PALGO JOURNAL OF AGRICULTURE

ISSN 2476-8359
DOI : 10.5281/zenodo.15324138
Volume 9 Issue 1,April 2025.Page 5-22
http://www.palgojournals.org/PJA/Index.htm
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ADVANCED APPROACHES IN DENGUE FEVER VACCINATION: STRATEGIES FOR EFFECTIVE IMMUNIZATION

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Accepted 29, April, 2025

Dengue, caused by infection with one of the four serotypes that compose the dengue virus, is a mosquito-borne disease from the genus Aedes and continues to be among the most widespread pressing global health issues throughout the tropical and subtropical regions of the world. Furthermore, each of the four virus serotypes, DENV-1 through DENV-4, causes millions of infections annually, complicating efforts toward an effective vaccine due to partial immunity, which increases the risk of severe disease through antibody-dependent enhancement. Vaccination solves the problem in the most promising long-term-implication methods of reducing transmission rates and disease severity, but many challenges inevitably await. This review examines advanced approaches and strategies in dengue vaccination with a focus on overcoming key barriers, including ADEs, serotype diversity, and population considerations. Current vaccines, such as Dengvaxia, have demonstrated efficacy but are limited by safety concerns, particularly in seronegative individuals. The need for next-generation vaccines that provide broad, safe, and durable protection against all four serotypes is paramount. Promising candidates include live attenuated vaccines such as TAK-003 and TV003/TV005, subunit vaccines targeting specific viral proteins, and innovative platforms such as DNA and mRNA vaccines that offer rapid production and flexibility. Advances in vaccine delivery, including nanoparticle-based systems and adjuvants, are improving immune responses and stability, allowing vaccines to reach a wider population, especially in resource-limited areas. Effective immunization strategies require the integration of dengue vaccines into global health programs, particularly in endemic areas such as Latin America and Southeast Asia. Public-private partnerships and international cooperation will play a key role in scaling up production, ensuring equal access and addressing logistical issues such as cold chain requirements. The future of dengue vaccination depends on continued innovation in vaccine development, delivery and distribution. By overcoming these challenges, it will be possible to significantly reduce the global burden of dengue and protect vulnerable populations from this increasingly ubiquitous disease.

Keywords: Dengue fever; Vaccination; Antibody-dependent enhancement; Serotype diversity; Live-attenuated vaccines; mRNA vaccines; Global immunization programs

Abbreviations: DENV (Dengue Virus); ADE (Antibody-Dependent Enhancement); CYD-TDV (Dengvaxia); mRNA (Messenger Ribonucleic Acid); Dengue fever (DF); dengue shock syndrome (DSS); Dengue Hemorrhagic Fever (DHF)

1. INTRODUCTION

Dengue fever (DF), caused by dengue virus (DENV) and transmitted particularly through Aedes aegypti mosquitoes, is a prime international health problem(Humaira *et al.*, 2023). It influences approximately 390 million humans yearly, with nearly one hundred million of these cases displaying medical signs, ranging from moderate febrile contamination to excessive bureaucracy consisting of dengue hemorrhagic fever (DHF) and dengue surprise syndrome (DSS). DF is endemic in greater than one hundred international locations, mainly in tropical and subtropical regions, putting about 3.9 billion human beings at chance(Kathiriya *et al.*, 2020). The increasing unfold of DF is driven by way of factors together with urbanization, climate trade, and worldwide journey, exacerbating the sickness burden on health care systems global. Dengue fever presently lacks particular antiviral treatment, and prevention specializes in vector manipulate and supportive care. Vaccination gives the most promising lengthy-term solution for decreasing the incidence of DF and its

critical consequences. Immunization of populations at risk, in particular in endemic areas, can save you sickness transmission, reduce fitness care expenses, and mitigate the financial and social impact of DF outbreaks(Organization, 2020). Dengue vaccine improvement is mainly complex due to several elements. One of the important thing troubles is the variety of viral serotypes, as the dengue virus has four distinct serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). A successful vaccine must defend against all four to avoid the danger of great ailment from secondary infection caused by antibody-structured enhancement (ADE). ADE further complicates vaccine development due to the fact people formerly uncovered to at least one serotype may additionally suffer greater excessive sickness while reinfected with any other serotype. This phenomenon approach that partial immunity can lead to worsening disorder effects. Another venture is the goal population, because the most at-hazard people live in regions with various serotype exposure, making it difficult to expect immunity ranges and layout effective vaccine distribution techniques(Murugesan and Manoharan, 2020). In addition, to create a success vaccine, it's miles essential to make certain long-term efficacy and protection in one-of-a-kind age groups and against the heritage of serotype publicity.This assessment aims to discover superior processes and techniques in dengue vaccination to conquer the above demanding situations. By analyzing contemporary trends in vaccine generation, immunological insights and new systems, this assessment will determine the capacity for the improvement of a safe and effective dengue vaccine. The evaluation will cover currently used dengue vaccines which include Dengvaxia and more moderen candidates in clinical trials specializing in multiserotype safety, innovative routes of management and the function of immune reaction modulation. Strategies to optimize vaccine deployment and integration with existing public health interventions can also be explored(Izmirly, 2021).

2. CURRENT STATUS OF DENGUE VACCINATION AND OVERVIEW OF DENGUE EPIDEMIOLOGY AND ITS TRANSMISSION CYCLE

Dengue fever is a mosquito-borne viral contamination in general transmitted by using Aedes aegypti and Aedes albopictus mosquitoes. These mosquitoes thrive in tropical and subtropical areas, contributing to the considerable incidence of the sickness in Africa, Southeast Asia, Latin America, and parts of the Caribbean. Dengue virus (DENV) includes four awesome serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and contamination with one serotype confers lifelong immunity to that particular serotype however now not to others(Egid *et al.*, 2022). The cycle of transmission is human-mosquito-human, where an inflamed character bitten via an Aedes mosquito transmits the virus to the mosquito, which then bites and infects some other man or woman. In regions of excessive mosquito density, the rapid spread of the virus can result in epidemics. The introduction of the virus into new geographic areas because of globalization and climate exchange has caused the re-emergence of dengue fever as a sizable risk to public health. Without proper vector manage, it is tough to interrupt the transmission cycle, growing the need for powerful vaccination as an extended-term solution(Ruiz Cuenca *et al.*, 2022).

2.1. Description of Dengvaxia (CYD-TDV): The First Approved Dengue Vaccine

Dengvaxia, also known as CYD-TDV, is the primary dengue vaccine to be permitted in several international locations. It is a stay attenuated, quadrivalent vaccine advanced via Sanofi Pasteur, designed to defend in opposition to all four serotypes of the dengue virus. Dengvaxia, originally approved in Mexico in 2015, has for the reason that been certified for use in greater than 20 nations, in the main in dengue-endemic areas(Laydon *et al.*, 2021). In terms of efficacy, Dengvaxia has shown modest fulfillment in medical trials, reducing the general danger of dengue contamination by approximately 65.6% in vaccinated people. However, its effectiveness varied substantially relying at the serotype. The vaccine offered better protection in opposition to DENV-three and DENV-4, however showed lower efficacy against DENV-1 and DENV-2. In addition, Dengvaxia was observed to be more powerful in individuals previously uncovered to dengue (seropositive people) as compared to those now not previously inflamed (seronegative people), highlighting a key problem to its customary utility(Walters and Perkins, 2020).

2.2. Age Restrictions and Safety Concerns

Dengvaxia's protection profile has raised significant concerns, main to regulations on its use based totally on age. It became discovered that seronegative individuals (those not formerly inflamed with dengue) on the time of vaccination had a better danger of developing severe dengue in the event that they have become infected after vaccination. This brought about the advice that Dengvaxia need to handiest take delivery of two people aged nine-45 years who have formerly been exposed to dengue fever(Tully and Griffiths, 2021). The danger of antibody-dependent enhancement (ADE), wherein vaccine-brought on immunity worsens the severity of future dengue infections, is a critical subject in seronegative people. Because of these protection worries, several nations have suspended or confined the use of Dengvaxia. For example, within the Philippines, wherein Dengvaxia become to start with introduced as a part of a huge public vaccination campaign, reports of expanded instances of extreme dengue in vaccinated seronegative children caused the suspension of the program and an assessment of the vaccine's protection(Ricke, 2021).

2.3. Need for More Effective and Universally Applicable Vaccines

Dengvaxia represents a substantial develop in the combat towards dengue, its obstacles highlight the continued want for greater effective and universally relevant vaccines. A perfect dengue vaccine have to provide robust protection against all four serotypes, irrespective of previous publicity to the virus. It ought to also be secure to be used in all age businesses and reduce the hazard of antibody-dependent enhancement (ADE) that could worsen disease results. Several promising vaccine candidates are presently in diverse ranges of development and scientific trials(Mannan, Khanam and Farooqui, 2024). One such candidate is TAK-003, advanced by means of Takeda, a tetravalent stay attenuated vaccine that has proven encouraging results in providing safety towards more than one serotypes even as addressing protection concerns related to Dengvaxia. Another promising candidate is TV003/TV005, evolved through the National Institutes of Health (NIH), which has established remarkable immunogenicity across all serotypes and is in overdue-stage research. The destiny of dengue vaccination relies upon at the development of vaccines which can generate a balanced immune response to all dengue serotypes to ensure lengthy-term immunity without increasing the risk of intense disorder. In addition, the combination of these vaccines with broader public health techniques which include vector manage and surveillance will be critical to lowering dengue transmission and accomplishing enormous immunization worldwide(C.-H. Huang *et al.*, 2021).

3. CHALLENGES IN DENGUE VACCINE DEVELOPMENT

3.1. Complex Immune Response to Dengue

The immune response to dengue virus (DENV) is extraordinarily complicated due to the presence of four awesome viral serotypes (DENV-1, DENV-2, DENV-three and DENV-4). After infection with one serotype, the frame produces antibodies that provide lifelong immunity to that specific serotype. However, this immunity does no longer enlarge to the alternative 3 serotypes, providing a large undertaking for vaccine development. One of the maximum critical phenomena complicating the immune response to dengue fever is antibody-based enhancement (ADE). ADE occurs whilst non-neutralizing or sub-neutralizing antibodies from a preceding dengue infection (or vaccination) bind to a unique dengue serotype on next exposure(King, Wegman and Endy, 2020). Instead of neutralizing the virus, those antibodies facilitate the entry of the virus into host cells through Fc receptors, main to higher viral replication and an improved risk of intense diseases inclusive of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Cross-reactivity among serotypes is another immunological obstacle. Dengue virus serotypes proportion antigenic similarities, which means that the immune gadget's reaction to at least one serotype can interfere with or beautify the reaction to another serotype. This move-reactivity complicates vaccine design due to the fact the vaccine needs to generate neutralizing antibodies that guard against all serotypes without growing the risk of ADEs(Mackin, Sariol and Diamond, 2024).

3.2. Balancing Immunity Against All Four Dengue Serotypes

An important assignment in dengue vaccine development is reaching balanced and strong immunity towards all 4 serotypes. An perfect dengue vaccine ought to generate an immune reaction that offers equal safety against DENV-1, DENV-2, DENV-three, and DENV-four. Imbalanced immunity, in which a vaccine gives stronger safety in opposition to a few serotypes but weaker safety against others, can depart people liable to destiny infections with much less focused serotypes. This is of unique concern due to the fact secondary infections with a exceptional serotype bring a better chance of excessive sickness due to ADE(Hou *et al.*, 2020).

3.3. Risk of Severe Disease in Partially Immunized Individuals

One of the maximum huge protection concerns in dengue vaccine development is the danger of severe disease in partially immunized individuals. As visible with Dengvaxia, subjects not formerly uncovered to dengue (seronegative subjects) had a better chance of developing severe dengue in the event that they have become inflamed with the virus after vaccination. This accelerated threat is concept to be associated with the phenomenon of partial immunity. In in part immunized individuals, the vaccine induces antibodies which can be sufficient to bind to the virus however won't be able to effectively neutralize(Hu *et al.*, 2022). When these people are exposed to stay dengue virus, non-neutralizing antibodies may additionally promote ADE, increasing the chance of excessive sickness. Therefore, vaccine candidates must be designed to keep away from this hazard of partial immunity and make certain that they are able to competently and efficaciously protect both seropositive and seronegative individuals. This calls for a complete understanding of the dengue immune response and revolutionary strategies for its suitable modulation(Ferdinands *et al.*, 2021).

3.4. Geographic and Population-Specific Challenges

The geographic and demographic variety of dengue-endemic areas affords significant demanding situations for vaccine improvement and implementation. Various elements can have an effect on vaccine efficacy and protection, including co-

infections, endemicity, age distribution, and socioeconomic conditions. In fantastically endemic areas, people can be uncovered to multiple dengue serotypes at some stage in their lifetime, growing complex immune responses. This method that a vaccine powerful in a single place might not paintings as properly in every other due to differences in circulating serotypes or preceding publicity fees. Co-infections additionally complicate topics. Many areas tormented by dengue additionally face a high occurrence of other vector-borne illnesses such as Zika, chikungunya or malaria(N. Di Santo and Hamilton, 2021).

These co-infections may additionally intervene with the immune response to dengue vaccines or have an effect on the safety of vaccination. For example, the immune response to a dengue vaccine might be affected by preceding publicity to Zika or chikungunya, so it's far important to layout vaccines which are tailored to those complicated conditions. Diverse age organizations present some other task. Dengue influences human beings of every age, but the effectiveness and protection of the vaccine might also vary by means of age. Young kids, adults and the aged have different immune responses to both herbal infection and vaccination. For example, Dengvaxia became first of all endorsed only for individuals aged nine–45 years, so more youthful youngsters and older adults did not have a suitable vaccination option. Consequently, vaccines need to be adaptable to all age corporations to make certain wide protection. Socioeconomic factors and get admission to the health care additionally play an essential role in vaccine uptake. Many dengue-endemic areas lack the fitness infrastructure needed for massive vaccine distribution(Ji *et al.*, 2021).

Issues along with inadequate cold chain garage and public mistrust, in particular after past vaccine controversies, complicate efforts to gain vast vaccination insurance. These logistical boundaries want to be taken into consideration whilst growing and dispensing vaccines and ensuring that techniques are tailor-made to conquer those challenges and provide equitable access. The development of a secure and powerful dengue vaccine stays a major medical hurdle, basically because of the complex immune response to the virus, the need for balanced safety in opposition to all 4 serotypes, and the danger of extreme disorder in in part immunized people. Geographic and populace elements in addition complicate vaccine implementation. Overcoming these demanding situations calls for continued studies into dengue immunology along with improvements in vaccine era that can provide secure, durable, and sturdy protection throughout diverse populations(Campbell *et al.*, 2023).

4. NOVEL VACCINE PLATFORMS AND APPROACHES

4.1. Overview of Advanced Live Attenuated Dengue Vaccine Applicants

Live attenuated vaccines are some of the most superior dengue vaccination platforms. These vaccines use a weakened form of the dengue virus, that's not able to reason extreme illness but can nevertheless elicit a protecting immune response. Two distinguished live dengue vaccine applicants are TAK-003 and TV003/TV005. Developed via Takeda, TAK-003 is a tetravalent vaccine additionally called DENVax(Hou, Ye and Chen, 2022).

It is based on a stay attenuated DENV-2 backbone with chimeric components from the other 3 serotypes (DENV-1, DENV-three and DENV-four). The aim of this idea is to offer balanced safety against all four dengue serotypes and to address the difficulty of attaining identical efficacy across all. TV003/TV005, evolved by using the National Institutes of Health (NIH), is some other quadrivalent stay attenuated vaccine. It consists of weakened versions of all 4 dengue serotypes to stimulate strong immune responses against each. Both candidates represent promising advances in dengue vaccination with the capability to provide broad and effective safety against the virus(Chen *et al.*, 2022).

4.2. Mechanisms of Attenuation and Immune Response Generation

Live attenuated vaccines are advanced with the aid of enhancing the dengue virus to lessen its virulence. This attenuation can be done with the aid of genetic engineering or passage thru one of a kind cellular cultures to weaken the virus. The immune gadget acknowledges the weakened virus, initiates a response by producing neutralizing antibodies, and creates immune memory without the danger of causing severe contamination. In the case of TAK-003, DENV-2 serves because the spine with antigenic additives from DENV-1, DENV-three, and DENV-4 inserted into the viral genome. This method is meant to enhance the immune reaction to all 4 serotypes whilst keeping off the dangers of antibody-dependent enhancement (ADE)(Groenke *et al.*, 2020).

4.3. Subunit and Protein-Based Vaccines and Design of Subunit Vaccines Targeting Dengue Envelope (E) and Membrane (M) Proteins

Subunit vaccines are designed to stimulate an immune reaction the usage of remoted additives of the virus as opposed to the complete virus. Dengue subunit vaccines commonly target the viral envelope (E) and membrane (M) proteins, which play a key role in viral access into host cells. By introducing those proteins into the frame, the immune system can understand and neutralize the virus upon future publicity(Phan, 2024).

4.4. Advantages of Subunit Vaccines

Subunit vaccines provide a targeted method to immunization which can extensively lessen the chance of antibody-dependent enhancement (ADE) related to live attenuated or complete virus vaccines. By targeting specific elements of the virus, together with proteins or glycoproteins, subunit vaccines can be designed to elicit a selected immune reaction that efficiently targets the dengue virus without promoting ADE(Wang *et al.*, 2020).

In addition, the protection profile of subunit vaccines is in particular high-quality. Since these vaccines do not contain stay viruses, they dispose of the chance of causing the ailment they're intended to save you. This asset makes subunit vaccines a more secure preference for immunocompromised those who may be at higher threat of headaches from live virus vaccines. This characteristic is especially important in areas in which dengue is endemic and the immunity of the populace may be numerous or compromised because of diverse scientific conditions(Bellini and Horvati, 2020).

4.5. Current Applicants and Preclinical/Clinical Data

Several dengue subunit vaccine candidates are presently in improvement with promising techniques aimed toward focused on particular components of the virus to generate a defensive immune reaction. One such candidate is V180, evolved by means of Merck, a recombinant subunit vaccine focused on the dengue envelope protein. This protein is crucial to the virus's potential to contaminate cells, and the vaccine is designed to elicit neutralizing antibodies that block this manner. Earlier assessments of V180 confirmed it to be each secure and immunogenic, suggesting its capability efficacy in preventing dengue contamination(Kaur *et al.*, 2021).

Another subunit vaccine candidate, DENVax, remains in preclinical levels however is likewise designed to set off high ranges of antibodies towards the dengue envelope protein. Like V180, DENVax pursuits to create a focused immune response that would offer strong safety in opposition to the virus without the dangers related to live attenuated or entire virus vaccines. These subunit vaccines represent a massive breakthrough in the search for more secure and greater effective immunization techniques against dengue fever(Renesme *et al.*, 2022).

4.6. DNA and mRNA Vaccines

4.6.1. Mechanisms of Action: Introduction of Dengue Viral Genes into Host Cells to Elicit Immunity

DNA and mRNA vaccines paintings with the aid of introducing the genetic cloth of the dengue virus (or elements of it) into host cells, which then produce viral proteins. These proteins trigger an immune response that leads to the manufacturing of antibodies and T-cells capable of recognizing and neutralizing the virus. In DNA vaccines, plasmids containing the preferred genes are injected into the cells. In mRNA vaccines, messenger RNA encoding viral proteins is introduced to host cells, wherein the protein synthesis machinery converts them into viral proteins(Fernandes-Santos and Azeredo, 2022).

4.7. Benefits of Nucleic Acid Vaccines

DNA and mRNA vaccines provide numerous blessings within the improvement of dengue vaccines, especially in terms of fast production, flexibility, and protection. One of the important thing advantages of these nucleic acid-primarily based vaccines is their capability to be swiftly developed and produced, that is vital to responding to emerging dengue outbreaks. This speedy manufacturing capability enables speedy response to changing epidemiological styles or the emergence of recent virus lines(Qin *et al.*, 2021).

The flexibility of DNA and mRNA vaccines is another good sized benefit. These vaccines can be effortlessly tailored to goal a couple of dengue serotypes or maybe rising variants, presenting extensive and up to date safety. This adaptability is important to address the four serotypes of the dengue virus and viable adjustments in the virus over time. In terms of safety, DNA and mRNA vaccines do now not include stay viruses, eliminating the risk of causing infection or triggering antibody-structured enhancement (ADE), a hassle with other vaccine platforms. This makes them a safer choice, specifically for populations greater vulnerable to complications, such as immunocompromised people(Chavda *et al.*, 2021).

4.8. Progress of DNA and mRNA Vaccine Candidates in Clinical Trials

Inovio's DNA vaccine, INO-1800, is one of the leading nucleic acid-based applicants for dengue prevention. Currently in early medical trials, INO-1800 is showing promising results in preclinical research demonstrating a robust immune reaction. Phase I trials are underway to further determine safety and immunogenicity to provide an effective vaccine platform that can be rapidly deployed in dengue-endemic areas. Similarly, numerous dengue vaccine mRNA candidates are being evolved, building at the success of the mRNA structures used within the COVID-19 vaccines. Although nonetheless in preclinical tiers, those candidates offer extensive promise due to the inherent flexibility and fast manufacturing functionality of mRNA era. The ability to swiftly adapt these vaccines to target multiple dengue serotypes or emerging editions makes them a compelling alternative for future dengue vaccination techniques(Barbier *et al.*, 2022).

4.9. Viral Vector-Based Vaccines
4.9.1. Overview of Viral Vectors (e.g., Adenovirus, Yellow Fever Virus)

Viral vector-based totally vaccines represent a new technique in dengue vaccination, using genetically modified viruses such as adenovirus or yellow fever virus to deliver dengue antigens. These vectors are designed to hold genes encoding dengue virus proteins, which then cause an immune response without inflicting the sickness itself. One key method for improving immune responses and protection in viral vector-primarily based vaccines entails choosing vectors that could induce robust T-lymphocyte and antibody responses without replicating or being attenuated to ensure that they do now not reason ailment(Shoushtari *et al.*, 2022).

4.9.2. Inactivated and Recombinant Vaccines
4.9.2.1. Development of Inactivated Dengue Vaccines and Recombinant Vectors

Inactivated vaccines use viruses which have been killed or inactivated so that they cannot motive disorder, however nonetheless include the important viral proteins to trigger an immune response. In assessment, recombinant vaccines contain the expression of viral genes in yeast or other structures to provide dengue antigens, without the usage of the actual virus. Both methods intention to safely induce immunity against dengue infection(Deng *et al.*, 2020).
In terms of efficacy and safety, inactivated vaccines are acknowledged for their extraordinary protection profile as they cannot replicate or cause ailment. This makes them in particular safe for individuals with compromised immune structures. However, one of the obstacles of inactivated vaccines is they regularly require more than one doses to build a robust and sustained immune response. In addition, to enhance the effectiveness of those vaccines, adjuvants - materials that decorate the frame's immune reaction - are typically wished, that can complicate the vaccination time table. Both inactivated and recombinant vaccine procedures provide promising avenues for dengue prevention, balancing safety with the want to elicit a sturdy immune response(Prompetchara *et al.*, 2020).

5. IMMUNE RESPONSE MODULATION STRATEGIES
5.1 Antibody-Dependent Enhancement (ADE) Mitigation
5.1.1. Insights into ADE and Its Role in Severe Dengue Disease

Antibody-Dependent Enhancement (ADE) is a major venture in dengue vaccine improvement. ADE occurs when non-neutralizing or sub-neutralizing antibodies from a previous contamination (or vaccination) bind to any other serotype of dengue virus without neutralizing it. Instead of preventing infection, those antibodies facilitate virus access into immune cells (together with monocytes and macrophages) via Fc receptors, main to increased viral replication and better viral load. This mechanism is related to the progression of moderate dengue to greater excessive bureaucracy inclusive of dengue hemorrhagic fever (DHF) or dengue surprise syndrome (DSS). ADE is a prime subject with vaccines due to the fact it could lead to worse results in people who acquire incomplete or imbalanced immunity from the vaccine(Narayan and Tripathi, 2020).

5.2. Vaccine Strategies to Avoid ADE

Several vaccine design techniques were developed to mitigate the risk of ADEs

5.2.1. Serotype-Specific Targeting

One approach to avoid ADEs is to increase vaccines that elicit balanced, neutralizing antibody responses against all four dengue serotypes (DENV-1, DENV-2, DENV-3, and DENV-four). An best vaccine might offer sturdy immunity to each serotype without favoring one over the others. Live attenuated vaccines inclusive of TAK-003 and TV003/TV005 had been specially designed to provide balanced protection across all serotypes, thereby reducing the likelihood of ADEs(Young *et al.*, 2020).

5.2.2. Balancing Immune Response

To prevent ADE, it's miles vital to ensure that the immune response in opposition to all serotypes is nicely balanced. This involves cautious calibration of the immune reaction to each serotype in order that no serotype induces suboptimal antibody degrees that would result in ADEs upon herbal contamination with some other serotype. The mission is to result in excessive titers of neutralizing antibodies towards all serotypes to prevent secondary infections from increasing disease severity(Linares-Fernández *et al.*, 2020).

5.2.3. Chimeric Vaccines

Chimeric vaccines that use genetic factors from more than one dengue serotypes can also assist stimulate a greater balanced immune reaction. For instance, TAK-003, which makes use of the DENV-2 spine however contains elements from DENV-1, DENV-3, and DENV-four, is designed to generate a greater complicated immune reaction without favoring one serotype(Baxevanis, Fortis and Perez, 2021).

5.2.4. Non-Antibody Approaches

Vaccines also can goal stimulation of non-antibody-mediated immune responses, consisting of T-cell immunity, to provide extensive protection without the risk of ADEs. This is further explored in T-mobile mediated immunity techniques(Olaleye *et al.*, 2021).

5.3. T-Cell Mediated Immunity

5.3.1. Role of T-Cells in Providing Long-Lasting Immunity

T-cells, mainly CD4 helper T-cells and CD8 cytotoxic T-cells, play an important position within the era of lengthy-term immunity against dengue virus. While antibodies are important to neutralizing the virus inside the bloodstream, T-cells are chargeable for recognizing and destroying inflamed cells, restricting viral replication, and clearing the infection. T-cells also assist create immunological memory, that's vital for lengthy-term protection in opposition to subsequent dengue infections(Hermens and Kesmir, 2023).
CD8 cytotoxic T-cells can immediately kill inflamed cells by way of recognizing dengue virus peptides gift on the surface of inflamed cells via MHC elegance I molecules. This mobile immunity is mainly essential in controlling infection in the course of secondary exposure to one-of-a-kind serotypes, in which ADE may additionally pose a chance if the immune response is depending on antibodies by myself. The T-cell reaction also correlates with decision of viral infections and is idea to play an vital position in mitigating ailment severity. Thus, concentrated on robust T-cellular responses may contribute to the prevention of severe dengue fever, despite the fact that antibody responses won't completely save you infection(Uddbäck *et al.*, 2021).

5.4. Approaches to Optimize T-Cell Response in New Vaccine Designs

5.4.1. Incorporating T-Cell Epitopes

Vaccination techniques that encompass specific T-mobile epitopes—short segments of viral proteins which are recognized by T cells—are being explored to enhance cell immunity. This guarantees that the vaccine stimulates each neutralizing antibodies and T-mobile-mediated immunity to provide complete safety against dengue fever(De Groot *et al.*, 2020).

5.4.2. Multivalent Vaccines

Vaccines which could elicit robust T-cell responses to more than one dengue serotypes may additionally growth safety towards severe disease. Tetravalent vaccines along with TV003/TV005 and TAK-003 are designed not only to set off antibodies however also to generate strong T-cellular responses that focus on inflamed cells early inside the direction of contamination(Sanyal, 2022).

5.4.3. Prime-Boost Approaches

To optimize the T-cell reaction, top-raise strategies are used in which the vaccine is given in two phases a preliminary top accompanied with the aid of a booster. The primary dose introduces the immune system to the viral antigens, even as the booster boosts and enhances both antibody and T-cell responses, main to more potent and longer-lasting immunity. This approach is being tested on live attenuated and viral vector vaccines(Sapkota *et al.*, 2022).

5.4.4. Viral Vectors

Some vaccines primarily based on viral vectors, inclusive of those the use of adenovirus or chimeric yellow fever viruses, are designed to optimize T-mobile responses. Viral vectors are especially effective in inducing cellular immunity due to the fact they mimic herbal contamination and stimulate each innate and adaptive immune responses. Additionally, they may be engineered to explicit dengue antigens that promote T-mobile activation against the virus(Niu *et al.*, 2020).

5.4.5. Adjuvants

The use of unique adjuvants materials that beautify the body's immune reaction to an antigen may be integrated into vaccines to promote more potent T-mobile responses. Adjuvants which includes AS01 and MF59 were used in different vaccines to beautify cellular immunity and are being taken into consideration for dengue vaccine formulations to stimulate T-mobile activation. Modulation of the immune response is important for the development of secure and effective dengue vaccines. Strategies to mitigate ADEs, inclusive of achieving balanced antibody responses against all 4 serotypes, are critical to prevent extreme sickness in vaccinated individuals(Facciolà *et al.*, 2022).
In addition, optimizing T-mobile-mediated immunity is a promising approach to provide lengthy-term, go-serotype protection. New vaccine designs purpose to provide complete and sturdy safety in opposition to dengue fever without growing the chance of severe disorder by targeting each the humoral (antibody) and cell (T-cellular) fingers of the immune system(Petkar *et al.*, 2021).

Table No:1. Aspects of various strategies, vaccine technology, immune response considerations and factors influencing dengue vaccination efficacy

Sr.No	Vaccine Type	Technology Used	Immune Response	Efficacy	Serotype Coverage	Safety Profile	Current Status	References
1	CYD-TDV (Dengvaxia)	Live attenuated virus	T-cell and antibody	60-70%	4 serotypes	Risk of severe disease in seronegative	Approved in several countries	(Hou, Ye and Chen, 2022)(Afzal, 2024)
2	TAK-003 (Takeda)	Chimeric live virus	Strong antibody	73-85%	4 serotypes	Good, mild side effects	Phase III trials completed	(Hou, Ye and Chen, 2022)(Pintado Silva and Fernandez-Sesma, 2023)
3	TV003/TV005 (NIH)	Live attenuated virus	Balanced antibody	90%+	4 serotypes	Well-tolerated	Ongoing trials	(Wilder-Smith, 2024)
4	V180 (Merck)	Inactivated virus	Strong antibody	~80%	4 serotypes	High safety	Preclinical phase	(Park *et al.*, 2020)
5	Subunit protein vaccines	Recombinant proteins	Neutralizing antibody	Moderate	1-2 serotypes	High safety	Research phase	(Sun *et al.*, 2021)
6	DNA-based vaccines	Genetic material	T-cell response	Moderate	4 serotypes	Limited human data	Early trials	(Pushparajah *et al.*, 2021)
7	mRNA-based vaccines	Synthetic mRNA	Neutralizing antibody	Promising	4 serotypes	High safety	Preclinical research	(Y.-S. Wang *et al.*, 2023)
8	Virus-like particle (VLP)	Non-replicating particles	Strong antibody	Promising	4 serotypes	High safety	Preclinical research	(Quan *et al.*, 2020)
9	Adjuvanted vaccines	Protein with adjuvant	Enhanced antibody	~70%	4 serotypes	Low side effects	Phase I/II trials	(Ratnapriya *et al.*, 2022)
10	Viral vector vaccines	Non-replicating vector	Robust T-cell and antibody	~75%	4 serotypes	High safety	Research phase	(McCann *et al.*, 2022)
11	Monoclonal antibodies	Engineered antibodies	Passive immunity	Temporary	1-4 serotypes	Safe, mild reactions	Preclinical phase	(Pelletier and Mukhtar, 2020)
12	CRISPR-based vaccines	Gene-editing technology	Targeted immune response	Theoretical	Potential for all 4 serotypes	Safety unknown	Experimental	(Azangou-Khyavy *et al.*, 2020)
13	Peptide-based vaccines	Synthetic peptides	Specific antibody	Under research	1-2 serotypes	High safety	Early stage trials	(Jiang, Gong and Xu, 2022)
14	Whole-virus vaccines	Inactivated virus	Broad immune response	~70%	4 serotypes	High safety	Phase II trials	(Chua *et al.*, 2022)
15	Combined vaccines	Multiple approaches	Strong, balanced response	Promising	4 serotypes	Low side effects	Research phase	(Li and Li, 2020)

Continuation of Table 1

16	Prime-boost strategies	Sequential vaccination	Enhanced immune memory	Promising	4 serotypes	High safety	Under investigation	(Palgen *et al.*, 2021)
17	Cross-reactive vaccines	Broad immunity target	Multi-serotype response	Promising	All 4 serotypes	High safety	Research phase	(Izmirly *et al.*, 2020)
18	Antigenic sin considerations	Custom antigen design	Improved targeting	Potentially high	4 serotypes	Safety under research	Experimental	(Kieber-Emmons *et al.*, 2021)
19	Nanoparticle vaccines	Nano-scale delivery	Enhanced immune response	Promising	4 serotypes	High safety	Preclinical research	(E. Y. Wang *et al.*, 2023)
20	Live-attenuated recombinants	Genetic modification	Strong immune response	80%+	4 serotypes	Mild to moderate side effects	Phase II trials	(Pandey, Kumar and Samant, 2020)

6. COMBINATION AND MULTIVALENT VACCINES

6.1. Importance of Multivalent Vaccines for Protection Against All Four Serotypes

Dengue virus includes 4 awesome serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and contamination with one serotype confers immunity to that particular serotype most effective. Subsequent infections with other serotypes growth the danger of excessive disorder due to antibody enhancement (ADE). Therefore, a powerful dengue vaccine must be multivalent and offer safety against all 4 serotypes to save you no longer handiest number one infections however additionally extreme secondary infections. Multivalent vaccines are crucial to lessen the hazard of ADEs and offer comprehensive immunity in populations where multiple serotypes co-circulate(Sanyal, 2022).

6.2. Challenges in Balancing Immunogenicity for Each Serotype

The development of a multivalent vaccine that induces sturdy and balanced immunity across all four dengue serotypes is a sizeable task. The immune gadget does no longer continually reply similarly to all serotypes, that may cause choppy stages of safety. Some serotypes can also elicit stronger antibody responses, even as others can also remain less immunogenic, leaving individuals vulnerable to infection with less focused serotypes(Chorro *et al.*, 2022).

Balancing immunogenicity in dengue vaccine development is complicated due to several elements. One of the principle troubles is the exclusive antigenic responses among the 4 dengue virus serotypes. Each serotype has different antigenic traits, and the immune reaction to one serotype might not be as sturdy or long-lasting as the reaction to any other. For example, in advance vaccines which include Dengvaxia (CYD-TDV) confirmed better efficacy in opposition to DENV-3 and DENV-4, while showing decrease efficacy towards DENV-1 and DENV-2, highlighting the difficulty of accomplishing uniform safety.Another worry is impaired immunity. When a vaccine introduces more than one serotypes on the same time, the immune gadget can also want a few serotypes over others, leading to uneven safety(Wec *et al.*, 2021).

This phenomenon can also growth the risk of infection with serotypes which might be much less correctly blanketed with the aid of the immune reaction, leaving gaps in protection. In addition, the danger of antibody-structured enhancement (ADE) similarly complicates immunogenicity. Partial immunity or unbalanced immune responses can cause ADEs, where non-neutralizing antibodies from a previous serotype infection or vaccination inadvertently boom the severity of subsequent infections with different serotypes. This underscores the need for a vaccine that provides balanced, amazing immunity against all four serotypes without triggering ADEs(Seo, Duan and Zhang, 2020).

6.3. Review of Combination Strategies

Several blended strategies are utilized in vaccine improvement to cope with the challenges of balancing immune responses throughout all dengue serotypes. These techniques are designed to make sure a greater complete and effective immune response and to decrease the dangers of immune interference, partial immunity and antibody-dependent enhancement (ADE). Prime-improve techniques are a key method that entails the management of doses a high dose to introduce the immune machine to antigens and a lift dose to bolster and prolong the immune response. This technique is especially effective for reinforcing both antibody and T-mobile responses throughout all dengue serotypes. In a homologous high-increase strategy, the identical vaccine is used for both the primary and booster doses(Zeyaullah *et al.*, 2022).

This approach complements the immune device's response to vaccine antigens and can cause more ordinary protection. Live attenuated vaccines together with TAK-003 and TV003/TV005 typically use this approach to reinforce immune responses and growth efficacy across distinctive dengue serotypes. On the opposite hand, the heterologous priming and booster approach involves the use of different vaccine platforms for the priming and booster doses. By stimulating humoral (antibody-mediated) and cell immune responses thru specific mechanisms, this approach can

enhance immunogenicity(Sun *et al.*, 2020).

7. VACCINE DELIVERY SYSTEMS

7.1. Advances in Vaccine Delivery Technology

7.1.1. Nanoparticle-Based Delivery

Nanoparticle-based totally transport systems have emerged as a promising innovation in vaccine transport. These structures contain the use of nanoparticles to encapsulate or gift antigens, which allows to enhance the immune response, improve vaccine stability, and permit focused delivery. Nanoparticles can be fabricated from various materials inclusive of lipids, polymers or proteins and are used to defend antigens from degradation while ensuring that they attain the right cells to result in immunity(Diaz-Arévalo, Nanopharmaceuticals and 2020, no date).

7.2. **Advantages of nanoparticle-based delivery**

7.2.1. Increased immunogenicity

Nanoparticles can mimic the scale and shape of viruses and assist them stimulate a stronger and more effective immune response. They additionally enhance antigen presentation to immune cells, leading to greater strong antibody production and T-cell activation(Jing Huang *et al.*, 2021).

7.2.2. Controlled release

Nanoparticles can be designed for managed or sustained launch, allowing the antigen to be supplied for an extended time period, enhancing immune memory and reducing the need for more than one doses(Lawrencia *et al.*, 2021).

7.2.3. Targeted delivery

Nanoparticles can be designed to goal precise cells or tissues, thereby increasing vaccine efficacy and decreasing capacity facet results. This targeting may be done by way of modifying the surface of the nanoparticles to especially bind to sure receptors on immune cells. Several dengue vaccine applicants are exploring nanoparticle-based totally delivery platforms, particularly for subunit and nucleic acid-based vaccines(Jain, 2020)(Huang *et al.*, 2022).

7.2.4. Adjuvants

Adjuvants are materials added to vaccines to decorate the immune reaction. Traditional vaccines frequently depend on live, weakened or inactivated viruses that inherently stimulate the immune device. However, for more recent vaccine systems consisting of subunit or DNA/mRNA vaccines, adjuvants play a key role in improving immunogenicity. They assist by means of selling more potent, longer-lasting immune responses with smaller doses of antigens and in a few cases assist to elicit both humoral (antibody) and cell (T-cellular) responses(Facciolà *et al.*, 2022)(Wu and Liu, 2021).

7.3. Innovative adjuvants

7.3.1. MF59

An oil-in-water emulsion that enhances the immune reaction with the aid of recruiting immune cells to the injection website online and promoting antigen uptake(Verma *et al.*, 2023).

7.3.2. AS01

A liposomal adjuvant that complements each humoral and T-cell mediated immune responses, used in vaccines consisting of the RTS malaria vaccine, S(Guerrero Manriquez and Tuero, 2021).

7.3.3. CpG oligodeoxynucleotides

These act as immune device stimulants, mimicking bacterial DNA and triggering the innate immune response, which in turn boosts the adaptive immune reaction. By combining the nanoparticles with an adjuvant, researchers can in addition boom the effectiveness of the vaccine and make sure that even low doses of antigens are especially effective(Bai *et al.*, 2021).

7.4. Innovations in Improving Vaccine Stability and Immune Activation

7.4.1. Thermostability and Cold Chain Independence

One of the principle demanding situations in vaccine shipping, mainly in tropical and useful resource-negative environments, is keeping the "cold chain" – the process of preserving vaccines at unique temperatures (usually among 2°C and 8°C) to prevent degradation. Maintaining this cold chain is logistically difficult and high priced, specifically in far off areas. The modern improvements cognizance on improving the thermal stability of vaccines, which permits them to be saved and transported at better temperatures without lack of effectiveness(Kumar *et al.*, 2022).

7.5. Techniques

7.5.1. Lyophilization (lyophilization)

This manner includes freeze-drying the vaccine to increase its shelf life and increase its balance at higher temperatures. The vaccine can then be reconstituted with sterile water or every other diluent simply earlier than management(Kumar *et al.*, 2022)(Williamson, Bachelder and Ainslie, 2024).

7.5.2. Encapsulation of nanoparticles

Nanoparticles now not most effective enhance immunogenicity but additionally enhance vaccine balance with the aid of shielding antigens from environmental factors which include temperature fluctuations and mild(Jessica Huang *et al.*, 2021).

7.5.3. Virosomes

These are lipid-based totally vesicles which can encapsulate antigens, stabilize them, and on the same time mimic the shape of viruses to enhance immune activation. These technologies purpose to lessen reliance on bloodless chain infrastructure and make vaccines greater available in dengue-endemic areas, specifically in rural and difficult-to-attain regions(Ali *et al.*, 2023).

7.5.4. Enhancing Immune Activation

In addition to balance, a important goal of recent transport structures is to improve immune activation(Schijns *et al.*, 2020).

7.5.5. Mucosal delivery

Administration of vaccines by using mucosal routes (which includes intranasal or oral) can stimulate local immune responses on the web page of virus entry (inclusive of the breathing or gastrointestinal tract), which may be mainly powerful for viruses which includes dengue. Mucosal vaccines have the gain of being needle-unfastened, making them easier to manage and greater acceptable in a few populations(Zhang *et al.*, 2021).

7.5.6. Microneedle Patches

Microneedle patches are a brand new shipping approach that uses a patch containing tiny needles to painlessly practice the vaccine to the pores and skin. This technique no longer best simplifies administration, however also improves immune responses by using concentrated on the considerable immune cells within the pores and skin. Microneedle patches are also more solid at higher temperatures, making them appropriate to be used in remote regions(Sheng *et al.*, 2021).

7.5.7. Impact of Delivery Systems on Vaccine Uptake and Coverage in Endemic Areas

Innovative vaccine shipping systems play a vital role in increasing vaccine uptake and coverage, especially in dengue-endemic areas where health infrastructure may be limited(Davies, Olivier and Amponsah-Dacosta, 2023).

7.5.8. Availability and simplified administration

Simplified vaccine delivery techniques along with microneedle patches, oral vaccines, or nasal sprays lessen the need for trained healthcare workers and the sterile situations required for traditional needle-based totally vaccines. This increases get right of entry to to vaccines in far off areas and can lead to better vaccination charges. For example, microneedle patches may be self-applied or administered by way of minimally educated employees, lowering the logistical burden on healthcare structures(Wessels, Rolles and Rink, 2020).

7.6. Overcoming public hesitation and increasing acceptance

New shipping structures, together with needle-free alternatives (eg, patches or mucosal sprays), are typically greater appropriate to the public, specifically in regions wherein worry of needles or mistrust of vaccination packages may additionally deter human beings from immunisation. The painful and invasive nature of traditional vaccinations is often a barrier to uptake, in particular in kids. Reducing those barriers can result in better adoption costs, especially in community-huge campaigns to save you dengue outbreaks(Cerda and García, 2021).

7.7. Improved cold chain logistics and cost efficiency

Technologies that enhance vaccine balance along with lyophilization or nanoparticle encapsulation can extensively lessen costs related to retaining a chilly chain at some point of vaccine transport and storage. In many dengue-endemic areas, cold chain infrastructure is limited or unreliable, leading to vaccine wastage and decreased efficacy. By increasing thermostability, vaccines may be delivered greater reliably and make sure that they attain the population that needs them most without degradation. This can also reduce the overall value of vaccination packages and cause them to greater sustainable in low-earnings settings(Han *et al.*, 2021).
Advances in vaccine shipping systems, together with nanoparticle-based totally technology, adjuvants, and innovations in thermostability, have the capacity to revolutionize dengue vaccination efforts. These improvements now not simplest enhance vaccine balance and immune activation, but also simplify management, making vaccines more handy and ideal in endemic areas. Using those technologies, vaccination campaigns in dengue-endemic regions can attain better insurance charges and feature a extra impact on controlling the unfold of the sickness. As these transport systems preserve to evolve, they provide a promising route to more powerful and broadly allotted dengue vaccines(Lin, Zhao and Lev, 2020).

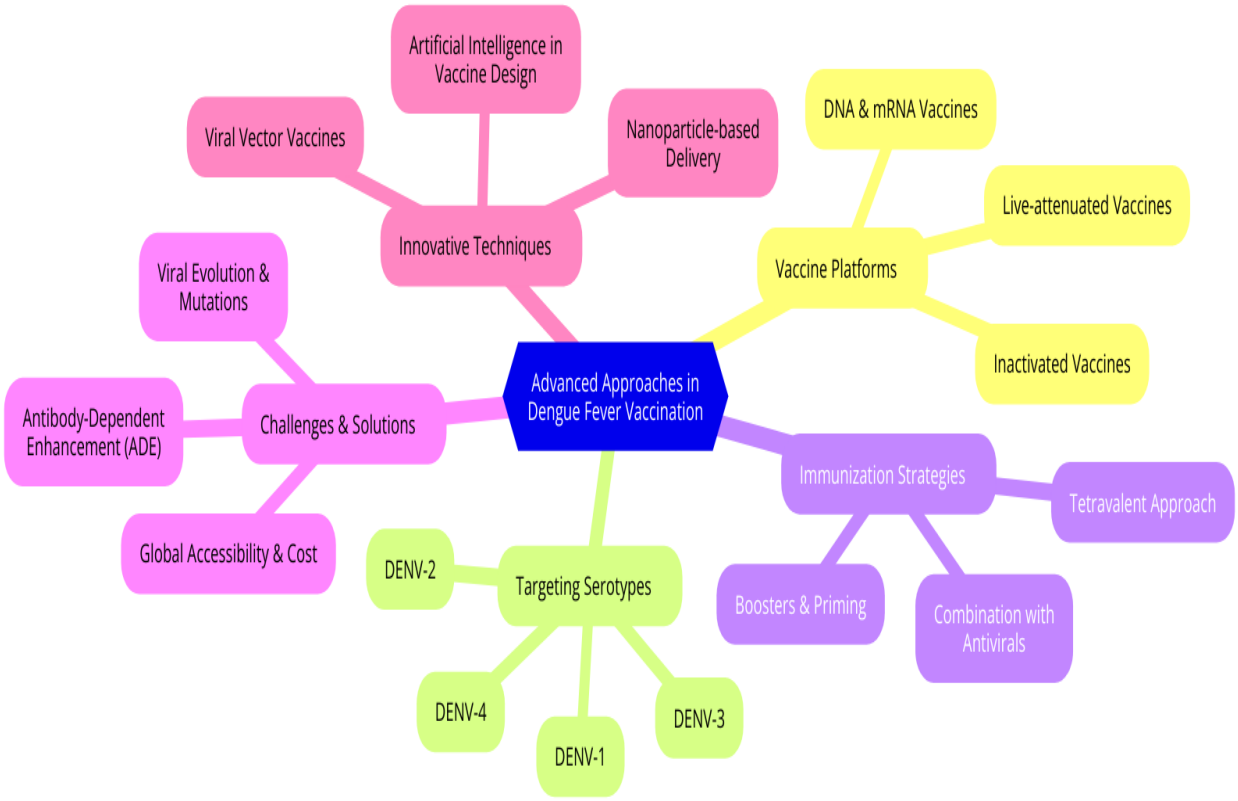

Figure No:1. Show the Advanced Approaches in Dengue Fever Vaccination

8. POPULATION-SPECIFIC CONSIDERATIONS FOR DENGUE VACCINATION

8.1. Age-Specific Vaccination Strategies

8.1.1. Children vs. Adults

Age is a essential element in dengue vaccination strategies because of differences in immune responses and disorder epidemiology in unique age agencies. Children and adults display different tiers of susceptibility to infection, ailment severity, and reaction to vaccines(Ha, 2021).

8.1.2. Children

Young kids are especially at risk of intense dengue fever (dengue hemorrhagic fever and dengue shock syndrome), especially in endemic regions wherein they're exposed to more than one serotypes at an early age. However, their immune gadget might also reply to vaccinations in another way in comparison to adults, now and again producing less robust antibody responses. In addition, protection concerns with Dengvaxia (CYD-TDV) have highlighted the accelerated threat of extreme dengue in seronegative youngsters, main to regulations on its use. For kids, vaccines have to no longer most effective be secure, but must also offer lengthy-term safety due to the better likelihood of multiple exposures over the years. Age-particular immunization packages often awareness on vaccinating school-elderly kids (9–16 years), as visible with Dengvaxia, because they are at better chance of secondary infections and serious outcomes(Annan *et al.*, 2023).

8.1.3. Adults

Adults, mainly the ones in endemic regions, who have already been uncovered to as a minimum one dengue serotype may additionally gain from vaccines such as Dengvaxia, which work better in seropositive individuals. Vaccination strategies for adults have to keep in mind occupational publicity (eg, in agricultural workers or dengue-prone city regions) and the opportunity of tour-associated dengue in non-endemic populations. The intention for adults is to provide comprehensive safety towards all serotypes, mainly those with a danger of secondary infections, which tend to be extra intense. Additionally, older populations may additionally have weaker immune responses to vaccines, necessitating formulations or dosing techniques that account for immunosenescence. In each age groups, vaccines need to strike a stability among safety and efficacy whilst ensuring minimum danger of serious effects which includes antibody-based enhancement (ADE)(Chong, Tan and Arasoo, 2023).

8.2. Importance of Vaccination in Endemic Regions

8.2.1. Latin America

Dengue transmission remains a vast trouble in lots of components of Latin America, with nations including Brazil, Mexico and Colombia going through tremendous sickness burdens. These countries revel in waves of epidemics that stress fitness structures, cause economic losses and cause hospitalizations. In such areas, vaccination plays a key role in decreasing severe instances and hospitalizations, as a consequence reducing stress on the health system. One of the main problems in Latin America is the superiority of more than one dengue serotypes. Co-move of different serotypes increases the chance of secondary infections, that are regularly extra extreme. Vaccines which includes TAK-003 and TV003/TV005, which aim to provide balanced immunity against all 4 serotypes, are essential in these regions to keep away from such extreme outcomes. Another key component is the infrastructure wanted for vaccination campaigns(Llau, Williams and Tejada, 2021).

While city centers typically have the sources wanted for massive-scale vaccination efforts, rural regions face good sized logistical demanding situations. Improving bloodless chain systems and the usage of vaccines that remain solid below less than ideal conditions could help make sure that even far flung regions can benefit from vaccination. Public perception and hesitancy approximately vaccination is likewise a critical issue. The Dengvaxia controversy within the Philippines had a ripple effect in different countries, shaking public confidence in dengue vaccination packages. Clear and transparent verbal exchange is wanted to clear up this trouble, in conjunction with training campaigns on the way to repair self-belief in more recent vaccines, mainly people with better safety profiles. By addressing those issues, vaccination can emerge as a cornerstone of dengue prevention in Latin America(dos Santos Ferreira *et al.*, 2021).

8.2.2. Southeast Asia

Southeast Asia is the primary consciousness of dengue fever, with countries such as Thailand, Indonesia and the Philippines experiencing excessive stages of endemicity. In this place, a combination of urbanization, in which Aedes aegypti mosquitoes thrive, and densely populated areas contribute to the unfold of the disorder. Southeast Asia faces similar demanding situations to Latin America, but with the added complexity of a tropical weather that helps 12 months-spherical transmission. One essential aspect for Southeast Asia is the want for non-stop vaccination applications. The consistent threat of dengue caused by the tropical climate manner that vaccination efforts cannot be restrained to outbreak intervals(Wong, Wong and AbuBakar, 2020).

Targeting faculty-age kids and excessive-risk adults, in particular all through off-height times, may want to help avoid seasonal fluctuations in cases and offer 12 months-spherical protection. Another problem is the hazard of co-infection with different mosquito-borne sicknesses such as Zika and chikungunya, which often circulate in the identical regions. Vaccination strategies have to take these risks into consideration, and integrating dengue vaccination with vector control measures, along with decreasing mosquito breeding sites, could provide extra comprehensive safety. Another trouble is overburdened healthcare structures. During a dengue outbreak, fitness care sources are frequently constrained, making it difficult to address different health priorities. By decreasing the occurrence of dengue via huge vaccination, these

structures could goal different vital fitness troubles and relieve a number of the pressure for the duration of outbreak intervals(Gao *et al.*, 2020).

8.3. Potential Vaccine Strategies for Travelers and Non-Endemic Populations

Travelers to dengue-endemic areas and populations living in non-endemic regions have exceptional vaccination wishes as compared to those residing in regions wherein dengue is endemic for the duration of the 12 months. Vaccination strategies for these populations are centered more on short-time period protection and lowering the hazard of significant infection during travel(Steffen, Chen and Leggat, 2023).

8.4. Travelers to Endemic Regions

Dengue poses a giant chance to international tourists travelling endemic regions inclusive of Southeast Asia, Latin America, and the Caribbean. Without broadly to be had dengue pre-publicity prophylaxis, vaccination is the excellent alternative for protection. Travelers require vaccines that provide brief-term, speedy-onset safety, preferably some weeks before travel. Single-dose vaccines consisting of live attenuated versions together with TV003/TV005 would be sensible to make sure compliance. Since many tourists are seronegative, vaccines need to be secure and powerful for this populace without growing the hazard of antibody-based enhancement (ADE)(Mischlinger *et al.*, 2020).

8.5. Non-Endemic Populations

In non-endemic populations, mass vaccination programs against dengue may not be vital, but there are specific situations where vaccination may want to nonetheless play a key function. Military employees deployed to dengue-endemic regions, as an instance, would benefit from pre-deployment vaccinations to prevent service-related ailments. Similarly, emergency or remedy workers responding to failures in areas with dengue fever may additionally require vaccination to keep away from infection for the duration of deployment(Argirion*et al.*, 2020).
In areas in which dengue is rising or re-rising, vaccination techniques should goal high-risk businesses, consisting of residents of regions where new outbreaks have befell. Tailoring dengue vaccination techniques to precise populations, thinking of factors which include age, endemicity and chance of publicity, is crucial for powerful implementation. This approach could help defend youngsters and adults in endemic regions and offer brief-term unmarried-dose vaccines for tourists and non-endemic populations, ultimately decreasing ailment transmission and public health influences international(Rocha, Pereira and Maia, 2022).

9. FUTURE DIRECTIONS IN DENGUE VACCINATION

The future of dengue vaccination could be very promising as subsequent-technology vaccine candidates cognizance on growing protection, efficacy and availability(Akter*et al.*, 2024). Integrating dengue vaccines into worldwide immunization packages and leveraging public-private partnerships might be vital to attain at-hazard populations. However, scaling up manufacturing and making sure equitable get right of entry to to vaccines will present demanding situations that require international cooperation, revolutionary financing mechanisms and continued commitment from governments, NGOs and the private area(Kamath and Aishwarya, 2024). Overcoming these demanding situations may be vital to accomplishing considerable dengue control and reducing the worldwide burden of the disease(Wang, 2024).

10. CONCLUSION

Dengue remains a major global health problem, especially in endemic areas. Vaccination is a critical means of disease prevention, but the complexity of the dengue virus, such as its 4 serotypes and the risk of antibody-based amplification (ADE), presents challenging situations. Current and other vaccine candidates, which include attenuated, subunit, and mRNA vaccines, offer hope for safer and stronger safety. Incorporating these vaccines into international immunization programs and ensuring equitable access through public-private partnerships is essential. Innovations in vaccine delivery systems, including nanoparticle-based platforms and thermostable formulations, may also be critical to increasing insurance coverage, particularly in low-resource settings. Overcoming challenges in production, distribution, and public opinion may be key to the success of global dengue vaccination efforts, long-term reductions in the disease burden, and halting major global epidemics.

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