



INFLUENZA VACCINATION IN PAEDIATRIC AND MATERNAL POPULATIONS IN NEPAL: CLINICAL RATIONALE AND EXPERT PERSPECTIVE

Infectious Disease

Dr Smriti Mathema*

Associate Professor of Paediatrics & Clinician Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu *Corresponding Author

Dr Anshu Poudel

Neonatologist, Department of Pediatrics and Neonatology, Koshi Hospital, Biratnagar, Nepal

Dr Nira Singh Shrestha

Director, Nepal Health Clinic, Mid Baneshwor, Kathmandu, Nepal. Head, Department of Gynecology & Obstetrics, MEDICITI Hospital, Lalitpur, Nepal

ABSTRACT

Influenza is an acute viral infection of the respiratory tract that contributes significantly to global morbidity and mortality, with a disproportionately higher burden in low- and middle-income countries such as Nepal. Pregnant women and children are particularly vulnerable, with an increased risk of severe illness and hospitalization following infection. This review evaluates the need for influenza vaccination in maternal and paediatric populations in Nepal and assesses vaccine acceptance in real-world clinical practice based on expert opinion. Focus group discussions were conducted with specialists in Pediatrics and Obstetrics & Gynecology and paediatrics, supported by a structured literature review. Findings indicate that limited surveillance data likely underestimate the true burden of influenza in Nepal. Maternal immunization is recognized as an effective strategy that provides protection to both mothers and infants through passive immunity, while annual paediatric vaccination from six months of age contributes to reducing disease burden. Despite concerns related to cost and accessibility, the overall benefits of influenza vaccination are perceived to outweigh its limitations. Strengthening surveillance systems, enhancing healthcare provider and community awareness, and establishing a clear national vaccination policy are essential to improve influenza vaccine uptake in Nepal.

KEYWORDS

Influenza, Maternal Influenza Immunization, Infant Influenza Vaccination, Nepal

INTRODUCTION

Influenza virus infection contributes significantly to global morbidity and mortality.¹ Pregnant women with influenza in immunocompromised state have an increased risk of illness and hospitalization compared with non-pregnant women, and maternal infections during pregnancy are associated with adverse outcomes such as low birth weight and preterm birth.² The risk of severe disease and hospitalization is particularly elevated during the second and third trimesters of pregnancy.³ Similarly, infants aged 0–6 months are highly susceptible to influenza-related complications, especially in the presence of underlying comorbidities such as cardiac, respiratory, neurological, or neuromuscular conditions.³ Maternal influenza immunization has been shown to reduce morbidity and mortality among both pregnant women and young infants.^{4–6}

Children experience high influenza attack rates and are important drivers of transmission within communities.^{7,8} Young children, particularly those under five years of age, are at increased risk of severe disease, hospitalization, and complications.^{9,10} Globally, a substantial proportion of influenza-related lower respiratory tract deaths in this age group occurs in developing countries.¹⁰ School-aged children facilitate rapid transmission due to close contact within classrooms, higher viral shedding, and limited pre-existing immunity.^{7,10}

According to the 2012 World Health Organization recommendations, pregnant women are the highest priority group for seasonal influenza vaccination, followed by other high-risk populations including children under five years, older adults, individuals with chronic medical conditions, and healthcare workers.^{11–13} Influenza complications are more frequently reported in low- and middle-income countries (LMICs) such as Nepal, where higher rates of hospitalization and influenza-related mortality are observed.^{14,15,16}

In this context, the present review aims to evaluate the need for influenza vaccination among pregnant women and children in Nepal and to assess the acceptance of influenza vaccination in real-world clinical settings based on expert opinion, with a focus on identifying existing gaps and opportunities to improve vaccine uptake in these high-risk populations.

Methodology

Focus group discussions conducted with 23 experts from Nepal qualified in Pediatrics and Obstetrics & Gynecology. During the meetings, the experts discussed current practices related to influenza vaccine uptake, shared their individual clinical experiences, and identified key barriers influencing vaccination acceptance among

pregnant women and children.

A literature search was conducted across databases such as PUBMED, COCHRANE, and Google Scholar using keywords including 'Nepal', 'Influenza', 'Influenza surveillance', 'Influenza vaccination', 'Pregnancy', and 'Children.' The findings from the literature were reviewed and shared with the expert panel to facilitate evidence-based discussions.

The experts provided insights on the current uptake of influenza vaccination, highlighted challenges and barriers to vaccine acceptance in real-world settings, and proposed strategies to improve vaccination coverage among these high-risk groups. A descriptive synthesis of the literature and expert opinions is presented below.

Prevalence of Influenza in Pregnant Women and Children Evidence

Pregnant women are at significantly increased risk of severe influenza-related complications, with studies indicating up to a fourfold higher risk of hospitalization, particularly during the second and third trimesters.¹² Infants aged 0–6 months also demonstrate a higher risk of severe influenza infection and hospitalization compared with older children.¹³

In a community-based study conducted in Sarlahi District of rural Nepal among 752 households, children (≤ 15 years) constituted a substantial proportion of the population and experienced higher rates of acute respiratory infections compared to adults¹. These findings highlight the considerable burden of respiratory illnesses in paediatric populations in Nepal, many of which are attributable to viral pathogens such as influenza¹⁴. School attendance further amplifies transmission dynamics, as children in close-contact settings facilitate the spread of respiratory viruses, including influenza^{8,13}. The frequent interaction among children, combined with higher viral shedding and lower pre-existing immunity, underscores their role as key drivers of influenza transmission within households and communities^{8,13}.

Expert Opinion

Globally, influenza activity shows variability in seasonal patterns and virus subtype circulation across regions¹⁶. Influenza activity in Nepal demonstrates a bimodal seasonal pattern, with a peak during January–February and a secondary peak during September–October, although year-round transmission is common¹⁷. Due to limited surveillance coverage, the true national burden may be underestimated²⁰. Nepal contributes to the WHO Global Influenza Surveillance and Response System (GISRS) through sentinel influenza-like illness (ILI) and severe acute respiratory infection

(SARI) surveillance with routine virological testing, reporting weekly data on influenza activity.^{19,20} Multiple sentinel surveillance sites perform RT-PCR testing and report findings through the National Influenza Centre (NIC) at the National Public Health Laboratory (NPHL), which identifies circulating influenza virus types.

Although population-specific prevalence in pregnant women and children is not distinctly reported, overall influenza positivity ranges from approximately 14% to 39%, with seasonal peaks up to around 40%²⁰. Within this system, children contribute substantially to reported cases, and pregnant women are recognized as high-risk groups for severe influenza.¹⁸

Clinically, influenza may present with moderate to severe symptoms. Different types of influenza A and B viruses can circulate either at different times or simultaneously among both adults and children.¹⁹ Influenza A is more frequently reported in adults, whereas influenza B is more common among children.¹⁹ Any unsubtype influenza virus circulation is further investigated to determine its type. Outpatient settings experience a high burden of paediatric respiratory infections during peak seasons, and severe cases requiring ICU admission are occasionally laboratory-confirmed as influenza.¹⁹

Influenza during pregnancy as an immunocompromised state can lead to serious maternal and neonatal complications, especially in low-resource settings such as Nepal.^{3,18} Pregnant women, particularly in later gestation or with comorbidities like diabetes or hypertension, are at higher risk of severe illness, including respiratory distress and ICU admission¹⁸. While early antiviral treatment helps, limited diagnostic tools often lead to empirical antibiotic use due to difficulty distinguishing viral from bacterial infections.¹⁸

In infants, especially those with risk factors such as immunocompromised status or bronchiolitis presenting with recurrent flu-like symptoms or influenza-like illness (ILI), the clinical overlap makes it difficult to distinguish influenza from other respiratory pathogens¹⁸.

Children under 5 years of age represent a significant proportion of Nepal's population (approximately 2.99 million)¹⁹. A 2018 study conducted by the National Influenza Centre (NIC), Nepal, among children under 5 years presenting with ILI (n = 424) reported that 14.6% (62/424) were influenza-positive by RT-PCR. Notably, a higher positivity rate was observed among hospitalized severe acute respiratory infection (SARI) cases within the same cohort (28%; 12/43)²¹. Influenza virus circulation occurred throughout the year, with a pronounced seasonal peak during the winter months (January–March).¹⁷

Furthermore, national NIC surveillance data from 2018 to 2022 indicate that influenza positivity among children under 5 years was 15.7% during the pre-COVID-19 period (2018–2019) and declined to 10.4% during the COVID-19 period (2020–2022)¹⁷. Despite this reduction, children under 5 years consistently demonstrated the highest influenza positivity rates compared with older age groups during 2020–2022¹⁷. Studies on the influenza burden in children under 5 years of age have been elaborated in Table 1. Co-infections among influenza-positive paediatric cases have also been reported and were predominant in children <5 years, underscoring the complexity of viral respiratory illness in this age band.²²

Influenza Burden in Nepal: Under-5 Children^{17,21,22}

Study Setting & Author	Year (s)	Population and Case definition	Key findings
Pediatric NIC descriptive Study - Sapkota <i>et al</i>	2018	Children <5 years with ILI (n=424)	Influenza positivity was 14.6% (62/424) by RT-PCR.
		Children <5 years with SARI (n=43)	Influenza positivity was 28% (12/43); higher positivity among severe hospitalized presentations
National influenza surveillance trends with NIC age-stratified subset - Shrestha <i>et al</i>	2018–2022	All ages; national reporting.	Average influenza positivity dropped from 39% (pre-COVID) to 14% (during COVID).

		Age group <5 years	Influenza Positivity rate was 15.7% pre-COVID and 10.4% during COVID among tested specimens with epidemiologic data.
Influenza positivity by age during COVID-19. - Shrestha <i>et al</i>	2020–2022	<5 years of age vs older ages	During COVID years, influenza positivity was highest in children <5 years of age versus individuals between age groups 5–14, 15–64, ≥65 years.

Protective Role of Influenza Vaccination During Pregnancy and in Children Evidence

In Nepal, pregnant women may be at increased risk of influenza infection due to immunocompromised state and intense household transmission dynamics, where close and prolonged contact with family members facilitates rapid spread of respiratory viruses, particularly during seasonal peaks. Given the structure of multigenerational households and high background influenza circulation, transmission within households remains a key contributor to infection risk, with repeated exposure increasing vulnerability among pregnant women¹. Influenza vaccination during pregnancy has been shown to reduce influenza cases and hospitalizations by approximately 40% and may also decrease severe pneumonia among infants^{2,3}. Vaccination confers passive immunity to infants through transplacental antibody transfer, providing protection during the first months of life when direct vaccination is not possible^{3,8}.

School-going children often serve as vectors for introducing infection into households, increasing risk among pregnant women. School outbreaks of influenza contribute to absenteeism and wider socioeconomic disruption.^{7,9} Annual influenza vaccination in children reduces illness and missed schooldays.⁹ School-based vaccination programs are associated with fewer illness-related school absences and lower community influenza hospitalization rates, suggesting both direct protection and indirect protection in the broader population.^{7,23}

Expert Opinion

Unvaccinated mothers and family members can transmit the virus to vulnerable populations. Vaccinating pregnant women not only protects them but also offers postnatal protection to their newborns.^{24,25} The “cocooning effect” of the influenza vaccine highlights the importance of vaccinating all household members and close contacts to shield infants.²⁶ Infants under 6 months of age are ineligible for influenza vaccination, making maternal and household immunization critical²⁷. A positive impact of vaccination in reducing the frequency and severity of seasonal respiratory illnesses in children has been observed.^{9,23}

Key Barriers to Influenza Vaccination Evidence

Influenza vaccination remains substantially underused in Nepal, largely due to limited awareness and insufficient provider recommendation. Evidence from a recent descriptive study among Nepalese pregnant women shows that although 96.4% had heard of the influenza vaccine, 74.4% were unaware that it is recommended during pregnancy, and 91.3% reported that their healthcare providers had not advised them to receive it. Major barriers in this study included lack of knowledge, limited recommendations by clinicians, and affordability.²⁸

Pediatricians frequently report limited time and competing clinical priorities as key barriers to providing influenza vaccine counseling, leading to reduced opportunities for patient education during routine encounters.²⁹

In government hospitals, heavy patient load and time pressure further limit the ability of doctors to counsel families on influenza vaccination. These observations align with evidence demonstrating that missed opportunities for influenza vaccination often occur when counseling time is insufficient or absent, despite parents being open to receiving recommendations when provided clearly and empathetically.²⁸

Expert Opinion

The benefits of the influenza vaccine outweigh the costs of vaccination.³⁰ Economic evaluations from LMICs show that influenza

vaccination is often cost-effective or cost-saving, largely by preventing medically attended illness and expensive hospitalizations in high-risk groups.^{31,32} A systematic review of LMIC studies reported that most (~88%) cost-effectiveness analyses judged at least one scenario per target group as cost-effective or cost-saving.³³ Experts highlighted that influenza vaccination is largely accessed through facility-based channels and is frequently an optional paid vaccine, with uptake limited by availability of updated seasonal vaccine, affordability, low awareness, and missed provider recommendation during ANC.²⁸ They also noted that operational constraints such as procurement/workforce gaps and cold-chain limitations that can affect consistent annual vaccination.^{35,36}

Vaccination Timing and Recommendations for Pregnant Women and Children

Evidence

Inactivated influenza vaccine is recommended in pregnancy (live attenuated influenza vaccine is not recommended) and may be administered in any trimester, ideally before peak circulation but also later in the season if missed.^{37,38} In Nepal, influenza circulates year round, and a randomized trial by Steinhoff et al. supports the safety and efficacy of year-round maternal influenza immunization for protecting both mothers and infants.³⁹ The authors also suggest that in areas with continuous influenza circulation, a universal strategy of influenza vaccination during pregnancy may provide better protection.³⁹

For children, guidance identifies those aged 6 months to <5 years as an important risk group; routine annual vaccination is recommended from 6 months of age, and children aged 6 months–8 years may require two doses ≥4 weeks apart if unvaccinated or incompletely vaccinated.^{37,40} Because infants aged <6 months cannot be vaccinated, maternal immunization provides protection during early infancy through transplacental antibody transfer.⁴¹

Expert Opinion

Influenza vaccination is routinely administered to pregnant women between 32 and 34 weeks of gestation, regardless of the season. In cases where patients present with flu-like symptoms or influenza-like illness (ILI), vaccination is deferred for two weeks to allow recovery, as the vaccine can still offer protection against other circulating strains.³⁷

For pregnant women recovering from flu-like symptoms, an average 2-week waiting period post-recovery is commonly recommended before vaccination.⁴²

Paediatricians play a crucial role in vaccine advocacy and improving influenza vaccine uptake, with training and exposure during medical education strengthening their ability to counsel caregivers effectively.⁴³ Influenza vaccination is recommended for all children aged ≥6 months, as it significantly reduces disease burden and complications.^{9,44} Mild acute illness (with or without low-grade fever) is not a contraindication to routine vaccination; therefore, immunization may be administered on schedule in otherwise clinically stable children with minor infections.⁴² Appropriate counselling and follow-up are particularly important in settings with fixed vaccination schedules to ensure completion of immunization.⁴³

Influenza Surveillance and Immunization Infrastructure in Nepal Evidence

The WHO Global Influenza Surveillance and Response System (GISRS) monitors influenza activity globally, including Nepal, to support strain tracking and public health response.⁴⁵ Nepal contributes to GISRS through a national influenza surveillance platform coordinated by the National Influenza Centre (NIC), housed within the National Public Health Laboratory (NPHL), Teku, Kathmandu.^{19,47} Nepal operates sentinel ILI (outpatient) and sentinel SARI (inpatient) surveillance with 13 ILI sites and 9 SARI sites across five districts, reporting weekly aggregated data via electronic reporting tools.¹⁹ Other sentinel surveillance sites for influenza also report RT-PCR results on influenza A and B subtypes to NIC for incorporating this information into the national database for further reporting from Nepal to GISRS and FLU Net. Laboratory confirmation is routinely performed for all enrolled ILI and SARI cases with RT-PCR on influenza A and B viruses with its subtypes, strengthening virologic attribution of respiratory illness.¹⁹

Nepal maintains influenza virological surveillance from different partners with national and sentinel components, including 16

virological surveillance sites and an average processing volume of approximately 62 samples per week. The country has RT-PCR capacity across 83 laboratories, with 100% reporting to the NIC, and also utilizes rapid diagnostic testing for influenza surveillance.^{19,47} The NIC (established in 2010) performs rapid influenza testing, RT-PCR, immunofluorescence assay (IFA), and virus isolation, and ships specimens to WHO Collaborating Centres 1–2 times per year for external characterization. Nepal reports influenza virological data to FluNet (weekly since 2012) and epidemiological data to FluID (weekly since 2019), with annual national reports supplemented by weekly International Health Regulations (IHR) bulletins.⁴⁶

Influenza Surveillance in Nepal^{19,46}

Domain	Nepal status	Details / remarks
NIC location & role	NIC is established and operates under NPHL (Teku, Kathmandu)	NIC established 2010
Routine assays at NIC	Available	Rapid influenza test, RT-PCR, IFA, virus isolation
Virus isolation capacity	Yes	NIC has virus isolation capability
Sequencing capacity	Yes	NPHL is leading Genomic Surveillance for Nepal
RT-PCR lab network	83 laboratories; 100% reporting to NIC	National network supports consolidated reporting via NIC
Reporting to FluNet	Yes	Reporting began 2012; weekly reporting
Reporting to FluID	Yes	Reporting began 2019; weekly reporting
Shipment to WHO Collaborating Centres	Yes	Ships to WHO Collaborating Centres 1–2 times/year
Integration of epidemiological + virologic data	Not integrated (routine linkage not in place)	Limits subgroup analyses (e.g., pregnancy, under-5) from routine surveillance outputs

IFA: Immunofluorescence Assay, RIDT: Rapid Influenza Diagnostic Test FluNet: WHO global platform for virological influenza surveillance (laboratory-confirmed virus reporting) FluID: WHO global platform for epidemiological influenza surveillance (tracking disease trend and impact), WHO CCs = WHO Collaborating Centres for Influenza

Vaccine Transport and Cold Chain in Nepal

Nepal's mountainous topography and dispersed settlements pose substantial logistical constraints for last-mile vaccine delivery, requiring transport over long distances and through highly variable ambient temperatures.⁴⁸ Influenza vaccines are freeze sensitive and therefore require a continuous cold chain of 2–8 °C during storage and transport; this is typically achieved using insulated passive cold chain equipment (e.g., cold boxes, vaccine carriers and refrigerated vans) to buffer against environmental temperature fluctuations.^{49,50} However, passive cold chain systems are vulnerable to inadvertent sub-zero exposure, most commonly due to incorrect handling of frozen packs (e.g., insufficient conditioning or direct contact between frozen packs and vials), which can compromise vaccine potency and increase wastage.^{51,52,53}

To reduce this risk especially during transport through cold conditions manufacturers are increasingly using freeze-preventive cold boxes and vaccine carriers. These include specially designed liners that keep vaccines separated from frozen packs, lowering the chance of freezing damage.^{51,53}

Field evaluations in Nepal indicate that freeze-preventive vaccine carriers maintained internal temperatures above 0 °C for >99% of monitored transport time, supporting improved protection of freeze-sensitive vaccines during outreach delivery.⁵⁴

In addition to equipment upgrades, risk-mitigation strategies include targeted training on correct packing practices, appropriate coolant selection and handling, and routine temperature monitoring (e.g., electronic loggers) to detect excursions early and preserve vaccine potency.^{50,51}

Expert Opinion

Current influenza testing is limited, especially in children, due to discomfort with swab procedures and lack of accessible testing.⁵⁵

There is a need for a centralized influenza surveillance system, like the successful MMR (Measles–Mumps–Rubella) program, which improved significantly after structured sample collection and digital tracking were introduced.⁵⁵

The issues related to vaccine handling include improper cold chain maintenance at pharmacies (e.g., storage in temperature unstable areas such as refrigerator doors) and incorrect administration practices.⁵⁰ Targeted, periodic training of pharmacists and pharmacy staff on vaccine storage, temperature monitoring, handling during transport, administration and preparation to address for any reaction or anaphylaxis is critical because vaccine quality is a shared responsibility from receipt to administration and requires consistent staff competency.^{50,56} In parallel, structured education for patients and caregivers is essential to improve awareness of correct vaccine storage and handling (e.g., avoiding home delivery without temperature control) and to reinforce confidence in vaccine safety and effectiveness.^{56,57}

Many remain hesitant toward influenza vaccination due to misconceptions about vaccine effectiveness and limited awareness.^{60,61} Some perceive vaccination as unnecessary unless illness occurs, while others deprioritize it because influenza is often viewed as a self-limiting infection.⁶⁰ In addition, the cost and the absence of regular, structured vaccination drives can further discourage uptake.^{60,61} Limited community health education reinforces these beliefs, resulting in missed opportunities for prevention.⁵⁵ Experts emphasized that sustained community education and clear risk communication are essential to improve understanding of influenza severity and acceptance of vaccination as a preventive measure.⁵⁵

Experts also highlighted the challenge of inconsistent availability of vaccines which can disrupt vaccination schedules.⁵⁷ The need for updated formulations based on WHO recommendations were also discussed.⁵⁷ Preferences for prefilled syringes over vials and the importance of consistent supply chains were emphasized.^{58,59} Overall, ensuring timely access, informed vaccine selection, and reliable logistics was seen as essential for effective influenza vaccination programs.⁵⁷ Prefilled syringes are single-use, ready-to-administer syringes that facilitate more rapid vaccination.⁵⁸ Prefilled syringes are also risk reducers, as they reduce the occurrence of handling errors and associated health hazard risks.⁵⁹

WHO prequalification is a global assurance process through which the World Health Organization independently evaluates vaccines for manufacturing quality, clinical performance, programmatic suitability, and ongoing production consistency.⁵⁷ WHO prequalified influenza vaccines meet internationally recognized standards of quality, safety, and efficacy. Prequalified inactivated influenza vaccines are available for pediatric and maternal populations, supporting regulatory acceptance, public procurement, and alignment with global immunization recommendations.⁵⁷ Their availability provides an essential evidence-based platform for considering influenza vaccination strategies in Nepal.⁵⁷

Low compliance with annual influenza vaccination is largely due to limited awareness, underestimation of disease severity, and lack of consistent public health messaging.⁶³ Experts emphasized the importance of improved education, continuous awareness efforts, effective communication, and policy support.^{55,61} Counselling and improved vaccine access were also suggested, along with practical approaches such as SMS reminders, which help improve annual vaccination rates by addressing forgetfulness and reinforcing the need for yearly immunization.⁶⁰

Participants emphasized the need for stricter policies and oversight to ensure safe, consistent, and cost-effective vaccine delivery.^{50,62} Experts opined that national professional health bodies in Nepal can play a key role by generating evidence on influenza burden, particularly in high-risk groups, leading awareness campaigns, to educate the community regarding the benefits of influenza vaccination.⁶⁰ They can also collaborate with healthcare professionals to enhance their knowledge and skills in managing influenza cases and promoting vaccination.^{50,63}

CONCLUSION

Maternal influenza immunization can reduce morbidity and mortality associated with influenza infection in pregnant women and infants. Vaccination during pregnancy has shown to reduce the incidence of preterm births and also confer protection to newborns through transplacental antibody transfer. Evidence from across the globe indicates that vaccination effectively reduces both the frequency and severity of seasonal respiratory illnesses in children. Despite these well-established benefits, influenza vaccination uptake in Nepal remains extremely low at approximately 1%, primarily due to misinformation, limited public awareness, lack of advocacy, and time constraints faced by healthcare providers in counseling patients and caregivers. To improve vaccine coverage, it is essential to strengthen awareness and education initiatives, equip healthcare providers with adequate training and communication tools, and integrate influenza vaccination into routine maternal and child healthcare services. Active involvement of healthcare professionals in advocacy efforts are crucial to promote acceptance and uptake of influenza vaccination among pregnant women and children in Nepal.

Source of Funding

The expert panel discussion was organized in collaboration with Abbott India Limited. This article is based on the experts' viewpoints. The views expressed and discussed in the meetings, as well as those presented in this paper, are the authors' independent views and not those of Abbott India Ltd.

Conflict of Interest

The authors received speakers' honorarium from Abbott India Limited for participation in the focus group discussion.

Ethical Approval: Not required

ACKNOWLEDGMENT

The authors sincerely acknowledge the valuable contributions of all healthcare professionals who participated in the focus group discussions. Their clinical insights and expertise were instrumental in shaping this work. We extend our gratitude to Dr. Kabita Keyal (Paediatrics, Sumeru City Hospital), Dr. Mandira Shrestha (Paediatrics, Nepal Medical College; Kathmandu Model Hospital; and Nepal Medicit Hospital), Dr. Binod Lal Bajracharya (Paediatrics, Washa Pasa), Dr. Shama Shakya (Paediatrics, Chhetrapati Free Clinic), Dr. Smriti Mathema (Paediatrics, Kathmandu Medical College), Dr. Anwesh Bhatta (Paediatrics, B&B Hospital), Dr. Nisha Jyoti Shrestha (Paediatrics, Kanti Children Hospital), Dr. Nikhil Agrawal (Paediatrics, Vayodha Hospitals), Dr. Nira Singh Shrestha (Gynaecology, Medicit Hospital), Dr. Neha Homagain (Gynaecology, Indira IVF Nepal), Mr. Jay Dev Yadav (Gynaecology, Himal Hospital Pvt. Ltd.), Dr. Arun Giri (Paediatrics, Nobel Medical College), Dr. Vijay Kumar Shah (Paediatrics, Nobel Medical College), Dr. Suresh Prasad Shah (Paediatrics, Neuro Hospital), Dr. Anshu Poudel (Paediatrics, Koshi Zonal Hospital), Dr. Prerana Dahal (Gynaecology, Biratnagar Asptal), Dr. Chandra Bhusan Jha (Paediatrics, Birat Medical College and Teaching Hospital), Dr. Suryakant Chaudhary (Paediatrics, Koshi Zonal Hospital), Dr. Nanda Kishwor Chaudhary (Paediatrics, Koshi Zonal Hospital), Dr. Deepraj Upadhaya Adhikari (Paediatrics, Birat Nursing Home Pvt. Ltd.), and Dr. Sandip Kumar Singh (Paediatrics, Nobel Medical College).

REFERENCES

- Newman KL, Stewart LM, Scott EM, Tielsch JM, Englund JA, et al. Assessment of indirect protection from maternal influenza immunization among non-vaccinated household family members in a randomized controlled trial in Sarlahi, Nepal. *Vaccine*. 2020;38(43):6826–6831.
- Omer SB, Richards JL, Madhi SA, Tapia MD, Steinhoff MC, Aqil AR, et al. Three randomized trials of maternal influenza immunization in Mali, Nepal, and South Africa: methods and expectations. *Vaccine*. 2015;33(32):3801–3812.
- Marshall H, McMillan M, Andrews RM, Macartney K, Edwards K. Vaccines in pregnancy: the dual benefit for pregnant women and infants. *Hum Vaccin Immunother*. 2016;12(4):848–856. doi:10.1080/21645515.2015.1127485
- King JC Jr, Stoddard JJ, Gaglani MJ, Moore KA, Magder L, McClure E. Effectiveness of school-based influenza vaccination. *N Engl J Med*. 2006;355:2523–2532.
- Piedra PA, Gaglani MJ, Kozinetz CA, Herschler G, Riggs M, Griffith M. Herd immunity in adults against influenza-related illnesses with use of trivalent live attenuated influenza vaccine in children. *Vaccine*. 2005;23:1540–1548.
- Loeb M, Russell ML, Moss L, Fonseca K, Fox J, Earn DJD, et al. Effect of influenza vaccination of children on infection rates in Hutterite communities: a randomized trial. *JAMA*. 2010;303:943–950.
- Gori M, Fappani C, Bianchi S, Tanzi E, Zuccotti GV, Amendola A. Exploring the pathway toward reduction of paediatric seasonal influenza burden: school-based vaccination and surveillance. *J Prev Med Hyg*. 2025;65(4):E469–E472.
- Yin JK, Heywood AE, Georgousakis M, King C, Chiu C, Isaacs D, et al. Indirect protection afforded by vaccinating children against seasonal influenza: a systematic review and meta-analysis. *Clin Infect Dis*. 2017;65(5):719–728.
- Centers for Disease Control and Prevention. Flu and children [Internet]. Atlanta: CDC;

- 2024 [cited 2026 May 18]. <https://www.cdc.gov/flu/highrisk/children.html>
10. World Health Organization. Influenza (seasonal) [Internet]. Geneva: WHO; 2025 [cited 2026 May 18]. Available from: [https://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))
11. World Health Organization. Vaccines against influenza: WHO position paper. *Wkly Epidemiol Rec.* 2012;87:461–476.
12. Hurwitz ES, Haber M, Chang A, Shope T, Teo S, Ginsberg M. Effectiveness of influenza vaccination of daycare children in reducing influenza-related morbidity among household contacts. *JAMA.* 2000;284:1677–1682.
13. Tsang TK, Fang VJ, Ip DKM, Perera R, So HC, Leung GM. Indirect protection from vaccinating children against influenza in households. *Nat Commun.* 2019;10:106.
14. GBD 2017 Influenza Collaborators. Mortality, morbidity, and hospitalizations due to influenza lower respiratory tract infections, 2017: an analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med.* 2019;7(1):69–89.
15. Zanobini P, Bonaccorsi G, Lorini C, et al. Global patterns of seasonal influenza activity, duration of activity and virus (sub)type circulation from 2010 to 2020. *Influenza Other Respi Viruses.* 2022;16(4):696–706. doi:10.1111/irv.12969
16. Coleman BL, Fadel SA, Fitzpatrick T, Thomas SM. Risk factors for serious outcomes associated with influenza illness in high- versus low- and middle-income countries: a systematic review and meta-analysis. *Influenza Other Respi Viruses.* 2018;12(1):22–29. doi:10.1111/irv.12504
17. Shrestha S, Jha P, Shrestha L, Chaudhary LB, Mulmi R, Govindakarnavar A, et al. Trend of influenza before and during the COVID-19 pandemic in Nepal—A study from 2018 to 2022. *PLoS One.* 2025;20(4):e0299610. doi:10.1371/journal.pone.0299610
18. Fischer WA 2nd, Gong M, Bhagwanjee S, Sevransky J. Global burden of influenza as a cause of cardiopulmonary morbidity and mortality. *Glob Heart.* 2014;9(3):325–336. doi:10.1016/j.ghart.2014.08.004
19. World Health Organization. National influenza programme: Nepal [Internet]. Geneva: World Health Organization; 2021 [cited 2026 May 18]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/363357/Nepal-eng.pdf>
20. Epidemiology and Disease Control Division (EDCD). National influenza surveillance reports. Kathmandu: Ministry of Health and Population, Government of Nepal; various years.
21. Sapkota A, Upadhyay BP. Prevalence and seasonality of influenza virus among pediatric population in Nepal, 2018. *Int J Infect Dis.* 2020;101(Suppl 1):526. Available from: [https://www.ijidonline.com/article/S1201-9712\(20\)32081-6/fulltext](https://www.ijidonline.com/article/S1201-9712(20)32081-6/fulltext)
22. Upadhyay BP, Banjara MR, Shrestha RK, Tashiro M, Ghimire P. Etiology of coinfections in children with influenza during 2015/16 winter season in Nepal. *Int J Microbiol.* 2018;2018:8945142. doi:10.1155/2018/8945142
23. Benjamin-Chung J, Arnold BF, Kennedy CJ, Mishra K, Pokpongkiet N, Nguyen A, et al. Evaluation of a citywide school-located influenza vaccination program. *PLoS Med.* 2020;17(8):e1003238. doi:10.1371/journal.pmed.1003238
24. Laibl VR, Sheffield JS. Influenza and pneumonia in pregnancy. *Clin Perinatol.* 2005;32(3):727–738.
25. Ciniola B, Conti MG, Terrin G, Sgrulletti M, Elfeky R, Carsetti R, et al. The protective role of maternal immunization in early life. *Front Pediatr.* 2021;9:638871. doi:10.3389/fped.2021.638871
26. White P, Baum D, Ross H, Falletta L, Reed M. Cocooning: influenza vaccine for parents and caregivers in an urban pediatric medical home. *Clin Pediatr.* 2010;49:1123–1128.
27. Moriarty LF, Omer SB. Infants and the seasonal influenza vaccine: a global perspective on safety, effectiveness, and alternate forms of protection. *Hum Vaccin Immunother.* 2014;10(9):2721–2728.
28. Mathema S, Uprety G, Baral P. Influenza vaccination during pregnancy: a descriptive study of knowledge, beliefs, and practices among Nepalese women. *J Perinat Soc Nepal.* 2024;3(1):11–14.
29. World Health Organization. Reducing missed opportunities for vaccination (MOV) [Internet]. Geneva: WHO; 2017 [cited 2026 May 18].
30. Kim DeLuca E, Gebremariam A, Rose A, Biggerstaff M, Meltzer MI, Prosser LA. Cost-effectiveness of routine annual influenza vaccination by age and risk status. *Vaccine.* 2023;41(29):4239–4248. doi:10.1016/j.vaccine.2023.04.069
31. Gharpure R, Chard AN, Cabrera Escobar M, Zhou W, Valleau MM, Yau TS, et al. Costs and cost-effectiveness of influenza illness and vaccination in low- and middle-income countries: a systematic review from 2012 to 2022. *PLoS Med.* 2024;21(1):e1004333. doi:10.1371/journal.pmed.1004333
32. Ostad-Ahmadi Z, Boccalini S, Daemi A, Mahboub-Ahari A. Cost-effectiveness analysis of seasonal influenza vaccination during pregnancy: a systematic review. *Travel Med Infect Dis.* 2023;55:102632. doi:10.1016/j.tmaid.2023.102632
33. NITAG Resource Center. Cost-effectiveness analysis of seasonal influenza vaccination during pregnancy: a systematic review [Internet]. [cited 2026 May 18]. Available from: <https://www.nitag-resource.org>
34. World Health Organization. Immunization coverage and planning: vaccine supply and access [Internet]. Geneva: WHO; [cited 2026 May 18].
35. Exemplars in Global Health. Vaccine delivery in Nepal: challenges [Internet]. [cited 2026 May 18].
36. Epidemiology and Disease Control Division (EDCD). Nepal. What one should know about seasonal influenza [Internet]. Kathmandu: Ministry of Health and Population; [cited 2026 May 18].
37. World Health Organization. Vaccines against influenza: WHO position paper – May 2022. *Wkly Epidemiol Rec.* 2022;97(19):185–208.
38. World Health Organization. How to implement influenza vaccination of pregnant women: an introduction manual for national immunization programme managers and policy makers [Internet]. Geneva: WHO; 2016 [cited 2026 May 18].
39. Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP) [Internet]. Atlanta (GA): CDC; 2025 [cited 2026 May 18].
40. Moriarty LF, Omer SB. Infants and the seasonal influenza vaccine: a global perspective on safety, effectiveness, and alternate forms of protection. *Hum Vaccin Immunother.* 2014;10(9):2721–2728.
41. World Health Organization. Influenza (seasonal) [Internet]. Geneva: WHO; 2025 [cited 2026 May 18].
42. Kroger A, Bahta L, Long S, Sanchez P. General best practice guidelines for immunization: best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Atlanta (GA): CDC; 2023.
43. Centers for Disease Control and Prevention. Flu and children [Internet]. Atlanta: CDC; 2024 [cited 2026 May 18]. Available from: <https://www.cdc.gov/flu/highrisk/children.html>
44. World Health Organization. Influenza surveillance outputs [Internet]. Geneva: WHO; [cited 2026 May 18].
45. World Health Organization. Global Influenza Surveillance and Response System (GISRS) [Internet]. Geneva: WHO; [cited 2026 May 18]. Available from: <https://www.who.int/teams/global-influenza-programme/global-influenza-surveillance-and-response-system>
46. World Health Organization. FluNet and FluID global platforms for influenza surveillance [Internet]. Geneva: WHO; [cited 2026 May 18]. Available from: <https://www.who.int/tools/fluNet>
47. World Health Organization. Strengthening influenza virological surveillance and laboratory capacity [Internet]. Geneva: WHO; [cited 2026 May 18].
48. World Health Organization. Nepal: WHO country cooperation strategy / immunization programme overview. Geneva: WHO; [cited 2026 May 18].
49. Pan American Health Organization. Cold chain resource center (vaccine storage temperatures) [Internet]. Washington (DC): PAHO; [cited 2026 May 18].
50. Centers for Disease Control and Prevention. Vaccine storage and handling toolkit [Internet]. Atlanta: CDC; 2023 (updated 2024) [cited 2026 May 18].
51. World Health Organization. Guidance on selecting, commissioning and using freeze-preventive vaccine carriers [Internet]. Geneva: WHO; 2021 Oct 25 [cited 2026 May 18].
52. World Health Organization. Guidance on selecting, commissioning and using freeze-preventive vaccine carriers (full text) [Internet]. Geneva: WHO; 2021 [cited 2026 May 18].
53. PATH. Preventing freezing in cold boxes and vaccine carriers [Internet]. Seattle: PATH; [cited 2026 May 18].
54. Kumar S, Lennon P, Muller N, Uranw S, Myundura M, Sibole A, et al. Using long-range freeze-preventive vaccine carriers in Nepal: A study of equipment performance, acceptability, systems fit, and cost. *Vaccine X.* 2022;10:100146.
55. Crosby LE, Real FJ, Cunningham J, Mitchell M. Overcoming vaccine hesitancy using community-based efforts. *Pediatr Clin North Am.* 2023;70(2):359–370.
56. World Health Organization. Cold chain and logistics management. Geneva: WHO; 2024. [cdn.who.int]
57. World Health Organization. Prequalification of health products. Geneva: WHO; 2026. Available from: <https://www.who.int/news-room/fact-sheets/detail/prequalification-of-medicines-by-who> [who.int]
58. Scheifele DW, Skowronski DM, King A, LaJeunesse CA, Bjornson GL, Parkyn H, Walken N, Stefura E. Evaluation of ready-to-use and multi-dose influenza vaccine formats in large clinic settings. *Can J Public Health.* 2000;91(5):329–332. [pmc.ncbi.nlm.nih.gov]
59. Benhamou D, Weiss M, Borms M, Lucaci J, Girgis H, Frolet C, Baisley WT, Shoushi G, Cribbs KA, Wenk M. Assessing the clinical, economic, and health resource utilization impacts of prefilled syringes versus conventional medication administration methods: a systematic review. *Ann Pharmacother.* 2024;58(9):921–934. [journals.sagepub.com]
60. Regan AK, Bloomfield L, Peters I, Effler PV. Randomized controlled trial of text message reminders for increasing influenza vaccination. *Ann Fam Med.* 2017;15(6):507–514. [annfammed.org]
61. Szilagyi PG, Duru OK, Casillas A, Ong MK, Vangala S, Tseng CH, Albertin C, Humiston SG, Clark E, Ross MK, Evans SA, Sloyan M, Fox CR, Lerner C. Text vs patient portal messaging to improve influenza vaccination coverage: a health system-wide randomized clinical trial. *JAMA Intern Med.* 2024;184(5):519–527. [pmc.ncbi.nlm.nih.gov]
62. Schmid P, Rauber D, Betsch C, Lidolt G, Denker ML. Barriers of influenza vaccination intention and behavior: a systematic review. *PLoS One.* 2017;12(1):e0170550. [journals.plos.org]
63. Alzeer AA, Alfantouk LA, Theneyan A, Bin Eid F, Almangour TA, Alshememry AK, Alhossan AA. The influence of demographics on influenza vaccine awareness and hesitancy among adults visiting an educational hospital in Saudi Arabia. *Saudi Pharm J.* 2021;29(2):188–193. [pmc.ncbi.nlm.nih.gov]