Considerations for Age-Based and Risk-Based Use of PCV15 and PCV20 among U.S. Adults and Proposed Policy Options

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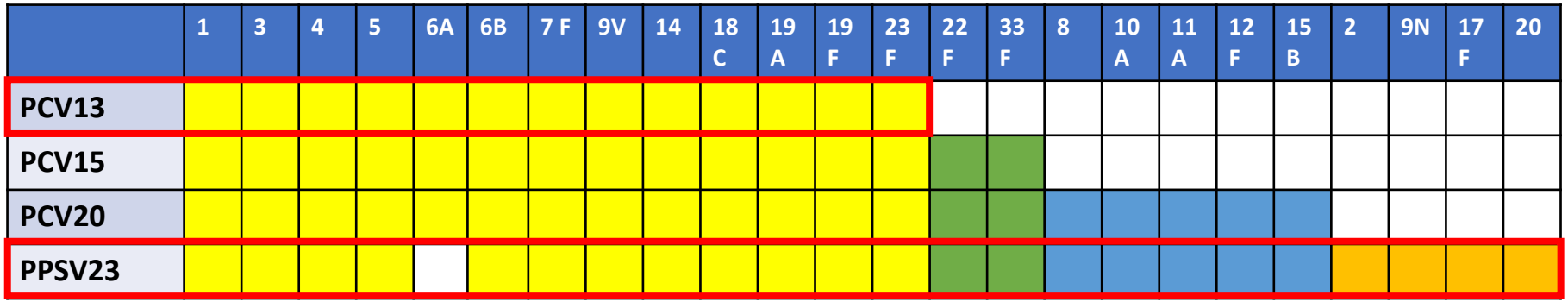
ACIP Meeting

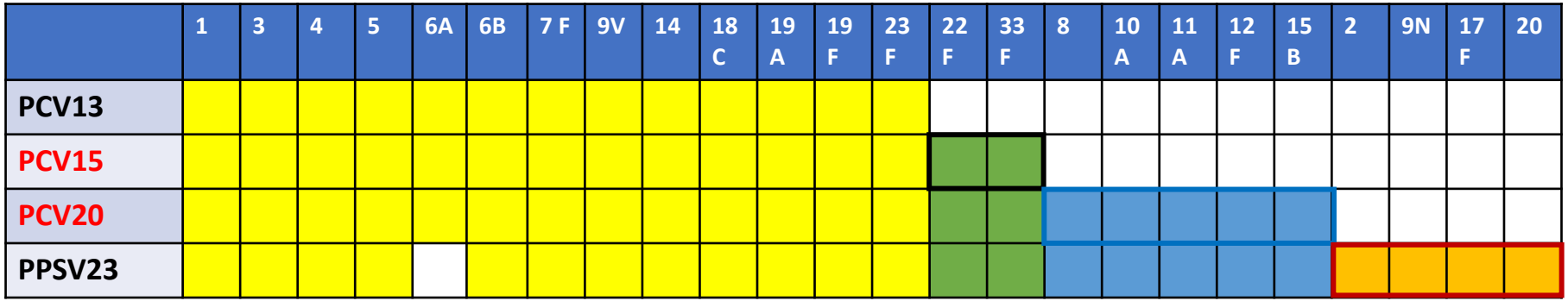
October 20, 2021

Serotypes Contained in Current and New Pneumococcal Vaccines



PCV13: 13-valent pneumococcal conjugate vaccine
PPSV23: 23-valent pneumococcal polysaccharide vaccine

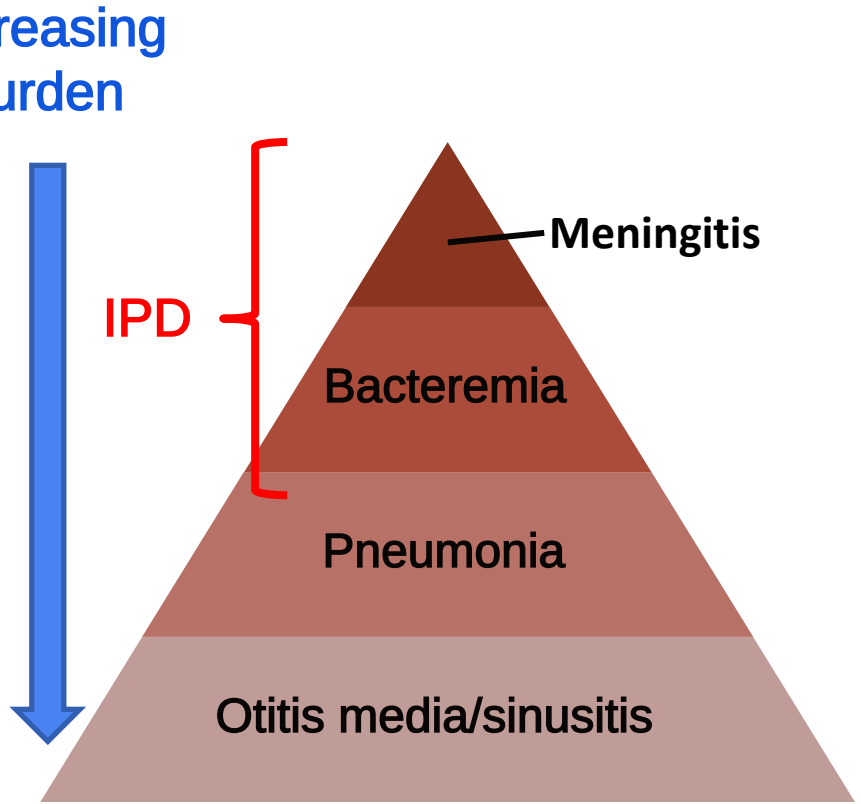
Serotypes Contained in Current and New Pneumococcal Vaccines



- **PCV15 non-PCV13**: includes serotypes **22F and 33F**
- **PCV20 non-PCV13**: includes serotypes **22F, 33F, 8, 10A, 11A, 12F, and 15B**
- **PPSV23 non-PCV20**: includes serotypes **2, 9N, 17F, and 20**

Pneumococcal disease

- Invasive pneumococcal disease (IPD)
  - e.g., meningitis, bacteremia, bacteremic pneumonia
- Non-invasive disease
  - e.g., non-bacteremic pneumonia



Estimated burden of pneumococcal disease in U.S. adults aged ≥19 years

- In 2017, **≥100,000** hospitalized pneumococcal pneumonia cases occurred[1]
- In 2019, **~30,000** IPD cases and **~3,000** IPD deaths occurred[2]
  - **~43%** of IPD in adults aged **≥65 years**
  - **~48%** of IPD in adults aged **19–64 years with risk-based indications**

>90% of the current adult IPD burden is in persons aged 19–64 years with risk-based indications and persons aged ≥65 years

1. CDC SNiPP, 2017; 2. CDC ABCs, 2018

Classification of Risk Groups: Chronic Medical Conditions vs. Immunocompromising Conditions

	19–64 years
None of the conditions listed below	No recommendation
Chronic medical conditions† (CMC)	**PPSV23**
Cochlear implant, CSF leak	**Both PCV13* and PPSV23**
Immunocompromising conditions	**Both PCV13* and PPSV23, repeat PPSV23 after 5 years**

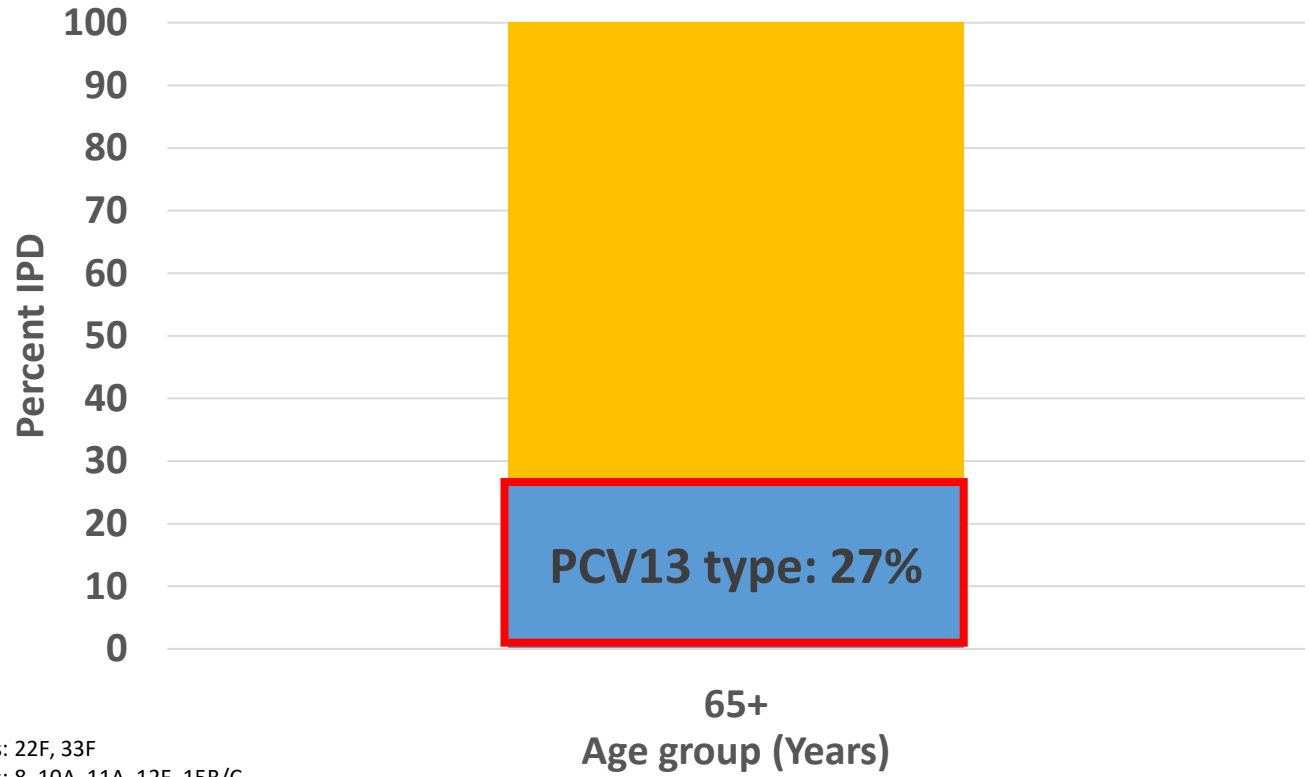
Chronic Medical Conditions (CMC)

Immunocompromising conditions (IC)

CSF: cerebrospinal fluid leak
PCV13: 13-valent pneumococcal conjugate vaccine
PPSV23: 23-valent pneumococcal polysaccharide vaccine

*If not previously given; †Examples include alcoholism, chronic heart/liver/lung disease, diabetes, cigarette smoking
https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf

Proportion of IPD by Serotype Groups in Adults aged ≥65 Years



ABCs 2018–2019

PCV15 non-PCV13 serotypes: 22F, 33F

PCV20 non-PCV15 serotypes: 8, 10A, 11A, 12F, 15B/C

PPSV23 non-PCV20 serotype: 2, 9N, 17F ,20

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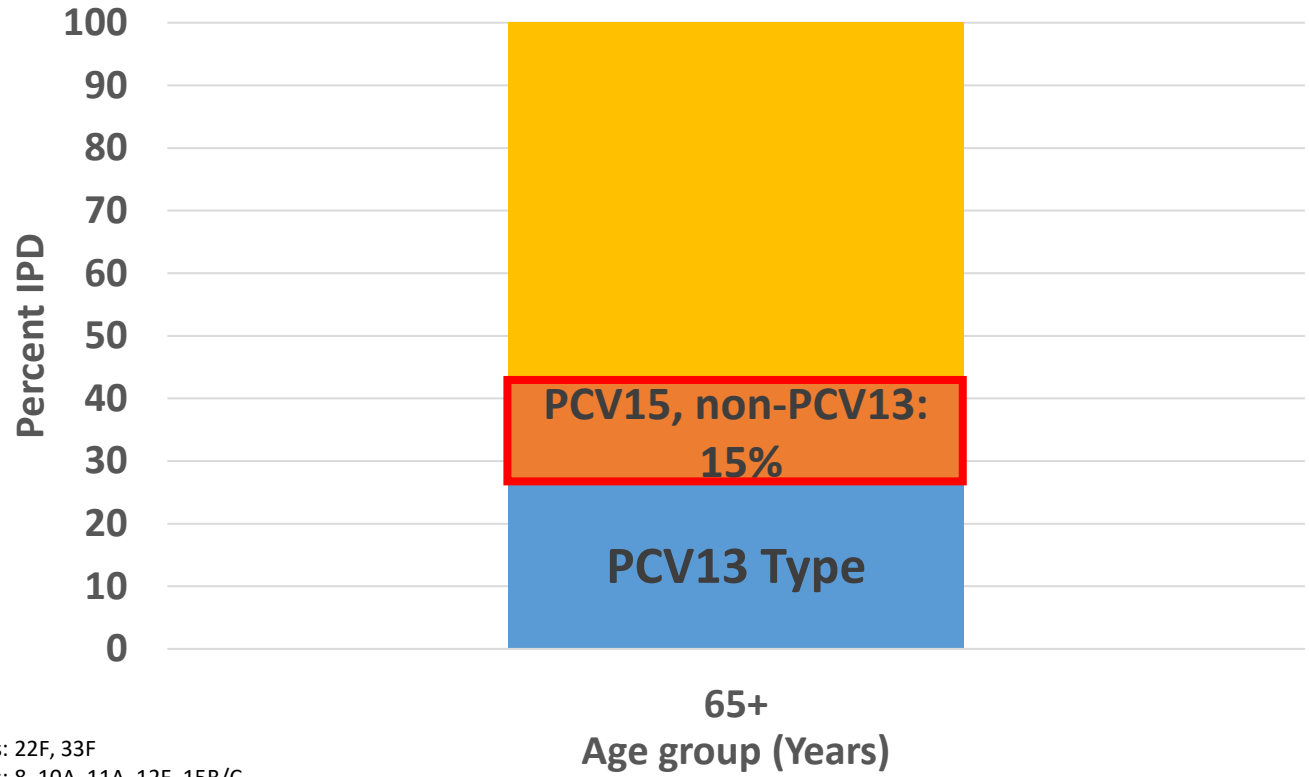

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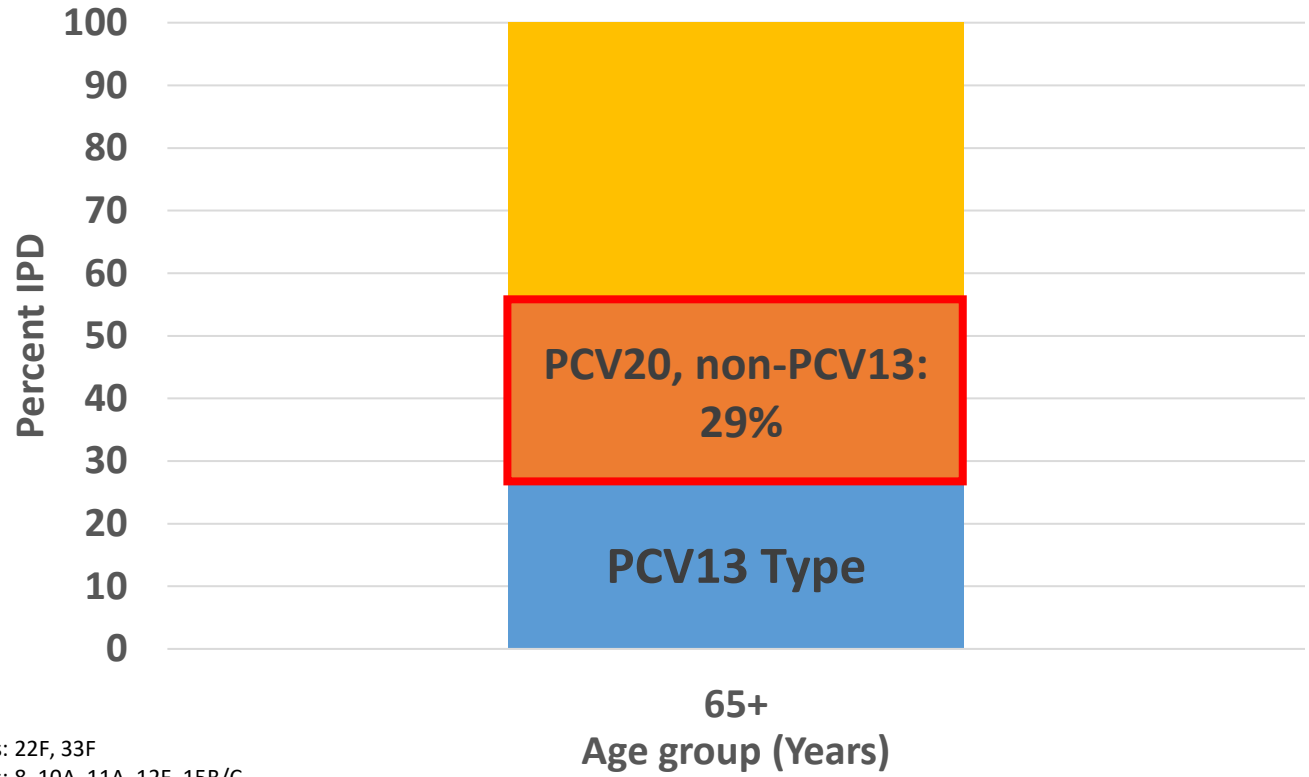

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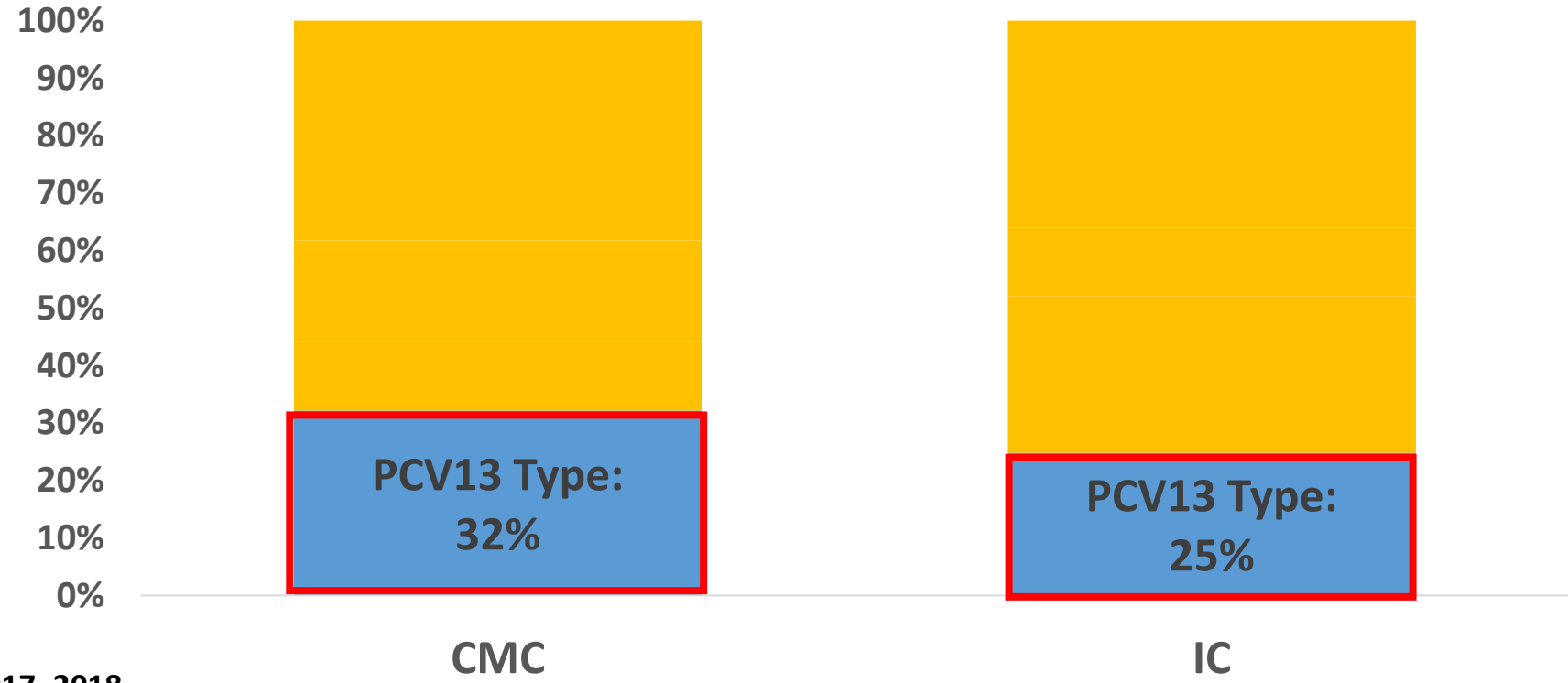
Proportion of IPD by Serotype Groups in Adults aged 19–64 Years with Risk-based Indications



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CMC: chronic medical conditions
IC: immunocompromising conditions

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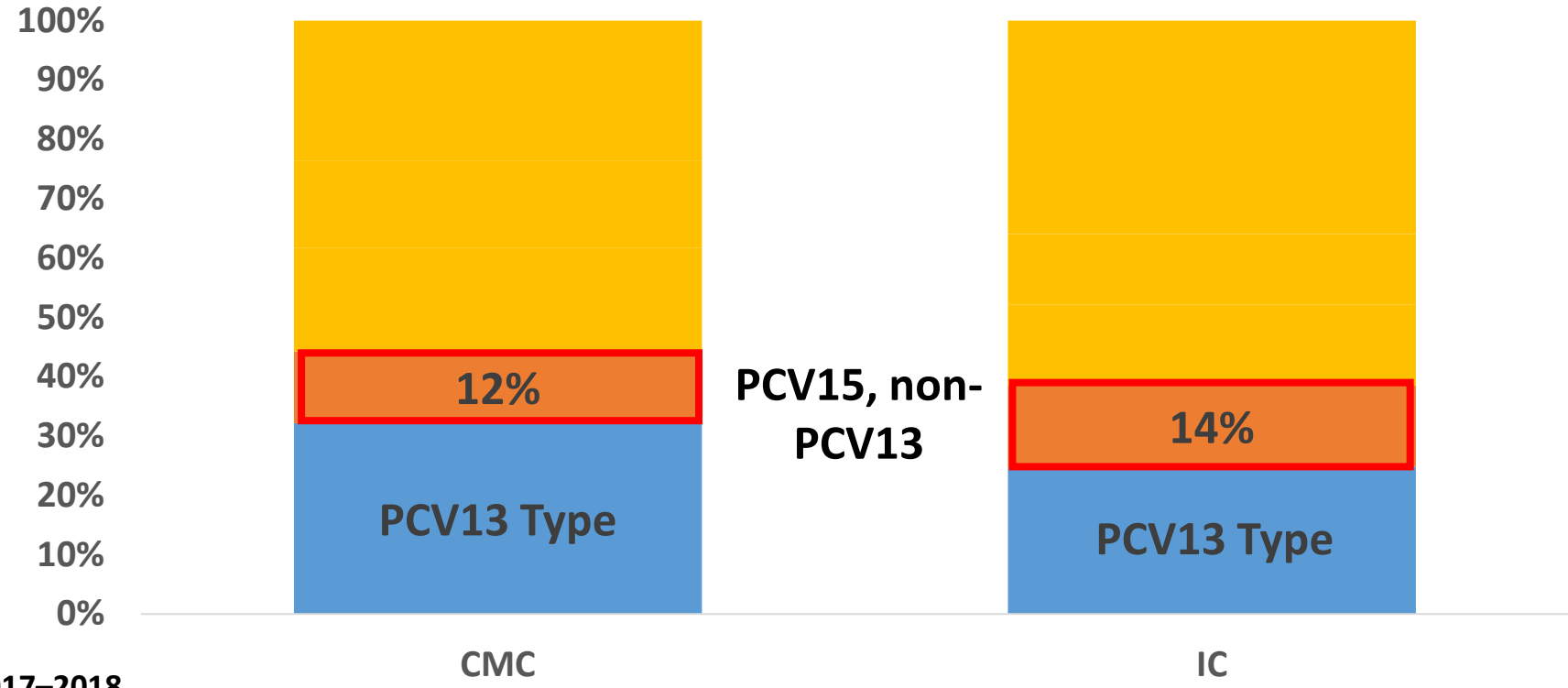

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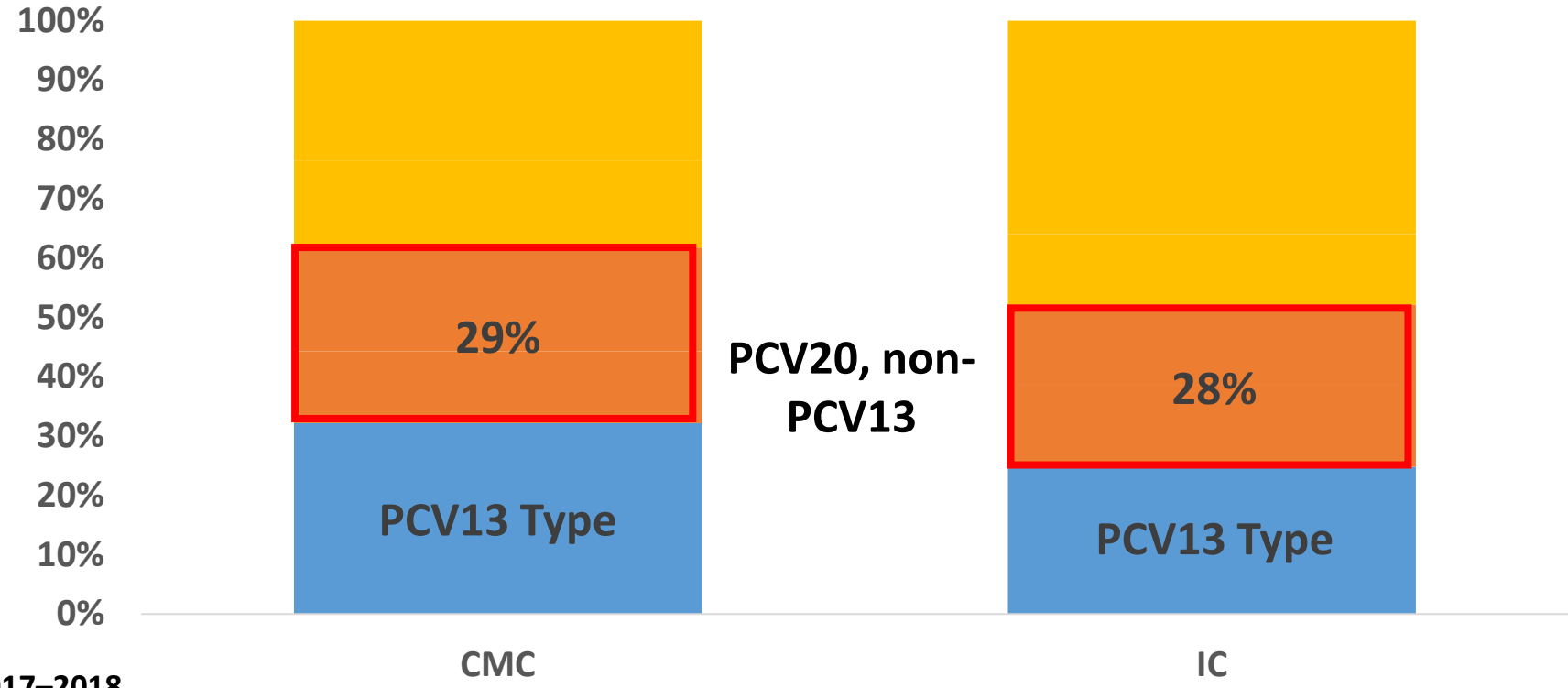

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Updated Policy Questions for Consideration

- Should **PCV20 alone OR PCV15 in series with PPSV23** be routinely recommended for US adults aged **≥65 years?**

- Should **PCV20 alone OR PCV15 in series with PPSV23** be recommended for U.S. adults aged **19–64 years** with certain underlying medical conditions or other risk factors*?

*alcoholism, chronic heart/liver/lung disease, cigarette smoking, diabetes mellitus, chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease or other hemoglobinopathies, CSF leak, or cochlear implant.

Current and Proposed Options for an Age-based Recommendation

<table>
<tr><th></th><th>Current Policy</th><th>Proposed Policy Option</th></tr>
<tr><td>None of the conditions listed below</td><td rowspan="2">PCV13* based on shared clinical decision making, PPSV23 for all</td><td rowspan="4">PCV20
OR
PCV15 and PPSV23</td></tr>
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PCV13: 13-valent pneumococcal conjugate vaccine, PCV15: 15-valent pneumococcal conjugate vaccine, PCV20: 20-valent pneumococcal conjugate vaccine, PPSV23: 23-valent pneumococcal polysaccharide vaccine

*If not previously given; †Examples include alcoholism, chronic heart/liver/lung disease, diabetes, cigarette smoking

https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf

Current and Proposed Options for a Risk-Based Recommendation

	Current policy	Proposed Policy Option
None of the conditions listed below	No recommendation	No recommendation
Chronic medical conditions† (CMC)	**PPSV23**	PCV20 **OR** PCV15 and PPSV23
Cochlear implant, CSF leak	**Both PCV13* and PPSV23**	
Immunocompromising conditions	**Both PCV13* and PPSV23, repeat PPSV23 after 5 years**	

PCV13: 13-valent pneumococcal conjugate vaccine
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https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf

Work Group Discussion Points on Proposed Options

- The **majority** of work group members in support of proposed options:
  - Either **PCV20 alone** or **PCV15+PPSV23** at age ≥65 years
  - Either **PCV20 alone** or **PCV15+PPSV23** for adults aged 19-64 years with certain underlying medical conditions or other risk factors*

*alcoholism, chronic heart/liver/lung disease, cigarette smoking, diabetes mellitus, chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease or other hemoglobinopathies, CSF leak, or cochlear implant.

Main Reasons Against the Proposed Options

- Prefer an age-based recommendation at **age 50** vs 65 years
  - May reduce disparity in disease burden in adults aged 50–64 years
  - May provide more opportunities to vaccinate adults before they develop underlying conditions

- Concerns with PCV15 options given need to use **in series with PPSV23**
  - Logistically more challenging to administer different vaccines in series
  - Need to know the vaccination history to correctly complete series
  - Can result in lower serotype coverage if series not completed

Age-based recommendation

age 50 vs. 65 years

Reasons for an Age-Based Recommendation at ≥65 years

- Due to **potential waning of immunity**, vaccination later in life may be favorable when risk of disease is higher

- Consistently **cost-saving** (lower cost and better health outcome compared to current recommendations) in cost-effectiveness analyses

- Proposed risk-based and age-based options still provide an **opportunity for higher PCV coverage**, which may prevent more disease compared with current recommendations and may address some health equity concerns

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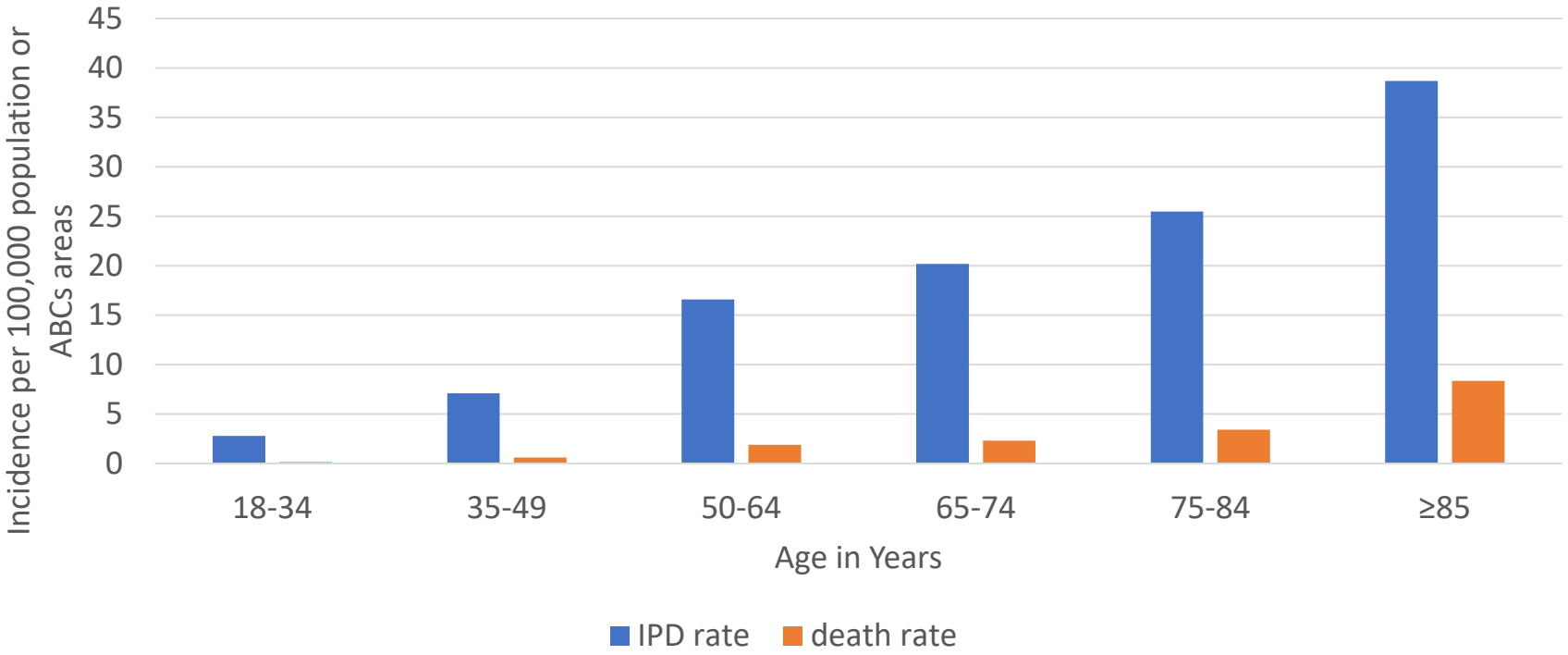
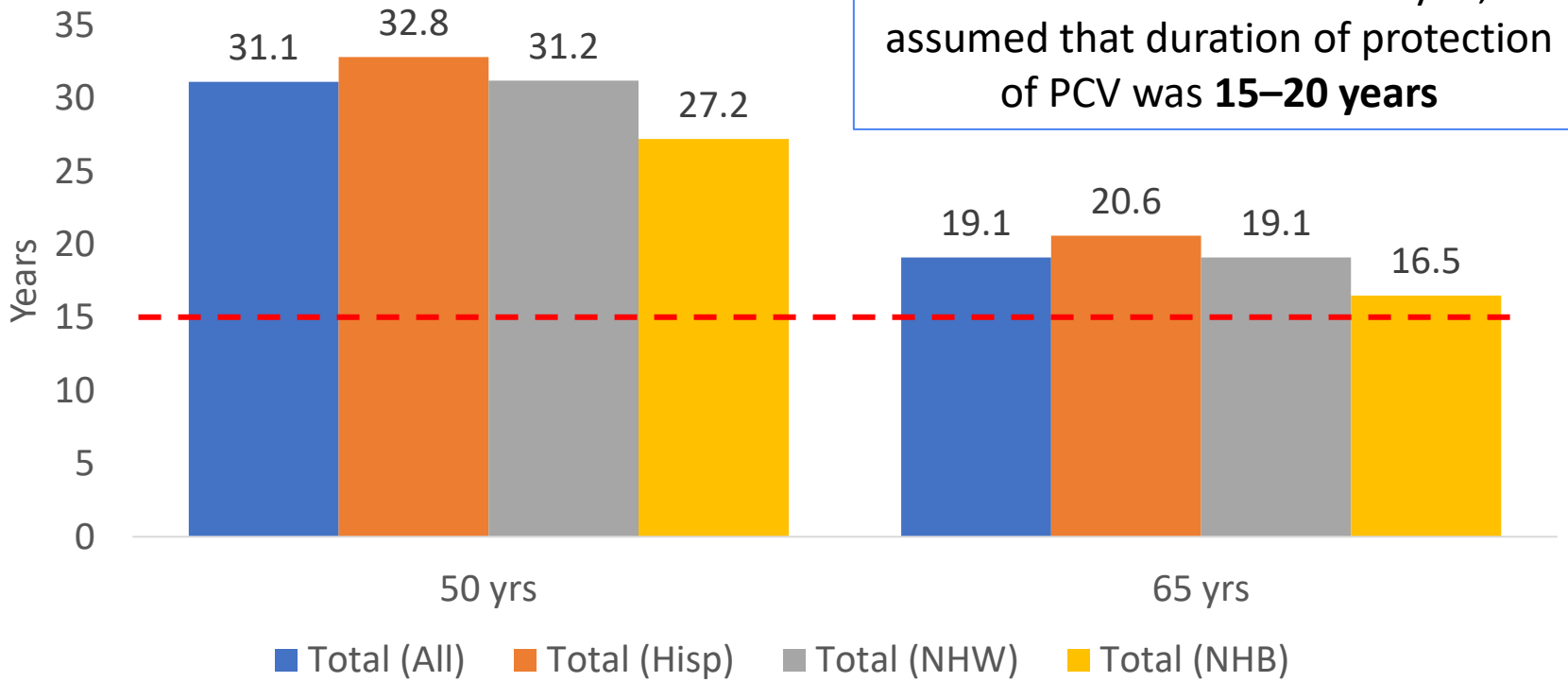
Risk of pneumococcal disease increases with increasing age.



ABCs Report: *Streptococcus pneumoniae*, 2018. https://www.cdc.gov/abcs/reports-findings/survreports/spneu18.html

Life Expectancy at Age 50 vs 65 by Race/Ethnicity, US, 2020

In cost-effectiveness analysis, assumed that duration of protection of PCV was **15–20 years**



CEA: cost-effectiveness analysis, Hisp: Hispanic, NHW: Non-Hispanic white, NHB: Non-Hispanic Black

https://www.cdc.gov/nchs/data/vsrr/VSRR10508.pdf

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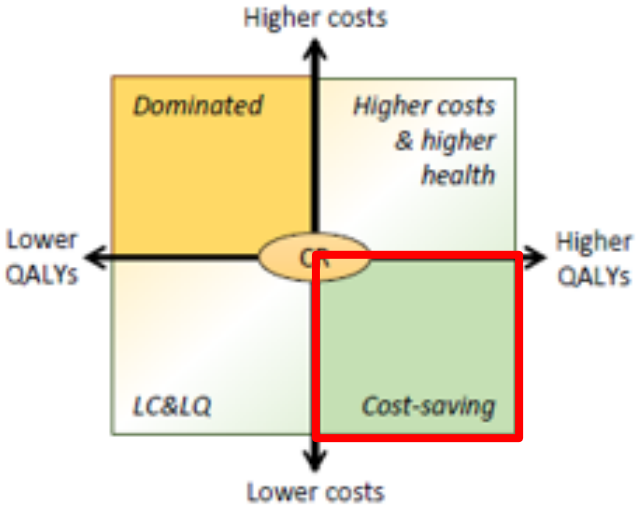

QALY: quality-adjusted life year

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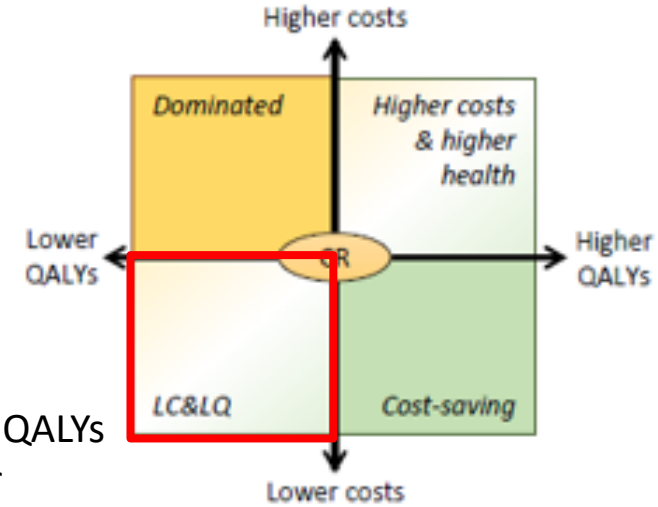


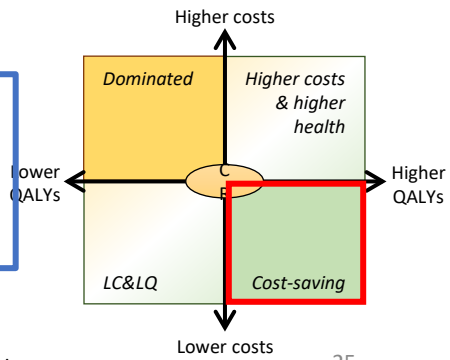
LC&LQ: Lower costs and lower QALYs
QALY: quality-adjusted life year

Age-based strategies, PCV20, CDC model

Scenario analyses, compared to current recommendations ($/QALY)

Analysis	Strategy	Base case	PCV waning 20 years	PCV coverage higher than in base case	Indirect effects	Lower PCV20 VE	**Health-improving scenarios**	**Cost-saving scenarios**
Age-based	PCV20 at age **65**	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	Cost-saving[a]	**5 of 5**	**5 of 5**
Age-based	PCV20 at age **50**	LC&LQ[b] (5,300,000)	Cost-saving[a]	7,000	Cost-saving[a]	LC&LQ[b] (944,000)	**3 of 5**	**2 of 5**

- **PCV20 at age 65 consistently showed that the intervention was "cost-saving" in different scenarios.**
- **PCV20 at age 50 resulted in worse health in some CDC scenarios.**



Sept 2021 ACIP meeting presentation

[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

[b] LC&LQ indicates a strategy yielded lower health outcomes (fewer QALYs, more episodes of disease) and lower costs than the comparator.

Age-based strategies, PCV20, CDC model

Scenario analyses, compared to current recommendations ($/QALY)

Analysis	Strategy	Base case	PCV waning 20 years	PCV coverage higher than in base case	Indirect effects	Lower PCV20 VE	**Health-improving scenarios**	**Cost-saving scenarios**
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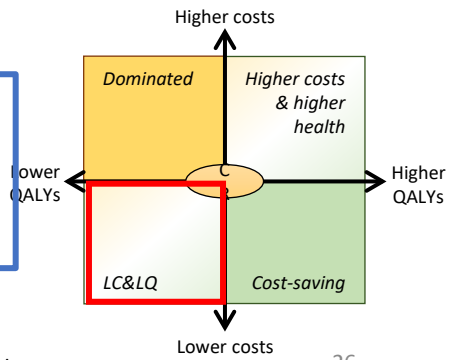

Sept 2021 ACIP meeting presentation, QALY: quality-adjusted life year

[a] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

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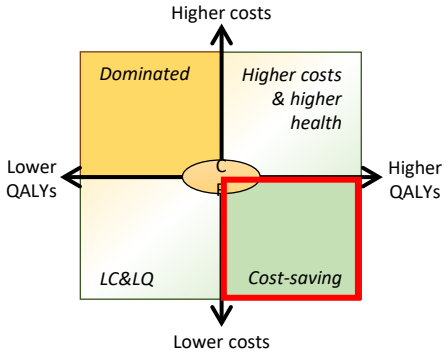
Age-based strategies, PCV20, all models

Compared to current recommendations ($/QALY)

Analysis	Strategy	CDC model	Merck model	Pfizer model
Age-based	PCV20 at age **65**	Cost-saving[a]	Cost-saving[a] to 39,000	Cost-saving[a]
Age-based	PCV20 at age **50**	LC&LQ[b]	174,000 to 514,000	18,000



- **CEA models from other groups showed PCV20 use at age 65 was "cost-saving" in most cases.**

Sept 2021 ACIP meeting presentation, QALY: quality-adjusted life year

[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.
[b.] LC&LQ indicates a strategy yielded lower health outcomes (fewer QALYs, more episodes of disease) and lower costs than the comparator.

Age-based strategy, PCV15+PPSV23, all models

Compared to current recommendations ($/QALY)

Analysis	Intervention	Comparator	CDC Model	Merck model
Age-based	PCV15+PPSV23 at age 50	Current recommendations	LC&LQ[a]	555,556 to 640,015
Age-based	PCV15+PPSV23 at age 65	Current recommendations	Cost-saving[b]	237,026 to 282,140 Sensitivity Analysis: Cost-saving

- **CDC model showed PCV15+PPSV23 at age 50 resulted in lower health outcomes**
- **Merck model showed PCV15+PPSV23 at age 50 was less cost-effective than age 65**

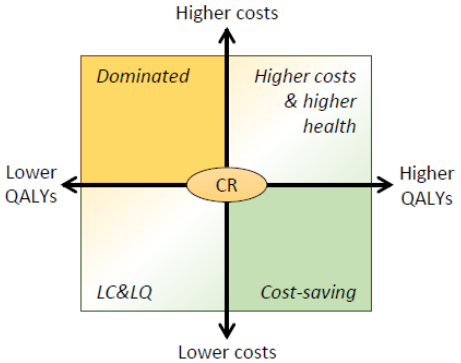
QALY: quality-adjusted life year

a. LC&LQ indicates a strategy yielded lower health outcomes (fewer QALYs, more episodes of disease) and lower costs than the comparator.
b. Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Age-based strategy, PCV15+PPSV23, all models

Compared to current recommendations

- **CDC CEA model showed that PCV15+PPSV23 at age 65 was "cost-saving" in all scenarios considered.**



Analysis	Strategy	Base case	PCV waning 20 years	Indirect effects	Higher PCV15 ST3 VE	**Health-improving scenarios**	**Cost-saving scenarios**
Age-based	PCV15+PPSV23 at age **65**	Cost-saving[a]	Cost-saving[a,b]	Cost-saving[a]	Cost-saving[a]	**4 of 4**	**4 of 4**

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[a.] Cost-saving indicates an intervention strategy yielded higher health outcomes (more QALYs, fewer episodes of disease) and lower costs than the comparator.

Reasons for an Age-Based Recommendation at ≥65 years

- Due to **potential waning of immunity**, vaccination later in life may be favorable when risk of disease is higher

- Consistently **cost-saving** (lower cost and better health outcome compared to current recommendations) in cost-effectiveness analyses

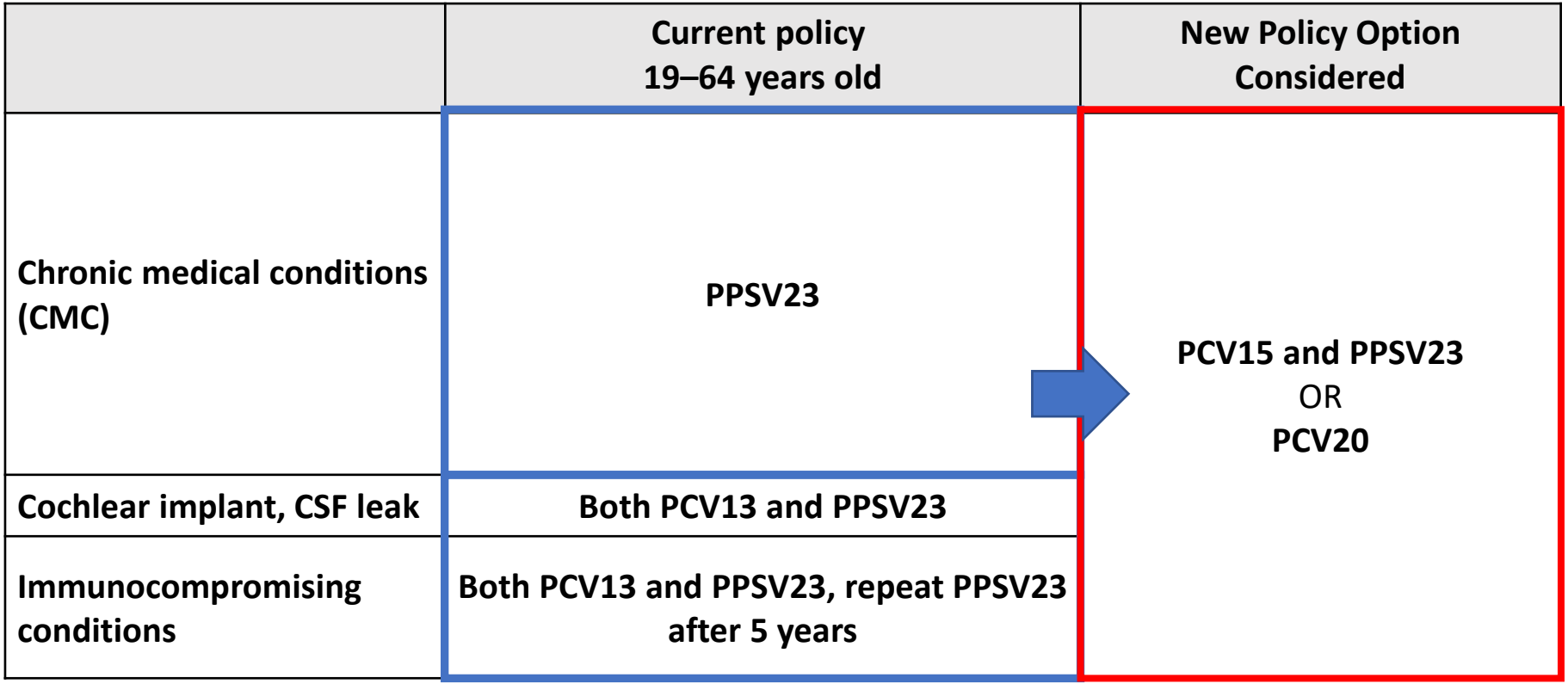
- Proposed risk-based and age-based options still provide an **opportunity for higher PCV coverage**, which may prevent more disease compared with current recommendations and may address some health equity concerns

Estimated Proportion of Adults aged 19–64 years with CMC/IC who Ever Received Pneumococcal Vaccination, NHIS 2018

	Sample size	%	(95% CI)
Overall	5,851	23.3%	(22.0, 24.6)
White	4,048	23.6%	(22.1, 25.2)
Black	696	25.7%	(21.8, 30.0)
Hispanic	656	18.5%	(15.2, 22.4)*
Asian	192	25.0%	(17.3, 34.5)
Other	259	25.8%	(19.3, 33.5)

National Health Interview Survey, 2018; CMC: chronic medical conditions; IC: immunocompromising conditions
*p<0.05 for comparisons with white as the reference.

The new risk-based policy option may help improve vaccine uptake in adults with indications.



*National Health Interview Survey, 2017–2018

Current and New Pneumococcal Vaccines: PCVs vs. PPSV23

	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																								
PCV15																								
PCV20																								
PPSV23																								

	PCV	PPSV23
Basic Vaccine Composition	Capsular polysaccharides conjugated to **CRM_{197} Carrier Protein**	Capsular polysaccharide antigens
Mechanism of action	T-cell **dependent**	T-cell **independent**
Memory B cell production	**Yes**	**No**

PCV: pneumococcal conjugate vaccine, PPSV23: 23-valent pneumococcal polysaccharide vaccine

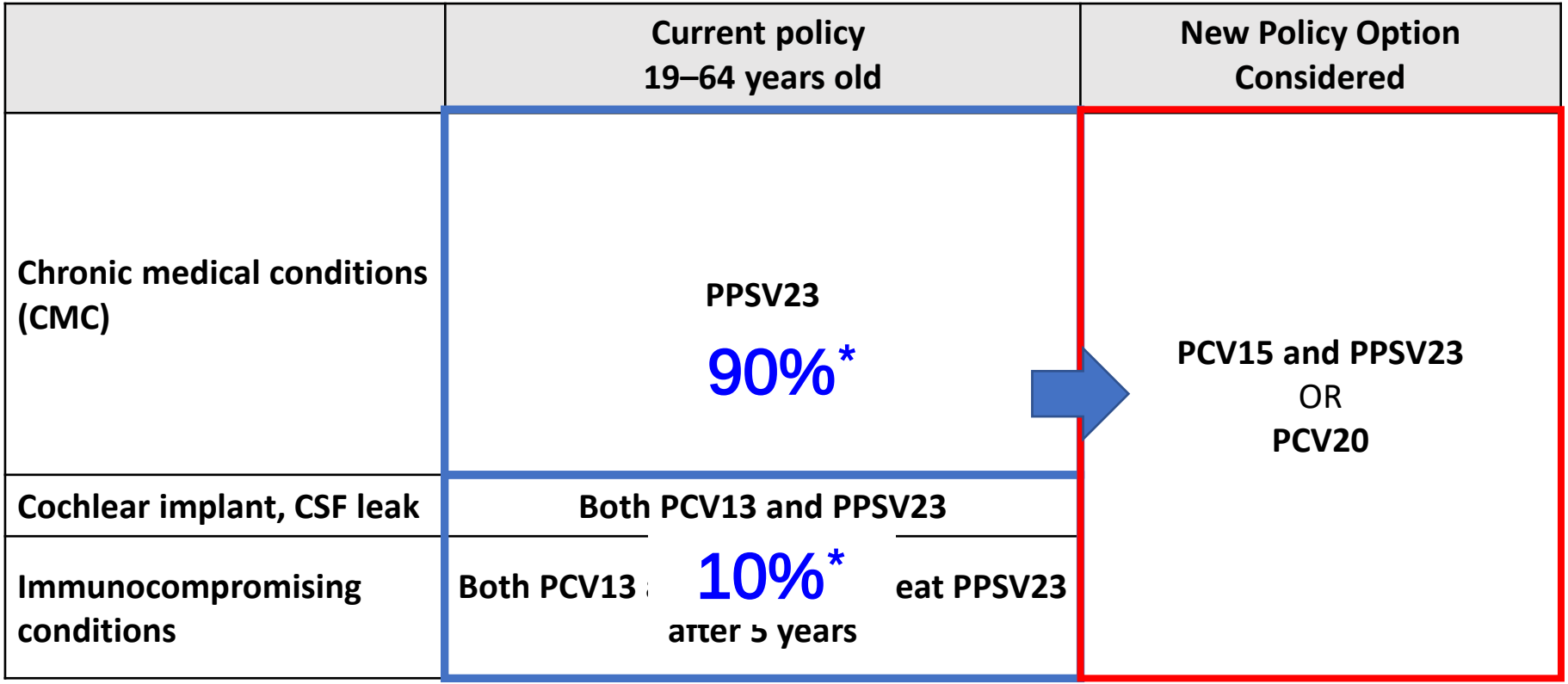
Key Vaccine Effectiveness/Waning Assumptions September CDC Model (base case)

	PCV	PPSV23
Duration of protection	15 years: **no decline for 5 yrs**[1], linear decline to 0 over 10yrs	15 years: linear decline to 0 over 15 years
Vaccine Effectiveness vs. Vaccine-type IPD*	Healthy/CMC: **75** (41.4, 90.8)[1] IC: **25.0** (13.8, 30.3)[2]	Healthy/CMC: **59.7** (47.4, 69.1)[3] IC: **7.9** (0, 34.2)[3]
Vaccine Effectiveness vs. Vaccine-type pneumonia*	Healthy: **66.7** (11.8. 89.3)[4] CMC: **40.3** (11.4, 60.2)[4] IC: **15.0** (4.7, 21.8)[2]	Healthy/CMC: **20** (0, 40)[5] IC: **6.7** (0, 13.3)[2]

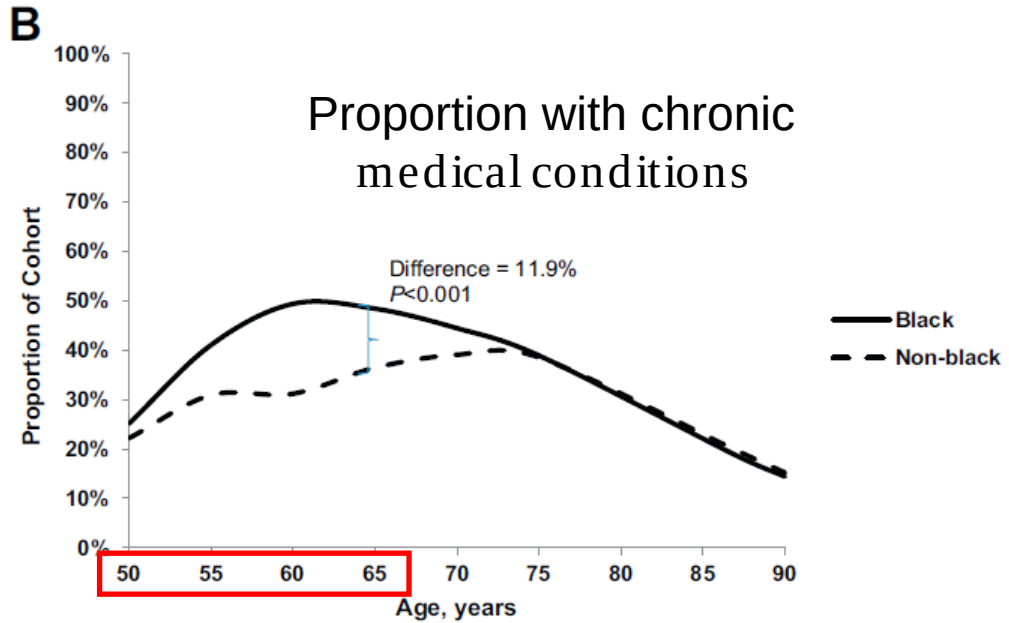
CMC: Chronic medical conditions, IC: immunocompromising conditions
Adapted from Leidner September 2021 ACIP Presentation
*For PCVs, different vaccine effectiveness assumptions were used against serotype 3 disease

1. Bonten et al. NEJM 2015, 2. Assumed 1/3 of healthy/CMC adults, Cho et al. Vaccine 2013, 3. Meta-analysis of Andrews 2012, Rudnick 2013, and Djennad 2018, restricting to PPSV23 VE within 5 years of vaccination , 4. Suaya et al. Vaccine 2018, 5. Lawrence et al. PLoS Med 2020

Under the new risk-based policy option, more adults will be recommended to receive new PCVs.



*National Health Interview Survey, 2017–2018



The new risk-based policy option may prevent more disease in populations with higher burden of chronic medical conditions before age 65 years.

Chronic medical conditions: chronic heart, lung, or liver disease; diabetes mellitus; alcoholism; asthma; cirrhosis

Nowalk et al. Journal of the National Medical Association 2019.

Use of PCV15 in series with PPSV23

Reasons for an PCV15+PPSV23 Series Option

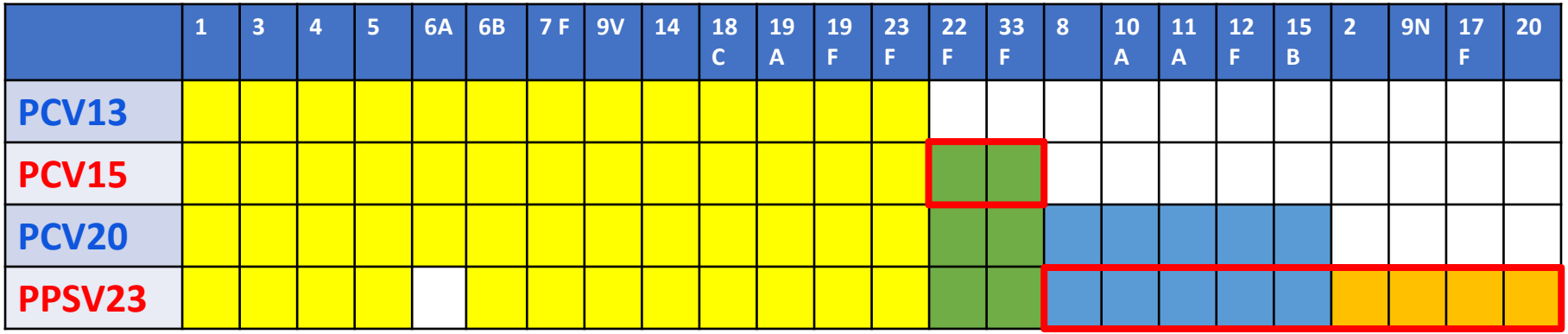
- **Provides broad serotype coverage**

- **Age-based use at age 65 was cost-saving** (lower cost and better health outcomes compared to current recommendations) according to CDC's cost-effectiveness analysis

- **PCV13+PPSV23 series** is currently used

Reasons for an PCV15+PPSV23 Series Option

- Provides broad serotype coverage



Reasons for an PCV15+PPSV23 Series Option

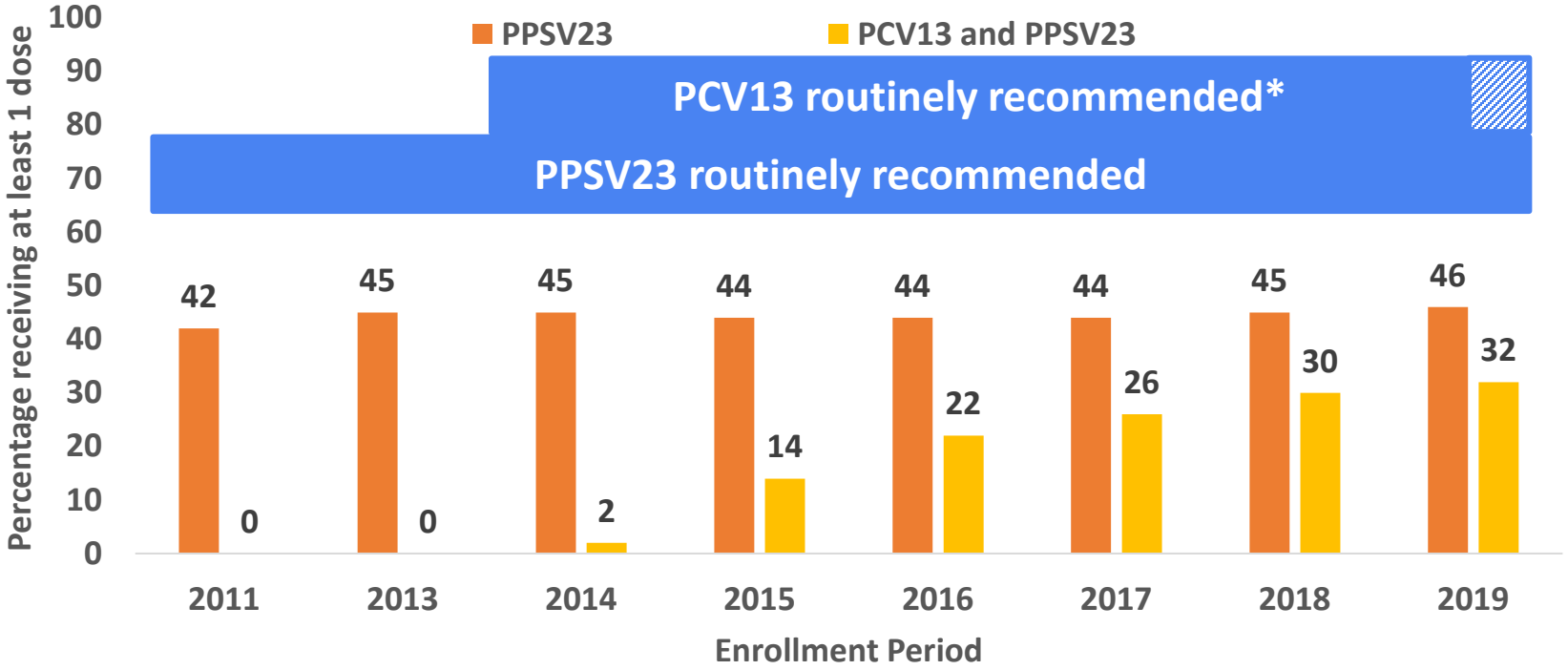
- Provides broad serotype coverage

- **Age-based use at age 65 was cost-saving** (lower cost and better health outcome compared to current recommendations) according to CDC's cost-effectiveness analysis

- **PCV13+PPSV23 series** is currently used
  - Adults aged ≥19 years with immunocompromising conditions, cochlear implant, cerebrospinal fluid (CSF) leak
  - Adults aged ≥65 years* based on shared clinical decision-making

*adults without immunocompromising conditions, cochlear implant, CSF leak

In Medicare beneficiaries aged ≥65 years, the proportion of adults who received both PCV13 and PPSV23 increased over time.



*In 2019, ACIP recommended shared clinical decision-making for PCV13 use in adults aged ≥65 years without immunocompromising conditions, CSF leak, or cochlear implant

Adapted from: Pneumococcal vaccination among U.S. Medicare beneficiaries aged ≥65 years, 2010–2019 | CDC

WG Discussion on Potential for a Preferential Recommendation

In favor of a preferential recommendation

- Implementation challenges with PCV15-PPSV23 series
- PCV20 is likely to provide improved protection against the 5 serotypes included in PPSV23 but not in PCV15

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20
PCV15																								
PCV20																								
PPSV23																								

WG Discussion on Potential for a Preferential Recommendation

Against a preferential recommendation:

- No studies **directly comparing PCV15 and PCV20** efficacy and safety
- The potential **impact of PCV20 use alone is unknown**
  - Clinical relevance of lower immunogenicity for PCV20 vs. PCV13 unknown
  - No data in immunocompromised adults
  - Losing protection against PPSV23, non-PCV20 serotypes

Summary of Evidence, PCV15-PPSV23 series: Benefits (VT-IPD, pneumonia, deaths)

- **PCV15-PPSV23 vs. PCV13-PPSV23 immunogenicity**:
  - In three phase 3 RCTs*, geometric mean titers (GMTs) and % seroresponders were higher in PCV15-PPSV23 recipients for some shared serotypes

*V114-016, V114-017, V114-018

Adapted from June 2021 ACIP presentation

Summary of Evidence from PCV20 studies: Benefits (VT-IPD, pneumonia, deaths)

- **PCV20 vs. PCV13 (comparison of 13 shared serotypes)**:
  - PCV20 recipients had **lower** responses by GMT and % seroresponders (12–13/13 serotypes)
    - Met noninferiority criteria for all shared serotypes by GMT ratio in phase 3 trials*.

	1	3	4	5	6 A	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																								
PCV20																								

*B7471007 (Phase 3), *Klein et al. 2021 (Phase 3), Hurley et al. 2021 (Phase 2)
Adapted from September 2021 ACIP presentation

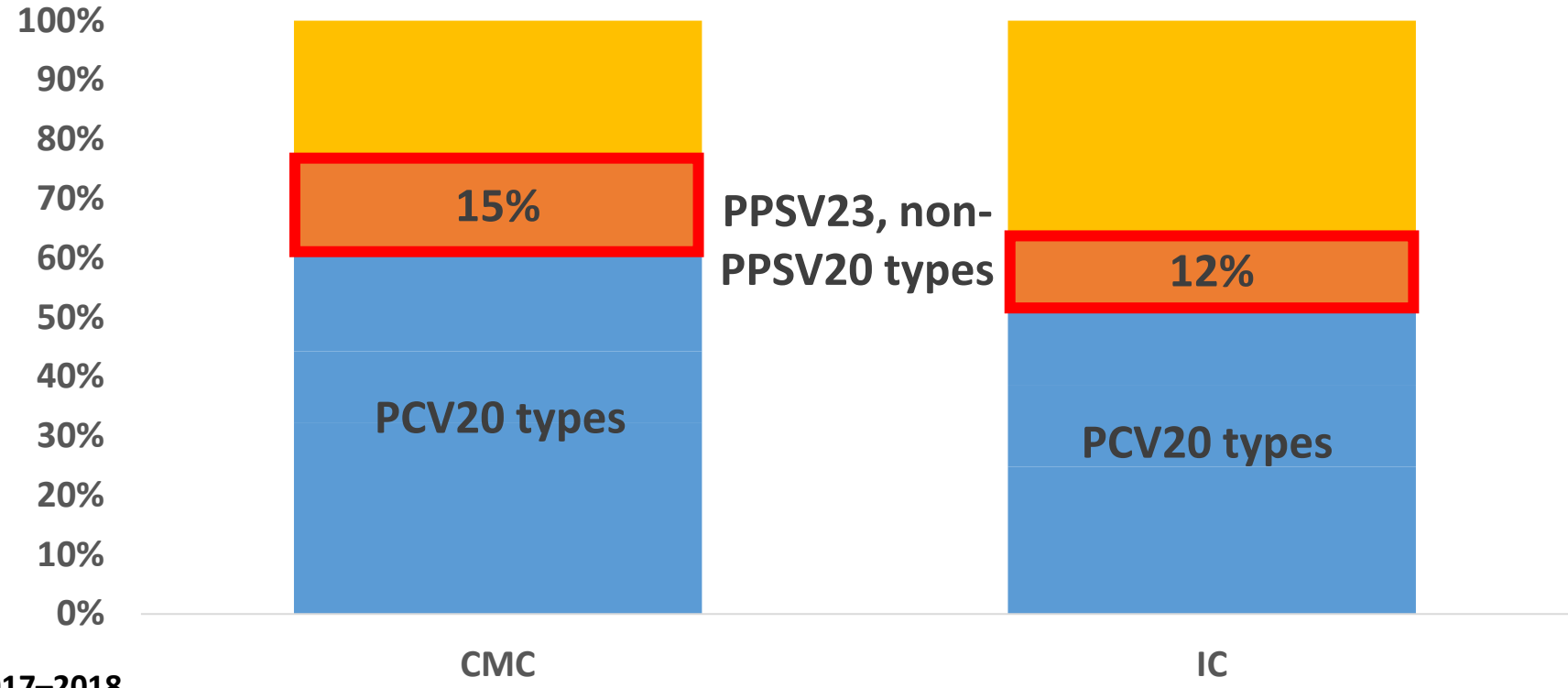
Summary of Evidence from PCV20 studies: Benefits (VT-IPD, pneumonia, deaths) in adults with CMC/IC

Certainty assessment							№ of patients		Results		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	comparison[e]	Relative effect	Absolute effect	
Vaccine effectiveness (Vaccine-type invasive pneumococcal disease, Vaccine-type non-bacteremic pneumococcal pneumonia, Vaccine-type pneumococcal mortality)											
2 [1,2,3]	Randomized studies	Not serious	Not serious	Very serious [a,b,c,d]	Not serious	Not serious	3417	2802	PCV20 vs. PCV13: Across all studies non-inferiority met for all 13 shared serotypes PCV20 had slightly lower immune responses vs. PCV13 for all 13 shared serotypes. PCV20 vs. PPSV23 (non-PCV13 serotypes): Non-inferiority met for all serotypes in at least one study, but ST8 inferior in some studies. PCV20 had greater immune responses vs. PPSV23 for 6 of 7 non-PCV13 shared serotypes.		3 Low

a. These are all immunogenicity studies and there are no correlates of protection.
b. B7471007, Klein et al., and Hurley et al. enrolled healthy adults (some with chronic stable conditions, but focus is not those with immunocompromising or chronic medical conditions).
c. B7471007 provided primary PCV20 vs PCV13 immunogenicity outcomes for adults ≥60 and then showed non-inferiority for PCV20 in 18-49 year-olds compared to PCV20 in 60-64 year-olds. Did not directly compare immunogenicity of PCV20 vs PCV13 in 18-49 year-olds.
d. Hurley et al. only enrolled 60-64 year -olds.
e. Patient no. based on minimum number of patients included in immunogenicity comparisons presented; some comparisons may have had more patients than this minimum.
f. No vaccine-related serious adverse events reported; sample size relatively small

1. B7471007 (Phase 3), 2. Klein et al. 2021 (Phase 3), 3. Hurley et al. 2021 (Phase 2)

Proportion of IPD by Serotype Groups in Adults aged 19–64 Years with Risk-based Indications

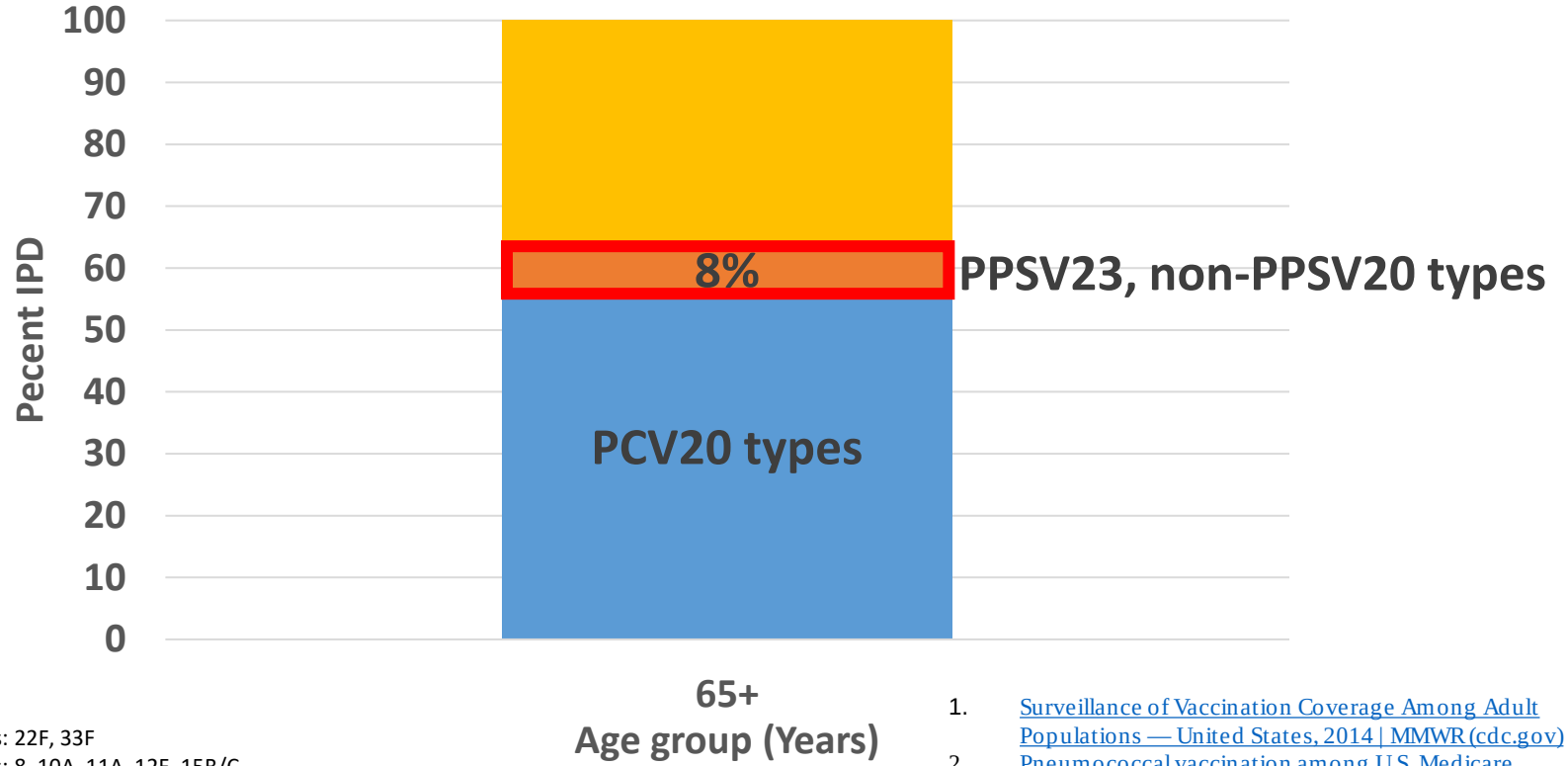


ABCs 2017–2018

PCV15 non-PCV13 serotypes: 22F, 33F
PCV20 non-PCV15 serotypes: 8, 10A, 11A, 12F, 15B/C
PPSV23 non-PCV20 serotype: 2, 9N, 17F ,20

CMC: chronic medical conditions
IC: immunocompromising conditions

In adults aged ≥65 years, additional serotypes contained in PPSV23 but not PCV20 comprise 8%, when PPSV23 coverage is 50–60%[1,2].



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PCV15 non-PCV13 serotypes: 22F, 33F
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1. Surveillance of Vaccination Coverage Among Adult Populations — United States, 2014 | MMWR (cdc.gov)
2. Pneumococcal vaccination among U.S. Medicare beneficiaries aged ≥65 years, 2010-2019 | CDC

Summary of WG Considerations: Age-Based at Age 50 vs. 65 years

In favor of age-based at age 50 years	In favor of age-based at age 65 years
• May reduce disparity in disease burden in adults aged 50–64 years • May provide more opportunities to vaccinate adults before they develop underlying conditions	• Potential for waning immunity makes it favorable to vaccinate later in life when risk of disease is higher • Consistently cost-saving* in cost-effectiveness analyses • Still provides an opportunity for higher PCV coverage in adults vs. current recommendations

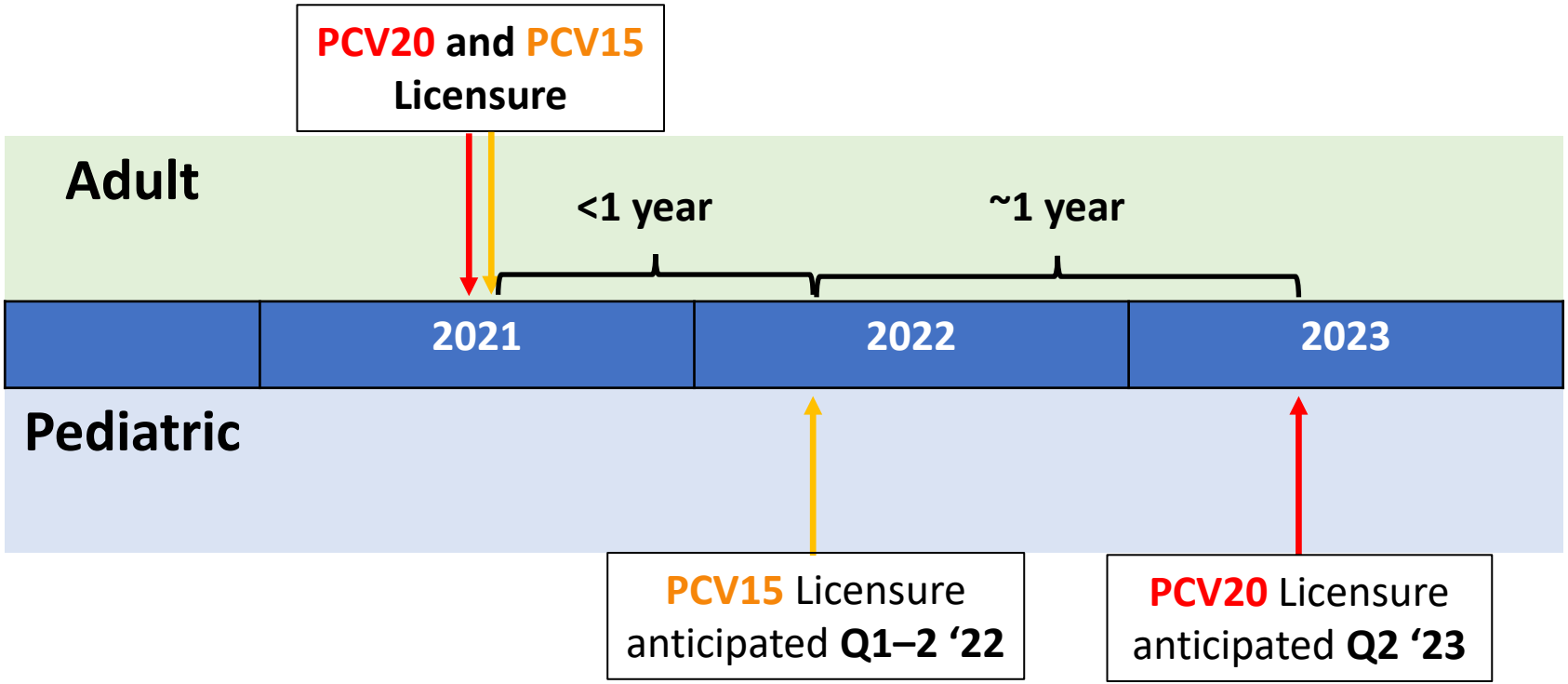
*lower cost and better health outcome compared to current recommendations

Summary of WG Considerations: PCV20 Use Alone OR PCV15+PPSV23

Advantages of PCV20 Use Alone	Disadvantages of PCV20 Use Alone
• Acceptable and feasible to implement a single vaccine option • Cost-saving* in cost-effectiveness analyses • Expected to provide better protection for the serotypes covered by PPSV23 alone	• Clinical significance of lower immunogenicity vs. PCV13 unknown • No data in immunocompromised adults • Losing protection against PPSV23, non-PCV20 serotypes
Advantages of PCV15+PPSV23	**Disadvantages of PCV15+PPSV23**
• Provides broad serotype coverage • Age-based use at age 65 was cost-saving* according to CDC's cost-effectiveness analysis	• Logistically more challenging to administer PCV15-PPSV23 vaccine series • Need to know vaccination history to correctly complete series • Can result in lower serotype coverage if series not completed

*lower cost and better health outcome compared to current recommendations

Unknown Impact of Use of New PCVs in Children in the Future on Adult Pneumococcal Disease Burden



Proposed Age-based Recommendation

Adults 65 years of age or older who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive a pneumococcal conjugate vaccine (either PCV20 or PCV15). If PCV15 is used, this should be followed by a dose of PPSV23.

Proposed Risk-based Recommendation

Adults aged 19 years of age or older with certain underlying medical conditions or other risk factors* who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive a pneumococcal conjugate vaccine (either PCV20 or PCV15). If PCV15 is used, this should be followed by a dose of PPSV23.

*alcoholism, chronic heart/liver/lung disease, cigarette smoking, diabetes mellitus, chronic renal failure, nephrotic syndrome, immunodeficiency, iatrogenic immunosuppression, generalized malignancy, human immunodeficiency virus, Hodgkin disease, leukemia, lymphoma, multiple myeloma, solid organ transplants, congenital or acquired asplenia, sickle cell disease or other hemoglobinopathies, CSF leak, or cochlear implant.

Discussion

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Thank you

For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov