

# **Burden of Illness of Respiratory Diseases in Africa, with a focus on Influenza.**

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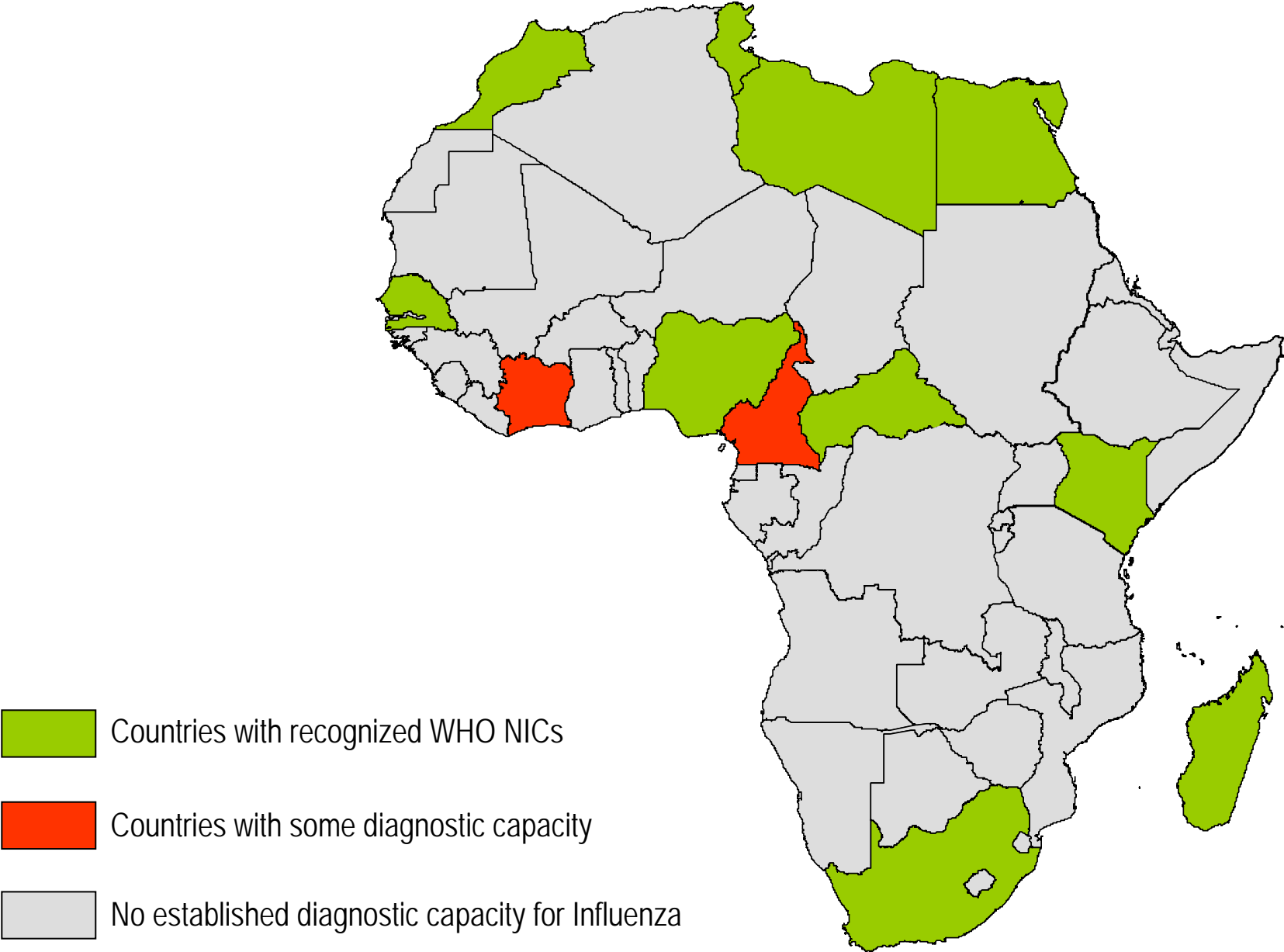
Respiratory and Meningeal Pathogens Research Unit, &

DST/NRF: Vaccine Preventable Diseases

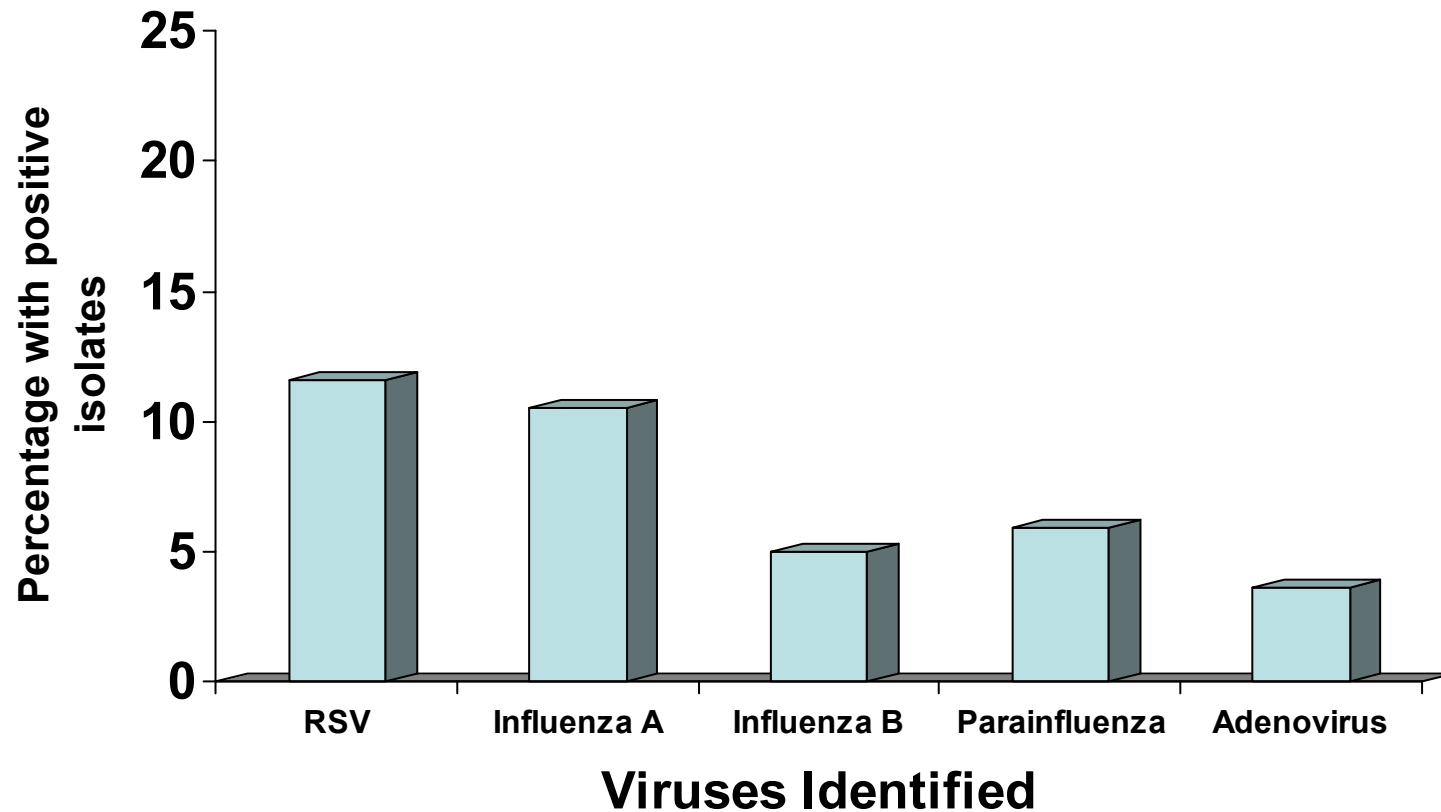


# Map of Influenza Diagnostic Capacity in Africa: 2005

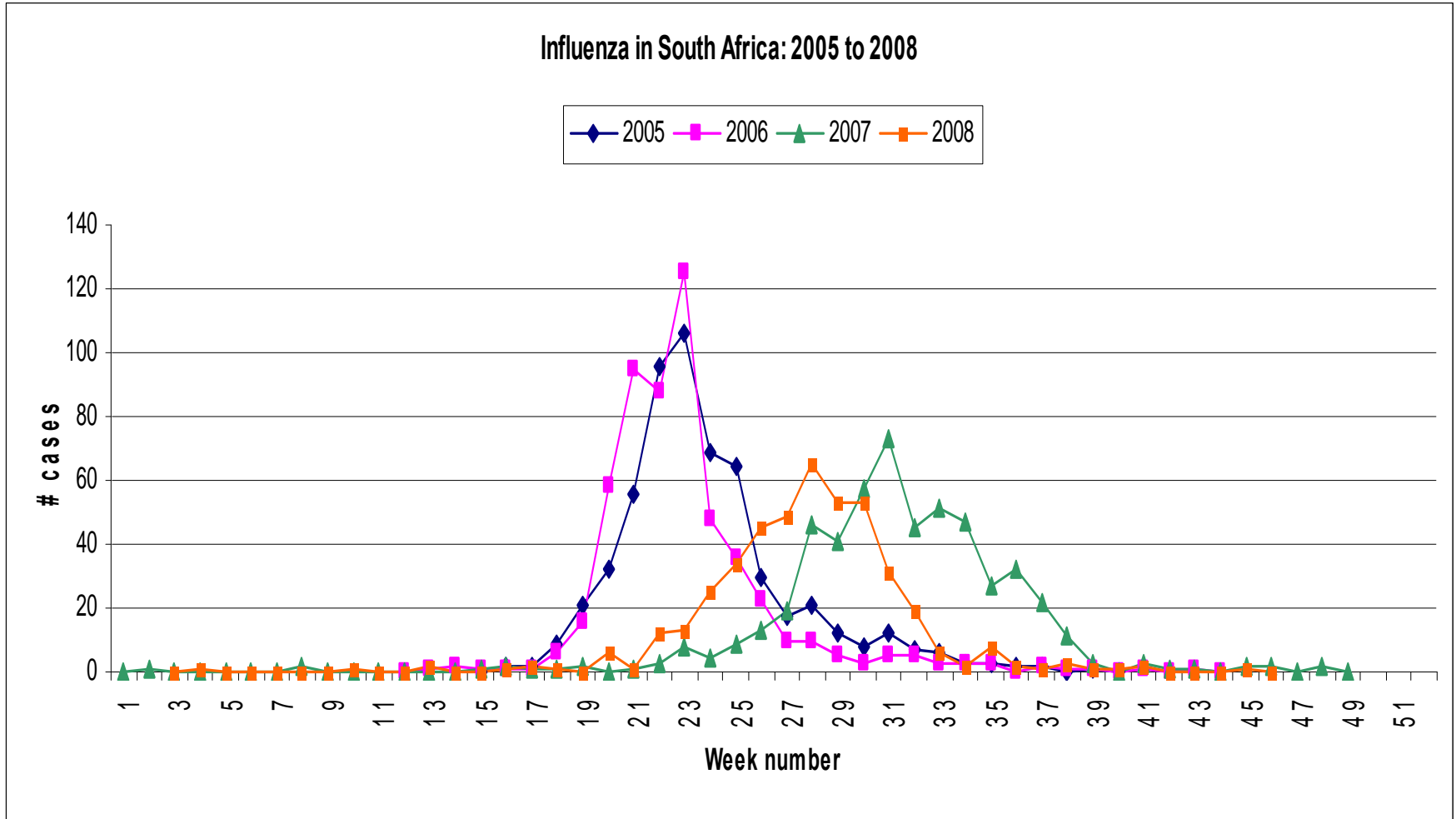
Courtesy: Stefano Tempia; CDC



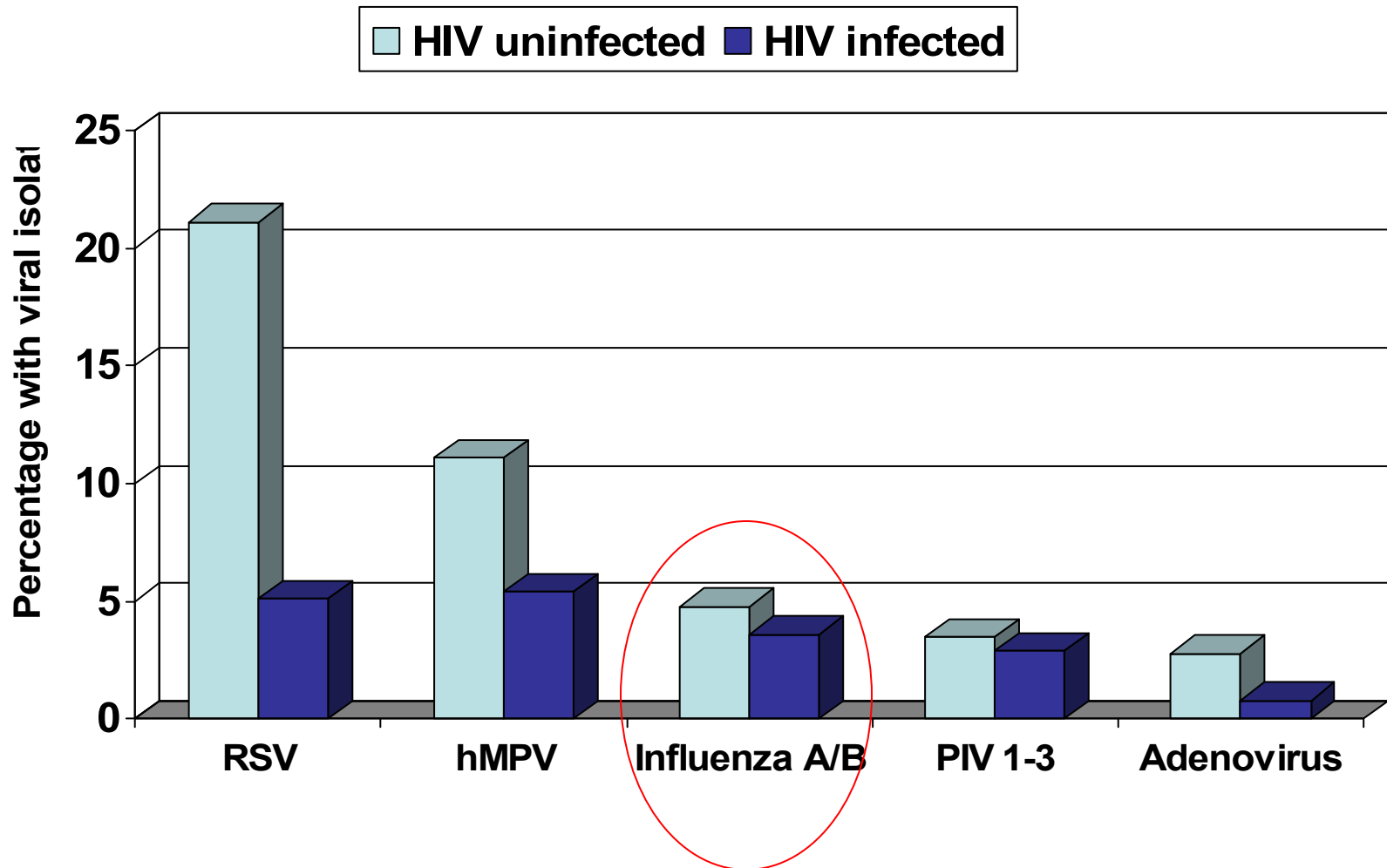
# Prevalence of Respiratory Viruses in African Infants less Than 3 Months (N=438) investigated with signs of possible infection (1991- 1992)



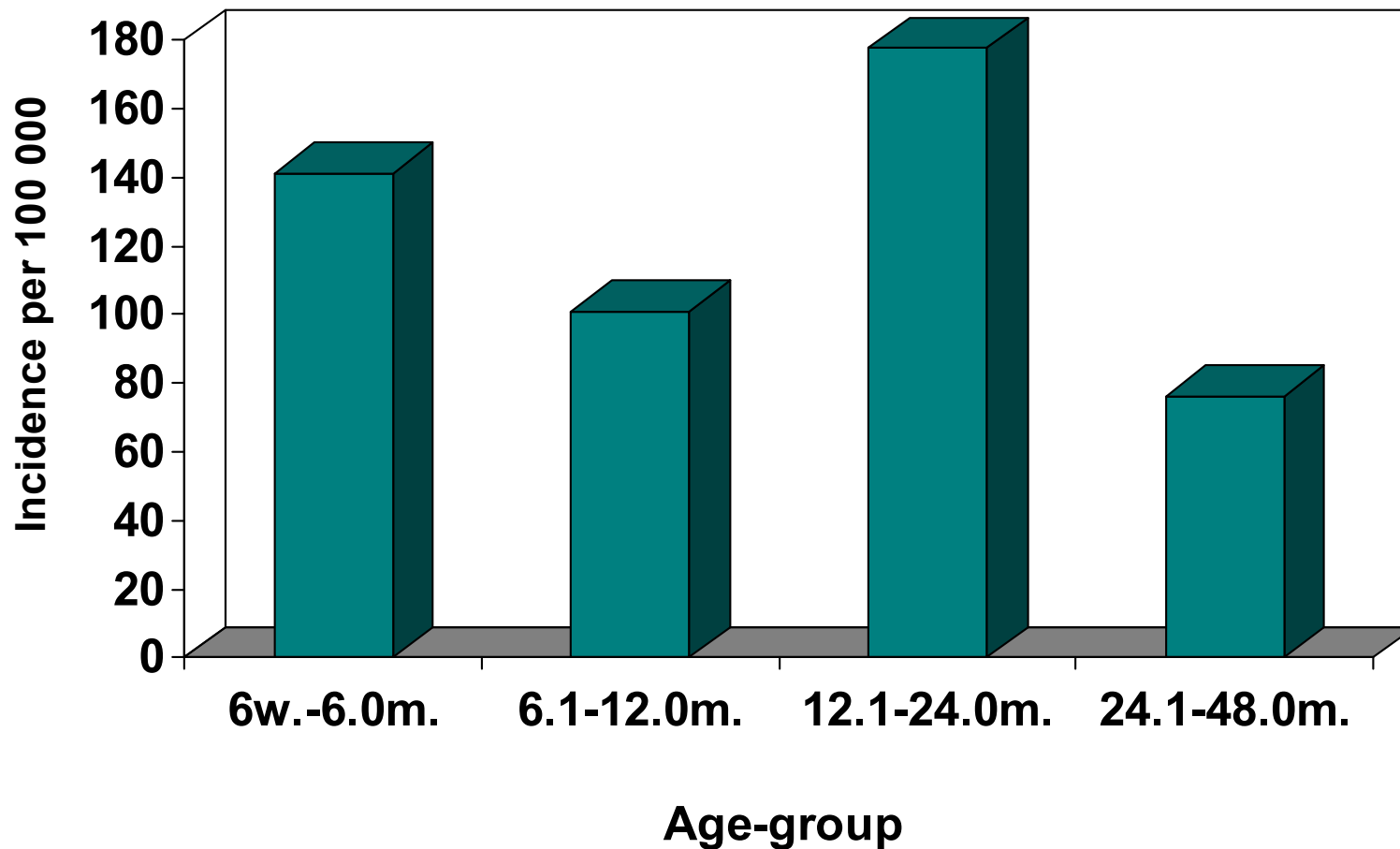
# Seasonality of Influenza Virus In South Africa.



# Prevalence Of Identifying Respiratory Viruses In PCV-unvaccinated Children Hospitalized With Lower Respiratory Tract Infections



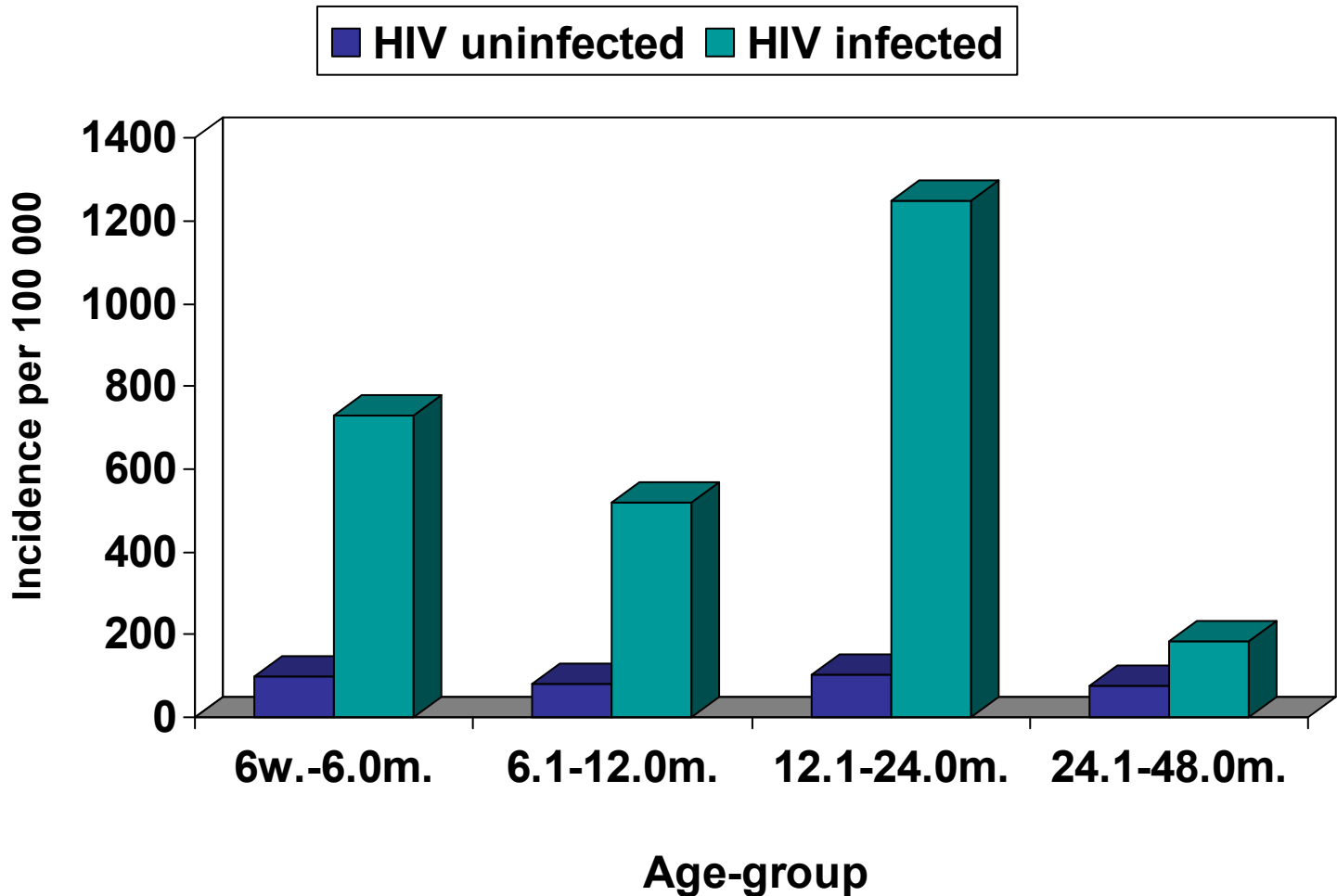
# Incidence Of Hospitalization For Confirmed Influenza Associated LRTI In Children (No PCV)



Unpublished data: S Madhi. PCV-9 Efficacy Trial; South Africa.

# Agegroup Incidence Of Hospitalization For Influenza Associated LRTI In Children Not Vaccinated With PCV

Unpublished data: S Madhi. PCV-9 Efficacy Trial; South Africa.



RR; 95%C.I. 7.8 (7.4-17.5) 6.5 (2.5-17.0) 12.1 (6.1-24.3) 2.5 (0.6-10.8)

Overall HIV+ vs. HIV-: R.R. 7.5 (4.7-11.8)

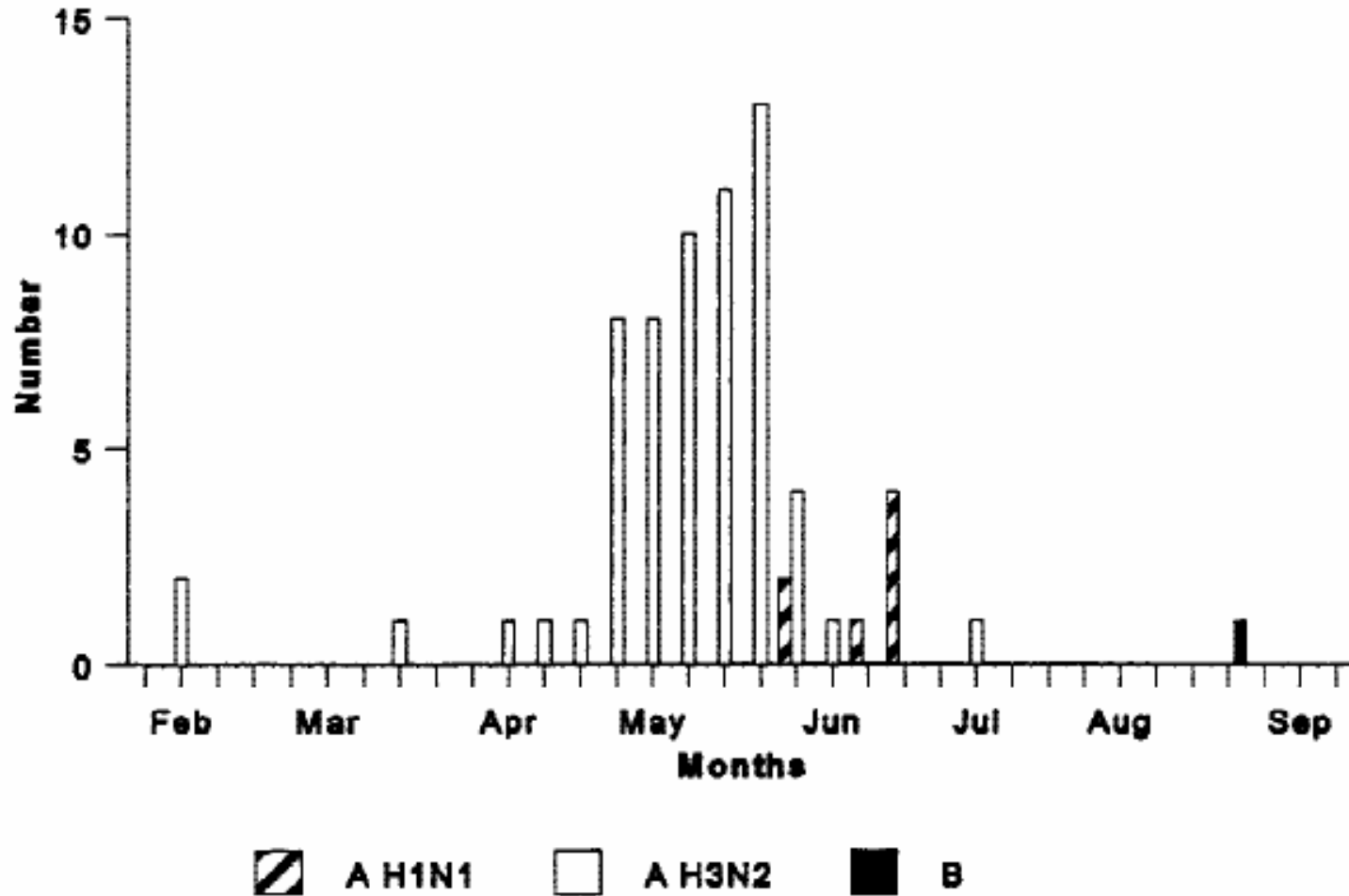
# Impact Of PCV On Hospitalization for Influenza Virus Associated Pneumonia

<b>Group: Per protocol</b>	<b>Vaccine</b>	<b>Placebo</b>	<b>Efficacy</b>	<b>95%C.I.</b>	<b>P value</b>
<b>Overall</b>	<b>30</b>	<b>53</b>	<b>43</b>	<b>11 to 64</b>	<b>0.01</b>
<b>HIV uninfected</b>	<b>21</b>	<b>32</b>	<b>34</b>	<b>-14 to 62</b>	<b>0.1</b>
<b>HIV infected</b>	<b>9</b>	<b>21</b>	<b>57</b>	<b>7 to 80</b>	<b>0.03</b>

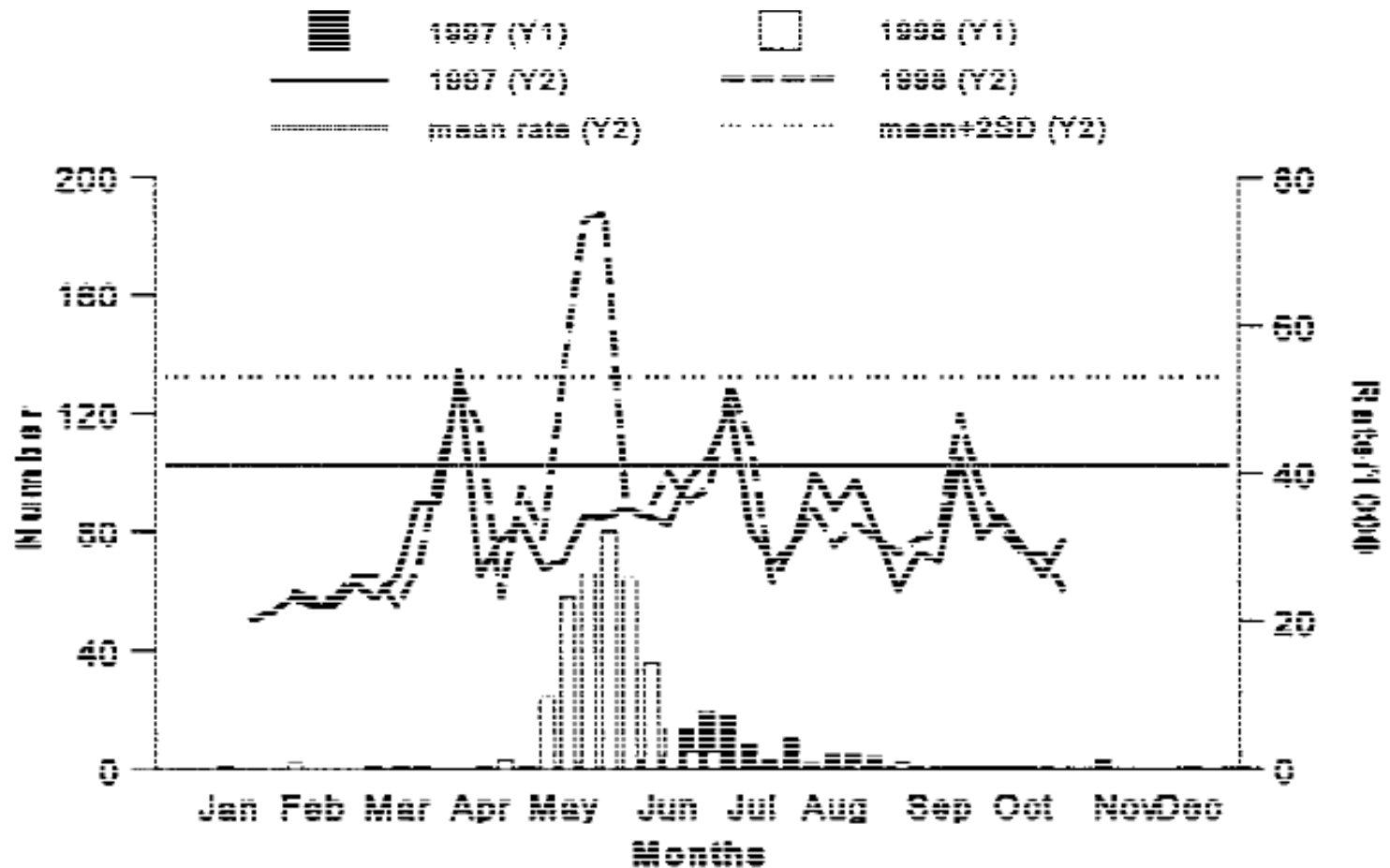
**Influenza Virus Predisposes to Pneumococcal Co-Infection Resulting in Severe Pneumonia Requiring Hospitalization.**

# **Impact of Influenza Virus Infection in School-Aged Children in South Africa**

# Distribution of the 1998 subttyped influenza isolates



# Distribution Of Influenza Isolates And School Absenteeism For 1997 And 1998.

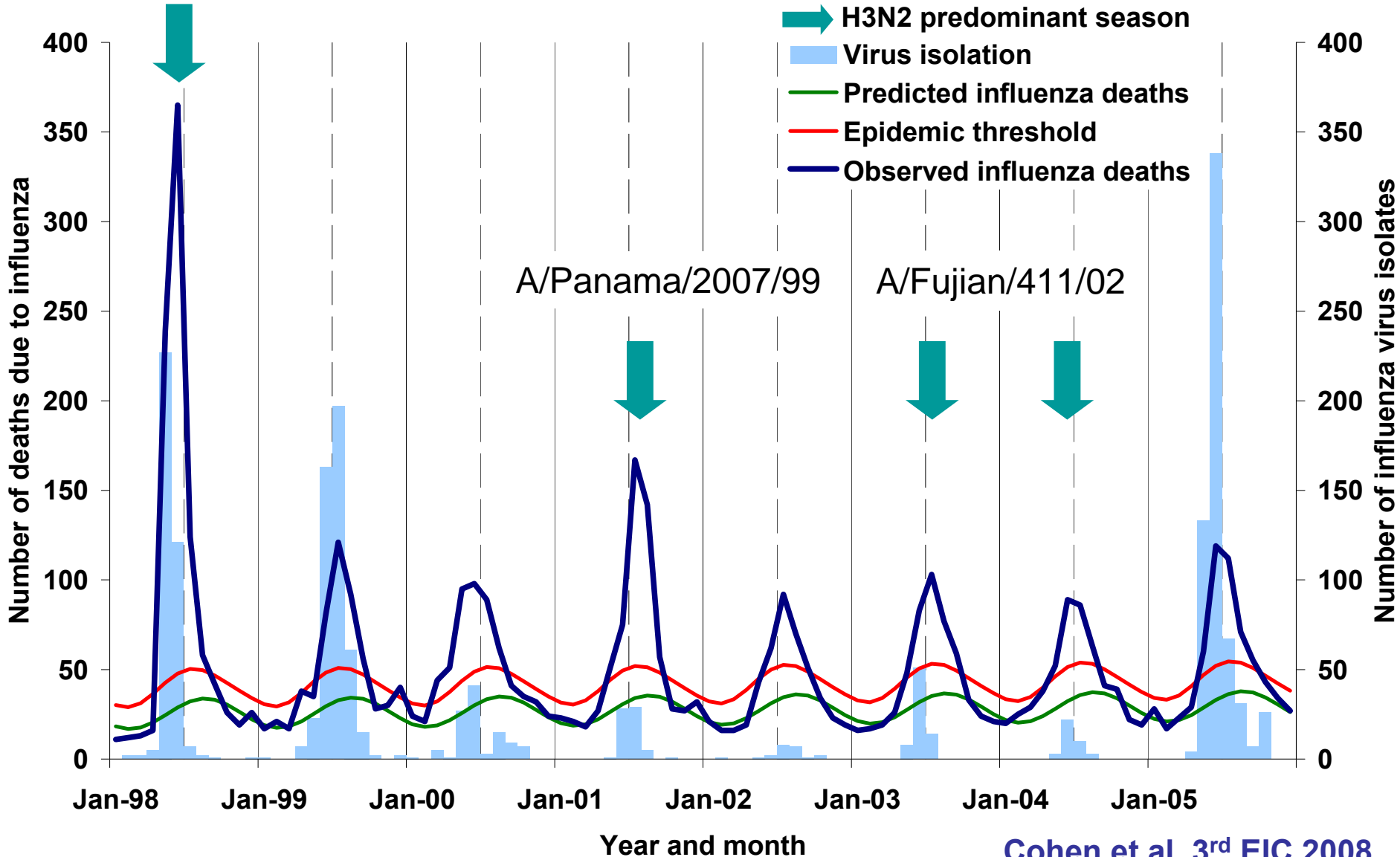


# **Impact of Influenza Virus Epidemics on Mortality in the Elderly in Africa**

# Observed and predicted influenza deaths and epidemic threshold; and number of influenza viral isolations by month, persons $\geq 65$ years, 1998-2005, South Africa

A/Sydney/5/97

years, 1998-2005, South Africa



# Seasonal influenza-related excess mortality $\geq 65$ years South Africa (SA) vs United States of America (USA) 1998-2005

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Cause of death	Age standardised deaths per 100,000 *		
	SA	USA	P+
All-cause	545	133	<0.001
Pneumonia & Influenza	63	21	0.002

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\* Standardised to the USA population in 2000

+ Wilcoxon rank sum test

# Novel H1N1 in South Africa in 2009

- 12 631 laboratory confirmed cases in SA (8 June to 1 Dec 2009)
  - 92 deaths
    - 28% (26/91) deaths in pregnant/ puerperium
    - 50% (19/38) HIV positive
    - 23% (20/85) no co-morbidities identified
  - In pregnant women, 95% (19/20) in 3<sup>rd</sup> trimester, 2 were <42 days post delivery
    - 68% (11/16) HIV positive
    - 18% (4/22) had documented active TB

**Randomised controlled trial of safety,  
immunogenicity and efficacy of trivalent  
inactivated influenza vaccine in African HIV  
infected adults**

# Methods

- A prospective double blind, randomized placebo-controlled trial was undertaken in HIV+ adults on stable first line antiretroviral treatment (ART) or ART naïve with CD4 cell count >100cells/ml in 2008
- Study participants were randomized to receive a single dose of placebo or TIV (Vaxigrip®), including vaccine strains A/Solomon Islands/3/2006 (H1N1)-like virus; A/Brisbane/10/2007 (H3N2)-like virus and B/Florida/4/2006-like virus, prior to the anticipated onset of the influenza season
- Oropharyngeal swabs were obtained from subjects responding to weekly short message text (SMS) reminders to attend the clinic for influenza-like symptoms and those with unsolicited visits for respiratory illness.

## Vaccine efficacy calculations for ITT efficacy cohort: confirmed influenza illness (n=506)

Outcome	Overall				
	TIIV N=255	Placebo N=251	Vaccine Efficacy	P	Rate Reduction
Influenza A or B	3 (0.06)	12 (0.25)	75.4% (14.2-93.0)	0.019	0.19
Influenza A H1N1	3 (0.06)	11 (0.23)	73.5% (5.1-92.5)	0.028	0.16

## Immune responses to H1N1 influenza virus strain in HIV infected adults to TIV or placebo

<b>Immunogenicity measure</b>	<b>TIV n=97</b>	<b>Placebo n=91</b>	<b>P-value</b>
Proportion with antibody response post- vaccine (%) <sup>1</sup>	65 (67%)	9 (10%)	<0.0001
Proportion with seroprotection post-vaccine (%) <sup>2</sup>	55 (57%)	10 (11%)	<0.0001

<sup>1</sup> Haemagglutinin inhibition antibody titre (HAI) response defined as either a 4-fold increase in titre from baseline or an increase from <1:10 to ≥1:10 in HAI titer from baseline to 4 weeks post-immunization.

<sup>2</sup> Seroprotection defined as HAI titre ≥1:40 at 4 weeks after immunization

## Conclusion:

- Paucity of influenza data from most of Africa.
- Influenza causes significant morbidity and mortality in South Africa.
- RCT demonstrated high efficacy of TIV vaccination against confirmed influenza disease in HIV+ adults.
- Influenza vaccination should be encouraged in Africa.