



# FRAMEWORK TO GUIDE INFLUENZA VACCINATION POLICY IN RESOURCE LIMITED SETTINGS – A CASE STUDY FROM SOUTH AFRICA

Meredith McMorrow, MD, MPH, FAAP

Influenza Program Director, CDC-South Africa

ANISE

Antananarivo, Madagascar

20 March 2018

# INTRODUCTION

- 2012 WHO POSITION PAPER ON INFLUENZA VACCINATION
  - Defined risk groups to be targeted for vaccination:
    - pregnant women,
    - children aged 6-59 months,
    - adults aged  $\geq 65$  years,
    - individuals with chronic medical conditions, and
    - healthcare workers
  - Encouraged collection of country-specific data on risk groups
  - SAGE recommended prioritization of pregnant women

# CHALLENGES FOR INFLUENZA POLICYMAKERS

- LIMITED HEALTH RESOURCES IN LMIC
  - Vaccine needs of high risk groups may exceed available resources for vaccine procurement
  - Prioritization among risk groups may be necessary
- DELIVERY MECHANISMS AND ASSOCIATED COSTS
  - Existing platforms (EPI, ANC) are limited to specific risk groups
  - Other risk groups may be harder to reach
  - Costs of hospitalization, consultation lower – may impact cost effectiveness
- LIMITED WHO GUIDANCE ON SEASONAL VACCINE PRIORITIZATION

# FRAMEWORK FOR INFLUENZA VACCINE POLICY

- EVIDENCE-BASED PRIORITIZATION OF RISK GROUPS
  - Combine existing data by risk group:
    - hospitalization/death rate
    - vaccine efficacy (VE)
    - vaccine coverage
- ESTIMATE FOR EACH RISK GROUP
  - Rate of hospitalizations/deaths potentially averted by vaccination
  - Estimates of hospitalizations/deaths potentially averted by current and target vaccination programs

# CASE STUDY

## ■ SOUTH AFRICA (2016)

- Population 55.9 million
- LMIC: per capita GDP USD5274
- HIV prevalence 12.7%
- Endemic TB

- ~318,000 cases notified in 2014

- >23 million people in one or more risk groups
- ~1 million doses of influenza vaccine administered in public sector and ~1 million doses in private sector annually



# FRAMEWORK INPUTS

- 2016 POPULATION ESTIMATES
  - Pregnant women: assumed equal to live births
  - HIV infected adults aged 15-64 years: Thembisa model
  - HCW: registered providers from medical and nursing councils
  - TB: 2014 estimate from WHO World TB Report
  - Chronic illness: SA NHANES survey data with adjustment for higher prevalence of comorbidities in HIV-infected
- HOSPITALIZATION RATES
  - Age and HIV-standardized rates derived from surveillance platforms (Tempia et al. IORV 2017)
  - Adjusted for increased relative risk/case-population ratio

# FRAMEWORK INPUTS

- MORTALITY RATES
  - Published rates from local data Cohen et al. CID 2017, Tempia et al. CID 2015, Walaza et al PLoS ONE 2015
  - Unpublished rates derived from Cohen et al. CID 2017
- VACCINE EFFICACY
  - Estimated using 1-RR using random effects Mantel-Haenszel model of published RCTs for pregnant women, infants 0-5 months, and children aged 6-23 months
  - HIV-infected adults Madhi et al. CID 2011
  - Elderly, TB-infected, chronic illness Darvishian et al Lancet ID 2014
  - Healthcare workers Demicheli et al. Cochrane Review 2014

# FRAMEWORK INPUTS

- VACCINE COVERAGE
  - Annual coverage estimates by target group from National Department of Health (W. Ramkrishna)
  - No estimate for HCW so assumed current coverage of 10% based on review of other LMIC (Haviari et al. HVI 2015)
- OTHER INPUTS
  - Cost of IIV USD 3 (range 2.80-3.95) from PAHO Revolving Fund
  - Mean duration of hospitalization by risk group from local surveillance
  - Expectation of life in years by age from WHO Global Health Observatory
- MONTE CARLO SIMULATION 5000 ITERATIONS POISSON DISTRIBUTION TO CALCULATE 95% CONFIDENCE INTERVALS



**Table 1. Population size, influenza-associated hospitalization rates, influenza-associated death rates, vaccine efficacy by high risk group, South Africa**

<b>Risk group</b>	<b>Mid-year population in South Africa (2016)</b>	<b>Rate of influenza-associated hospitalization per 100,000 py (95% CI)</b>	<b>Rate of influenza-associated death per 100,000 py (95% CI)</b>	<b>Vaccine efficacy* in risk group (95% CI)</b>
Pregnant women	1,198,861	378.8 (237.7-534.8)	12.6 (7.2 - 18.0)	61% (43-73%)
HIV-infected adults aged 15-64 years	6,604,709	256.3 (179.4 - 333.2)	64.7 (38.3 - 81.1)	76% (9-96%)
Children aged 6-23 months	1,729,502	324.1 (237.6 – 417.8)	23.4 (5.1 – 26.5)	35% (-41-70%)
Adults aged ≥65 years	2,909,122	194 (144 - 256)	169.3 (81.0-324.6)	58% (40-70%)
Healthcare workers	566,393	60.6 (45.5 – 75.8)	20.9 (9.4-29.0)	60% (53-66%)
Adults & children with TB	318,193	282.7 (193.5-377.4)	164 (144 - 174)	Unknown
Chronic illness in persons aged 5-64 years	9,863,353	42.4 (31.8 – 53.7)	24.4 (15.4 – 35.3)	Unknown

**Table 2. Potential hospitalizations averted per 100,000 vaccinated, potential deaths averted per 100,000 vaccinated, and vaccine coverage by high risk group, South Africa**

<b>Risk group</b>	<b>Potential hospitalizations averted per 100,000 vaccinated (95% CI)</b>	<b>Potential deaths averted per 100,000 vaccinated (95% CI)</b>	<b>2016 influenza vaccine coverage</b>	<b>Target vaccine coverage</b>
Pregnant women	256.3 (146.1 -403.0)	15.5 (9.0-22.7)	14%	40%
HIV-infected adults aged 15-64 years	190.9 (24.5-390.6)	48.2 (6.1 - 102.3)	3%	20%
Children aged 6-23 months	111.6 (1.1 – 238.3)	8.0 (0.1 - 18.3)	3%	32%
Adults aged ≥65 years	111.0 (70.3 – 160.7)	96.6 (26.2 - 180.9)	2%	10%
Healthcare workers	36.1 (26.5-46.3)	12.5 (6.6 - 18.7)	10%	80%
Adults & children with TB	162.0 (96.6 – 245.1)	95.0 (64.0 – 127.3)	3%	20%
Chronic illness in persons aged 5-64 years	29.4 (15.5 – 44.7)	16.7 (8.3 - 28.3)	3%	20%

**Table 3. Estimated hospitalizations and deaths potentially averted in current and target influenza vaccination programs, South Africa, 2016**

<b>Risk group</b>	<b>Estimated hospitalizations averted by current program (95% CI)</b>	<b>Estimated hospitalizations averted by target program (95% CI)</b>	<b>Estimated deaths averted by current program (95% CI)</b>	<b>Estimated deaths averted by target program (95% CI)</b>
Pregnant women	430 (245-676)	1229 (701-1933)	26 (15-38)	74 (43-109)
HIV-infected adults aged 15-64 years	378 (49-774)	2522 (324-5160)	96 (12-203)	637 (81-1351)
Children aged 6-23 months	58 (1-124)	618 (6-1319)	4 (0-9)	44 (1-101)
Adults aged ≥65 years	65 (41-93)	323 (205-467)	55 (37-74)	276 (186-370)
Healthcare workers	20 (15-26)	164 (120-210)	7 (4-11)	57 (30-85)
Adults & children with TB	15 (9-23)	103 (61-156)	9 (6-12)	60 (41-81)
Chronic illness in persons aged 5-64 years	87 (46-132)	580 (306-882)	49 (25-84)	329 (164-558)
<b>TOTAL</b>	<b>1054 (405-1849)</b>	<b>5,538 (1722-10,126)</b>	<b>247 (99-431)</b>	<b>1478 (545-2656)</b>

# SUMMARY OF RESULTS

- LMIC may have different disease rates, care-seeking behavior, and few platforms for vaccine delivery which may supersede this framework
- Adults aged  $\geq 65$  years rank highest in potential deaths averted per 100,000 vaccinated, but are a challenging risk group to reach with vaccination services
- Lower vaccine efficacy and the need for 2 doses of influenza vaccine in children aged 6-23 months who have not been previously vaccinated reduced averted burden

# LIMITATIONS

- POPULATION ESTIMATES
  - Available for most but challenging to estimate chronic illness prevalence
- LIMITED DATA ON VACCINE EFFICACY
  - No published data on VE in persons with TB infection
  - Specific studies on some chronic illnesses but impact on VE unlikely to be similar across all disease classes
- LIMITED TO IIV - ONLY PRODUCTS LICENSED IN SOUTH AFRICA
- DID NOT ASSESS IMPACT OF VACCINATION ON DISEASE TRANSMISSION

# CONCLUSIONS & FUTURE STUDIES

- Risk group prioritization may be necessary in many LMIC
- This framework may be helpful for policymakers to make evidence-based decisions about seasonal influenza vaccine prioritization
- Depending on available data, the framework may also provide useful guidance during pandemics
- More rigorous cost and cost-effectiveness studies are planned in South Africa to further inform influenza vaccine policies

# ACKNOWLEDGEMENTS

- Co-authors: Stefano Tempia, Sibongile Walaza, Florette Treurnicht, Wayne Ramkrishna, Eduardo Azziz-Baumgartner, Shabir Madhi, Cheryl Cohen
- National Department of Health Communicable Disease Cluster
- Prof. Demetre Labadarios and team at the Human Science Research Council for access to South Africa National Health and Nutrition Survey (SA NHANES) data
- National Pneumonia Sentinel Surveillance Team of surveillance officers, laboratorians, and participants



For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://www.cdc.gov)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

