A nationwide study on the impact of pneumococcal conjugate vaccination on antibiotic use and ventilation tube insertion in Denmark 2000-2014

Michael F. Howitz[a], Zitta B. Harboe[b,c], Helene Ingels[d],
Palle Valentiner-Branth[e], Kåre Mølbak[e], Bjarki D. Djurhuus[f,g]

a) Department of ENT Head & Neck Surgery, Nordsjællands Hospital
b) Department of Microbiology and Infection Control, Statens Serum Institut
c) Department of Infectious Diseases, Rigshospitalet
d) Department of Pediatrics, Næstved Hospital
e) Department of Infectious Disease Epidemiology, Statens Serum Institut
f) Epidemiology, Biostatistics and Biodemography, University of Southern Denmark
g) Department of ENT Head & Neck Surgery, Zealand University Hospital

Pneumococcal conjugate vaccine (PCV)

PCV7: Covers 7 serotypes
Introduced in Denmark in 2007

PCV13: Covers 13 serotypes
Introduced in Denmark during 2010

A decrease in **invasive pneumococcal disease** demonstrated in many countries

Pneumococcal conjugate vaccine (PCV)

Invasive pneumococcal disease in Denmark after PCV13:

- ↓ 71% in <2-year-olds
- ↓ 21% in total population

Harboe ZB, Dalby T, Weinberger DM, Benfield T, Molbak K, Slotved HC, et al. Impact of 13-valent pneumococcal conjugate vaccination in invasive pneumococcal disease incidence and mortality. Clin Infect Dis 2014; 59(8):1066-73.

Pneumococcal conjugate vaccine (PCV)

Invasive pneumococcal disease in Denmark after PCV13:

- 71% in <2-year-olds
- 21% in total population

However looking at the costs…

98% is from **non-invasive infections**

TABLE 4
Costs* of pneumococcal disease in a cohort of 340,000 Canadian children from six months to nine years of age

	Costs to health system	Costs to families	Costs to society
Meningitis	$649,000	$97,000	$746,000
Hospitalized bacteremia	$1,070,000	$655,000	$1,725,000
Nonhospitalized bacteremia	$34,000	$71,000	$105,000
Hospitalized pneumonia	$5,022,000	$4,108,000	$9,130,000
Nonhospitalized pneumonia	$1,261,000	$7,748,000	$9,009,000
Acute otitis media	$15,148,000	$69,008,000	$84,156,000
Myringotomy with ventilation tube insertion	$16,872,000	$3,958,000	$20,830,000
Total	$40,224,000	$85,477,000	$125,701,000

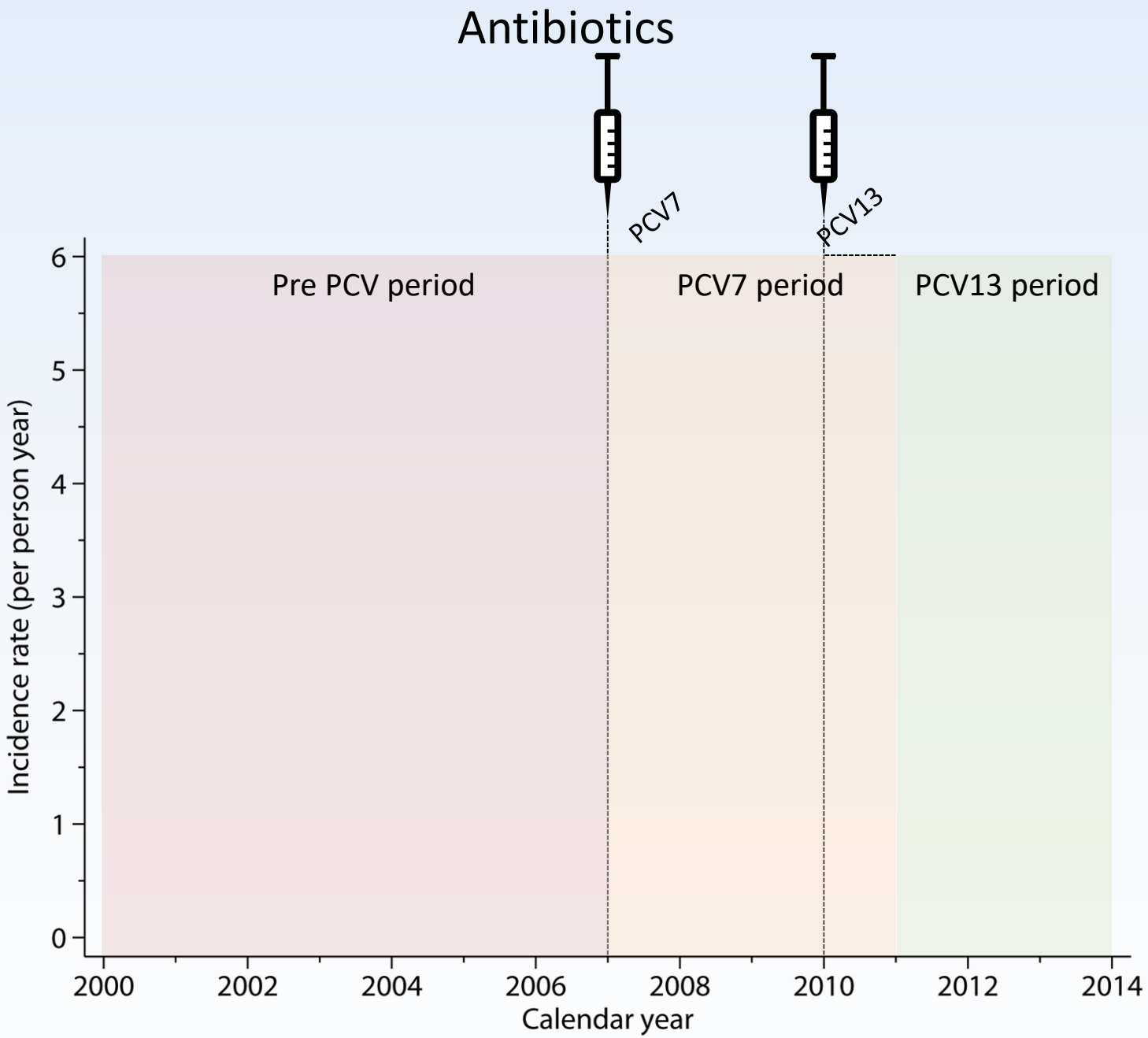
**Excluding costs of sequelae and productivity losses associated with deaths and disabilities. Assuming 22% of all cases of pneumonia, 19% of all cases of acute otitis media, and 50 % of all cases of myringotomy with ventilation tube insertion are attributable to* S pneumoniae

Petit G, De Wals P, Law B, Tam T, Erickson LJ, Guay M, et al. Epidemiological and economic burden of pneumococcal diseases in Canadian children. Can J Infect Dis 2003; 14(4):215-20

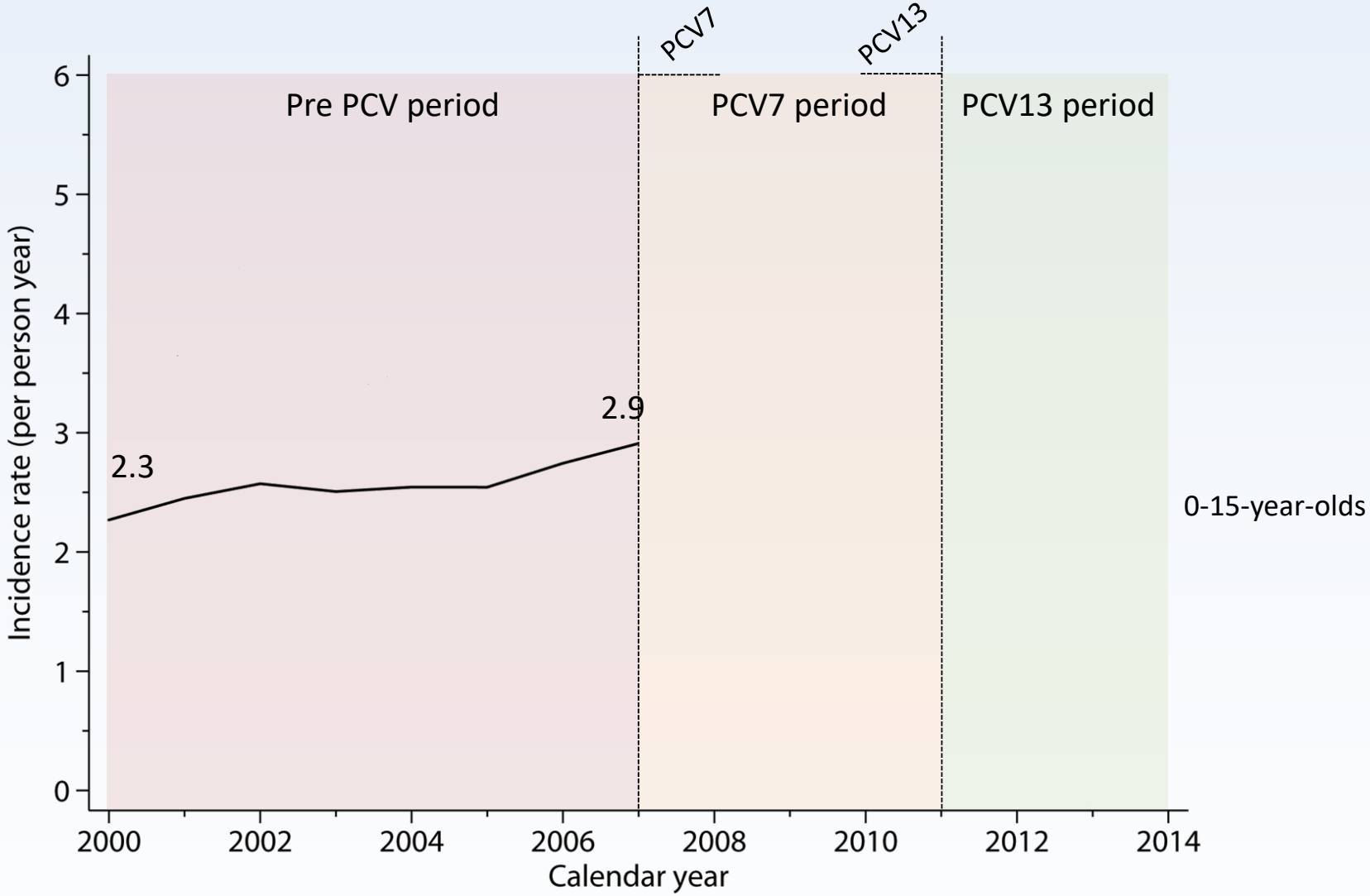
Antibiotics

The Danish National Prescription Registry

2000-2014: 41,466,000 defined daily doses purchased to 0-15-years-olds


Antibiotics
PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per person year)
0
1
2
3
4
5
6
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year

Antibiotics



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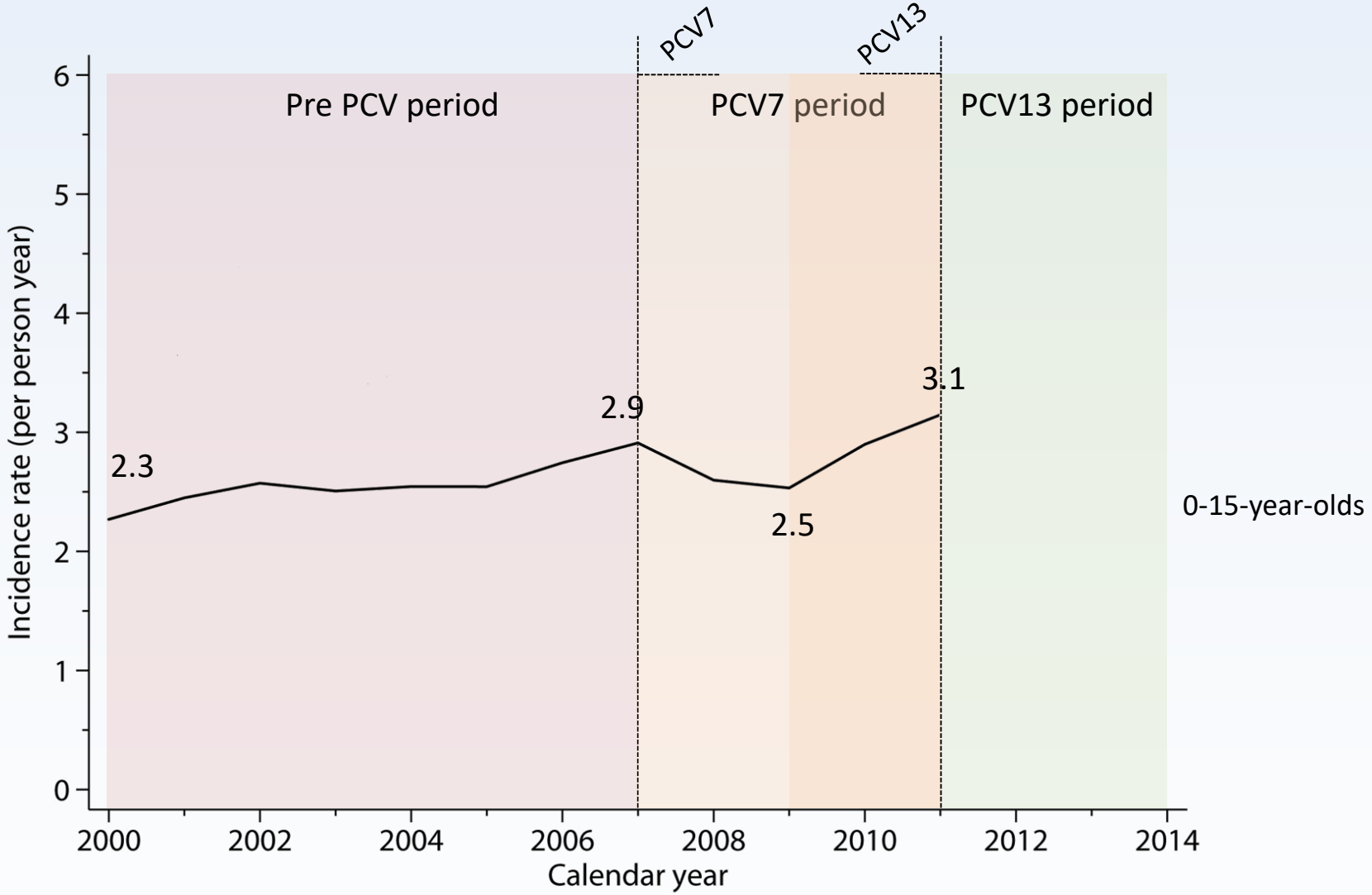

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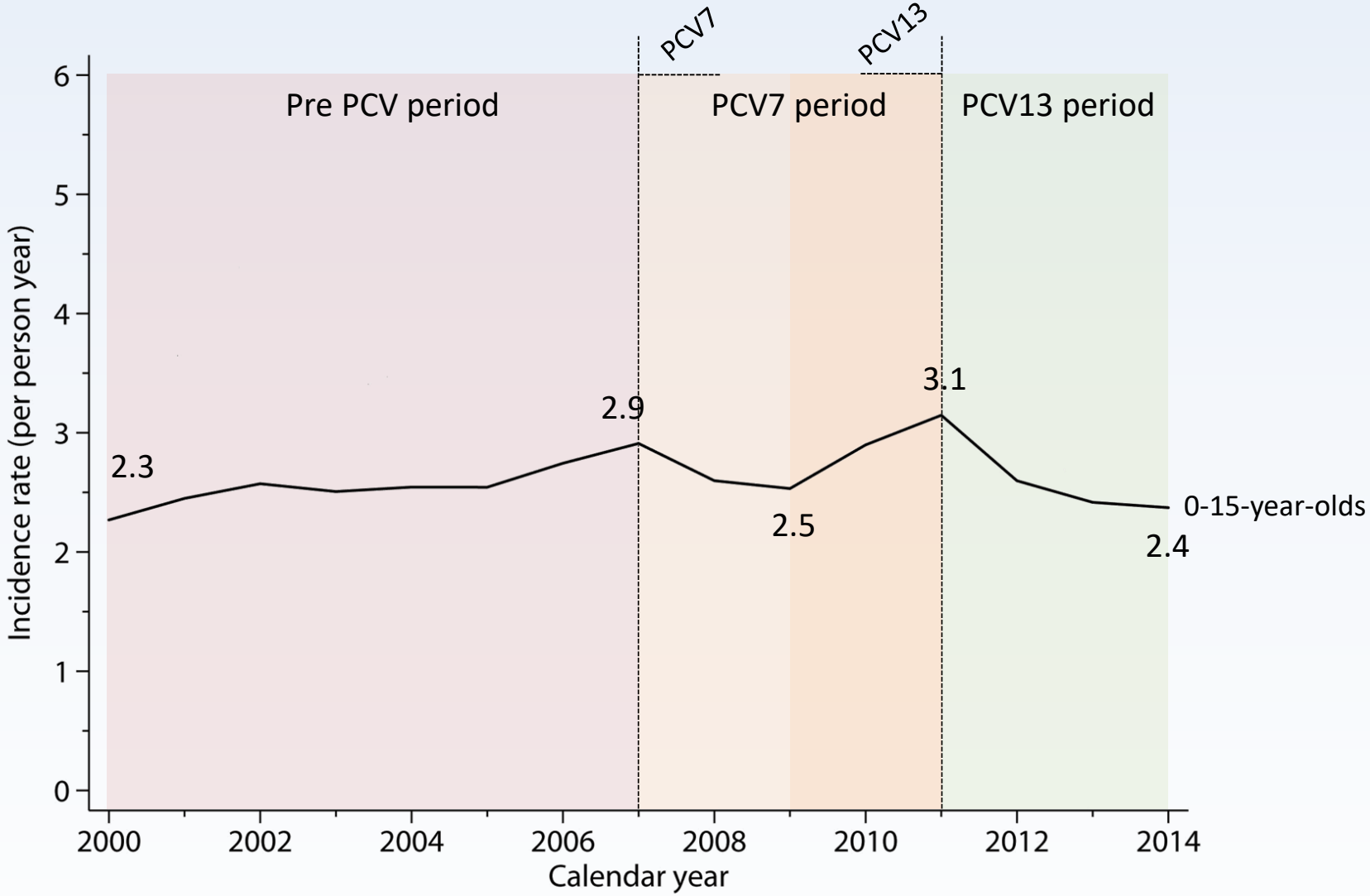

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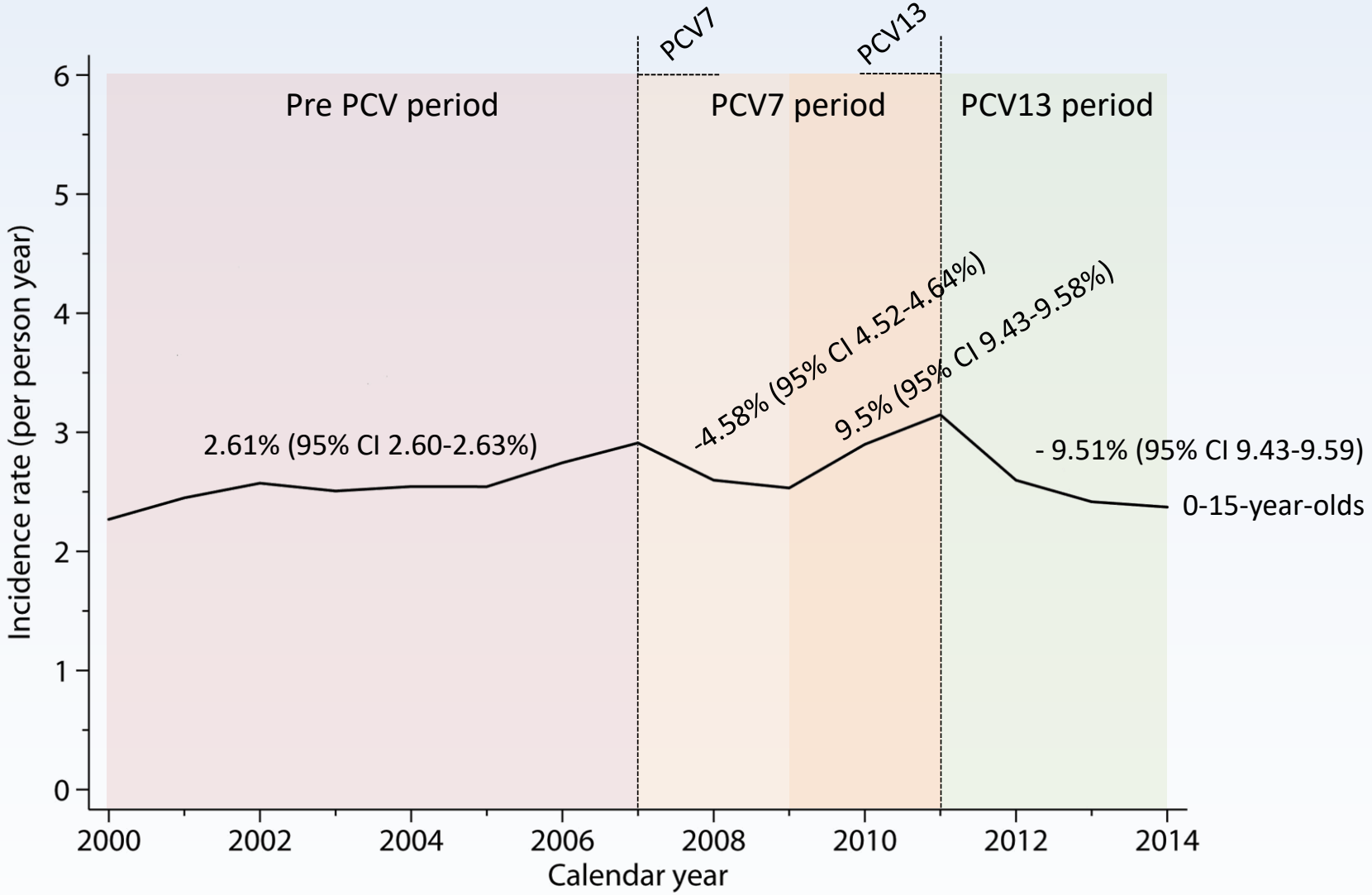

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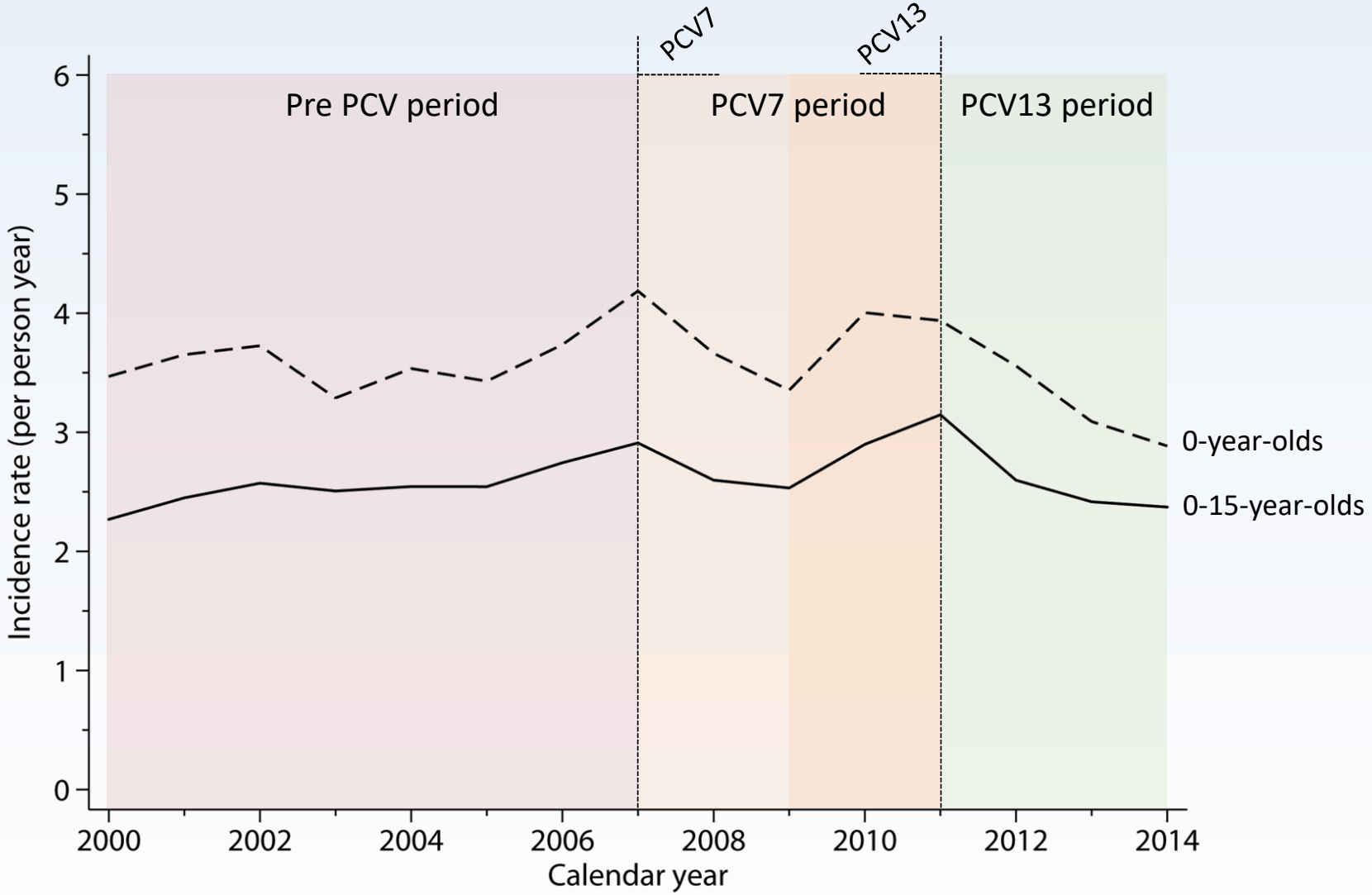

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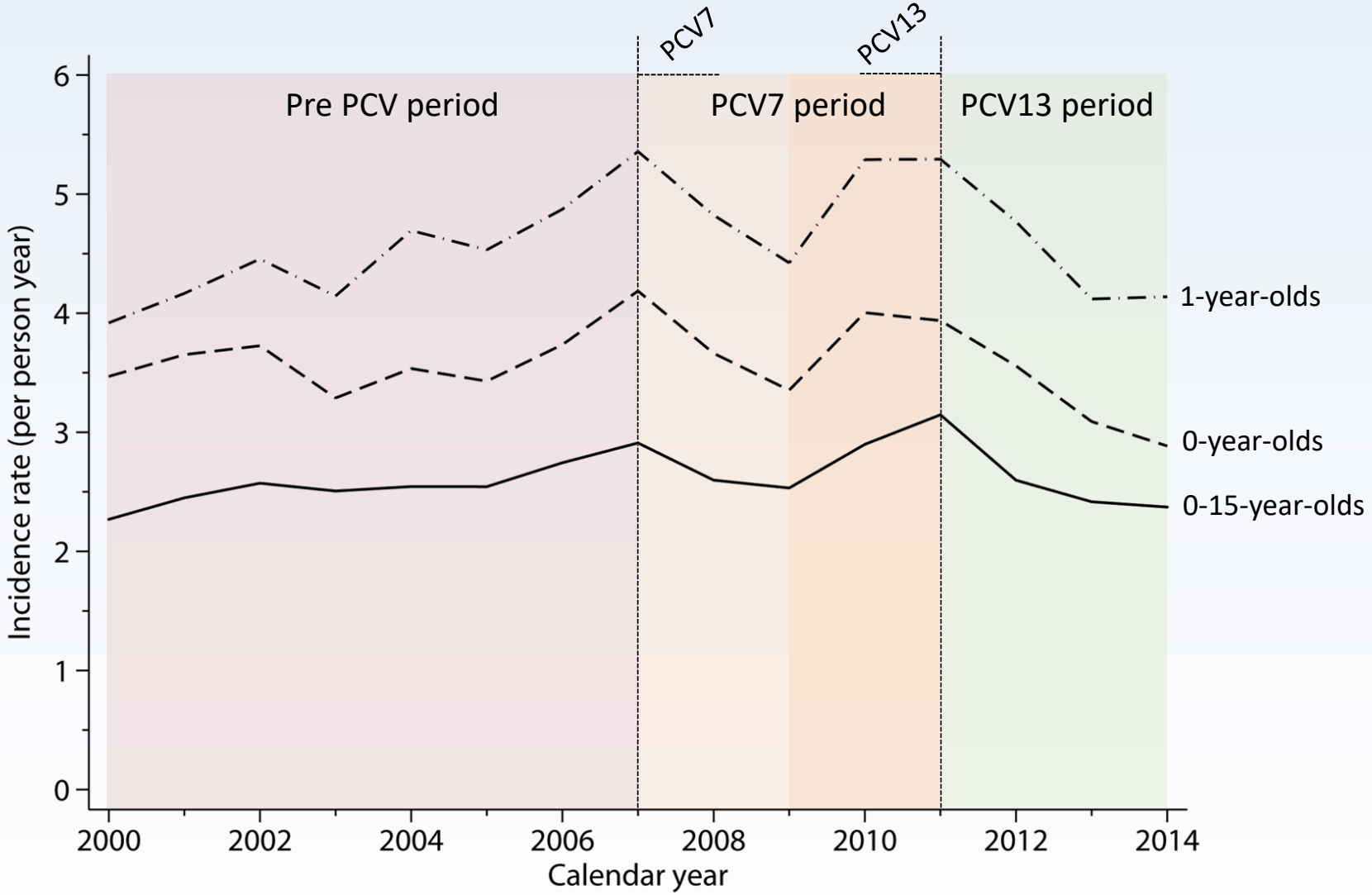
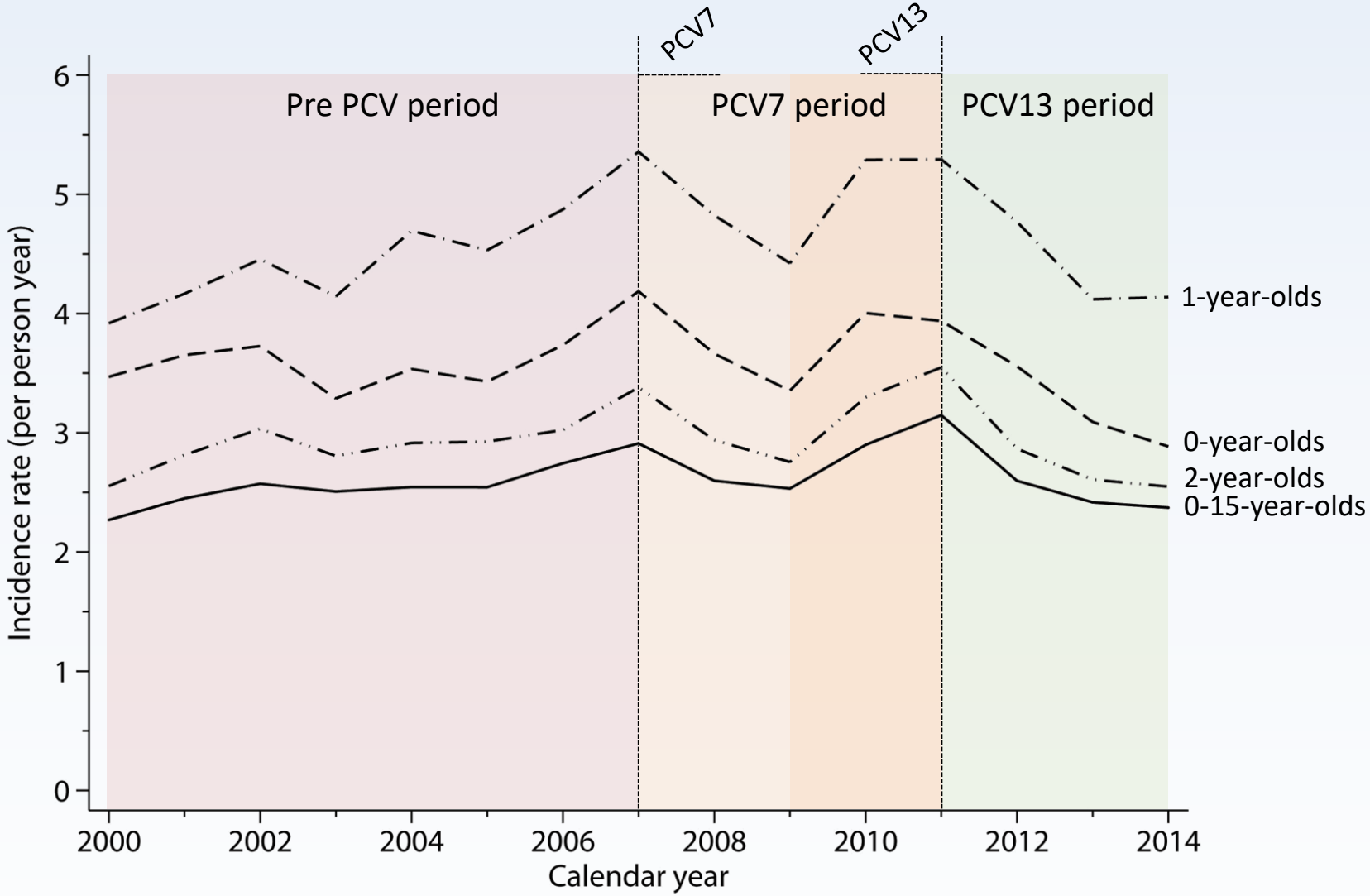


Antibiotics

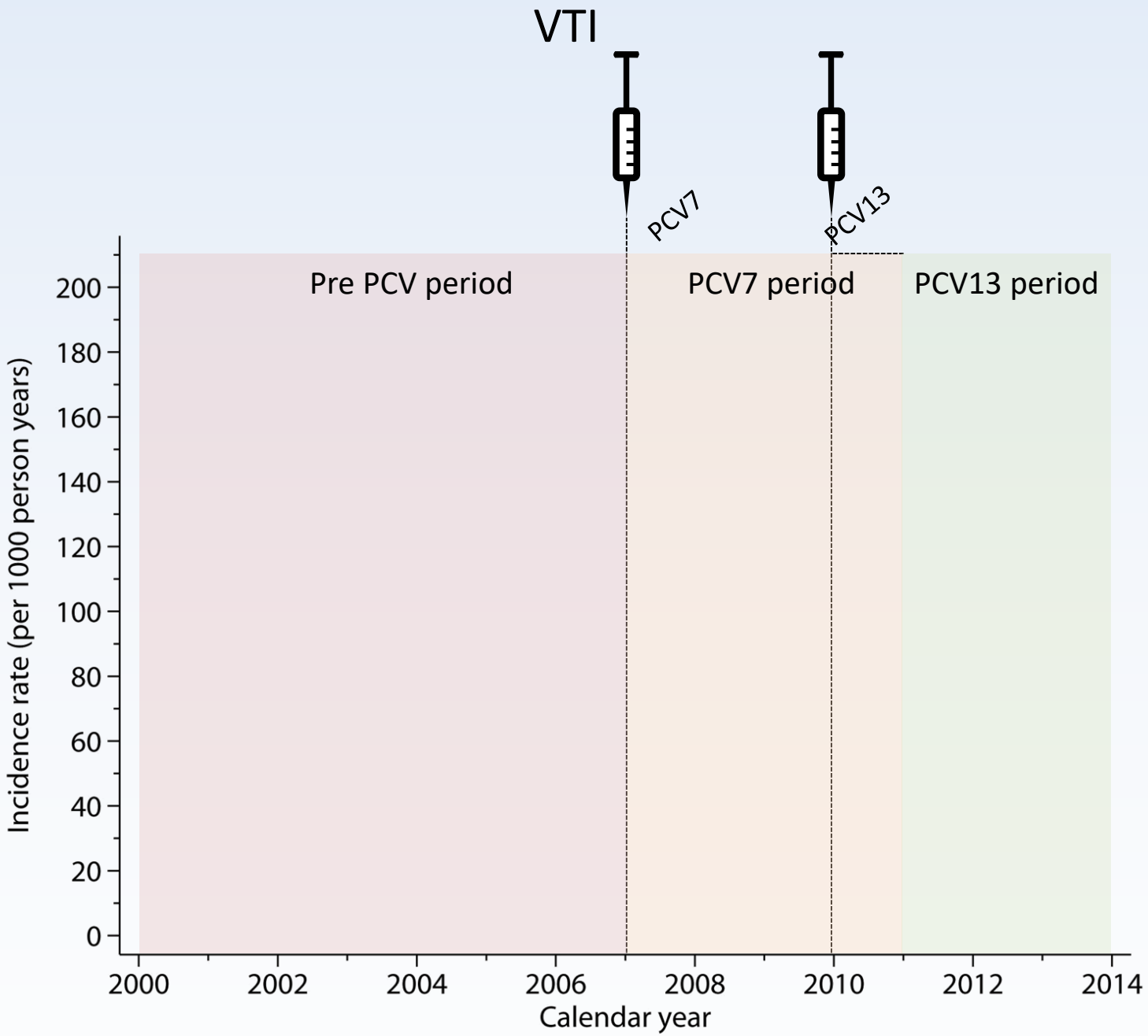


Ventilation Tube Insertions
(VTI)

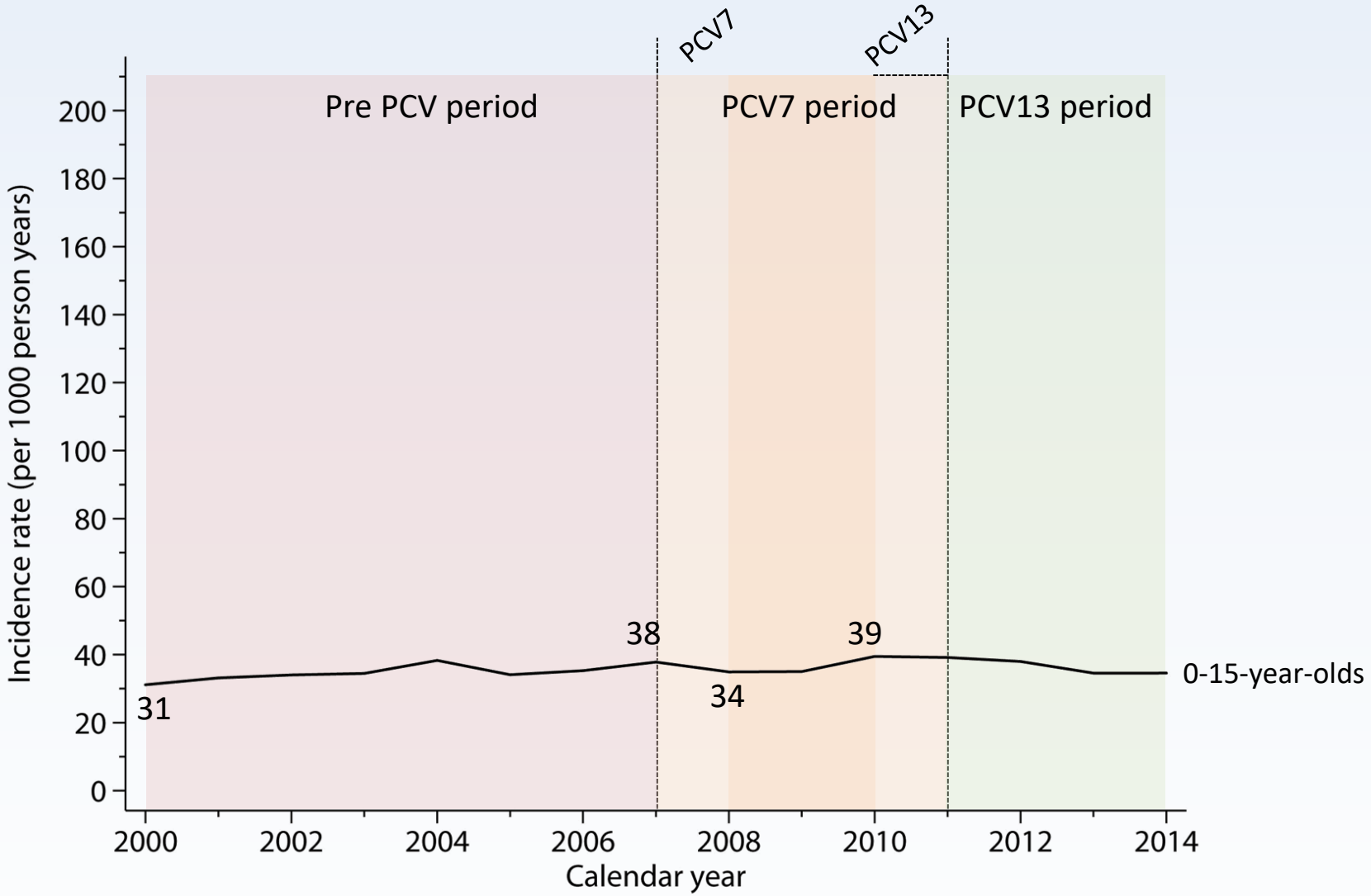
The Danish National Health Service Register

The Danish National Hospital Register

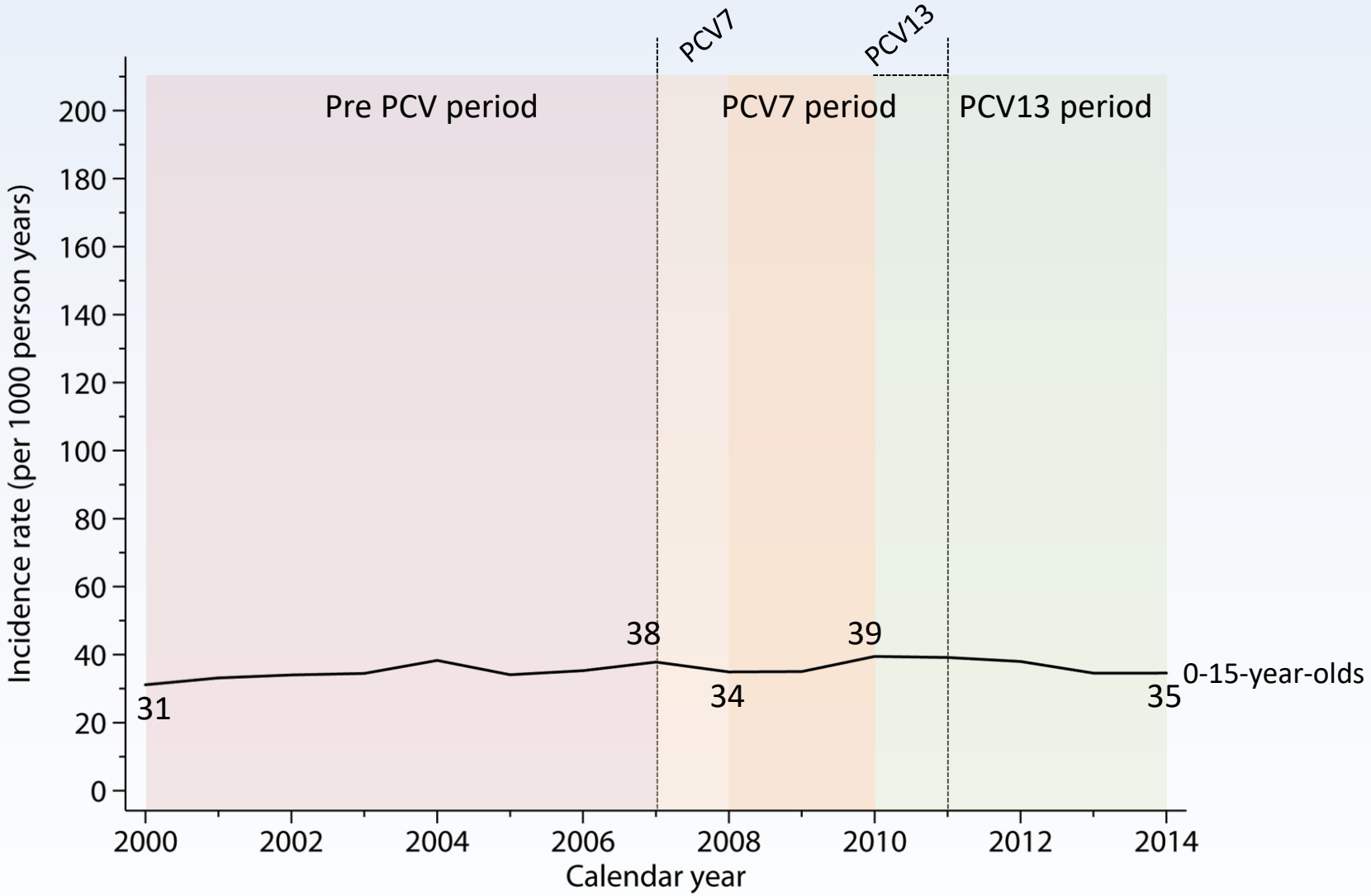
2000-2014: 552,925 uni- or bilateral VTI's in 0-15 year-olds


VTI
PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per 1000 person years)
0
20
40
60
80
100
120
140
160
180
200
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year

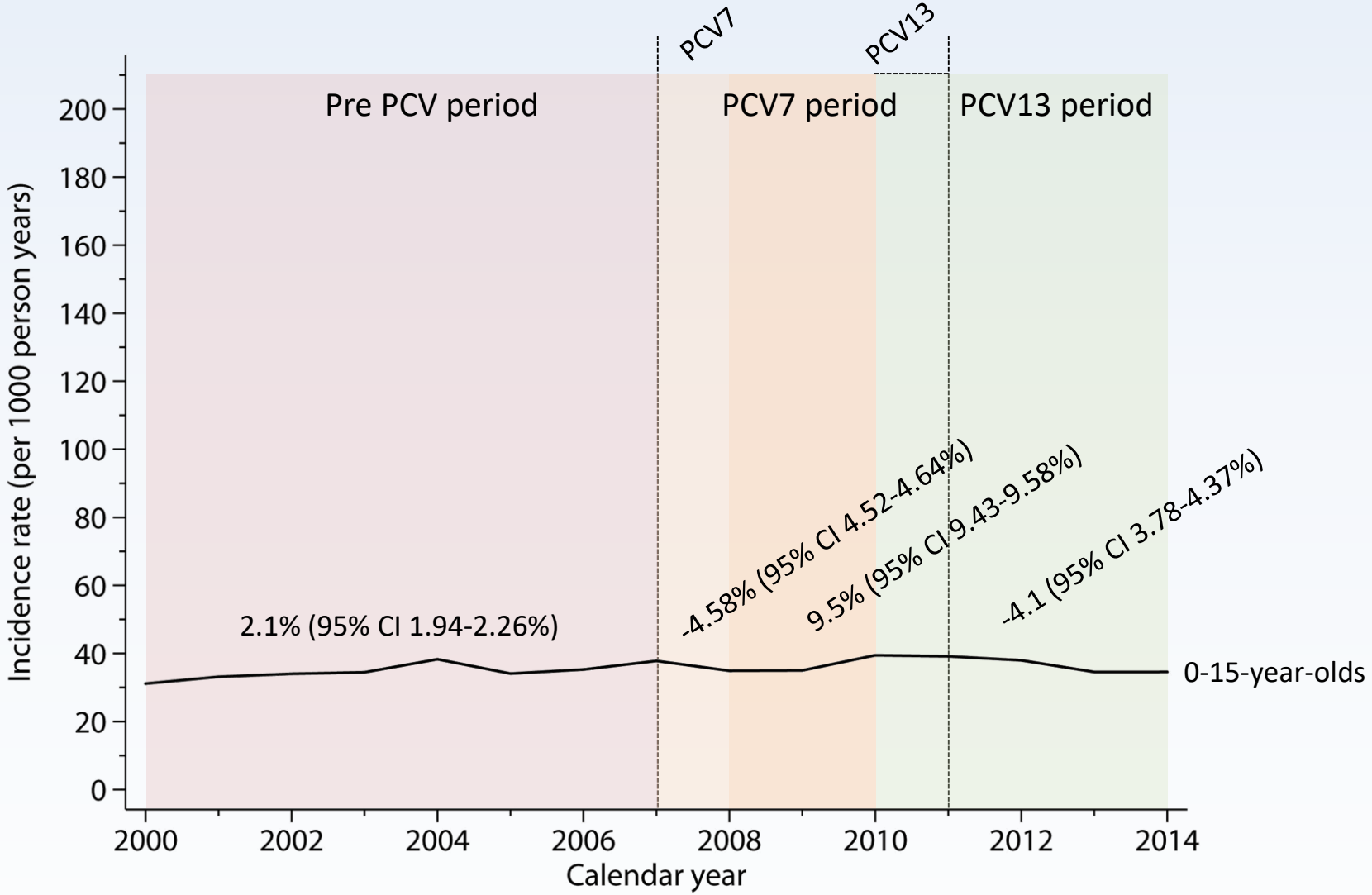
VTI


PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per 1000 person years)
200
180
160
140
120
100
80
60
40
20
0
38
39
31
34
0-15-year-olds
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year

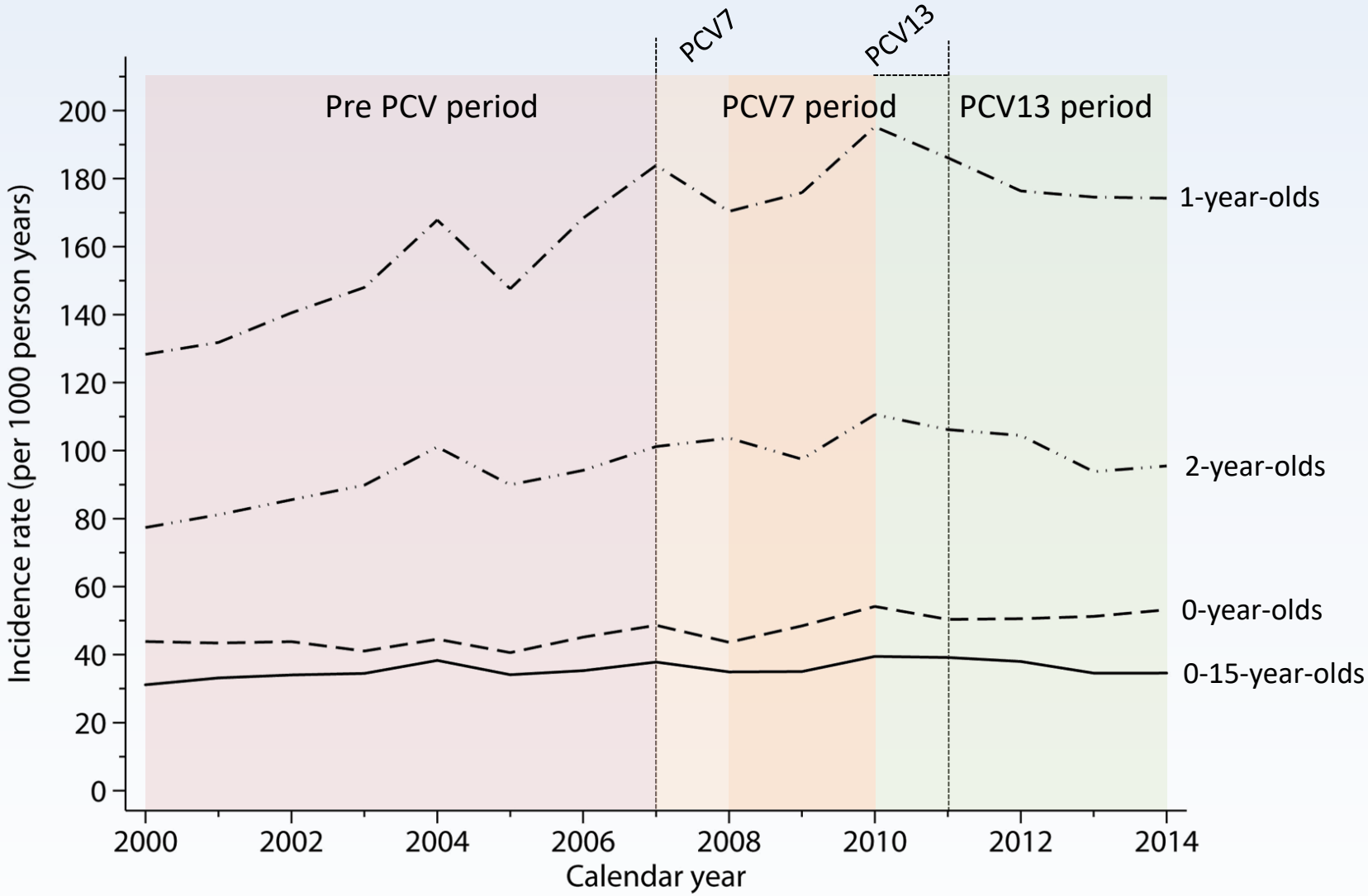
VTI


PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per 1000 person years)
0
20
40
60
80
100
120
140
160
180
200
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year
31
38
34
39
35
0-15-year-olds

VTI


PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per 1000 person years)
0
20
40
60
80
100
120
140
160
180
200
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year
2.1% (95% CI 1.94-2.26%)
-4.58% (95% CI 4.52-4.64%)
9.5% (95% CI 9.43-9.58%)
-4.1 (95% CI 3.78-4.37%)
0-15-year-olds

VTI


PCV7
PCV13
Pre PCV period
PCV7 period
PCV13 period
Incidence rate (per 1000 person years)
0
20
40
60
80
100
120
140
160
180
200
2000
2002
2004
2006
2008
2010
2012
2014
Calendar year
1-year-olds
2-year-olds
0-year-olds
0-15-year-olds

Summing up

Antibiotics:

- **Decrease after introduction of PCV7 & PCV13**
  - **Causality likely**

VTI:

- **Short decrease in 2007**
  - **Causality questionable**
- **Decreasing since 2010**
  - **PCV13 could be partly responsible**

Antibiotics:

	Pre PVC (2000-2007)	PCV7 (2008-2010)	PCV13 (2011-2014)	
	Increasing (2000-2007)	**Decreasing (2008-2009)**	**Increasing (2010-2011)**	**Decreasing (2012-2014)**
0-15-year-olds	1.0261 (1.0260-1.0263)	0.9542 (0.9536-0.9548)	1.0951 (1.0943-1.0959)	0.9048 (0.9043-0.9052)
0-year-olds	1.0159 (1.0153-1.0165)	0.9532 (0.9511-0.9553)	1.0754 (1.0727-1.0781)	0.8878 (0.8861-0.8895)
1-year-olds	1.0384 (1.0378-1.0389)	0.9448 (0.9429-0.9466)	1.0804 (1.0781-1.0827)	0.9037 (0.9022-0.9051)
2-year-olds	1.0265 (1.0258-1.0272)	0.9369 (0.9346-0.9392)	1.1110 (1.1080-1.1140)	0.8845 (0.8827-0.8862)
3-year-olds	1.0279 (1.0272-1.0286)	0.9367 (0.9343-0.9390)	1.1135 (1.1105-1.1166)	0.8881 (0.8863-0.8898)
4-year-olds	1.0266 (1.0259-1.0273)	0.9451 (0.9426-0.9476)	1.1170 (1.1138-1.1203)	0.8905 (0.8886-0.8923)

95% confidence intervals are given in brackets.

VTI:

	Pre PVC	PCV7		PCV13
	Increasing (2000-2007)	**Decreasing (2008)**	**Increasing (2009-2010)**	**Decreasing (2011-2014)**
0-15-year-olds	1.021 (1.019-1.023)	0.909 (0.899-0.920)	1.079 (1.072-1.086)	0.965 (0.962-0.968)
0-year-olds	1.010 (1.004-1.015)	0.967 (0.929-1.007)	1.092 (1.068-1.116)	0.996 (0.986-1.007)
1-year-olds	1.049 (1.046-1.052)	0.943 (0.923-0.962)	1.065 (1.053-1.077)	0.972 (0.967-0.978)
2-year-olds	1.035 (1.031-1.039)	0.991 (0.964-1.018)	1.041 (1.026-1.057)	0.965 (0.958-0.973)
3-year-olds	1.019 (1.015-1.024)	0.947 (0.918-0.976)	1.049 (1.031-1.067)	0.961 (0.953-0.969)
4-year-olds	1.003 (0.999-1.008)	0.892 (0.862-0.925)	1.078 (1.057-1.100)	0.952 (0.943-0.961)

95% confidence intervals are given in brackets.