

# Improving Influenza Vaccine Uptake in Low- and Lower-Middle-Income Countries: A Synthesis of Interventions and Strategic Recommendations

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Seasonal influenza continues to impose a significant health and economic burden on low- and lower-middle-income countries (LLMICs), where vaccine uptake remains critically low. Despite proven benefits of vaccination, the implementation of successful influenza vaccination strategies in these regions is hindered by a complex interplay of multiple barriers, including limited resources, evidence gaps, infrastructural challenges, and socio-cultural factors. Although lessons from high-income countries offer valuable insights, their direct application in resource-constrained settings without contextual adaptation is often ineffective. Exploring the underlying barriers and developing successful interventions tailored to the unique realities of LLMICs is critical, as influenza poses a threat for the next potential pandemic. Multifaceted strategies incorporating culturally informed and risk group-specific interventions, including healthcare provider engagement for vaccine recommendations, promoting local research, leveraging existing platforms, strengthening surveillance systems, and fostering international and domestic support, can facilitate inclusive evidence-based policymaking.

**Keywords.** developing countries; influenza; intervention; health policy; vaccines.

## INTRODUCTION

Seasonal influenza imposes a significant global public health challenge. Fifteen percent of the global population is infected by the influenza virus each year [1]. The World Health Organization (WHO) links influenza to 3–5 million cases of severe respiratory illness and 290 000–650 000 fatalities annually [2]. The challenges are most apparent in low-income countries (LICs) and lower-middle-income countries (LMICs) by World Bank income category, where the prevalence of respiratory infections is high and the influenza vaccination is rarely utilized [3–5]. As a result, the burden affects the low- and lower-middle-income countries (LLMICs) disproportionately.

From 2014 to 2018, there was a net increase in the number of countries with national seasonal influenza vaccination policies. The 15 new countries of 2018 included only 2 LICs and 9 upper-middle-income countries (UMICs) and high-income countries (HICs). Policies were most frequent in the WHO Region of the Americas and the WHO European Regions and less frequent in other regions [6]. Eighty-five percent of nations without a policy belong to the LLMICs, which constitute 40% of the world's population and have a high influenza burden [7]. High-income countries and some UMICs have developed robust interventions to improve their seasonal influenza vaccination coverage. These include public health campaigns, easy vaccine access and availability, and health policies for high-risk populations [6, 8, 9]. These interventions have significantly reduced the frequency and intensity of influenza outbreaks in HICs.

However, the interventions implemented in HICs are, in most cases, if not all, not suitable for low-income settings due to differences in demographic and socioeconomic factors. Hence, many flu-specific strategies did not work well when implemented in low-income settings. Learning from what worked in HICs is important, but it is also equally important to have a deeper understanding of the unique challenges LLMICs face.

This analysis investigates the complexities of seasonal influenza vaccine (SIV) interventions in LICs and LMICs and the reasons behind the less effectiveness of HIC models in these regions. The analysis considers socioeconomic, cultural,

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infrastructural, and policy-related factors, offering insights into tailored strategies that could improve the effectiveness of influenza vaccination programs in LLMICs.

### THE BURDEN OF SEASONAL INFLUENZA IN LLMICs

The scarcity of high-quality health burden data from LLMICs obscures the actual picture of the impact of influenza. However, the latest modeling study by Iuliano et al [2] reveals that, compared to HICs and UMICs, influenza-associated mortality had a wider range in LLMICs (112 881–420 841 annual deaths), and Southeast Asia, Eastern Mediterranean, and Sub-Saharan Africa showed the greatest variation. The highest proportion (25%) of total global influenza-associated respiratory deaths belonged to Southeast Asia, 8 out of 11 countries of which belong to the LLMICs. The proportion of total influenza-associated respiratory deaths in LMICs alone across all age groups was 36% of total deaths [2].

Approximately 0.5–29 per 100 000 children under 5 years old died annually due to influenza-associated illness across the countries of sub-Saharan Africa, where 28 out of 47 belong to the LLMIC group [2]. Another previous meta-analysis showed that the risk of severe outcomes in the children <5 years old age group was 50% higher than the older age group and pregnant women had an increased risk of 66% of severe outcomes than nonpregnant women in the low- and middle-income nations [10].

Cost analyses are rarely standardized across nations. Low- and lower-middle-income countries are very underrepresented in such studies or very few works are available. As a result, the true economic impact of seasonal influenza in LLMICs is unclear. Nonetheless, reviews have found that compared to high-income economies, direct costs in LLMICs were lower, and productivity losses through indirect costs were higher [11]. The national economic burden of influenza illness among the general population was 0.01%–7% of the national health expenditure and highest in Bangladesh, an LMIC [7]. It was also

found that India’s overall economic losses from the pandemic influenza ranged from \$9.3 to \$33.6 billion, or 1.8 to 5.8 percentage points of Gross domestic product (GDP) [11].

Seasonal influenza presents significant public health challenges in the LLMICs. The complex interplay among limited healthcare resources, low vaccination and high mortality rates, economic impact due to direct and indirect healthcare costs, loss of productivity, underreporting due to incomplete and inadequate surveillance, and lack of vaccination strategies and policies results in a high national burden of the disease (Figure 1). In resource-constrained settings of the LLMICs, limited resources is one of the primary and the most influential factors that control the rest of the crucial dynamics for influenza management and vaccination strategies. Inadequate resource restricts the surveillance capacity, local research on the vaccine efficacy, cost-effectiveness and other evidence generation [12]. Lack of an effective surveillance system hampers accurate and adequate data collection, resulting in evidence gaps, which include seasonality of the disease, circulating strains and local monitoring of the vaccine effectiveness [13].

Economic considerations, coupled with evidence gaps, affect the national influenza vaccination policy, strategy and finally vaccination [12]. The evidence gap and inadequate resources are themselves direct barriers to local vaccine uptake [12]. Influenza vaccination reduces the infection and the severity of the disease, and vice versa. High infection rates and increased severity of the disease due to the lack of vaccination cause high mortality, increased healthcare costs, and loss of productivity, all 3 of which add up to the national burden of disease.

### INFLUENZA VACCINE UPTAKE ACROSS ALL RISK GROUPS IN LLMICs

#### Vaccine Uptake

The scenario of the SIV uptake rate in the LLMICs is very upsetting (Table 1). Only 2 out of 26 (8%) countries belonging to LICs

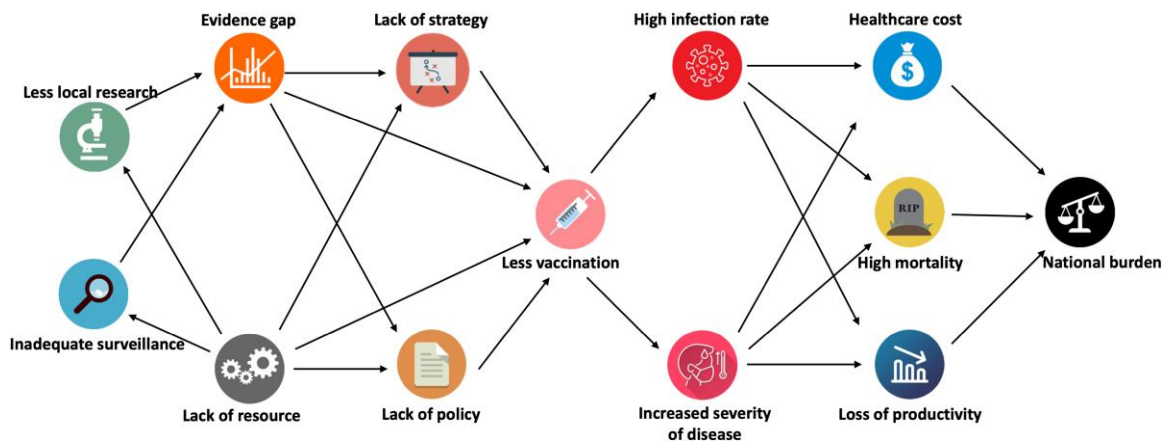


Figure 1. Flowchart of the dynamics of high national burden of influenza in low-resource settings.

**Table 1. Latest Reported Seasonal Influenza Vaccine Uptake Rates by September 2024 in LLMICs According to the World Bank 2025 Fiscal Year [5, 14]**

Country	Seasonal Influenza Vaccine Uptake Rate (%)				
	Health Care Workers	Children Under 5 Years Old	Pregnant Women	Elderly Individuals (>65 years)	Individuals With Chronic Medical Conditions
Low-income countries (4/26) (GNI per capita \$1145 or less in 2023) [5]					
Afghanistan	18 (2021) [15]	...	...	...	...
DPRK	...	96.4 (2022)	...	96.4 (2022)	...
Guinea-Bissau	...	60 (2010) [16]	...	...	...
The Sierra Leone	6.5 (2006) [17]	91 (2020)	...	...	...
Lower-middle-income countries (19/51) (GNI per capita \$1146 to \$4515 in 2023) [5]					
Bangladesh	4.6 (2022) <sup>a</sup>	...	...	...	...
Bhutan	50.41 (2023)	74 (2023)	50 (2023)	79 (2023)	100 (2023)
Bolivia	34 (2023)	31.19 (2023)	49 (2023)	55 (2023)	100 (2022)
Côte d'Ivoire	82 (2023)	...	...	...	...
Egypt, Arab Rep	30.7 (2019) [18]	...	...	...	...
Honduras	91 (2023)	47 (2023)	67 (2023)	73 (2023)	100 (2022)
India	4.4 (2012) [19]	...	...	1.1 (2017–18) [20]	2.1 (2017–18) [20]
Jordan	100 (2019)	...	...	...	...
Kenya	...	20 (2019)	...	...	...
Kyrgyz Rep	72 (2023)	29 (2023)	2.24 (2023)	3.5 (2023)	13 (2023)
Lebanon	100 (2023)	...	...	100 (2023)	100 (2023)
Morocco	50 (2019)	...	1 (2016) [21]	...	68 (2019)
Nicaragua	100 (2023)	100 (2015)	98 (2023)	97 (2022)	100 (2023)
Pakistan	21 (2022) [22] 44 (2021) [23]	...	...	...	...
Philippines	...	.....	...	23 (2023)	...
Tajikistan	88 (2023)	...	...	...	...
Tunisia	64 (2021)	...	4.6 (2019) [24]	...	19.4 (2018–19) [25]
Uzbekistan	100 (2023)	94 (2023)	0 (2020)	97 (2023)	100 (2021)
Vietnam	48 (2017) [26]	...	...	...	...

Literature was manually searched on Google Scholar and PubMed for the countries that have not reported their data to the above-mentioned database through the WHO-UNICEF joint reporting form.

Abbreviations: LLMICs, low- and lower-middle-income countries; WHO, World Health Organization; GNI, gross national income; DPRK, The Democratic People's Republic of Korea.

<sup>a</sup>Hassan MZ, unpublished data.

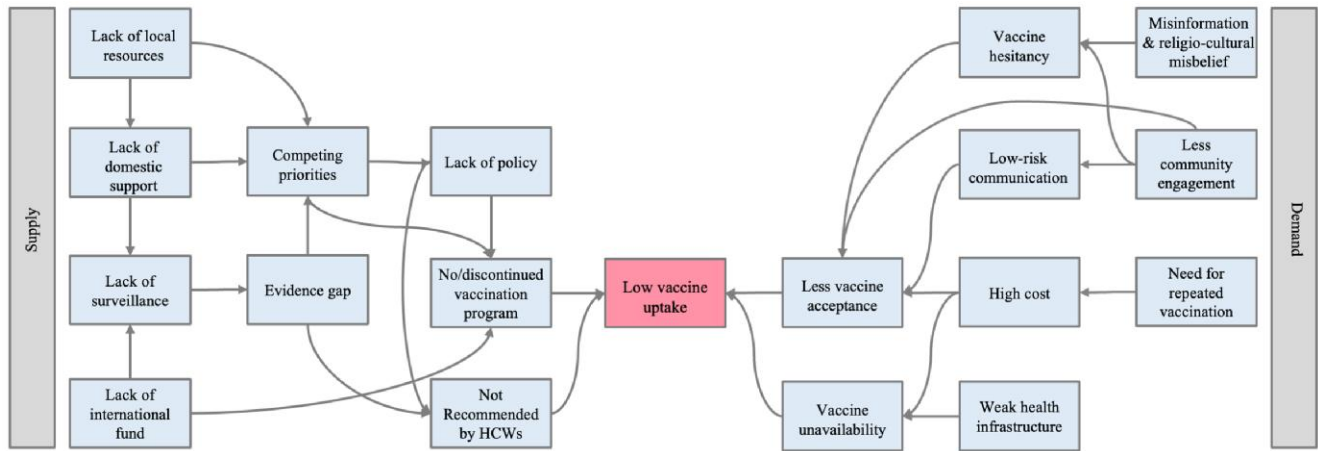
have ever reported their national influenza vaccine uptake rates through the WHO-UNICEF joint reporting form until 2024. Besides the absence of up-to-date data, the reliability of the data is also questionable for some countries. The unavailability of data for most of the LICs indicates a critical gap in the vaccination efforts for the high-risk groups in most of the countries.

Healthcare workers (HCWs) were the most vaccinated group in the LMICs, although the number is scanty. Fourteen out of 51 (28%) LMICs have ever reported national influenza vaccination data of at least one risk group through the joint reporting form till 2024. Rates of 5 other countries were found in the literature, although those were not nationally representative data. In 2023, 8 countries reported vaccinating HCWs, except for 2, the remaining 6 countries had 72%–100% vaccination rates. Bhutan (74%) and Uzbekistan (94%) had high vaccination rates in under 5 children recently. Nicaragua had almost full coverage (98%) of pregnant mothers in 2023. Out of the 7 countries that reported on the elderly population in 2023, Bhutan, Honduras, Lebanon, and Uzbekistan had high vaccination rates. Only Bhutan, Lebanon, and Nicaragua reported

100% vaccination rates in individuals with chronic diseases in 2023. Although Bolivia, Honduras, and Uzbekistan reported 100% coverage in the previous years, their current status remains unknown. Although the coverage is very high in a few of the countries, it is critically low in most.

#### Why Vaccine Uptake Is Low in LLMICs

During 2023, nearly a billion doses of SIVs were procured globally, but <3% were consumed in LLMICs [27]. Vaccine uptake in LLMICs is influenced by and is a result of complex interplay of a combination of barriers including accessibility issues, vaccine hesitancy and systemic challenges such as healthcare infrastructure limitations and socioeconomic factors (Figure 2). We can roughly categorize the determinants into two groups: supply-related and demand-related factors. On the supply side, economic barriers can be multifaceted and the lack of domestic financial support and international funds for establishment and maintenance of seasonal influenza surveillance and vaccination programs is the most critical aspect [12]. Evidence gap in influenza-related burden, burden averted by,



**Figure 2.** Determinants of low vaccine uptake in resource-limited settings.

and cost-effectiveness of the vaccination also obliterate the urgency and priority of national vaccination programs. Lack of surveillance is responsible for the local evidence gap related to morbidity, mortality, seasonality, circulating strains, local outbreaks, etc. that play critical role in the formulation of effective policy and strategy [28]. Competing health priorities often overshadow the threats posed by influenza infection in low-resource settings.

On the other side, vaccine acceptance is dependent on multiple factors, such as misinformation, religious and cultural belief, community engagement, and high cost which collectively hinders the demand growth. Low vaccine acceptance is often a result of knowledge gap of the receiver due to inadequate risk communication due to inadequate community engagement [12]. Social, cultural, behavioral, and religious beliefs, misconceptions, and misinformation prevail in some communities, which have direct impact on vaccine acceptance and uptake [29].

### SUCCESSFUL INTERVENTIONS USED TO INCREASE INFLUENZA VACCINE UPTAKE IN HICS AND UMICS

The approach to interventions for increasing the influenza vaccine uptake widely varies between countries, depending on their national economy. Robust healthcare system, adequate public awareness, and substantial funding opportunities contribute to widespread vaccination policies and higher vaccination coverage in HICs and UMICs. However, despite economic growth, UMICs may face barriers like withdrawal of international support that ultimately curb their capacity leading to logistical insufficiency [30].

#### Healthcare Workers

Our investigation into the interventions revealed some successful interventions among different risk groups across the HICs and UMICs (Table 2). Interventions with multiple

components, such as educational materials, reminders, flexible or worksite delivery, and committed staff coordination, were more successful than single interventional studies. Where the uptake rate was only 45% despite free vaccination, an increment to 86% was seen in just a single season [31]. Flexible worksite delivery when implemented alongside educational interventions played a pivotal role in another large scale influenza vaccination campaign among HCWs in Brazil [35]. A unique intervention like filling up a mandatory declination statement if the vaccine is declined along with reminders and incentives gave rise to an additional 25% increase in the vaccine uptake rate even when HCWs had to pay for their shots [32]. Finland being the first country to mandate flu vaccines for HCWs nationwide achieved almost 30% increase in the first season [36]. The implementation of mandatory flu vaccination is a controversial strategy. However, research indicates that these regulations can greatly help achieve the benchmark immunization rate of 75%, safeguarding both patients and health-care workers [59].

#### Adults With Comorbidities

A computerized reminder system generating individualized preventive care reminders for inpatients admitted to a general medicine service, which were displayed to their physicians, was found to yield a 50% higher vaccination rate than in the control group [38]. Standing order program (SOP) can effectively increase vaccination rates and reduce missed opportunities by enabling nonphysician medical personnel to assess patients' immunization status and needs, allowing them to administer vaccinations without direct involvement from a physician [60]. Multiple studies with SOP intervention combined with provider or receiver education programs successfully increased the influenza vaccine uptake rate by 9%–43% among the comorbid adults [39–42]. We believe that hospitalization

**Table 2. Interventions Used to Increase Influenza Vaccine Uptake Across Various Risk Groups by World Bank Income Category [5]**

Place of Study	Author (Year)	Type of Study	Previous Interventions or Components (Before and Continued During the Intervention Program/Used in Control Group in Case of Trial)	New Interventions or Components (Added to Previous Season/Used in Intervention Group in Trial)	Study Population (at Baseline/Intervention and Control Group)	Outcome Measure (at Baseline/Intervention Group)	Outcome Measure (at Endline/Intervention Group)	Increase in Outcome Measure (From Baseline/Intervention Group)	
<b>HICs and UMICs</b>									
<b>HCW</b>									
United States	McCullers et al (2006) [31]	Influenza vaccine campaign	<ul style="list-style-type: none"> <li>Free vaccine</li> <li>Educational campaign</li> </ul>	<ul style="list-style-type: none"> <li>Reminders</li> <li>Flexible and worksite delivery</li> <li>Feedback</li> <li>Dedicated staff assignment</li> </ul>	702	Vaccine uptake	45%	86%	41%
	Ribner et al (2008) [32]	Influenza vaccine campaign	<ul style="list-style-type: none"> <li>No free vaccine</li> <li>Educational material</li> <li>Flexible and worksite delivery</li> <li>Feedback</li> </ul>	<ul style="list-style-type: none"> <li>Reminder</li> <li>Incentives</li> <li>Mandatory declination statement</li> </ul>	9214	Vaccine uptake	43%	67%	24%
Spain	de Juanes et al (2007) [33]	Cohort study	<ul style="list-style-type: none"> <li>Free vaccine</li> <li>Educational material</li> <li>Reminder</li> </ul>	<ul style="list-style-type: none"> <li>Flexible and worksite delivery</li> </ul>	5718	Vaccine uptake	21%	40%	19%
	Lupiá et al (2010) [34]	Before after trial	<ul style="list-style-type: none"> <li>Free vaccine</li> <li>Educational material</li> <li>Flexible and worksite delivery</li> </ul>	<ul style="list-style-type: none"> <li>Reminders</li> <li>Incentives</li> <li>Feedback</li> </ul>	4783	Vaccine uptake	24%	37%	13%
Brazil	Lopes et al (2008) [35]	Influenza vaccine campaign	<ul style="list-style-type: none"> <li>Free vaccine</li> </ul>	<ul style="list-style-type: none"> <li>Educational material</li> <li>Educational sessions</li> <li>Flexible and worksite delivery</li> </ul>	20 000	Vaccine uptake	6%	45%	39%
Finland	Hämäläinen et al (2021) [36]	...	Unknown	Mandatory vaccination	821	Vaccine uptake	68.2%	95.4%	27.2%
Austria	Boyer et al (2023) [37]	Intervention study	NA	<ul style="list-style-type: none"> <li>Residents:</li> <li>Reminders</li> <li>Educational session</li> <li>Educational material</li> <li>Worksite delivery</li> </ul>	377 (Residents)	Vaccine uptake	5.8%	19.1%	13.3%
			HCW:	<ul style="list-style-type: none"> <li>Reminder</li> <li>Educational session</li> <li>Worksite delivery</li> <li>Free vaccine—incentives</li> </ul>	234 (HCW)	Vaccine uptake	1.3%	19.7%	18.4%

**Table 2. Continued**

Place of Study	Author (Year)	Type of Study	Previous Interventions or Components (Before and Continued During the Intervention Program/Used in Control Group in Case of Trial)	New Interventions or Components (Added to Previous Season/Used in Intervention Group in Trial)	Study Population (at Baseline/Intervention and Control Group)	Outcome Measure (at Baseline/Intervention Group)	Outcome Measure (at Endline/Intervention Group)	Increase in Outcome Measure (From Baseline/Intervention Group)
<b>HICs and UMICs</b>								
<b>Adults with Comorbidities</b>								
United States	Dexter et al (2001) [38]	RCT study	Reminders not displayed	<ul style="list-style-type: none"> <li>• Rule-based computerized reminders displayed to the physicians</li> </ul>	10 065 (inpatients) Intv = 4995 Ctrl = 5070	Vaccine uptake 1.0%	51.4%	50.4%
	Bourdet et al (2003) [39]	Nonrandomized trial study	None	<ul style="list-style-type: none"> <li>• Eligibility screening (by pharmacists)</li> <li>• SOP (by pharmacists)</li> <li>• Patient education</li> </ul>	1303 (inpatients) Intv = 542 Ctrl = 761	Vaccine uptake Ctrl = 0.8%	Intv = 9.8%	9%
	Donato et al (2007) [40]	Nonrandomized trial study	None	<ul style="list-style-type: none"> <li>• Intv 1 = Physician reminders</li> <li>• Intv 2 = SOP</li> <li>• Intv 3 = SOP with a provider education program</li> </ul>	654 (inpatients) Intv 1 = 287 Intv 2 = 197 Intv 3 = 170	Vaccine uptake ...	Intv 1 = 3% Intv 2 = 21% Intv 3 = 43%	43%
	Rees et al (2011) [41]	Prepost intervention study	None	<ul style="list-style-type: none"> <li>• SOP</li> <li>• Visual and verbal reminders</li> <li>• Electronic alerts</li> </ul>	5846 (inpatients) Pre = 2538 Post = 3308	Vaccine uptake (Preintv = average 45%;	Postintv = 78%)	33%
	Cohen et al (2015) [42]	Prepost intervention study	Automated clinical reminder system for patients	<ul style="list-style-type: none"> <li>• Hospital-wide campaign</li> <li>• EMR embedded vaccine order</li> <li>• Reminders</li> <li>• SOP on discharge</li> </ul>	Not reported	Vaccine uptake (Preintv = 60%;	Postintv = ~80%),	20%
Spain	Esteban-Vasallo et al (2019) [43]	quasi-experimental prepost intervention study	None	SMS reminders	69 040 Case = 60 205 Ctrl = 8835	Vaccine uptake 7.1%	9.3%	2.2%

**Table 2. Continued**

Place of Study	Author (Year)	Type of Study	Previous Interventions or Components (Before and Continued During the Intervention Program/Used in Control Group in Case of Trial)	New Interventions or Components (Added to Previous Season/Used in Intervention Group in Trial)	Study Population (at Baseline/Intervention and Control Group)	Outcome Measure Type	Outcome Measure (at Baseline/Intervention Group)	Outcome Measure (at Endline/Intervention Group)	Increase in Outcome Measure (From Baseline/Intervention Group)
<b>HICs and UMICs</b>									
<b>Older adults</b>									
United States	Veltri et al (2009) [44]	Intervention study	NA	<ul style="list-style-type: none"> <li>SOP (for pharmacists)</li> <li>Patient education</li> </ul>	5855 (inpatients <65 y)	Encounter rates	27%;	55%	28%
Thailand	Worasathit et al (2015) [45]	Quasi-experimental trial	None	Video-led educational intervention	2693 Intv = 1402 Ctrl = 1291	Willingness to pay	72.2%	82.1%	9.9%
Hong Kong	Leung et al (2017) [46]	RCT	None	Educational session (face to face for 3 min)	529 Intv = 265 Ctrl = 264	Vaccine uptake	25%	33.6%	8.6%
China	Wu et al (2022) [47]	Quasi-experimental pragmatic trial	Educational material	Pay-it-forward (free vaccine)	150	Vaccine uptake	20%	60%	40%
	Jiang et al (2022) [48]	Community-based RCT	None	Video-led educational intervention	350 Intv = 175 Ctrl = 175	Vaccine uptake	3.4%	10.3%	6.9%
<b>Pregnant women</b>									
United States	Ogburn et al (2007) [49]	Retrospective Cohort	Provider education, screening protocol, vaccine availability	SOP (for nurses)	NA	Vaccine uptake	2003–2004 1%	2004–2005 37%	36%
	Mouzoon et al (2010) [50]	Retrospective cohort	Standard care: routine ANC	<ul style="list-style-type: none"> <li>SOP</li> <li>Provider education</li> <li>Provider feedback</li> <li>Routine ANC</li> <li>Provider reminder</li> </ul>	2023	Vaccine uptake	2003–2004 2.5%	2008–2009 (37.4%)	35%
	Sherman et al (2012) [51]	Retrospective cohort	Standard care: routine ANC	<ul style="list-style-type: none"> <li>Provider feedback</li> <li>Routine ANC</li> <li>Provider reminder</li> </ul>	1367	Vaccine uptake	2003 14.7%	2005 51.6%	36.9%
	Stockwell et al (2014) [52]	RCT	Usual care, standard automated telephone appointment reminders	SMS reminder	1187 Intv = 593 Ctrl = 594	Vaccine uptake	2003 46.6%	2005 49.3%	2.7%
	Meharry et al (2014) [53]	RCT	Standard care: routine ANC	<ul style="list-style-type: none"> <li>Pamphlet</li> <li>Educational material</li> <li>A verbalized benefit statement: “vaccinating pregnant woman also benefits the young infant”</li> </ul>	133 Intv 2 = 36 Ctrl = 49	Vaccine uptake	47%	86%	39%

**Table 2. Continued**

Place of Study	Author (Year)	Type of Study	Previous Interventions or Components (Before and Continued During the Intervention Program/Used in Control Group in Case of Trial)	New Interventions or Components (Added to Previous Season/Used in Intervention Group in Trial)	Study Population (at Baseline/Intervention and Control Group)	Outcome Measure Type	Outcome Measure (at Baseline/in Control Group)	Outcome Measure (at Endline/in Intervention Group)	Increase in Outcome Measure (From Baseline/in Intervention Group)
<b>HICs and LMICs</b>									
Greece	Maltezou et al (2019) [54]	Cross-sectional	NA	<ul style="list-style-type: none"> <li>• Recommendation (from obstetrician)</li> <li>• Educational material (leaflet)</li> </ul>	304	Vaccine uptake	<2%	19.5%	17.5%
Under 5 children Hong Kong	Yeung et al (2018) [55]	RCT	VSS	<ul style="list-style-type: none"> <li>• Educational material</li> <li>• Semi-completed forms to utilize the subsidy</li> <li>• Contacts of VSS clinics</li> <li>• SMS reminder</li> </ul>	833 Intv = 416 Ctrl = 417	Vaccine uptake	13%	Year 1: 35% Year 2: 38%	Year 1: 22% Year 2: 25%
China	Wu et al (2022) [47]	Quasi-experimental pragmatic trial	Educational material	Pay-it-forward (free vaccine for the next person)	150	Vaccine uptake	53%	88%	35%
Australia	Tuckerman et al (2023) [56]	RCT	<ul style="list-style-type: none"> <li>• Vaccine availability</li> <li>• Clinical nudge (Vaccine reminder stickers on clinical notes for physicians)</li> </ul>	<ul style="list-style-type: none"> <li>• SMS reminder</li> <li>• Parent-level nudge (educational advice for in patients)</li> <li>• Clinical nudge</li> </ul>	600 Intv = 298 Ctrl = 302	Vaccine uptake	Ctrl 26.2%	Intv 38.6%	12.4%
<b>LMICs and LMICs</b>									
Pregnant women Nicaragua	Arriola et al (2018) [57]	Survey	NA	Recommendation and offer by physician	1223	Vaccine uptake	5% (not recommended or offered)	95% (both recommended and offered)	90%
Tunisia	Dhaouadi et al (2022) [24]	CS	NA	Recommendation by physician	1157	Willingness to receive in the next pregnancy	4.6%	81% (recommended but not offered) 74.5% (will receive if recommended by doctor)	76% 70% 56%

**Table 2. Continued**

Place of Study	Author (Year)	Type of Study	Previous Interventions or Components (Before and Continued During the Intervention Program/Used in Control Group in Case of Trial)	New Interventions or Components (Added to Previous Season/Used in Intervention Group in Trial)	Study Population (at Baseline/Intervention and Control Group)	Outcome Measure Type	Outcome Measure (at Baseline/in Control Group)	Outcome Measure (at Endline/in Intervention Group)	Increase in Outcome Measure (From Baseline/in Intervention Group)
HICs and LMICs									
Pakistan	Khan et al (2015) [58]	CS	NA	Recommendation by physician	283	Willingness to receive in the next pregnancy	0% (unvaccinated population)	87% (willing to accept vaccine if offered)	56% (will receive if recommended by doctor)
Adults with comorbidities Tunisia	Kharroubi et al (2021) [25]	CS	NA	Recommendation by physician	1 191	Willingness to receive in the next season	19.4%	64.7%	41%

Abbreviations: ANC, antenatal care; CS, cross-sectional study; Ctrl, control group; EMR, electronic medical record; HCW, healthcare worker; HICs, high-income countries; Intv, intervention group; LICs, low-income countries; LMICs, lower-middle-income countries; NA, not applicable; RCT, randomized control trial; SMS, short message service; SOP, standing order procedure; UMICs, upper-middle-income countries; VSS, Vaccination Subsidy Scheme.

provides an opportunity to reach the target population in an environment where appropriate intervention from the health-care provider end can modify the recipients' health-seeking behavior. These findings emphasize the importance of systemic changes inside the healthcare institution, particularly at the point of care to influence the provider behavior.

**Older Adults**

Community-based strategies, including educational interventions, video resources, and “pay-it-forward” models, were used for older adults. A recent study in China achieved a 40% higher vaccine uptake in the intervention group using the “pay-it-forward” method, where the intervention group were offered to voluntarily donate any amount of money for a future participant [47]. Although this method yielded a high vaccine uptake, we believe the scenario in the LMICs and LICs would be different due to the high cost of the vaccine in comparison to the cost of living. Video-led educational intervention in Thailand was found to increase the willingness to pay for the vaccine [45]. Gains in these populations were generally lower than institutional interventions like SOP and patient education by HCWs or inpatient settings in older adults with comorbidities. However, these small changes are still significant as the baseline uptake rates are traditionally low.

**Pregnant Women**

Provider-focused interventional strategies including provider reminders, provider education and standing order programs were prevalent among different studies on pregnant mothers. A retrospective cohort study revealed that provider-focused reminders alone increased the influenza vaccine uptake by 37% within 2 consecutive seasons in this population [51]. A similar increase in vaccine uptake was reported in 5 seasons by integrating provider-focused interventions and standing orders with the standard routine antenatal care for pregnant mothers [50]. However, SOP for nurses to screen for and administer influenza vaccine without consulting a physician alone gave rise to 36% vaccine uptake in one season in the United States [49]. Tailored verbal messages for the mothers were highly effective when used alongside educational materials [53].

**Under 5 Children**

Several intervention strategies were evaluated to improve the influenza vaccination rates in children under 5 years old. The Hong Kong government launched the Childhood Influenza Vaccination Subsidy Scheme (VSS) in 2015 to promote and support influenza vaccination [61]. A randomized control trial in Hong Kong found 13% vaccine uptake after subsidy in the control group, whereas the intervention group parents receiving explanatory telephone call, contacts of VSS clinics, prefilled vaccination forms, and short message service (SMS) reminders multiple times showed 35% and 38% uptake rates in the next 2

consecutive years [55]. The pay-it-forward method in China attained a 35% rise in the uptake [47]. The combination of financial support, parental education, and repeated reminders can effectively raise the flu vaccine uptake in the minors.

## EVIDENCE FROM LLMICS

Studies where vaccine uptake or other related outcomes were measured before or after an intervention were extremely scarce. We have included all available open-access literature from LLMICs till September 2025 in this review (Table 2). A Pakistani study in 2015 found that 56% of participating pregnant women would receive the influenza vaccine during their next pregnancy if their doctors recommended it [58]. Similar findings were recorded in Tunisia, where 74.5% of pregnant women expressed their willingness to receive it in their next pregnancy if recommended by the doctors [24]. A survey in Nicaragua revealed that the influenza vaccine uptake among pregnant women who were neither recommended nor offered the vaccine was only 5%. Whereas the uptake rate was 76% higher among the group which was recommended and 90% higher among those who were both recommended and offered [57]. Similar results were seen in the case of adults with comorbidities in Tunisia as well [25].

Vaccine recommendation by HCWs has always played a pivotal role in enhancing vaccine uptake among patients, as HCWs are key players in shaping public health practices and behavior. When seeking medical advice, patients typically trust their healthcare providers more than any other sources. Therefore, a recommendation from physicians, nurses, or other HCWs related to patient care is proven to significantly improve the vaccination uptake in different vaccines [62].

## STRATEGIES AND RECOMMENDATIONS TO IMPROVE INFLUENZA VACCINE UPTAKE IN LLMICS

Promising influenza vaccine uptake strategies and interventions in LLMICs should be characterized by multiple interrelated attributes, including demonstrable effectiveness, contextual appropriateness, financial feasibility within existing health systems, cost-effectiveness, scalability, and sustainability [63]. Studies have shown that multicomponent interventions, particularly those addressing both demand and supply barriers, are more effective and sustainable than single-component approaches [64]. In LLMIC contexts, with prevalent resource constraints and inequities in access, interventions must additionally demonstrate affordability and integration within existing platforms. Finally, to ensure long-term sustainability and responsiveness to changing epidemiological and behavioral dynamics, continuous monitoring, evaluation, and adaptation are necessary [65].

We propose a pragmatic, phased framework for influenza vaccination in LLMICs balancing feasibility with impact. In such settings, a hybrid approach where national-level policy

and international or combined financing provide an enabling environment, while community-based or grassroots strategies drive demand generation and local acceptability. Targeting some of the high-risk groups rather than attempting universal coverage initially, strategies may integrate into existing platforms (Figure 3). Key points from the framework are further discussed in detail below.

### Local Evidence Generation

Comprehensive, context-specific data regarding influenza vaccination, including the facilitators, barriers, willingness to pay, etc., among various at-risk populations and socioeconomic groups, are crucial for developing tailored interventions. The Health Ministry, universities, and other research organizations should conduct such studies, essential to enhance the vaccine coverage and support evidence-based policy formulation.

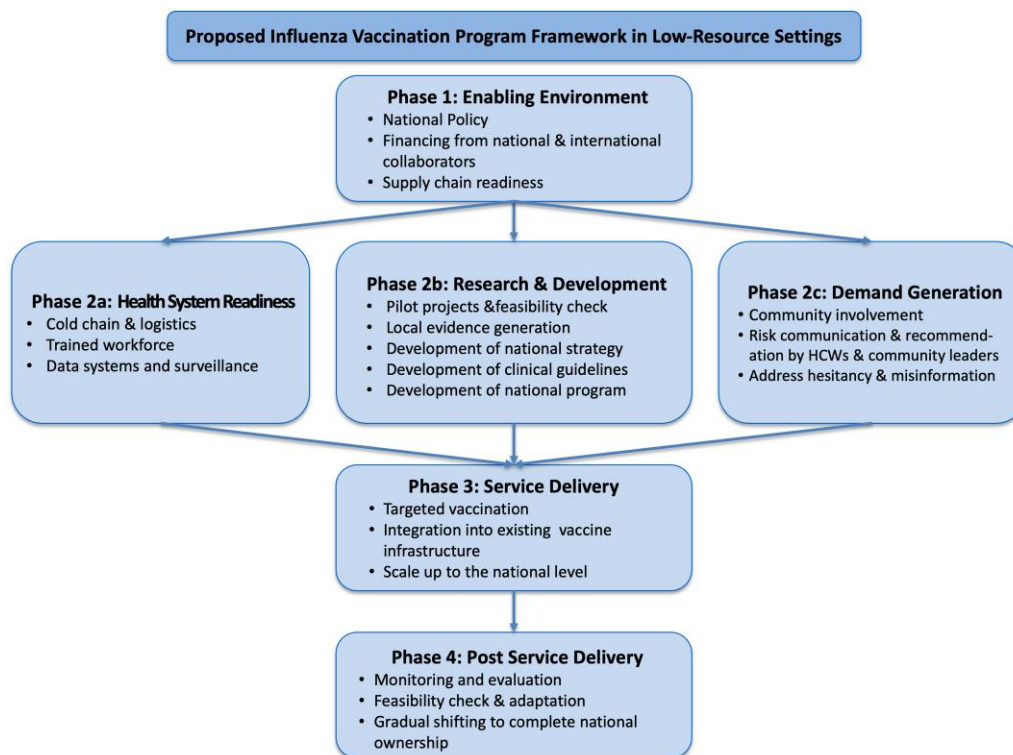
To understand the cultural, behavioral, and socioeconomic aspects impacting vaccination decisions, qualitative research is essential in addition to extensive quantitative studies. The WHO has developed effective tools to understand the behavioral and social drivers (BeSD) of vaccination [65]. The cost-effectiveness and burden averted by vaccination analyses on the potential reduction of hospitalizations, deaths, and health expenditure attributable to vaccination offer compelling perspectives and valuable insights for policymakers and health economists. Such studies play crucial roles in justifying competitive investments in vaccination programs in resource-constrained settings in the LLMICs.

### National Vaccination Strategy and Clinical Guidelines

National guidelines are standardized, evidence-based, but non-mandatory principles for the management of a specific illness. These formal official documents are developed by the government health authority assigned professional body aimed at establishing a standard and consistent clinical practice across the nation [66]. National guidelines recommending a specific vaccine are found to successfully enhance the uptake of that vaccine in the target population [67]. Although there are multiple international guidelines, we believe that recommending SIV in the national guidelines of the lower and middle-income countries with proper and adequate local evidence can play a pivotal role in motivating and encouraging healthcare providers to recommend and prescribe it to their patients, which in turn will increase the vaccine uptake.

### International Stakeholder Engagement and Domestic Support for a Feasible Financial Approach

A feasible financial approach is inevitable for a sustainable influenza vaccination program. For instance, the Task Force for Global Health supported the introduction of influenza vaccination in Mongolia beginning in 2016 through its Partnership for Influenza Vaccine Introduction [68]. They provided vaccines,



**Figure 3.** Proposed structured framework for implementing a comprehensive influenza vaccination program in resource-constrained settings.

technical assistance, and program development support. Over subsequent years, this support enabled the country to strengthen delivery systems, expand coverage, and progressively increase domestic vaccine procurement. By around 2022, Mongolia had initiated a transition toward a fully country-financed and sustained influenza vaccination program [68]. Their approach illustrates a scalable pathway from external support to national ownership based on programmatic implementation evidence.

International organizations such as the WHO, Gavi, the Vaccine Alliance, UNICEF, and the World Bank play a crucial role in enhancing vaccination coverage in LLMICs, where weak public health infrastructure, limited resources, and competing health priorities interplay to hinder the overall process. Despite economic growth, many middle-income countries have high underimmunized children due to funding gaps as they become too wealthy to qualify for aid from international organizations but not wealthy enough to implement or finance their own vaccination programs [30]. The withdrawal of international funds directly affects supply chain maintenance, vaccine affordability and availability, vaccine infrastructure, etc., resulting in stagnant or declining immunization rates [30].

Local, regional, and global players may support in such cases through financial assistance, technical support, and policy advocacy. Gavi's cofinancing policy can assist LMICs in acquiring

affordable influenza vaccines and strengthening the cold chain infrastructure for vaccine storage and distribution [69]. The Influenza Vaccine Project of the Program for Appropriate Technology in Health is facilitating several initiatives in partnership with both public and private sectors to promote the advancement of promising influenza vaccinations that are accessible and affordable for individuals in low-resource countries [70]. Expanding local vaccine production through public-private partnerships can meet domestic needs and also improve regional influenza vaccine coverage by supplying vaccines to neighboring countries at a lower cost, balancing the interests of both the public and private sectors, ensuring equitable funding competition, and creating a level playing field [66].

#### Context-Specific and Risk-Group-Tailored Interventions

We have identified a range of targeted interventions from the HICs and UMICs to enhance influenza vaccination uptake among high-risk populations in LMICs in this review. These interventions can be implemented individually or in combination, depending on the local context, for maximum output (Table 3). Their feasibility in LLMICs depends totally on adaptation rather than replication. Pilot projects supported by external partners in selected regions or facilities can subsequently be scaled up and integrated into national programs through a phased approach. This iterative approach allows learning, capacity building, and gradual transition to domestic financing.

**Table 3. Risk Group–specific Potential Interventions to Enhance Influenza Vaccination Coverage in LLMICs Derived From the Interventions From High- and Upper-Middle-Income Countries**

Risk Group	Potential Interventions
HCW	<ul style="list-style-type: none"> <li>• Subsidized or free vaccination</li> <li>• Mandatory vaccination</li> <li>• Incentives</li> <li>• Flexible and worksite delivery</li> <li>• Mandatory declination statement</li> <li>• Reminders</li> </ul>
Older adults	<ul style="list-style-type: none"> <li>• Physician recommendation</li> <li>• SOP (for pharmacists)</li> <li>• Patient education</li> <li>• Video-led educational intervention</li> <li>• Pay-it-forward (free vaccine)</li> </ul>
Under 5 children	<ul style="list-style-type: none"> <li>• Physician recommendation (from pediatrician)</li> <li>• Subsidized or free vaccination</li> <li>• Parent education</li> <li>• Inclusion in national immunization guideline</li> <li>• Reminders</li> <li>• Kindergarten-based vaccination campaign</li> <li>• Parent-level nudge</li> </ul>
Pregnant Women	<ul style="list-style-type: none"> <li>• Physician recommendation (from obstetrician)</li> <li>• SOP (for nurses)</li> <li>• Inclusion in ANC guideline</li> <li>• Provider education</li> <li>• Provider feedback</li> <li>• Pregnant mother education</li> <li>• Health slogan</li> </ul>
Adults with comorbidities	<ul style="list-style-type: none"> <li>• Physician recommendation</li> <li>• SOP (by pharmacists)</li> <li>• Physician reminders</li> <li>• Hospital-wide campaign</li> <li>• Patient education</li> <li>• Caregiver education</li> <li>• Visual and verbal reminders</li> <li>• Inclusion in national guideline</li> </ul>

Abbreviations: ANC, antenatal care; HCW, healthcare worker; LLMICs, low- and lower-middle-income countries; SOP, standing order procedure.

Countries can begin with subsidized or free vaccines along with a flexible and worksite delivery system for the HCWs. Later, interventions such as mandatory vaccination or mandatory declination forms can be implemented for maximum uptake [34, 36, 37].

Inclusion in national guidelines and provider-based education will effectively enhance the vaccine uptake in the rest of the risk groups, as physician recommendation is found to effectively raise the uptake rate in all risk groups. Hospital-based interventions such as outdoor and indoor campaigns for pregnant mothers, sick children and adults with comorbidities can positively impact the patient, parent, and caregiver knowledge, perception, and acceptability [24, 25, 54, 57, 58].

Community-based interventions such as school-based campaigns for children and community engagement for older adults and free or subsidized vaccines for them at specific vaccination clinics are also found to positively impact the influenza vaccination rate [55]. Standing order procedures for nurses and pharmacists have been proven to increase vaccine

uptake among pregnant women and older adults with or without comorbidities, as they empower nonphysician healthcare providers who frequently engage with these risk groups [42, 44, 49, 50, 56].

### Culturally Sensitive Strategies for Community Engagement and Risk Communication

Vaccine hesitancy in many settings is strongly influenced by religious and cultural beliefs, which are significant obstacles to vaccination in LICs and LMICs. Religious and cultural beliefs shape perceptions of health, illness, and medical interventions. Local faith actors play powerful roles in both promoting and inhibiting immunization uptake [71]. Misconceptions about vaccine ingredients, concerns about permissibility within religious frameworks, and reliance on traditional healing practices can reduce acceptance of immunization. Additionally, the spread of misinformation within close-knit social and religious networks can amplify fears and skepticism. Many outbreaks of vaccine-preventable diseases, such as poliomyelitis, measles, and pertussis, in the LLMICs and even in the HICs, can be linked to undervaccinated or nonvaccinated communities [72]. Such circumstances can be effectively addressed through Community-based participatory research and integrated knowledge translation principles [73]. Studies found that faith-based organizations and religious leaders had a vital role in establishing trust, mitigating barriers, enhancing vaccine uptake and tailoring campaigns during the COVID-19 vaccination initiatives [74].

Therefore, when targeting underserved or diverse communities for vaccines like influenza, effective immunization campaigns must include culturally sensitive community engagement and communication strategies. Health authorities can build trust, encourage uptake and reduce vaccine hesitancy by designing tailored messages and delivery methods relevant and respectful to the local context, recognizing the cultural beliefs, values, and traditions of target communities.

### Using Existing Vaccine Infrastructure and Learning From COVID-19

The COVID-19 pandemic has exposed fundamental gaps in healthcare infrastructure, preparedness, and response mechanisms worldwide, particularly in LLMICs. Pandemic preparedness and prevention is no longer an option, but rather a national obligation. Experiences from COVID-19 vaccination programs can pave the way for LLMICs to adopt adult vaccination programs. Rather than establishing entirely new systems, integrating new vaccines into preexisting platforms, such as national immunization programs like the Expanded Program on Immunization (EPI), the COVID-19 vaccination programs for adults, etc., can improve efficiency, reduce costs, and accelerate implementation [28]. Cold chain systems established for COVID-19, digital health records to enable tracking of coverage, urban and rural distribution networks to improve access

in hard-to-reach areas, and trained healthcare workers can readily support the adult influenza vaccine programs [28].

Bhutan has leveraged existing vaccine infrastructure to introduce and gradually scale up the seasonal influenza vaccination program. Later, they used the same infrastructure for the COVID-19 vaccination [66]. Thailand has set a regional benchmark by progressively expanding its influenza vaccination policy from initially targeting healthcare workers in 2005 to covering all high-risk groups by 2009. Both childhood and adult vaccination are integrated with the EPI under the national program [66]. This phased approach of leveraging existing vaccine apparatus to enable gradual capacity building while prioritizing vulnerable populations holds lessons for LLMICs over the globe.

## CONCLUSION

This review shows that low influenza vaccine uptake in LLMICs is a multifaceted issue rooted in systemic limitations, cultural barriers, and policy gaps. While strategies from HICs offer valuable insights, their direct application without contextual adaptation in low-resource settings is often impractical. Tailored interventions based on cultural sensitivity, risk group specificity, and local evidence are necessary. National vaccination strategies, inclusive clinical guidelines, physician recommendations, and standing orders empowering nonphysician HCWs can effectively bridge current gaps. Furthermore, coordinated support from both domestic key players and international stakeholders is crucial for sustainable improvements.

## Notes

**Author contributions.** S. H. and M. Z. H. jointly conceptualized the research idea. S. H. prepared the initial draft with input from M. Z. H. S. H. incorporated M. Z. H.'s comments and inputs on the draft. All authors reviewed and approved the final version of the manuscript.

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**Data availability.** No primary data were generated or analyzed in this study. All data are derived from publicly available sources and are cited within the article.

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