Online (BanglaJOL) portal for regionally indexed studies. The search terms were Booleaned with MeSH headings such as "dengue," "dengue hemorrhagic fever," "Bangladesh," "South Asia," "Aedes," "vector control," "transmission dynamics," "socioeconomic burden," and "vaccine. Literature searches were conducted from January 2016 to December 2024, including recent outbreaks during this time. Hand search of reference lists of key articles was also done to find additional relevant articles that were not electronically indexed to capture the regional publications, another snowballing method to be used when searching for regional publications.

2.3. Eligibility Criteria

Peer-reviewed, English-language studies addressing dengue epidemiology, transmission, clinical burden, socioeconomic impact, or public health response in South Asia were included, with priority given to Bangladesh-based evidence. Studies from other regions were retained only where they offered comparative insight or described interventions, such as vaccination or *Wolbachia*-based vector control, with relevance to the South Asian context. Editorials, conference abstracts, and studies limited to basic virology without public health relevance were excluded.

2.4. Synthesis Approach

Given the diversity of included study designs, a thematic synthesis method was used rather than statistical pooling. Extracted evidence was organized around a four-part framework encompassing disease burden, ecological and climatic drivers, health-system capacity, and policy response, allowing comparison across sections and identification of recurring gaps.

2.5. Limitations

As a narrative rather than systematic review, this method is subject to selection bias and does not include formal quality appraisal of individual studies. The restriction to English-language sources may exclude relevant Bengali-language operational reports, and rapidly evolving 2023–2024 outbreak data may be incompletely represented in peer-reviewed literature at the time of writing.

Chapter - 3
Results

3.1. Regional Burden of Dengue Disease

Over the last ten years, every country in South Asia has seen dengue cases climb, and all four viral serotypes are now circulating together throughout the region. The table below shows how the reported case load and serotype mix have grown across South Asian nations during this period.

Table 01: The table below shows how the reported case load and serotype mix have grown across South Asian nations.

LRRRL Country	Largest outbreak (cases)	Year	Deaths	Dominant serotypes
Bangladesh	**321,179**	**2023**	**1,705**	**DENV-1, DENV-2, DENV-3, DENV-4**
India	**233,251**	**2022**	**303**	**DENV-1,DENV-2, DENV-3, DENV-4**
Sri Lanka	**186,101**	**2017**	**440**	**DENV-2, DENV-3**
Nepal	**54,784**	**2022**	**88**	**DENV-1, DENV-2, DENV-3**
Pakistan	**53,498**	**2021**	**249**	**DENV-1, DENV-2, DENV-3**
Myanmar	**31,288**	**2022**	**192**	**DENV-1, DENV-2, DENV-3**
Bhutan	**3,599**	**2023**	**6**	**DENV-1, DENV-2**

Of all the countries in the region, India carries the heaviest total case load. A pooled analysis of multiple studies put nationwide seroprevalence at roughly 48.7 percent, with case fatality varying between 0.5 and 3.5 percent depending on the state (Ganeshkumar et al., 2018). India's surveillance data point to a steady climb in both the number of cases and the geographic reach of the disease - the number of districts reporting dengue grew from around 60 in 2010 to more than 250 by 2023. Actual infection numbers are almost certainly far higher than what gets officially recorded: one modeling study put India's yearly infection count somewhere between 6 and 33 million, dwarfing the 100,000 to 200,000 cases captured by formal surveillance. This gap comes down to the weaknesses of a passive reporting

system, the fact that many infections are mild or symptom-free, and low levels of lab-confirmed testing.

Pakistan has been hit by a series of major outbreaks, each larger than the last: more than 21,000 cases in Lahore in 2011, over 50,000 across Karachi and Peshawar in 2019, and above 53,000 in 2021. Flooding in 2022, which submerged roughly a third of the country, left behind extensive pools of standing water that gave Aedes mosquitoes ample breeding ground and helped prolong transmission. Efforts to control dengue in Pakistan have also been complicated by the shift of health responsibilities to provincial governments, which has split up surveillance and vector-control work.

Sri Lanka's worst outbreak came in 2017 - more than 186,000 cases and 440 deaths, driven mainly by DENV-2. That outbreak stood out for how severe it was: fatality rates climbed above those seen in earlier outbreaks, and a larger share of patients developed severe forms of the disease. Later outbreaks in 2019 and 2023 were smaller in scale but persistent, pointing to dengue having become a fixture of ongoing transmission in the country. Sri Lanka's surveillance system ranks among the strongest in the region cases must be reported by law, and the country maintains sentinel monitoring sites along with regular serotype tracking, giving it a model that other South Asian countries can learn from.

Nepal, once viewed as having only low levels of dengue, has watched the disease spread into districts at much higher elevations, with back-to-back record-breaking outbreaks in 2022 and 2023 (Rimal et al., 2024). The 2022 outbreak was especially notable over 54,000 cases spread across all seven provinces because it showed that dengue can now take hold above 1,500 meters, an altitude once thought too high for Aedes mosquitoes to survive. Researchers link this expansion to a warming climate, which has pushed the range of Aedes aegypti and Aedes albopictus into higher terrain, combined with more people traveling from dengue-endemic lowland regions into highland areas that previously saw little to no transmission.

Bhutan and Myanmar have also reported climbing case counts, though the data coming out of both countries is less complete. Bhutan's first significant outbreak hit in 2019 with over 5,000 cases, followed by another in 2023 topping 3,500. In Myanmar, ongoing political turmoil has limited the quality of surveillance data, but reported cases have grown from under 5,000 a

year before 2015 to over 30,000 in 2022. The Maldives hasn't recorded any large outbreaks during the period under review, but it has seen scattered transmission, and the dense population of its capital, Malé, provides conditions where an outbreak could easily take off.

Region-wide, dengue has shifted from occasional epidemic spikes to an ongoing, endemic presence punctuated by seasonal surges a pattern that echoes what Southeast Asia went through roughly twenty years earlier. Figure 2 maps out the major milestones in dengue's emergence across South Asian countries.

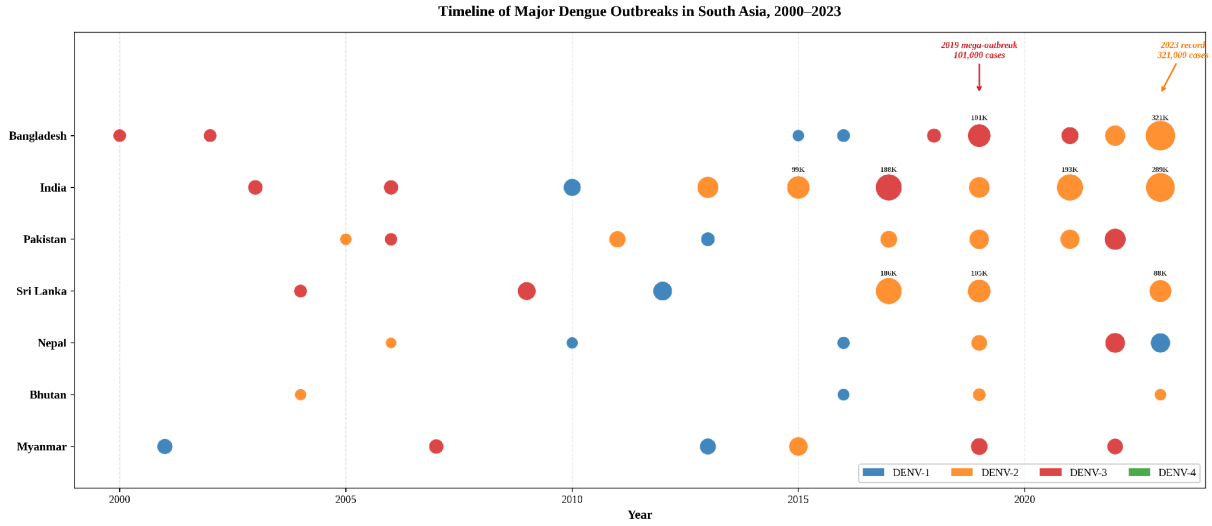

Figure 1. Timeline of major dengue outbreaks in South Asia, 2000–2023.

3.2. Country-Specific Burden

The uneven distribution of dengue's impact across South Asia comes down to differences in how sensitive each country's surveillance is, how much diagnostic capacity exists, along with variation in climate, urban growth, and the strength of vector-control programs. India's official case counts are probably the furthest from reality, given its enormous population, its reliance on passive rather than active surveillance, and low rates of laboratory confirmation. One seroprevalence study carried out in Chennai from 2010 to 2012 found that 93 percent of adults between 18 and 65 showed signs of a past dengue infection suggesting that in dense urban centers, almost everyone eventually gets exposed. Comparable studies out of Delhi, Mumbai, and Kolkata found seroprevalence running between 50 and 80 percent among adults.

In Pakistan, the dengue burden centers on Punjab and Sindh provinces, home to the major cities of Lahore and Karachi. The 2011 Lahore outbreak marked a turning point, leading Punjab to set up a provincial dengue control program credited with bringing case numbers down in the years that followed. Even so, the program's results have been inconsistent, and the outbreaks of 2019 and 2021 showed that keeping the disease under control long-term is still an uphill battle.

Sri Lanka's dengue burden is striking given how small its population is. The 2017 outbreak more than 186,000 cases among roughly 22 million people produced one of the highest per-capita attack rates ever recorded anywhere in the world. Researchers attribute this to several factors converging at once: a DENV-2 strain that hadn't been the dominant type in the years before, a population broadly susceptible to infection, and heavy monsoon rains that created ample breeding conditions.

3.3. Shared Ecological and Demographic Determinants

Two ecological forces stand out as the main reason dengue transmission rises and falls together across South Asia: rainfall tied to the monsoon, and fast, unplanned urban growth. The region's climate is shaped by the Southwest monsoon, running from June through September, which brings the warm, humid air and pools of standing water that let Aedes mosquito populations surge (Mamenun et al., 2024). Once temperatures sit between 25 and 30°C, the virus develops faster inside the mosquito, cutting the time between a mosquito's infected blood meal and its ability to transmit the virus from roughly 10 to 15 days at 25°C down to just 5 to 7 days at 30°C. Because of this temperature sensitivity, the window for transmission is shorter in the cooler northern stretches of South Asia Nepal, and the northern parts of India and Pakistan and stretches longer in the warmer south and along the coast.

Urban growth adds to these climate effects. South Asia's cities are expanding by more than 2.5 percent a year, with much of that growth happening in informal settlements that lack reliable water, sanitation, and waste services. Cities like Dhaka, Delhi, Mumbai, Karachi, and Colombo share the same risk factors: extremely dense populations (over 20,000 people per square kilometer in core areas), households that store water because supply is unreliable, and gaps in waste collection all of which add up to prime breeding conditions for Aedes aegypti (Lim et al., 2020). Informal settlements make up somewhere between roughly 25 percent of

the urban population in Colombo and over 40 percent in Dhaka and Mumbai. These settlements typically have homes without window screens, water storage born of unreliable supply, and inconsistent trash pickup that leaves discarded containers lying around as breeding sites.

Urbanization's link to dengue isn't a straight line. Early on, transmission tends to stay confined to a handful of urban centers, as was true in Bangladesh before 2016. As cities keep growing, transmission spreads out geographically, and the line between "urban" and "rural" cases starts to blur. Bangladesh illustrates this well: the share of dengue cases reported from outside Dhaka rose from under 10 percent before 2016 to over 40 percent by 2023, as Aedes habitat pushed into peri-urban and rural zones.

3.4. Seasonal and Climatic Patterns of Transmission

Across South Asia, dengue cases typically peak in the months immediately after the monsoon, from August through November. This timing results from the interaction of rain and heat: monsoon rains fill breeding sites, and the warmth that follows accelerates the virus's development inside mosquitoes. A gap of roughly one to two months between peak rainfall and peak case counts consistently appears across the region, reflecting the time needed for eggs to hatch, larvae to mature, and adult mosquitoes to become capable of transmitting the virus after biting an infected person.

That said, the seasonal rhythm isn't identical everywhere. Sri Lanka sees two separate peaks a smaller one during the Southwest monsoon (May to July) and a bigger one during the Northeast monsoon (October to December). In southern India, cases stay elevated more continuously through the year rather than spiking sharply, since the climate is warmer and breeding sites are available almost year-round. In Nepal, by contrast, the transmission window is squeezed into the post-monsoon stretch from September to November, a reflection of the cooler conditions found at higher elevations.

Rising temperatures tied to climate change are stretching out the transmission season on both ends starting earlier in spring and lasting later into autumn. Bangladesh's 2023 outbreak is a good example: it started in May, ahead of the usual June–July onset, and ran all the way into December. More frequent and intense bursts of heavy rain are creating irregular waves of

new breeding sites, while warmer winter minimum temperatures are letting Aedes mosquitoes survive through seasons that used to kill them off.

3.5. Cross-Border Mobility and Transmission Dynamics

Because South Asia's land borders are so porous, people moving across them are helping carry new dengue serotypes from one country to another, making it harder for any single nation to control the disease on its own. The region has some of the busiest land borders anywhere, crossed daily by huge numbers of traders, migrant workers, and people visiting family. The India-Bangladesh border alone stretches over 4,000 kilometers among the longest in the world with tens of thousands of people estimated to cross it every day. Genetic tracing of the virus has shown DENV strains moving across this border, with versions found in West Bengal and Assam closely matching those circulating in Dhaka (Cruz et al., 2023). Likewise, the DENV-2 Cosmopolitan strain that became dominant in Bangladesh has since turned up in Nepal and eastern India, pointing to spread across borders.

Along the India-Nepal border, where citizens can move freely between the two countries, dengue has been able to travel from India's endemic lowlands into parts of Nepal that had never seen the disease before. The widespread 2022 Nepal outbreak, which touched all seven provinces, was likely triggered by several separate introductions from India, then amplified by favorable weather once it took hold locally. The India-Pakistan border sees more restricted crossing, but still enough traffic at official checkpoints that genetic studies have found shared DENV strains between the two nations.

Right now, there's no coordinated regional system for tracking dengue, and countries generally don't share surveillance data with each other in real time. As a result, cross-border spread tends to be identified only after the fact if it's caught at all rather than functioning as an early warning system for neighboring countries. The WHO's South-East Asia Regional Office has begun working to build up regional surveillance, including plans for a shared dengue laboratory network, but the effort has moved slowly, and countries still share relatively little epidemiological or virological data with one another.

3.6. Dengue in Bangladesh: Trajectory from Historical Emergence to Hyperendemic Transmission

3.6.1. Early Emergence and Initial Outbreaks

The first documented dengue cases in Bangladesh date back to 1964, when a small cluster appeared in Dhaka under the clinical label "Dhaka fever." Patients presented with fever, rash, and joint pain a picture consistent with classic dengue fever and the cluster was thought to stem from the virus being carried in by travelers arriving from abroad. Despite this early appearance, the disease did not take hold as a sustained transmission cycle until 36 years later. Why transmission stayed dormant for so long isn't fully understood, but it was probably due to some combination of Dhaka's lower population density at the time, climate conditions less suited to Aedes breeding, and a lack of repeated virus introductions.

The country's first major outbreak arrived in 2000, with around 5,500 hospitalized cases and 93 deaths (Hossain et al., 2023a). It was centered in Dhaka, and DENV-3 emerged as the leading serotype. A case fatality rate near 1.7 percent was strikingly high, a reflection of how little clinical experience existed at the time for managing dengue and the fact that no national treatment protocols were yet in place. In response, the Directorate General of Health Services (DGHS) set up a dengue surveillance system, and the country's first clinical management guidelines were drawn up.

From 2000 through 2015, dengue stayed largely a sporadic, outbreak-driven disease concentrated in Dhaka, without much geographic spread. Notable flare-ups occurred in 2002 (roughly 6,100 cases), 2004 (about 4,000 cases), and 2011–2012 (approximately 1,500 and 600 cases respectively), while the years between outbreaks typically saw fewer than 1,000 cases reported annually. Serological studies from this era point to DENV-1 and DENV-2 as the main circulating serotypes, with DENV-3 turning up only now and then (Mutsuddy et al., 2019). This on-and-off pattern fits what's typically seen in the early stages of dengue establishing itself in a population outbreaks flare when enough susceptible people have accumulated and a new serotype gets introduced, rather than transmission running continuously.

3.6.2. Shift from Episodic Outbreaks to Endemic and Hyperendemic Circulation

2016 proved to be a pivotal year, with case counts topping 6,000 for the first time since 2002. What made the 2016 outbreak notable was DENV-1 rising to dominance after years of only occasional detection. Because this serotype had been largely missing from circulation for so long, a substantial pool of susceptible people had built up especially children born after the previous DENV-1 wave which likely fueled the scale of the outbreak.

The 2019 outbreak, with more than 100,000 confirmed cases and 164 deaths, marked the definitive shift into hyperendemic transmission (Sharif et al., 2024). Several things set it apart. It was the first time all four serotypes were confirmed circulating simultaneously, with DENV-3 genotype I making up roughly 78 percent of typed samples and the remaining share split among DENV-1, DENV-2, and DENV-4. It was also the first outbreak with cases confirmed in all eight of Bangladesh's administrative divisions, showing that dengue had moved well beyond Dhaka to become a truly nationwide issue. On top of that, a larger share of cases progressed to severe dengue than in prior outbreaks, and the death toll of 164 was the highest recorded to that point.

Case numbers dropped in 2020 and 2021, to about 1,400 and 28,000 respectively, before the 2022 outbreak climbed back to around 62,000 cases. Then 2023 broke every previous record, with over 300,000 cases and more than 1,500 deaths (Sarker et al., 2024). The dip in 2020–2021 was likely tied to COVID-19 mobility restrictions, which cut down on human movement and may have reduced contact between people and Aedes mosquitoes, along with reduced care-seeking, since febrile patients may have stayed away from health facilities out of fear of catching COVID-19. The 2023 outbreak brought several worrying developments: a case fatality rate around 0.5 percent, higher than in previous years; an earlier-than-normal start in May; a transmission season that stretched all the way into December; and DENV-2 re-emerging as a major driver of severe disease.

A number of factors likely combined to drive the surge in 2023. A more virulent strain of the DENV-2 Cosmopolitan C genotype appeared in southwest Bangladesh and was linked to more severe illness (Setu et al., 2025). Immunity across the population may have waned during the COVID-19 period, when dengue transmission was comparatively low, leaving more people susceptible. Unplanned urban growth and the spread of water storage containers

pushed Aedes habitat into peri-urban and rural areas, widening the geographic reach of transmission. And when hospitals reached capacity during the busiest weeks, delays in starting fluid management for incoming patients likely contributed to the elevated death toll.

3.6.3. National Trends in Case Counts and Mortality

Table 2 traces the epidemiological path of dengue in Bangladesh through the three phases of its shift from outbreak disease to endemicity. It shows the progression from sporadic, Dhaka-centered transmission, through a transitional period of geographic spread, to the current hyperendemic phase, in which all four serotypes circulate across all 64 districts and case counts have reached levels never seen before. The case fatality rate has also crept upward over time from 0.4–0.5 percent during 2000–2015 to 0.5 percent or higher in the 2019 and 2023 outbreaks, suggesting that gains in clinical management have not kept pace with worsening disease severity.

LLLL Phase & Period & Key characteristics & Dominant serotype Sporadic & 2000–2015 & Isolated outbreaks, Dhaka-centric, fewer than 6,000 cases per year & DENV-1, DENV-2 (Hossain et al., 2023a) Transition & 2016–2018 & Rising baseline, geographic spread begins & DENV-1, DENV-2, DENV-3 (Mutsuddy et al., 2019) Hyperendemic & 2019–2023 & All 4 serotypes, all 64 districts, record outbreaks & DENV-2, DENV-3 dominant (Sarker et al., 2024)

Even with gaps in the data, the national case figures trace a clear upward path. Average annual reported cases rose from about 2,000 during the sporadic phase (2000–2015), to roughly 35,000 during the transitional phase (2016–2018), to more than 120,000 during the hyperendemic phase (2019–2023). The share of cases reported from outside Dhaka grew from under 10 percent before 2016 to more than 40 percent by 2023, tracking the geographic spread of transmission. The case fatality rate, though it fluctuates, has trended upward overall, moving from an average of 0.5 percent in the sporadic phase to 0.5 percent or higher during the hyperendemic phase.

3.6.4. Spatial Expansion and District-Level Distribution

Dengue transmission in Bangladesh has moved from being centered on Dhaka to occurring nationwide, across all 64 districts. The 2019 outbreak was the first to produce confirmed cases in every district, and that pattern has held in the years since. Dhaka still reports the highest raw case numbers, but the share of cases coming from elsewhere in the country climbed from under 10 percent before 2016 to more than 40 percent in 2023 (Rafi et al., 2020). This geographic spread stems from several forces: Aedes aegypti and Aedes albopictus moving into districts where they weren't previously established, aided by better transport links and increased movement of goods and people; a growing number of water storage containers in peri-urban and rural areas where municipal water service is unreliable; and rising population density in district towns, which supports sustained transmission.

Case distribution across districts is far from even. In 2023, just five districts Dhaka, Chattogram, Khulna, Barishal, and Rajshahi accounted for roughly 70 percent of all reported cases, leaving the other 59 districts to account for the remaining 30 percent. This concentration tracks with higher population density, more abundant Aedes breeding sites, and stronger diagnostic capacity in urban centers. That said, the share of cases coming from lower-density districts has been climbing, and a number of districts that reported zero cases before 2019 have since seen sustained transmission a sign that dengue is taking root in places once considered free of the disease. Figure 3 maps the geographic spread of dengue incidence across Bangladesh's 64 districts.

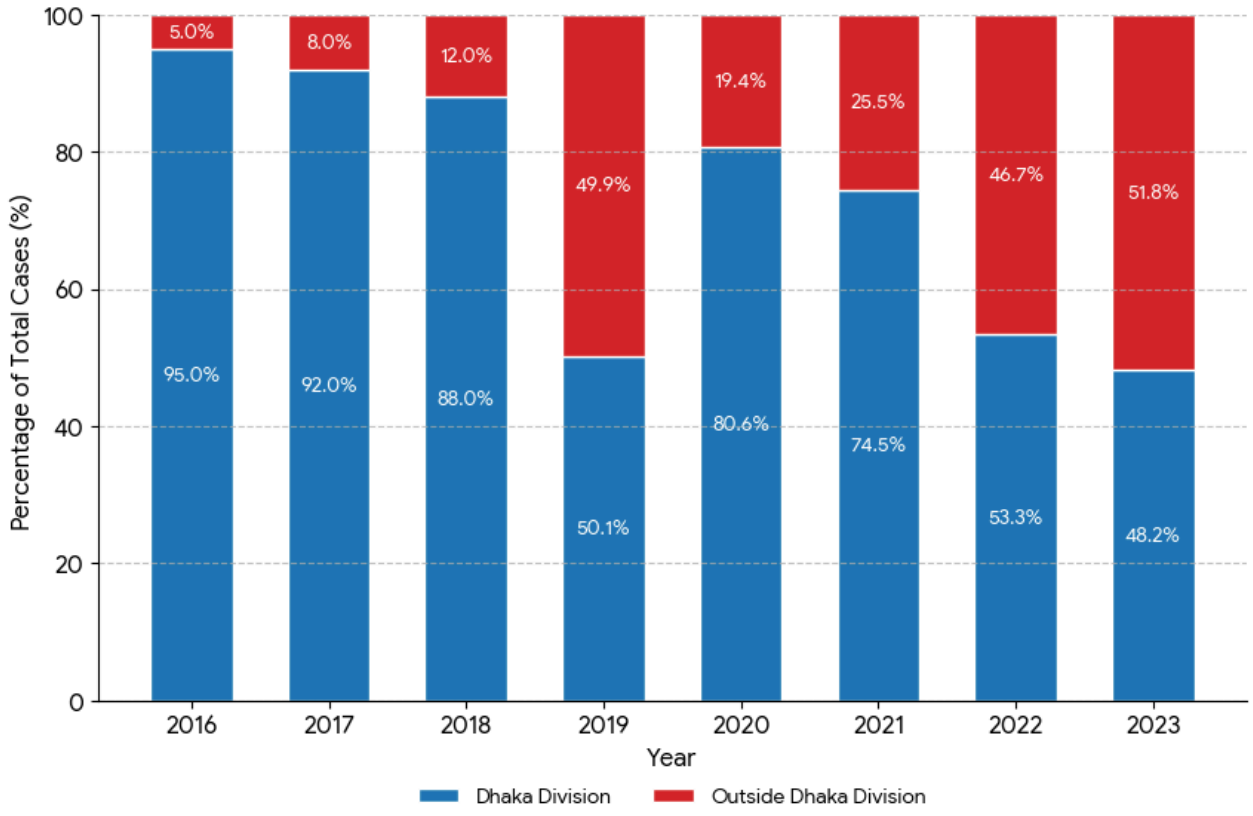

Figure 2. Dengue cases across Bangladesh, 2016–2023.

3.6.5. Seasonal Trends in Case Occurrence

Dengue in Bangladesh follows a fairly predictable seasonal rhythm: cases start climbing in June and July as the monsoon arrives, peak between August and October in the post-monsoon stretch, and taper off from November into December as temperatures cool. This pattern comes from the combined effect of rainfall, heat monsoon rains generate plentiful breeding sites, while post-monsoon warmth speeds up the virus's development inside mosquitoes. A lag of roughly one to two months between peak rainfall and peak case counts shows up consistently across the country, reflecting the time it takes for Aedes eggs to hatch, larvae to mature, and adult mosquitoes to become capable of transmitting the virus.

The 2023 season broke from this pattern somewhat, with transmission stretching later into December likely tied to a delayed monsoon withdrawal and warmer-than-usual autumn temperatures. This extended season is a cause for concern, since it shortens the gap between epidemics during which vector-control efforts could otherwise be ramped up, and it adds to the total number of infections in a given year. Climate projections suggest Bangladesh's

transmission season will keep lengthening over time, starting earlier in spring and ending later in autumn, as average temperatures rise and monsoon patterns grow less predictable.

3.6.6. Patterns Across Urban, Peri-Urban, and Rural Settings

The line between urban and rural dengue transmission in Bangladesh has grown increasingly indistinct. Dengue was once thought of as a city disease, concentrated in Dhaka and a handful of other large urban centers, a pattern rooted in the ecology of Aedes aegypti, which favors dense human populations and plentiful artificial containers for laying eggs. But several shifts have worn away that urban-rural divide.

For one, Aedes albopictus, a secondary vector that tolerates cooler temperatures better and tends to breed outdoors, has spread into peri-urban and rural parts of Bangladesh. Unlike Aedes aegypti, it isn't as reliant on artificial containers and can breed in natural sites like tree holes and the base of leaves, as well as in man-made containers. Its spread into rural areas has been helped along by more water storage containers, discarded tires, and other artificial containers showing up in rural settings.

Beyond that, population density in peri-urban and rural areas has been climbing as populations grow and cities expand into the surrounding countryside, creating conditions that favor Aedes aegypti breeding. Peri-urban zones, which mix agricultural and residential land use, frequently deal with unreliable water supply and poor solid-waste management, both of which favor mosquito breeding.

Finally, better transport connections between cities and the countryside make it easier for infected individuals to travel from urban areas, where transmission is ongoing, into rural areas where a larger pool of susceptible people may exist. This lines up with a "source-sink" model of dengue spread, where urban centers act as sources of the virus that periodically seed outbreaks among susceptible rural populations.

3.6.7. Populations at Elevated Risk

Children, older adults, pregnant women, and people with underlying health conditions face a disproportionately higher risk of severe dengue and death in Bangladesh. Looking at the 2019 and 2023 outbreaks, the case fatality rate was highest among adults aged 40 to 60 a pattern that differs from Southeast Asia, where severe dengue skews toward children, and may

reflect a population where secondary infections predominate (Haider et al., 2023). Severe disease being concentrated in adults rather than children carries implications for clinical care, since adult patients are more likely to have comorbidities that complicate fluid management, and for vaccine strategy, since the age group at greatest risk may not match the age group typically targeted by pediatric vaccination campaigns.

Pregnant women make up a particularly vulnerable group, as dengue infection during pregnancy raises the risk of preterm birth, low birth weight, and maternal hemorrhage (Howard-Jones et al., 2023). Pregnancy-related physiological shifts, including increased plasma volume and hemodilution, can mask the hemoconcentration that normally signals plasma leakage, making severe dengue harder to diagnose. Managing dengue during pregnancy calls for close monitoring of both mother and fetus, and delivery should ideally happen at a facility equipped to handle obstetric hemorrhage.

Patients with diabetes, hypertension, and chronic kidney disease face significantly worse odds of severe outcomes. One study found a threefold increase in mortality risk among dengue patients with chronic kidney disease (Lee et al., 2023). The reasons behind this elevated risk are varied: diabetes and hypertension are linked to endothelial dysfunction, which may worsen plasma leakage; chronic kidney disease disrupts fluid balance, complicating the fluid management central to treating severe dengue; and medications used for these conditions, including ACE inhibitors and NSAIDs, may interact with how dengue affects the body.

Chapter - 4
Virology & Molecular Epidemiology

4.1. Virus structure

The dengue virus is a single-stranded, positive-sense RNA virus that is a member of the family Flaviviridae and genus Flavivirus. Its roughly 11 kilobase genome codes for a single polyprotein that is broken down into seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) and three structural proteins (capsid, pre-membrane/membrane, and envelope) by host and viral proteases. The capsid protein encapsulates the viral RNA, the envelope protein mediates receptor binding and membrane fusion during viral entry, and the pre membrane protein serves as a chaperone for the envelope protein during virion assembly before being cleaved to the mature membrane protein during virion egress. These structural proteins make up the viral particle. The non structural proteins are involved in pathogenesis, immune evasion, and viral replication: NS1 is secreted from infected cells and plays a role in plasma leakage by activating complement and disrupting the endothelial glycocalyx; NS3 is a helicase and protease; and NS5 is an RNA dependent RNA polymerase that also serves as a methyltransferase.

Since genotype replacement events, in which a previously circulating genotype is replaced by a new genotype, are frequently linked to variations in epidemic severity, the genotype classification is clinically and epidemiologically significant. The 1980s and 1990s saw the appearance of severe dengue in an area where it had previously been uncommon due to the substitution of the DENV-2 Asian/American genotype in the Americas by the Southeast Asian genotype. Similar to this, genotype changes in DENV-1 and DENV-3 have been linked to more severe outbreaks in Asia.

4.2. Serotype

Based on phylogenetic analysis of the envelope gene or full genome sequences, dengue viruses are further divided into genotypes within each serotype. There are five genotypes of DENV 1 (I through V), six genotypes of DENV 2 (Asian I, Asian II, Cosmopolitan, American, Southeast Asian/American, and Sylvatic), five genotypes of DENV 3 (I through V), and four genotypes of DENV 4 (I through IV). The potential for an epidemic, pathogenicity, and ability to cause serious illness can differ among genotypes within the same serotype.

The immunopathogenesis of severe dengue is largely dependent on the cross-reactive but non neutralizing antibody responses elicited by the four serotypes, which share about 65% amino acid identity. Cross-reactive antibodies may enable antibody-dependent enhancement (ADE) following future infection with a different serotype. Infection with one serotype provides lifetime homotypic immunity but only temporary heterotypic protection (Rathore et al., 2020). Higher viral loads and increased immunological activation arise from ADE, which happens when sub-neutralizing quantities of cross-reactive antibodies attach to the virus and make it easier for it to enter Fc-gamma-receptor-bearing cells, such as monocytes and macrophages. The main obstacle to developing a dengue vaccine is the ADE phenomenon, which is the cause of the elevated risk of severe dengue linked to secondary heterotypic infections.

4.3. Bangladesh-specific molecular epidemiology

The DENV-2 Cosmopolitan genotype replaced the previously prevalent DENV-2 Asian I genotype in Dhaka during a significant genotype replacement event that took place between 2017 and 2018 (Suzuki et al., 2019). The Cosmopolitan genotype has been linked to significant epidemics in several nations and is extensively dispersed throughout South and Southeast Asia. Over the course of about a year, the Cosmopolitan genotype replaced the Asian I genotype in Dhaka, which was linked to a rise in DENV-2 cases. Although the exact mechanisms underlying genotype replacement are unknown, they may involve variations in viral fitness, such as replication efficiency, mosquito vector transmission efficiency, and the ability to elude pre-existing immunity. DENV-3 genotype I was the most common serotype by 2020–2021, and genetic analysis of isolates from Dhaka in 2021 verified this genotype's ongoing dominance (Jahan et al., 2023). A novel DENV-2 Cosmopolitan C genotype strain that was found in Bangladesh's southwest and linked to greater severity made the 2023 epidemic noteworthy (Setu et al., 2025). During the 2018 epidemic in Dhaka, co-circulation of DENV-3 genotype I and DENV-2 Cosmopolitan genotype was observed, demonstrating the pattern of concurrent transmission of multiple serotypes that has defined the hyperendemic phase (Ahmad et al., 2020).

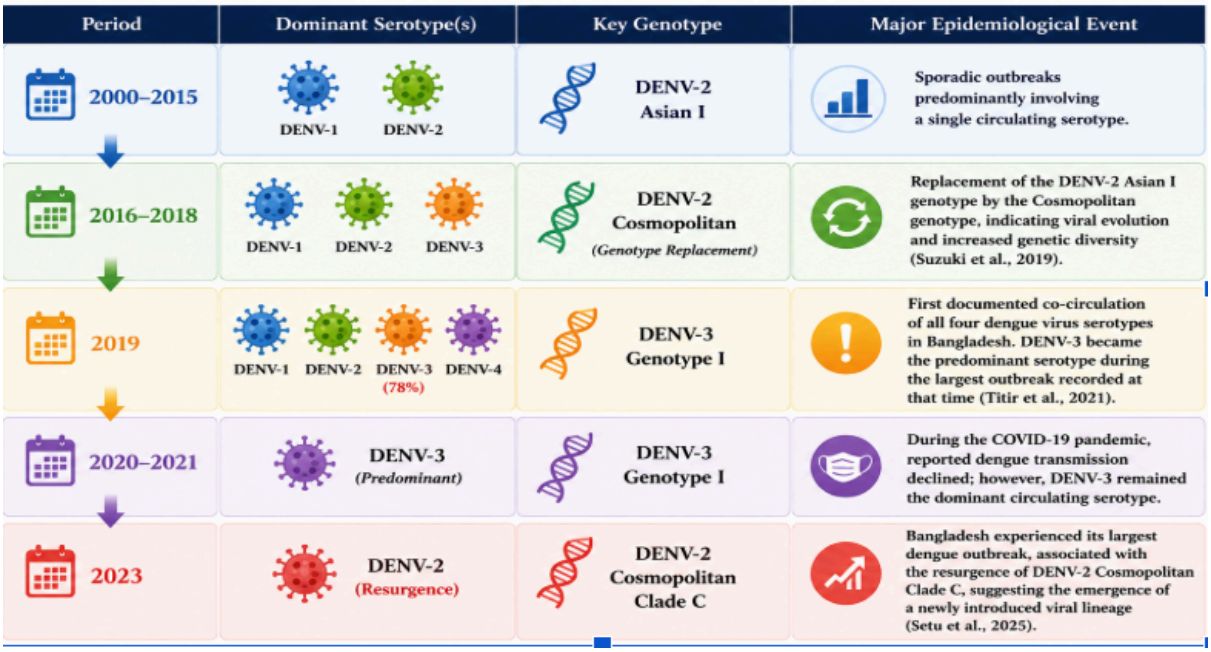

Figure 3: Temporal Distribution of Dengue Virus Serotype and Genotype Shifts in Bangladesh (2000 - 2023) (generated with Gemini)

4.4. Serotype Shifts in terms of Outbreaks and Severity

While serotype shifts are linked to more severe outbreaks, Bangladesh's lack of regular genetic surveillance makes it more difficult to identify newly developing aggressive strains. Large outbreaks were preceded by the genotype replacing the DENV-2 Asian I genotype in 2017 and the subsequent dominance of DENV-3 genotype I in 2019, indicating that genotype alterations can act as early warning indicators. Nevertheless, molecular surveillance in Bangladesh is still restricted to a few research facilities, mostly in Dhaka, and is not included into the country's overall surveillance framework. Because sequencing is done on convenience samples after the fact, it is not as useful for responding to outbreaks in real time. The population immunity profile acts as a bridge in the link between serotype shifts and outbreak severity. A substantial pool of susceptible people, especially children born since the last outbreak of that serotype, are available to fuel transmission when a serotype that has been absent from the population for a number of years is reintroduced. This pattern is demonstrated by the 2023 outbreak, which witnessed the resurgence of DENV-2, and the 2019 outbreak, which was dominated by DENV-3 following several years of DENV-3 absence. The likelihood of secondary heterotypic infections, which are linked to an increased risk of severe dengue, is increased when numerous serotypes co-circulate.

4.5. Life cycle

According to (Kuhn, Zhang, Rossmann, & Pletnev, 2020), the dengue virus's reproductive cycle consists of several crucial stages, one of which is the point at which an infected Aedes mosquito bites a human.

a. Entry: The dengue virus travels via the skin and targets the entire bitten area, acting as a virus carrier. It binds to many of the cells that are often known for eliminating disease, such as monocytes, dendritic cells, macrophages, and others.

b. Attachment and Entry into Cells: By incorporating (or mimicking) the envelope protein function, which involves the cell receptors separating from the cell surface, the virus can change the cell. The viruses enter cells via binding to cellular receptors through endocytosis, a form of receptor-mediated endocytosis, which is a more intricate (affinity to) process that takes place at the cellular level.

c. Release of Viral RNA: After entering the cell, the virus enters the endosome. One can cause the viral membrane to fuse with the endosomal membrane in the endosome's acidic environment. The viral RNA genome can then be released into the host cell's cytoplasm as a result.

d. Replication: The antiviral ribosomes use the viral RNA as a template to translate the viral progeny proteins. After the proteins involved in this process have completed their tasks, the replication complex is created to replicate the RNA.

e. Production, Assembly and Maturation: In the initial phases, host cells supply the cells that the endoplasmic reticulum and golgi apparatus used to produce viral particles. As they gain their unique infectious traits, the immature viruses mature into their mature versions.

f. Release: These recycled particles are able to infect other cells after being exocytosed from the host cell. The virus uses its host as a vehicle for additional transmission or amplification as the cycle repeats, emphasizing how repetitive it is.

The host's immune system activates during the whole infection process, including the removal of any pre-existing viruses. The severity of the illness is influenced by the complexity of the dengue virus's interaction with the host immune system.

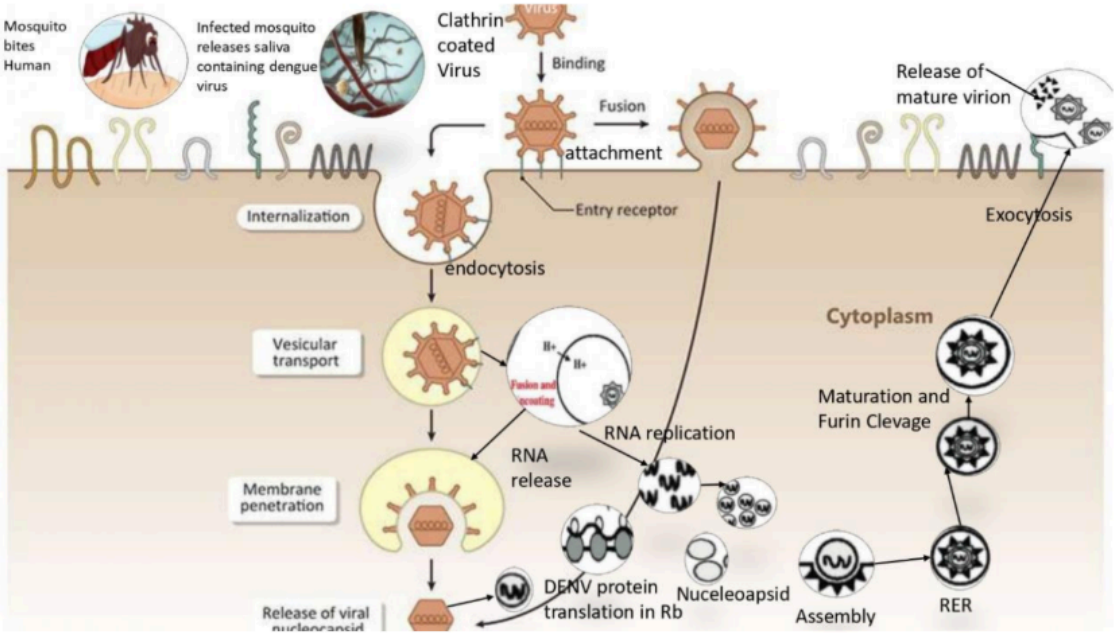

Figure 4: Dengue Virus Life Cycle

4.6 Limitations of Molecular Surveillance In Regards to Bangladesh

Dengue molecular surveillance in Bangladesh is constrained by a number of variables. First, there are only about 500 DENV sequences from Bangladesh that have been added to GenBank, most of which are from Dhaka. This gives an inadequate picture of the dynamics of viral transmission and diversification. Second, convenience samples usually from hospitalized patients in Dhaka are used for sequencing, which may not be indicative of the larger population of circulating viruses. Third, the scope and promptness of molecular monitoring are constrained by the expense of sequencing, the scarcity of sequencing reagents and equipment, and the lack of qualified staff in phylogenetic analysis and bioinformatics. Fourth, research labs do sequencing on an as-needed basis without coordination or standardization due to the lack of a national program for molecular surveillance. Viral sequence diversity did not significantly differ between severity categories in a study of DENV genetic diversity in severe and non severe cases in Dhaka between 2018 and 2022, indicating that host factors may be more significant than viral genetic variation in determining clinical outcomes (Rahim et al., 2023). However, genotype alterations are usually discovered months after they occur due to the lack of rigorous, prospective molecular

surveillance, and the association between certain virus genotypes and clinical severity in the Bangladeshi context is still poorly understood.

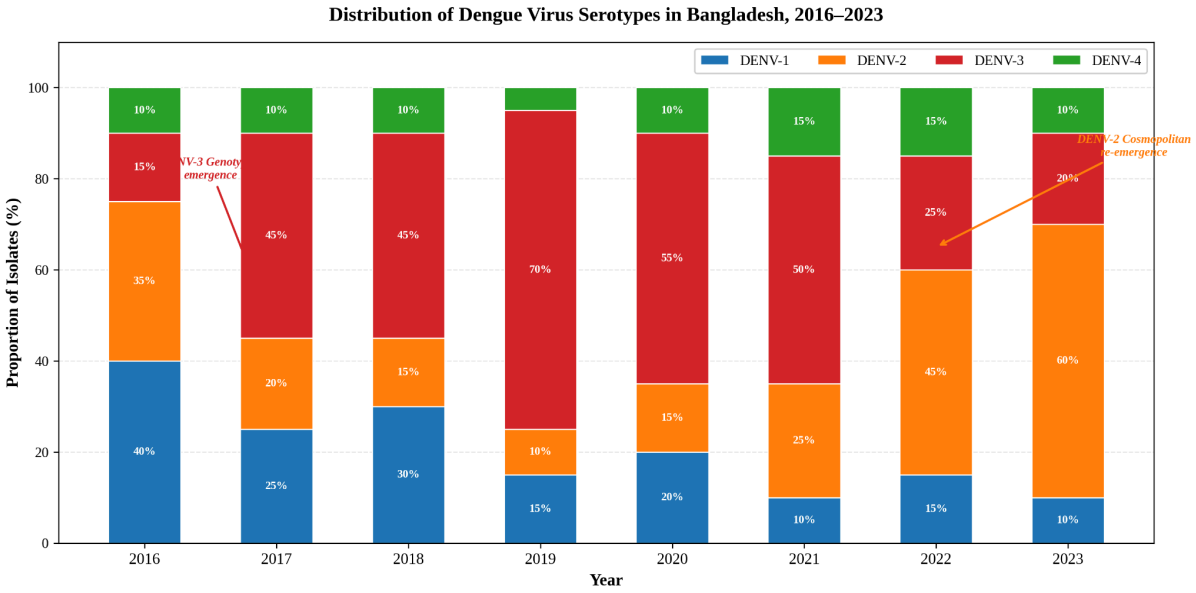

Figure 5: Dengue virus serotype distribution in Bangladesh, 2016–2023

Chapter - 5
Clinical Features

5.1 Symptoms

The clinical spectrum of dengue infection includes mild, undifferentiated fever, characteristic dengue fever, severe dengue with plasma leakage, hemorrhage, and organ damage, and silent infection (which is thought to make up 50–80% of all infections). Since the true disease burden is significantly higher than the number of clinically apparent cases, the percentage of asymptomatic infections has significant implications for both surveillance and transmission dynamics. Asymptomatic individuals can act as a reservoir for virus transmission to mosquitoes. The ratio of asymptomatic to symptomatic infections varies depending on the circulating serotype and the immune profile of the population. Asymptomatic infections are more common in primary infections and in children. The annual seroconversion rate in a community-based cohort study in Dhaka was estimated to be 12.5%; however, the percentage of seroconversions linked to clinically evident disease was not ascertained (Dhar-Chowdhury et al., 2017). Seroprevalence surveys, which identify prior infection regardless of whether it was clinically apparent, offer a more comprehensive view of the actual disease burden than passive surveillance of clinically obvious cases due to the high percentage of silent infection.

The 2009 WHO classification divides symptomatic dengue into dengue without warning signs, dengue with warning signs, and severe dengue.

a. **Without Warning Signs:**

Fever with at least two of the following symptoms nausea, vomiting, rash, aches and pains, positive tourniquet test, leukopenia, or any warning sign are indicative of dengue without warning. High temperature (usually 39 to 40C), severe headache, retro-orbital pain, myalgia, arthralgia (the distinctive "breakbone fever"), and a maculopapular rash that develops three to five days after the onset of fever are the hallmarks of the febrile phase, which lasts two to seven days. Abdominal discomfort, nausea, and vomiting are frequent gastrointestinal symptoms, and their occurrence may be a sign that the illness will worsen. Fever (100%), headache (78%), myalgia (65%), and retro-orbital pain (52%) were the most frequent presenting symptoms in a study of 319 serologically confirmed dengue patients in northern Bangladesh during the 2019 outbreak (Rafi et al., 2020). The frequency of these symptoms was in line with the typical dengue fever presentation seen in other endemic areas. However, compared to several Southeast Asian settings, the percentage of cases presenting

with warning symptoms (31%) was higher, potentially indicating delayed presentation to care. Patients who arrived at the hospital later were more likely to exhibit warning signs and develop a severe illness, the median period from symptom onset to hospital presentation was four days.

b. Warning Signs:

The emergence of warning signs, such as persistent vomiting, abdominal discomfort, mucosal bleeding, lethargy, hepatomegaly, and a rising hematocrit with quickly falling platelet count, are indicative of the critical phase, which usually occurs around the time of defervescence (days 3 to 7 of sickness) (Tayal et al., 2022). The foundation of the WHO clinical care algorithm is the identification of warning symptoms, which identify patients who are at high risk of developing severe dengue and who need prompt fluid resuscitation. A warning indicator of gastrointestinal involvement and potential impending plasma leakage is persistent vomiting, which is defined as three or more bouts in a 24 hour period. Hepatic congestion and hepatic capsule stretching are hypothesized to be the causes of abdominal pain, which is frequently described as severe and persistent. The thrombocytopenia and capillary fragility that define the critical period are reflected in mucosal bleeding, including epistaxis and gingival hemorrhage. Hypoperfusion of the central nervous system may be the cause of lethargy and restlessness. A liver edge palpable more than 2 cm behind the costal border is known as hepatomegaly, and it indicates hepatic congestion and may be linked to high transaminases. The most accurate test indicator of the development of severe dengue is a rising hematocrit with a rapidly declining platelet count because it signals oncoming shock and plasma leakage.

c. Progression of Severe Dengue:

Significant bleeding, significant organ damage, or severe plasma leakage that results in shock (dengue shock syndrome) are characteristics of severe dengue. A narrow pulse pressure (less than 20 mm Hg), hypotension, and symptoms of poor peripheral perfusion, such as oliguria, delayed capillary refill, and chilly extremities, are the hallmarks of dengue shock syndrome. Increased vascular permeability, which permits plasma to escape from the intravascular to the extravascular compartment and causes hemoconcentration and hypovolemia, is part of the pathogenesis of dengue shock syndrome. Dengue shock syndrome

can develop into irreversible shock and death if it is not identified and treated quickly with intravenous fluid resuscitation. Although it happens in a small percentage of severe dengue patients, severe bleeding which includes cerebral hemorrhage, menorrhagia, and gastrointestinal bleeding is linked to a high death rate. Thrombocytopenia, platelet dysfunction, coagulopathy, and endothelial dysfunction are all factors that contribute to dengue's bleeding tendency. Even in the absence of shock and hemorrhage, severe organ impairment, such as acute liver failure, acute kidney injury, myocarditis, and encephalopathy, can happen due to the virus's direct cytopathic action or the effects of immune-mediated tissue damage.

5.2 Crucial Biomarkers for Severe Dengue

Rising hematocrit with concurrent thrombocytopenia is the most reliable laboratory predictor of progression to severe dengue in South Asian populations. Thrombocytopenia (platelet count below 150,000 per cubic millimeter) is nearly universal in dengue infection, and a platelet count below 50,000 per cubic millimeter is associated with increased risk of bleeding. The nadir platelet count typically occurs on day 5 to 7 of illness, coinciding with the critical phase, and platelet counts begin to recover during the recovery phase. The mechanism of thrombocytopenia in dengue is multifactorial and includes bone marrow suppression, immune-mediated platelet destruction, and platelet consumption due to disseminated intravascular coagulation.

The hallmark of plasma leakage and the primary criterion for diagnosing dengue shock syndrome is hemoconcentration, which is defined as an increase in hematocrit of 20 percent or greater from baseline. However, the existence of anemia or polycythemia at baseline, the effects of fluid resuscitation (which may conceal hemoconcentration), and the lack of a known baseline value for the majority of patients complicate the interpretation of hematocrit.

Leukopenia, increased liver enzymes (especially aspartate aminotransferase), hypoalbuminemia, and hyponatremia are other common laboratory abnormalities (Rathore et al., 2020). Liver involvement is indicated by elevated transaminases, which are more common in severe dengue than in dengue without warning signals. In severe instances, these levels may surpass 1,000 IU per liter. Due to increased vascular permeability, albumin is lost from the intravascular compartment, which is reflected in hypoalbuminemia. Severe dengue

frequently results in hyponatremia, which can be caused by the syndrome of improper antidiuretic hormone secretion or the consequences of fluid resuscitation with hypotonic solutions.

5.3 Different Clinical Approach According to Age

Dengue symptoms vary according to age. Dengue may manifest as an undifferentiated febrile disease in newborns and young children, and it may be challenging to elicit the characteristic symptoms of headache, retro-orbital discomfort, and myalgia. The classic presentation is more prevalent in older kids and adults. Age also affects the risk of severe dengue: in South Asia, especially Bangladesh, severe dengue is increasingly documented in adults, whereas in Southeast Asia, it has historically been most frequent in children. In contrast to the juvenile predominance seen in Southeast Asia, the 2019 and 2023 outbreaks in Bangladesh were notable for the large percentage of severe cases and deaths among adults aged 40 to 60 years (Haider et al., 2023).

The population's immune nature may be reflected in the age shift in severe dengue in South Asia. Adults in populations where dengue has been common for decades are more likely to have had many infections, and secondary heterotypic infections increase the risk of severe dengue. Because adult patients are more likely to have comorbidities that make fluid management more difficult, the prevalence of severe disease in adults has implications for both clinical management and vaccine policy. This is because the age group at highest risk may not be the same as the age group that pediatric vaccination programs target.

5.4 Poor Outcome of Individual Variables (Predictors)

Risk factors for severe outcomes identified in Bangladeshi and regional studies include secondary infection (as indicated by a high IgG to IgM ratio in the acute phase), diabetes mellitus, hypertension, chronic kidney disease, obesity, and delayed presentation to care. In hospital mortality predictors among hospitalized adults with dengue include age over 40 years, the presence of acute kidney injury, elevated transaminases more than five times the upper limit of normal, and the need for mechanical ventilation (Lee et al., 2023). The identification of these predictors has implications for triage, as patients with multiple risk factors should be prioritized for close monitoring and early intervention.

5.5. Diagnosis and Limitations of resources

5.5.1 Clinical Diagnosis

The WHO 2009 case classification, which defines probable dengue as an acute febrile illness with two or more of the following headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, or leukopenia, occurring in a dengue-endemic area, is the basis for the clinical diagnosis of dengue. However, the patient's age, the clinician's experience, and the circulating serotype all affect how sensitive this clinical case definition is. The WHO clinical case definition has a sensitivity of roughly 60 to 70 percent when compared with laboratory confirmation, according to studies from Bangladesh. This means that even when clinicians correctly apply the criteria, a significant percentage of dengue cases are missed (Hossain et al, 2023b).

The overlap between dengue and other feverish conditions exacerbates the limits of clinical diagnosis. Clinical criteria alone cannot reliably differentiate dengue from chikungunya, Zika, leptospirosis, typhoid fever, or malaria in the early febrile phase. Although laboratory confirmation is necessary for an appropriate diagnosis due to the lack of pathognomonic clinical characteristics, clinical diagnosis is still the major method of case detection because laboratory testing is not widely available in Bangladeshi healthcare institutions.

5.5.2. Laboratory Reports

IgM serology is most helpful after day five of illness, but NS1 antigen testing offers the maximum sensitivity during the early febrile phase (days 1 to 5 of illness). A viral non-structural protein released by infected cells, the NS1 antigen can be seen in serum from the first day of fever until roughly day 7 or 9. It is the recommended test for early diagnosis since its sensitivity is higher than 90% during the first three days of sickness. But after day five, NS1 sensitivity starts to decrease, and in secondary infections, pre-existing NS1 antibodies may create immunological complexes that make NS1 detection less sensitive.

IgG antibodies develop soon after IgM and last for years, whereas IgM antibodies start to show up around day 4 or 5 of sickness and last for two to three months (Tai et al., 2017). The timing of sample collection must be taken into account when interpreting IgM and IgG results. Although it cannot differentiate between primary and secondary infection, a single

positive IgM test during the acute phase is consistent with a recent dengue infection. In the acute phase, a high IgG-to-IgM ratio indicates secondary infection, which is linked to an increased risk of severe dengue.

With the added benefit of detecting the infecting serotype, RT-PCR gives the best sensitivity and specificity; nevertheless, it necessitates appropriate equipment, reagents, and skilled staff. The WHO recommends a combination of NS1 antigen testing and IgM serology for endemic settings, with RT-PCR reserved for specific cases.

5.5.3. Limitations of Diagnosis

The cost of diagnostic tests (NS1 rapid tests cost about USD 3 to 5, or one to two days' wages for many households), the scarcity of testing in public-sector primary care facilities, and the concentration of RT-PCR capacity in a few tertiary and research laboratories are some of the obstacles to laboratory confirmation in Bangladesh. Patients must pay for all diagnostic expenses due to the lack of a national health insurance program, which creates a financial barrier that disproportionately impacts the poor (Das et al, 2017).

Local differences in access to laboratory confirmation are caused by the concentration of diagnostic capability in urban regions. District-level hospitals usually rely on clinical diagnosis reinforced by complete blood count, and Dhaka is home to over 70% of the nation's NS1 testing and RT-PCR capabilities. One significant gap in the diagnostic landscape is the lack of accessible, accurate, and user-friendly point of care diagnostic assays in primary care settings.

5.5.4 Underreporting And Misclassification

The majority of Bangladeshi healthcare facilities rely on clinical diagnosis without laboratory confirmation, which leads to significant underreporting. Only 7 to 15% of symptomatic dengue cases were reported by the national surveillance system between 2012 and 2015, according to a Bayesian modeling study of dengue incidence in Dhaka. Underreporting was most noticeable in non-outbreak years and in facilities outside of Dhaka (Sharmin et al, 2016). Those from lower-income households, who are less likely to seek care at facilities that report to the surveillance system, and those from rural locations, where diagnostic capability is limited, are disproportionately underreported.

The underestimating of the dengue burden is also a result of misclassification. The dengue monitoring system does not record dengue cases that are mistakenly identified as other fever infections, such as typhoid, malaria, or chikungunya. On the other hand, the estimated dengue burden may be overstated if instances of other feverish conditions are mistakenly identified as dengue. Although the overall impact of misclassification on dengue monitoring accuracy is uncertain, given the prevalence of clinical diagnosis without laboratory confirmation, it is likely that the true burden is far higher than the reported burden.

5.5.5 Surveillance Case Definitions

Regional comparison is hampered by the inconsistent use of WHO monitoring case definitions among South Asian nations. Although its application has been inconsistent, the WHO 2009 case classification was intended to increase the sensitivity of severe dengue detection and to standardize reporting across nations. Severe dengue is not consistently reported across facilities in Bangladesh, and the country's surveillance system employs a reduced case definition that falls short of the WHO warning signals classification.

5.6. Treatment

5.6.1 Treatment of Dengue Without Warning Signs

As long as they can tolerate oral fluids, maintain sufficient urine output, and have consistent access to daily follow up, patients with dengue who do not exhibit warning signs can typically be treated as outpatients. The main goal is to avoid dehydration by consuming enough oral fluids, such as water, fruit juices, soups, or oral rehydration solution (ORS). According to the World Health Organization [WHO], 2009, the Centers for Disease Control and Prevention, 2025, patients should be informed to seek medical attention right away if they experience warning signs like persistent vomiting, severe abdominal pain, mucosal bleeding, lethargy, or decreased urine output.

The recommended antipyretic and analgesic for treating fever and pain in cases of simple dengue is paracetamol (acetaminophen). Because they impair platelet function and raise the risk of gastrointestinal and mucosal bleeding, aspirin, ibuprofen, diclofenac, naproxen, and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided, especially during the critical phase of dengue infection (WHO, 2009; Simmons et al., 2012).

Patients should undergo regular clinical assessment during the febrile and early critical phases, including monitoring of hematocrit, platelet count, body temperature, hydration status, and urine output. Daily reassessment allows clinicians to identify early signs of plasma leakage or hemoconcentration before shock develops, thereby reducing the risk of severe complications (WHO, 2012; Guzman et al., 2016).

5.6.2 Treatment of Dengue With Warning Signs

Due to their high risk of developing severe dengue, patients who exhibit warning signs must be admitted to the hospital. Persistent vomiting, severe stomach discomfort, clinical fluid accumulation, mucosal bleeding, hepatomegaly, lethargy, restlessness, and an increasing hematocrit with rapidly decreasing platelet counts are warning signals. Continuous monitoring is made possible by hospital admission during the crucial stage when plasma leakage is most likely to happen (WHO, 2009, CDC, 2025).

Intravenous isotonic crystalloid solutions, such as normal saline or Ringer's lactate, constitute the cornerstone of treatment for patients with warning signs. Fluid replacement should be carefully titrated according to blood pressure, pulse pressure, urine output, hematocrit, and clinical improvement. Excessive fluid administration should be avoided because plasma reabsorption during the recovery phase may result in pulmonary edema or heart failure (WHO, 2012).

Throughout hospitalization, close clinical and laboratory monitoring is crucial. Early detection of deteriorating plasma leakage or bleeding is made possible by serial assessments of hematocrit and platelet count, as well as regular evaluation of vital signs, capillary refill time, respiratory status, and urine output. According to WHO (2009) and Lee et al (2022), blood transfusion is only advised when there is noticeable clinical bleeding rather than only thrombocytopenia.

5.6.3 Treatment of Severe Dengue

Severe bleeding, severe organ dysfunction involving the liver, kidneys, heart, or central nervous system, or severe plasma leakage resulting in shock or respiratory difficulty are the hallmarks of severe dengue, a medical emergency. Patients should be referred right away to

an intensive care unit or high dependency unit where quick intervention and ongoing monitoring are available (WHO, 2009).

Aggressive but carefully controlled intravenous fluid resuscitation remains the most important therapeutic intervention for dengue shock syndrome. Isotonic crystalloid solutions should be administered promptly, with infusion rates adjusted according to clinical response, hematocrit, urine output, and hemodynamic status. Colloid solutions may be considered in patients who fail to respond adequately to crystalloid therapy despite appropriate fluid replacement (WHO, 2012, Simmons et al, 2012).

Blood pressure, heart rate, oxygen saturation, hematocrit, electrolyte concentrations, renal function, liver enzymes, serum lactate, and urine output must all be continuously monitored in patients with severe dengue. Clinicians can quickly detect prolonged shock, organ failure, or fluid overload with this kind of intense monitoring and modify treatment as necessary (Guzman et al, 2016).

Blood component therapy, which includes packed red blood cells and fresh frozen plasma when necessary, should be used to treat clinically substantial bleeding. Patients with active significant bleeding or those in need of urgent invasive treatments should be the only ones to receive platelet transfusions due to low platelet counts. Clinical outcomes have not been shown to improve with routine preventive platelet transfusion (Lye et al, 2017; WHO, 2009).

5.6.4 Age Specific Treatment

a. Children: Children are particularly vulnerable to rapid plasma leakage because of their smaller circulating blood volume and limited physiological reserve. Fluid therapy should therefore be administered according to body weight, with careful monitoring of urine output, hematocrit, pulse pressure, and capillary refill time. Early recognition of compensated shock and prevention of fluid overload are essential for improving survival in pediatric dengue patients (WHO, 2012, Yacoub & Wills, 2014).

b. Adults: With proper oral hydration, paracetamol medication, and daily monitoring, the majority of healthy persons with uncomplicated dengue can be effectively treated as outpatients. Because these comorbidities significantly raise the risk of severe dengue and mortality, adults with diabetes mellitus, hypertension, obesity, cardiovascular

disease, chronic kidney disease, or chronic liver disease need to be closely monitored (WHO, 2022; Guzman et al, 2016).

c. Older Individuals: Fluid management is especially difficult for older persons since they often exhibit unusual clinical symptoms and have reduced cardiovascular and renal reserve. Therefore, it is important to monitor cardiac function, renal function, electrolyte balance, and symptoms of fluid excess when administering intravenous fluids. Due to their greater incidence of serious illness and mortality, older people should typically have a lower hospitalization threshold (WHO, 2022).

d. Pregnant Women: Pregnant women infected with dengue require specialized multidisciplinary care because infection is associated with increased risks of maternal hemorrhage, preterm delivery, fetal distress, and vertical transmission. Careful fluid therapy is essential to maintain maternal circulation while minimizing pulmonary edema. Continuous fetal monitoring and coordinated obstetric management are recommended, particularly in women with severe thrombocytopenia or active bleeding (WHO, 2022, Paixão et al, 2018).

5.7. Dengue Vaccine

a. History of Dengue Vaccine Research

In recent decades, the development of a vaccine for this infection has been a major global health priority, considering that dengue infection is becoming more common all over the world. The study of vaccines started in the middle of the last century as researchers realised there was a need for a vaccine against the four dengue virus serotypes. But vaccine development was especially difficult due to immunity to the first serovar not conferring total immunity to other serovars. Moreover, the possible occurrence of secondary infection with a different serotype could predispose to severe infection through complex immune mechanisms (Pintado Silva and Fernandez-Sesma, 2023). Due to this, studies have been done to develop a tetravalent vaccine that can induce a globular immune response associated with all four serotypes at the same time. The advent of biotechnology (immunology and virology) has greatly facilitated the study of vaccines and the development of several promising vaccine candidates. The most prominent is Dengvaxia (CYD-TDV) - the first licensed dengue vaccine - and the development of the new vaccines TV003, TV005 and TAK-003.

b. Dengvaxia (CYD-TDV)

CYD-TDV or Dengvaxia was created by Sanofi Pasteur and is the only dengue vaccine to be approved by regulators. A live attenuated quadrivalent vaccine that provides immunity against all four dengue virus serotypes. During clinical trials with thousands of people, it had been shown that Dengvaxia could decrease the incidence of symptomatic dengue and severe dengue disease in people who had been previously infected with the dengue virus. The vaccine was a major development in preventing dengue as it was the first proof of the ability of vaccination to help curb the dengue burden in endemic areas (Thomas and Yoon, 2019). After the trials, Dengvaxia was launched in several countries which are mostly prone to dengue. But, post-licensure studies have shown some crucial safety issues, especially in people who had never had a dengue infection before, and this has given rise to a reconsideration of its use.

c. Emerging Dengue Vaccines

Given the constraints of the first dengue vaccine used (Dengvaxia or CYD TDV), which has led to an increase in side effects in the population's younger age groups, researchers have been prompted to work on safer and more effective vaccine candidates (Hershan, 2023). The development of new-generation dengue vaccines is attempting to develop a strong and balanced immunity to all four serotypes of the dengue virus, with reduced risk of antibody-dependent enhancement (ADE). Several promising vaccine candidates are undergoing clinical evaluation, such as TAK-003, TV003 and TV005. Furthermore, new vaccine platforms using biotechnology techniques could generate new vaccines that could make them more efficient, safe, and readily available (Anumanthan et al., 2025). These are the vaccines that may soon lead to a lesser impact of Dengue on the global scale, and therefore better health in endemic areas.

1. TV003 and TV005 Vaccine Candidates

TV003 and TV005 are live attenuated tetravalent dengue vaccine candidates, developed by the United States National Institutes of Health (NIH). All these vaccines have been formulated to elicit a balanced immune response towards all four serotypes of the dengue

virus. TV003 and TV005, unlike Dengvaxia (which was effective to different extents in those who had been exposed to or not exposed to dengue previously), have yielded promising results in both seropositive and seronegative patients (Bouzidi et al., 2026). TV003 includes four serotypes of dengue virus (DENV), all of which are weakened versions and have been found to induce high levels of neutralising antibody response after just one dose. The vaccine has generally been well accepted in clinical trials and has been able to induce immunity to several serotypes in one. In addition, studies with controlled human infection models showed strong protection against viral challenge with dengue virus (Tricou et al., 2020). While TV003 contains an intermediate dose of the DENV-2 component, TV005 is modified to include a greater dose of this component. This formulation was created to augment the immune response to DENV-2, which was less extensively immunogenic in previous vaccine development candidates. The clinical trial results demonstrate that TV005 induces well-balanced antibody responses against all four serotypes and has a favourable safety profile. TV003 and TV005 may have one of their most important of all their benefits, as they may help achieve widespread protection following a single dose, which would ease vaccination programs in endemic countries. People have shown great interest in them because of their promising clinical performance, and they can be an alternative to the current vaccines. Long-term efficacy, duration of immunity and large-scale implementation strategies are being continually assessed.

2. TAK-003 Vaccine

Another important dengue vaccine candidate is TAK-003, which is developed by Takeda Pharmaceuticals. It is a live-attenuated tetravalent vaccine that consists of an attenuated DENV-2 backbone containing genetic material from DENV-1, DENV-3 and DENV-4. This design seeks to elicit broad efficacy across all 4 serotypes of Dengue Virus.TAK-003 has been shown to give significant protection against the severity of dengue infection and hospitalisation in large-scale Phase III clinical trials. The vaccine is effective in a wide age range and geographical area; thus, it could be a viable vaccine for large-scale use (Yan et al., 2025). In contrast to previous vaccines, TAK-003 has shown promising activity against both seropositive and seronegative individuals, but further studies need to be conducted to evaluate long-term effects.Safety assessments have shown that TAK-003 is generally tolerable, and that the majority of any adverse effects that occur are mild or moderate – for

example, injection site reaction, headache and fatigue. The vaccine has a good safety footprint, which has led to approval in several countries. Studies are ongoing into the persistence of vaccine-induced immunity and whether the vaccine is effective against the various serotypes of dengue in circulation over longer time periods (Huang et al., 2021).

Chapter-6
Aedes Mosquito Distribution

6.1 Biology

Aedes mosquitoes, especially Aedes aegypti and Aedes albopictus, are tiny, dark-colored insects that belong to the Culicidae family and have characteristic white patterns on their legs and thorax. Many medically significant arboviruses, such as dengue, Zika, chikungunya, and yellow fever, are mostly spread by it. Aedes aegypti is a highly anthropophilic insect that lives in close proximity to human settlements and prefers to feed on human blood. Albopictus consumes both humans and animals and is more opportunistic. Both sexes of mosquitoes typically consume plant nectar for energy, but only females consume blood meals, which supply the proteins required for egg formation. Under ideal environmental conditions (25–30°C), the life cycle's four separate stagesegg, larva, pupa, and adult, are usually finished in 7–10 days. Individual eggs are laid by females on the inner walls of water-filled containers slightly above the waterline. These eggs are remarkably resistant to desiccation, meaning they can withstand dry circumstances for several months before being submerged in water.

The aquatic larval stage consists of four instars in which the larvae actively consume organic waste, algae, and microorganisms before changing into non feeding pupae, from which adults emerge. The early morning and late afternoon are when adult Aedes mosquitoes are most active during the day. Ae. aegypti typically has a flying range of less than 200 meters, which causes limited transmission near breeding grounds. Carbon dioxide, body heat, skin smells, wetness, and visual stimuli are among the sensory cues that mediate host-seeking behavior. After consuming an infectious blood meal, the dengue virus first enters the mosquito's midgut, spreads via the hemocoel, and, after an extrinsic incubation time of about 8 to 12 days, reaches the salivary glands, allowing for transmission during future blood meals.

Aedes mosquitoes are particularly well adapted to urban and peri-urban settings because environmental factors like temperature, humidity, rainfall, urbanization, and the availability of artificial water-holding containers have a significant impact on their vector competence and survival. Aedes mosquitoes are among the most effective vectors of dengue virus transmission globally due to their high reproductive capability, frequent human biting activity, many blood-feeding events within a single gonotrophic cycle, and close interaction with human environments.

6.2 Ecology

Through behavioral changes that enhance its vectorial capacity, Aedes aegypti, the main urban dengue vector, has adapted to the Dhaka environment. These include oviposition in clean water containers, which are common in urban environments, multiple feeding attempts per gonotrophic cycle, which increases the likelihood of virus acquisition and transmission, and indoor resting, which lessens exposure to outdoor insecticide applications (Gutirrez et al, 2020). Aedes aegypti is a very effective vector that may maintain transmission even at comparatively low mosquito concentrations because of its adaptation to the urban environment. Aedes albopictus, a secondary vector that prefers outdoor breeding grounds and has a higher tolerance to cold, has spread into Bangladesh's peri-urban and rural areas. Aedes albopictus may reproduce in both artificial and natural containers, such as tree holes and leaf axils, and is less reliant on artificial ones. Dengue transmission has spread geographically outside of the urban core, where Aedes aegypti is predominant, thanks to its spread into rural regions. The location of Aedes positive breeding containers found in Dhaka during the 2019 outbreak is summarized in Figure 6, which emphasizes the preponderance of water storage containers as the most productive larval habitat.

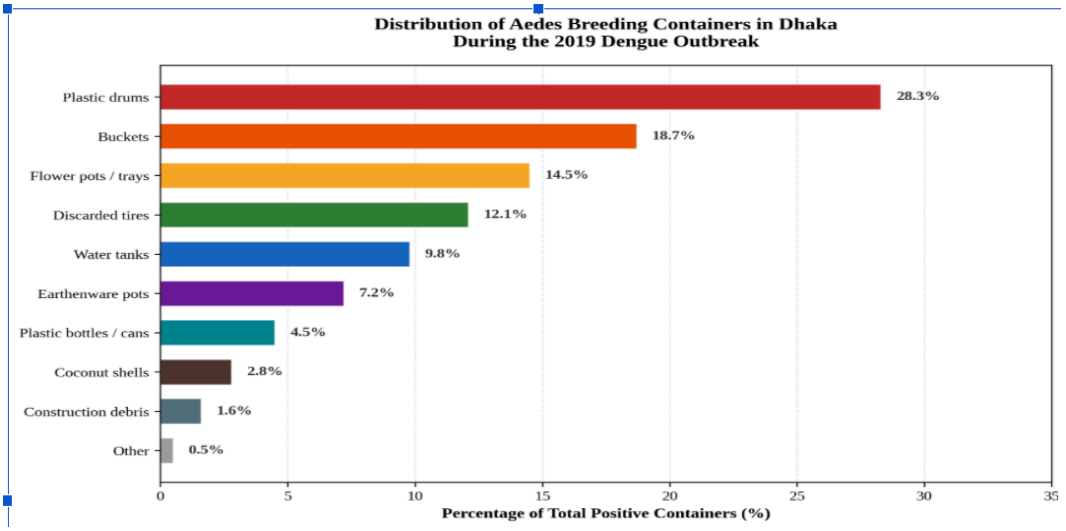

Figure 6: Distribution of Aedes breeding containers identified in Dhaka during the 2019 outbreak.

6.3 Environmental Factors of Transmission and Risk in the Perspective of Bangladesh

6.3.1 Effect Of Climate and Monsoon

The best climatic indicators of dengue incidence in Dhaka and other metropolitan areas are temperatures between 25 and 30 degrees Celsius and rainfall with a lag of one to two months. A 1C increase in monthly mean temperature was linked to a 25–30% increase in dengue cases in the following month, while a 10-mm increase in monthly rainfall was linked to a 5–8% increase in incidence two months later, according to a count regression analysis of climate factors and dengue incidence in Dhaka between 2000 and 2019 (Hossain et al., 2023b). The time it takes for Aedes eggs to hatch, larvae to grow, and adult mosquitoes to become contagious after feeding on a viremic host is reflected in the lagged effect of rainfall.

The ideal temperature and rainfall ranges for dengue transmission were found using a generalized linear regression model that looked at threshold effects. The highest dengue incidence was linked to maximum temperatures of 30 to 33C and monthly rainfall of 200 to 400 mm (Hossain, 2023). Reduced transmission was linked to temperatures above 35C, which may indicate the detrimental effects of intense heat on Aedes survival and activity. The bidirectional association between temperature-rainfall patterns and dengue prevalence in Dhaka is depicted in the Figure below

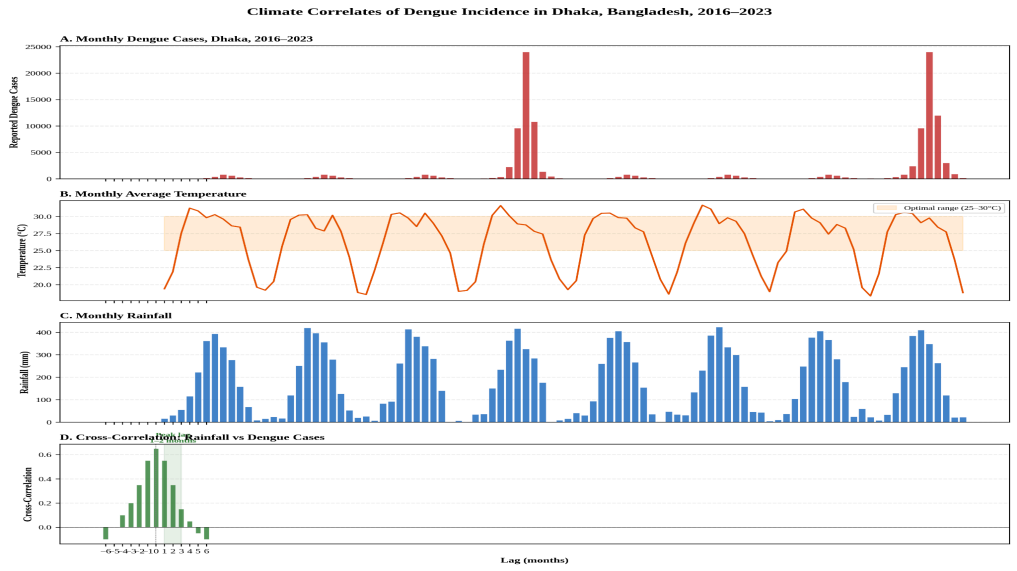

Figure 7: Climate correlates of dengue incidence in Dhaka, Bangladesh, 2016–2023.

6.3.2 Temperature, Rainfall, and Humidity

The relationship between dengue transmission and climate variables is intricate and clearly nonlinear. The length of the Aedes life cycle (from egg to adult), the extrinsic incubation period of the virus within the mosquito, the biting rate of adult female mosquitoes, and the lifespan of adult mosquitoes are all impacted by temperature. In order to optimize the likelihood that an infected mosquito would survive long enough to spread the virus, the ideal temperature for dengue transmission is roughly 25 to 30C, where the extrinsic incubation time is 5 to 10 days. Although rainfall provides Aedes mosquito breeding grounds, there is a nonlinear correlation between rainfall and dengue incidence. While moderate rainfall produces the standing water that is perfect for Aedes breeding, heavy rainfall can flood out larval habitats, temporarily lowering Aedes populations. Rainfall's temporal distribution is just as significant as its overall amount: Aedes breeding is more conducive to intermittent rainfall that alternates between wet and dry periods than to continuous heavy rainfall. Since adult Aedes mosquitoes are susceptible to desiccation, humidity has an impact on their survival. higher mosquito survivability and, thus, higher transmission are linked to relative humidity levels exceeding 60%. Dengue transmission is consequently facilitated by Bangladesh's high humidity during the monsoon and post-monsoon seasons, whereas the seasonal fall in transmission may be attributed to the winter's reduced humidity. The climatic appropriateness for dengue transmission is expected to rise over the next few decades in terms of both geographic breadth and seasonal duration, according to climate change estimates for Bangladesh that indicate increases in both mean temperature and the frequency of intense rainfall events. The section on research gaps goes into further depth about how climate change affects dengue spread in Bangladesh.

6.3.3 Rapid Urbanization and Increasing Population Density

Dhaka has become a year-round Aedes breeding ground due to unplanned urbanization, peri-urban growth, and reliance on water storage containers. The population of Dhaka increased from over 6 million in 1990 to over 22 million in 2024, with a large portion of this growth taking place in informal settlements where households store water in drums, buckets, and tanks and the municipal water supply is sporadic. Dhaka has one of the greatest population densities in the world, more than 20,000 people per square kilometer in its core urban areas and the close proximity of human hosts to Aedes breeding sites promotes

effective transmission. Water storage drums (34 percent of positive containers), discarded tires (18 percent), flower pots and trays (15 percent), and construction-site water accumulations (12 percent) were the most productive Aedes breeding containers, according to a cross-sectional entomological survey of 12 wards in Dhaka during the 2019 outbreak (Ahsan et al., 2020). In every ward surveyed, the Breteau index (number of positive containers per 100 households) was greater than 20, which is far higher than the WHO threshold of 5 for pandemic risk. The high Breteau index is a sign of widespread Aedes breeding and a lack of source reduction in vector control efforts.

Through the buildup of water in building materials, on rooftops, and in basements, the construction industry, which operates across Dhaka, generates more breeding grounds. Development sites are a major and unappreciated source of Aedes reproduction due to the quick speed of development and the absence of enforcement of building standards requiring the removal of standing water.

6.3.4 Stationary Waterbody and Traditional Household Practices

One of the main causes of Aedes proliferation in Dhaka and other Bangladeshi cities is the sporadic municipal water supply. Households store water in a variety of containers, such as drums, buckets, tanks, and earthenware pots, many of which are either uncovered or insufficiently covered, when water is only accessible for a few hours each day. For Aedes aegypti, which favors clean, standing water for oviposition, these containers offer perfect larval habitat. Knowledge, attitudes, and socioeconomic conditions all affect how households store water and dispose of solid waste. A survey of youth in Bangladesh found that while 72 percent of respondents correctly identified mosquitoes as the dengue vector, only 34 percent could identify at least three breeding-site elimination practices, and knowledge was significantly lower among respondents from lower-income households (Siddique et al., 2024). The gap between knowledge and practice is a recurring theme in dengue prevention research: knowledge of dengue transmission does not necessarily translate into sustained breeding-site elimination behavior.

6.3.5 Waste and Sanitation

Inadequate solid waste management is a major contributor to Aedes breeding in Bangladesh. Discarded containers, including plastic bottles, cans, cups, and tires, accumulate water during

the monsoon and provide larval habitat for Aedes mosquitoes. The coverage of municipal solid waste collection in Dhaka is estimated at approximately 50 to 60 percent, with the remainder of solid waste disposed of informally, often in open lots, drains, and water bodies. The informal disposal of solid waste creates scattered breeding sites that are difficult to identify and eliminate through centralized vector control programs. Dhaka's drainage system, which is intended to transport wastewater and stormwater, is frequently clogged with solid waste, resulting in stagnant water that acts as a breeding ground for Aedes. The issue is made worse by infrequent drain repair and the expansion of informal settlements on drainage channels. Therefore, improving drainage and solid waste management is a top priority for preventing dengue, but it necessitates intersectoral cooperation between the water and sanitation, health, and municipal agencies.

6.3.6 Human Transportation and Migration

Through a number of mechanisms, human migration and mobility contribute to the dengue outbreak in Bangladesh. Driven by economic opportunities, internal migration from rural areas to Dhaka raises the city's population density and the number of vulnerable people exposed to Aedes breeding sites. As workers who contract the virus in Dhaka return to their home villages during the harvest season, seasonal migration for agricultural labor which is widespread in Bangladesh may spread the virus from urban to rural areas. New serotypes may enter Bangladesh through international migration, especially the movement of Bangladeshi laborers to and from dengue-endemic nations in the Middle East and Southeast Asia. Human migration over the porous India-Bangladesh border is an important mode of virus introduction, according to phylogenetic evidence for cross-border movement of DENV genotypes between Bangladesh and India.

Chapter-7

Economic Burden of Dengue

7.1. Direct Cost

Dengue has evolved into a persistent economic concern affecting both household finances and national healthcare systems (World Health Organization [WHO], 2024 Direct medical expenses include physician consultations, diagnostic testing, intensive care management, medications, hospital admissions, intravenous fluid therapy, and follow-up healthcare services. Patients dealing with severe dengue need repeated laboratory monitoring, blood transfusions, prolonged hospitalizations, and intensive supportive care, which significantly increases healthcare expenditures. Not only that, but during large outbreaks, hospitals experience shortages of medical personnel, diagnostic equipment, beds, and essential supplies, increasing operational costs and reducing healthcare efficiency increasing operational costs and reducing healthcare efficiency increasing operational costs and reducing healthcare efficiency.

Table 02: Societal cost of illness due to dengue fever, per person per episode (US$).

Type of cost	**Cost component**	**Overall**	
Direct Medical	**Diagnostic (e.g., CBC, NS1)**	**0.44**	**0.61**
	Medicine	**2.58**	**3.53**
	Medical Materials (e.g., syringe, cannula)	**0.12**	**0.17**
	Staff personnel (e.g., doctor, nurse)	**37.02**	**50.74**
Total direct medical	**40.17**		**55.05**
	Shared personnel (e.g., admin officer, accountant)	**12.04**	**16.51**
	Transport (e.g., ambulance)	**0.14**	**0.19**
	Food cost	**8.06**	**11.05**

Direct non-medical	**Stationeries (e.g., pen, print, paper, photocopy)**	**0.97**	**1.33**
	Utilities (e.g., electricity, water, telephone)	**8.21**	**11.25**
	Laundry	**0.43**	**0.6**
	Capital items (e.g., furniture, machineries)	**0.71**	**0.97**
	Building (e.g., study ward/sq. feet)	**2.22**	**3.05**

The above table demonstrates the cost of illness from a societal perspective. The average societal cost of a dengue patient was USD 479.02, whereas for the patients treated in public and private hospitals, the average societal cost for illness was USD 567 and USD 342, respectively. Considering the treatment cost by the provider, direct medical cost was 8.4% which was the main cost driver followed by the indirect cost (6.8%). In between public and private hospitals, private hospitals are profit-maximizers as the entire treatment cost is incurred by the patient.

If we compare the average cost per dengue case, we observed that the average cost per dengue case in Bangladesh was lower than the average cost of dengue per episode in Thailand (US$ 573), Malaysia (US$ 947), Indonesia (US$ 791 to US$ 1250), Venezuela (US$ 627), Brazil (US$ 676), Panama (US$ 1,065) and higher than from India (US$ 432.2), Pakistan (US$ 358), Sri Lanka (US$ 32 to US$ 330) and in many North American countries like El Salvador (US$ 457), Guatemala (US$ 418) and Cambodia (US$11)(Mahmud et al., 2023). Although our study observed that the total societal treatment cost of dengue was comparatively higher than that of the neighboring countries. This might be due to various reasons such as the differences in study settings (e.g., urban vs rural), sampling strategy (e.g., local vs national) and even for the seasonal variations . For instance, a study conducted in Colombo, Sri Lanka observed that the cost of hospitalization of an adult dengue patient was US$ 196 to US$ 866 in a dengue epidemic year (Mahmud et al., 2023).. A recent cost-estimation study in India reported that the costs per hospitalized non-fatal and fatal

dengue illnesses were about US$ 325 and US$ 36,385 respectively . Therefore, the results might be different varying on the contexts, which further urges that priority should be given to conduct a multi-country study in near future.

The findings highlighted the substantial economic burden of dengue among Dhaka city dwellers, which stresses on the urgent need for an effective national prevention strategy to perform considerable cost-savings besides reducing morbidity(Hung et al., 2020).. Therefore, policy-makers should consider the treatment cost of dengue infections, particularly among the poor in the population while balancing the benefits of introducing potentially effective dengue preventive programs such as vaccine introduction.

7.2. Indirect Costs

Indirect economic losses exceed direct healthcare costs as dengue initially affects economically productive age groups. Generally, individuals infected with dengue require several weeks to recover before returning to their normal lives. And during this span of time, absenteeism from school and work causes substantial losses for both household and national economies. Businesses may experience reduced productivity because of employee illness, and parents lose working days while caring for infected children. In countries, due to the recurrent dengue epidemics, cumulative productivity losses take place, resulting in an overall economic burden. consisted of 18% of the total societal cost of illness comes from the indirect cost such as income and productivity loss of patients and caregivers.

A systematic review of productivity costs from dengue episodes in Asia estimated that the mean number of workdays lost per episode ranged from 7 to 14 days for hospitalized cases and 3 to 5 days for ambulatory cases, with the total indirect cost representing 45 to 65 percent of the overall economic burden (Hung et al., 2020).

In Thailand, a study of household costs of hospitalized dengue illness in a semi-rural setting found that indirect costs, primarily from lost wages of patients and caregivers, accounted for 56 percent of the total household cost, and that 22 percent of households experienced catastrophic health expenditure (Tozan et al., 2017). The economic impact extends beyond the acute episode: households that finance dengue care through high-interest informal loans or asset sales may experience long-term financial consequences.

7.3. Household Financial Burden

The financial hardship associated with dengue care extends beyond the direct and indirect costs of the acute episode. Households that finance care through borrowing or asset sales may experience long-term consequences, including reduced household food security, school dropout among children whose families can no longer afford educational expenses, and the intergenerational transmission of poverty through asset depletion (Legorreta-Soberanis et al.,2017).

Table 03: Cost burden and catastrophic health expenditure in different socio-economic conditions, US$.

groupIncome	Average monthly income (US$)	Average total OOP cost (US$)	OOP cost as a percentage of monthly household income
Poorest quintile	**131.41**	**183.07**	**139.31%**
2nd quintile	**248.99**	**235.83**	**94.71%**
3rd quintile	**369.40**	**265.13**	**71.77%**
4th quintile	**574.65**	**338.65**	**58.93%**
Upper quintile	**1704.61**	**616.61**	**36.17%**
Overall	**561.71**	**316.51**	**56.35%**

groupIncome	Average monthly income (US$)	Average total OOP cost (US$)	OOP cost as a percentage of monthly household income
Poorest quintile	**131.41**	**183.07**	**139.31%**
Rich-poor ratio	**0.16**	**0.04**	**25.97%**
Rich poor difference	**1573.20**	**433.53**	**-103.14%**

The financial hardship is regressive: households in the lowest income quintile spend a significantly higher proportion of their income on dengue care than those in higher quintiles, and are more likely to finance care through borrowing or asset sales. The concentration of specialized dengue care in urban tertiary hospitals means that rural and peri-urban populations face additional costs for transportation and accommodation, as well as delays in accessing appropriate care.

7.4. Out-of-Pocket Expenditure

The predominance of out-of-pocket financing in Bangladesh's health system means that the financial burden of dengue care falls disproportionately on households. The cost of a single dengue hospitalization includes diagnostic tests (NS1 antigen, complete blood count), medications (antipyretics, antiemetics, intravenous fluids), hospital bed charges, and, in severe cases, platelet transfusions and intensive care. The financial burden of dengue care is not limited to the acute episode. Households that finance care through high-interest informal loans or asset sales may experience long-term financial consequences that persist for years after the illness has resolved. The intergenerational transmission of poverty through health-related financial shocks is a well- documented phenomenon in low-income settings, and dengue is likely to contribute to this cycle in Bangladesh.

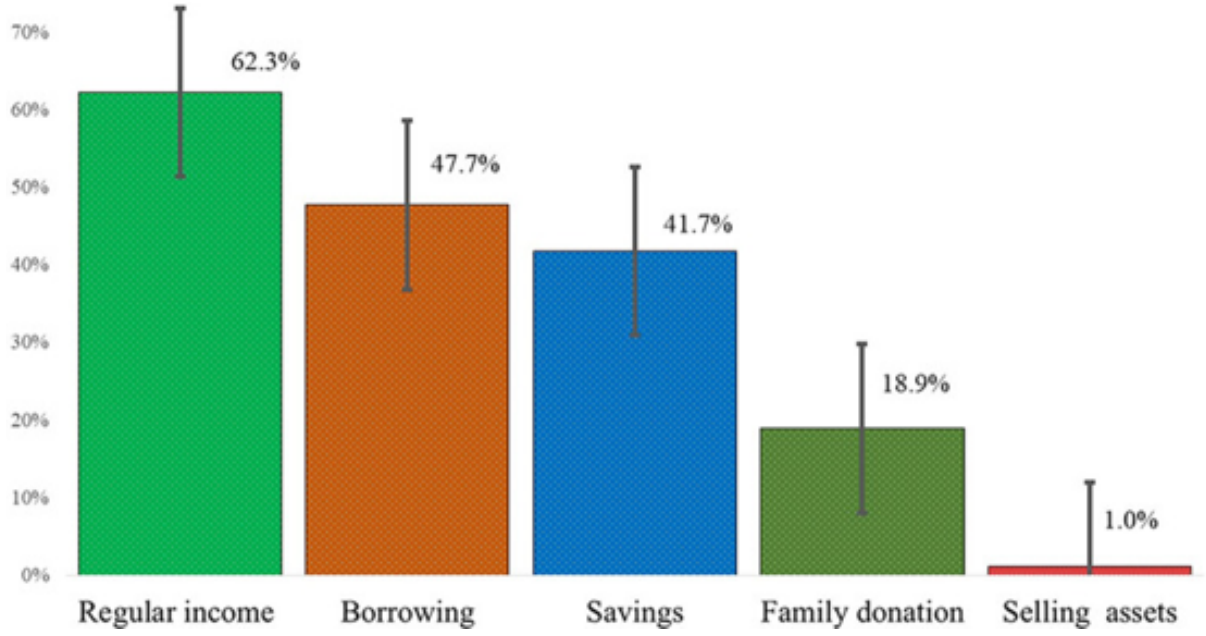

Figure 8: Coping strategies (multiple responses).

The above diagram illustrates that the majority of the household relies on their regular income, which is 62.3%, making it the primary source of their healthcare finance. On the other hand, a good proportion of money depends on borrowing money and personal savings, which are 47.7% and 41.7%, respectively. This substantial amount of money on dengue treatment indicates that this treatment places a considerable financial pressure on households. Moreover, 18.9% of households received financial assistance from family members or relatives, whereas only 1.0% reported selling assets to bear treatment costs. The overall findings indicate that dengue imposes a significant economic burden on households.

Chapter-8

Prevention and Control Strategies

8.1 Personal Protection

In the prevention of dengue transmission, it is very important to maintain personal protective measures. Safety measures like long sleeve cloths, installation of window and door screens,mosquito nets for infants and adults, mosquito repellents containing DEET or picaridin are used. Protective measures during the day should be taken against *Aedes* mosquitoes as they are primarily daytime biters.To create public awareness about mosquito breeding habits, dengue symptoms, and preventive practices, public education campaigns through television, radio, newspapers, and social media should be widely used.

8.2 Vector Control Strategies

Vector control is one of the most effective strategies for reducing dengue transmission. By limiting human-vector contact and eliminating breeding sites, the population of *Aedes* mosquitoes can be decreased. Effective vector control includes proper solid waste disposal, regular removal of stagnant water from domestic and public areas, environmental management, and maintenance of water storage containers to prevent mosquito breeding (Noman et al., 2023). The mosquito population can also be suppressed through the application of larvicides and targeted insecticide fogging during outbreaks. Chemical control, along with larvicides and targeted insecticides, is highly effective in reducing dengue cases (Siddique et al., 2024). Moreover, in certain settings, biological control methods such as using larvivorous fish or bacterial larvicides provide environmentally sustainable alternatives. To achieve long-term and sustainable dengue control, the World Health Organization recommends Integrated Vector Management (IVM), which combines environmental, biological, and chemical control methods with surveillance and public education.

8.3Environmental Management

Environmental management, including the improvement of water supply, sanitation, and solid waste management, is a critical but underutilized component of dengue prevention inBangladesh. The provision of reliable, piped water supply would reduce the need for household water storage, eliminating a major source of Aedes breeding sites. The improvement of solid waste collection and disposal would reduce the accumulation of discarded containers that serve as larval habitat. The maintenance of drainage systems would reduce the accumulation of stagnant water in urban areas.However, environmental management requires intersectoral coordination between the health sector, municipal

authorities, and the water and sanitation sector, which has been inconsistent in Bangladesh. The lack of a dedicated national dengue control program with the authority to coordinate these activities across sectors is a critical barrier to the implementation of environmental management for dengue prevention.

8.4 Chemical and Biological Control Methods

Larviciding with *Bacillus thuringiensis israelensis (Bti)* or temephos has been piloted in selected wards of Dhaka, but coverage has been limited and the emergence of temephos resistance in Aedes populations has been reported in several districts. Bti, a biological larvicide, is effective against Aedes larvae and has a favorable environmental safety profile, but its application requires trained personnel and regular reapplication, which have been challenging to sustain. Wolbachia-mediated biocontrol, which involves the introduction of Wolbachia-infectedAedes mosquitoes that are refractory to dengue virus infection, has shown promise in field trials in Indonesia, Vietnam, and Brazil, but has not yet been evaluated in Bangladesh(Olliaro et al., 2018). The Wolbachia approach has the advantage of being self-sustaining, asWolbachia-infected mosquitoes pass the bacterium to their offspring, and of not requiring the repeated application of insecticides. However, the approach requires the establishment of a mosquito rearing and release facility, community acceptance of mosquito releases, and long-term monitoring of Wolbachia prevalence in the Aedes population.

8.5 Effective Surveillance System

An effective surveillance system is vital for dengue control. Through the Directorate General of Health Services, laboratory confirmation, mosquito population monitoring, and improved case reporting, Bangladesh has strengthened its disease surveillance. Early detection of outbreaks is essential to prepare healthcare facilities for increased patient loads and to implement timely vector control measures. By using early tests such as NS1 antigen and antibody tests, hospitals and clinics are encouraged to diagnose dengue promptly. Additionally, through quick supportive treatment, especially fluid management, the risk of severe complications and death from dengue can be greatly reduced. Patients are advised to seek immediate medical care if they show warning signs like persistent vomiting, severe abdominal pain, bleeding, or difficulty breathing. The use of aspirin and non-steroidal anti-inflammatory drugs is discouraged because these medications can increase bleeding risk, while paracetamol is recommended for fever management.

Chapter-9

Future Prospects and Vaccination for Dengue Control

9.1. Current global Vaccine Landscape

In tropical and sub-tropical regions of more than 100 countries, dengue emerged as one of the fastest-growing mosquito-borne viral diseases. Due to the existence of four antigenically distinct dengue virus serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) the effective development of a dengue vaccine has been quite challenging. Infection with one serotype provides lifelong protection to that particular serotype but temporary protection to other serotypes. The risk of dengue severity increases if infection with another serotype happens by antibody-dependent enhancement (ADE). Therefore, an ideal vaccine should give protection against all the serotypes.In recent years, two vaccines have received regulatory approval in several countries, and other vaccine candidates are in clinical trials. These developments have offered new opportunities to complement conventional vector control strategies and transformed the global dengue prevention landscape.

9.1.1. Licensed Dengue Vaccines

The first vaccine licensed for public use back in 2015 was Dengvaxia®, developed by Sanofi Pasteur. It is a live attenuated tetravalent vaccine that protects against all dengue serotypes. Through large phase III clinical trials, it was demonstrated that Dengvaxia reduces both dengue symptoms and hospitalizations of seropositive individuals. However, following subsequent infection, post-licensure studies revealed that vaccination of seronegative individuals increased the risk of severe dengue and hospitalization. Therefore,World Health Organization(WHO) recommends this vaccine for individuals with laboratory-confirmed previous dengue infection. Before the administration of the vaccine, pre-vaccination serological testing is required.

The second licensed one is named as Qdenga®, developed by Takeda Pharmaceuticals. This vaccine is a live attenuated tetravalent vaccine derived from the DEV2 strain. It demonstrated protection against both seropositive and seronegative individuals in clinical trials unlike Dengvaxia. The Phase III TIDES trial showed that TAK-003 massively reduced hospitalization, virologically confirmed dengue, and severe disease across multiple endemic countries. It demonstrated 61 percent efficacy against virologically confirmed dengue and 84 percent efficacy against hospitalization over 4.5 years of follow-up in a phase 3 trial, with no evidence of increased risk in seronegative recipients (Biswal et al., 2020; Tricou et al., 2024).

The favorable safety profile of TAK-003 in seronegative individuals is a significant advantage over CYD-TDV, as it eliminates the need for pre-vaccination serostatus screening.

Butantan-DV, a single-dose live-attenuated tetravalent vaccine, demonstrated 80 percent efficacy against virologically confirmed dengue over two years in a phase 3 trial in Brazil, with a favorable safety profile across serostatus groups (Kallás et al., 2024). The single-dose regimen of Butantan-DV is a significant practical advantage, as it simplifies vaccine delivery and reduces the cost of vaccination.

A phase 2 trial of the TV005 tetravalent dengue vaccine in dengue-endemic Bangladesh demonstrated safety and durable immunogenicity across serotypes and age groups, providing the first clinical evidence of dengue vaccine performance in the Bangladesh population (Walsh et al., 2023).

The TV005 trial is an important step toward the introduction of a dengue vaccine in Bangladesh, but further studies are needed to evaluate efficacy in the Bangladesh epidemiological context.

Clinical studies reported lowered protection against DENV-3 and DENV-4 and sustained protection particularly against DENV-1 and DENV-2 for several years after vaccination.

9.2. Relevance for South Asia

The relevance of dengue vaccines for South Asia is high, given the region's large population, high disease burden, and limited capacity for sustained vector control. A vaccine that is safe, effective, and affordable could substantially reduce the disease burden and the economic cost of dengue. However, the deployment of dengue vaccines in South Asia faces several challenges.

First, the epidemiological context in South Asia, characterized by the co-circulation of all four serotypes and a high prevalence of secondary infections, is complex, and the efficacy of vaccines may vary by serotype and by prior exposure history. Second, the health systems of South Asian countries have limited capacity for vaccine delivery, particularly for vaccines that require multiple doses or pre-vaccination screening. Third, the cost of vaccines, which is likely to be substantial, may exceed the willingness and capacity to pay of both governments and households.

Comparison of Leading Dengue Vaccine Candidates

Vaccine	Developer	Type	Dosing	VCD Efficacy	Hospitalized Efficacy	Serostatus Effect	WHO Status
CYD-TDV (Dengvaxia)	Sanofi Pasteur	Live attenuated chimeric YF-17D	3 doses 0/6/12 mo	56–61%	67–80%	Seronegative: ↑ risk	Licensed (>9 yrs, seropositive)
TAK-003 (Qdenga)	Takeda	Live attenuated chimeric DENV-2	2 doses 0/3 mo	61–80%	84–95%	Better in seropositive	Licensed (>6 yrs)
Butantan-DV (TV003)	Butantan Institute	Live attenuated tetravalent	1 dose	73–80%	89%	Robust across serostatus	Phase 3 completed

Efficacy color codes: ≥80% 60–79% <60%

Figure 9: Comparison of leading dengue vaccine candidates.

9.3. Prospects for Future Innovation

Researchers are working on developing five types of vaccines: live attenuated vaccines (introduced vaccines), chimeric live attenuated vaccines (introductory vaccines), inactivated vaccines (dormant vaccines), subunit or component affixed vaccines (subunit or component attached vaccines), and nucleic acid-based vaccines (strand-like vaccines). Goals for every form are the inhibition of dengue microbes with contradictory capacities and effectiveness. Another example of innovative vaccine approaches are chimera live-attenuated vaccines, which are created by combining the genes from different sources. Meanwhile, those based on nucleic acid harness the power of DNA copies of specific dengue viral genes introduced to the cells for the eventual production of an immune response.

Besides developing vaccines, it is being examined widely whether antiviral drugs can replace vaccines or not. Vaccination is one of the most feasible measures against Dengue disease. In the future, antiviral drugs could also be explored to relieve or prevent disease symptoms when the first dengue outbreak is noticed. The development of these drugs involves the screening of compounds, which are look for being able to disturb the viral proteins, which are

responsible for viral replication. Viral pathogenesis and immunopathogenesis born by the research investigated how a virus causes the disease and severe symptoms including dengue

hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Some studies propose that, on the one hand, the genetic makeup of the virus is very important, as in the case where the virus is rapidly replicating, and more important in the second case, where the protection of the body against the infection plays a greater role.

Dengue fever also faces the issues of climate changes which are serious. These changes may contribute the future spread and impact of this disease. In the wake of the global climate changes, i.e. the rises in temperature and changes in rainfall patterns, the habitats conducive to the amplification of the Aedes mosquito, the primary agent for the spread of a number of viruses including dengue virus, are expected to expand. This can therefore results to increase in dengue fever incidences and even the extend of its geographical distribution. Projections of climate change consequences indicate that the geographical distribution of dengue's burden, epidemic potential for denguees, and geographical distribution are subjects of active research by the scientists and professors, who have revealed that dengue cases are more possible to increase due to climatic factors.

Next-generation mRNA-based dengue vaccines and antiviral agents offer promising future alternatives, but integrated vector control plus vaccination strategies are needed for sustainable impact. Computational and reverse vaccinology approaches have been used to design mRNA-based dengue vaccine candidates targeting conserved epitopes across all four serotypes, though these remain in preclinical development (Mukhtar et al., 2022). The success of mRNA vaccines for COVID-19 has generated interest in the application of mRNA technology to dengue, and several candidates are in early-stage development. Antiviral development for dengue has been challenging, as the virus's intracellular replication cycle offers limited targets for small-molecule inhibitors, and no dengue-specific antiviral has yet reached clinical use (O. et al., 2021). The development of a safe, effective, and affordable antiviral for dengue would be a major advance, as it would provide a therapeutic option for patients with severe dengue, for whom current management is limited to supportive care.

References

Ahmad, F. U., Paul, S. K., Aung, M. S., Mazid, R., Alam, M., Ahmed, S., Haque, N., Hossain, M. A., Paul, S., Sharmin, R., & Kobayashi, N. (2020). Co-circulation of dengue virus type 3-genotype I and type 2-Cosmopolitan genotype in 2018 outbreak in Dhaka, Bangladesh. *New Microbes and New Infections*. https://doi.org/10.1016/j.nmni.2019.100629.

Ahsan, A., Haider, N., Kock, R., & Benfield, C. (2020). Possible Drivers of the 2019 Dengue Outbreak in Bangladesh: The Need for a Robust Community-Level Surveillance System. *Journal of Medical Entomology*. https://doi.org/10.1093/jme/tjaa150.

Bagahizel, A. M., & Elkhatim, H. S. (2023). Assessment of the readiness and response toward the dengue fever outbreak (2019) in Sudan: a qualitative exploration. *BMC Public Health*. https://doi.org/10.1186/s12889-023-17020-9.

Bhowmik, K. K., Ferdous, J., Baral, P. K., & Islam, M. S. (2023). Recent outbreak of dengue in Bangladesh: A threat to public health. *Health Science Reports*. https://doi.org/10.1002/hsr2.1210.

Biswal, S., Borja-Tabora, C., Vargas, L. M., Velásquez, H., Alera, M. T., Sierra, V., Rodriguez-Arenales, E. J., Yu, D., Wickramasinghe, V. P., Moreira, E. D., Fernando, A. D., Gunasekera, D., Kosalaraksa, Espinoza, F., López-Medina, E., Bravo, L., Tuboi, S., Hutagalung, Y., Garbes, P., … Kosalaraksa, P. (2020). Efficacy of a tetravalent dengue vaccine in healthy children aged 4–16 years: a randomised, placebo-controlled, phase 3 trial. *The Lancet*. https://doi.org/10.1016/s0140-6736(20)30414-1.

Cruz, Z. V. da, Araujo, A. L., Ribas, A., & Nithikathkul, C. (2023). Dengue in Timor-Leste during the COVID-19 phenomenon. *Frontiers in Public Health*. https://doi.org/10.3389/fpubh.2023.1057951.

Das, S., Sarfraz, A., Jaiswal, N., & Das, P. (2017). Impediments of reporting dengue cases in India. *Journal of Infection and Public Health*. https://doi.org/10.1016/j.jiph.2017.02.004.

Dhar-Chowdhury, P., Paul, K. K., Haque, C. E., Hossain, S., Lindsay, L. R., Dibernardo, A., Brooks, W. A., & Drebot, M. A. (2017). Dengue seroprevalence, seroconversion and risk factors in Dhaka, Bangladesh. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0005475.

Ganeshkumar, P., Murhekar, M. V., Poornima, V., Saravanakumar, V., Sukumaran, K., Anandaselvasankar, A., John, D., & Mehendale, S. M. (2018). Dengue infection in India: A systematic review and meta-analysis. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0006618.

Gutirrez, E. H. J., Walker, K. R., Ernst, K. C., Riehle, M. A., Davidowitz, G., Gutiérrez, E. H. J., Walker, K. R., Ernst, K. C., & Riehle, M. A. (2020). Size as a Proxy for Survival in Aedes aegypti (Diptera: Culicidae) Mosquitoes. *Journal of Medical Entomology*. https://doi.org/10.1093/jme/tjaa055.

Haider, N., Hasan, M. N., Khalil, I., Tonge, D., Hegde, S., Chowdhury, M. A. B., Rahman, M., Khan, M. H., Ansumana, R., Zumla, A., & Uddin, M. J. (2023). The 2022 dengue outbreak in Bangladesh: hypotheses for the late resurgence of cases and fatalities. *Journal of*

Medical Entomology. https://doi.org/10.1093/jme/tjad057.

Hasan, M. M., Sahito, A. M., Muzzamil, M., Mohanan, P., Islam, Z., Billah, Md. M., Islam, M. J., & Essar, M. Y. (2022). Devastating dengue outbreak amidst COVID-19 pandemic in Bangladesh: an alarming situation. *Tropical Medicine and Health*. https://doi.org/10.1186/s41182-022-00401-y.

Hossain, M. S., Noman, A. A., Mamun, S. A. A., & Mosabbir, A. A. (2023a). Twenty-two years of dengue outbreaks in Bangladesh: epidemiology, clinical spectrum, serotypes, and future disease risks. *Tropical Medicine and Health*. https://doi.org/10.1186/s41182-023-00528-6.

Hossain, S. (2023). Generalized Linear Regression Model to Determine the Threshold Effects of Climate Variables on Dengue Fever: A Case Study on Bangladesh. *Canadian Journal of Infectious Diseases and Medical Microbiology*. https://doi.org/10.1155/2023/2131801.

Hossain, S., Chowdhury, P. B., Easty, I. A., Bashar, K., Islam, Md. M., Hasan, Md. A., Tusar, Md. K., & Rashid, M. B. (2023b). Association of climate factors with dengue incidence in Bangladesh, Dhaka City: A count regression approach. *Heliyon*. https://doi.org/10.1016/j.heliyon.2023.e16053.

Howard-Jones, A. R., Pham, D., Sparks, R., Maddocks, S., Dwyer, D. E., Kok, J., & Basile, K. (2023). Arthropod-Borne Flaviviruses in Pregnancy. *Microorganisms*. https://doi.org/10.3390/microorganisms11020433.

Hung, T. M., Shepard, D. S., Bettis, A. A., Nguyen, H. A., McBride, A., Clapham, H. E., & Turner, H. C. (2020). Productivity costs from a dengue episode in Asia: a systematic literature review. *BMC Infectious Diseases*. https://doi.org/10.1186/s12879-020-05109-0.

Jahan, A., Paul, S. K., Nasreen, S. A., Haque, N., Roy, S., Sultana, M., Hossain, T., Nila, S., Ahmad, F. U., Ahmed, S., Aung, M. S., Kobayashi, N., & Nila, S. S. (2023). Genetic Characterization of the Dengue Virus Type 3 Genotype I Prevailing in Dhaka, Bangladesh, 2021. *Vector-Borne and Zoonotic Diseases*. https://doi.org/10.1089/vbz.2023.0025.

Kabir, K. M. A., Hagishima, A., & Tanimoto, J. (2020). Hypothetical assessment of efficiency, willingness-to-accept and willingness-to-pay for dengue vaccine and treatment: a contingent valuation survey in Bangladesh. *Human Vaccines & Immunotherapeutics*. https://doi.org/10.1080/21645515.2020.1796424.

Kallás, E. G., Cintra, M. A. T., Moreira, J. A., Patiño, E. G., Braga, P. E., Tenório, J. C. V., Infante, V., Palacios, R., Lacerda, M. V. G. de, Pereira, D. B., Fonseca, A. J. da, Gurgel, R. Q., Coelho, I. C.-B., Fontes, C. J. F., Marques, E. T. A., Romero, G. A. S., Teixeira, M. M., Siqueira, A. M., Barral, A. M. P., … Nogueira, M. L. (2024). Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults. *New England Journal of Medicine*. https://doi.org/10.1056/nejmoa2301790.

Kayesh, M. E. H., Nazneen, H., Kohara, M., & Tsukiyama-Kohara, K. (2024). An effective pan-serotype dengue vaccine and enhanced control strategies could help in reducing the severe dengue burden in Bangladesh–A perspective. *Frontiers in Microbiology*. https://doi.org/10.3389/fmicb.2024.1423044.

Lee, I.-K., Lee, N.-Y., Huang, W.-C., Hsu, J.-C., Tai, C.-H., Yang, C. H., Huang, C.-H., Lin,

C.-Y., Chang, K., & Chen, Y.-H. (2023). In-hospital mortality predictors among hospitalized adults and those with chronic kidney disease with dengue. *Journal of Microbiology Immunology and Infection*. https://doi.org/10.1016/j.jmii.2023.08.004.

Lee, J.-S., Mogasale, V., Lim, J. K., Carabali, M., Lee, K.-S., Sirivichayakul, C., Dang, D. A., Palencia-Florez, D. C., Nguyen, T. H. A., Riewpaiboon, A., Chanthavanich, P., Villar, L., Maskery, B. A., & Farlow, A. (2017). A multi-country study of the economic burden of dengue fever: Vietnam, Thailand, and Colombia. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0006037.

Legorreta-Soberanis, J., Paredes-Solís, S., Morales-Pérez, A., Nava-Aguilera, E., Santos, F. R. S. los, Dimas-Garcia, D. L., Ledogar, R. J., Cockcroft, A., & Andersson, N. (2017). Household costs of dengue illness: secondary outcomes from a randomised controlled trial of dengue prevention in Guerrero state, Mexico. *BMC Public Health*. https://doi.org/10.1186/s12889-017-4304-x.

Lim, J. T., Han, Y., Dickens, B. S. L., Choo, E. L. W., Chew, L. Z. X., & Cook, A. R. (2020). Revealing two dynamic dengue epidemic clusters in Thailand. *BMC Infectious Diseases*. https://doi.org/10.1186/s12879-020-05666-4.

Mahmud, A. S., Bhattacharjee, J., Baker, R. E., & Martinez, P. P. (2023). Alarming trends in dengue incidence and mortality in Bangladesh. *The Journal of Infectious Diseases*. https://doi.org/10.1093/infdis/jiad529.

Mamenun, Koesmaryono, Y., Sopaheluwakan, A., Hidayati, R., Dasanto, B. D., & Aryati, R. (2024). Spatiotemporal Characterization of Dengue Incidence and Its Correlation to Climate Parameters in Indonesia. *Insects*. https://doi.org/10.3390/insects15050366.

Miah, Md. M., Hossain, M. B., Jannat, S. N., Karim, Md. R., Rahman, Md. R., Arafat, Y., & Pingki, F. H. (2024). Assessing the impact of climatic factors on dengue fever transmission in Bangladesh. *Aerobiologia*. https://doi.org/10.1007/s10453-024-09814-0.

Mukhtar, M., Wajeeha, A. W., Bibi, N., & Sahar Sadaf Zaidi, N. us. (2022). IJMS, Vol. 23, Pages 13911: Engineering Modified mRNA-Based Vaccine against Dengue Virus Using Computational and Reverse Vaccinology Approaches. *International Journal of Molecular Sciences*. https://doi.org/10.3390/ijms232213911.

Mutsuddy, P., Jhora, S. T., Shamsuzzaman, A. K. M., Kaisar, S. M. G., Khan, N. A., & Khan, M. N. A. (2019). Dengue Situation in Bangladesh: An Epidemiological Shift in terms of Morbidity and Mortality. *Canadian Journal of Infectious Diseases and Medical Microbiology*. https://doi.org/10.1155/2019/3516284.

Nadjib, M., Setiawan, E., Putri, S., Nealon, J., Beucher, S., Hadinegoro, S. R., Permanasari, V. Y., Sari, K., Wahyono, T. Y. M., Kristin, E., Wirawan, D. N., & Thabrany, H. (2019). Economic burden of dengue in Indonesia. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0007038.

Noman, A. A., Das, D., Nesa, Z., Sharzana, F., Riaz, B. K., Sharower, G., Rahman, M. M., Tariquzzaman, Md., & Hasan, Md. R. (2023). Importance of Wolbachia-mediated biocontrol to reduce dengue in Bangladesh and other dengue-endemic developing countries. *Biosafety and Health*. https://doi.org/10.1016/j.bsheal.2023.03.003.

O., J., Gutiérrez-Barbosa, H., Chua, J. V., Deredge, D. J., & Obi, J. O. (2021). Current Trends and Limitations in Dengue Antiviral Research. *Tropical Medicine and Infectious Disease*. https://doi.org/10.3390/tropicalmed6040180.

Okoye, E. C., Mitra, A. K., Lomax, T., Nunaley, C., Okoye, E. C., & Mitra, A. K. (2024). Dengue Fever Epidemics and the Prospect of Vaccines: A Systematic Review and Meta-Analysis Using Clinical Trials in Children. *Diseases*. https://doi.org/10.3390/diseases12020032.

Olliaro, P., Fouque, F., Kroeger, A., Bowman, L., Velayudhan, R., Santelli, A. C., Garcia, D., Ramm, R. S., Sulaiman, L. H., Tejeda, G. S., Morales, F. C., Gozzer, E., Garrido, C. B., Quang, L. C., Gutierrez, G., Yadon, Z. E., & Runge-Ranzinger, S. (2018). Improved tools and strategies for the prevention and control of arboviral diseases: A research-to-policy forum. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0005967.

Patterson, J., Sammon, M., & Garg, M. (2016). Dengue, Zika and Chikungunya: Emerging Arboviruses in the New World. *Western Journal of Emergency Medicine*. https://doi.org/10.5811/westjem.2016.9.30904.

Pilot, E., Murthy, G. V. S., & Nittas, V. (2020). Understanding India's urban dengue surveillance: A qualitative policy analysis of Hyderabad district. *Global Public Health*. https://doi.org/10.1080/17441692.2020.1767674.

Rafi, A., Mousumi, A. N., Ahmed, R., Chowdhury, R. H., Wadood, A., & Hossain, G. (2020). Dengue epidemic in a non-endemic zone of Bangladesh: Clinical and laboratory profiles of patients. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0008567.

Rahim, R., Hasan, A., Phadungsombat, J., Hasan, N., Ara, N., Biswas, S. M., Nakayama, E. E., Rahman, M., & Shioda, T. (2023). Genetic Analysis of Dengue Virus in Severe and Non-Severe Cases in Dhaka, Bangladesh, in 2018–2022. *Viruses*. https://doi.org/10.3390/v15051144.

Rathore, A. P., Farouk, F. S., & John, A. L. St. (2020). Risk factors and biomarkers of severe dengue. *Current Opinion in Virology*. https://doi.org/10.1016/j.coviro.2020.06.008.

Rimal, S., Shrestha, S., Paudel, S. W., Shah, Y., Bhandari, G., Pandey, K., Kharbuja, A., Kapandji, M., Gautam, I., Bhujel, R., Takamatsu, Y., Bhandari, R., Klungthong, C., Shrestha, S. K., Fernandez, S., Malavige, G. N., Pandey, B. D., Urano, T., Morita, K., … Dumre, S. P. (2024). Molecular and Entomological Characterization of 2023 Dengue Outbreak in Dhading District, Central Nepal. *Viruses*. https://doi.org/10.3390/v16040594.

Runge-Ranzinger, S., Kroeger, A., Olliaro, P., McCall, P. J., Tejeda, G. S., Lloyd, L. S., Hakim, L., Bowman, L. R., Horstick, O., & Coelho, G. (2016). Dengue Contingency Planning: From Research to Policy and Practice. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0004916.

Sarker, R., Roknuzzaman, A. S. M., Emon, F. A., Dewan, S. M. R., Hossain, Md. J., & Islam, Md. R. (2024). A perspective on the worst ever dengue outbreak 2023 in Bangladesh: What makes this old enemy so deadly, and how can we combat it? *Health Science Reports*. https://doi.org/10.1002/hsr2.2077.

Scott, L. J. (2016). Tetravalent Dengue Vaccine: A Review in the Prevention of Dengue

Disease. *Drugs*. https://doi.org/10.1007/s40265-016-0626-8.

Sebastianelli, A., Spiller, D., Carmo, R., Wheeler, J., Nowakowski, A., Jacobson, L. V., Kim, D., Barlevi, H., Cordero, Z. E. R., Colón-González, F. J., Lowe, R., Ullo, S. L., & Schneider, R. (2024). A reproducible ensemble machine learning approach to forecast dengue outbreaks. *Scientific Reports*. https://doi.org/10.1038/s41598-024-52796-9.

Seth, A., Sevdalis, N., Ismail, Z., Hadinegoro, S. R., Larson, H. J., & Pangestu, T. (2024). Antiscience, Vaccine Hesitancy, and Pandemic Responses: Highlights from the Asia Pacific Summit on Infectious Diseases and Immunization. *Vaccines*. https://doi.org/10.3390/vaccines12121336.

Setu, Md. A. A., Das, P. K., Ahammed, T., Saha, S., Hasan, A., K., S. K. P., Das, S., Ahamed, T., Hossain, K. M. A., Al-Emran, H. M., Hossain, M. A., & Jahid, I. K. (2025). Dengue Virus Serotype 2 Cosmopolitan C Genotype Reemerges With a New Strain in Southwest Region of Bangladesh. *Transboundary and Emerging Diseases*. https://doi.org/10.1155/tbed/8275099.

Sharif, N., Opu, R. R., Saha, T., Masud, A. I., Naim, J., Alsharif, K. F., Alzahrani, K. J., Alvarado, E. S., Noya, I. D., Torre Díez, I. D. la, & Dey, S. K. (2024). Evolving epidemiology, clinical features, and genotyping of dengue outbreaks in Bangladesh, 2000–2024: a systematic review. *Frontiers in Microbiology*. https://doi.org/10.3389/fmicb.2024.1481418.

Sharmin, S., Glass, K., Viennet, E., & Harley, D. (2016). A Bayesian approach for estimating under-reported dengue incidence with a focus on non-linear associations between climate and dengue in Dhaka, Bangladesh. *Statistical Methods in Medical Research*. https://doi.org/10.1177/0962280216649216.

Siddique, A. B., Omi, N. T., Rasel, S. M., Hoque, S. S. B., Rahman, N., Sarker, S., Ghosh, A., Ahmed, I., Akash, Y., Ahmed, A., & Sikder, Md. T. (2024). Assessment of perceived dengue risk and prevention practices among youth in Bangladesh. *Scientific Reports*. https://doi.org/10.1038/s41598-024-54238-y.

Suzuki, K., Phadungsombat, J., Nakayama, E. E., Saito, A., Egawa, A., Sato, T., Rahim, R., Hasan, A., Lin, M. Y.-C., Takasaki, T., Rahman, M., Shioda, T., & Nakayama, E. E. (2019). Genotype replacement of dengue virus type 3 and clade replacement of dengue virus type 2 genotype Cosmopolitan in Dhaka, Bangladesh in 2017. *Infection Genetics and Evolution*. https://doi.org/10.1016/j.meegid.2019.103977.

Tai, A. Y., McGuinness, S. L., Robosa, R., Turner, D., Huang, G. K. L., Leder, K., Korman, T. M., Thevarajan, I., Stewardson, A. J., Padiglione, A. A., & Johnson, D. F. (2017). Management of dengue in Australian travellers: a retrospective multicentre analysis. *The Medical Journal of Australia*. https://doi.org/10.5694/mja16.01056.

Tambo, E., Chen, J.-H., Zhou, X.-N., & Khater, E. I. M. (2016). Outwitting dengue threat and epidemics resurgence in Asia-Pacific countries: strengthening integrated dengue surveillance, monitoring and response systems. *Infectious Diseases of Poverty*. https://doi.org/10.1186/s40249-016-0148-3.

Tayal, A., Kabra, S. K., & Lodha, R. (2022). Management of Dengue: An Updated Review. *The Indian Journal of Pediatrics*. https://doi.org/10.1007/s12098-022-04394-8.

Titir, S. R., Paul, S. K., Ahmed, S., Haque, N., Nasreen, S. A., Hossain, K. S., Ahmad, F. U., Nila, S. S., Khanam, J., Nowsher, N., Amin, A. M. M. A., Khan, A. U., Aung, M. S., & Kobayashi, N. (2021). Nationwide Distribution of Dengue Virus Type 3 (DENV-3) Genotype I and Emergence of DENV-3 Genotype III during the 2019 Outbreak in Bangladesh. *Tropical Medicine and Infectious Disease*. https://doi.org/10.3390/tropicalmed6020058.

Tozan, Y., Ratanawong, P., Sewe, M. O., Wilder-Smith, A., & Kittayapong, P. (2017). Household costs of hospitalized dengue illness in semi-rural Thailand. *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0005961.

Tricou, V., Yu, D., Reynales, H., Biswal, S., Saez-Llorens, X., Sirivichayakul, C., Lopez, P., Borja-Tabora, C., Bravo, L., Kosalaraksa, P., Vargas, L. M., Alera, M. T., Rivera, L., Watanaveeradej, V., Dietze, R., Fernando, L., Wickramasinghe, V. P., Moreira, E. D., Fernando, A. D., … Wallace, D. (2024). Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4·5-year results from a phase 3, randomised, double-blind, placebo-controlled trial. *The Lancet Global Health*. https://doi.org/10.1016/s2214-109x(23)00522-3.

Walsh, M.-C. R., Alam, M. S., Pierce, K. K., Carmolli, M., Alam, M., Dickson, D. M., Bak, D. M., Afreen, S., Nazib, F., Golam, K., Qadri, F., Diehl, S. A., Durbin, A. P., Whitehead, S. S., Haque, R., & Kirkpatrick, B. D. (2023). Safety and durable immunogenicity of the TV005 tetravalent dengue vaccine, across serotypes and age groups, in dengue-endemic Bangladesh: a randomised, controlled trial. *The Lancet Infectious Diseases*. https://doi.org/10.1016/s1473-3099(23)00520-0.

Weerasinghe, N. P., Bodinayake, C. K., Wijayaratne, W. M. D. G. B., Devasiri, I. V., Dahanayake, N. J., Kurukulasooriya, M. R. P., Premamali, M., Sheng, T., Nicholson, B. P., Ubeysekera, H. A., Silva, A. D. de, Østbye, T., Woods, C. W., Tillekeratne, L. G., & Nagahawatte, A. D. S. (2022). Direct and indirect costs for hospitalized patients with dengue in Southern Sri Lanka. *BMC Health Services Research*. https://doi.org/10.1186/s12913-022-08048-5.

Zaheer, S., Tahir, M. J., Ullah, I., Ahmed, A., Saleem, S. M., Shoib, S., & Asghar, M. S. (2022). Dengue outbreak in the times of COVID-19 pandemic: Common myths associated with the dengue. *Annals of Medicine and Surgery*. https://doi.org/10.1016/j.amsu.2022.104535.

.Centers for Disease Control and Prevention. (2024). *Life cycle of Aedes mosquitoes*. https://www.cdc.gov/mosquitoes/about/life-cycle-of-aedes-mosquitoes.html

Facchinelli, L., Badolo, A., & McCall, P. J. (2023). Biology and behaviour of *Aedes aegypti* in the human environment: Opportunities for vector control of arbovirus transmission. *Pathogens, 12*(3), 435. https://doi.org/10.3390/pathogens12030435

Nosten, F., et al. (2023). *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) ecology, biology, behaviour, and implications on arbovirus transmission in Thailand: Review. *One Health, 16*, 100555. https://doi.org/10.1016/j.onehlt.2023.100555

Shafiei, R., et al. (2025). *Aedes aegypti* and dengue: Insights into transmission dynamics and viral lifecycle. *Epidemiology & Infection, 153*, e130. https://doi.org/10.1017/S0950268825100320

Christofferson, R. C., & Mores, C. N. (2020). Linking mosquito ecology, traits, behavior, and disease transmission. *Trends in Parasitology, 36*(4), 393–403. https://doi.org/10.1016/j.pt.2020.02.001

Guzman, M. G., Harris, E., et al. (2016). Dengue. *The Lancet, 385*(9966), 453–465. https://doi.org/10.1016/S0140-6736(14)60572-9

Lee, I. K., Liu, J. W., & Yang, K. D. (2022). Clinical characteristics and management of severe dengue. *Journal of Microbiology, Immunology and Infection, 55*(1), 1–10.

Lye, D. C., Lee, V. J., Sun, Y., Leo, Y. S., et al. (2017). Lack of efficacy of prophylactic platelet transfusion for severe thrombocytopenia in adult dengue patients. *Clinical Infectious Diseases, 64*(2), 205–212.

Paixão, E. S., Teixeira, M. G., & Costa, M. C. N. (2018). Dengue during pregnancy and adverse fetal outcomes: A systematic review and meta-analysis. *The Lancet Infectious Diseases, 18*(8), 857–865.

Simmons, C. P., Farrar, J. J., Nguyen, V. V., & Wills, B. (2012). Dengue. *New England Journal of Medicine, 366*(15), 1423–1432. https://doi.org/10.1056/NEJMra1110265

World Health Organization. (2009). *Dengue: Guidelines for diagnosis, treatment, prevention and control*. WHO.

World Health Organization. (2012). *Handbook for clinical management of dengue*. WHO.

World Health Organization. (2022). *Guidelines for the clinical diagnosis and treatment of dengue, chikungunya, and Zika*. WHO.

Yacoub, S., & Wills, B. (2014). Predicting outcome from dengue. *BMC Medicine, 12*, 147. https://doi.org/10.1186/s12916-014-0147-9