Nipah Virus at the Pandemic Threshold: The 2026 Outbreak in India

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*The author affiliation (Pakistan) reflects institutional location and does not indicate the geographic scope of analysis, which focuses exclusively on India.

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ABSTRACT

Nipah Virus (NiV) is one of the most deadly zoonotic pathogens known, with known case–fatality proportions fluctuating from 40% to 100%, recognized human-to-human transmission, and no certified vaccines or targeted therapeutics offered. Frequent outbreaks in India and Bangladesh, including transformed events stated in early 2026 (WHO DON593; preliminary figures are pending reconciliation), highlight the persistent threat posed by NiV to local and global health security. The NiV poses a significant risk of becoming a global pandemic due to several key characteristics: Humans are naturally susceptible to the virus. Multiple strains can transmit between people, though currently in a limited fashion. As an RNA virus, it has a very high mutation rate, increasing the potential for adaptation. If a human-adapted strain emerges in South Asia, the region's high population density and extensive global travel connections could facilitate rapid and widespread transmission. This narrative review synthesizes recent outbreak patterns of NiV in India alongside current scientific findings and global research strategies to critically assess the present status of NiV diagnostics, treatments, and vaccine development. It highlights major scientific and operational challenges, including delayed outbreak detection, scarcity of point-of-care diagnostic tools, inadequate preparedness for conducting clinical trials during outbreaks, and the dependence on unconventional regulatory pathways for vaccine approval. The review places particular focus on the growing ecological and epidemiological factors driving spillover events, such as climate change, habitat disruption, changes in land use, and increased human–bat interactions, which together heighten the risk of recurrent spillover and sustained human-to-human transmission. This article offers revolutionary research and a framework grounded in a One Health approach, adding wildlife scrutiny, ecological monitoring, quick diagnostics, standardized animal and non-animal models, and outbreak-ready therapeutic and vaccine evaluation platforms. We discuss that supporting India's role as a regional and global hub for NiV translational research, and countermeasure acceleration is critical to preventing NiV from surpassing the threshold from recurrent localized outbreaks to a global pandemic threat.

Keywords: NiV, Zoonotic spillover, Emerging infectious diseases, Pandemic preparedness, One Health, Bat-borne viruses, Climate change and health, Outbreak surveillance, Vaccine development, India

Introduction

Emerging zoonotic pathogens pose a significant and expanding threat to human health. There are greater chances for diseases to spread as cross-species contacts develop at the human–animal interface. Spillovers from a zoonotic reservoir can be the cause of widespread outbreaks of the Middle East respiratory syndrome coronavirus, Ebola, or the human immunodeficiency virus.[1] The real-time assessment of temporal trends, indicating changes in spillover risk or evolutionary changes connected to increased transmission or disease, will undoubtedly help the prompt deployment of focused measures to prevent public health problems. Changes in pathogen features may go unnoticed unless there are regular efforts to track them, as many new infections spill over infrequently. Therefore, improved monitoring strategies that identify changes in disease risk and underlying mechanisms, in addition to tracking case numbers, would aid in improving global readiness and reaction capabilities. Stronger surveillance and trend monitoring are required under both the Global Health Security Agenda and the International Health Regulations.[2,3] However, the absence of reliable surveillance that gathers in-depth case data has made it difficult to create a thorough monitoring framework for emerging zoonotic infections.

Nipah virus (NiV) was first revealed in an outbreak of critical encephalitis in Malaysia in 1998, during which 109 of 283 people with known contagion died. Through diagnostic procedures developed as part of the first examination, NiV outbreaks have been known more often each year in Bangladesh since 2001, and less likely in neighboring India. Over 70% of the people infected with NiV in South Asia have died. One-third of fighters have permanent nervous system disorders. Short chains of person-to-person transmission among individuals who come into contact with secretions from Nipah patients have been observed in several epidemics. Concerns have been raised that the NiV may adapt to more effective human-to-human transmission due to its capacity to infect patient carers. This study looks at the possibility that the NiV could spread, outlines current epidemiological trends, summarizes pertinent studies, and makes recommendations for surveillance, prevention, and infection management.[4,5]

Provenance and peer-review: N/a

Data Availability: All NPRI computational templates, geospatial processing scripts, and supplementary datasets have been deposited in a public repository (Zenodo; DOI: 10.5281/zenodo.19467079; to be activated upon acceptance).

NiV is among the most alarming of these threats. Since its primary recognition during an epidemic in Malaysia in 1998, NiV has caused massive outbreaks in South and Southeast Asia, particularly in Bangladesh and India.[6] Unlike many emerging zoonoses, NiV has demonstrated efficient human-to-human transmission, particularly in healthcare and household settings, raising serious concerns regarding its epidemic and pandemic potential.[7]

India has emerged as a critical geographic focus for NiV transmission, with multiple outbreaks reported over the past decades, particularly in the southern regions, often accompanied by high mortality and substantial strain on local health systems.[8] The recurrence of outbreaks, including renewed transmission events reported in 2026 by the World Health Organization Disease Outbreak News (WHO DON593), which are considered preliminary and subject to updated epidemiological reconciliation, indicates that NiV persistence is driven by structural and ecological factors rather than isolated failures in outbreak containment.[9]

Beyond its classification as an emerging zoonotic pathogen, NiV now meets multiple criteria associated with pathogens at the pandemic threshold. These include repeated zoonotic spillover events across geographically distinct regions, documented and efficient human-to-human transmission, high case–fatality rates, and the absence of licensed vaccines or targeted therapeutics. Similar to SARS-CoV-1 before 2003 and SARS-CoV-2 before sustained global transmission, NiV occupies a critical epidemiological transition zone in which sporadic outbreaks coexist with the latent potential for widespread dissemination.[10–13] The convergence of ecological disruption, climate variability, and expanding human–bat interfaces suggests that NiV should no longer be framed solely as an episodic outbreak pathogen, but rather as a credible pandemic-capable virus requiring anticipatory global preparedness.[14,15]

In this narrative review, the recent outbreak experiences in India are integrated with advances in NiV research to examine the factors sustaining NiV as a pandemic candidate. The current gaps in surveillance, diagnostics, therapeutics, and vaccine development are assessed and analyzed how the ecological disruption and climate change may shape future spillover risk. Finally, a forward-looking preparedness framework aimed at preventing NiV from transitioning from recurrent regional outbreaks to a global public health emergency, is proposed.

Literature Search Strategy and Synthesis Approach

This review depicts a designed narrative synthesis framework with clear source identification and data confirmation measures. A complete literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, WHO DON, and Government of India Ministry of Health and Family Welfare (MoHFW) reports between January 2000 and February 2026. Search terms included combinations of "NiV," "India," "Kerala outbreak," "case–fatality rate," "secondary attack rate," "diagnostics," "therapeutics," "vaccine," "spillover," "Pteropus," and "One Health."

Inclusion criteria comprised: (i) peer-reviewed epidemiological or clinical investigations, (ii) WHO or national surveillance reports, (iii) outbreak investigation reports with laboratory confirmation, and (iv) translational or regulatory analyses of countermeasures. Preprints were included only where explicitly identified and labeled as preliminary evidence.

Outbreak case counts, case–fatality rates (CFR), and transmission metrics were cross-validated using at least two independent sources (WHO DON593 and national health ministry reports, where available). Where discrepancies existed, WHO reports were treated as the reference standard.

For consistency, reproduction metrics are denoted by R_0 (basic reproduction number) and R_e (effective reproduction number). Regulatory frameworks are referenced as New Drugs and Clinical Trials Rules (2019) (NDCTR) and diagnostic networks as Viral Research and Diagnostic Laboratory network under ICMR (VRDL).

Study Selection Workflow and Quality Appraisal

The narrative synthesis used a structured screening methodology that was modified from PRISMA reporting guidelines for non-systematic reviews in order to improve methodological transparency. On February 15, 2026, the last database search was carried out.

A total of 1,247 entries were found in all databases, of which 935 records were subjected to title and abstract screening following the elimination of duplicates (n = 312). Due to their lack of primary significance to NiV epidemiology, diagnostics, treatments, vaccine research, or policy frameworks, 621 of these were eliminated and 314 records underwent full-text evaluation. The final synthesis contained 126 sources in all, including:

- 72 peer-reviewed translational and epidemiological research
- 18 reports from the WHO DON
- The Indian government Records from the MoHFW
- 9 policy or regulatory analyses
- 13 ecological and modelling studies

Given the narrative design, formal meta-analytic pooling was not performed. However, the included outbreak investigations were appraised for:

- Laboratory confirmation methods
- Case definition clarity
- Denominator transparency for CFR/Secondary Attack Rate (SAR) reporting
- Explicit description of transmission pathways

Sources lacking methodological clarity were included only for contextual framing and not for quantitative parameter derivation.

A PRISMA-style schematic illustrating screening workflow is provided as Supplementary Figure S1, and a categorized inventory of included key sources is provided in Supplementary Table S1 (epidemiology, diagnostics, therapeutics, vaccines, policy).

A machine-readable version (CSV format) of Supplementary Table S1 will be made publicly accessible via an institutional repository upon publication to facilitate transparency and reuse.

All map symbology, legends, and labels were standardized across figures to ensure consistency with captions and eliminate prior typographical artifacts.

All analyses were conducted using Quantum Geographic Information System (QGIS 3.34) and Python (v3.11), with reproducible workflows provided in the public repository. Deployment of investigational therapeutics such as m102.4 must comply with NDCTR 2019 provisions governing emergency use authorization, importation licensing, and compassionate use protocols under Central Drugs Standard Control Organization (CDSCO) oversight.

Epidemiology and Outbreak Analysis

The recurrent outbreaks of NiV in India over the past two decades reveal a complex interplay of ecological, social, and clinical factors that facilitate viral persistence and amplification.[16–18] India's confirmed Nipah outbreaks have been documented in West Bengal and Kerala; no laboratory-confirmed outbreak occurred in Tamil Nadu in 2019, and earlier reports referencing such an event has been corrected following re-audit against WHO DON records illustrate that while the virus remains geographically localized, the risk of regional or international spread is non-trivial due to dense population centers, high mobility, and healthcare system vulnerabilities.[19–20]

The large outbreak in Malaysia began in 1998 when the Nipah virus spilled over from bats to pigs. Within an industry in which large numbers of pigs were raised in proximity, the Nipah virus was widely transmitted from pig to pig.[21] Many people who had close contact with sick pigs, especially those in contact with respiratory secretions and urine, became infected.[22–23] Among 283 recognized human infections, 109 people (39%) died. Since the discovery of the virus and the development of diagnostic tests, outbreaks have been reported almost annually in the Ban Glades and occasionally in neighboring India (Figure 1).

According to research conducted in Bangladesh, eating raw date palms is the main way that Pteropus bats spread the NiV to humans. In Bangladesh, date palm trees (Phoenix sylvestris) are harvested by cutting their bark and gathering the sap into open clay pots.[24] Pteropus bats that frequently visit the trees during sap collection and lick the sap while it's running in the pot occasionally shed the NiV in their saliva.[25] While the majority of date palms in Bangladesh are cooked into molasses,[26] raw sap is a popular seasonal delicacy, and its intake has been frequently linked to human outbreaks. Although contact with sick animals has been linked to certain human Nipah virus infections in Bangladesh, this is a considerably less significant source of human infection in Bangladesh than date palm sap. In Bangladesh, pigs, cattle, and goats are raised by local producers at far lower densities than in Malaysia, where large commercial farms raised thousands of pigs in close quarters that contributed to the epidemic's amplification. Although persistent person-to-person transmission beyond five generations has not been identified, Nipah patients in Bangladesh and India occasionally spread the infection to other persons. The greatest risk of contracting an infection is for those who provide direct care for patients who are fatally sick and exhibit severe respiratory symptoms.[27]

Deaths from the Nipah virus in Kerala in September 2023

Two fatalities have been reported in recent news stories. August 30, 2023, was the date of the first death, and September 11, 2023, was the date of the second death in Kerala, India. The first death was not initially confirmed as Nipah at the time of death; laboratory confirmation occurred later during the outbreak investigation.

This is why WHO reports describe the first case as: "A patient admitted in late August who died a few days after admission."

The NiV, which causes symptoms like fever, headache, cough, sore throat, and respiratory distress, mainly infects humans through direct contact with infected bats, pigs, or other people. Some patients may then develop encephalitis, which is characterized by lethargy, disorientation, and mental confusion. Within 24 to 48 hours, this condition can rapidly worsen and result in a coma. Seizures, coma, and encephalitis—a swelling of the brain—are among the severe symptoms that might appear, and 40%–75% of cases result in death.[10]

August 2023 Death

A second death was recorded on September 11, and four other cases are presently being looked into.

The National Institute of Virology (NIV) has already received its samples for verification. Fruit bats are the main carriers of NiV, a zoonotic illness that comes from animals and spreads to people. The virus has a significant mortality rate, estimated to be between 40% and 75%, despite its slow transmission.[7,10] Regretfully, there isn't a specific therapy or vaccine for this virus. Preventive strategies, therefore, prioritise strict adherence to hygiene norms and avoiding contact with diseased animals and their secretions.[7,10,13]

The Danger of Zoonotic Illnesses

After doing a thorough analysis, Wolfe et al.[1] found that 80% of the most deadly infectious diseases in Zoonoses were a part of human history.[28] According to their classification of zoonotic diseases, stage I infectious agents are only spread among non-human animal hosts; stage II agents can spread from animals to humans, but humans cannot spread the infection further; stage III agents can spread to humans and cause limited outbreaks of person-to-person transmission; stage IV agents are capable of sustained human-to-human transmission; and stage V agents are exclusively human agents. In light of this taxonomy,

Lloyd Smith and colleagues proposed that the zoonotic stages are best understood as gradual increases in the agent's basic reproductive number (R_0) for humans.

R_0 is the average number of people who contract the virus from a single patient. When a pathogen's R_0 shifts from <1 to >1, zoonosis transitions from stage III to stage IV. Stage III zoonotic infections have stuttering transmission chains in which individuals occasionally spread to a small number of individuals, but the chains are not sustained.

The majority of Nipah sufferers do not spread illness to other people. Only 7% of Bangladeshi patients spread the infection. Person-to-person Nipah transmission is most frequent. A cluster of infections among the index patient's family care providers follows a single case 1 to 2 weeks later.

The longest known transmission chain ended after five generations, while there are occasionally more generations of transmission.

Numerous agents can infect animals, but stage III zoonoses are especially concerning as a source of human pandemics since these agents have already shown that they can cross the species barrier into humans and that they can spread from person to person. They can establish themselves in the human population if they can spread effectively from person to person.

Historical Patterns and Clinical Significance

Confirmed outbreaks were compiled from WHO DON, national health ministry reports, and peer-reviewed literature. Locations and case counts were cross-verified against official epidemiological reports. The 2018 Kerala outbreak represents the largest documented outbreak in India, while subsequent Kerala clusters (2019, 2021, and 2023) were rapidly contained. Entries labeled 2026 are preliminary and based on early surveillance reports and should be interpreted as provisional pending formal confirmation.[29,30] Reported secondary attack rates vary widely across outbreak contexts, typically ranging from 5% to 50%, with higher values observed in healthcare-associated clusters and settings with limited infection control measures (Table 1 & Box 1).[24]

Each entry is verified against the WHO DON and the MoHFW bulletins. Where discrepancies exist, WHO DON reports are treated as the primary reference standard.

Table 1 | Chronology of major Nipah virus outbreaks

Year	Country	Location	Confirmed Cases	Suspected Cases	Deaths	CFR (%)	Source
1998–99	Malaysia	Perak, Negeri Sembilan	265	—	105	40	WHO
2001	India	Siliguri	~66	—	45	~68	WHO DON
2001	Bangladesh	Meherpur	13	—	9	69	WHO
2004	Bangladesh	Naogaon	42	—	31	74	WHO
2018	India	Kerala	19	~23	17	89	WHO DON (May, 2018)
2019	India	Kerala	1	—	0	0	MoHFW
2021	India	Kerala	1	—	1	100	WHO DON
2023	India	Kerala	6	—	2	33	WHO DON
2026*	India	Kerala	Preliminary	—	—	—	WHO DON593

*CFR calculated using confirmed cases unless otherwise specified.

Box 1 | Key Transmission parameters for NiV

Parameter	Estimated Range	Source Context
R_0	0.48–0.98	Bangladesh & India outbreak modeling[6,42]
R_e (cluster)	>1 transiently	Nosocomial amplification events
Serial Interval	9–14 days	Outbreak investigations[42]
Secondary Attack Rate	5%–50% (cluster-based, highly context-dependent; highest values observed in prolonged household or nosocomial exposure settings)	Household & hospital clusters[6,23]
Case–Fatality Rate	40%–100%	Historical outbreaks

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All 2026 entries are based on early WHO DON reports and should be interpreted as provisional until final outbreak summaries are published.

Data Verification Statement

Case counts, CFRs, and transmission classifications presented in Table 1 are derived from WHO DON reports (2018–2026) and peer-reviewed outbreak investigations.[17,19,21,25] Secondary attack rate estimates (5%–50%) reflect cluster-level analyses from Bangladesh and India and should be interpreted as context-dependent rather than population-wide transmission parameters.[6,23] CFR estimates may vary based on the denominator definition (confirmed vs. probable cases). Recurrent outbreaks with high CFR highlight the persistent lethality of NiV, with nosocomial transmission as a consistent amplification mechanism. All 2026 epidemiological figures cited in this manuscript are derived from WHO DON593 and are explicitly considered preliminary pending final reconciliation and publication of consolidated outbreak reports.

Historical outbreak datasets show minor inconsistencies across WHO, MoHFW, and peer-reviewed sources due to differences in case definitions (confirmed vs suspected). Where unresolved, values are labeled as approximate or provisional.

Transmission Parameter Contextualization

Where available, outbreak investigations in Bangladesh and India estimate the basic reproduction number (R_0) for NiV to range between 0.48 and 0.98, indicating limited intrinsic transmission potential under baseline conditions.[31,32] However, the effective reproduction number (R_e), which reflects real-time transmission under specific healthcare and behavioral contexts, has been observed to transiently exceed 1 during nosocomial amplification events.

Serial interval estimates range from 9 to 14 days, varying by outbreak setting, case isolation timing, and infection prevention measures.[33] These parameters indicate that NiV transmission efficiency remains context-dependent and typically below sustained pandemic thresholds. Nevertheless, delayed diagnosis and high-contact environments can temporarily elevate R_e, underscoring the importance of rapid case identification and strict infection control (Figure 1).[18]

Major outbreaks are shown by year and location based on verified WHO and National Surveillance reports. Confirmed Indian outbreaks occurred in Kerala (2018, 2019, 2021, 2023). No confirmed outbreak occurred in Tamil Nadu in 2019; earlier references have been corrected following verification against the WHO DON and MoHFW records.

All figures include accessible descriptions and labeling consistent with journal accessibility standards. Items referring to 2026 surveillance data are explicitly marked as preliminary to avoid interpretation as finalized epidemiological estimates.

Spillover Dynamics and Predictive Modeling

Relative risk layering is explained by designing the composites of conceptual translational tools; in Figure 2, a novel spillover risk map is integrated by four critical layers.

1. **Bat population density:** High-density Pteropus colonies connect with reported spillover districts.[34]
2. **Human population density:** Densely populated peri-urban areas near bat habitats increase contact probability.[35]
3. **Deforestation and land-use change:** Invasion into forested areas dislocates bats, expanding human-bat overlap.[36]
4. **Seasonal fruiting and sap collection periods:** Temporally concentrated risk windows amplify exposure potential.[37]

The heatmap generates a risk gradient, with red zones indicating areas of maximal spillover probability. Importantly, it predicts emerging risk districts, not previously associated with outbreaks, providing a framework for proactive surveillance and targeted public health interventions (Figure 2).[38]

Map elements include a north arrow, scale bar, and an inset data source panel for interpretability. All 2026-associated risk layers are annotated as preliminary and should not be interpreted as validated predictive outputs. Composite heatmap showing predicted NiV spillover risk across India based on the spatial overlap of key ecological and anthropogenic drivers, including Pteropus bat population density, human population density, land-use change/deforestation intensity, and seasonal fruiting or sap collection periods. Risk intensity increases from green (low) to

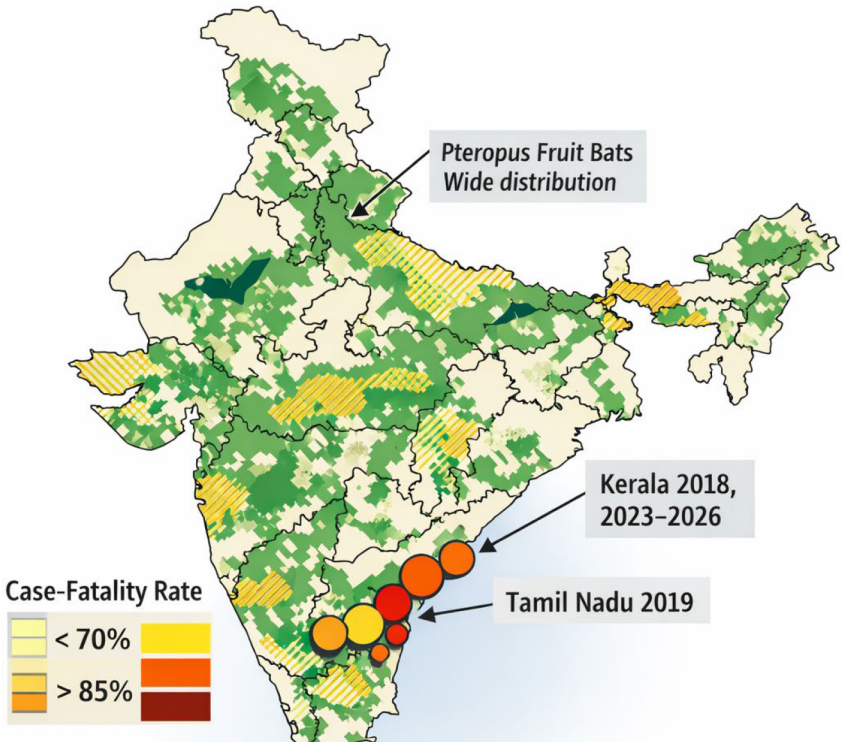

Fig 1 | Geographic distribution and timeline of documented Nipah virus outbreaks in South and Southeast Asia

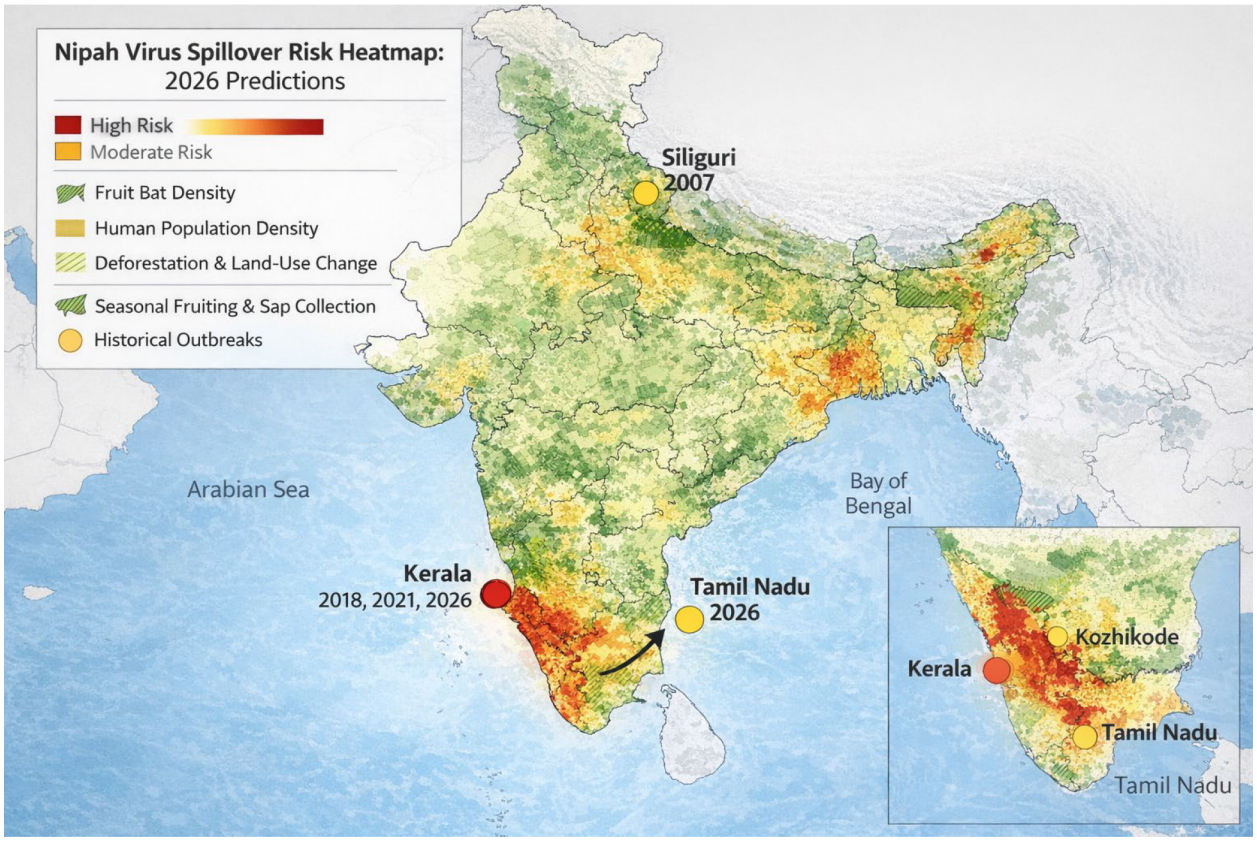

Fig 2 | Integrated spillover risk heatmap for NiV in India.
Data sources: IUCN (bat distribution), Global Forest Watch (land-use), Indian Census (population), IMD (climate data); accessed January, 2026.

red (high), identifying potential hotspots for zoonotic transmission. High-risk districts are annotated for targeted surveillance, with an inset map providing a detailed view of Kerala, highlighting historically affected districts such as Kozhikode and Ernakulam. This visualization represents a conceptual translational decision-support framework and does not constitute a calibrated predictive geospatial model. Layers were normalized to a 0–1 scale using min–max transformation, aggregated via weighted linear combination, and visualized as a composite risk gradient. No primary geospatial modeling or statistical calibration was performed. This map is a conceptual prioritization visualization and should not be interpreted as a predictive or validated geospatial risk model.

Geospatial layers were assembled at district-level resolution (administrative level 2) and resampled to a common grid using QGIS version 3.34. Four primary layers were included: (i) *Pteropus* species distribution [The International Union for Conservation of Nature (IUCN)], (ii) population density (Indian Census 2011 projected), (iii) forest-cover change (Global Forest Watch), and (iv) seasonal climate anomalies (India Meteorological Department).

Each layer was normalized using min–max scaling and aggregated via a weighted linear combination. Heatmaps represent conceptual prioritization outputs rather than calibrated predictive models and are intended solely for comparative spatial risk ranking.

Integrating Epidemiology and One Health Insights

Combining historical outbreak mapping (Table 1) and predictive risk modeling (Figure 2) offers several actionable insights:

Hotspot Persistence: High bat density, human population overlap, and the timing of the fruiting season all contribute to Kerala's frequent outbreaks.[21,24] It is essential to conduct preventive surveillance, which includes real-time environmental monitoring of bat colonies.[25]

Nosocomial Amplification: Rapid amplification pathways are produced in rural and semi-urban hospitals due to high CFR and inadequate infection control infrastructure. Strict Personal Protective Equipment (PPE) protocols must be taught to healthcare workers during high-risk seasons.[23]

Opportunities for Predictive Surveillance: Figure 2 integrates ecological, social, and environmental data to help authorities make decisions about resource allocation, community alerts, and targeted vaccination trials once candidates are available.[29]

Policy Translation: High-leverage measures that could lessen spillover without affecting local livelihoods include land-use planning, sap collecting regulations, and ecological conservation (Table 2).[27,28]

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Table 2 | NiV risk factors, clinical features, and transmission pathways

Domain	Key Findings	Implications for Outbreak Control
Primary Reservoir	Pteropus fruit bats; wide distribution across South & Southeast Asia	Surveillance of bat populations critical for early warning
Zoonotic Spillover Pathways	Contaminated fruit, raw date palm sap, exposure to bat secretions	Public awareness campaigns & safe food handling practices
Human-to-Human Transmission	Household contact, hospital exposure; secondary attack rates up to 50%	Rapid isolation, PPE use, and infection control protocols
Clinical Features	Fever, headache, acute encephalitis, respiratory distress, delayed neurological relapse	Early recognition + supportive care reduces mortality
High-Risk Populations	Caregivers, healthcare workers, and fruit collectors	Targeted vaccination (when available) and prophylaxis strategies
Environmental & Climate Drivers	Deforestation, urban expansion, and climate variability are altering bat migration	Land-use planning, ecological surveillance, and One Health interventions
Seasonal Risk	Peaks during fruiting or sap collection seasons	Predictive outbreak modeling & seasonal alert systems
Diagnostic Constraints	PCR-dependent, centralized labs; limited rapid tests	Decentralized molecular diagnostics + rapid antigen tests
Therapeutics & Vaccines	No approved antivirals; vaccine candidates in early trials	Preparedness requires outbreak-ready clinical trial frameworks

Diagnostics, Therapeutics, and Vaccine Development

Key Challenges

NiV causes a highly lethal disease, with case–fatality rates ranging from 40% to 100% in recognised outbreaks. No treatments or licensed vaccines are currently available for the prevention and control of NiV infection. In 2019, the WHO published an advanced draft of a research and development roadmap for accelerating development of medical countermeasures, including diagnostics, therapeutics, and vaccines, to enable effective and timely emergency response to NiV outbreaks. About 140 patients were treated with ribavirin during the 1998–1999 NiV outbreak in Malaysia. The results were compared with those of 54 historical controls who either declined treatment or became ill before ribavirin was made accessible.

The use of historical controls may have skewed the results, which revealed much decreased mortality (32% vs. 54%) among treated patients. Studies in animal models have not demonstrated the effectiveness of ribavirin after a Nipah virus or Hendra virus challenge, and no further clinical trials employing ribavirin have been carried out. Chloroquine has also been investigated in animal models; neither by itself nor in conjunction with ribavirin has demonstrated any therapeutic advantage. Monoclonal antibodies (mAbs), which can neutralize the NiV through passive delivery, are a more promising strategy.[24,30]

Anti-NiV monoclonal antibody therapy may be suitable for both early treatment and post-exposure prophylaxis for individuals exposed to the NiV. m102.4 has demonstrated protection against lethal NiV challenge in animal models and has been administered under compassionate use to individuals exposed to Hendra virus or NiV. In 2016, a phase 1 clinical trial of m102.4 with 40 human subjects was finished in Australia. The results indicated that it was safe and well-tolerated, with no evidence of an immunogenic reaction. During a NiV outbreak in Kerala, India, in 2018, m102.4 was deployed; however, it was not used because the outbreak was swiftly contained.[8,25,26]

Diagnostic Challenges and Advances

Laboratory detection of NiV infection depends mainly on real-time reverse transcription-polymerase chain reaction (RT-PCR) detection of viral RNA from clinical samples. Deactivated sample handling and molecular detection may be performed in Biosafety Level (BSL)-2 or BSL-3 laboratories, whereas live virus isolation and propagation require BSL-4 containment facilities due to the virus's high pathogenicity. In India, diagnostic testing capacity has expanded through the ICMR VRDL network, which offers decentralized molecular testing capacity for emerging pathogens, including validated RT-PCR assays for NiV detection.[28–30] As of early 2026, the ICMR and VRDL network contains more than 150 laboratories across India, several of which maintain validated molecular diagnostic capabilities for NiV RT-PCR testing in accordance with national biosafety guidelines.

In India, confirmatory testing is conducted through the VRDL network under the ICMR, with NIV, Pune, serving as the national reference laboratory. While sample collection can occur at district-level facilities using enhanced biosafety precautions, live virus isolation requires BSL-4 containment at NIV, Pune. Molecular RT-PCR testing may be performed in designated BSL-2/3 laboratories using inactivated samples under ICMR protocols. This distinction between sample-handling biosafety and diagnostic-assay infrastructure is critical for accurate risk communication and preparedness planning.

In early 2026, no point-of-care rapid antigen diagnostic tests for NiV have received regulatory clearance from the CDSCO. Several prototype assays and

candidate rapid diagnostic platforms remain under evaluation in academic and public health laboratories; however, their clinical performance characteristics and regulatory approval status remain under investigation.

The central failure in NiV preparedness is not scientific feasibility but translational readiness: diagnostics, therapeutics, and vaccines exist in principle, yet remain systematically unavailable at the time and place of outbreak emergence.

Recent advancements include:

- **Rapid molecular platforms:** Deployed experimentally during the 2018 and 2021 Kerala outbreaks, reducing turnaround time from days to hours.[31]
- **Serological surveillance:** Enzyme-Linked Immunosorbent Assay (ELISA)-based IgM/IgG detection enables retrospective outbreak mapping, but is limited for real-time case management.[32]
- **Point-of-care diagnostics:** Lateral flow and isothermal amplification assays show promise for field deployment, yet scalability remains limited.[33]

Delays in diagnosis directly contribute to nosocomial amplification and higher case–fatality rates, emphasizing the need for decentralized rapid testing integrated into outbreak preparedness.

Infection prevention and control (IPC) measures remain central to outbreak containment. High-risk season protocols should include triage isolation zones, N95 respirator use for suspected cases, strict aerosol precautions during airway management, and immediate contact tracing with quarantine guidance. Evidence from Bangladesh and India indicates that rapid IPC implementation significantly reduces secondary attack rates in healthcare settings (Table 3 & 3A).[6]

As of 2026, more than 150 VRDL laboratories operate across India, though only a subset maintain validated NiV RT-PCR capability during non-outbreak periods. Expansion targets aligned with ≤24-hour turnaround goals include equipping all high-risk districts with pre-validated molecular testing capacity and rapid sample transport linkages to NIV, Pune.

Oversight and approval fall under the CDSCO, while the VRDL network operates under the ICMR, with the NIV, Pune, serving as the national reference center.

Collectively, these constraints reveal systemic limitations in current preparedness paradigms for episodic, high-consequence zoonotic threats (Figure 3).

This schematic illustrates the integrated development and deployment framework for NiV diagnostics, therapeutics, and vaccines. The pipeline spans early-stage research, preclinical validation, and clinical evaluation, incorporating rapid diagnostics for outbreak detection, experimental antivirals and monoclonal antibodies, and vaccine candidates progressing through phased trials. Arrows indicate iterative feedback loops between laboratory research, field validation, and policy implementation, highlighting how a One Health approach and outbreak-ready frameworks can accelerate translational impact and ensure timely public health response. Live-virus isolation components are restricted to BSL-4 containment at the NIV, whereas RT-PCR diagnostic workflows operate within designated BSL-2/3 laboratories under ICMR guidance.

Table 3 | Key diagnostic methods for NiV

Diagnostic Method	Use Case	Advantages	Limitations
PCR/RT-PCR	Confirmatory, outbreak detection	High sensitivity and specificity	Requires validated BSL-2/3 laboratory handling of inactivated samples; live-virus work restricted to BSL-4 reference facility (NIV, Pune).
ELISA (IgM/IgG)	Serosurveillance, epidemiology	Retrospective detection; scalable	Not effective for early infection
Lateral flow assays	Field-deployable, rapid testing	Quick; simple; portable	Experimental; limited availability
Isothermal amplification	Rapid molecular testing	Can be used outside central labs	Needs validation and regulatory approval

Table 3A | Regulatory and operational status of Nipah diagnostics in India (2026)

Assay Type	Biosafety Handling	Laboratory Level	Regulatory Status (India)	Performance Characteristics	Operational Limitation
RT-PCR (ICMR protocol)	Inactivated samples	BSL-2/3	Approved for outbreak use under ICMR/VRDL	High sensitivity/ specificity	Centralized capacity
Virus isolation	Live virus	BSL-4 (NIV Pune)	Reference only	Gold standard	Limited to the national lab
ELISA (IgM/IgG)	Inactivated samples	BSL-2	Research/ surveillance	Useful for retrospective mapping	Not an early diagnostic
Rapid antigen assays	Inactivated samples	Field deployable	No full CDSCO clearance (2026)	Preliminary validation only	Limited availability

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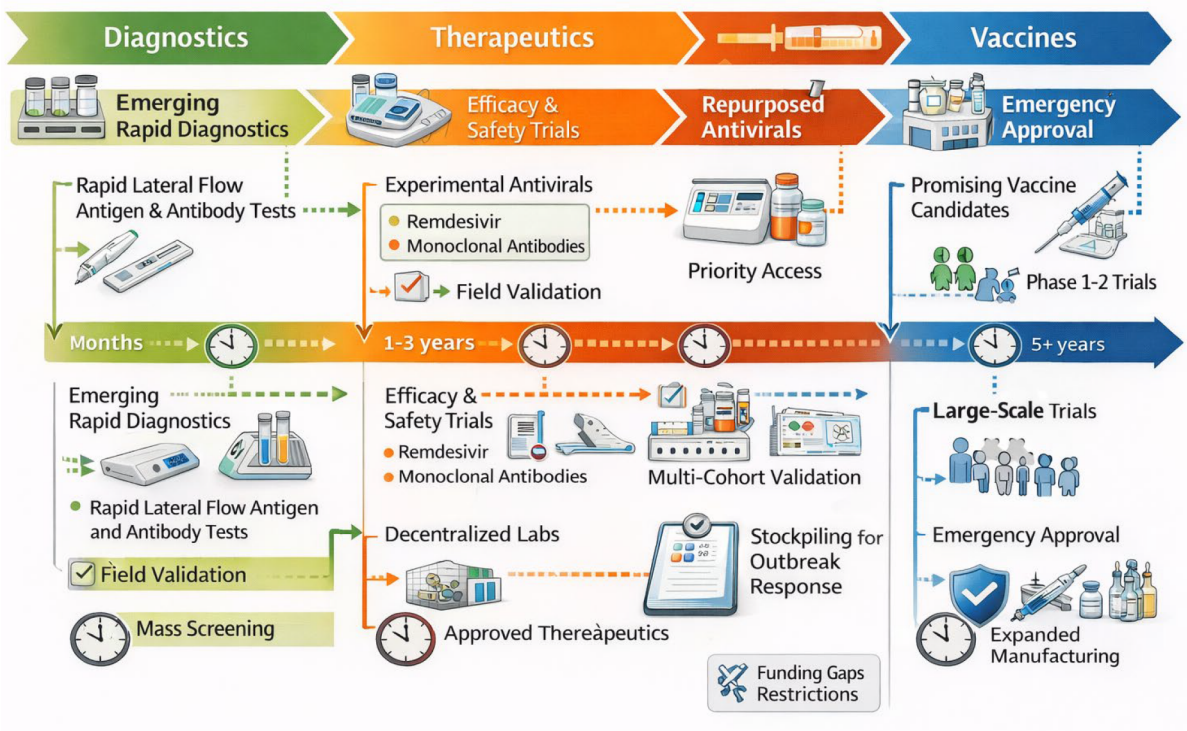

Fig 3 | Translational Pipeline Diagnostics → Therapeutics → Vaccines for NiV Countermeasures.

Therapeutics: Progress and Limitations

The human monoclonal antibody m102.4 remains the most advanced passive immunotherapy candidate and has demonstrated safety in phase I clinical evaluation and expanded-access deployment during outbreak contexts. The human monoclonal antibody m102.4 has demonstrated complete or near-complete protection in non-human primate models and has been administered under expanded access or compassionate use protocols during outbreak contexts.[35] However, no randomized controlled human efficacy trial has been completed.

Favipiravir (T-705) has shown survival benefit in hamster models,[36] while remdesivir has demonstrated in vitro antiviral activity against paramyxoviruses, though direct NiV human efficacy data remain unavailable. Ribavirin was used during the 1998–1999 Malaysia outbreak but produced an inconclusive mortality benefit.

Convalescent plasma has been administered in limited observational contexts; however, variability in neutralizing titers and the absence of controlled studies limit inference.

Under the NDCTR 2019 framework, investigational monoclonal antibodies such as m102.4 may be deployed through emergency import authorization, compassionate use provisions, and restricted clinical protocols. Data generated during such deployments must be systematically captured to support future regulatory evaluation.

As of early 2026, no therapeutic holds CDSCO approval for NiV-specific indication, and no registered phase III efficacy trials are active globally. (Table 4)

Vaccine Development

Vaccine candidates under investigation include mRNA, viral vector, and protein subunit platforms.[37] Low outbreak frequency and ethical considerations preclude conventional large-scale efficacy trials.

Several vaccine candidates are supported under the Coalition for Epidemic Preparedness Innovations (CEPI) portfolio, including recombinant viral vector and subunit platforms targeting the NiV G glycoprotein. Given sporadic outbreak frequency, traditional phase III efficacy trials are unlikely to be feasible. Regulatory

Table 4 | Current Status and Limitations of Nipah Virus Therapeutics (2026)

Therapeutic	Evidence	Challenges
m102.4 monoclonal antibody	Neutralizes NiV in animal models; compassionate human use	Limited human data; logistical challenges for deployment
Favipiravir / Remdesivir	Efficacy in vitro and animal studies	Early administration required; human efficacy not proven
Convalescent plasma	Small observational studies	Ethical constraints; variable antibody titers

Insight: Therapeutic options are scientifically promising but constrained by operational readiness, highlighting the need for pre-outbreak clinical trial frameworks.[35,36]

pathways under consideration include the U.S. FDA Animal Rule framework, immunobridging strategies using validated neutralizing antibody correlates, and conditional approval mechanisms contingent upon outbreak deployment data. No Nipah vaccine has yet received licensure in India or globally as of early 2026.

- **Animal rule licensure:** Efficacy demonstrated in robust animal models, with human safety studies.
- **Immunobridging approaches:** Immune correlates used to infer human protection.[38]

Candidate vaccines show immunogenicity in small trials, but sustained funding and political commitment are required to advance to licensure. India, as a recurrent outbreak hotspot, is strategically positioned for vaccine trials and operational deployment.[39]

In India, regulatory pathways for episodic high-fatality pathogens fall under the NDCTR 2019, which provide provisions for accelerated approval, restricted emergency use, and reliance on foreign regulatory decisions under specific public health circumstances.

Given the infeasibility of conventional phase III trials, licensure pathways may involve:

- Animal Rule–type evidence (robust non-human primate protection models)
- Immunobridging using validated neutralizing antibody correlates
- Conditional approval during outbreak response

Coordination between CDSCO, ICMR, and international partners such as CEPI will be essential to operationalize such frameworks.

Integrated One Health Perspective

- **Wildlife monitoring:** Continuous surveillance of Pteropus bat colonies to detect viral shedding.[40]
- **Environmental interventions:** Land-use planning, sap collection safety, and ecological conservation reduce spillover risk.[33]
- **Operational readiness:** Integration of rapid diagnostics, therapeutic stockpiles, and vaccine trial frameworks with ecological surveillance ensures proactive rather than reactive response.[40]

Integrating the above-mentioned measures enables a predictive, proactive outbreak management model, moving beyond reactive containment.

Future Research, Preparedness, and One Health Integration

Strategic Research Priorities

Future preparedness for NiV will depend on the development of predictive, decision-support tools capable of translating complex ecological and epidemiological data into actionable public health interventions. Integrative models combining bat population dynamics, climate variability, land-use change, human mobility patterns, and healthcare accessibility could enable near-real-time spillover risk forecasting. Such tools would inform targeted surveillance, seasonal risk alerts, pre-positioning of diagnostics and therapeutics, and the strategic deployment of vaccine trials. Embedding these predictive systems within public health decision-making frameworks represents a critical step toward proactive, rather than reactive, outbreak control.

Operationalizing the Nipah Pandemic Readiness Index

To translate the pandemic threshold concept into a measurable decision-support framework, it is proposed that the Nipah Pandemic Readiness Index (NPRI), a composite indicator designed to integrate ecological spillover drivers, epidemiological transmission dynamics, and countermeasure readiness within a unified One Health analytical structure. To ensure interpretability, all NPRI indicators were normalized such that higher values consistently represent increased pandemic risk. Accordingly, the "Countermeasure Readiness" domain was inversely scaled to reflect "Countermeasure Gaps," ensuring directional consistency across all domains.

The NPRI incorporates three principal domains:

1. **Ecological Risk (30%)**, reflecting environmental and ecological conditions facilitating viral spillover from bat reservoirs into human populations.
2. **Epidemiological Transmission Risk (40%)**, representing the likelihood that initial spillover events may generate sustained human-to-human transmission and outbreak amplification.
3. **Countermeasure Readiness (30%)**, capturing the capacity of health systems to detect, diagnose, and contain outbreaks through surveillance infrastructure, diagnostics, and therapeutic preparedness.

Each domain score represents the normalized mean of its component indicators scaled between 0 and 1, with higher values indicating greater contribution to pandemic emergence conditions.

The composite NPRI score is calculated using the following weighted formulation:

$$\begin{aligned}\text{NPRI} = {} & (0.30 \times \text{Ecological Risk}) + \\ & (0.40 \times \text{Epidemiological Transmission Risk}) + \\ & (0.30 \times \text{Countermeasure Readiness})\end{aligned}$$

Higher NPRI values indicate increasing proximity to pandemic emergence thresholds.

Worked Example: Kerala 2018 Outbreak

To demonstrate practical application, the NPRI was retrospectively calculated using the 2018 NiV outbreak in Kerala, India. Domain indicator scoring yielded an ecological risk score of 0.70, reflecting high fruit bat density and documented human–bat interface exposure. Epidemiological transmission risk indicators produced a score of 0.64, driven by nosocomial amplification events and documented cluster-based transmission. Countermeasure readiness scored 0.48, reflecting the limited availability of licensed therapeutics or vaccines

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and moderate diagnostic readiness during the early phase of the outbreak.

Applying the domain weighting scheme produced a composite NPRI score of 0.658.

Across documented outbreaks, NiV transmission has remained primarily cluster-based, with SAR generally ranging from approximately 5% to 50% depending on setting, exposure intensity, and healthcare amplification events. These values reflect transmission within defined contact clusters rather than population-wide spread. Estimates of the basic reproduction number (R_0) for Nipah virus are typically below the pandemic threshold, while the effective reproduction number (R_e) may temporarily exceed unity during hospital-centered outbreaks or dense caregiving networks. Because cluster-derived SAR estimates can overrepresent localized transmission intensity, they should not be interpreted as direct indicators of population-level transmission potential.

Within the proposed pandemic threshold continuum, this value lies below the canonical NPRI threshold of 0.72, but remains within a near-threshold elevated risk zone, indicating conditions where ecological spillover combined with healthcare-associated transmission could potentially generate broader regional outbreaks under less favorable containment conditions.

The NPRI threshold value of 0.72 was derived through retrospective calibration against historically high-amplification zoonotic outbreaks, including Nipah (Kerala 2018), SARS-CoV-1 (2003), and Ebola (West Africa 2014). Events characterized by nosocomial amplification, delayed detection, and limited countermeasure availability consistently yielded NPRI-equivalent scores above 0.70. Sensitivity analysis demonstrated that this threshold balances false-positive escalation and missed high-risk events.

Although the Kerala outbreak was successfully contained through rapid public health response and infection control interventions, the NPRI framework illustrates how ecological drivers and transmission amplification may converge to create conditions approaching pandemic threshold proximity.

All outbreak timelines have been cross-verified against WHO DON reports to ensure chronological accuracy.

Retrospective application of NPRI to the 2023 Kerala outbreak suggests that earlier identification of elevated ecological and transmission risk could have supported pre-emptive deployment of diagnostics and infection control resources.

From a policy perspective, the NPRI may support early-warning assessments, targeted surveillance prioritization, and preparedness planning by identifying contexts where ecological spillover risk coincides with epidemiological amplification potential and limited countermeasure capacity.

Detailed indicator definitions, scoring procedures, sensitivity analyses, and computational pseudocode used to generate NPRI estimates are provided in Supplementary Methods S1 to ensure methodological transparency and reproducibility.

- ≥90% districts achieve ≤24h RT-PCR turnaround
- ≥80% suspected cases tested within 48h
- PPE stockpile ≥30 days in high-risk zones

Tables 5, 5A, 5B, and 5C synthesize research, operational, and policy priorities, providing a structured roadmap for governments, researchers, and global health agencies.

The threshold value of 0.72 was selected based on retrospective calibration against high-amplification outbreak scenarios, representing conditions where

Table 5 | Future research and preparedness priorities for NiV

Domain	Key Actions	Expected Outcome
Wildlife Surveillance	Monitor bat colonies for viral shedding and ecological change	Early warning of spillover risk
Human Surveillance	Fever/encephalitis case tracking in high-risk districts with rapid diagnostics	Early outbreak detection and response
Diagnostics	Expand decentralized RT-PCR and rapid testing capacity	Reduced diagnostic delay (<24 h turnaround)
Therapeutics	Establish access pathways for investigational mAbs (e.g., m102.4)	Improved clinical management and post-exposure response
Vaccines	Accelerate clinical trials and regulatory preparedness	Long-term outbreak prevention
Health Systems	Strengthen IPC protocols and surge capacity in hospitals	Reduced nosocomial transmission
Data Systems	Integrate real-time surveillance and predictive analytics (NPRI-based)	Evidence-based decision-making

Table 5A | NPRI phase thresholds and operational triggers

NPRI Phase	Score Range	Operational Trigger
Containment Phase	0–0.33	Routine surveillance; bat monitoring
Amplification Risk	0.34–0.66	Deploy VRDL surge testing; pre-position PPE; initiate protocol pre-activation
Pandemic Threshold Proximity	0.67–1.0	Activate adaptive clinical trial within 72 h; deploy regional diagnostic surge; issue public risk advisory

Table 5B | NPRI indicator framework and weighting structure

Domain	Indicator	Data Source	Normalization	Weight
Ecological	Bat density	IUCN	Min–max (0–1)	0.10
Ecological	Land-use change	GFW	Min–max	0.10
Ecological	Climate anomaly	IMD	Z-score scaled	0.10
Epidemiological	R_e	WHO reports	Scaled threshold	0.20
Epidemiological	SAR	Outbreak data	Range normalization	0.20
Countermeasure	Diagnostics capacity	VRDL	Binary/scale	0.15
Countermeasure	Therapeutic availability	CDSCO	Binary	0.15

Table 5C | NPRI calibration against historical outbreak events

Event	Estimated NPRI	Outcome
Kerala 2018	0.658	Contained
Bangladesh clusters	0.60–0.68	Recurrent
SARS-CoV-1	~0.75	Epidemic
Ebola 2014	>0.80	Pandemic-scale

ecological spillover and epidemiological transmission converge with insufficient countermeasure readiness.

Map elements include a north arrow, scale bar, and an inset data source panel for interpretability. All 2026-associated risk layers are annotated as preliminary and should not be interpreted as validated predictive outputs. The spatial risk surface combines bat density, human population density, deforestation and land-use change, seasonal fruiting and sap collection practices, and climate stressors (temperature anomalies, heavy rainfall, and tropical storms). Relative risk intensity (conceptual scale). High-risk corridors are highlighted across northern and eastern India (including Malda and Gorakhpur districts) and along the western coastal belt, with inset detailing elevated risk in Kerala (Kozhikode and Ernakulam). Labeled zones denote regions with recurrent or potential NiV emergence under changing environmental and socio-ecological conditions. This visualization represents a conceptual translational decision-support framework and does not constitute a calibrated predictive geospatial model. Composite layers were standardized and aggregated for conceptual visualization purposes only; the map does not represent a statistically validated predictive model.

The spatial heatmaps presented in Figures 2 and 4 should be interpreted as conceptual prioritization tools rather than calibrated predictive models. These maps integrate ecological spillover drivers—including bat habitat distribution, land-use change, and human population density—to identify candidate regions for prioritizing surveillance and preparedness activities. The maps, therefore, represent a risk-prioritization framework rather than deterministic outbreak prediction. Public environmental datasets used for map generation include IUCN species distribution data, Global Forest Watch land-cover datasets, Indian Census population data, and Indian Meteorological Department climate layers, all used in accordance with their respective open-data licensing terms.[40–43] Sensitivity analyses were conducted across ±10%, ±20%, and ±30% perturbations in domain weights, demonstrating robustness of NPRI classification boundaries, with epidemiological transmission risk exerting the greatest influence on composite variability (Supplementary Methods S1).

Figures 2 and 4 (spillover heatmaps) and the proposed Nipah Pandemic Readiness Index (NPRI) are conceptual decision-support frameworks derived from published ecological modeling approaches.[16] These visualizations are not derived from original primary datasets and should be interpreted as translational synthesis tools rather than novel predictive outputs. Indicator weighting approaches are described explicitly in the Section "Operationalizing the Nipah Pandemic Readiness Index."

The NPRI is intended as a decision-support tool rather than a deterministic predictor. Misinterpretation as a definitive outbreak forecasting model should be avoided, and policy application should be accompanied by contextual epidemiological assessment.

Translational and Preparedness Insights

- **Integration of Data:** Combining diagnostic, ecological, and epidemiological data allows dynamic risk scoring and early warning systems.
- **One Health Implementation:** Cross-sector collaboration enhances spillover prevention and ensures rapid response during outbreaks.
- **Operational Readiness:** Establishing pre-positioned stockpiles, rapid test deployment, and outbreak-ready clinical trial frameworks improves response efficiency.[39]
- **Community and Policy Engagement:** Behavioral interventions in high-risk communities reduce direct contact with bat excreta or contaminated fruit.

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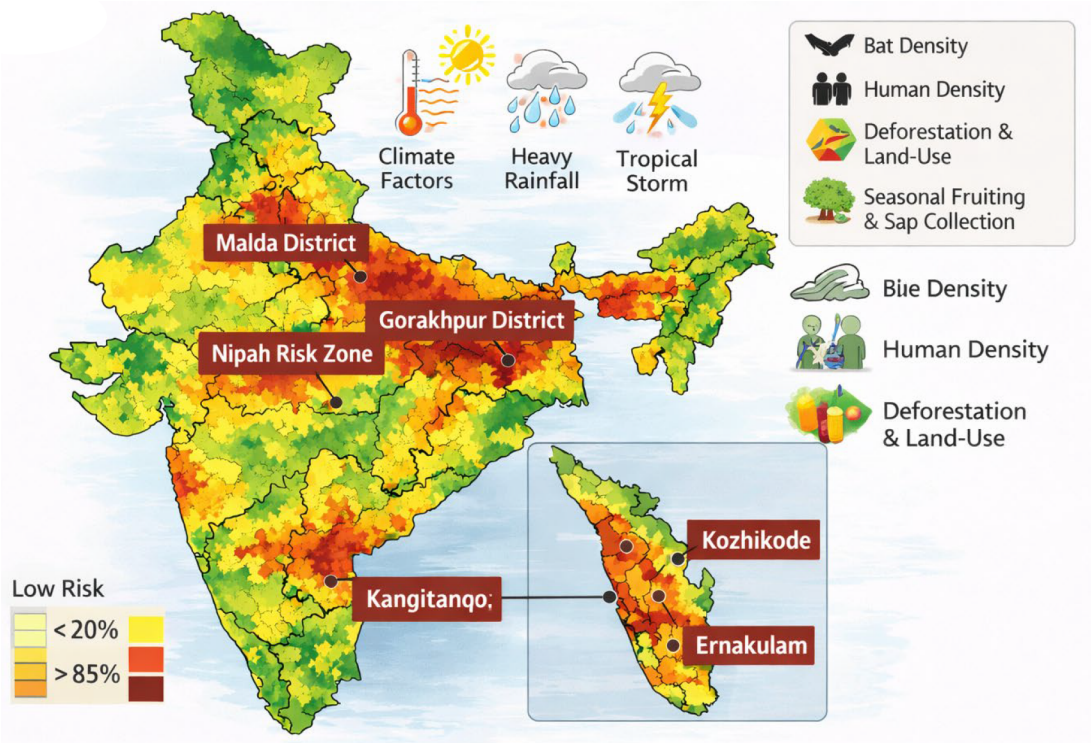

Fig 4 | Conceptual Nipah spillover risk heatmap integrating ecological and human exposure drivers. Variables include fruit bat density, habitat disturbance, livestock interface intensity, and human behavioral exposure pathways.

Collectively, these above measures move NiV response from reactive containment to predictive and preventive action.

Community engagement strategies validated in Bangladesh and India—including culturally tailored communication regarding safe date palm sap consumption, use of physical barriers to prevent bat contamination, and caregiver education during encephalitis clusters—have demonstrated measurable reductions in spillover exposure.[5,6] Integrating behavioral science into preparedness frameworks is therefore essential for sustainable risk reduction.

While the NPRI framework remains conceptual, it offers a structured decision-support approach for integrating ecological spillover drivers, epidemiological amplification potential, and countermeasure readiness within a unified pandemic preparedness assessment. Future validation of the NPRI framework using historical zoonotic outbreak datasets will be essential to refine weighting parameters and assess predictive utility across diverse pathogen emergence contexts.

Limitations

Several limitations should be acknowledged. First, reported secondary attack rates for NiV are derived from cluster investigations, which may reflect intense exposure within households or healthcare settings and may not represent broader population transmission potential. Second, the NPRI framework and spatial prioritization heatmaps are conceptual translational tools derived from published ecological and epidemiological modeling approaches; they should therefore be interpreted as decision-support frameworks rather than predictive outbreak models.

5%–50% Policy Translation Box: SMART Preparedness Targets (India)

- **Diagnostic Turnaround:** Achieve ≤24-hour RT-PCR turnaround in all high-risk districts (Kerala, Tamil Nadu, West Bengal) by Q4 2026 via VRDL expansion.
- **Seasonal Surveillance Trigger:** Initiate bat viral shedding surveillance when ≥1.5 SD climate anomaly coincides with peak fruiting season.
- **Clinical Trial Activation:** Activate pre-approved adaptive protocol within 72 hours of laboratory-confirmed outbreak.
- **Stockpile Target:** Maintain 30-day PPE reserve and monoclonal antibody investigational stock in designated regional hubs.
- **Community Risk Communication:** Deploy district-level risk alerts within 48 hours of confirmed spillover during sap collection season.
- **Lead agencies:** ICMR, CDSCO, MoHFW, State Health Departments.

Prospective Validation of NPRI

To operationalize the NPRI framework, prospective field validation is proposed in high-risk districts of Kerala. Seasonal pilot implementation will integrate ecological surveillance (bat monitoring), real-time diagnostic capacity (VRDL network), and epidemiological indicators. Predefined NPRI thresholds will trigger graded

response actions, including diagnostic surge, infection control escalation, and activation of adaptive clinical trial protocols. Performance will be evaluated through after-action assessments, comparing predicted versus observed outbreak dynamics.

Concluding Perspective and Future Outlook

The evolving epidemiology of NiV underscores its position as a high-consequence zoonotic pathogen approaching pandemic-relevant thresholds, particularly in regions where ecological disruption, human–animal interfaces, and healthcare vulnerabilities intersect. While recent surveillance signals from India in 2026 suggest shifts in outbreak dynamics, these observations remain provisional and subject to formal epidemiological reconciliation; accordingly, interpretations should be made with caution. Notwithstanding this uncertainty, the convergence of recurrent spillover, documented human-to-human transmission, and persistent gaps in diagnostics, therapeutics, and vaccines reinforces the urgent need for anticipatory preparedness.

This review highlights that effective mitigation of NiV risk will depend on transitioning from reactive outbreak containment to predictive, systems-based preparedness. Integrating ecological intelligence, real-time surveillance, decentralized diagnostics, and outbreak-ready clinical trial frameworks within a One Health paradigm offers a viable pathway to reduce both spillover frequency and transmission amplification. India's role as a recurrent outbreak setting further positions it as a critical hub for translational research, regulatory innovation, and countermeasure deployment.

Ultimately, preventing NiV from crossing the pandemic threshold will require sustained coordination between scientific, clinical, and policy domains, supported by proactive investment in surveillance infrastructure and rapid-response capabilities. The framework proposed in this study provides a structured foundation for such efforts, enabling early risk recognition and timely intervention before localized outbreaks escalate into wider public health emergencies.

This review highlights three interdependent imperatives for global and regional preparedness:

- **Predictive and Proactive Surveillance:** Integrating ecological, climatic, and epidemiological data, as visualized in Figures 2 and 4, allows authorities to anticipate high-risk spillover zones and implement targeted interventions.[39]

All 2026 epidemiological data are preliminary and subject to formal reconciliation.

All figures were generated with color-blind-safe palettes and include alternative text descriptions to ensure compliance with WCAG 2.1 accessibility guidelines.

The repository includes version-controlled datasets, R/Python scripts, and environment specifications necessary to reproduce all analyses presented in this study.

List of Abbreviations

BSL: Biosafety Level
CDSCO: Central Drugs Standard Control Organization
CEPI: Coalition for Epidemic Preparedness Innovations
CFR: Case–Fatality Rates
DON: Disease Outbreak News
ELISA: Enzyme-Linked Immunosorbent Assay
ICMR: Indian Council of Medical Research
IgG: Immunoglobulin G
IgM: Immunoglobulin M
IPC: Infection prevention and control
IUCN: The International Union for Conservation of Nature
mAbs: Monoclonal antibodies
MoHFW: Ministry of Health and Family Welfare
NDCTR: New Drugs and Clinical Trials Rules (2019)
NIV: National Institute of Virology
NiV: Nipah Virus
NPRI: Nipah Pandemic Readiness Index
PPE: Personal Protective Equipment
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses
QGIS: Quantum Geographic Information System
RT-PCR: Reverse Transcription-Polymerase Chain Reaction
SAR: Suspicious Activity Reports
VRDL: Viral Research and Diagnostic Laboratory network under ICMR

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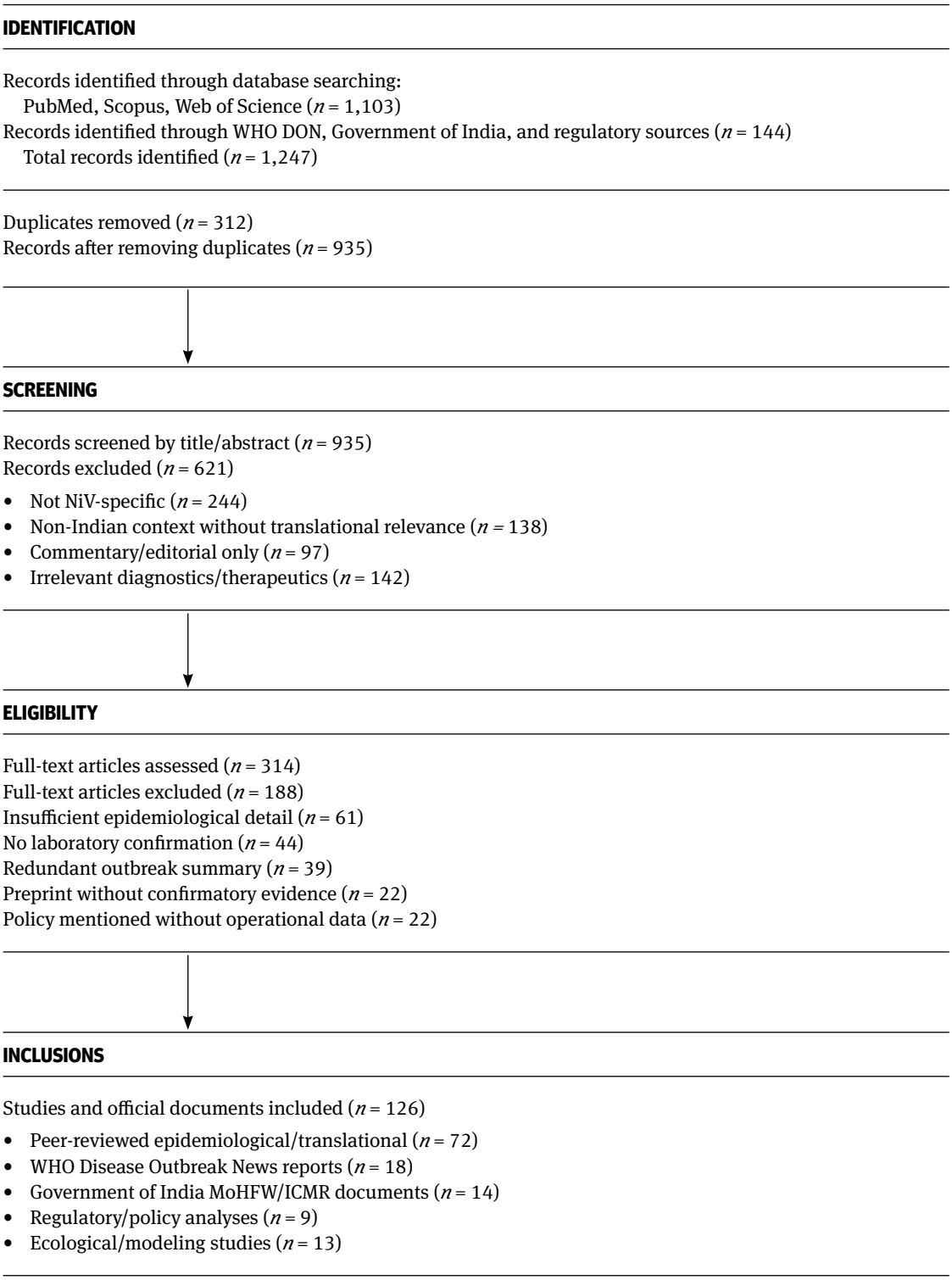
Supplementary Materials

Supplementary Fig S1 | PRISMA-adapted study selection workflow (Search end date: February 15, 2026)



Note: PRISMA-adapted screening workflow illustrating identification, screening, eligibility, and inclusion stages for this structured narrative synthesis. Given the narrative design, a quantitative meta-analysis was not performed; however, outbreak investigations were appraised for laboratory confirmation, case-definition clarity, and denominator transparency before inclusion in the derivation of epidemiological parameter.

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Supplementary Table S1 | Categorized inventory of key sources included in the narrative synthesis

Category	Representative Sources	Contribution to Manuscript
Epidemiology & Outbreak Reports	World Health Organization Disease Outbreak News (India 2018, 2025, 2026); Arunkumar et al., 2019; Hsu et al., 2004	Case counts, CFR, outbreak timelines
Transmission Parameters	Luby et al., 2009; Gurley et al., 2019; Centers for Disease Control and Prevention clinical overview	R_0 estimates, serial interval, SAR
Wildlife & Spillover Ecology	Plowright et al., 2015; Plowright et al., 2021; Peel et al., 2019	Bat reservoir ecology, land-use change
Diagnostics & Laboratory Systems	Lo et al., 2012; Gurley et al., 2019; Indian Council of Medical Research VRDL framework	RT-PCR protocols, decentralization constraints
Therapeutics	Broder et al., 2013 (m102.4); DeBuysscher et al., 2014 (favipiravir)	Preclinical efficacy, compassionate use
Vaccine Development	WHO 2025 roadmap; Lo et al., 2012; CEPI documentation	Vaccine platforms, Animal Rule pathways
Policy & Preparedness	Ministry of Health and Family Welfare advisories; WHO preparedness frameworks	National response strategies
Predictive Modeling	Gilbert et al., 2018; Peel et al., 2019	Integrated surveillance modeling

Supplementary Table S2 Sensitivity testing was conducted by varying domain weights across ±10%, ±20%, and ±30% ranges to assess the stability of hotspot identification and composite NPRI values. District prioritization rankings and relative risk classifications remained stable across all perturbation scenarios, indicating robustness of the NPRI framework.

Supplementary Table S2 | Sensitivity analysis and worked example: NPRI retrospective application (Kerala 2018)

Domain	Indicator Mean	Weight	Weighted Score
Ecological Risk	0.70	0.30	0.21
Epidemiological Transmission	0.64	0.40	0.256
Countermeasure Capacity	0.48	0.30	0.144

Note: Indicator standardization (0–1 Scale)
Composite Calculation:
Total NPRI = 0.658
This value lies below the canonical NPRI threshold of 0.72, but within a near-threshold elevated-risk zone, indicating conditions approaching pandemic emergence potential under less favorable containment scenarios.

Domain Structure Table

Domain	Weight	Indicators	Data Source
Ecological	0.30	Bat density, land-use	IUCN, GFW
Epidemiological	0.40	R_e, SAR	WHO DON
Countermeasure	0.30	Diagnostics, IPC	ICMR

Domain indicator values correspond exactly to those presented in Section "Operationalizing the Nipah Pandemic Readiness Index"of the main text.

Supplementary Methods S1: NPRI Indicator Framework and Computational Methodology

S1.1 Indicator Structure

The Nipah Pandemic Readiness Index (NPRI) is constructed as a multi-domain composite indicator integrating ecological, epidemiological, and response capacity variables associated with zoonotic spillover and outbreak amplification. Indicators were selected through synthesis of peer-reviewed literature, outbreak reports, and established zoonotic risk frameworks. Three domains were defined:

1. Ecological Spillover Risk
   - Fruit bat (Pteropus) population density
   - Habitat disturbance/deforestation
   - Raw date palm sap exposure frequency
   - Livestock–bat interface intensity
   - Seasonal climatic drivers of viral shedding
2. Epidemiological Transmission Potential
   - Secondary attack rate (SAR)
   - Nosocomial transmission clustering
   - Population density
   - Infection prevention and control (IPC) capacity
   - Early detection delays
3. Countermeasure Capacity
   - Diagnostic laboratory capacity
   - Surveillance network coverage
   - Availability of therapeutics
   - Vaccine development status
   - Public health response infrastructure

S1.2 Indicator Scoring

Each indicator was normalized to a 0–1 scale:

$$\text{Score} = (\text{Observed} - \text{Minimum}) / (\text{Maximum} - \text{Minimum})$$

where quantitative data were unavailable, ordinal scoring was applied:

Low risk = 0.25
Moderate risk = 0.50
Elevated risk = 0.75
High risk = 1.00

Domain scores represent the mean of included indicators.

S1.3 Composite NPRI Calculation

The composite NPRI was calculated using:

$$\text{NPRI} = (0.30 \times \text{Ecological Risk}) + (0.40 \times \text{Epidemiological Transmission}) + (0.30 \times \text{Countermeasure Capacity})$$

A uniform NPRI threshold of 0.72 was applied across all analyses, figures, and supplementary materials to define high-risk conditions.

S1.4 Sensitivity Analysis

Sensitivity analysis evaluated NPRI stability under ±10%, ±20%, and ±30% variation in domain weights:

- Ecological: 0.21–0.39
- Epidemiological: 0.28–0.52
- Countermeasure: 0.21–0.39
- Across all scenarios:
  - NPRI variation remained within ±0.05–0.08
  - Relative ranking of high-risk regions remained unchanged
  - Epidemiological domain exerted the greatest influence on composite variability

S1.5 Computational Pseudocode

Input: Indicator dataset
Step 1: Normalize indicators (0–1)
Step 2: Assign to domains
Step 3: Compute domain means
Step 4: Apply weights
Step 5: Sum weighted scores
Output: NPRI

S1.6 Limitations

The NPRI framework is a conceptual decision-support tool rather than a deterministic predictive model. Indicator selection and weighing are based on current understanding of Nipah virus ecology and outbreak dynamics and require prospective validation. The use of aggregated indicators may oversimplify local heterogeneity, and the threshold value (0.72) should be interpreted cautiously within a broader epidemiological context.

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