Adult Vaccine Space:
General Overview of the Current Vaccine Preventable Infections (VPIs) in the Adult Population

Univ.-Prof. Dr. med. habil.

JOE SCHMITT
Potential Conflicts of Interest

- VP & Global MDSCA Lead Viral Vaccines, Pfizer (to May 2021)
- Scientific and Strategic Advisor, Vaccelerate, Cologne University
- Editor-in-Chief, Global Health Press, Singapore
- Consultant to Governments
- Consultant to Start-Ups
Current Vaccines (Routine)

Maternal Immunization (5)
- TdaP
- Influenza
- COVID19
  (Recommended, not licensed)
- (RSV) (if licensed)

Infants, Toddlers (≥11+4)
- DTaP-Hib-IPV-HBV
- PCV
- Rotavirus
- Influenza
- MenACWY,
- Men B
- (TBE ≥1 yr)
- MMR-V

School Entry/Adolescents (≥6)
- Missed Vx
- Boosters TdaP
- Influenza
- COVID19
- Men ACWY
- MenB
- HPV
- (TBE)

Adults (≥3)
- Missed Vx (MMR)
- Boosters TdaP(-IPV)
- COVID19
- Influenza
- HPV
- TBE
- HAV
- HBV
- Occupational Vx
- (RSV if licensed)

≥65 yrs (≥4)
- Missed Vx (MMR)
- Boosters TdaP(-IPV)
- COVID19
- Influenza
- PCV/(PPV23)
- Zoster
- TBE
- MenACWY
- MenB

Maternal Immunization (5)
Infants, Toddlers (≥11+4)
School Entry/Adolescents (≥6)
Adults (≥3)
≥65 yrs (≥4)
## Medical need based on special host/exposure

<table>
<thead>
<tr>
<th>Traveller</th>
<th>Underlying Diseases</th>
<th>B-&amp;T-cell Defect/ Cancer*</th>
<th>Emerging Infections</th>
<th>Lack of Health Care Resources</th>
</tr>
</thead>
</table>
| - Boosters  
- TBE (FSME)  
- HAV  
- HBV  
- Influenza  
- MenACWY  
- MenB  
- JE  
- Typhoid  
- Rabies  
- Yellow fever  
- Cholera  
- Dengue | - Boosters  
- Influenza  
- PCV  
- MenB/ACWY  
- (risk-based Vx) | - Influenza  
- PCV  
- MenACWY  
- MenB  
- H. influenzae b  
- HBV  
- Boosters | - COVID19 VOCs  
- Avian influenza  
- Monkeypox  
- CEPI / WHO-list | Monkeypox  
Ebola |

* If sufficient immune responses can be reasonably expected
## Adult Immunization Schedule – CDC - COVID19

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19</td>
<td>2- or 3- dose primary series and booster (<a href="#">see notes</a>)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age based recommendation</th>
<th>+ risk factor or other indication</th>
<th>Shared decision</th>
<th>No recommendation, Not applicable</th>
</tr>
</thead>
</table>
Opinion: COVID19 vaccination 2023 and beyond

- One (or several ?) annual boosters, including variants of concern for risk subjects and for those with occupational indication.
- Combination with influenza vaccines would be beneficial.
- Research should focus on how carriage and acquisition can be reduced for any respiratory pathogen.
# Adult Immunization Schedule – CDC – Influenza

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COVID-19</strong></td>
<td>2- or 3- dose primary series and booster <em>(see notes)</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Influenza inactivated (IIV4)</em> or <em>Influenza recombinant (RIV4)</em></td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Influenza live attenuated (LAIV)</em></td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**LAIV**

*Fluenz® no longer authorized by EMA as MAH withdrew for commercial reasons*
OECD: Influenza-Vaccine Uptake 2021 Adults ≥65 years

DE: 47.3%
Opinion: Influenza vaccination

Influenza vaccines ...

- are far away from being ideal vaccines (modest efficacy)
- uptake is **way** too low
- **Cell culture based platform** needed for pandemic preparedness
- Both, **HD and MF59-based / enhanced vaccines** should be recommended (pandemic preparedness) for specific groups
# Adult Immunization Schedule – CDC – TdaP-IPV

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus, diphtheria, pertussis</td>
<td>1 dose Tdap each pregnancy; 1 doseTd/Tdap for wound management (see notes)</td>
<td>1 dose Tdap, then Td or Tdap booster every 10 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Age based recommendation**
- + risk factor or other indication

**Recommended when + risk factor or other indication**

**Shared decision**

**No recommendation, n.a.**
Opinion: TdaP (-IPV)

- Tetanus: Italy has highest EU-ccase numbers (?)
  - The incidence of reported tetanus in Italy decreased from 0.5/100 000 in the 1970s to 0.2/100 000 in the 1990’s. … the case-fatality ratio decreased from 68% to 39%. Italy has the highest reported number of tetanus cases in European countries. Elderly women are the most affected: … 60% in the 1970s to 76% in the 1990s. Vaccination campaigns need to be conducted to target this group, and the surveillance of tetanus has to be improved to identify additional groups of population at risk.

- Diphtheria: Outbreak among immigrants in Germany
  - [Outbreak of imported diphtheria with Corynebacterium diphtheriae among migrants arriving in Germany, 2022](Eurosurveillance)

- Pertussis: TdaP every 10 years – or 5 doses sufficient for life? Monovalent aP available elsewhere

- IPV: The art of ending … (4 doses of trivalent vaccine sufficient (?)�)
  - Search for unvaccinated pockets (e.g. religious beliefes, „alternative thinking“, …)
  - In 2022, cases of poliomyelitis (PM) related to circulating vaccine derived polioviruses (cVDPV) occurred in unvaccinated persons in non-endemic countries. cVDPV2 in London (UK) sewage water raised public health concerns even more. Consequently, poliovirus vaccination coverage in non-endemic countries needs to be elucidated.
# Adult immunization Schedule – CDC – MMR

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>1 or 2 doses depending on indication (if born in 1957 or later)</td>
<td>For healthcare personnel, (see notes)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation Type</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age based recommendation</td>
<td>+ risk factor or other indication</td>
<td>Shared decision</td>
<td>No recommendation, n.a.</td>
<td></td>
</tr>
</tbody>
</table>
## Adult Immunization Schedule – CDC – VZV/Zoster

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Varicella (VAR)</strong></td>
<td>2 doses</td>
<td>2 doses</td>
<td></td>
<td>2 doses</td>
</tr>
<tr>
<td>(if born in 1980 or later)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Zoster recombinant (RZV)</strong></td>
<td>2 doses</td>
<td></td>
<td>2 doses</td>
<td></td>
</tr>
<tr>
<td>(see notes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age based recommendation</th>
<th>+ risk factor or other indication</th>
<th>Shared decision</th>
<th>No recommendation, n.a.</th>
</tr>
</thead>
</table>
## Herpes Zoster Vaccines

<table>
<thead>
<tr>
<th></th>
<th>Recombinant Zoster Vaccine</th>
<th>Live Zoster Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brand name</strong></td>
<td>Shingrix®</td>
<td>Zostavax®</td>
</tr>
<tr>
<td><strong>Vaccine Type</strong></td>
<td>Subunit vaccine</td>
<td>Live vaccine</td>
</tr>
<tr>
<td><strong>Antigen</strong></td>
<td>VZV glycoprotein E (50µg) and the AS01B adjuvant system</td>
<td>Oka/Merck varicella virus 19,400 PFU</td>
</tr>
<tr>
<td><strong>Use in highly immuno-compromised patients</strong></td>
<td>Under investigation, currently no data</td>
<td>Contraindicated</td>
</tr>
<tr>
<td><strong>Efficacy against Zoster</strong></td>
<td>91.3% (95% CI = 86.8–94.5)</td>
<td>38% (95% CI = 25–48)</td>
</tr>
<tr>
<td><strong>Efficacy against PHN</strong></td>
<td>88.8% (95% CI = 68.7–97.1)</td>
<td>66.8% (95% CI = 43.3–81.3)</td>
</tr>
<tr>
<td><strong>Duration of protection</strong></td>
<td>Modest waning of protection over 4 years following vaccination</td>
<td>Substantial decrease over time Maximal protection 9 – 11 years</td>
</tr>
<tr>
<td><strong>Safety profile</strong></td>
<td>Favorable Injection site reactions 45 – 78%</td>
<td>Favorable Injection site reactions 48%</td>
</tr>
</tbody>
</table>

PHN – Post-herpetic neuralgia


>1350 PFU Oka strain in the pediatric VZV formulation
## Adult Immunization Schedule – HPV

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human papillomavirus</strong> (HPV) 🌟</td>
<td>2 or 3 doses depending on age at initial vaccination or condition</td>
<td>27 through 45 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Opinion: HPV

- **Comprehensive HPV/genital cancer program needed, male and female vx.**
  - Stop routine PCR-testing for HPV-serotypes
  - Value of annual screening vs value of >95% participation every 5 years

- **Booster with 9-valent product: 3 doses**
  - Implementation is lacking
# Adult immunization Schedule – *Pneumococcus*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥ 65 years</th>
</tr>
</thead>
</table>
| **Pneumococcal** (PCV15, PCV20, PPSV23)    | 1 dose PCV15 followed by PPSV23  
OR  
1 dose PCV20 ([see notes](#)) |             |             |             |           |

See Notes

See Notes
Pathogenesis of *S. pneumoniae* Diseases

- Colonization
- Direct Infection
- Invasive Pneumococcal Disease (IPD)
- Metastatic Disease

- Otitis Media
- Pneumonia
- Sepsis & Bacteremia
- Meningitis, Arthritis
Pneumococcal CAP Represents the Majority of Pneumococcal Disease\textsuperscript{1,2}


**Pneumococcal Community Acquired Pneumonia**

- **pCAP**

**Invasive Pneumococcal Disease**\textsuperscript{1}

- **IPD**

**Meningitis**

**Bacteremia**

**Bacteremic pneumonia**

**Non-bacteremic pneumonia**

75\%\textsuperscript{2} to 91\%\textsuperscript{3} of pneumonia in adults

The majority of pneumococcal pneumonia cases in adults are non-bacteremic\textsuperscript{2}
Pipelines of Vaccine Producers for Next-generation PCVs

<table>
<thead>
<tr>
<th>Serotype</th>
<th>4</th>
<th>6B</th>
<th>9V</th>
<th>14</th>
<th>18C</th>
<th>19F</th>
<th>23F</th>
<th>1</th>
<th>5</th>
<th>7F</th>
<th>3</th>
<th>6A</th>
<th>19A</th>
<th>22F</th>
<th>33F</th>
<th>8</th>
<th>10A</th>
<th>11A</th>
<th>12F</th>
<th>15B</th>
<th>2</th>
<th>9N</th>
<th>17F</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPSV23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPV23: **25µg*/polysaccharide
PCV15: 2.0 µg/polysaccharide (except serotype 4: 4.0 µg) individually conjugated to CRM$_{197}$
PCV13, PCV20: 2.2µg/polysaccharide (except serotype 4: 4.4 µg) individually conjugated to CRM$_{197}$

See respective EPARs
Opinion: Pneumococcal Vaccines for Adults

- **PPV23 has a modest effect on IPD, none on non-bacteremic pneumonia**
  - CDC (2015): Japanese study (Maruyama et al.) owns misclassification of cases
  - Gessner 2019: lack of internal and external validity
  - Effectiveness is short-lived, no immunological memory (Andrews, PHE 2012)
  - PPV23 doubled the risk for IPD in AIDS patients (d-b-r study in Uganda (French 2000))

- **PCV 15 / PCV 20 and beyond: Decision criteria – for discussion**
  (roughly same price, 10 doses: € 767,35)
  - Both products licensed based on safety-serological /non-inferiority to PCV13
  - Do lower titers make a difference? - Herd protection more relevant?
  - Impact/effectiveness against **serotypes 3 and 19A**
  - Size of local **strain coverage AND case number reduction** regarding
    - 22F, 33F (PCV15) **PLUS** 8, 10A, 11A, 12F, 15B (PCV20)
  - With excellent surveillance in place, we will only know 1-5 years after licensure (or never) if one vaccine is superior to the other

**IMPLEMENTATION IS WHAT MATTERS**
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>19-26 years</th>
<th>27-49 years</th>
<th>50-64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis A</strong> (HepA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2, 3, or 4 doses depending on vaccine</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis B</strong> (HepB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2, 3, or 4 doses depending on vaccine or condition</td>
<td></td>
</tr>
<tr>
<td><strong>Meningococcal A, C, W, Y</strong> (MenACWY)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 or 2 doses depending on indication, <a href="#">see notes</a> for booster recommendations</td>
<td></td>
</tr>
<tr>
<td><strong>Meningococcal B</strong> (MenB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 or 3 doses depending on vaccine and indication, <a href="#">see notes</a> for booster recommendations</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19 through 23 years</td>
<td></td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b</strong> (Hib)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 or 3 doses depending on indication</td>
<td></td>
</tr>
</tbody>
</table>

Reminder: Eculizumab (Soliris®) inhibits terminal complement activation
TBE – Basics

1. **TBE**: CNS infection caused by the TBE virus (TBEV)

2. **Transmission**: Ticks, unpasteurized milk/products, transplantation, aerosols

3. **Occurrence**: UK to Japan, polar circle to northern Tunisia (forest belt EurAsia)

   - **Seasonality**: 95% of cases occurring May to November
   - **Incidence**: <1/10⁵ to >30/10⁵, unpredictable variations
   - **3 “classic” TBEV subtypes**: European, Siberian, Far-Eastern
   - **2 potential new subtypes**: (Baikalian; Himalayan)

4. **3 Manifestations**: no symptoms – non-CNS diseases – CNS infection

5. **Sequelae**: <46% of patients; in children mainly mental sequelae

6. **Case fatality**: 0.5–20%

7. **Specific therapy**: Not licensed / not available

8. **Local authorities, E-CDC, WHO recommend vaccination as best way for prevention

---

**TBE Risk definition based on ECDC criteria for arboviruses:**

- **Predisposed**: Area and ticks suitable to sustain TBEV circulation
- **Imperiled**: TBEV identified in appropriate ticks
- **Affected**: TBE cases reported
- **Endemic**: Annual cases reported

Dobler et al. (2022) The TBE Book (GHP), Singapore
Opinion - TBE

- Hugely underdiagnosed
- Low Vaccine uptake even in risk areas and among risk subjects
- Most ridiculous vaccination schedule for any vaccine
  - High effectiveness after 3 doses; 10-year boosters in Switzerland and Finland (but not in EMA label)
- Recommended as a travel vaccine for Europe and Asia (e.g. China) in the USA
Soon to come?
Electronic ARI-Case Reports based on self-testing
GAPS in Adult Vaccination in EU
Most EU-countries own Vaccine Recommendations, but no Vaccination Program with:

- Goals
- Plan
- Implementation
- Evaluation
Vaccination Programmes consist of:

**Goals:**
- A) Future needs
- B) Current targets

**Plan:**
- A) One, comprehensive
- B) Current updates

**Implementation:**
- A) Responsibilities/Account.
- B) Government PR

**Evaluation:**
- A) Uptake by population
- B) Burden of Disease
Thank you!