

NIPAH VIRUS VACCINE: PROGRESS AND CHALLENGES FOR ZOO NOTIC SPILLOVER PREVENTION

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Abstract

Nipah virus (NiV) is a highly pathogenic bat-borne and zoonotic virus. It has epidemic and pandemic potential due to its high case fatality rate, capacity for human-to-human transmission and broad host range. Since its discovery in 1998 in Malaysia, recurrent episodes in India and Bangladesh highlight the urgent need for effective preventive strategies. This review examines recent progress in NiV vaccine development, including viral vector, subunit, DNA, mRNA, and virus-like particle platforms, and discusses the major scientific and operational barriers limiting their translation into field use. Key challenges include limited clinical evaluation opportunities, strain diversity, manufacturing constraints, cold-chain requirements, and weak outbreak preparedness in high-risk settings. The review also highlights the importance of integrating vaccine development with surveillance, early detection, and One Health-based prevention strategies. Strengthening these linked approaches will be essential for improving preparedness and reducing the risk of future Nipah virus outbreaks.

INTRODUCTION

Nipah virus (NiV) is a zoonotic paramyxovirus that causes bat-borne diseases in humans and animals. This virus is part of the genus henipavirus and family paramyxoviridae. Since its initial discovery in 1998, during an encephalitis outbreak among pig farmers in Malaysia, the virus has caused repeated outbreaks in South and Southeast Asia, particularly in Bangladesh, India, and the Philippines (Singh et al., 2019). Infection in humans has been ascribed to consuming and ingesting the infected bat secretions on the date palm sap and physical contact with infected

animals, particularly pigs (Islam et al., 2016; Yadav et al., 2022). Human-to-human infection can occur secondarily through respiratory droplets and body fluids, and it is more prevalent in health facilities (Gazal et al., 2022; Kalter et al., 2023). Genomic analysis revealed that NiV exhibits high genetic variability across outbreaks and that envelope glycoproteins play an important role in viral attachment and entry (De Campos et al., 2024). It is also closely linked to the Hendra virus and henipaviruses (Gupta et al., 2020; Singh et al., 2019). The concept of genomic variability is also among the factors required to identify therapeutic

and vaccine targets (Seib et al., 2009; Ullah et al., 2025; Ullah et al., 2026). No approved NiV vaccinations or antivirals are currently available; therefore, the focus is on the prevention plan (McLean & Graham, 2019; Singh et al., 2019). Some premature designs include live-attenuated vaccines, inactivated virus preparations, and protein subunits, with the newest designs being mRNA-based and either in preclinical or early clinical development (Broder et al., 2013; Foster et al., 2022; Wang, 2022a).

The genomic structure revealed that it is a negative-sense, single-stranded RNA virus with a

genome of 18 kb. Furthermore, it expresses six structural proteins: nucleocapsid (N), phosphoprotein (P), matrix (M), fusion (F), glycoprotein (G), and large polymerase (L) (Yadav et al., 2022). Electron microscopy shows that it is a closed structure with a typical herringbone pattern observed on the virion, measuring 40 to 600 nm in diameter. The viral genome is encapsidated by the N protein to form a ribonucleoprotein complex, transcribed and replicated by the P and L proteins. M protein keeps the virions stable and facilitates budding.

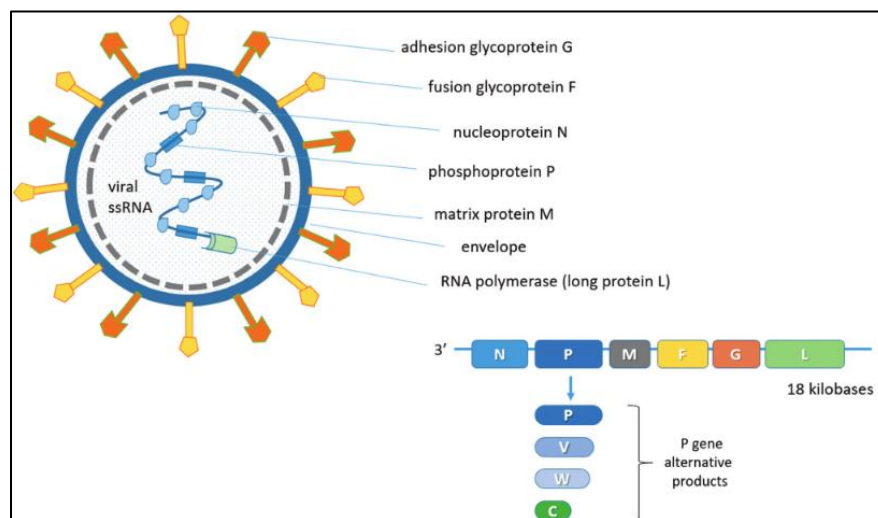


Figure 1: Genomic structure of NiV virus

F and G glycoproteins are important contributors to host cell entry and are classified as targets of primary vaccines. The G protein binds to ephrin-B2 and ephrin-B3 receptors on the host cell, and the F protein facilitates the fusion of the membranes to enable viral RNA entry into the cytoplasm (Salleh, 2025). These envelope proteins are vital in infection as well as in eliciting a strong immune response, which makes them important in developing vaccines (Murin et al., 2019). Further molecular studies are expanding the understanding of NiV reproduction and virulence, and could develop therapeutic and vaccination strategies that disrupt virus entry or genome replication (Chakraborty et al., 2024).

Epidemiology and Transmission

After the discovery in 1998, a mass outbreak of encephalitis among pig farmers was followed by the mass culling of more than one million pigs (Satterfield et al., 2016). This occurrence identified pigs as a critical intermediate host that can enhance the transmission of the virus between bats and humans. NiV has become an annual or periodical public health menace in Bangladesh since that time, and a recurrent menace in India (Cimaroli, 2024). NiV outbreaks have also been reported in the Philippines, with the first cases reported in 2018, followed by additional outbreaks in 2019, all of which were linked to contact with infected fruit bats (Banerjee et al., 2019).

Fruit bats (*Pteropus* spp.), particularly *Pteropus vampyrus* and *Pteropus hypomelanus* are the natural reservoir of NiV, with viral shedding found in saliva, urine and faeces (Sendow et al., 2010; Sendow et al., 2006). Such secretions often pollute food and water sources and provide cross-species opportunities. The consumption of raw date palm sap is one of the most well-documented spillover routes that gets contaminated by bat saliva or urine during collection. Several studies in Bangladesh have continued to attribute an outbreak to this cultural practice (Khan, 2024). However, it is not necessarily transmitted by food. Zoonotic events have occurred in Malaysia and

India, where pig farming is an overlapping habitat with bats (Wong et al., 2007). Pigs can also serve as amplifying hosts, releasing large quantities of the virus and exposing humans to greater risk. There are also instances of human-to-human transmission in various outbreaks, specifically in healthcare facilities. Caregivers, family members, and healthcare workers are at high risk of infection because infected patients can transmit the virus via respiratory droplets, saliva, urine, and other body fluids. In Bangladesh and India, nosocomial transmission has been particularly problematic, with poor infection-control practices exacerbating outbreak severity.

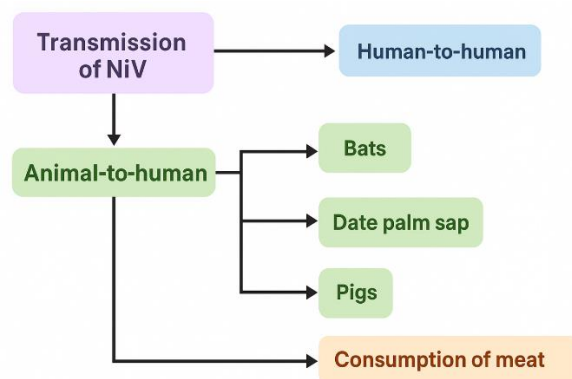
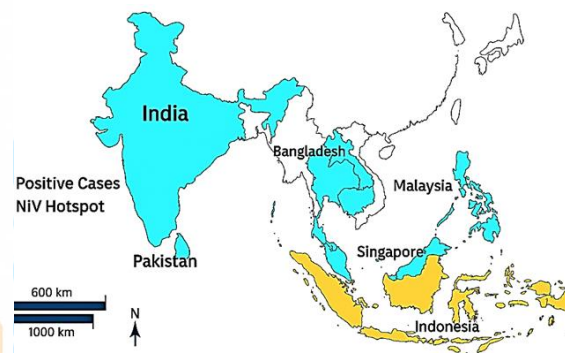


Figure 2: Transmission pathways and epidemiology map NiV



NiV outbreaks are considered serious because the reported fatality rate ranges from 40 to 75 per cent, depending on the location and the capacity of health care professionals to respond to the outbreak (Paul et al., 2023). Case fatality rates tend to be very high in Bangladesh (above 70 %), whereas in India, death rates have been between 40 and 75 % in different outbreaks. Differences in outbreak identification, health care facilities, and access to treatment can explain this variability. Although there are no reported human infections (as of May 2023) in Indonesia, in a few studies, NiV RNA and antibodies were detected in bat populations. *P. vampyrus* transmitted niV-strains that were directly related to those in Malaysia in Sumatra, and survey serology of *P. vampyrus* populations in Kalimantan, Sumatra and Java (Nidom et al., 2025). These findings indicate that Indonesia is a potential hot spot. It is thought that the co-occurrence of large populations of bats,

high populations of pigs and high human-animal contact enhance the potential risk of spillovers. The same simulation studies show that when bat ecology overlaps with agricultural activities, this creates an optimal environment for NiV emergence (Nikolay et al., 2021).

The frequency of cases in Bangladesh and India and the discovery of the virus in bats in Indonesia, Malaysia, and the Philippines all make substantially more powerful systems of surveillance, educating communities, and collaboration across countries essential. Health-related institutions should implement interventions to reduce high-risk behaviours, including excessive consumption of raw date palm sap, farm biosecurity, and infections within healthcare institutions.

NiV infection exhibits substantial clinical heterogeneity, with cases ranging from asymptomatic infection to severe and fatal disease.

The incubation period is approximately 4 to 14 days, but some reports indicate a longer incubation period of 45 days, thus making it difficult to contain the outbreak of this disease (Gazal et al., 2022; Thakur & Bailey, 2019).

Early clinical manifestation is not specific and includes headache, myalgia, vomiting and sore throat. All these flu-like symptoms may set in over a couple of days (Banerjee et al., 2019). Neurological manifestations and abnormalities, such as dizziness, drowsiness, altered mental status, seizures, and focal neurological deficits, can then occur in patients with a viral encephalitis (Ramphul et al., 2018). The most common acute condition is encephalitis, which is characterized by the inflammation of the brain and can cause coma in some patients within 24-48 hours (Bruno et al., 2022). The respiratory system is also often involved, with some patients developing acute respiratory distress syndrome (ARDS), which is manifested by cough, dyspnea and hypoxia. NiV is a very fatal disease as it affects the respiratory and central nervous systems (Cohen et al., 2024).

The case fatality rate (CFR) ranges from 40 to 75 %, and in some outbreaks in Bangladesh, it has reached 90%. Severe encephalitis, multi-organ dysfunction or respiratory failure are the most frequently occurring causes of death. Personality change, repeated convulsions, and cognitive impairment are some of the long-term neurological effects of a concussion (Mickeviciene et al., 2007). Additionally, the risks of NiV are also demonstrated by the cases of relapsed and delayed encephalitis months to years after the first infection (Sayed et al., 2019). Clinically, the local differences have also been noted. In Malaysia, the consequences of outbreaks were more connected to encephalitis, whereas in both Bangladesh and India, respiratory symptoms were even more prevalent, which raises the possibility of human-to-human transmission (Sharma et al., 2021). These differences may reflect a variety of strain or context-dependent transmission.

Though there have been no confirmed cases of NiV in humans recorded in Pakistan, its geographical location, ecological conditions, and agricultural activities make it vulnerable to spillover cases. India and Bangladesh are the

neighbouring countries of Pakistan, and since 2001, the two countries have faced frequent outbreaks (Singh et al., 2019). Considering the porous borders, the trade within the boundaries, and ecological cross-corridors, the possibility of spillover across the borders into Pakistan should not be ignored. Further, the distribution of *Pteropus giganteus* and other species in the country indicates a reservoir-host interface as observed in other neighbouring countries (Khan et al., 2022). The pig populations in Pakistan are not as significant as those in Malaysia and the Philippines, although other domestic animals can be used as incidental hosts, such as goats, cattle and horses. Of greater concern, the rural and peri-urban regions of the country are heavily populated, and people, animals, and bats are in close contact, increasing the chances of viral spillover. In these regions, the healthcare setup is likely to be resource-limited, and this may further complicate matters in case human-to-human transmission occurs. Practices in Bangladesh and India demonstrate that nosocomial infections in hospitals can contribute meaningfully to the severity of the outbreak (Shahida et al., 2016).

Pakistan is potentially in a precarious position due to its proximity to confirmed outbreak zones and a lack of surveillance and diagnostic capabilities (Iqbal et al., 2024; Mehmooda et al., 2025). NiV serological and human and livestock gaps in preparedness are due to the lack of systematic bat surveillance or NiV serological studies. Moreover, because of climatic and ecological transformations, such as deforestation and urbanization, the level of contact between bats and livestock, as well as people and bats, is on the rise, increasing the likelihood of zoonotic spillover (Esposito et al., 2023).

Management of Nipah Virus Disease

Effective management of the NiV outbreak requires accurate diagnosis. Molecular and serological tests are considered to be laboratory-confirmed. Reverse transcription polymerase chain reaction (RT-PCR) is the gold standard for detecting viral RNA in blood, throat swabs, urine or cerebrospinal fluid (Corless et al., 2002). Moreover, real-time quantitative RT-PCR tests

offer higher sensitivity and are faster, enabling timely identification of cases during outbreaks (Sule & Oluwayelu, 2020). The isolation of viruses at biosafety level 4 (BSL-4) is extremely conclusive, but seldom practised in clinical practice, as it requires a high level of biosafety. Serological assays are conducted using an enzyme-linked immunosorbent assay (ELISA), which detects IgM and IgG antibodies in both acute and convalescent samples, providing evidence of recent or past infection (Bastos et al., 2020). Lateral flow assays are new point-of-care diagnostics under development (Bruno et al., 2022).

There are currently no licensed antivirals against NiV infection. Supportive care is the mainstay of treatment and involves keeping the patient's body hydrated, helping to maintain the respiratory system and the neurological symptoms (Peghin & Danziger-Isakov, 2019). Ribavirin has undergone only small-scale clinical trials, and some studies indicate significant benefit (Li et al., 2023). Remdesivir is a broad-spectrum antiviral drug, which was developed for treating other RNA viruses, that is protective in animal models of NiV infection, but has not been tested adequately in humans (Sun, 2020). Favipiravir also showed a partial effect in experimental studies. The viral glycoprotein G-directed m102.4 monoclonal antibody has shown promising safety in nonhuman primates and has been used on a compassionate basis in Australia, but it is not generally available (Wang, 2022b).

Prevention is crucial, and public health strategies aim to reduce the risk of spillover and human-to-human transmission. Preventing the use of raw date palm sap by using bamboo skirts on collection pots in Bangladesh has reduced contact with bat secretions (Cimaroli, 2024). In farming environments, it is important to enhance farm biosecurity and reduce pig-bat interactions as seen in the Malaysian outbreak (Chan et al., 2021). Nosocomial transmission requires strict infection prevention and control (IPC) measures, such as isolation of suspected cases, the use of personal protective equipment (PPE) and adherence to barrier nursing protocols in healthcare settings. Public awareness campaigns and involving communities are crucial in vulnerable areas,

especially rural areas, where cultural practices pose a higher risk for exposure (Vaughan & Tinker, 2009). At the global level, NiV has been ranked by WHO as a priority pathogen under the Research and Development Blueprint, which supports and stresses the need for accelerated research on diagnostics and vaccines (Kojom & Singh, 2021).

Nipah Virus Vaccines and Preparedness

The lack of vaccines against the NiV has spurred extensive research into various vaccine platforms. The emphasis has been on inducing robust humoral and cellular immunity, particularly against the viral glycoproteins (G and F), which play a critical role in viral attachment and fusion. The following list of strategies that have proven encouraging in animal models and preclinical trials includes DNA vaccines, virus-like particles (VLPs), viral vectors, and mRNA vaccines (Singh et al., 2019).

DNA Vaccines

DNA vaccines will consist of plasmids encoding NiV antigens, enabling host cells to express viral proteins that elicit immune responses. Studies in animal models have shown that DNA vaccines encoding the G or F glycoproteins can elicit neutralizing antibodies and T cell responses (Singh et al., 2019). They have the benefits of being stable, easy to manufacture, and safe. DNA vaccines, however, have lower immunogenicity than other platforms and must be optimized or adjuvanted to be effective (Kozak & Hu, 2023).

Virus-Like Particles (VLPs)

They are non-infectious and highly immunogenic VLPs that replicate the form of a virus but lack genetic material. Co-expression of structural proteins (M, F and G) into NiV VLPs has been observed to provoke strong immune responses and protection in preclinical models (Libbey et al., 2011). The immune system is better recognized by its ability to present the antigens in natural folds. However, large-scale production and stability issues can make them really hard to put to use in outbreak situations when they are needed the most (Rele, 2020).

Viral Vector Vaccines

Some recombinant viral vectors have also been identified as the most promising NiV vaccine development vectors, such as vesicular stomatitis virus (VSV) or adenoviruses. primates fully protected with a single dose of a recombinant VSV expressing NiV glycoproteins, which may have potential as an outbreak response vaccine. (Monath et al., 2022). Likewise, NiV antigen recombinant measles virus vectors have demonstrated immunogenicity in animal models (Broder et al., 2013). For all these advances, safety considerations with live viral vectors, particularly across immunocompromised populations, have been a major concern (Woolsey et al., 2023).

mRNA Vaccines

With the success of COVID-19 vaccines, mRNA platforms have now been developed to adapt to NiV. Hamster models of mRNA encapsulated within lipid nanoparticles encoding prefusion

stabilized F and G proteins elicited robust neutralizing antibody and T cell responses with protection from challenge with the killing virus. mRNA vaccines: high scalability, flexibility against viral variants, high immunogenicity. The use of cold-chain storage, however, creates logistical challenges in resource-restricted and rural areas where NiV outbreaks have regularly been reported.

When examined against real-world needs, thermostability, single-dose efficacy, and rapid scale-up outweigh marginal immunogenicity gains. ChAdOx1 and VSV vectors score highest for outbreak containment (ring vaccination), while VLP and DNA platforms are promising for livestock or long-term preventive use. mRNA remains scientifically robust but logistically impractical for low-resource rural settings. Therefore, platform selection should not be “best science wins,” but “best fit for context.”

Table 1: Contextual suitability of current Nipah virus vaccine platforms for real-world deployment

Criterion	VSV Vector	ChAdOx1	mRNA	DNA	VLP
Thermostability	Moderate; requires cold chain	Good stability	Poor (frozen storage)	Moderate	Excellent
Production Cost	Moderate	Moderate	High	Low	Moderate
Dosing	Single	Single	Two	Multiple	Single
Outbreak Use Speed	Rapid scalable	Moderate	Rapid	Slow	Slow
Field Suitability	Good	Good	Limited	Limited	High (if scalable)

Proposed Roadmap for NiV Vaccine Development and Deployment

Accepting the point of the comparative analysis of the platforms of vaccines, one could see that scientific innovation will not be the key to the Nipah virus (NiV) vaccination success. The prevalent one is the compatibility of the nature of the vaccine to the conditions of deploying it, i.e. the nature of the epidemiological situation, the presence of the needed infrastructure and socio-economic environment in the affected regions. In this manner, we are able to get a three-level roadmap that would incorporate technological

preparedness and operational feasibility into a One Health framework.

Tier 1 - Vaccination upon Outbreaks (Ring Vaccination and Emergency Use)

The level is only interested in the rapid containment of the emerging clusters in Bangladesh and India, among other areas of risk. The best includes a single-dose efficacy vaccine platform that is fast immunogenic and scalable manufacturing capacity-based vaccine platform, such as VSV-based and ChAdOx1 vectors vaccine programs. They are flexible to the adoption of the

use of ring-vaccination methods and can be put in place within days after the outbreaks. In order to operationalize this tier, local health authorities in coordination with CEPI and WHO are supposed to assist in making pre-approved emergency stockpiles and regulatory expediency mechanisms of compassionate or emergency use.

Tier 2 - Livestock and Reservoir Control

In light of the specified role of pigs and Pteropus bats in spill over, a compensatory level of immunity is provided by selective immunization of animal hosts. The right vaccine to use at this stage will be the VLP and DNA vaccines, which can be re-engineered to be used in veterinary settings and can be manufactured in large quantities with minimal cost. These processes within the scheme of monitoring the farming and wild animals would decrease the rate of amplification and transmission of the virus. The tier involves the close cooperation of the veterinary services, wildlife biologists and the rest of the population through a One Health surveillance network.

Tier 3 Pre-emptive Community Protection.

Long-term prevention requirements in endemic or high-risk populations are cheap, thermostable and conveniently administered formulations, which the rural health systems can manage. The future iterations can be made capable of being room temperature stable and allow a single visit to be performed without additional follow-up to allow potential VLP, DNA or viral-vector vaccines to be integrated into regular immunization efforts or even into dedicated campaigns. High-risk districts should be a priority of the economic modelling, and NiV vaccination is to be incorporated with the already existing platforms (polio or COVID-19 vaccination campaigns).

This pyramid will make NiV vaccine development a situation-specific optimization game, rather than a race to the top in terms of laboratory efficacy. Any platform will be based on the price of the location and how it will be used. The following stage of conducting research should be during the case of veterinary and preventive situations, setting platform-specific deployment rules in the event of an outbreak. The development of low-volume

delivery equipment and thermostable formulations that were modified to suit the conditions in the tropics. New adaptive trial designs would be innovative, allowing for the measurement of disease outbreaks that happen at sporadic timepoints that would not introduce any delay in licensure. Enhancing cross-border communication of information and community participation to offer equal access and privacy.

Such a roadmap eventually gives a viable map on how the success of the laboratory can be translated into sustainability regarding the protection of the region. It bridges the scientific innovation with field realities, therefore translating NiV vaccine development out of theoretical preparedness to actual pandemic preparedness.

Monoclonal Immunoprophylaxis

Although not strictly vaccines, monoclonal antibodies such as m102.4 against the NiV G protein have been developed as prophylactic and/or therapeutic agents. In animal models, m102.4 gave good protection after challenge with NiV and has been used on a compassionate basis in humans (Chakraborty et al., 2024). Antibody-based interventions are costly and scale poorly, although promising.

Antibody-Based

Issues and Prospects.

Despite promising results, there are still a number of challenges ahead. Cross-protection of vaccines against NiV in the advent of genetic differences between the Malaysian and Bangladesh strains may not occur (Tan et al., 2024). Furthermore, the sporadic and geographically limited nature of outbreaks makes the design of large-scale human clinical trials challenging (Lauer et al., 2017). These barriers can only be tackled through creative designs of trials, global partnerships, or investing in One Health surveillance systems.

The combination of next-generation technologies like mRNA and VLPs with field-ready platforms that meet the need for delivery provides hope for future licensure. Importantly, for a vaccine to be successful, it has to be affordable, thermostable, and deployable in rural outbreak-prone areas. With the persistence of efforts in science and

policy, it may be possible in the near future to take an NiV vaccine for licensing (Marzouk & Alajaji, 2025). Despite significant progress in preclinical research, translating promising Nipah virus (NiV)

vaccine candidates into licensed products remains complex. Challenges range from viral diversity and trial design limitations to manufacturing, governance, and public acceptance issues.

Table 2. Nipah Virus Vaccine Platforms, Advantages, Limitations, and Key Findings

Vaccine Platform	Antigen/Target	Key Findings	Advantages	Limitations	References
DNA vaccines	Plasmid DNA encoding NiV G or F glycoproteins	Induced neutralizing antibodies and T-cell responses in animal models	Easy to produce; stable; safe	Generally weak immunogenicity; often requires multiple doses or adjuvants	Singh et al., 2019; McLean & Graham, 2019
Virus-like particles (VLPs)	Structural proteins (M, F, G) assembled into VLPs	Strong humoral and cellular immune responses; protective in preclinical models	Mimics native virus; highly immunogenic; non-infectious	Large-scale production difficult; stability issues	Walpita et al., 2011; Thakur & Bailey, 2019
Viral vector vaccines	Recombinant VSV, measles virus, adenovirus expressing NiV G or F	Single-dose protection in nonhuman primates: robust immune response	High immunogenicity; rapid outbreak use potential	Safety concerns in immunocompromised individuals	Broder et al., 2013; Foster et al., 2022; Monath et al., 2022
mRNA vaccines	mRNA encoding prefusion-stabilized F and G proteins, lipid nanoparticle-encapsulated	Induced strong antibody and T-cell responses; complete protection in hamsters	Rapid design and production; adaptable to variants; potent immunogenicity	Cold-chain requirements, cost, and distribution challenges	Wang et al., 2022; Gazal et al., 2022
Monoclonal antibody-based immunoprophylaxis	m102.4 targeting NiV G protein	Provided post-exposure protection in animal models; compassionate human use reported	High specificity; therapeutic potential	Expensive; not scalable as a vaccine substitute	Foster et al., 2022

Table 3. Key challenges and potential solutions for advancing Nipah virus (NiV) vaccine development and deployment

Challenge Area	Description / Limitation	Proposed Solutions and Strategic Approaches
Genetic and Antigenic Diversity	The existence of multiple NiV lineages (Malaysia vs. Bangladesh) raises concern over cross-protection. Current vaccines may not provide broad coverage.	• Employ consensus antigen or mosaic immunogen design to cover conserved epitopes across strains. • Use computational epitope mapping and structure-guided design to identify cross-neutralizing targets. • Establish reference strains and neutralization standards via WHO/CEPI coordination.
Limited Clinical Trial Feasibility	Low incidence and sporadic outbreaks make large-scale efficacy trials impractical.	• Apply the U.S. FDA “Animal Rule” or equivalent WHO pathways for approval based on validated animal models. • Develop adaptive and ring vaccination trial designs activated during outbreaks. • Maintain pre-approved “ready-to-activate” protocols in endemic regions.
3. Manufacturing and Cold-Chain Constraints	Cold storage, especially for mRNA and VSV platforms, limits deployment in tropical settings.	• Prioritize thermostable or lyophilized formulations and microneedle/intranasal delivery systems. • Leverage CEPI’s 100 Days Mission and LMIC manufacturing hubs for rapid scale-up. • Integrate NiV vaccines into regional stockpiles for emergency use.
4. Governance, Funding, and Global Coordination	Fragmented funding and a lack of commercial incentive slow progress between outbreaks.	• Strengthen CEPI-WHO-Gavi collaboration for end-to-end vaccine pipelines. • Create advance market commitments (AMCs) to sustain manufacturer interest. • Develop cross-border regulatory pathways and regional emergency stockpiles.
5. Socio-behavioural and Ethical Barriers	Vaccine hesitancy and poor healthcare access hinder uptake in rural populations.	• Implement community engagement and culturally sensitive communication within a One Health framework. • Combine NiV immunization with existing health campaigns (polio, COVID-19). • Promote equitable access through government-NGO collaboration.

Conclusion

Nipah virus remains an example of the growing distance between laboratory creation and its practical application in the process of controlling zoonotic diseases. However, the capacity to be inserted into the environment, where NiV evolves, is what defines the actual preparedness to deal with the pandemic due to a phenomenal number of vaccine platforms designed through scientific

approaches, among which are, but not limited to, viral vectors and VLPs, DNA or mRNA constructs. The synthetic evidence in this review indicates that the success of a technology is not enough, but the most intriguing is deployability- the ability to reach thermostability, low cost and scalability and even that, without the logistic limitations of South and Southeast Asia. The

given analysis pays specific attention to the operational and economic considerations of the NiV vaccine development in comparison with the prior reviews and presents the consideration of the risk environment in the area, that is, in Pakistan. Although they are not present in human cases, as of yet, Pakistan not only has the same ecological niche as Pteropus bat groups, but also has porous borders with NiV-carrying nations and does not have sufficient resources in health, which makes it one of the most important test cases of the preventive preparedness. This background indicates that inefficient surveillance systems and a lack of diagnostic capabilities can make a difference in the quick adoption of the vaccine, which is what is being addressed in the proposed roadmap.

When it comes to the future, however, it is essential to mention that the application of a three-pronged approach that entails the involvement of scientists, policy-makers, and manufacturers should be applied to the development of the NiV vaccine. The areas of research that should be considered by the researchers include how to come up with cross-lineage immunogens and thermostable formulations, which can be applied in the field. The policymakers ought to come up with regulatory channels using the Animal Rule and adaptive trial model to expedite approval within the low-incidence settings. In the meantime, global organizations, especially CEPI, WHO and Gavi, should invest in regional capacity to manufacture vaccines and equal procurement systems in such a way that NiV vaccines can be made available to rural people within days, as opposed to months, of an outbreak. Lastly, restricted access to NiV risk assessment and vaccine preparedness would be recommended to be incorporated in the One Health strategy of such countries as Pakistan, which would connect the monitoring in the wildlife, livestock and human healthcare preparedness. This survey redefines Nipah prevention, not as a discovery race, but as a deployment issue, a mentality that must be overcome to convert preclinical promise into a workable scientific use.

REFERENCES

- Banerjee, S., Gupta, N., Kodan, P., Mittal, A., Ray, Y., Nischal, N., Soneja, M., Biswas, A., & Wig, N. (2019). Nipah virus disease: A rare and intractable disease. *Intractable & rare diseases research*, 8(1), 1-8.
- Bastos, M. L., Tavaziva, G., Abidi, S. K., Campbell, J. R., Haraoui, L.-P., Johnston, J. C., Lan, Z., Law, S., MacLean, E., & Trajman, A. (2020). Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. *bmj*, 370.
- Broder, C. C., Xu, K., Nikolov, D. B., Zhu, Z., Dimitrov, D. S., Middleton, D., Pallister, J., Geisbert, T. W., Bossart, K. N., & Wang, L.-F. (2013). A treatment for and vaccine against the deadly Hendra and Nipah viruses. *Antiviral research*, 100(1), 8-13.
- Bruno, L., Nappo, M. A., Ferrari, L., Di Lecce, R., Guarnieri, C., Cantoni, A. M., & Corradi, A. (2022). Nipah virus disease: epidemiological, clinical, diagnostic and legislative aspects of this unpredictable emerging zoonosis. *Animals*, 13(1), 159.
- Chakraborty, C., Saha, S., & Bhattacharya, M. (2024). Recent advances in immunological landscape and immunotherapeutic agent of Nipah virus infection. *Cell Biochemistry and Biophysics*, 82(4), 3053-3069.
- Chan, O. S., Bradley, K. C., Grioni, A., Lau, S. K., Li, W.-T., Magouras, I., Naing, T., Padula, A., To, E. M., & Tun, H. M. (2021). Veterinary Experiences can Inform One Health Strategies for Animal Coronaviruses. *EcoHealth*, 18(3), 301-314.
- Cimaroli, A. (2024). *Climate Change and Nipah virus: exploring the links between climate variability, extremes, and zoonotic spillover in Bangladesh* [Politecnico di Torino].
- Cohen, S. M., Hatton, K. W., & Cereda, M. (2024). Dyspnea and Respiratory Distress in the Neuro ICU. In *Textbook of Neurointensive Care: Volume 1: Neuroanatomy, Diagnostic Assessment, Disease Management* (pp. 143-158). Springer.

- Corless, C. E., Guiver, M., Borrow, R., Edwards-Jones, V., Fox, A. J., Kaczmarski, E. B., & Mutton, K. J. (2002). Development and evaluation of a 'real-time' RT-PCR for the detection of enterovirus and parechovirus RNA in CSF and throat swab samples. *Journal of medical virology*, 67(4), 555-562.
- De Campos, G. M., Cella, E., Kashima, S., Alcântara, L. C. J., Sampaio, S. C., Elias, M. C., Giovanetti, M., & Slavov, S. N. (2024). Updated insights into the phylogenetics, phylodynamics, and genetic diversity of Nipah virus (NiV). *Viruses*, 16(2), 171.
- Esposito, M. M., Turku, S., Lehrfield, L., & Shoman, A. (2023). The impact of human activities on zoonotic infection transmissions. *Animals*, 13(10), 1646.
- Foster, S. L., Woolsey, C., Borisevich, V., Agans, K. N., Prasad, A. N., Deer, D. J., Geisbert, J. B., Dobias, N. S., Fenton, K. A., & Cross, R. W. (2022). A recombinant VSV-vectored vaccine rapidly protects nonhuman primates against lethal Nipah virus disease. *Proceedings of the National Academy of Sciences*, 119(12), e2200065119.
- Gazal, S., Sharma, N., Gazal, S., Tikoo, M., Shikha, D., Badroo, G. A., Rashid, M., & Lee, S.-J. (2022). Nipah and Hendra viruses: deadly zoonotic paramyxoviruses with the potential to cause the next pandemic. *Pathogens*, 11(12), 1419.
- Gupta, A. K., Kumar, A., Rajput, A., Kaur, K., Dar, S. A., Thakur, A., Megha, K., & Kumar, M. (2020). NipahVR: a resource of multi-targeted putative therapeutics and epitopes for the Nipah virus. *Database*, 2020, baz159.
- Iqbal, A., Ahmed, B., Gulzada, M., Khan Rohilla, A. R., Nawaz, Y., Ayoub, A., Ali, M., Zafar, J., Khan, M. S., & Wajid, M. (2024). Prevalence of communicable and non-communicable diseases among school going children. *History of Medicine*, 10(2), 1703-1723.
- Islam, M. S., Sazzad, H. M., Satter, S. M., Sultana, S., Hossain, M. J., Hasan, M., Rahman, M., Campbell, S., Cannon, D. L., & Ströher, U. (2016). Nipah virus transmission from bats to humans associated with drinking traditional liquor made from date palm sap, Bangladesh, 2011–2014. *Emerging infectious diseases*, 22(4), 664.
- Kalter, H. D., Setel, P. W., Deviany, P. E., Nugraheni, S. A., Sumarmi, S., Weaver, E. H., Latief, K., Rianty, T., Nandiaty, F., & Anggondowati, T. (2023). Modified Pathway to Survival highlights importance of rapid access to quality institutional delivery care to decrease neonatal mortality in Serang and Jember districts, Java, Indonesia. *Journal of global health*, 13, 04020.
- Khan, A. K. M. D. (2024). *Bat hunting and illnesses: A case of Mahanta community in Bangladesh* © University of Dhaka].
- Khan, S. A., Imtiaz, M. A., Islam, M. M., Tanzin, A. Z., Islam, A., & Hassan, M. M. (2022). Major bat-borne zoonotic viral epidemics in Asia and Africa: A systematic review and meta-analysis. *Veterinary medicine and science*, 8(4), 1787-1801.
- Kojom, L. P., & Singh, V. (2021). A review on emerging infectious diseases prioritized under the 2018 WHO research and development blueprint: lessons from the Indian context. *Vector-Borne and Zoonotic Diseases*, 21(3), 149-159.
- Kozak, M., & Hu, J. (2023). The integrated consideration of vaccine platforms, adjuvants, and delivery routes for successful vaccine development. *Vaccines*, 11(3), 695.
- Lauer, M. S., Gordon, D., Wei, G., & Pearson, G. (2017). Efficient design of clinical trials and epidemiological research: is it possible? *Nature Reviews Cardiology*, 14(8), 493-501.
- Li, G., Hilgenfeld, R., Whitley, R., & De Clercq, E. (2023). Therapeutic strategies for COVID-19: progress and lessons learned. *Nature reviews Drug discovery*, 22(6), 449-475.

- Libbey, J. E., Kennett, N. J., Wilcox, K. S., White, H. S., & Fujinami, R. S. (2011). Lack of correlation of central nervous system inflammation and neuropathology with the development of seizures following acute virus infection. *Journal of virology*, 85(16), 8149-8157.
- Marzouk, E., & Alajaji, A. I. (2025). Preventive Immunology for Livestock and Zoonotic Infectious Diseases in the One Health Era: From Mechanistic Insights to Innovative Interventions. *Veterinary Sciences*, 12(10), 1014.
- McLean, R. K., & Graham, S. P. (2019). Vaccine development for Nipah virus infection in pigs. *frontiers in Veterinary Science*, 6, 16.
- Mehmooda, M. I., Khana, M. S., Shaffiqueb, S., Alic, H., & Wajida, M. (2025). Community knowledge, attitude and practices towards dengue in urban and suburban populations of Okara (Punjab, Pakistan). *International Journal of Natural Medicine and Health Sciences*, 4(1), 38-45.
- Mickevičienė, D., Schrader, H., Stovner, L., Surkiene, D., Obelienienė, D., & Sand, T. (2007). A prospective study on the relationship between the severity of concussion and post-traumatic symptoms. Seventeenth Meeting of the European Neurological Society 16–20 June 2007, Rhodes, Greece,
- Monath, T. P., Nichols, R., Tussey, L., Scappaticci, K., Pullano, T. G., Whiteman, M. D., Vasilakis, N., Rossi, S. L., Campos, R. K., & Azar, S. R. (2022). Recombinant vesicular stomatitis vaccine against Nipah virus has a favorable safety profile: Model for assessment of live vaccines with neurotropic potential. *PLoS pathogens*, 18(6), e1010658.
- Murin, C. D., Wilson, I. A., & Ward, A. B. (2019). Antibody responses to viral infections: a structural perspective across three different enveloped viruses. *Nature microbiology*, 4(5), 734-747.
- Nidom, R. V., Indrasari, S., Prakoso, D., Nidom, A. N., & Afifah, B. (2025). Comprehensive surveillance and molecular detection of the Nipah virus in fruit bats (*Pteropus vampyrus*) across Indonesia: Insights from 2023 to 2024. *International Journal of One Health*, 11(1), 171-177.
- Nikolay, B., Dos Santos, G. R., Lipsitch, M., Rahman, M., Luby, S. P., Salje, H., Gurley, E. S., & Cauchemez, S. (2021). Assessing the feasibility of Nipah vaccine efficacy trials based on previous outbreaks in Bangladesh. *Vaccine*, 39(39), 5600-5606.
- Peghin, M., & Danziger-Isakov, L. (2019). Prevention and treatment of respiratory virus infection. In *Infectious Diseases in Solid-Organ Transplant Recipients: A practical approach* (pp. 107-129). Springer.
- Ramphul, K., Mejias, S. G., Agumadu, V. C., Sombans, S., Sonaye, R., & Lohana, P. (2018). The killer virus called Nipah: a review. *Cureus*, 10(8).
- Rele, S. (2020). Emerging outbreaks and epidemic threats: the practicality and limitations in the development and manufacturing of treatments for Coronavirus (COVID-19). *Polymorphism*, 4, 45-52.
- Salleh, M. Z. (2025). Structural biology of Nipah virus G and F glycoproteins: Insights into therapeutic and vaccine development. *European Journal of Microbiology and Immunology*.
- Satterfield, B. A., Dawes, B. E., & Milligan, G. N. (2016). Status of vaccine research and development of vaccines for Nipah virus. *Vaccine*, 34(26), 2971-2975.
- Sayed, A., Bottu, A., Qaisar, M., Mane, M., & Acharya, Y. (2019). Nipah virus: a narrative review of viral characteristics and epidemiological determinants. *Public Health*, 173, 97-104.
- Seib, K. L., Dougan, G., & Rappuoli, R. (2009). The key role of genomics in modern vaccine and drug design for emerging infectious diseases. *PLoS genetics*, 5(10), e1000612.

- Sendow, I., Field, H., Adjid, A., Ratnawati, A., Breed, A., Darminto, Morrissey, C., & Daniels, P. (2010). Screening for Nipah virus infection in West Kalimantan province, Indonesia. *Zoonoses and Public Health*, 57(7-8), 499-503.
- Sendow, I., Field, H. E., Curran, J., Morrissey, C., Meehan, G., Buick, T., & Daniels, P. (2006). Henipavirus in Pteropus vampyrus bats, Indonesia. *Emerging infectious diseases*, 12(4), 711.
- Shahida, S., Islam, A., Dey, B., Islam, F., Venkatesh, K., & Goodman, A. (2016). Hospital acquired infections in low and middle income countries: root cause analysis and the development of infection control practices in Bangladesh.
- Sharma, A., Bhyan, S. J., & Malik, A. (2021). A perspective review of deadly viral diseases: An era of viruses. *Int. J. Basic Clin. Pharmacol*, 10(1038), 2319-2003.
- Singh, R. K., Dhama, K., Chakraborty, S., Tiwari, R., Natesan, S., Khandia, R., Munjal, A., Vora, K. S., Latheef, S. K., & Karthik, K. (2019). Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies—a comprehensive review. *Veterinary Quarterly*, 39(1), 26-55.
- Sule, W. F., & Oluwayelu, D. O. (2020). Real-time RT-PCR for COVID-19 diagnosis: challenges and prospects. *The Pan African Medical Journal*, 35(Suppl 2), 121.
- Sun, D. (2020). Remdesivir for treatment of COVID-19: combination of pulmonary and IV administration may offer additional benefit. *The AAPS journal*, 22(4), 77.
- Tan, F. H., Sukri, A., Idris, N., Ong, K. C., Schee, J. P., Tan, C. T., Tan, S. H., Wong, K. T., Wong, L. P., & Tee, K. K. (2024). A systematic review on Nipah virus: global molecular epidemiology and medical countermeasures development. *Virus Evolution*, 10(1), veae048.
- Thakur, N., & Bailey, D. (2019). Advances in diagnostics, vaccines and therapeutics for Nipah virus. *Microbes and infection*, 21(7), 278-286.
- Ullah, A., Aslam, M., Ismael, S., Ahmad, M., Umar, A., Khan, M. U., & Khan, M. S. (2025). Structural and Function Impact of ERCC2 Gene variants in Xeroderma Pigmentosum: An Integrative Computational and Docking Analysis. *In Silico Research in Biomedicine*, 100111.
- Ullah, A., Aslam, M., Umar, A., Ahmad, M. Z., Khan, M. U., & Khan, M. S. (2026). In Silico Identification of Pathogenic RAPSIN Mutations and Ligand Interactions in Congenital Myasthenic Syndromes. *In Silico Research in Biomedicine*, 100241.
- Vaughan, E., & Tinker, T. (2009). Effective health risk communication about pandemic influenza for vulnerable populations. *American journal of public health*, 99(S2), S324-S332.
- Wang, Z. (2022a). Architecture and antigenicity of the Nipah virus attachment glycoprotein. *Biophysical Journal*, 121(3), 29a.
- Wang, Z. (2022b). *Structure-guided vaccine, antibody and drug discovery*. University of Washington.
- Wong, S., Lau, S., Woo, P., & Yuen, K. Y. (2007). Bats as a continuing source of emerging infections in humans. *Reviews in medical virology*, 17(2), 67-91.
- Woolsey, C., Borisevich, V., Fears, A. C., Agans, K. N., Deer, D. J., Prasad, A. N., O'Toole, R., Foster, S. L., Dobias, N. S., & Geisbert, J. B. (2023). Recombinant vesicular stomatitis virus-vectored vaccine induces long-lasting immunity against Nipah virus disease. *The Journal of clinical investigation*, 133(3).

Yadav, P. D., Sahay, R. R., Balakrishnan, A., Mohandas, S., Radhakrishnan, C., Gokhale, M. D., Balasubramanian, R., Abraham, P., Gupta, N., & Sugunan, A. (2022). Nipah virus outbreak in Kerala State, India amidst of COVID-19 pandemic. *Frontiers in public health*, 10, 818545.

