

Challenges

Conjugate Pneumococccal Vaccines

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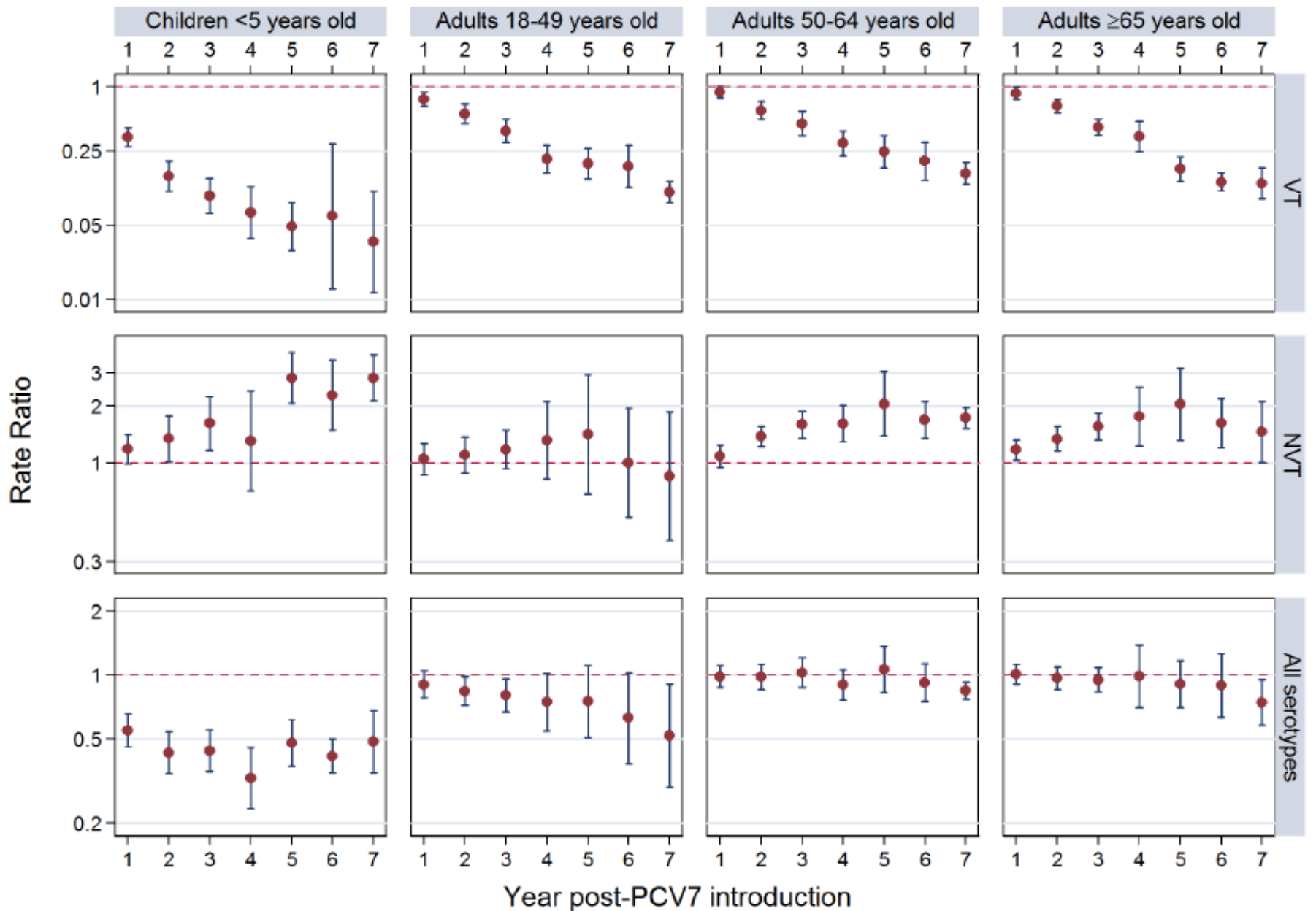
Mount Sinai Hospital

University of Toronto

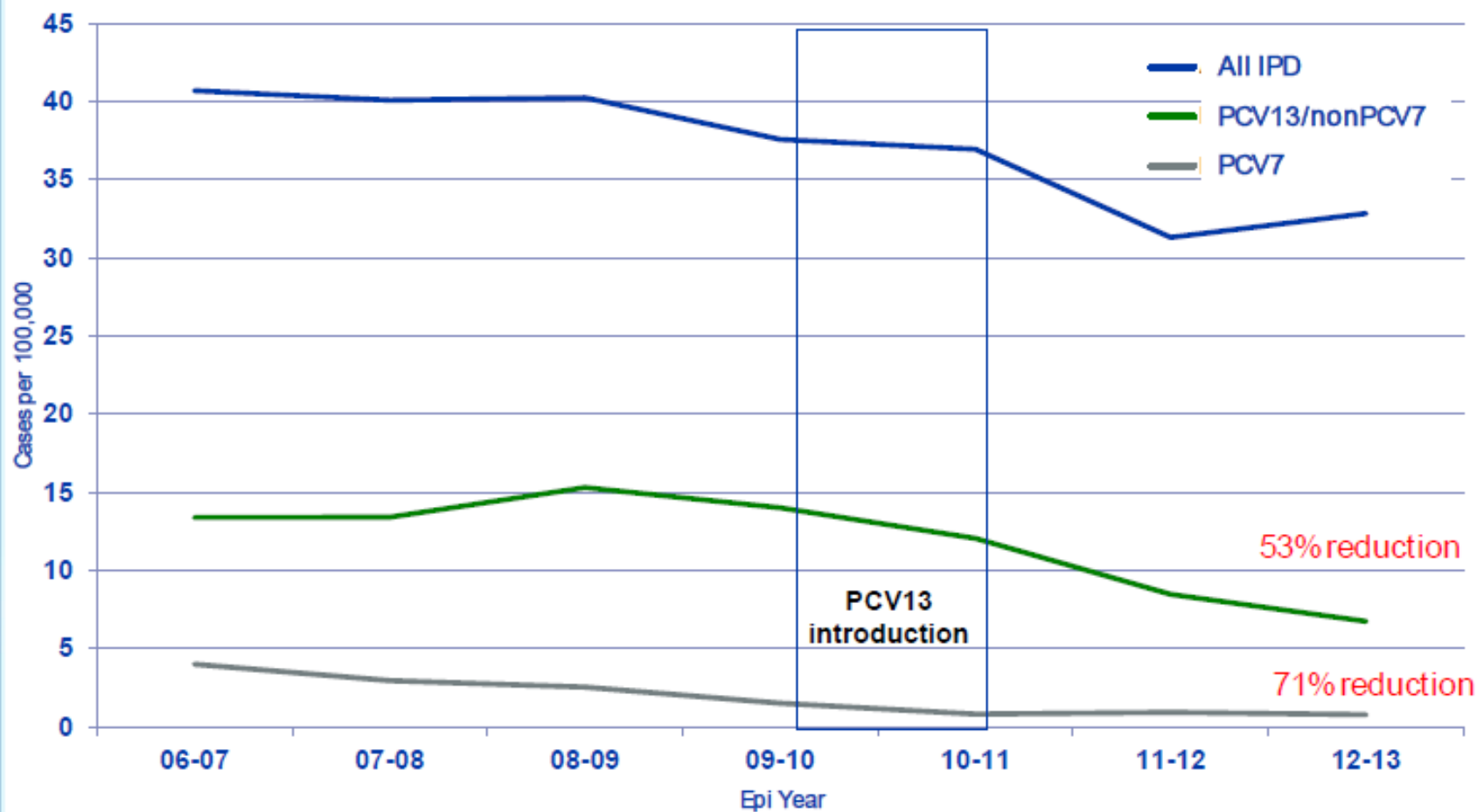
Disclosures

- I have research funding and have participated in advisory boards for Merck, GSK and Pfizer

Where are we?



Herd effects on IPD: Incidence of Invasive Pneumococcal Disease Among Adults ≥ 65 Years by Serotype, 1998-2013



Active Bacterial Core Surveillance, unpublished

PCV13 herd effects on non-bacteremic pneumonia, 2011-2012

	All-cause pneumonia	Invasive pneumococcal disease	Non-invasive pneumococcal or lobar pneumonia	Empyema
<2 years	21% (14 to 28)*	64% (47 to 75)*	40% (14 to 59)*	50% (22 to 68)*
2-4 years	17% (7 to 27)*	55% (16 to 75)*	33% (-3 to 56)	46% (21 to 64)*
5-17 years	-3% (-20 to 11)	25% (-24 to 54)	51% (29 to 66)*	37% (13 to 54)*
18-39 years	12% (6 to 17)*	37% (20 to 51)*	32% (17 to 44)*	-8% (-25 to 6)
40-64 years	2% (-2 to 6)	13% (-1 to 26)	25% (16 to 33)*	-4% (-13 to 3)
≥65 years	3% (-1 to 6)	29% (16 to 40)*	34% (27 to 41)*	-1% (-10 to 7)

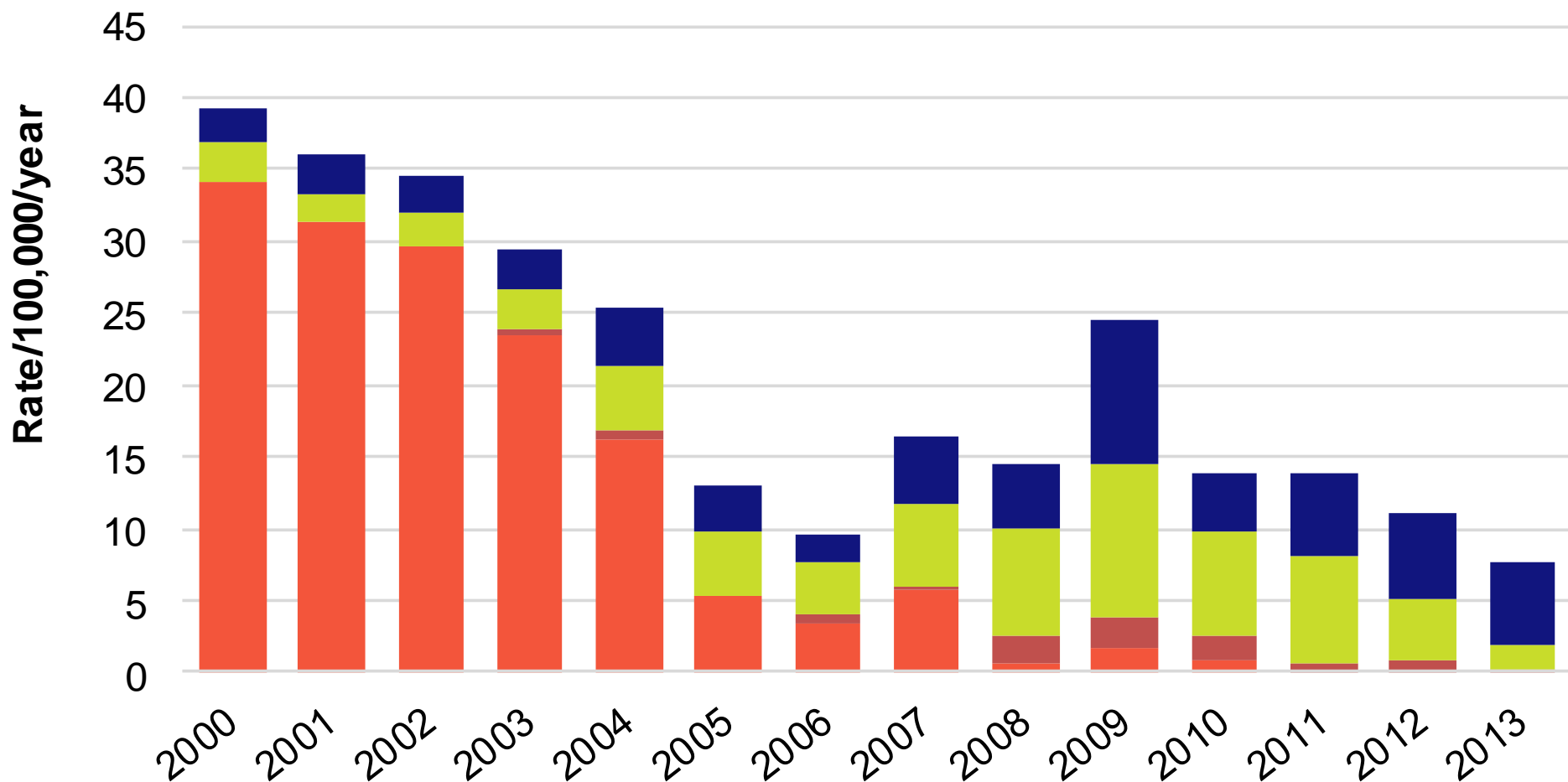
Data are percentage change (95% CI) according to our model. Assumes vaccine coverage at March, 2012 level.

*Significant reduction ($p < 0.05$).

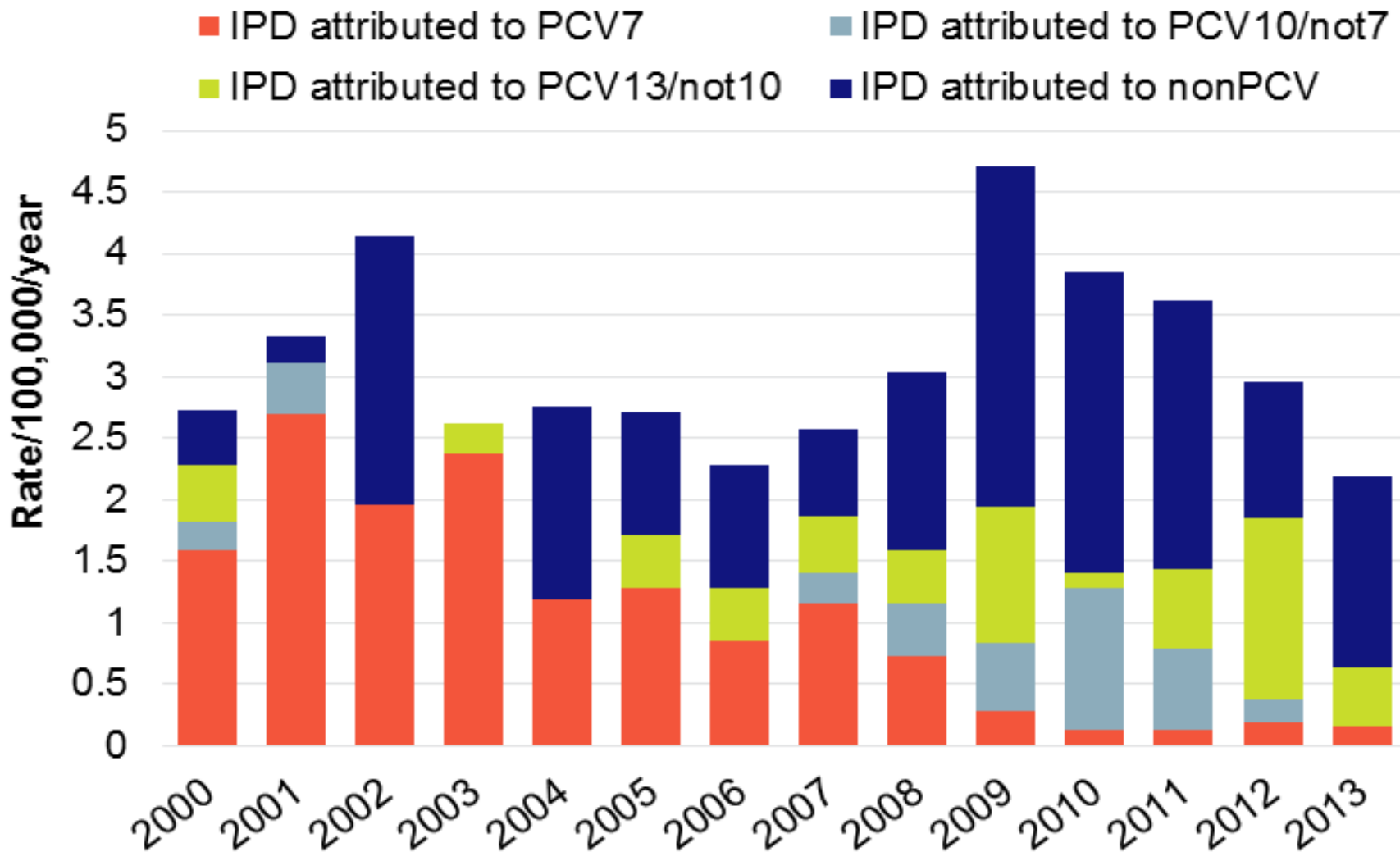
Table 3: Proportion of seasonal admissions to hospital averted by vaccination per season at coverage achieved in March, 2012

Rate of IPD in children <5 years, TIBDN

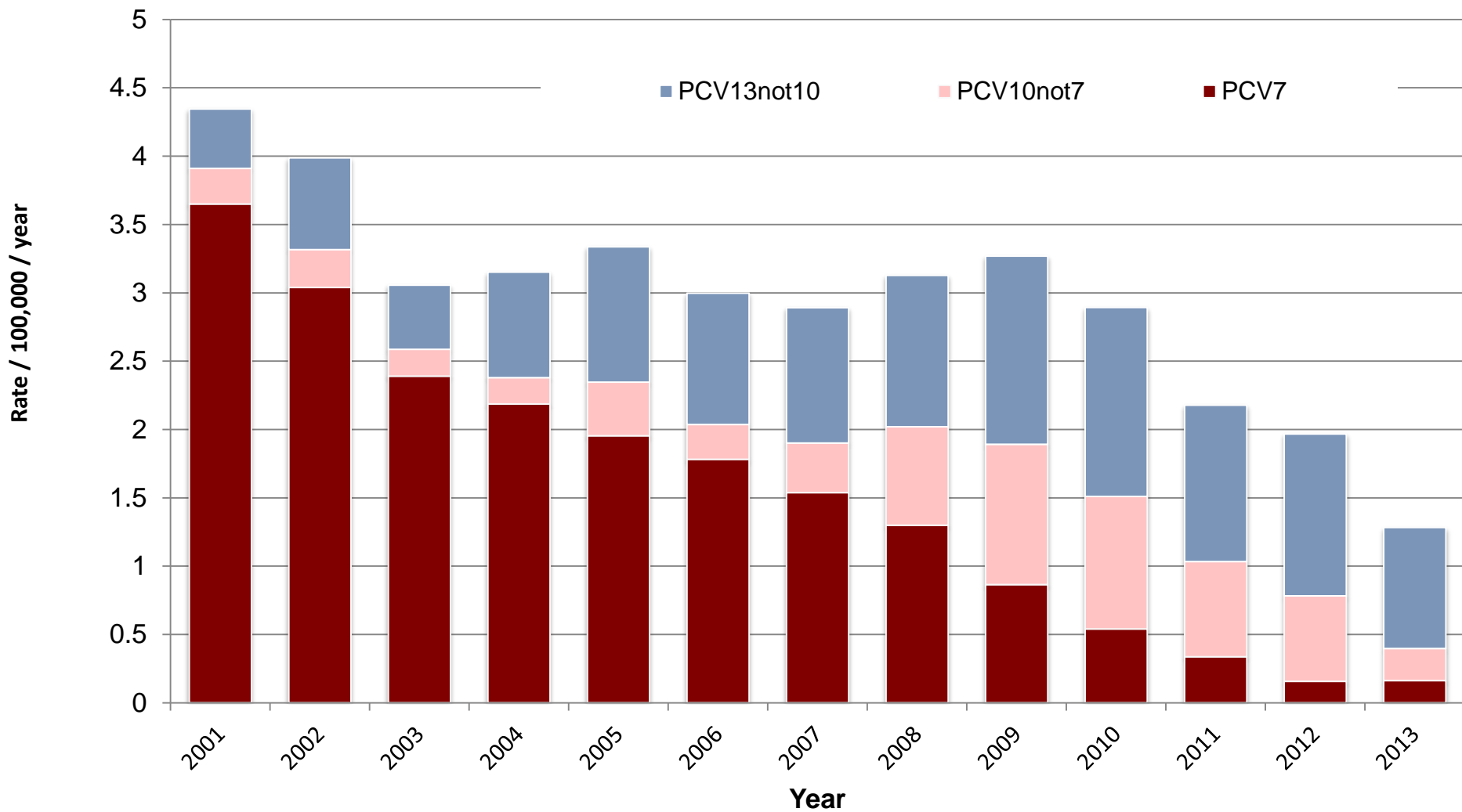
- IPD attributed to PCV7
- IPD attributed to PCV10/not7
- IPD attributed to PCV13/not10
- IPD attributed to nonPCV



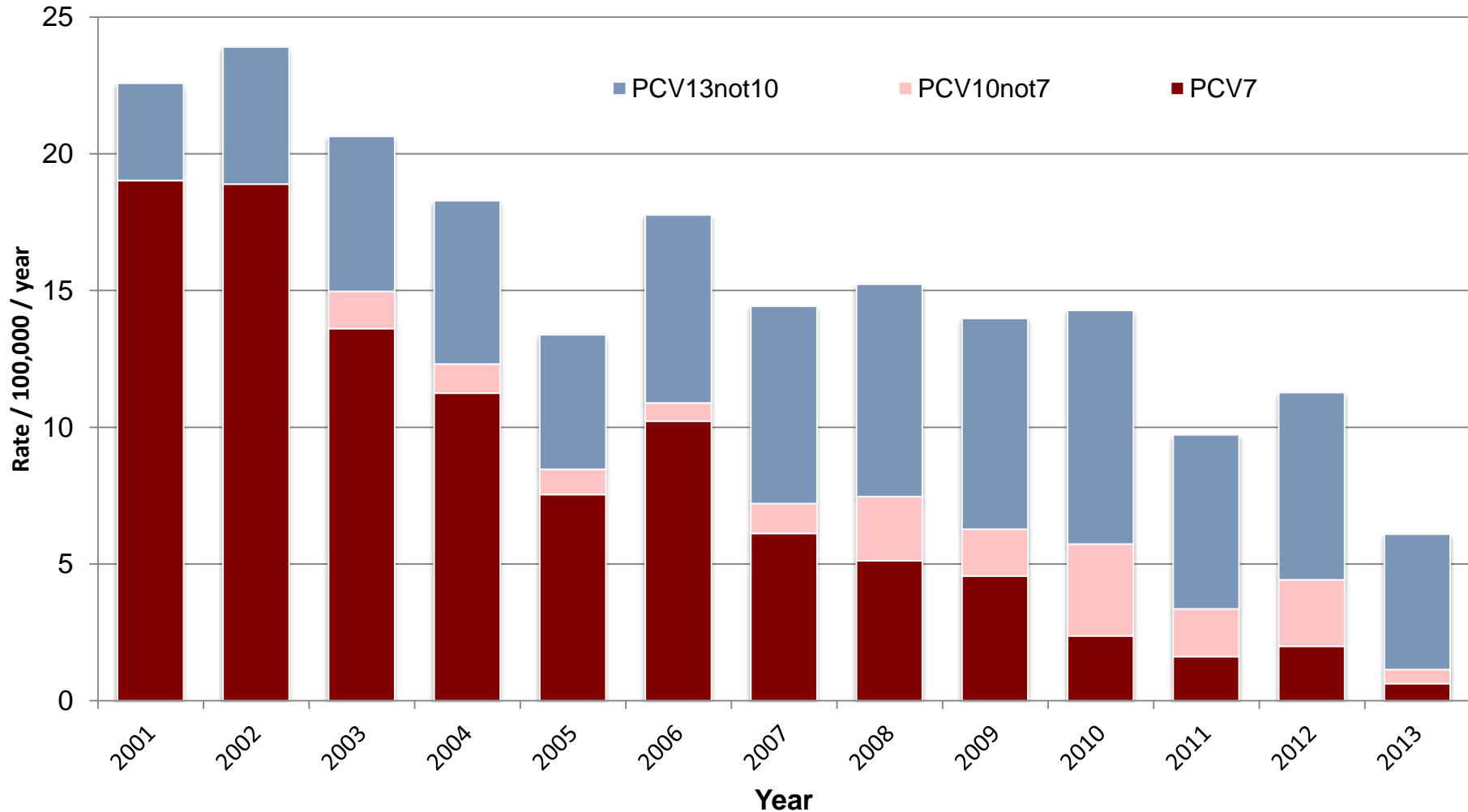
Rate of IPD in children 5-14 years, TIBDN



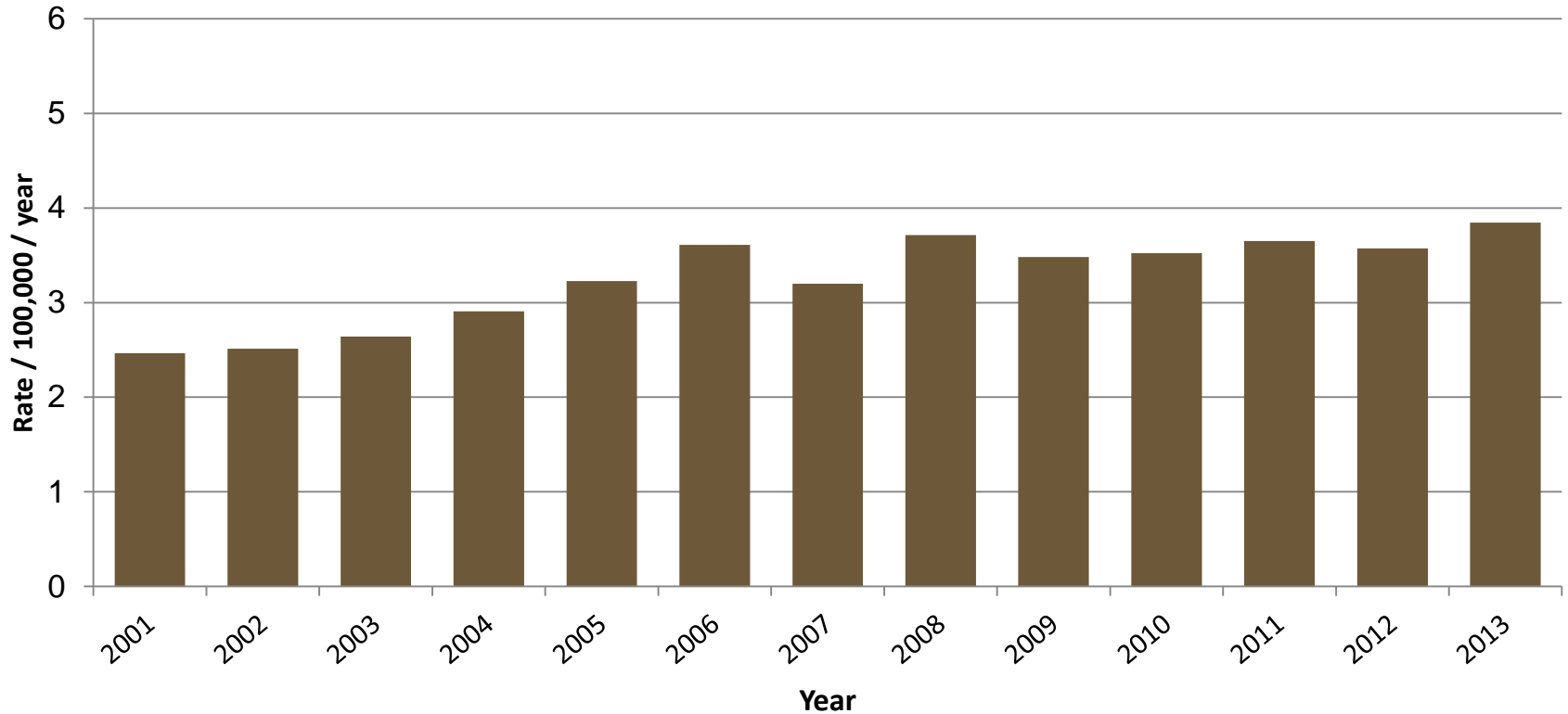
Rate of IPD due to conjugate vaccine serotypes in adults 15-49 years, TIBDN



Rate of IPD due to conjugate vaccine serotypes in adults ≥ 65 years, TIBDN



Rate of IPD due to conjugate vaccine serotypes in all adults, TIBDN



PCV13 in adults

- NACI/ACIP recommend PCV13 and PPV23 for adults with immunocompromising conditions

Incidence of IPD in immunosuppressed adults, TIBDN, 1995-2013

	Cases per 100 000 persons/year	Rate ratio (95% CI)
General population	8.3	
HIV	87.1	10.9 (9.3 – 12.6)
Hematological malignancy		
Acute leukemia	318.3	38.5 (34.9 – 41.9)
Chronic leukemia	312.8	38.1 (35.6 – 40.5)
Lymphoma	140.6	17.2 (15.1 – 19.3)
Myeloma	821.6	100.7 (98.7 - 102.8)
Sickle cell disease	220.5	26.5 (23.3 – 29.6)
Systemic autoimmune disease ^b	35.1	4.2 (2.1 – 6.3)
Immunosuppressive therapy		
COPD	31.6	5.5 (4.2 – 6.9)
Asthma	15.5	1.9 (0.8 – 2.9)
Inflammatory bowel disease	35.4	4.8 (3.7 – 5.9)
Rheumatoid arthritis	47.5	6.1 (4.9 – 7.2)

Efficacy of PCV in immunocompromised persons

PCV	Condition	Age	Location	VE against IPD	VE against pneumonia
PCV9	HIV	Children (2-5yrs)	S. Africa	65% (24-86%)	13% (-7,29%)
PCV7	HIV	Adults	Malawi	74% (30-90%)	
PCV7	Sickle cell disease	Children (<10yrs)	US	81% (19-96%)	

PCV13 in adults

- NACI/ACIP recommend PCV13 and PPV23 for adults with immunocompromising conditions
- ACIP recommend PCV13 for adults 65 years and over

Results: Sensitivity Analyses Adding PCV13 to Existing Recommendation

	Base	Higher QALY Decrements	Low Price	Higher QALY + Low Price	Cohort in 2019
Cost/QALY gained	\$62,065	\$54,183	\$12,270	\$10,711	\$272,621
Cost/Life-year gained	\$40,949	\$40,949	\$8,095	\$8,095	\$169,974

What are the challenges?

	Age group (in years)			
	All	<15	15-64	>=65
	(N=2115)	(N=137)	(N=1080)	(N=898)
	N	N (%)	N (%)	N (%)
Immunocompromising conditions				
Chronic renal failure	296	1 (0.7)	79 (7.3)	216 (24.1)
HIV	288	4 (2.9)	274 (25.4)	10 (1.1)
Hepatic cirrhosis	279	1 (0.7)	206 (19.1)	72 (8.0)
Hematological malignancy				
Leukemia	212	56 (40.9)	60 (5.6)	96 (10.7)
Myeloma	199	0 (0.0)	71 (6.6)	128 (14.3)
Lymphoma	179	5 (3.7)	81 (7.5)	93 (10.4)
Other ^a	18	0 (0.0)	3 (0.3)	15 (1.7)
Organ/bone marrow transplant	149	19 (13.9)	106 (9.8)	24 (2.7)
Asplenia	112	11 (8.0)	75 (6.9)	26 (2.9)
Systemic Lupus Erythematosus	85	2 (1.5)	69 (6.4)	14 (1.6)
Sickle cell disease	43	24 (17.5)	18 (1.7)	1 (0.1)
Primary Immunodeficiency ^b	55	6 (4.4)	32 (2.9)	17 (1.9)
Immunosuppressive therapy ^c	453	20 (14.6)	179 (16.6)	254 (28.3)

Should older/immunocompromised
adults receive booster doses?

Efficiency of PPV23 in preventing IPD, TIBDN, 1996-2011 (indirect cohort analysis)

Age group	Underlying illness	VE (95%CI) 0-5 years post PPV23	VE (95% CI) >5 years since PPV23
All ages	Overall	46% (31-58)	34% (11-51)
15-64 years	Overall	55% (31-71)	19% (-51-57)
	Chronic illness, no immunosuppression	56% (-11, 82)	51% (-100,88)
	Immunosuppressed	49% (17-69)	0% (-112-49)
>65 years	Overall	41% (20-57)	34% (6-54)
	Chronic illness, no immunosuppression	50% (23-68)	42% (5-64)
	Immunosuppressed	0 (-61-42)	0 (-154-30)

Estimating PCV13 –type disease burden among adults 65 years or older in a setting of herd effects

Estimated US cases without direct PCV13 use in adults

Outcome (PCV13 type)	2013	2015 (20% reduction due to herd effects*)	2019 (86% reduction due to herd effects*)
IPD	2,660	2,130	370
Inpatient CAP	56,380	45,100	7,890
Outpatient CAP	82,410	65,930	11,540
Total CAP	138,790	111,030	19,430

*Based on post-PCV7 experience

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Distribution of serotypes IPD, TIBDN, 2012/13

