Policy considerations and market opportunities for mRNA seasonal influenza vaccines

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### Policy and Market Considerations Relevant to mRNA Influenza Vaccines

**Are they needed?**
- Relative priority versus other pathogens
  - Disease Burden
  - Pandemic preparedness

**Can they be integrated into existing immunization programs?**
- Adult target groups
  - Life-course vaccination
  - Staffing / training
  - Cold chain

**Will there be sufficient demand?**
- Acceptability, knowledge among target groups

**Economic feasibility**
- Costs of program delivery
- Costs of vaccines

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What data or information are needed to support decisions on influenza vaccination investments in LMICs?
Influenza Burden and Epidemiology

- Seasonality varies by country
- Defined epidemic periods in most countries
- Year-round disease in tropical regions

Is transmitted every year in every country

Legend:
- 1 peak [37]
- 1 peak + yr-round [5]
- 2 peaks [18]
- 2 peaks + yr-round [8]
- yr-round [2]
- No data / NA [154]
Influenza Burden and Epidemiology

- Seasonality varies by country
- Defined epidemic periods in most countries
- Year-round disease in tropical regions

High attack rates worldwide

- 7-10% of all persons are infected each year

548 million – 1.2 billion illnesses each year

1. Iuliano A D, et al 2018; 2 Lafond K, GRIPP study group, 2016
Influenza Burden and Epidemiology

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High attack rates worldwide
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Substantial disease burden
- 291,000 and 646,000 respiratory deaths
- Underestimated because non-respiratory outcomes aren’t well counted

Influenza is associated with:
- 9.5% of pediatric respiratory hospitalizations worldwide
- 14% with acute lower respiratory hospitalizations among adults
- 5.4 million LRI hospitalizations annually in adults

Influenza Burden and Epidemiology

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High attack rates worldwide

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Substantial disease burden

- 291,000 and 646,000 respiratory deaths
- Underestimated because non-respiratory outcomes aren’t well counted

Burden disproportionately among low-income settings

- Higher risk of death and hospitalization compared with HICs
- Especially in SE Asia and African regions

- Children <5 years in developing countries are 3X more likely to be hospitalized than those in industrialized countries
- Rates of LRI are highest in adults in Africa and SE Asia

Influenza deaths by age and county income classification

- Children under 5 years in developing countries are 3X more likely to be hospitalized than those in industrialized countries
- Rates of LRI are highest in adults in Africa and SE Asia

Benefits of vaccination against influenza

- Vaccine effectiveness is variable from year to year, by type/subtype, by age, etc\(^1\)
- Overall, VE is modest but perhaps better in preventing severe outcomes (hospitalizations, ICU admissions, deaths) \(^2,3\)
- Can prevent non-respiratory outcomes, such as cardiac events, exacerbations of COPD and diabetes\(^1\)
- Large disease burden reduction based on high attack rate
- Vaccine cost-effective in most settings \(^4\)

Potential benefits of “better” vaccines

• Improved influenza vaccines a priority public health goal
  • Universal Influenza Vaccines - >160 candidates in late pre-clinical or clinical phase development
  • Influenza Vaccine R&D Roadmap developed
  • Full Value of Improved Vaccines for Influenza (FVIVA) initiative underway
• Recent model demonstrated increase cost-effectiveness of influenza vaccines with increased VE, longer duration of protection and breadth
• Potential for increased demand
• Better tools for pandemic response

2. Waterlow NR, et al. BMC Medicine 2023
“Data have shown that countries that had seasonal influenza vaccination programs before the 2009 influenza pandemic were better able to import and use vaccines than countries without such programs.”


Review of African country vaccine responses to 2009 pandemic resulted in a recommendation to “promote seasonal vaccination programs” as a readiness tool for the next pandemic

Mihigo et al. J Infect Dis 2012

“Our findings suggest that robust seasonal influenza vaccine programs increase national familiarity with the management of influenza vaccines and therefore enhance pandemic preparedness.”

Porter et al. 2019 Vaccine
Value of influenza vaccination for pandemic / epidemic responses

Ongoing evaluation of COVID vaccine responses
- Using WHO COVID vaccine Post-introduction Evaluation tool (cPIE)
- Up to 20 countries
- Evaluating the effect of influenza vaccination on COVID vaccine response

**Most countries reported:**
- Repurposing influenza pandemic preparedness plans, including NDVPs, for COVID-19 response
- Using influenza platforms to reach shared target groups with COVID-19 vaccine
- Repurposing influenza microplans for efficient vaccine distribution
- Adapting influenza communication materials to shared target groups

*Compiled data from 61 countries with and without programs (WHO Dashboard) * Existing Influenza Programs in 2019 and 2020
Policy and Market considerations relevant to mRNA influenza vaccines

Are they needed?
Relative priority versus other pathogens
- Disease Burden
- Pandemic preparedness

Seasonal Influenza Vaccination programs
- Target the same risk groups as pandemic/epidemic vaccines
- Given annually in campaigns – recurring practice
- Health workers central to acceptance / recommendations

For effective pandemic vaccination programs:
- Regulatory expertise
- Vaccine policy / effective NITAGs
- Distribution systems to access target groups
- High vaccine acceptance
- Monitoring programs (AEFI, coverage, ?VE)
Can they be integrated into existing immunization programs?

- Adult target groups
- Life-course vaccination
- Staffing / training
- Cold chain

Challenges
- Adult vaccination programs nascent
- Many countries don’t have existing influenza vaccination programs

• Experience with COVID vaccine implementation is foundation for influenza integration
• Lessons / best practices from PIVI in LMICs demonstrate programmatic feasibility
• Co-administration with other vaccines not an obstacle
• Tools for influenza vaccination program development available
  • Health worker guidelines
  • SAGE recommendations
  • Influenza Post-introduction evaluation tool
Policy and Market considerations relevant to mRNA influenza vaccines

Will there be sufficient demand?

Acceptability, knowledge among target groups

• Data from LMICs with recent influenza vaccine introduction indicate high acceptability among target groups

  12 country survey of HWs (n=10,281) and PW (n=8,556)
  • High acceptance by HWs overall (74%), lower in countries with SIV programs
  • 85% HWs would recommend vaccines to patients
  • Health workers who accept vaccines for themselves were 12 times more likely to recommend vaccines to their patients

<table>
<thead>
<tr>
<th></th>
<th>No vaccination program</th>
<th>Vaccination program present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would accept free vaccines</td>
<td>81%</td>
<td>61%</td>
</tr>
<tr>
<td>Would pay for vaccine</td>
<td>60%</td>
<td>46%</td>
</tr>
</tbody>
</table>

• Data from PIVI, indicate growing demand over time, with increased government purchase

Challenges

• Low awareness in many countries / target groups
• COVID hesitancy may affect influenza vaccine acceptance

References:
1. McCarron et al., Global influenza vaccine knowledge, attitudes, and practices among health workers (in press);
2. Bresee, Vaccine 2019; 3. Bresee, Options for the Control of Influenza, Belfast, 2022
Policy and Market considerations relevant to mRNA influenza vaccines

**Economic feasibility**

- Incremental costs of program delivery perhaps lower given COVID investments
- Compelling CE data for developing the value proposition
- Existing WHO Costing Tools to estimate the costs of program delivery

But,

- Vaccine costs barrier to introduction and expansion for influenza vaccines in LMICs
- Data on costs of delivery are sparse and need to be better understood in a context of co-delivery with other vaccines

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Needs and possible way ahead

Needs
- Data on mRNA vaccine performance in relevant populations
  - Vaccine safety profile must be similar to existing vaccines
  - Increased VE would strengthen the value proposition
- Build evidence base for value of influenza prevention in diverse settings
  - Disease burden
  - Cost-effectiveness
  - Pandemic / epidemic preparedness
- Experience with influenza vaccine implementation
  - Understand implementation strategies
  - Refine estimates of program costs
  - Learn and shape stakeholder perspectives and acceptance
- Ensure equitable vaccine access
  - Mechanisms to ensure affordable vaccines
  - National policy development

Possible way ahead
Multi-country (or regional) demonstration project to provide the value proposition for LMICs / vaccine manufacturers / stakeholders
- Provide vaccines for target groups (e.g., HWs)
  - Co-deliver with COVID vaccines
- Support policy development
- Conduct panel of implementation research to assess
  - feasibility
  - actual costs
  - country needs (e.g., staffing, training, cold-chain, etc.)
  - acceptability/demand over time
  - Vaccine safety