Guideline for the Vaccination of HIV-infected Adolescents & Adults

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Declarations
Outline

• Introduction

• Guideline

• Vaccines with strong local evidence for use

• Vaccines that are recommended but local data lacking

• Vaccines with no recommendation
When immunization rates are high, the wider community is protected including:

Infants who are too young to receive their vaccines.

Older adults at risk of serious diseases.

People who take medication that lowers their immune systems.
Southern African HIV Clinicians Society

• Promotes evidence-based HIV Healthcare in Southern Africa
• Society supports & strengthens capacity of its members
  • Deliver high quality HIV prevention, care & treatment services
• Activities;
  • Journals and publications
  • **Practice Guidelines**
  • Meetings (CPD-accredited CME)
  • Conference
  • Clinical Resources
  • Policy and Advocacy
• Society is a NPC
• Membership includes doctors, nurses, pharmacists & other health care professionals
Introduction

THE AGE OF VACCINES

The advent of routine childhood vaccination has led to dramatic declines in many contagious diseases in the United States. Maintaining these gains there and spreading these success worldwide is challenge for public health. By Tony Scully.

A HISTORY OF DISEASE REDUCTION

An analysis of weekly disease surveillance recorded at the state level by the US Centre for Disease Control and Prevention reveals how many major threats to public health have been affected by the introduction of a vaccine; an estimated 103 million cases of childhood diseases since 1924.

Vaccines are now widely regarded as an effective and cheap tool for improving health

Importance of full immunization throughout life and its role in achieving the 2030 Sustainable Development Goals
Whole Life Approach to Immunization

• Importance of vaccination
  • Prevention to avert health spending
  • Prevention is a “best buy”

• Vaccines seen as a solution for national & economic security

• Dual function of vaccines
Vaccination essential element for promoting

• Health equity

• Economic equity (reducing medical & non-medical costs)

• Social equity – access to the health care system

• Vertical equity intervention- vaccines for diseases of poverty
Guideline Development

• Experts in the field of vaccination
  • Vaccines for Africa Initiative (VACFA)
• National Institute for Communicable Diseases (NICD)
• Academics
• Private Sector
• Rural health
• Pediatricians & Physicians
• South African Cochrane Centre
• Full day workshop
• Presentation of local data
• Discussion
• Recommendation
  • Consensus if no local data
• Draft of guidelines
  • Evidence based
  • Based on best international practice
  • Circulated and comments received

• Review of guideline recommendation
  • Every 3-5 years
  • Identify gaps in local data –help inform future guidelines
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

TABLE 1: Vaccination guidelines for HIV-infected adolescents and adults.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Safety CD4 count</th>
<th>Doses for unvaccinated adults</th>
<th>Booster</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR vaccine</td>
<td>Measles, mumps, rubella seronegative</td>
<td>&gt; 200 cells/mL</td>
<td>2 doses (20 days apart)</td>
<td>-</td>
<td>Mainly indicated in measles seronegative HIV-infected women of childbearing age. Pregnancy should be avoided for 1 month after vaccination.</td>
</tr>
<tr>
<td>influenza</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td>yearly</td>
<td>-</td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV13)</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td>-</td>
<td>Given with IPV23 but must be given first</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPV23)</td>
<td>RS</td>
<td>&gt; 200 cells/mL</td>
<td>1 dose</td>
<td>&gt; 10 years</td>
<td>Given with PCV13 but given 8 weeks after PCV13. Can be given to patients with CD4 count &lt; 200 cells/mL if on ART and VL suppressed. Maximum of 2 booster doses: 1 booster dose in patients &gt; 83 years. Poor response if CD4 cell count &lt; 200 cells/mL and VL not suppressed.</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>R</td>
<td>Any</td>
<td>4 doses (40 µg) or 3 doses (20 µg)</td>
<td>Not clear awaiting evidence</td>
<td>-</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>RS – travel, MSM, IV drug users</td>
<td>&gt; 200 cells/mL</td>
<td>2 doses</td>
<td>10 years</td>
<td>-</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>RS</td>
<td>Any</td>
<td>2 doses</td>
<td>5 years</td>
<td>-</td>
</tr>
<tr>
<td>Tetanus-diphtheria (Td)</td>
<td>R</td>
<td>Any</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pertussis (acellular)</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td>10 years</td>
<td>Given in pregnancy combined with tetanus-diphtheria (DTPa/Td)</td>
</tr>
<tr>
<td>Poliovirus inactivated</td>
<td>RS</td>
<td>&gt; 200 cells/mL</td>
<td>3 doses</td>
<td>None</td>
<td>-</td>
</tr>
<tr>
<td>Human papilloma virus (HPV)</td>
<td>RS – females, MSM</td>
<td>Any</td>
<td>2 doses</td>
<td>None</td>
<td>May be considered if CD41 count &gt; 400 cells/mL.</td>
</tr>
<tr>
<td>Zoster</td>
<td>RS</td>
<td>&gt; 200 cells/mL</td>
<td>1 dose</td>
<td>-</td>
<td>Only use if CD4 count &gt; 200 cells/mL</td>
</tr>
</tbody>
</table>

MMR, measles, mumps, and rubella; R, recommended; RS, recommended in selected individuals; NR, not recommended; VL, viral load; HIVAb, hepatitis B surface antibody; MSM, men who have sex with men.
South Africa

- 7 million South African are HIV-infected
- ~3 million on ART
- Estimated ART coverage 42%
Trends in prevalence of selected opportunistic infections associated with HIV/AIDS in Uganda
WHY Vaccinate HIV population

• Have impaired host defenses
• Increased risk of vaccine preventable diseases
• Prevent severe forms of disease
• Shared transmission routes (HIV)
• For specific risk behaviours or comorbidities
Vaccine Preventable Disability

Catastrophic disability

- Defined as a loss of independence in ≥ 3 ADL
- 72% who experience catastrophic disability have been hospitalized
- Leading causes of catastrophic disability
  1. Strokes
  2. CHF
  3. Pneumonia and influenza
  4. Ischemic heart disease
  5. Cancer
  6. Hip fracture

Ferrucci et al. JAMA 277:728, 1997
1 = Very fit
2 = Well
3 = Well, with treated chronic disease
4 = Apparently vulnerable
5 = Mildly frail
6 = Moderately frail
7 = Severely frail
8 = Very severely frail
9 = Terminally ill
Low Vaccine Coverage in HIV

- Coverage rates among HIV patients reportedly low
  - In US influenza vaccination coverage 25-43%
  - In France influenza coverage is 30.9%

- Multifactorial
  - Lack of knowledge of current vaccine recommendations
  - Lack of infrastructure in clinics to provide vaccines
  - Concerns about vaccine safety
  - Insurers not willing to pay for vaccines
Vaccines with strong local evidence for Use
Influenza

• Responsible for a 10-fold increased mortality rate

• In SA influenza kills between 6 000-11 000 people every year
  • Half of these deaths are in the elderly
  • About 30% in HIV-infected individuals

• Highest rates of hospitalization
  • The elderly (65 years and older)
  • HIV-infected people
  • Pregnant women
  • Children less than five years
**Key Points:**

- Influenza causes substantial mortality in Soweto, South Africa.
- The peak burden of mortality experienced in children <1 year age and HIV-infected adults aged 25-64 years.
- HIV infected individuals experienced a higher estimated rate of death in all age groups.
- Other risk factors for death were the presence of non-HIV underlying illness and co-infection with *S.pneumoniae*.
Influenza Vaccination of Pregnant Women and Protection of Their Infants

Shabir A. Madhi, M.D., Ph.D., Clare L. Cutland, M.D., Locadia Kuwanda, M.Sc., Adriana Weinberg, M.D., Andrea Hugo, M.D., Stephanie Jones, M.D., Peter V. Adrian, Ph.D., Nadia van Niekerk, B.Tech., Florette Treurnicht, Ph.D., Justin R. Ortiz, M.D., Marietjie Venter, Ph.D., Avy Violari, M.D., Kathleen M. Neuzil, M.D., Eric A.F. Simões, M.D., Keith P. Klugman, M.D., Ph.D., and Marta C. Nunes, Ph.D., for the Maternal Flu Trial (Matflu) Team*

Influenza vaccination in HIV-infected individuals: Systematic review and assessment of quality of evidence related to vaccine efficacy, effectiveness and safety

Cornelius Remschmidt*, Ole Wichmann, Thomas Harder

Conclusion: This systematic review indicates that TIV is effective in preventing influenza infection in HIV-infected adults but not in young children. For both age-groups, only limited evidence exists for other outcomes, indicating a need for further studies.

Vaccine 2014; 32:5585-5592
Influenza

- 1 dose yearly
- Irrespective of CD4+ cell count, HIV viral load or pregnancy status
Pneumococcal

• HIV-infected individuals have a 35 to 60 fold increase of invasive IPD
  • Higher rates of bacteremia
  • Often at risk of recurrent pneumococcal infections
  • Associated with a 2-fold higher mortality rate

• Some good reasons why vaccination important in this population

• 3 main concerns previously
  • Lack of consensus on protective levels
  • Optimal timing of immunization
  • Durability of response and protection

• Vaccines available
  • Polysaccharide vaccine (PPV23)
  • Conjugate vaccine (PCV13)
Antiretroviral Therapy as Prevention of … Pneumococcal Infections?
Figure 1. Incidence of invasive pneumococcal disease per 100,000 person-years of follow-up among HIV-infected patients by transmission group, Denmark, 1995–2012. Periods: pre–combination antiretroviral therapy (cART), 1995–1996; early cART, 1997–1999; late cART, 2000–2012. Abbreviations: cART, combination antiretroviral therapy; IDUs, injecting drug users; MSM, men who have sex with men; PYFU, person-years of follow-up.
The persisting burden of invasive pneumococcal disease in HIV patients: an observational cohort study

Reed AC Siemieniuk\(^1\),\(^2\), Dan B Gregson\(^3\),\(^4\) and M John Gill\(^1\),\(^3\)*

Conclusions: Despite universal access to intensive measures to prevent pneumococcal disease including the widespread use of HAART and PPV-23 immunization, the incidence of IPD remains high in HIV patients with its associated morbidity and mortality.

BMC Infectious Diseases 2011, 11:314
Persistent High Burden of Invasive Pneumococcal Disease in South African HIV-Infected Adults in the Era of an Antiretroviral Treatment Program

Marta C. Nunes¹, Anne von Gottberg², Linda de Gouveia², Cheryl Cohen³, Locadiah Kuwanda¹, Alan S. Karstaedt⁴, Keith P. Klugman²,⁵, Shabir A. Madhi¹,²*

Conclusion: Despite a stable prevalence of HIV and the increased roll-out of HAART for treatment of AIDS patients in our setting, the burden of IPD has not decreased among HIV-infected adults. The study indicates a need for ongoing monitoring of disease and HAART program effectiveness to reduce opportunistic infections in African adults with HIV/AIDS, as well as the need to consider alternate strategies including pneumococcal conjugate vaccine immunization for the prevention of IPD in HIV-infected adults.
Risk factors for IPD - GERMS data
- Diabetes mellitus (most common)
- Chronic lung disease
- Heart disease
- Renal disease
- Liver disease

HIV-infection
- Most affected age 25-44 years (40% on ART)

Fig 3a. Incidence of invasive pneumococcal disease (IPD) amongst HIV-uninfected and HIV-infected persons by age category, South Africa, 2008.
Immunogenicity: Opsonophagocytic Activity Following One and Two Doses of PCV13 and PPV23: Serotype 1

Paradiso PR. Clin Infect Dis 2012; 55: 259-64
This Study adds to evidence supporting current pneumococcal vaccination recommendations combining the conjugate and polysaccharide pneumococcal vaccines in the United States and Europe for HIV-infected individuals.
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

• **Pneumococcal**
  - All HIV-infected regardless of CD4+ with suppressed viral load
  - Prime-boost approach
  - PCV13 followed by PPV23 eight weeks later
  - PCV13 alone is sufficient
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

• Hepatitis B
  • Prevalence in HIV-infected individuals ranges 0.4%-23%
  • Administration of vaccine shown to be safe
  • Four-double-dose regimen
  • Best responses in those with undetectable VL & CD4+ >200 cells/µL
Diphtheria Outbreaks in South Africa

- 15 cases occurred in eThekwini, KZN province 2015
  - most cases occurred in people who were not vaccinated or partially vaccinated
- 2 confirmed cases 2016- KZN
- Diphtheria kills 1, infects 3 in Western Cape – August 2017
  - 4 lab-confirmed cases & 1 asymptomatic carrier
- 3 cases (aged 20, 11 & 10 yrs), KZN province since March 2018
  - 2 of the cases have demised
- Catch-up campaign
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

- Tetanus-diphtheria (Td)
  - Vaccinated irrespective of CD4+ count
  - Booster vaccine every 10 years (until more data available)
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

- Human papilloma virus
  - In SA HPV- preteen girls 9-13 yrs- regardless of HIV status
  - Recommended for all HIV-infected adult men (MSM) & women,
  - Can be given regardless of CD4+ count, ART use or viral load

S Afr J HIV Med 2018; 19(1)
Vaccines that are recommended but either local data lacking or warranted in select cases
Pertussis

The Pertussis Problem

Stanley A. Plotkin
Department of Pediatrics, University of Pennsylvania, Philadelphia

Pertussis is resurgent, and many cases are occurring in vaccinated children and adolescents. In countries using acellular vaccines, waning immunity is at least part of the problem. This article discusses possible improvements in those vaccines.

Clinical Infectious Diseases January 2014

Re-emergence of pertussis: what are the solutions?

Figure 1. Pertussis cases by year in the USA from 1922 to 2010. The number of cases of whooping cough has been increasing steadily since the 1980s. Reprinted with permission from [2], © Elsevier 2012.
Bordetella pertussis Infection in South African HIV-Infected and HIV-Uninfected Mother–Infant Dyads: A Longitudinal Cohort Study

Conclusions. Bordetella pertussis identification was common among young infants with respiratory illness, most of whom were too young to be fully protected through direct vaccination. Vaccination of pregnant women might be a valuable strategy in a setting such as ours to prevent B. pertussis–associated illness in women and their young infants.

Review

Pertussis in Africa: Findings and recommendations of the Global Pertussis Initiative (GPI)

Rudzani Muloiwa, Nicole Wolter, Ezekiel Mupere, Tina Tan, A.J. Chitkara, Kevin D. Forsyth, Carl-Heinz Wirsing von König, Gregory Hussey

Vaccine 36 (2018) 2385–2393
Risk of pertussis with HIV infection and exposure

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Risk ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anukam (2004)</td>
<td>22.82 (6.93, 75.14)</td>
</tr>
<tr>
<td>Kayina (2015)</td>
<td>1.57 (0.64, 3.90)</td>
</tr>
<tr>
<td>Barger-Kamate (2016)</td>
<td>1.43 (0.44, 4.65)</td>
</tr>
<tr>
<td>Muloiva (2016)</td>
<td>3.01 (1.15, 7.90)</td>
</tr>
<tr>
<td>Nunes (2016)</td>
<td>3.01 (1.15, 7.90)</td>
</tr>
<tr>
<td>Soofie (2016)</td>
<td>1.70 (0.85, 3.40)</td>
</tr>
<tr>
<td>du Plessis (2018)</td>
<td>1.62 (0.85, 3.10)</td>
</tr>
<tr>
<td></td>
<td>1.87 (0.96, 3.69)</td>
</tr>
</tbody>
</table>

Overall (I-squared = 75.7%, p = 0.001)

HEU vs HUU: 2.37 (1.08, 5.13)

HIV+ vs HUU: 1.39 (0.98, 1.96)

Overall (I-squared = 27.9%, p = 0.236)

Risk ratio – risk of pertussis increases with HIV exposure (blue) or infection (red)

Slide courtesy of Dr Muloiva
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

- **Pertussis**
  - Emerging epidemiological data on burden of pertussis in HIV endemic countries
  - Only pregnant women regardless of CD4+ count or viral load
  - Recommend acellular vaccine

*S Afr J HIV Med 2018; 19(1)*
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

• **Meningococcal**
  • Should be considered
  • 2 dose schedule (12 weeks apart)
  • Booster every 5 years

• **Hepatitis A**
  • Recommended in high risk groups
    • MSM, IV drug users, travel, chronic liver disease
  • Ideally vaccinate those with CD4+ count >200

_S Afr J HIV Med 2018; 19(1)_
Vaccines with no recommendations
Systematic review

Varicella zoster virus-associated morbidity and mortality in Africa – a systematic review

Hannah Hussey1*, Leila Abdullahi2, Jamie Collins3, Rudzani Muloiya4, Gregory Hussey2 and Benjamin Kagina5

Methods

- Developed search query
- Applied the search query in 9 databases: (PubMed, Web of Science, CENTRAL, Scopus, Africa-Wide, PDQ-Evidence, Wholis, Embase and CINAHL.)
- Screened studies for eligibility
- Data extraction and analysis
<table>
<thead>
<tr>
<th>Author (year of publication)</th>
<th>Country</th>
<th>Setting</th>
<th>Study Design</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajayi, G. O., et al. (2011)</td>
<td>Nigeria</td>
<td>Health facility</td>
<td>cohort</td>
<td>70</td>
</tr>
<tr>
<td>Asiki, G., et al. (2015)</td>
<td>Uganda</td>
<td>Community</td>
<td>case-control</td>
<td>166</td>
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<tr>
<td>Ben Fredj, N., et al. (2012)</td>
<td>Tunisia</td>
<td>Both</td>
<td>case-control</td>
<td>102</td>
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<tr>
<td>Compston, L. I., et al. (2009)</td>
<td>Ghana</td>
<td>Both</td>
<td>cross-sectional</td>
<td>412</td>
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<tr>
<td>Hannachi, N., et al. (2011)</td>
<td>Tunisia</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>404</td>
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<tr>
<td>Nahdi, I., et al. (2012)</td>
<td>Tunisia</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>126</td>
</tr>
<tr>
<td>Nahdi, I., et al. (2013)</td>
<td>Tunisia</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>47</td>
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<tr>
<td>Poulsen, A., et al. (2005)</td>
<td>Guinea-Bissau</td>
<td>Community</td>
<td>cohort</td>
<td>45000</td>
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<tr>
<td>Schaftenaar, E., et al. (2014)</td>
<td>South Africa</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>405</td>
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<tr>
<td>Schoub, B. D., et al. (1985)</td>
<td>South Africa</td>
<td>Community</td>
<td>cross-sectional</td>
<td>244</td>
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<tr>
<td>Selim, H. S., et al. (2007)</td>
<td>Egypt</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>322</td>
</tr>
<tr>
<td>Siddiqi, O. K., et al. (2014)</td>
<td>Zambia</td>
<td>Health facility</td>
<td>cross-sectional</td>
<td>331</td>
</tr>
</tbody>
</table>
Geographical distribution and design included studies

Included studies come from 13 countries
Prevalence of VZV infection by serology

- 10 studies reported use of serology
- 7 of the ten studies measured IgG,
- 2 tested both IgG and IgM
- One study antibody not stated
- No standard definition of seropositivity
- Seroprevalence ranged from 21.9% in hospitalized Kenyan children to 100% in elderly patients in rural Uganda
- Children showed lower prevalence than adults
Sero-prevalence of VZV

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Positive</th>
<th>Sample</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schoub 1985</td>
<td>0.90 (0.86, 0.94)</td>
<td>220</td>
<td>244</td>
<td>South Africa</td>
</tr>
<tr>
<td>Sixl 1987</td>
<td>0.55 (0.50, 0.60)</td>
<td>209</td>
<td>380</td>
<td>Cape Verde</td>
</tr>
<tr>
<td>Ghebrekidan 1999</td>
<td>0.66 (0.62, 0.71)</td>
<td>299</td>
<td>450</td>
<td>Eritrea</td>
</tr>
<tr>
<td>Admani 2008</td>
<td>0.23 (0.17, 0.30)</td>
<td>42</td>
<td>182</td>
<td>Kenya</td>
</tr>
<tr>
<td>Compston 2009</td>
<td>0.51 (0.46, 0.56)</td>
<td>211</td>
<td>412</td>
<td>Ghana</td>
</tr>
<tr>
<td>Ajayi 2011</td>
<td>0.63 (0.50, 0.74)</td>
<td>44</td>
<td>70</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Hannachi 2011</td>
<td>0.80 (0.76, 0.84)</td>
<td>323</td>
<td>404</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Schaftenaar 2014</td>
<td>0.89 (0.85, 0.92)</td>
<td>360</td>
<td>405</td>
<td>South Africa</td>
</tr>
<tr>
<td>Leung 2015</td>
<td>0.95 (0.92, 0.97)</td>
<td>274</td>
<td>288</td>
<td>Kenya</td>
</tr>
<tr>
<td>Asiki 2015</td>
<td>1.00 (0.98, 1.00)</td>
<td>166</td>
<td>166</td>
<td>Uganda</td>
</tr>
<tr>
<td>Overall (I^2 = 98.8%, p = 0.000)</td>
<td>0.75 (0.59, 0.88)</td>
<td></td>
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</tr>
</tbody>
</table>
Prevalence of VZV infection by PCR

Most studies (8) looked at special cohorts of patients
  • 5 studies - patients with neurological disease
  • 2 studies - patients with ocular disease
  • Only one study was in “regular” VZV disease

Difficult to extrapolate to general population
PCR prevalence of VZV

<table>
<thead>
<tr>
<th>Study</th>
<th>Estimate (95% CI)</th>
<th>Positive</th>
<th>Sample</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selim 2007</td>
<td>0.01 (0.00, 0.02)</td>
<td>2</td>
<td>322</td>
<td>Egypt</td>
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<tr>
<td>Compston 2009</td>
<td>0.00 (0.00, 0.01)</td>
<td>0</td>
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<td>Ghana</td>
</tr>
<tr>
<td>Nahdi 2012</td>
<td>0.03 (0.01, 0.08)</td>
<td>4</td>
<td>126</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Ben Fredj 2012</td>
<td>0.05 (0.02, 0.11)</td>
<td>5</td>
<td>102</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Benjamin 2013</td>
<td>0.00 (0.00, 0.02)</td>
<td>0</td>
<td>183</td>
<td>Malawi</td>
</tr>
<tr>
<td>Nahdi 2013</td>
<td>0.30 (0.22, 0.39)</td>
<td>38</td>
<td>126</td>
<td>Tunisia</td>
</tr>
<tr>
<td>Siddiqi 2014</td>
<td>0.04 (0.02, 0.07)</td>
<td>13</td>
<td>331</td>
<td>Zambia</td>
</tr>
<tr>
<td>Laaks 2015</td>
<td>0.16 (0.10, 0.24)</td>
<td>21</td>
<td>129</td>
<td>South Africa</td>
</tr>
</tbody>
</table>

= average prevalence

Prevalence of PCR positive varicella-zoster cases
What about incidence?

A Household Study of Chickenpox in Guinea-Bissau: Intensity of Exposure is a Determinant of Severity

A. Poulsen1,2,*,†, K. Qureshi1,†, I. Lisse1,2, P.-E. Kofoed3, J. Nielsen1,2, B. F. Vestergaard4 and P. Aaby1,2

ORIGINAL STUDIES

Varicella Zoster in Guinea-Bissau
Intensity of Exposure and Severity of Infection

Anja Poulsen, MD,† Fernando Cabral, MD,* Jens Nielsen,† Adam Roth, MD, PhD,† Ida Maria Lisse, MD,† Bent Faber Vestergaard, MD,† and Peter Aaby, MD†
Incidence (cont....)

Poulsen et al: 2 community based studies in Guinea Bissau
Used both serology and clinical case definition

2002 – 441 cases per 100 000 population
• Median age of 3 years for the cases
• Pneumonia – 2%
• Bacterial skin infection – 44%
• Cough – 24%
• Conjunctivitis – 4%
• Diarrhoea – 2%

2005 – 3420 cases per 100 000 population
• Median age of 4.4 years for the cases
• Pneumonia 10%
• Case-fatality rate – 0.13%
Clinical case definition for herpes zoster

**4410 cases per 100 000 population overall**

- Median age of cases 32 (range 26-39) years
- Median CD4 128 cells at ART initiation
Mortality and HIV infection

**Mortality** - Two studies reported mortality:

- Poulsen et al. 2005 reported a fatality rate of 0.13% - varicella
- Siddiq et al. 2014 had a 30.8% mortality - CNS infection

9 studies had data on HIV

Rubaihayo - Incidence was 1340 cases per 100 000 population pre-ART
  - 330 cases per 100 000 population after ART became available

Compston – Healthy HIVneg seroprevalence 45%
  - Symptomatic HIVpos seroprevalence 57%
  \[ OR=1.6 \ (95\% \ CI, \ 1.1-2.6) \]

Evidence of HIV impact on both seroprevalence & incidence
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

• Varicella
  • Limited data on vaccination in adolescents or adults
  • In Africa- lack of epidemiologic & socio-economic data
Herpes Zoster Vaccine

• HIV-infected persons at risk for VZV reactivation
  – Estimated incidence of 3.2 cases per 100 person-years
• Limited data on use of vaccine in HIV
• May be considered in HIV
  – History of varicella or zoster or
  – VZV positive without history of varicella vaccination
  – ≥60 years CD4 count ≥200 cells/mm³
• Benefits of zoster vaccine
  – Reduce incidence of shingles
  – Reduce severity of disease
  – Reduce occurrence of post-herpetic neuralgia

• Concerns that remain
  – Lack of data on ideal dosing schedule
  – Safety & efficacy
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

• Zoster
  – No data in Africa to support use of this vaccine
Measles outbreaks and surveillance update in South Africa, January-September 2017
Measles was confirmed in a 29-year-old Somali migrant worker in South Africa, who had spent the last 9 months visiting family in Djibouti city, Djibouti. He presented to hospital in Cape Town 12 days after returning by direct air travel with a 7 hour airport transfer in Nairobi, with a 6 day history of fever, conjunctivitis, dry cough, vomiting and diarrhoea, followed on day 7 by a red maculopapular facial rash with subsequent spread to his upper extremities and abdomen. There was no other travel history, nor contact with any persons with known measles or a febrile illness and rash. He received pre-travel health information through his travel company and was vaccinated against Yellow Fever. There is no formal documentation of his measles vaccination status, but his brother indicated that he underwent all routine childhood vaccinations in Somalia.

**Measles was confirmed on urine PCR** on [Thu 18 Jan 2018] at the Groote Schuur Hospital Virology Laboratory, National Health Laboratory Service. The patient was discharged in a stable condition for isolation at home, to be followed up by the Groote Schuur Hospital Infectious Diseases Clinic, a member of the Geosentinel Travel Surveillance Network. A serum sample for measles IgM will be tested for surveillance purposes. The Groote Schuur Hospital Infection Prevention team is aiding the Western Cape Provincial Department of Health’s Communicable Disease Control Unit to optimise infection control, and begin contact tracing.

Published on ProMED 25th January 2018
Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa

- **Measles, mumps & rubella (MMR)**
  - Contra-indicated with CD4+ counts <200 cells.

- **Polio**
  - Exceedingly rare in SA
  - Live vaccine contra-indicated in HIV
  - Inactivated recommended for those infected with HIV

_S Afr J HIV Med 2018; 19(1)_)
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Safety CD4+ count</th>
<th>Doses for unvaccinated adults</th>
<th>Booster</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR vaccine</td>
<td>Measles, mumps or rubella seronegative</td>
<td>≥ 200 cells/mL</td>
<td>2 doses (28 days apart)</td>
<td>Protection likely lifelong</td>
<td>Mainly indicated in measles seronegative HIV-infected women of childbearing age. Pregnancy should be avoided for 1 month after vaccination</td>
</tr>
<tr>
<td>Influenza</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td>Yearly</td>
<td>-</td>
</tr>
<tr>
<td>Pneumococcal Conjugated (PCV13)</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td></td>
<td>Given with PPV23 but must be given first</td>
</tr>
<tr>
<td>Pneumococcal Polysaccharide (PPV23)</td>
<td>R</td>
<td>≥ 200 cells/mL</td>
<td>1 dose</td>
<td>5–10 years</td>
<td>Given with PCV13 but given 8 weeks after PCV13. Can be given to patients with CD4 count &lt; 200 cells/mL if on ART and VL suppressed. Maximum 2 booster doses, 1 booster dose in patients &gt; 65 years. Poor response if CD4+ cell count &lt; 200 cells/mL and VL not suppressed</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>R</td>
<td>Any</td>
<td>4 doses (40 µg) or 3 doses (20 µg)</td>
<td>Not clear awaiting evidence</td>
<td>-</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>R – travel, MSM, liver disease</td>
<td>≥ 200 cells/mL</td>
<td>2 doses</td>
<td>10 years</td>
<td>-</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>R</td>
<td>Any</td>
<td>2 doses</td>
<td>5 years</td>
<td>-</td>
</tr>
<tr>
<td>Tetanus-diphtheria (Td)</td>
<td>R</td>
<td>Any</td>
<td></td>
<td>10 years</td>
<td>Given in pregnancy combined with tetanus-diphtheria (DTPa/dTpa)</td>
</tr>
<tr>
<td>Pertussis-acellular</td>
<td>R</td>
<td>Any</td>
<td>1 dose</td>
<td>10 years</td>
<td>-</td>
</tr>
<tr>
<td>Poliomyelitis-inactivated</td>
<td>R</td>
<td>≥ 200 cells/mL</td>
<td>3 doses</td>
<td>none</td>
<td>-</td>
</tr>
<tr>
<td>Human papilloma virus (HPV)</td>
<td>R – females, MSM</td>
<td>Any</td>
<td>2 doses</td>
<td>none</td>
<td>-</td>
</tr>
<tr>
<td>Varicella</td>
<td>NR</td>
<td>-</td>
<td></td>
<td></td>
<td>May be considered if CD4+ count &gt; 400 cells/mL</td>
</tr>
<tr>
<td>Zoster</td>
<td>R</td>
<td>≥ 200 cells/mL</td>
<td>1 dose</td>
<td>none</td>
<td>Only use if CD4+ count ≥ 200 cells/µL</td>
</tr>
</tbody>
</table>

MMR, measles, mumps, and rubella; R, recommended; RS, recommended in selected individuals; NR, not recommended; VL, viral load; HBsAb, hepatitis B surface antibody; MSM, men who have sex with men.
**Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications**

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>INDICATION</th>
<th>Pregnancy</th>
<th>Immuno-compromising conditions (excluding HIV infection)</th>
<th>HIV infection CD4+ count (cells/µL)</th>
<th>Men who have sex with men (MSM)</th>
<th>Kidney failure, end-stage renal disease, on hemodialysis</th>
<th>Heart disease, chronic lung disease, chronic alcoholism</th>
<th>Asplenia and persistent complement component deficiencies</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
<th>Healthcare personnel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td></td>
<td></td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)</td>
<td>1 dose Tdap each pregnancy</td>
<td><img src="image" alt="Substitute Tdap for Td once, then Td booster every 10 yrs" /></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>Contraindicated</td>
<td><img src="image" alt="2 doses" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 21 yrs" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Female</td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
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<tr>
<td>Human papillomavirus (HPV) Male</td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td><img src="image" alt="3 doses through age 26 yrs" /></td>
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<td><img src="image" alt="3 doses through age 26 yrs" /></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>Contraindicated</td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
<td><img src="image" alt="1 dose" /></td>
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<td><img src="image" alt="1 dose" /></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>Contraindicated</td>
<td><img src="image" alt="1 or 2 doses depending on indication" /></td>
<td><img src="image" alt="1 or 2 doses depending on indication" /></td>
<td><img src="image" alt="1 or 2 doses depending on indication" /></td>
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<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td><img src="image" alt="1 dose" /></td>
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</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td><img src="image" alt="1, 2, or 3 doses depending on indication" /></td>
<td><img src="image" alt="1, 2, or 3 doses depending on indication" /></td>
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<td><img src="image" alt="1, 2, or 3 doses depending on indication" /></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td><img src="image" alt="2 or 3 doses depending on vaccine" /></td>
<td><img src="image" alt="2 or 3 doses depending on vaccine" /></td>
<td><img src="image" alt="2 or 3 doses depending on vaccine" /></td>
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<tr>
<td>Hepatitis B</td>
<td><img src="image" alt="3 doses" /></td>
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</tr>
<tr>
<td>Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4)</td>
<td><img src="image" alt="1 or more doses depending on indication" /></td>
<td><img src="image" alt="1 or more doses depending on indication" /></td>
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</tr>
<tr>
<td>Meningococcal B (MenB)</td>
<td><img src="image" alt="2 or 3 doses depending on vaccine" /></td>
<td><img src="image" alt="2 or 3 doses depending on vaccine" /></td>
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</tbody>
</table>

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**Recommended Adult Immunization Schedule United States - 2016**

MMWR February 4 2016
Conclusion

• Are opportunities to expand immunization for HIV-infected Adolescents & Adults

• Vaccinate during stable disease

• Communicate with patients about the importance of vaccination and the availability of vaccines

• Vaccination is the most cost effective intervention of 21st century
Saving Lives: Integrating Vaccines for Adults Into Routine Care

When immunization rates are high, the wider community is protected including:

- Infants who are too young to receive their vaccines.
- Older adults at risk of serious diseases.
- People who take medication that lowers their immune systems.