

# Influenza country achievements-South Africa

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National Institute for Communicable Diseases

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health

Department:  
Health  
REPUBLIC OF SOUTH AFRICA



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# Outline

- Surveillance for influenza in South Africa
  - Brief description of surveillance programmes
- Data from surveillance
  - Seasonality and intensity of influenza seasons
  - Risk groups for severe influenza-associated illness
  - Strain characterisation
  - Vaccine effectiveness
- Influenza policy
- Conclusion

# South Africa

- Middle income
- Temperate climate
- Population HIV prevalence 13% in 2016
- 5.5 million living with HIV in 2014
- 500,000 new TB cases each year



## Leading causes of death 2013-2015

Causes of death (based on ICD-10)	2013			2014			2015		
	Rank	Number	%	Rank	Number	%	Rank	Number	%
Tuberculosis (A15-A19)**	1	41 904	8,8	1	39 495	8,3	1	33 063	7,2
Diabetes mellitus (E10-E14)	5	23 133	4,9	3	23 966	5,0	2	25 070	5,4
Cerebrovascular diseases (I60-I69)	4	23 158	4,9	2	24 131	5,1	3	22 879	5,0
Other forms of heart disease (I30-I52)	6	22 189	4,7	4	22 928	4,8	4	22 215	4,8
Human immunodeficiency virus [HIV] disease (B20-B24)	3	23 825	5,0	6	22 729	4,8	5	21 926	4,8
Influenza and pneumonia (J09-J18)	2	24 345	5,1	5	22 813	4,8	6	20 570	4,5



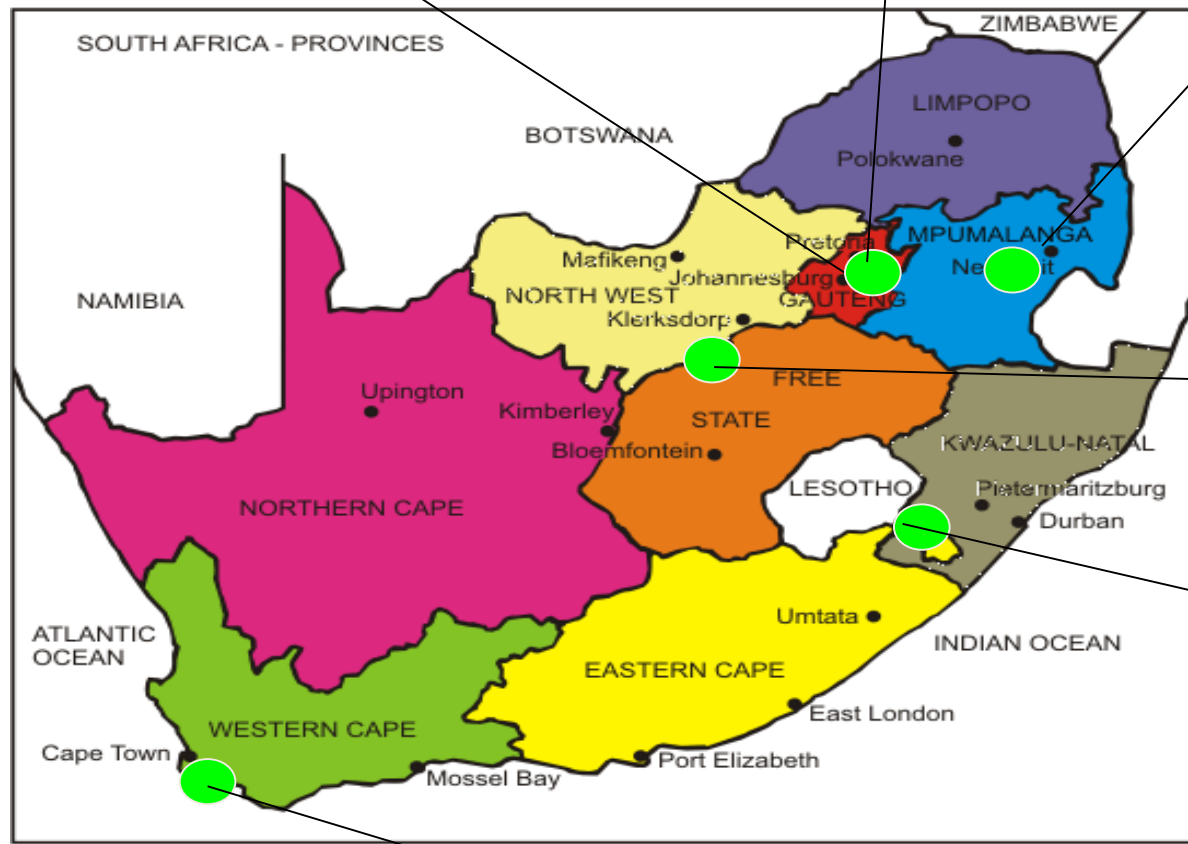
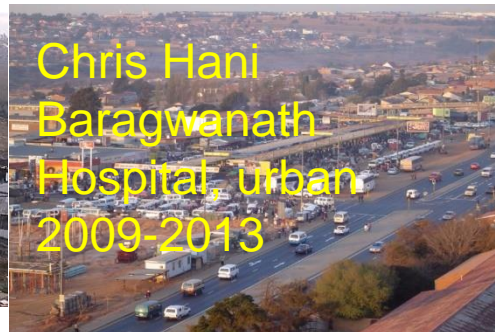
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# Influenza surveillance programmes in South Africa

Program	Period	Coverage	Population	Cases	Main Objectives
<b>Viral Watch</b>	1984-current	National sentinel	Mainly private some public	ILI	<ul style="list-style-type: none"> <li>• Timing and geographic variation</li> <li>• Characterize strains</li> <li>• Annual vaccine effectiveness</li> </ul>
<b>Enhanced viral watch</b>	2009-current	National sentinel	Public sector	SARI	<ul style="list-style-type: none"> <li>• Identify SARI in all 9 provinces</li> </ul>
<b>Severe acute respiratory tract infection (SARI)</b>	2009-current	Sentinel Sites in 5 Provinces (GP, KZN, MP, NWP,WC)	Public sector	SARI/ SCRI	<ul style="list-style-type: none"> <li>• Trends and burden of SARI</li> <li>• Identify high risk groups</li> <li>• Estimate severity of annual influenza seasons</li> </ul>
<b>Respiratory Consultations</b>	2005-current	GP, WCP, KZN, FSP, GP, NW, WC	Private sector	Hospitalisations	<ul style="list-style-type: none"> <li>• Seasonal and annual trends in hospital admissions</li> <li>• Timing of the influenza season</li> </ul>
<b>Influenza-associated mortality</b>	1997-2008	National	Public and private	Deaths	<ul style="list-style-type: none"> <li>• Estimate influenza-associated excess mortality</li> </ul>
<b>Influenza-like illness</b>	2012-current	Sentinel Sites in 3 provinces (MP,KZN, NW)	Public sector	ILI	<ul style="list-style-type: none"> <li>• Describe the burden and aetiology of outpatient ILI</li> </ul>
<b>Influenza surveillance</b>	2011	Sentinel sites in 1 province (GP)	Public sector	Hospitalisations	<ul style="list-style-type: none"> <li>• Trends and burden of influenza-associated illness in peds ,adults and pregnant women</li> </ul>



# Pneumonia surveillance sites, South Africa-2009 - 2017



Red Cross Hospital and Mitchell's Plain Hospital- urban

# Influenza surveillance-influenza like illness (viral watch), 1984-2017

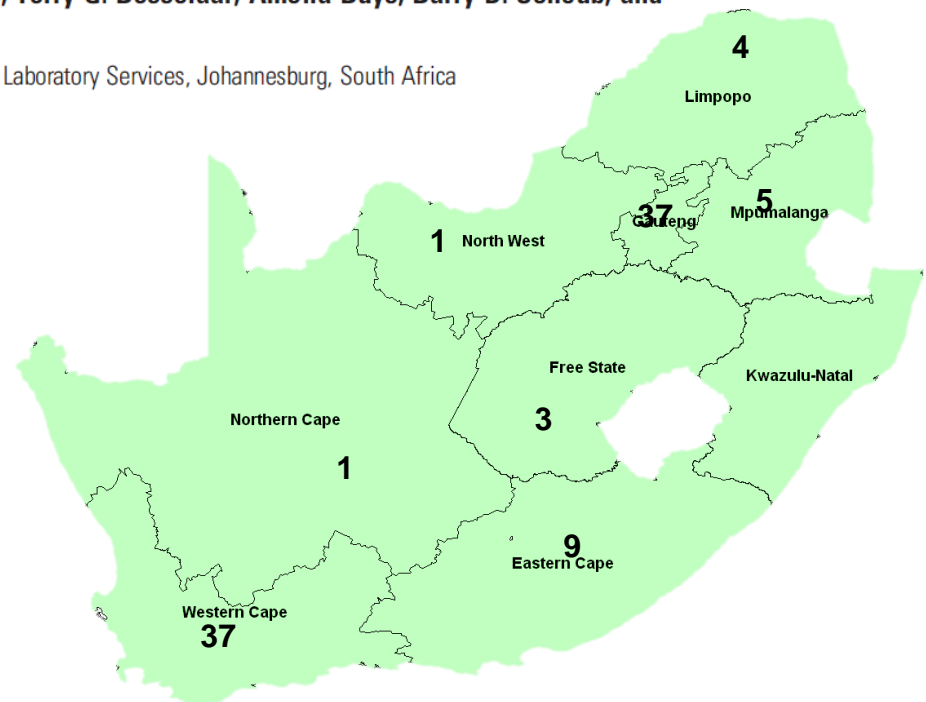
## Twenty-five Years of Outpatient Influenza Surveillance in South Africa, 1984–2008

Johanna M. McAnerney, Cheryl Cohen, Jocelyn Moyes, Terry G. Besselaar, Amelia Buys, Barry D. Schoub, and  
Lucille Blumberg

National Institute for Communicable Diseases of the National Health Laboratory Services, Johannesburg, South Africa

*The Journal of Infectious Diseases* 2012;206(S1):S153–8

**97 sites in 2017**

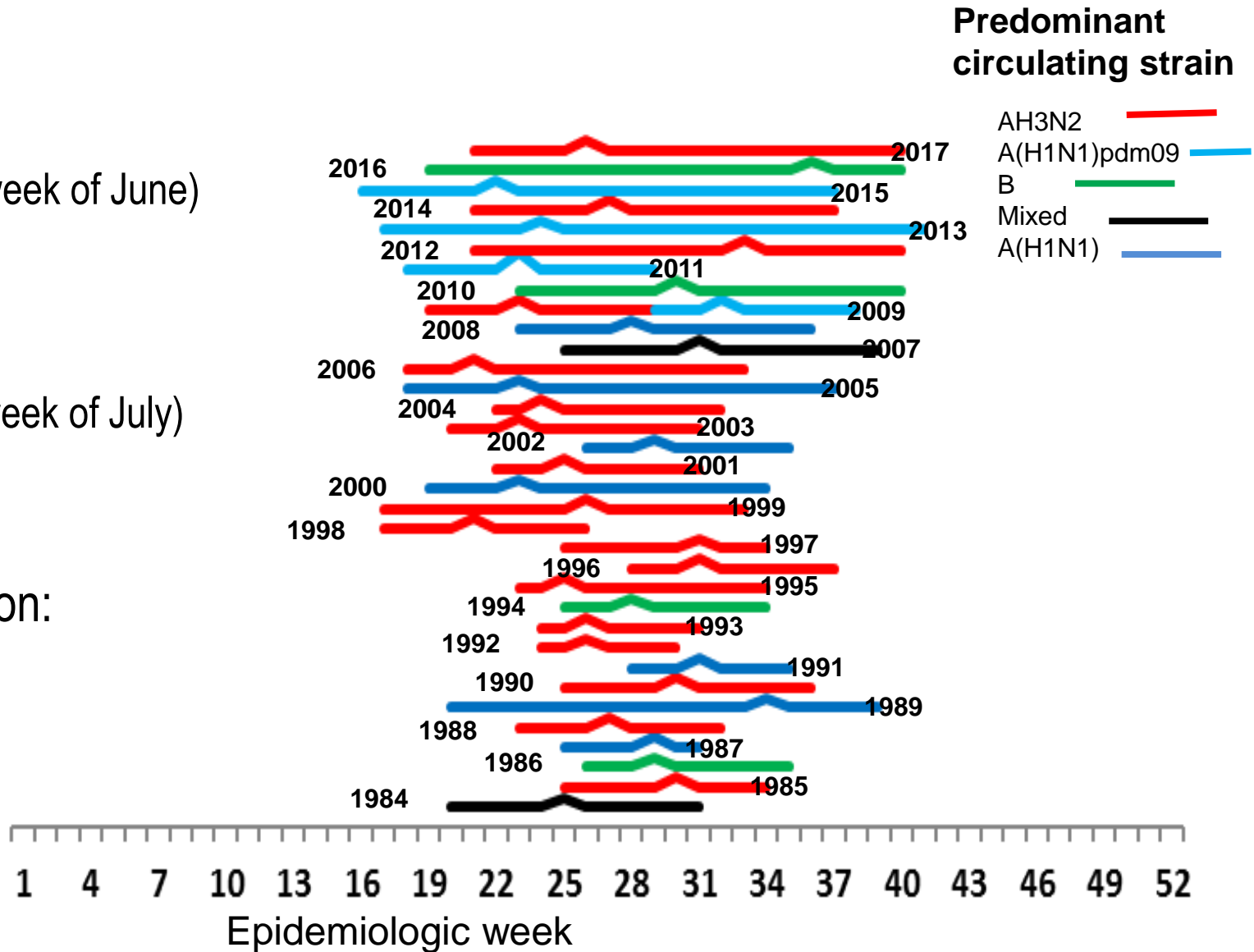


# Influenza seasons, South Africa 1984-2017

Mean onset:  
 Week 22 (1<sup>st</sup> week of June)  
 Range 16 -28

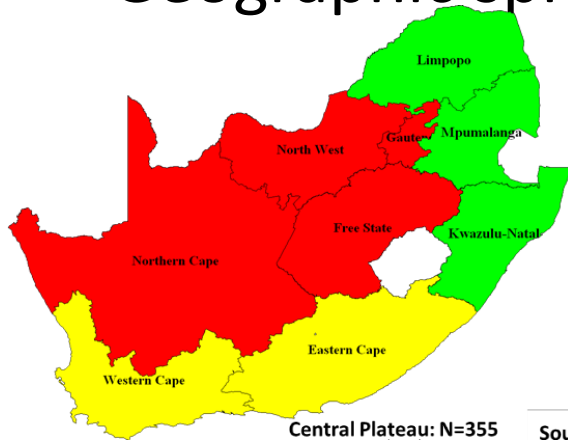
Mean peak:  
 Week 27 (2<sup>nd</sup> week of July)  
 Range 21 - 35

Mean duration:  
 14 weeks  
 Range 7 - 18

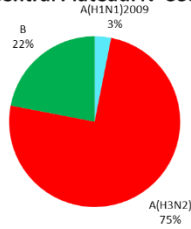


# Variations in season

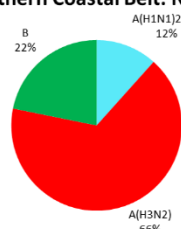
- Geographic spread: 2017



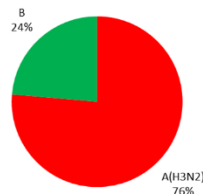
Central Plateau: N=355



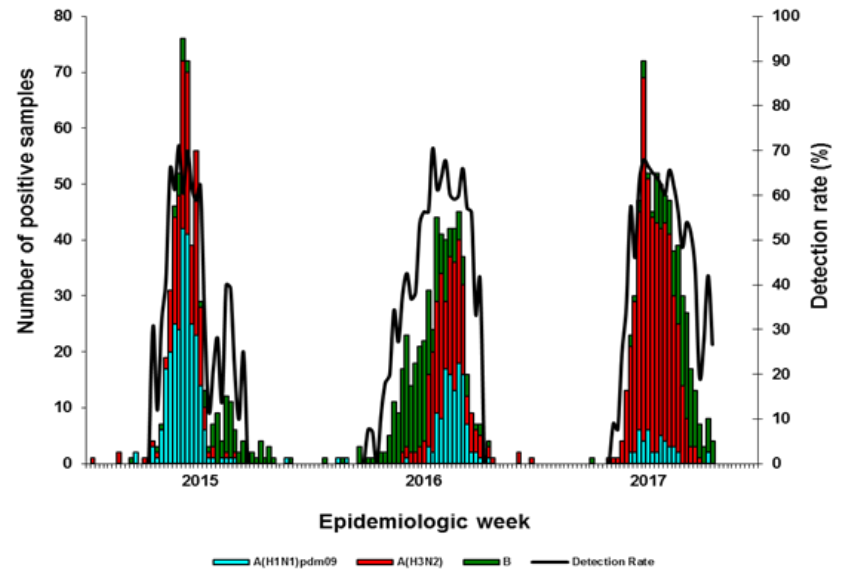
Southern Coastal Belt: N=275



NE Subtropical: N=52



## Influenza detections by type & subtype, influenza-like illness, South Africa 2015-2017



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Division of the National Health Laboratory Service



**Measures to determine intensity and severity of the South African influenza season**

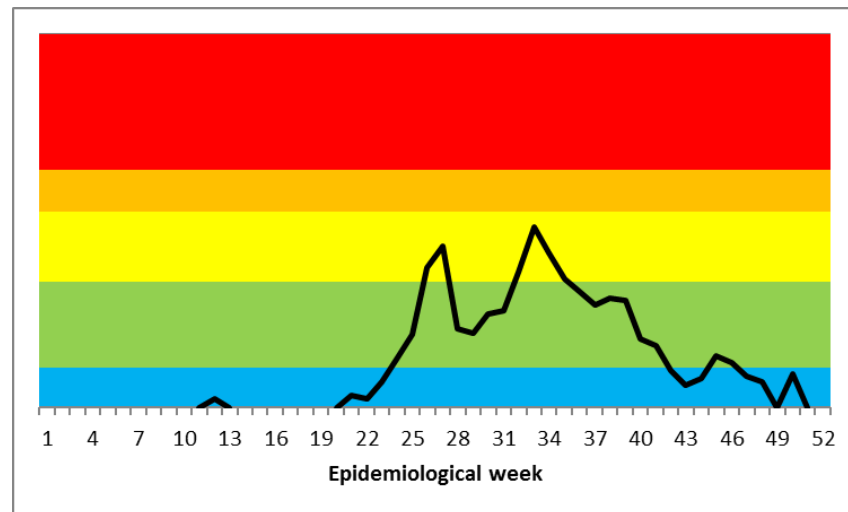
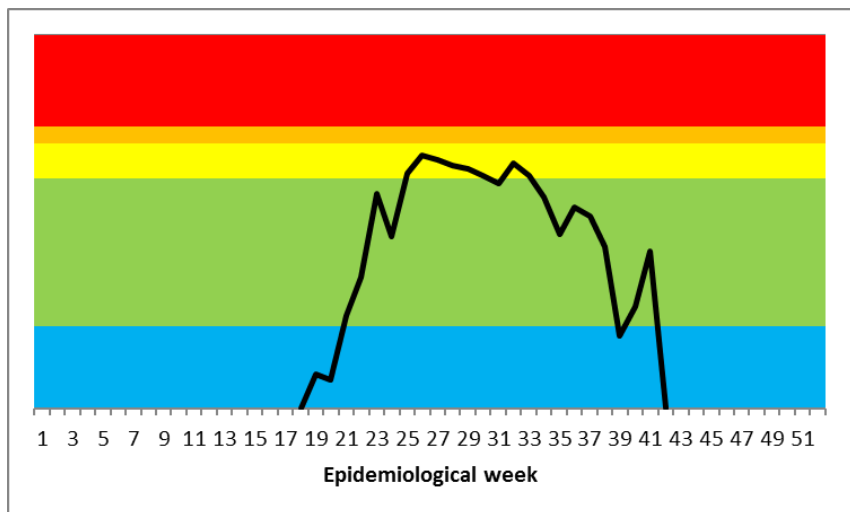
# MEM Thresholds

- Thresholds set using up to 10 years historical data
- Used 40<sup>th</sup>, 90<sup>th</sup> & 97.5<sup>th</sup> percentiles
  - Below seasonal threshold
  - Low activity (>seasonal threshold, <40%)
  - Moderate activity (≥40%, but <90%)
  - High activity (≥90%, but <97.5%)
  - Very high activity (≥97.5%)
- Transmissibility
  - Influenza detection rates for ILI- private practitioners (viral watch) & public health clinics
- Severity
  - Influenza detection rates for National syndromic surveillance for pneumonia (NSSP) & proportion hospitalised in Respiratory consultation and hospitalisations (RCHS)
- Impact on the healthcare system
  - ?

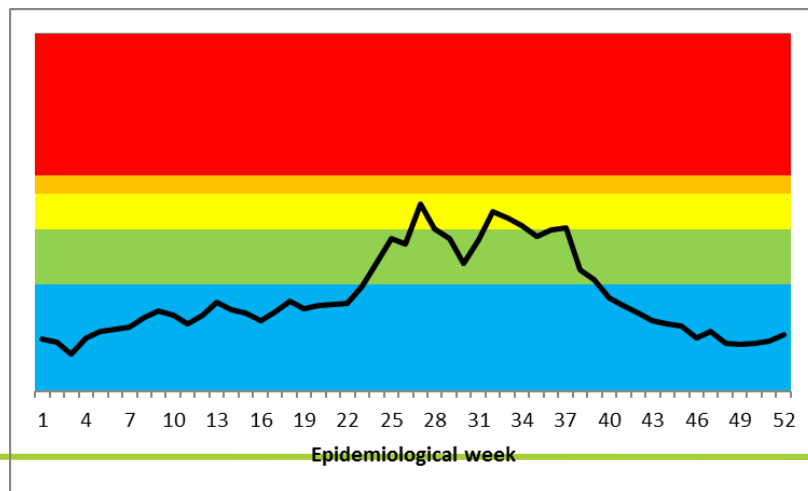
# 2017 Season: Thresholds based on 2012-2016 data: Transmissibility

ILI – Viral watch (Private practitioners)

ILI -Public health clinics



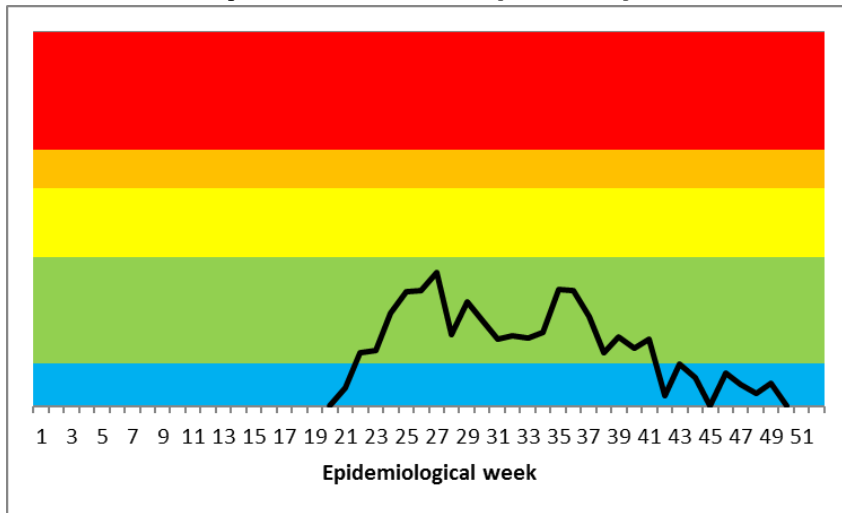
Respiratory consultations and hospitalisation: Out Patients



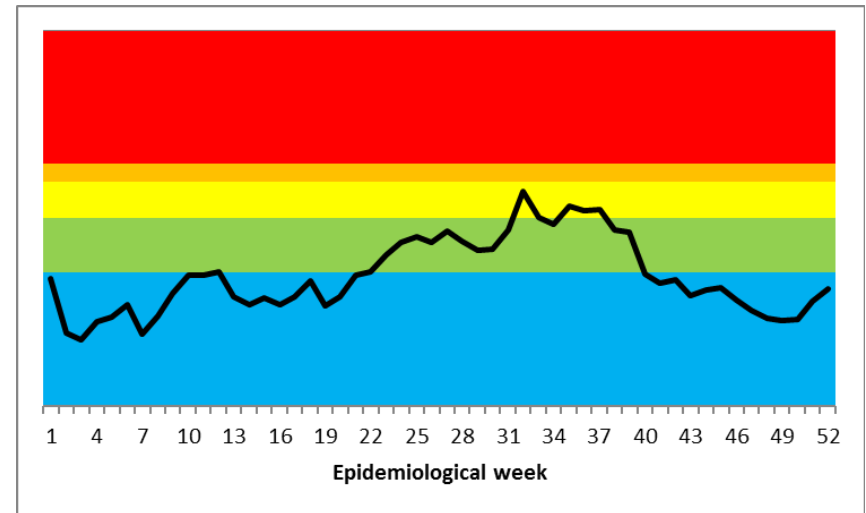
	Very High
	High
	Moderate
	Low
	Below Threshold

# 2017 Season: Thresholds based on 2012-2016 data: Severity of disease

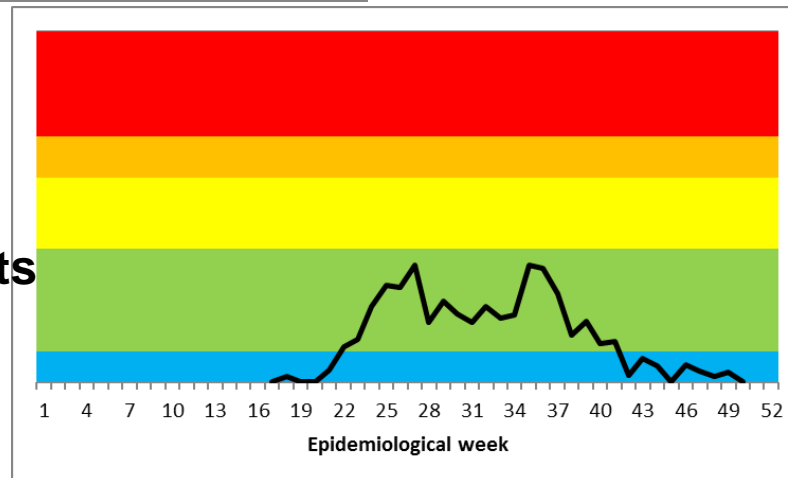
## National syndromic surveillance for pneumonia (NSSP)



## Respiratory consultations and hospitalisation (RCHS) – In Patients



## NSSP X RCHS-In Patients

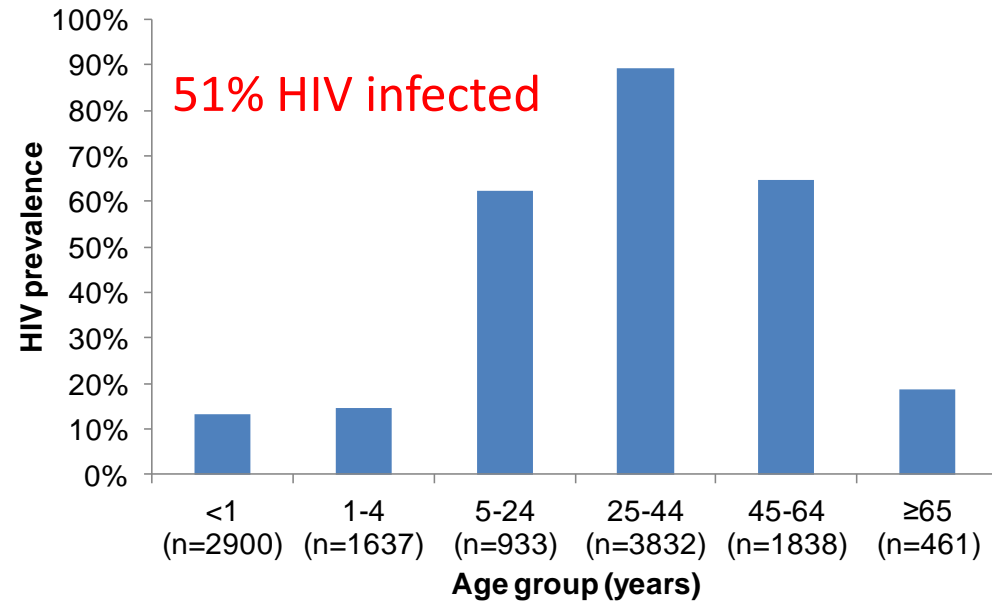


	Very High
	High
	Moderate
	Low
	Below Threshold

# **BURDEN AND RISK GROUPS FOR SEVERE INFLUENZA**

# Patients with influenza-associated acute lower respiratory-tract infection (ALRI), South Africa, 2009-2011

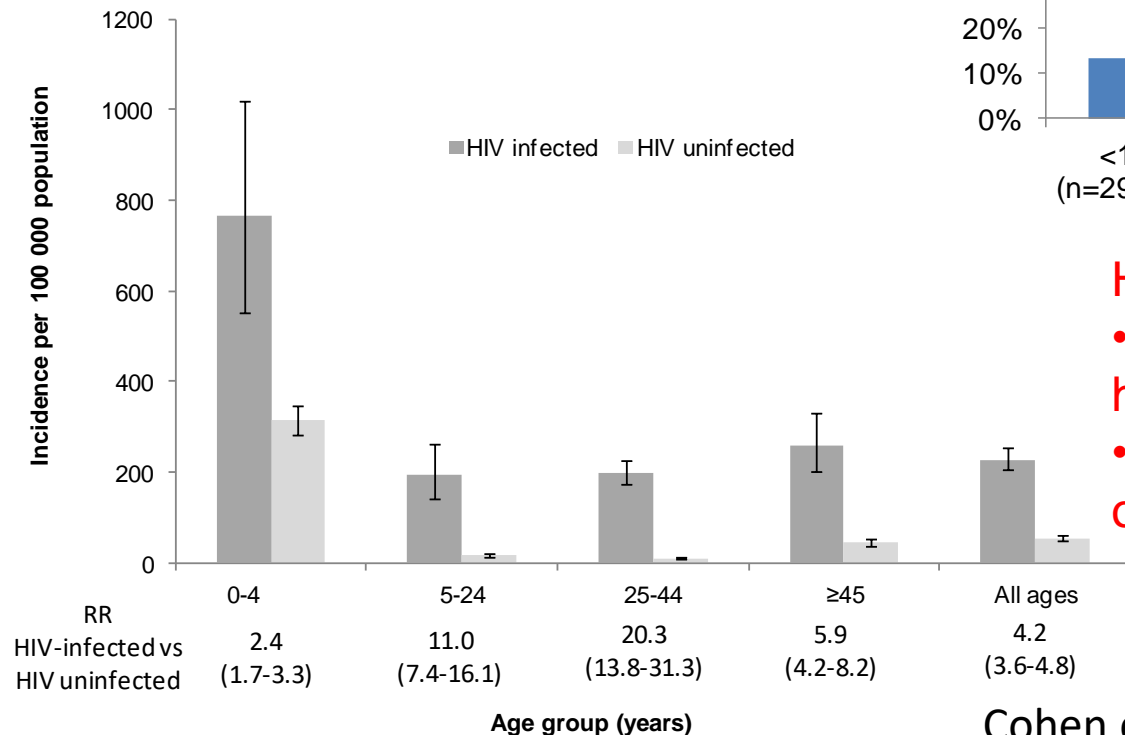
HIV prevalence by age group



HIV-infected individuals have

- 3-6 times higher incidence of hospitalisation
- 6 times greater odds of death once hospitalised

Incidence by HIV status and age group

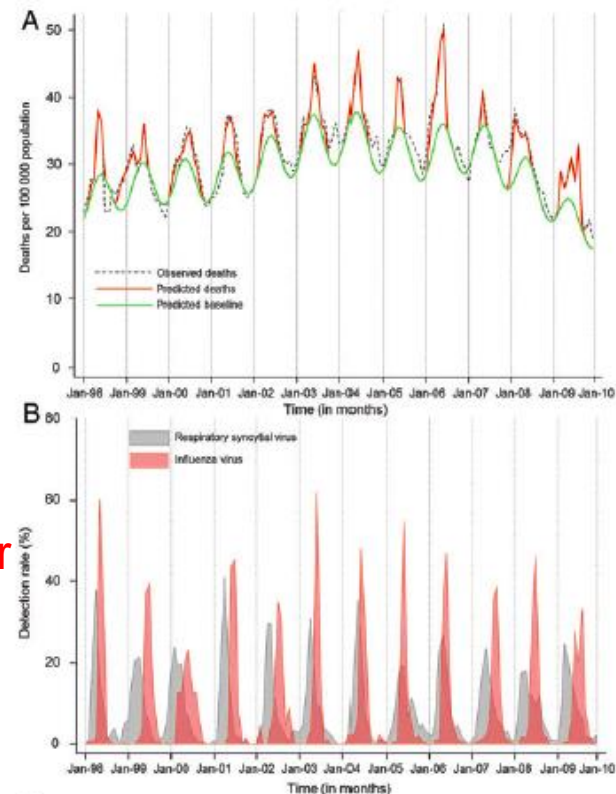




# Mortality Associated With Seasonal and Pandemic Influenza and Respiratory Syncytial Virus Among Children <5 Years of Age in a High HIV Prevalence Setting—South Africa, 1998–2009

Stefano Tempia,<sup>1,2,3</sup> Sibongile Walaza,<sup>3</sup> Cecile Viboud,<sup>4</sup> Adam L. Cohen,<sup>1,2</sup> Shabir A. Madhi,<sup>3,5,6</sup> Marietjie Venter,<sup>3,7</sup> Johanna M. McAnerney,<sup>3</sup> and Cheryl Cohen<sup>3,8</sup>

Highest rate of influenza-associated mortality in <1 year HIV-infected ~12 times more likely to die of influenza



**Table 4. Estimated Seasonal Influenza and Respiratory Syncytial Virus Mean Annual Associated Deaths and Relative Risk for Mortality Due to HIV Infection in Children <5 Years of Age in South Africa, 1998–2009<sup>a</sup>**

Cause of Death	Mean Annual Excess Deaths								Relative Risk (HIV-Positive vs HIV-Negative) (95% CI)
	Total			HIV-Positive		HIV-Negative			
	No., Mean (95% CI)	Rate <sup>b</sup> , Mean (95% CI)	Percentage Mortality Over Model Baseline, Mean (95% CI)	No., Mean (95% CI)	Rate <sup>b</sup> , Mean (95% CI)	No., Mean (95% CI)	Rate <sup>b</sup> , Mean (95% CI)		
Seasonal influenza virus									
All respiratory									
<1 y	240 (117–368)	22 (11–34)	4 (2–7)	72 (33–110)	162 (79–246)	168 (83–257)	16 (8–25)	10.1 (8.7–11.7)	
1–4 y	212 (110–313)	5 (2–7)	9 (7–11)	71 (36–104)	52 (28–78)	141 (73–208)	3 (2–5)	15.4 (11.2–21.1)	
<5 y	452 (227–681)	8 (4–13)	5 (4–8)	143 (69–214)	83 (42–123)	309 (157–466)	6 (3–9)	11.5 (9.6–12.6) <sup>c</sup>	

**Incidence rates, incident rate ratios and case-fatality ratios among children <6 months of age hospitalised with influenza-associated severe acute respiratory illness (SARI), in Soweto, South Africa, 2010-2011**

Organism	Incidence rates per 100 000 population	Incidence rate ratio (IRR)	CFR n/N (%)	OR
HUU	412 (325-515)	Reference	1/64 (2)	Reference
HEU	503 (354-693)	1.2 (0.8-1.8)	2/33 (6)	4.1 (0.4-46.6)
HIV infected	2516 (1300-4394)	<b>6.1 (3.0-11.3)</b>	2/10 (20)	<b>15.8 (1.3-193.9)</b>

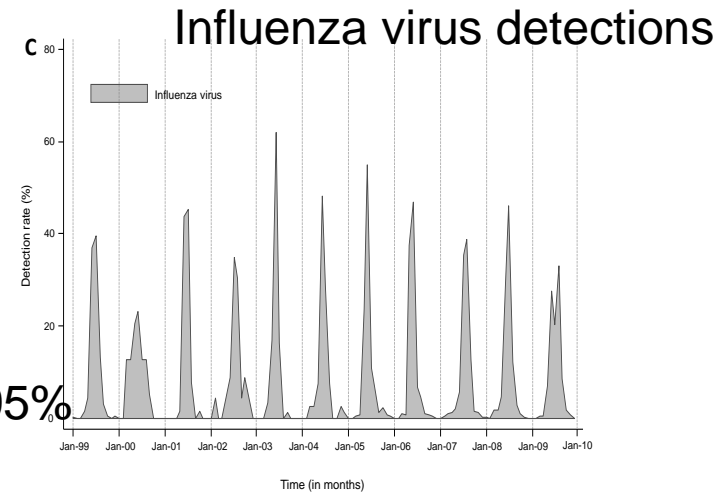
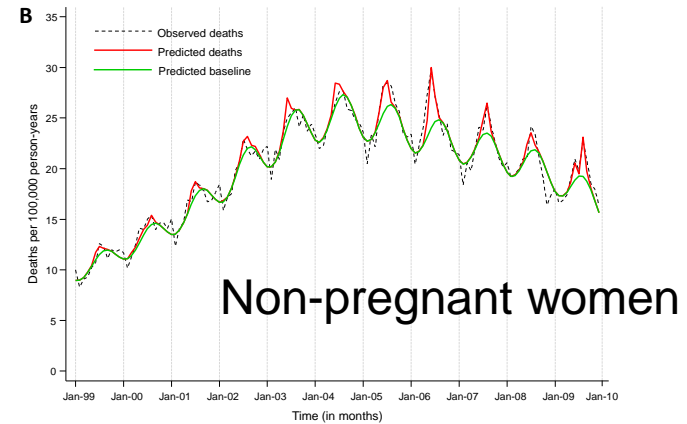
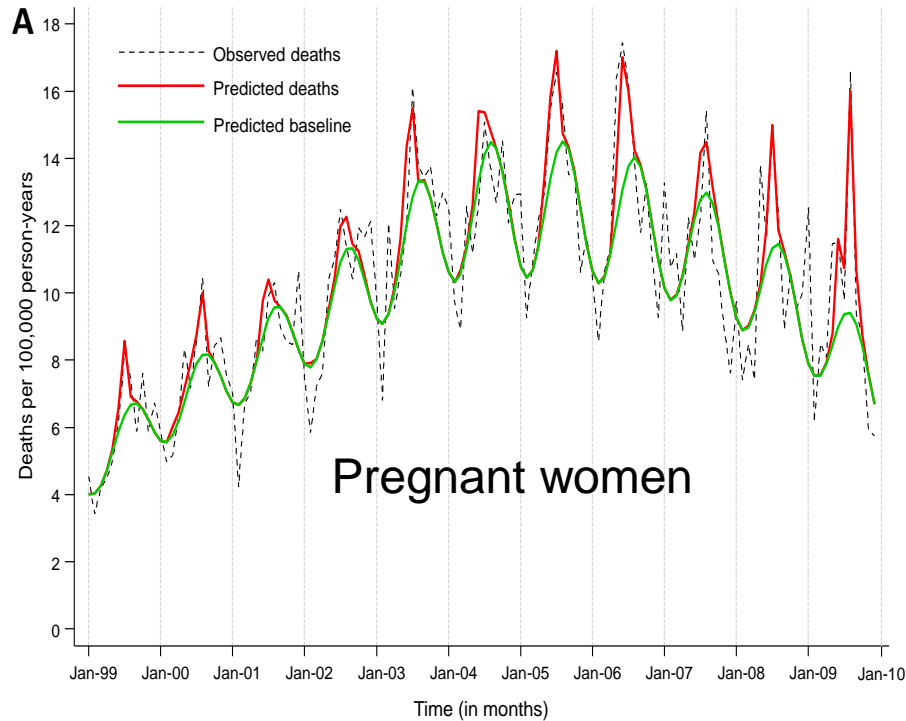
HUU – HIV unexposed uninfected, HEU – HIV exposed uninfected, HI – HIV infected  
 CI – confidence interval

# In- and Out-of-hospital Mortality Associated with Seasonal and Pandemic Influenza and Respiratory Syncytial Virus in South Africa, 2009–2013

Cheryl Cohen,<sup>1,2</sup> Sibongile Walaza,<sup>1,2</sup> Florette K. Treurnicht,<sup>1,2</sup> Meredith McMorrow,<sup>3,4,5</sup> Shabir A. Madhi,<sup>1,2,6</sup> Johanna M. McAnerney,<sup>1</sup> and Stefano Tempia<sup>3,4</sup>

- Estimated 11800 annual seasonal influenza-associated deaths in South Africa
- Influenza accounts for ~ 4% of respiratory deaths
- Highest burden of influenza-associated all cause-mortality in  $\geq 75$  years
- Increased mortality in  $< 5$  years and 20-64 years

# Mortality Associated with Seasonal and Pandemic Influenza among Pregnant and Non-Pregnant Women of Childbearing Age in a High HIV Prevalence Setting – South Africa, 1999-2009



•Pregnant women **seasonal** influenza-associated mortality compared to non-pregnant women **RR 2.8** 95% CI 2.1-3.7

•HIV infected RR 2.9 95% CI 2.1-3.7

•HIV-uninfected RR 2.4 95% CI 2.1-2.7

•In 2009 **pandemic** RR **3.2** 95% CI 2.3-4.1

# Excess Mortality Associated with Influenza among Tuberculosis Deaths in South Africa, 1999–2009

Sibongile Walaza<sup>1,4\*</sup>, Cheryl Cohen<sup>1,4</sup>, Ananta Nanoo<sup>1</sup>, Adam L. Cohen<sup>2,3</sup>, Johanna McAnerney<sup>1</sup>, Claire von Mollendorf<sup>1,4</sup>, Jocelyn Moyes<sup>1,4</sup>, Stefano Tempia<sup>1,2,3\*</sup>

- Influenza-associated PTB deaths
  - 5 x greater than non-TB respiratory deaths in **HIV infected** (RR 5.2 95%CI 4.6-5.9)
  - 60 x greater than non-TB respiratory deaths in **HIV uninfected**

Individual level data supportive.

A On multivariable analysis, patients co-infected with tuberculosis and influenza as compared to patients with tuberculosis only were at increased risk of death (aRRR 3.1, 95% CI 1.1-8.9).

Walaza et al BMC Infectious Diseases 2015

Deaths per 100,000 population



**Factors associated with death among hospitalised individuals aged  $\geq 15$  years with severe respiratory illness testing tuberculosis positive at two sentinel surveillance sites, South Africa, 2010-2016 (n=1075)**

Characteristics		Case fatality rate	Adjusted odds ratio (95% CI)	P value
Age group	15-24	8/129 (6)	1	
	25-44	69/656 (11)	1.5 (0.7-3.3)	0.286
	45-64	32/258 (13)	1.8 (0.8-3.9)	0.181
	$\geq 65$	7/36 (19)	<b>3.6 (1.2-11)</b>	<b>0.026</b>
HIV status	Negative	20/168 (12)	1	
	Positive	87/848 (10)	0.9 (0.5-1.6)	0.756
Influenza infection	Negative	108/1033 (10)	1	
	Positive	8/42 (19)	<b>2.3 (1.1-5.2)</b>	<b>0.045</b>
Duration of symptoms prior admission	$\leq 7$ days	20/258 (8)	1	
	$> 7$ days	94/786 (12)	1.5 (0.9-2.5)	0.114



**Factors associated with death among hospitalised individuals aged  $\geq 15$  years with severe respiratory illness testing influenza positive at two sentinel surveillance sites, South Africa, 2010-2016 (n=232)**

Characteristics		Case fatality rate	Adjusted odds ratio (95% CI)	P value
Age group	15-24	1/19 (5)	1	
	25-44	8/131 (6)	1.0 (0.1-8.9)	0.989
	45-64	6/57 (10)	2.5 (0.3-24.2)	0.417
	$\geq 65$	3/25 (12)	5.1 (0.4-65.9)	0.210
HIV status	Negative	4/66 (6)		
	Positive	14/156 (9)	2.0 (0.5-8.8)	0.337
Tuberculosis	No	10/190 (5)	1	
	Yes	8/42 (19)	<b>4.5 (1.5-13.2)</b>	<b>0.007</b>
Duration of symptoms prior admission	$\leq 7$ days	6/109 (5)	1	
	> 7 days	12/120 (10)	1.6 (0.6-4.7)	0.355

# VACCINE EFFECTIVENESS

# Effectiveness of seasonal influenza vaccine

- Since 2005 data collected on vaccine history
  - Vaccine coverage very low in South Africa
- Test-negative case control studies were conducted amongst patients enrolled as part of the Viral Watch programme (ILI in private practitioners) to estimate VE.
  - Patients in whom influenza was detected were considered cases and those who tested negative for influenza were unmatched controls
  - Only specimens collected during the annual influenza season were included in the VE analysis.
  - Patients who met the ILI case definition, had a known influenza vaccine history, and were 6 months or older were included in the VE analysis.

# Vaccine receipt and vaccine effectiveness by influenza type and subtype adjusted for age, underlying medical condition & timing within season: 2010-2017

Year	Predominant circulating strain	n/N(%)	Vaccine effectiveness Confidence interval (95%)
2010	Influenza B	310/585 (53)	<b>48.2 (13.8, 68.8)</b>
2011	A(H1N1)pdm09	561/698 (80)	<b>44.0 (12.1, 64.3)</b>
2012	A(H3N2)	360/586 (61)	22.8 (-29.7, 54.1)
2013	A(H1N1)pdm09	539/797 (67)	<b>77.8 (49.0, 90.3)</b>
2014	A(H3N2)	335/473 (71)	17.9 (-76.8, 61.9)
2015	A(H1N1)pdm09	251/490 (51)	<b>61.2 (13.8, 82.5)</b>
2016	A(H3N2)	207/523 (40)	18.1 (-54.9, 56.7)
	Influenza B	202/523 (39)	
2017	A(H3N2)	481/653 (74)	33.82 (-10.5, 60.4)

# Influenza Epidemiology and Vaccine Effectiveness among Patients with Influenza-Like Illness, Viral Watch Sentinel Sites, South Africa, 2005–2009

Genevieve M. Ntshoe<sup>1\*</sup>, Johanna M. McAnerney<sup>2</sup>, Stefano Tempia<sup>3</sup>, Lucille Blumberg<sup>1</sup>, Jocelyn Moyes<sup>2</sup>, Amelia Buys<sup>2</sup>, Dhamari Naidoo<sup>4</sup>, Marietjie Venter<sup>2</sup>, Terry Besselaar<sup>4</sup>, Barry D. Schoub<sup>5</sup>, Bernice N. Harri: Cheryl Cohen<sup>2\*</sup>

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www.influenzajournal.com

Original Article

## Effectiveness and knowledge, attitudes and practices of seasonal influenza vaccine in primary healthcare settings in South Africa, 2010–2013

Johanna M. McAnerney,<sup>a</sup> Sibongile Walaza,<sup>a</sup> Adam L. Cohen,<sup>b,c</sup> Stefano Tempia,<sup>a,b,c</sup> Amelia Buys,<sup>a</sup> Marietjie Venter,<sup>a</sup> Lucille Blumberg,<sup>a</sup> Jazmin Duque,<sup>b,d</sup> Cheryl Cohen<sup>a</sup>

<sup>a</sup>National Institute for Communicable Diseases (NICD) of the National Health Laboratory Services (NHLS), Johannesburg, South Africa. <sup>b</sup>U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA. <sup>c</sup>U.S. Centers for Disease Control and Prevention, Pretoria, South Africa. <sup>d</sup>Battelle Atlanta, Atlanta, GA, USA.

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www.influenzajournal.com

Short Article

## Evaluation of influenza vaccine effectiveness and description of circulating strains in outpatient settings in South Africa, 2014

Johanna M. McAnerney,<sup>a</sup> Florette Treurnicht,<sup>a</sup> Sibongile Walaza,<sup>a,b</sup> Adam L. Cohen,<sup>c,d</sup> Stefano Tempia,<sup>a,c,d</sup> Senzo Mtshali,<sup>a</sup> Amelia Buys,<sup>a</sup> Lucille Blumberg,<sup>a</sup> Cheryl Cohen<sup>a,b</sup>

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SHORT REPORT

WILEY

## Estimating vaccine effectiveness in preventing laboratory-confirmed influenza in outpatient settings in South Africa, 2015

Johanna M. McAnerney<sup>1</sup> | Sibongile Walaza<sup>1</sup> | Stefano Tempia<sup>1,2,3</sup> | Lucille Blumberg<sup>1</sup> | Florette K. Treurnicht<sup>1</sup> | Shabir A. Madhi<sup>1,4</sup> | Ziyaad Valley-Omar<sup>1,5</sup> | Cheryl Cohen<sup>1</sup>

<sup>1</sup>National Health Laboratory Services (NHLS), National Institute for Communicable Diseases (NICD), Johannesburg, South Africa

<sup>2</sup>Influenza Division, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA

<sup>3</sup>Influenza Program, U.S. Centers for Disease Control and Prevention, Pretoria, South Africa

<sup>4</sup>Faculty of Health Sciences, Medical Research Council Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand, Johannesburg, South Africa

Trivalent seasonal influenza vaccine effectiveness during the 2015 season in South Africa was assessed using a test-negative case control study design. Influenza A(H1N1)pdm09 was the dominant circulating strain. Overall influenza vaccine coverage was 3.2% (29/899). The vaccine effectiveness estimate, against any influenza virus infection, adjusted for age, underlying conditions and timing within season was 46.2% (95% CI: -23.5 to 76.5), and 53.6% (95% CI: -62.6 to 80.3) against influenza A(H1N1)pdm09.

# **GENETIC CHARACTERISATION OF INFLUENZA VIRUSES AND ANTIVIRAL RESISTANCE**



## Genetic characterisation of influenza viruses and antiviral resistance

- A(H1N1)pdm09 strains from 2017 were in sub-lineage 6B.1
- All A(H3N2) strains were within the genetic subgroup 3C.2a1
- Influenza B viruses sequenced grouped predominantly with B/Yamagata lineage viruses
- No genetic mutations associated with reduced susceptibility to oseltamivir was observed

# National influenza policy

## Goals of the National Influenza Policy

- Reduce influenza transmission and disease
- Establish sustainable influenza surveillance programme
- Ensure security of supply for seasonal and pandemic influenza vaccines
- Ensure national influenza epidemic and pandemic preparedness
- Ensure appropriate treatment and care for individuals infected with influenza
- Generate an evidence base for rational decision making related to influenza control and prevention activities
- Promote studies on influenza at the Human-Animal Interface

## National Influenza Policy and Strategic Plan

2017 to 2021

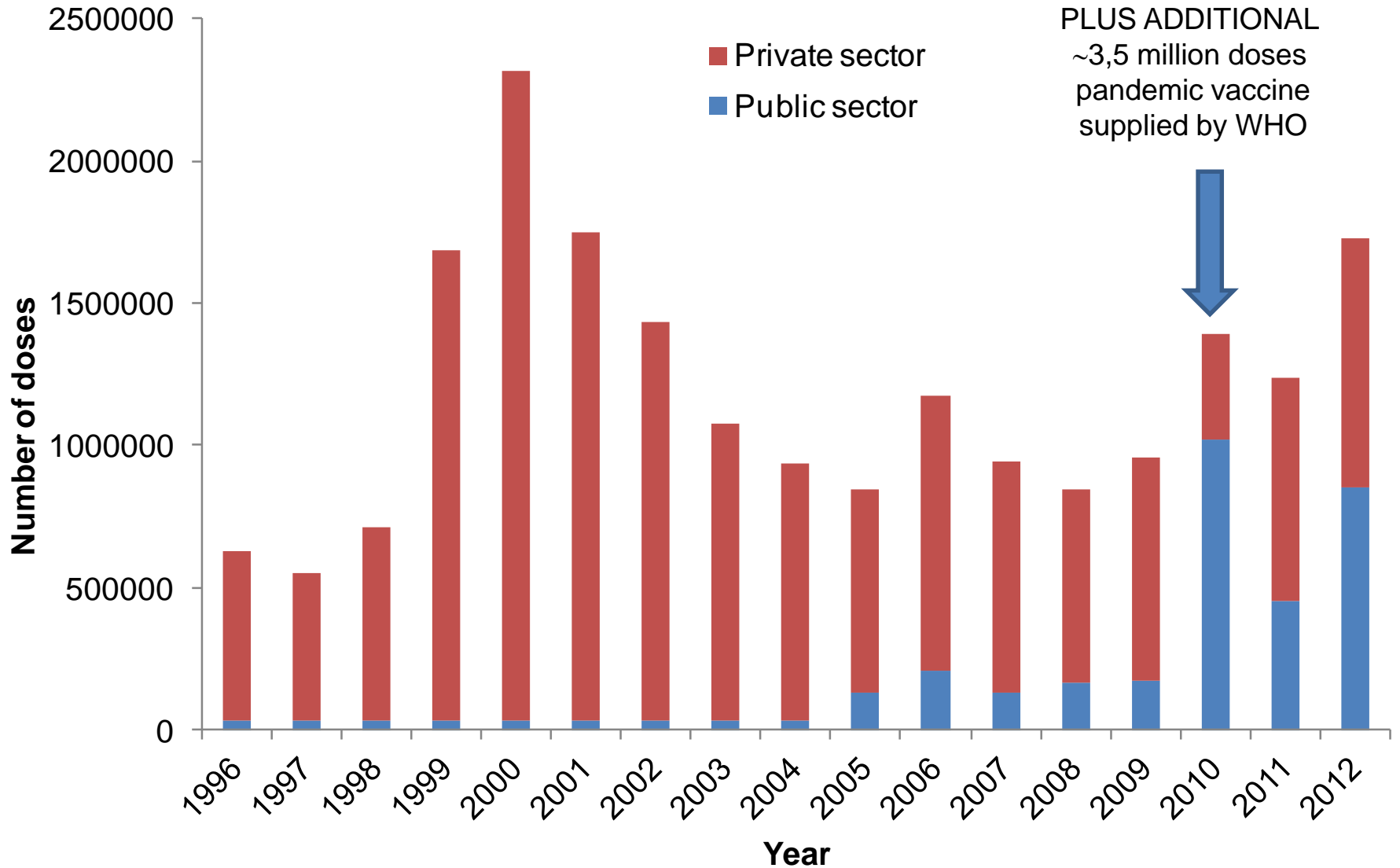
<http://www.health.gov.za/index.php/component/phocadownload/category/339-national-influenza-policy-#>



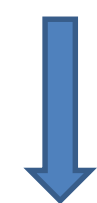
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# Annual number of influenza vaccine doses distributed, South Africa, 1996-2012



PLUS ADDITIONAL  
~3,5 million doses  
pandemic vaccine  
supplied by WHO



Population 1996 - 40,5 million

Population 2011 - 51.7 million

# Groups recommended for influenza vaccination

1. Pregnant women – irrespective of the stage of pregnancy, or postpartum (within 2 weeks after delivery)
2. HIV infected individuals
3. Individuals with underlying medical conditions (including tuberculosis)
4. Persons over the age of 65 years

## **Other groups that would benefit**

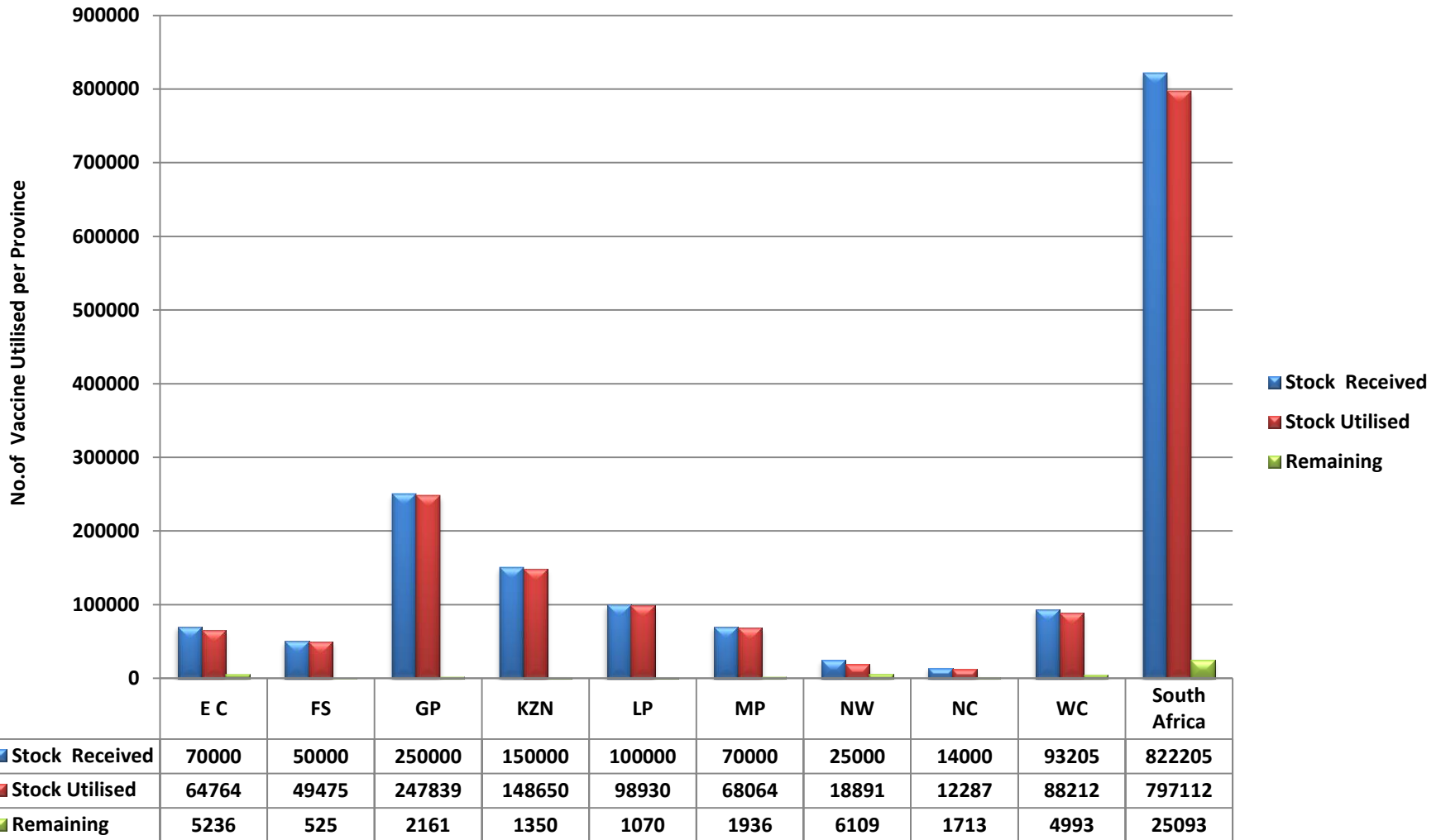
1. Healthcare workers
2. Residents of old-age homes, chronic care and rehabilitation institutions.  
individual who are morbidly obese ( $BMI \geq 40 \text{ kg/m}^2$ )
3. Adults and children who are family contacts of individuals at high-risk
4. Any persons wishing to protect themselves from the risk of contracting influenza

# Numbers of individuals in groups targeted for influenza vaccination in South Africa, 2011

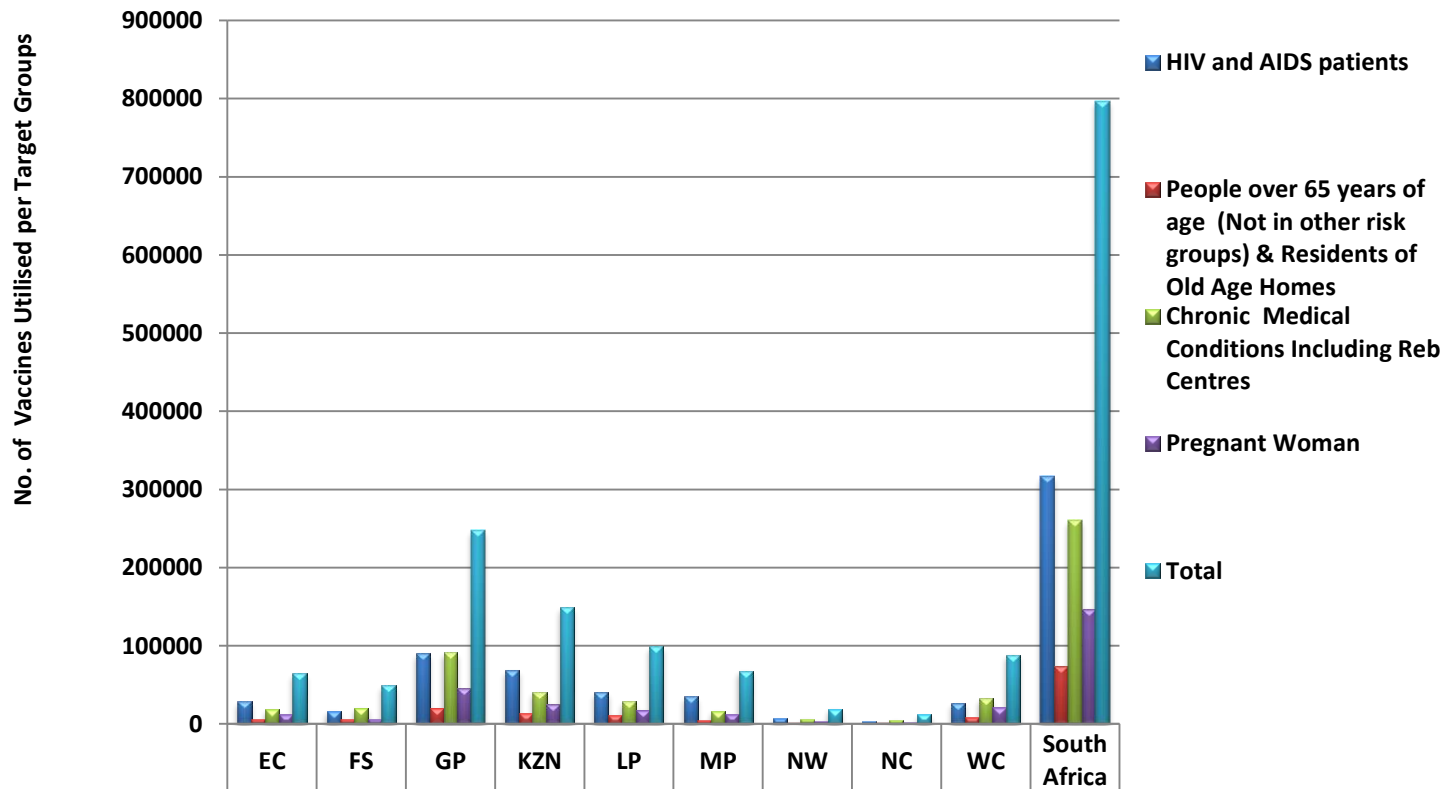
Target group	Number
Children $\leq 5$ years	5 189 528
Adults $\geq 65$ years	2 538 955
All pregnant women	852 831
Pregnant women (HIV-uninfected)	595 276
Pregnant women (HIV-infected)	257 555
HIV-infected (5-64 years, not pregnant)	5 023 017
Tuberculosis and without HIV infection (5-64 years)	138 953
Specific high-risk underlying conditions (5-64 years)	6 643 032
Health care workers	72 000
TOTAL	20 458 316

**PARADOX: Many more in risk groups than available doses**

# Influenza utilization by province, Department of Health vaccination campaign, South Africa 2017



# Influenza vaccination by target groups, Department of Health vaccination campaign, 2017



	EC	FS	GP	KZN	LP	MP	NW	NC	WC	South Africa
<b>HIV and AIDS patients</b>	28770	16436	90345	68421	40479	34735	7175	3222	26688	316271
<b>People over 65 years of age (Not in other risk groups) &amp; Residents of Old Age Homes</b>	5673	6004	20496	13907	11639	4449	1650	1833	7995	73646
<b>Chronic Medical Conditions Including Reb Centres</b>	18305	20416	91468	40904	28905	16375	6293	4932	32547	260145
<b>Pregnant Woman</b>	12016	6619	45530	25418	17907	12505	3773	2300	20982	147050
<b>Total</b>	64764	49475	247839	148650	98930	68064	18891	12287	88212	797112



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## Influenza

# NICD Recommendations for the diagnosis, prevention, management and public health response

[http://www.nicd.ac.za/wp-content/uploads/2017/03/Influenza-guidelines-final\\_24\\_05\\_2017.pdf](http://www.nicd.ac.za/wp-content/uploads/2017/03/Influenza-guidelines-final_24_05_2017.pdf)





# Conclusion

- Established surveillance for influenza
- Robust data for burden estimates and risk groups
- Data to guide prioritisation for influenza vaccination available
- Influenza policy and guidelines in place
- Data to assess impact of influenza in health systems not available
- Influenza vaccine cost effectiveness data ?



# THANK YOU



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