

Priority Needs Of PLWH: Use Of Pneumococcal Vaccine in PLWH

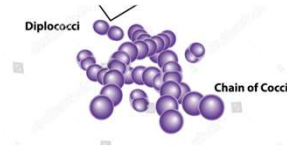
Yunus Moosa

AWACC: 31 October 2025

Outline

1. Nature of disease
2. Risk factors
3. Burden in HIV
4. Consequences
5. Prevention – a strategy worth considering
6. Introduce Pneumococcal Vaccine
7. Immunogenicity, safety, efficacy
8. Steps to improve adult vaccination coverage in clinical practice
9. Summary & take-home message

Pneumococcal disease refers to a wide range of infections caused by *Streptococcus pneumoniae*



- Ear infections
- Sinus infections
- Pneumonia
- Bacteremia
- Meningitis
- Sepsis

Invasive Pneumococcal Disease (IPD)

Isolation from sterile site:

Blood, pleural, pericardial, peritoneal fluid, joint, CSF

1. Pneumonia with bacteremia
2. Meningitis
3. Bacteremia

Colonization – infection - disease

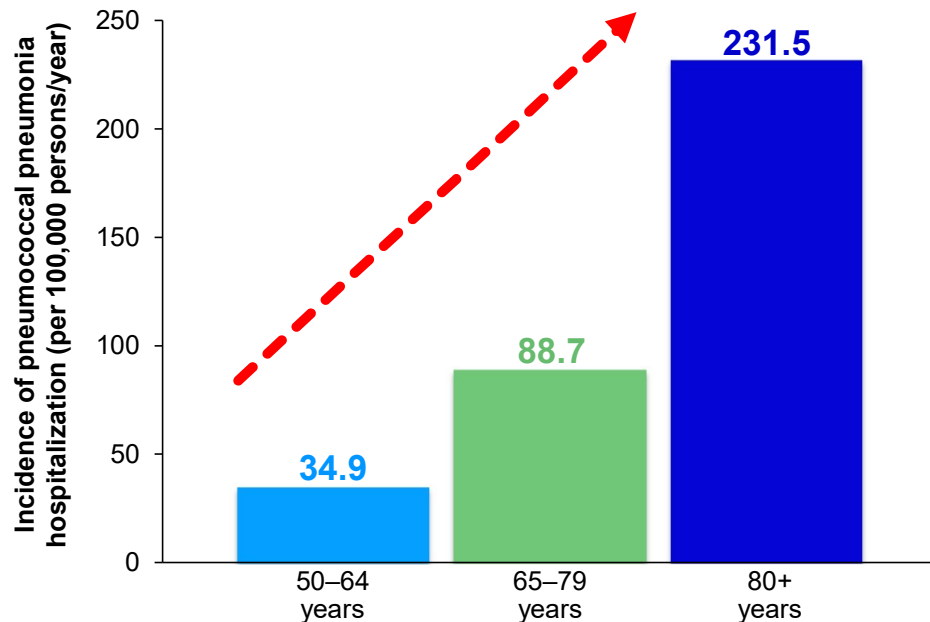
Risk in pneumococcal infection relates risk of infection and
probability poor outcome



Age is a Risk factor for Pneumococcal Pneumonia: (Immunosenescence) – hospitalization for Pneumonia, IPD

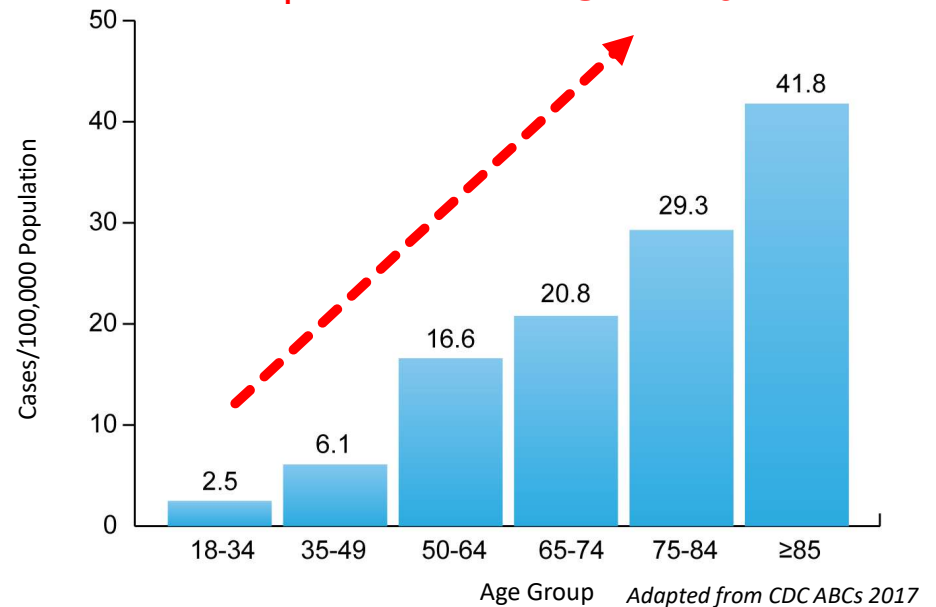
Incidence of Hospitalization for Pneumococcal Pneumonia

Data from a population-based prospective cohort study in adults ≥ 50 years of age (N=2,025,730) in Catalonia, Spain, 2015¹



Adapted from Vila-Corcoles A, et al Incidence and Risk of Pneumococcal Pneumonia in Adults with Distinct Underlying Medical Conditions: A Population-Based Study. *Lung*. 2020;198(3):481-489.

Rate of IPD per 100,000 of the Adult Population in the US in 2017



Pneumonia with bacteremia, meningitis, bacteremia

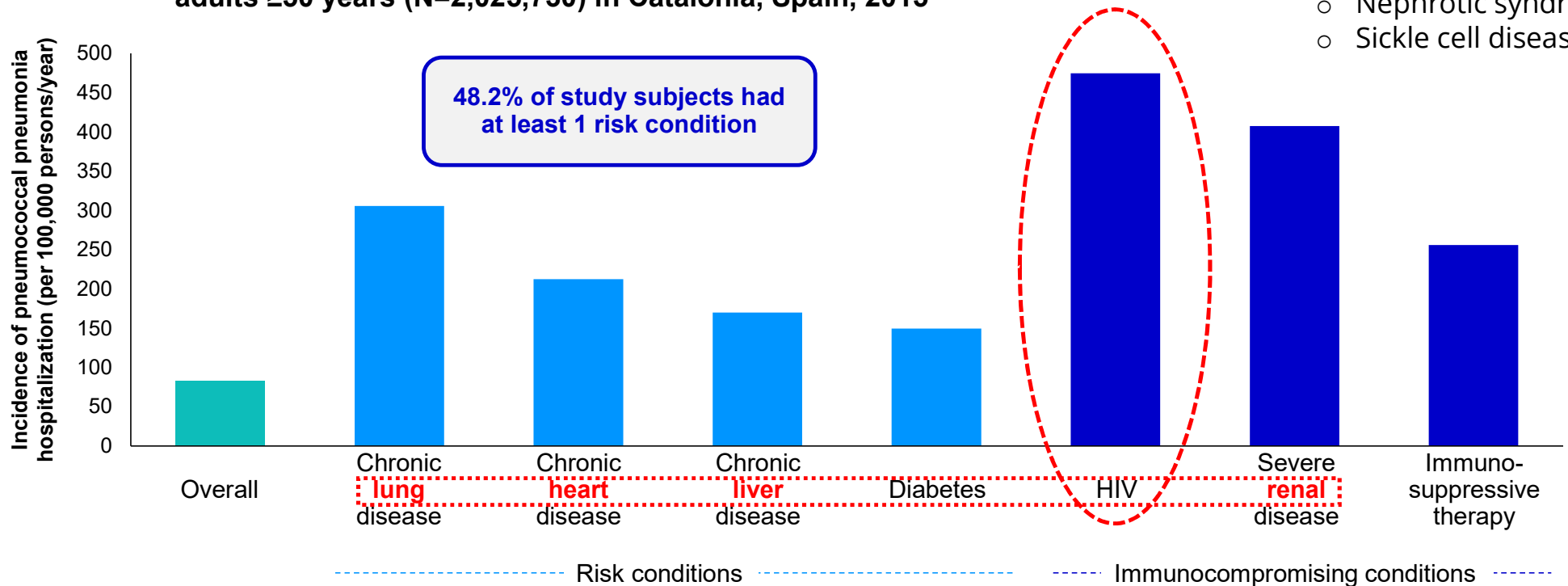
18-34 vs. ≥ 85 (17-fold increase)

1. Vila-Corcoles A, et al. *Lung*. 2020;198(3):481-489. 2. Ciabattini A, et al. *Semin Immunol*. 2018;40:83-94.

Medical Conditions Increase Risk of Pneumococcal Pneumonia

- Alcoholism
- Cerebrospinal fluid leak
- Cochlear implant
- Smoking
- Nephrotic syndrome
- Sickle cell disease (spleen)

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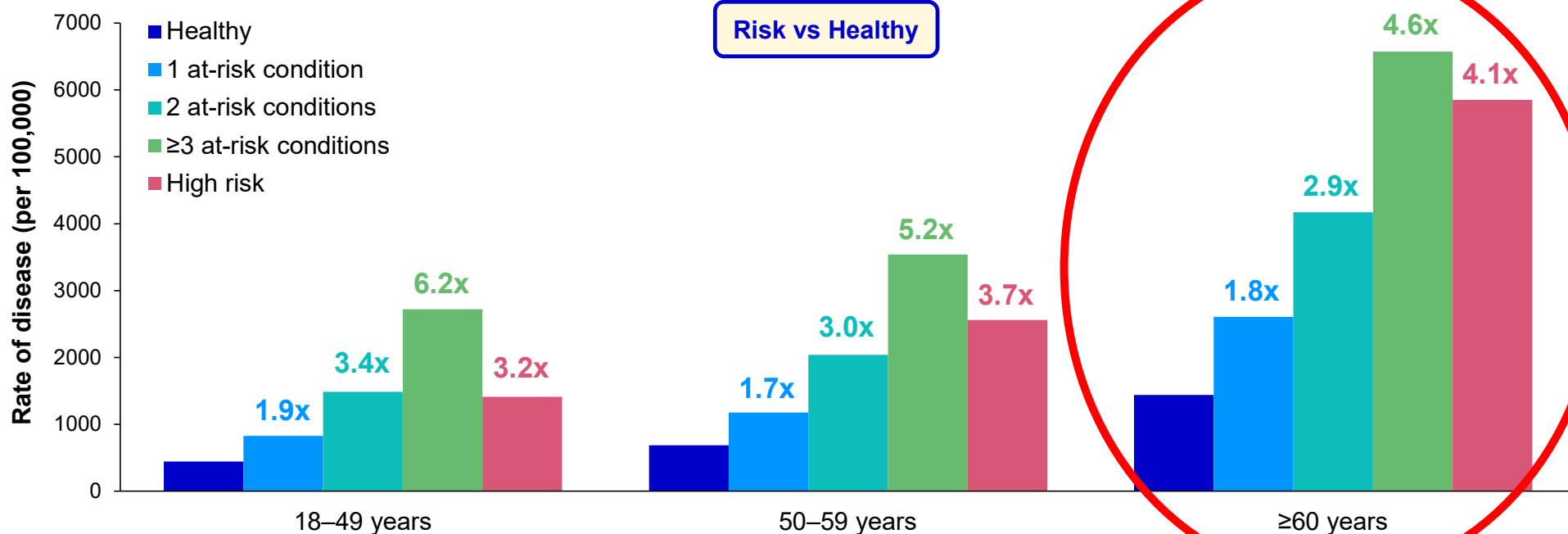
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Combination of multiple conditions increase risk of pneumonia

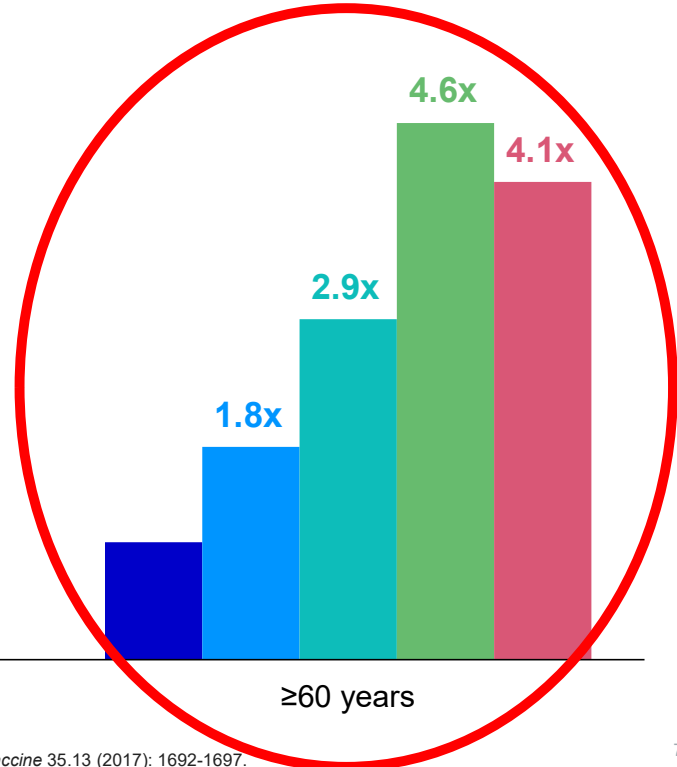


Risk Stacking

Rates of all-cause pneumonia among adults ≥18 years of age,*
by number of comorbidities, Germany, 2009–2012

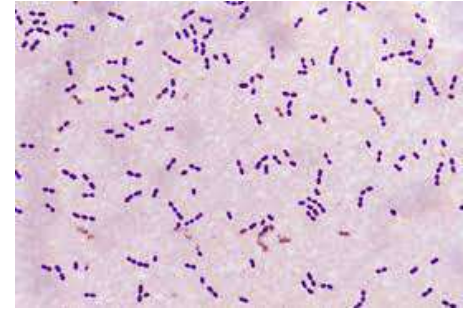


Stacking in HIV
Victims of a successful ART programme



Morton, Jacob B., et al. "Risk stacking of pneumococcal vaccination indications increases mortality in unvaccinated adults with Streptococcus pneumoniae infections." *Vaccine* 35.13 (2017): 1692-1697.
*Persons aged 18–49 years, 50–59 years, and ≥60 years contributed a total of 5.7 million, 2.0 million, and 3.5 million person-years of observation, respectively. Pelton SI, et al. *BMC Infect Dis.* 2015;15:470.

Pneumococcus in HIV



- Colonization rate/load - 35-to-60-fold increase risk of IPD
- Irrespective of CD4⁺ counts
- Irrespective of viral suppression
- Higher rates of bacteremia, recurrence and mortality
- Added risk from smoking, and excessive alcohol
- Despite the increased uptake of ART PLHIV remain susceptible IPD

GERMS-Annual-Review-2023 - in SA

Of all patients with IPD that were tested for HIV 50% were positive

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. Klugman^{2,5}, Shabir A. Madhi^{1,2*}

SA Study looked at IPD in hospitalized HIV positive adults during three periods
(2003-04 early-HAART 2005-06 intermediate-HAART, 2007-08 established-HAART)

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.

HIV likely drives the burden of IPD in SA

Consequences



Consequences of CAP are serious:

Hospitalizations, re-hospitalizations, morbidity and mortality.

In a **US, prospective, population-based, cohort study** among adults
18+ years of age **hospitalized for CAP** in Louisville, KY*:



A total of **8284 hospitalizations** were due to CAP during the 2-year study period



Of **3789 adults** hospitalized d/t CAP in first year of the study:

~9%

Re-hospitalized for CAP due to a new episode during the same study year

13%

Died within 30 days of hospitalization due to CAP

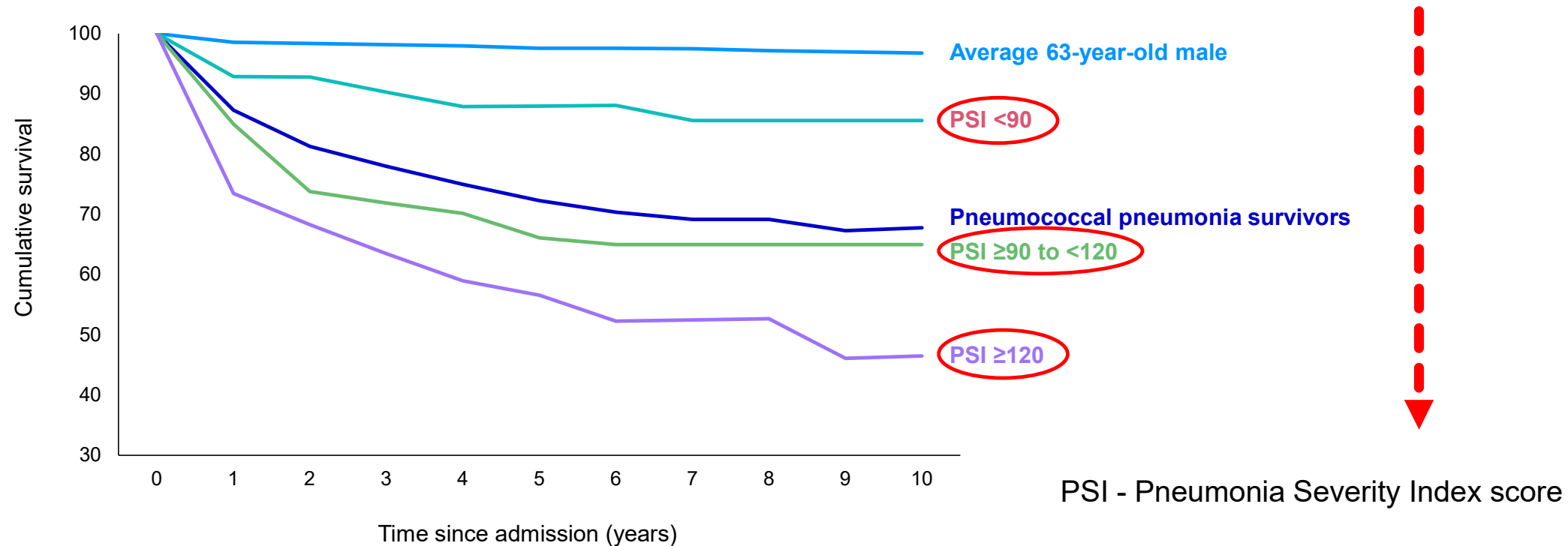
~31%

Died within 1 year of hospitalization due to CAP

Pneumococcal Pneumonia - associated with **Reduced Long-Term Survival**

Kaplan-Meier plots cumulative 10-year survival of 344 patients* with pneumococcal pneumonia compared with the expected 10-year survival of an average 63-year-old male

Long term survival is related to severity of Pneumonia



*Patients who survived past 1 month were also stratified based on PORT score severity index (PSI) at the time of admission. Sandvall B, et al. *Clin Infect Dis*. 2013;56(8):1145-1146.

Pneumonia also aggravates existing Health Conditions taking weeks/months to return to Baseline



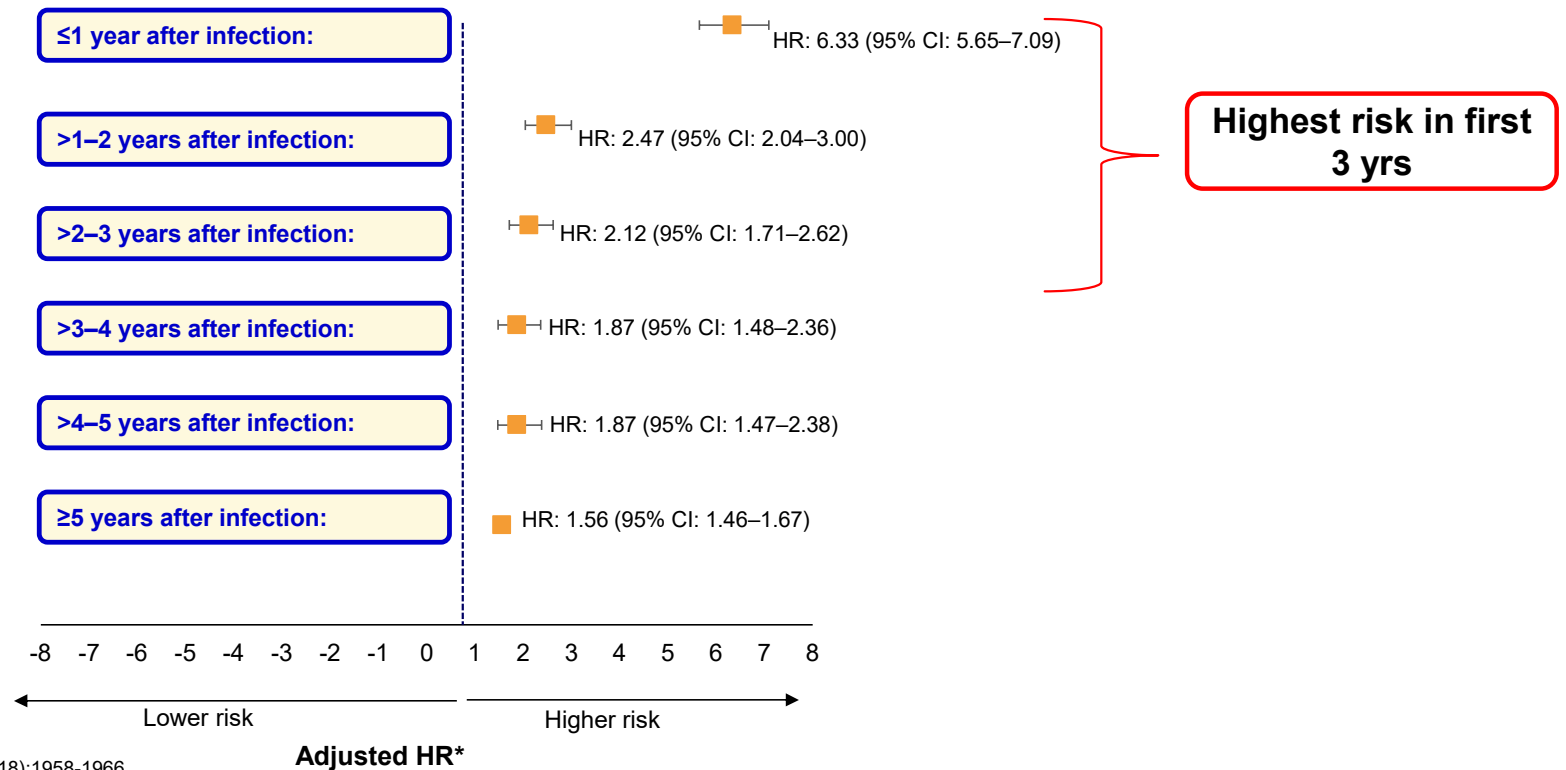
Prevalence and duration of health conditions reported as worsened by pneumonia

Health condition	Reported worsening (%)	Days until return to baseline
Asthma	23.0	24.8
COPD	24.4	52.4
Chronic bronchitis	12.2	32.8
Chronic emphysema	8.6	60.0
High blood pressure	20.1	21.6
Heart disease	5.9	38.7
Diabetes	9.8	18.0
Other	8.5	48.3

A content-valid questionnaire assessing pneumonia symptoms and comorbid conditions was administered online to adults aged ≥ 50 years with a recent diagnosis of CAP

Unmasks/aggravates of conditions:

Risk of CVD following pneumonia/sepsis persists for > 5 yrs in adults - Sweden, 1969–2010



Prevention is better than cure

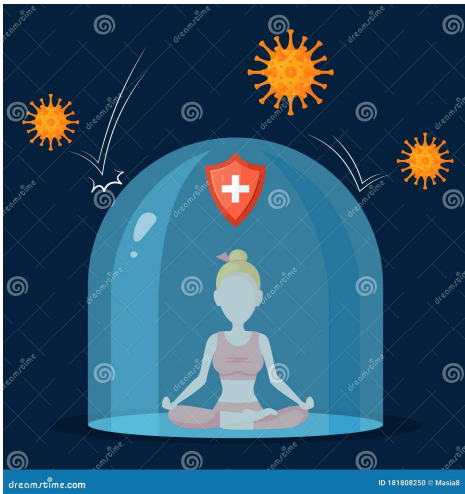
Reduces spending on health

Often the “best buy”

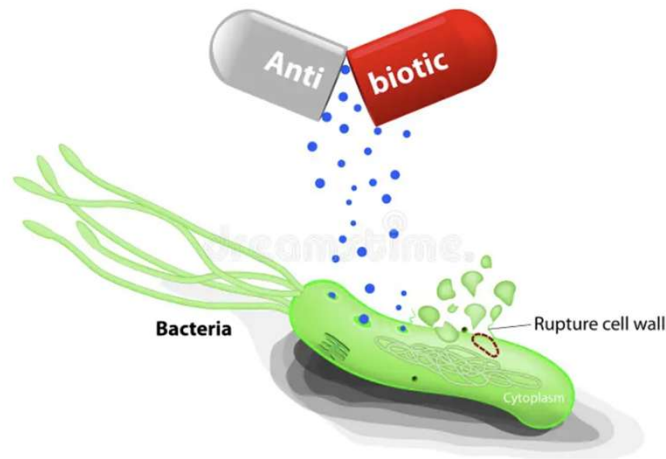


How to prevent Pneumococcal Disease

Live in a bubble



Prophylactic Antibiotic



Train the immune system





Vaccines do more than protect the Individual

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

Vulnerable

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.

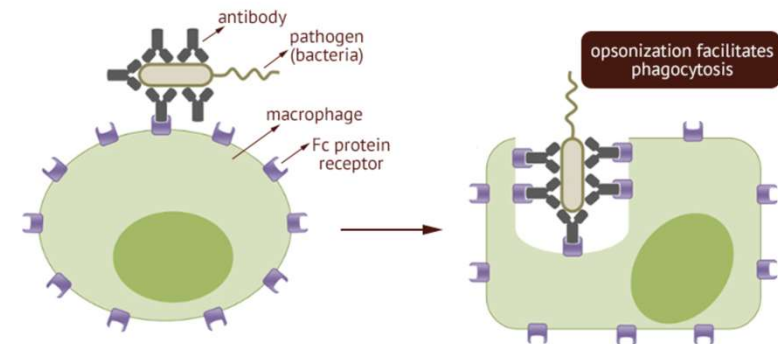
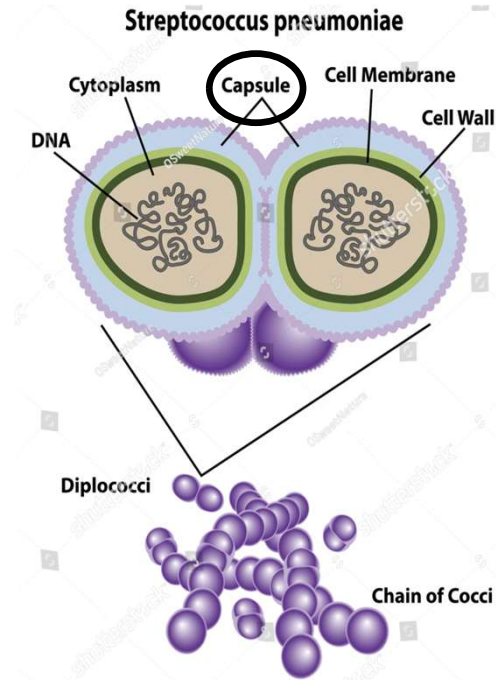


Basis of the Vaccine

Main virulence factor: Polysaccharide Capsule

- Capsule protects against phagocytosis
- Over 90 distinct polysaccharide capsular antigens
- Polysaccharide Ag differentiates strains (serotyping)
- **Protection is serotype specific**

For full protection from all strains vaccine will need to include over 90 distinct polysaccharide capsular antigens.



Fc receptor-mediated Opsonization
(Image source: philpoteducation)

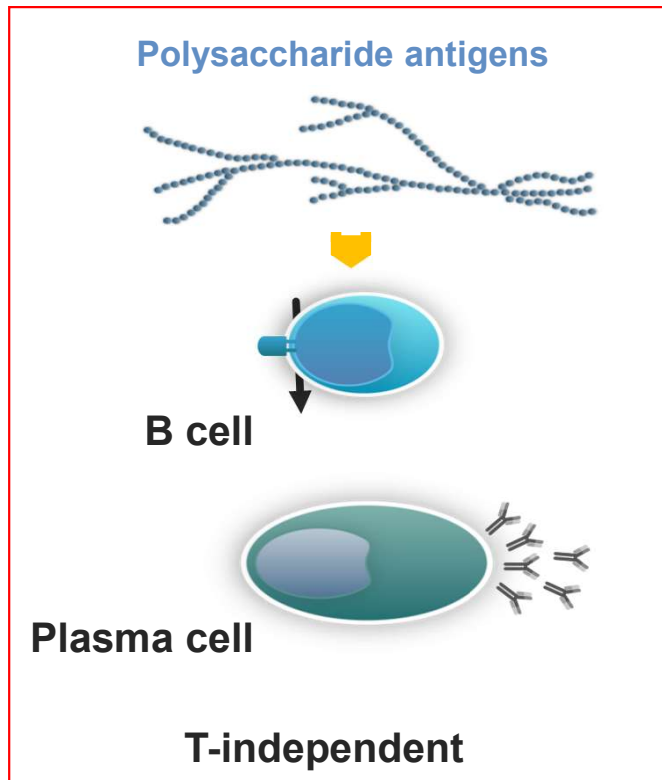
Which pneumococcal vaccine!!

23-valent pneumococcal polysaccharide vaccine (PPV23), comprising capsular antigens of 23 pneumococcal serotypes

13-valent pneumococcal conjugate vaccine (PCV13), containing capsular polysaccharide antigens of 13 pneumococcal serotypes, **independently conjugated to a protein carrier**

Serotypes Contained in Current and New Pneumococcal Vaccines																								
	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20
PCV13	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓											
PPSV23	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Pneumococcal Vaccines: Polysaccharide vs. Conjugate

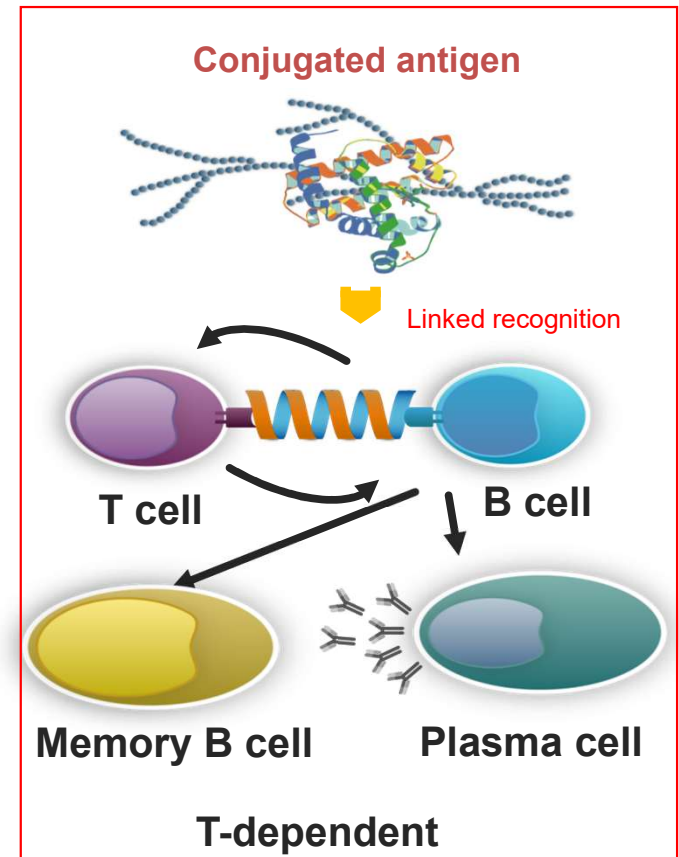


Immunogenic carrier protein



+

=



The conjugation of a polysaccharide to a carrier protein leads to the interaction with T cells resulting in the release of functional antibodies and production of memory B cells ^{1,2}

What does this mean for the immune response?


Polysaccharide vaccine T-independent response	Conjugated vaccines T-dependent
No Memory Limited isotype switching Limited impact - nasopharyngeal carriage Hyporesponsiveness at re-vaccination	Longer lasting Protection Anamnestic (Memory) response rapid and greater response with re-exposure to a pathogen Isotype switching – IgG/IgA Affinity maturation Reduces nasopharyngeal carriage

PCV13 vs. PPV23

Immunogenicity & Safety

Across all relevant age adult groups

- PCV13 has been evaluated in immunogenicity and safety studies **globally** and **in India**^{1,2,3}
- **PCV13 elicits a robust immune response to vaccine serotypes**³
- Immune responses to PCV13 were non-inferior to PPV23 and were statistically significantly greater for the majority of common serotypes^{1,2}

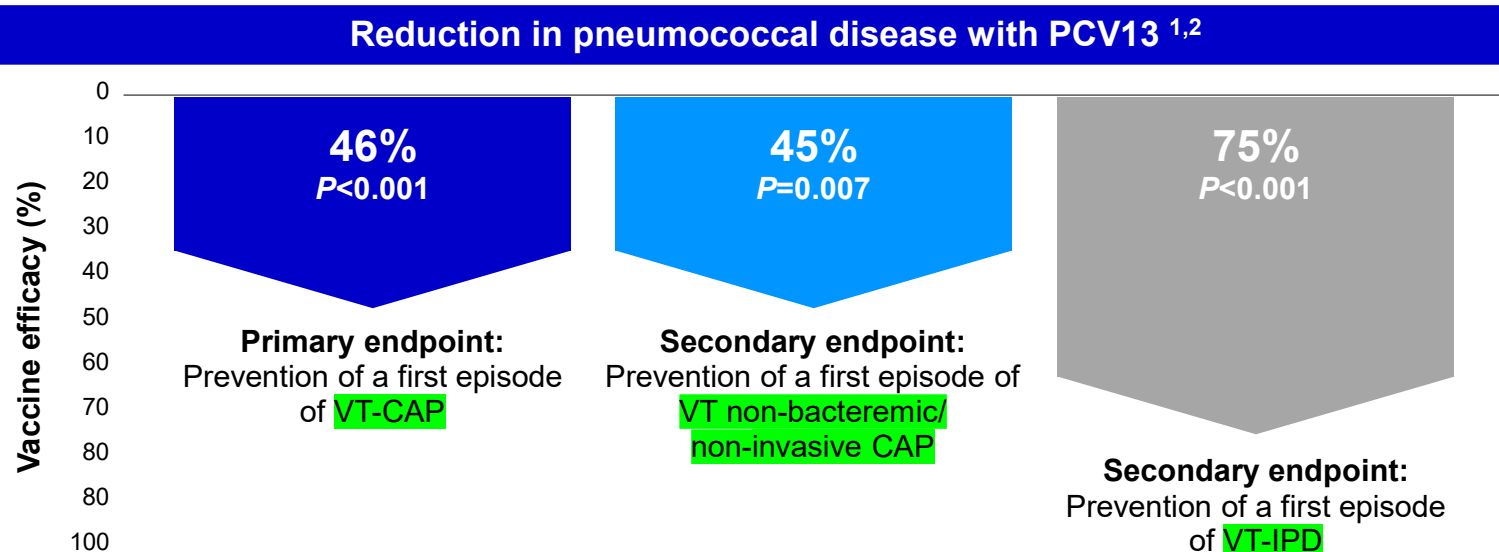
Author	Study population	Analysis	Key findings
Jackson <i>et al</i> 2013	Age 50–59 years (n=403) Age 60-64 years (US; n=831)	Single dose of PCV13 versus PPSV23 (study duration: 12 months)	PCV13 induces a greater functional immune response than PPSV23 for the majority of serotypes covered by PCV13.
Jackson <i>et al</i> 2013	Age >70; previously vaccinated with PPSV23 at least 5 years earlier (US, Sweden; n=936)	Sequential vaccination separated by 1 year (study duration: 13 months):	In adults aged 70 years and older previously vaccinated with PPSV23, <u>PCV13 was significantly more immunogenic</u> than PPSV23
Solanki <i>et al</i> 2017 	Individuals aged 50-65 years (India; n=999)	Open-label, single-arm study for PCV13	<u>PCV13 elicited a robust immune response</u> Well tolerated in Indian adults aged 50-65 years

1. Jackson LA, Gurtman A, van Cleeff M, Jansen KU, Jayawardene D, Devlin C, *et al*. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naive adults. *Vaccine* 2013;31:3577-84.

2. Jackson LA, Gurtman A, Rice K, Pauksens K, Greenberg RN, Jones TR, *et al*. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults 70 years of age and older previously vaccinated with 23-valent pneumococcal polysaccharide vaccine. *Vaccine* 2013;31:3585-93.

3. Solanki BB, Juergens C, Chopada MB, Supe P, Sundaraiyer V, Le Dren-Narayanan N, *et al*. Safety and immunogenicity of a 13-valent pneumococcal conjugate vaccine in adults 50 to 65 years of age in India: An open-label trial. *Hum Vaccin Immunother* 2017;13:2065-71.

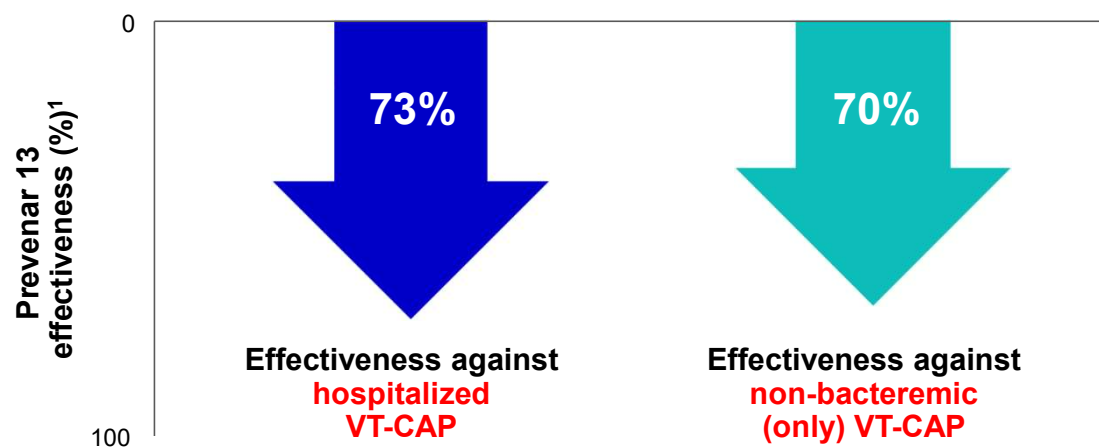
PCV13 Demonstrated Efficacy Against a First Episode of VT-CAP in Adults Aged 65 Years and Older



In one of the largest vaccine trials ever conducted in adults 65 years and older, PCV13 demonstrated efficacy against **VT non-invasive pneumococcal pneumonia as well as against invasive disease**

CAP=community-acquired pneumonia; CAPiTA=Community-Acquired Pneumonia Immunization Trial in Adults; VT=vaccine type.
1. Bonten MJ, et al. *N Engl J Med*. 2015;372(12):1114-1125. 2. Prevnar 13 (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM₁₉₇ Protein]) Prescribing Information, Wyeth Pharmaceuticals LLC, 2019.

Efficacy Results From the CAPiTA RCT Confirmed by TND Study in a Real-World Setting



Study limitations¹

- Observational in nature
- Low Prevenar 13 uptake in study
- Serotype-specific vaccine effectiveness and stratified analyses not possible
- May be susceptible to selection bias or confounding factors
- Overall number of CAP cases was relatively small (n=68)

PCV13 reduced the risk for **hospitalized VT-CAP** by 73% in adults aged 65+ years, including those with comorbid conditions, complementing the vaccine efficacy observed in CAPiTA^{1,2}

CAP=community-acquired pneumonia; CAPiTA=Community-Acquired Pneumonia Immunization Trial in Adults; RCT=randomized controlled trial; RWE=real-world effectiveness; VT=vaccine type.

1. McLaughlin JM, et al. *Clin Infect Dis*. 2018;67(10):1498-1506. 2. Bonten MJ, et al. *N Engl J Med*. 2015;372(12):1114-1125.

PCV13 Adult Clinical Program

A total of **7 European and US studies** assessed the safety of Prevenar 13 in 48,806 adults aged 18 to 101 years, including those with risk conditions¹

Immunogenicity

Immune responses to PCV13 were non-inferior to those elicited by PPV23¹

Efficacy

Statistically significant reductions in first episode of vaccine-type CAP and IPD with PCV13 in adults 65 and older¹

Safety

The safety profile of PCV13 was consistent across all populations, including those who were previously vaccinated with PPV23¹

Efficacy in High-Risk Populations (Open-label studies)

PCV13 elicits an immune response in **HIV-infected**.

PCV13 elicited higher immune responses for all vaccine serotypes than baseline. Each subsequent dose resulted in increased immunogenicity¹

Vaccine Recommendations for adult recommendations are **age** and **risk** based

- Adults **≥65 years** are at increased risk for pneumococcal disease.
- Adults of **all ages** are also at **increased risk** for pneumococcal disease if they have:
 - Alcoholism
 - Cerebrospinal fluid leak
 - Chronic **heart, lung, kidney, or liver** disease
 - Cochlear implant
 - Diabetes
 - **HIV infection**
 - Cancer, solid organ transplant, or immunosuppression Nephrotic syndrome
 - Sickle cell disease, a damaged spleen, or no spleen
- Adults who **smoke cigarettes** are also at increased risk for pneumococcal disease.
- **Chronic lung illnesses** that increase an adult's risk for pneumococcal disease include chronic obstructive lung disease, emphysema, and asthma.

1. Pneumococcal disease: Risk Factors and How It Spreads [Internet]. 2022 [cited 23 September 2022]. Available from: <https://www.cdc.gov/pneumococcal/about/risk-transmission.html>

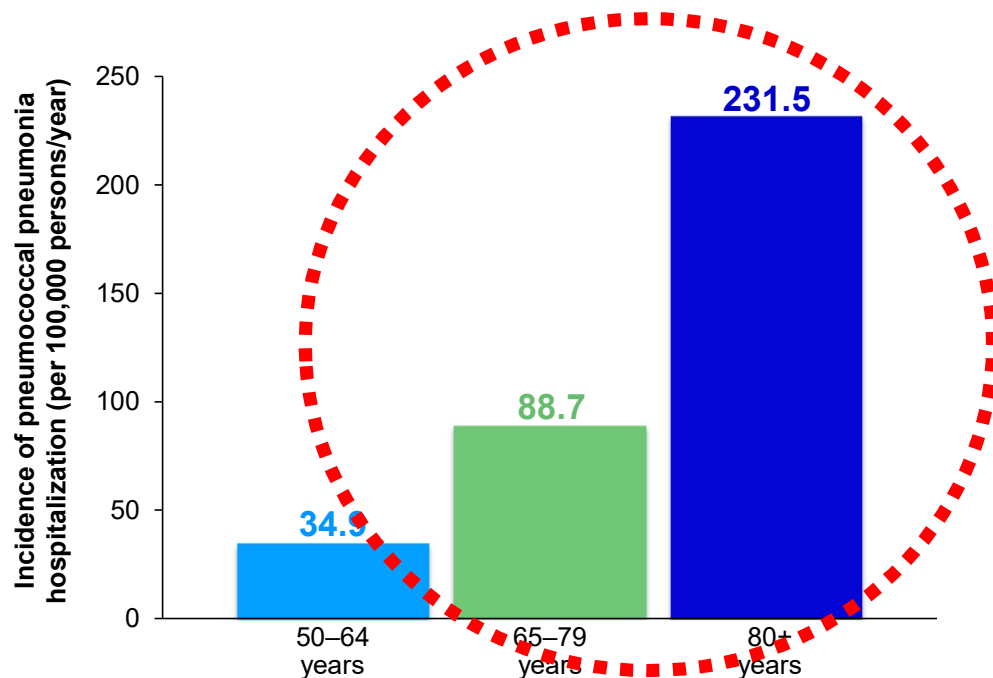
2. Pneumococcal Disease in Adults and the Vaccines to Prevent It [Internet]. 2022 [cited 23 September 2022]. Available from: <https://www.cdc.gov/pneumococcal/resources/prevent-pneumococcal-factsheet.html>

3. HIV- Human Immunodeficient Virus Syndrome

Age is a Risk factor for Pneumococcal Pneumonia: (Immunosenescence) – hospitalization for Pneumonia, IPD

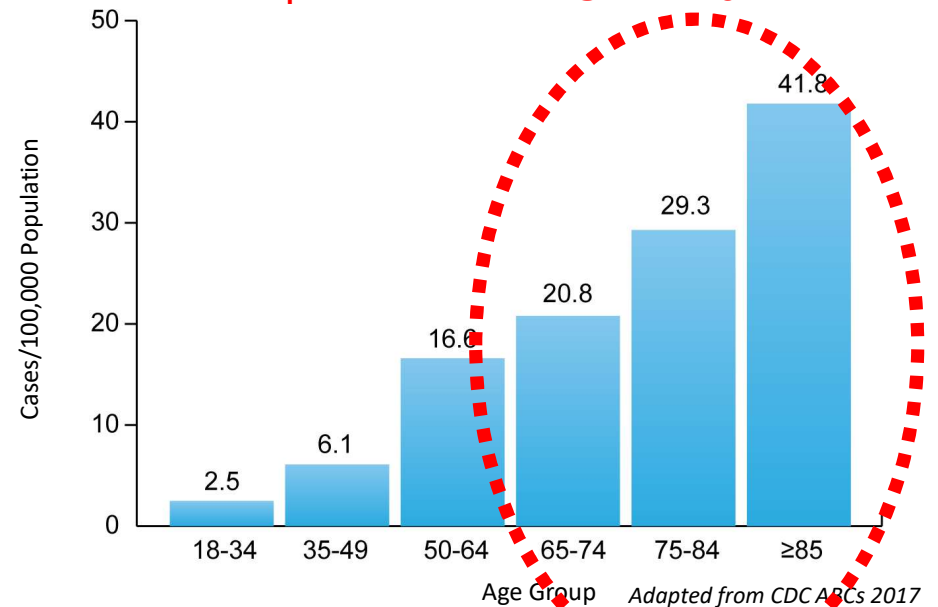
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Rate of IPD per 100,000 of the Adult Population in the US in 2017



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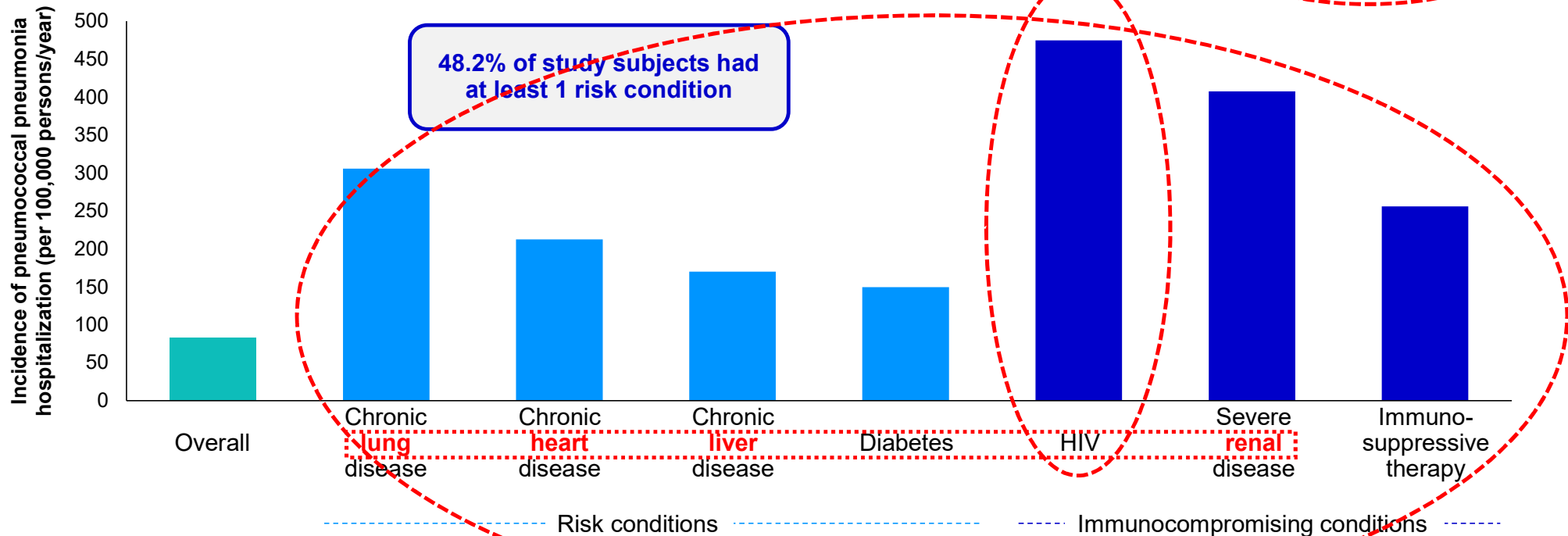
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- Cerebrospinal fluid leak
- Cochlear implant
- Smoking
- Nephrotic syndrome
- Sickle cell disease (spleen)

Pneumococcal pneumonia population-based prospective cohort study adults ≥50 years (N=2,025,730) in Catalonia, Spain, 2015



48.2% of study subjects had at least 1 risk condition

----- Risk conditions ----- Immunocompromising conditions -----

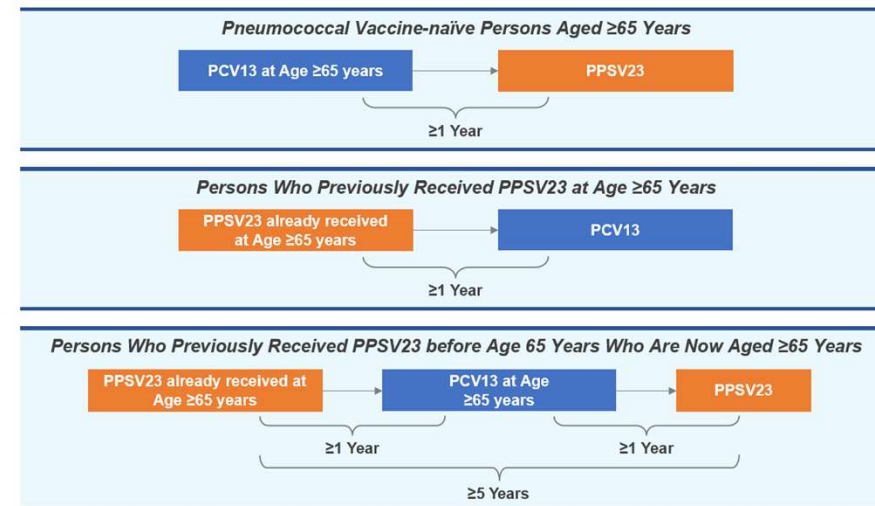
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Guidelines for the vaccination of HIV-infected adolescents and adults in South Africa



Pneumococcal

- All HIV-infected regardless of CD4 preferably with suppressed VL
- **Prime-boost approach recommended**
- PCV13 followed eight weeks later by PPSV23
- PCV13 alone is sufficient



Improving Vaccination Coverage

Make adult vaccination a standard of care

- Adult vaccination rates are extremely low.
- Most adults are NOT aware that they need vaccines.
- At every visit assess patients' vaccination status;
- At every opportunity - **Recommend, Repeat, Remind Review.**
- Institute a program for vaccine administration
- Clearly record administration date to plan following vaccines.



Conclusion

- Pneumococcal disease in high-risk groups have significant morbidity and mortality
- HIV is a particular concern in SA especially with risk stacking due to the aging HIV population with NCDs
- Vaccines have an important role in reducing disease burden
- Clinicians can play a vital role in promoting vaccines
- Note: currently in SA vaccine is available for childhood immunization, NAGI is contemplating adult vaccination as an option.

Acknowledgements

- Pfizer
- Richard Lessels

Thank You

