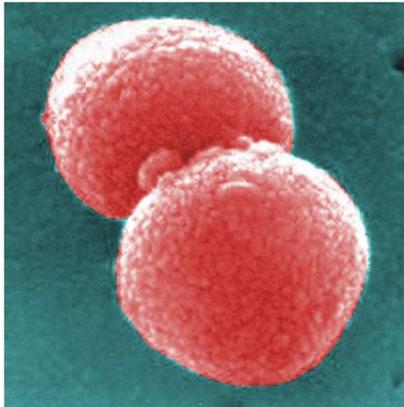


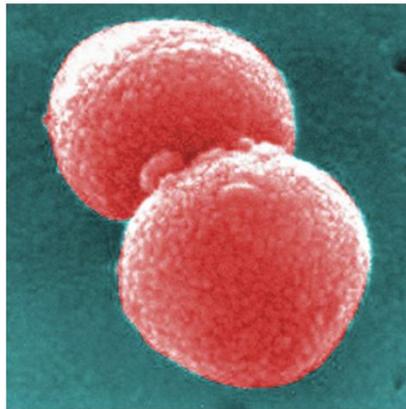
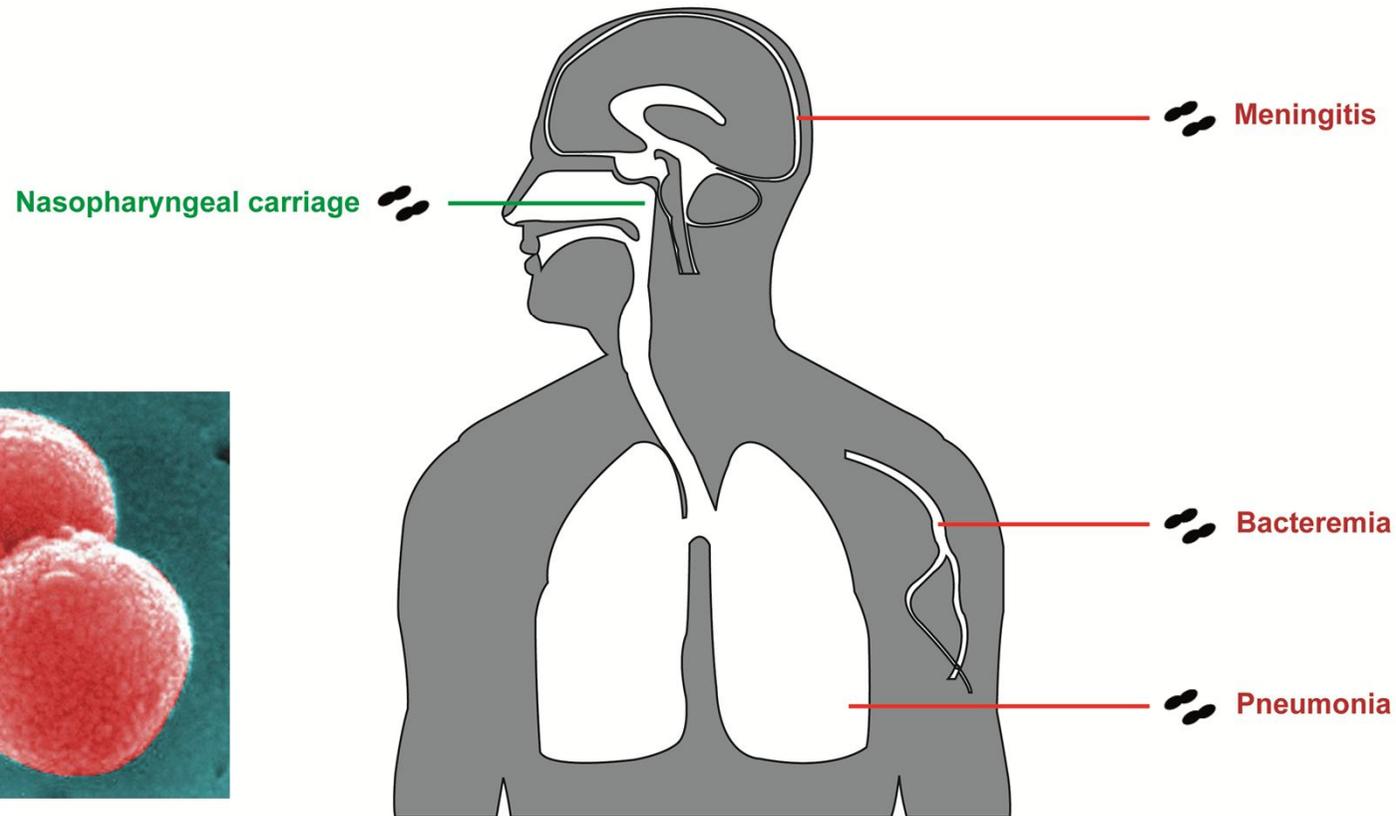
The role of ZmpC in the clinical manifestation of invasive pneumococcal disease

Amelieke J.H. Cremers
A mirror between North and South
14-11-2014

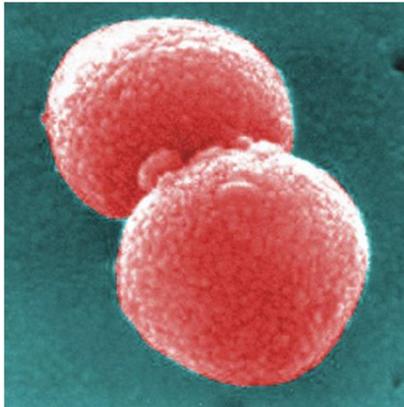
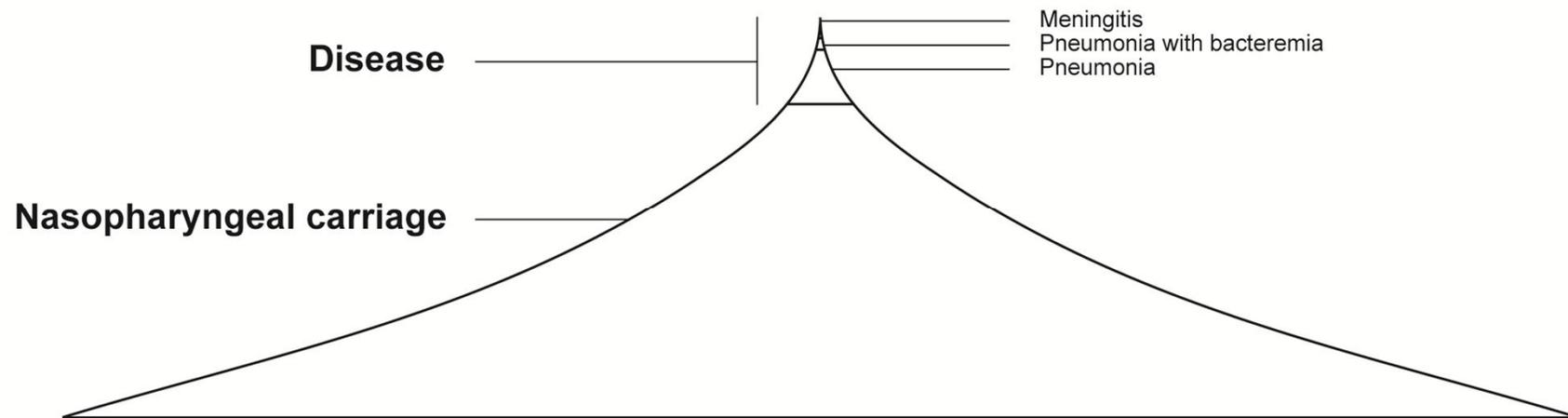
Streptococcus pneumoniae



Streptococcus pneumoniae

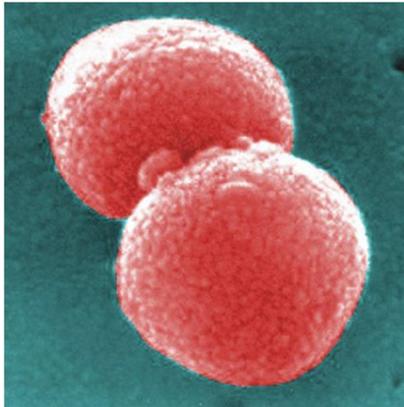


Streptococcus pneumoniae



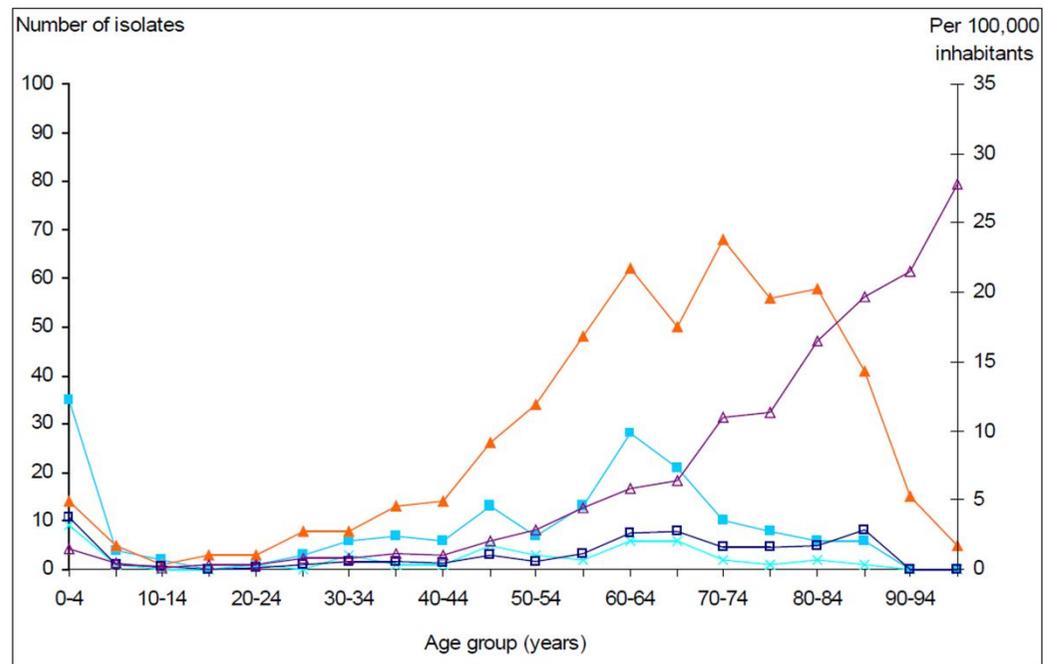
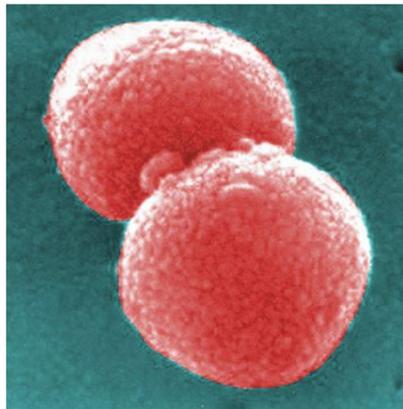
Streptococcus pneumoniae

Invasive pneumococcal disease (IPD)



Streptococcus pneumoniae

Invasive pneumococcal disease (IPD)

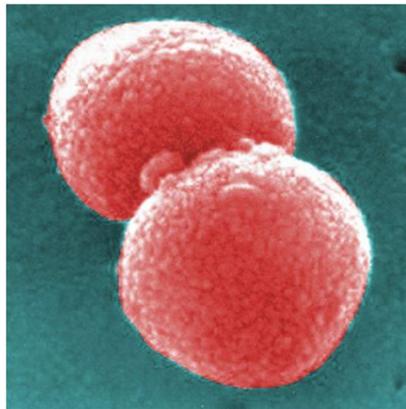


Distribution of *S. pneumoniae* isolates received in 2010 according to age

Annually 1.6 million deaths worldwide

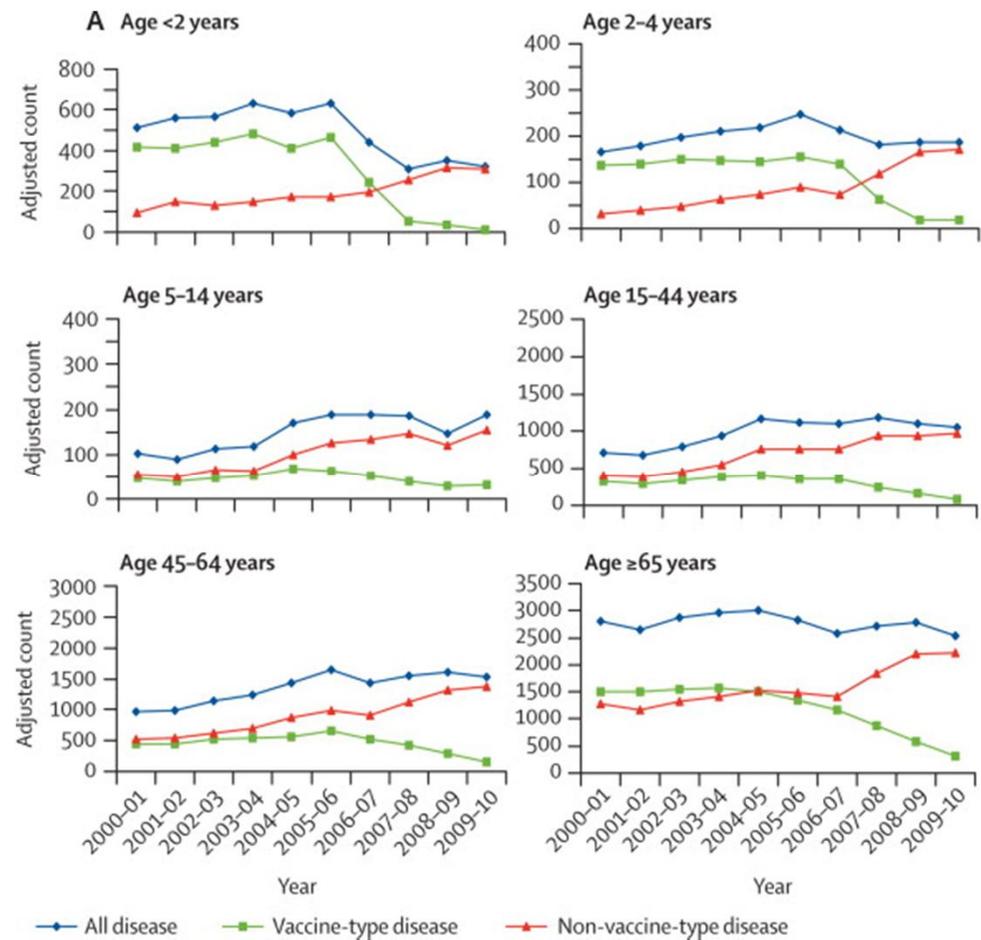
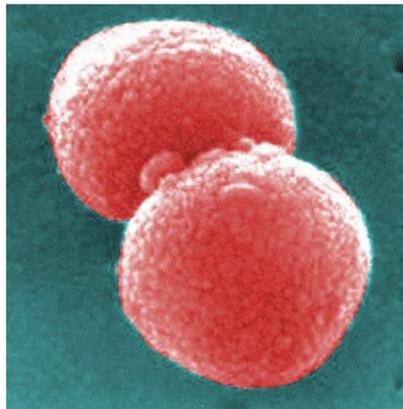
Streptococcus pneumoniae

Serotype – prevention



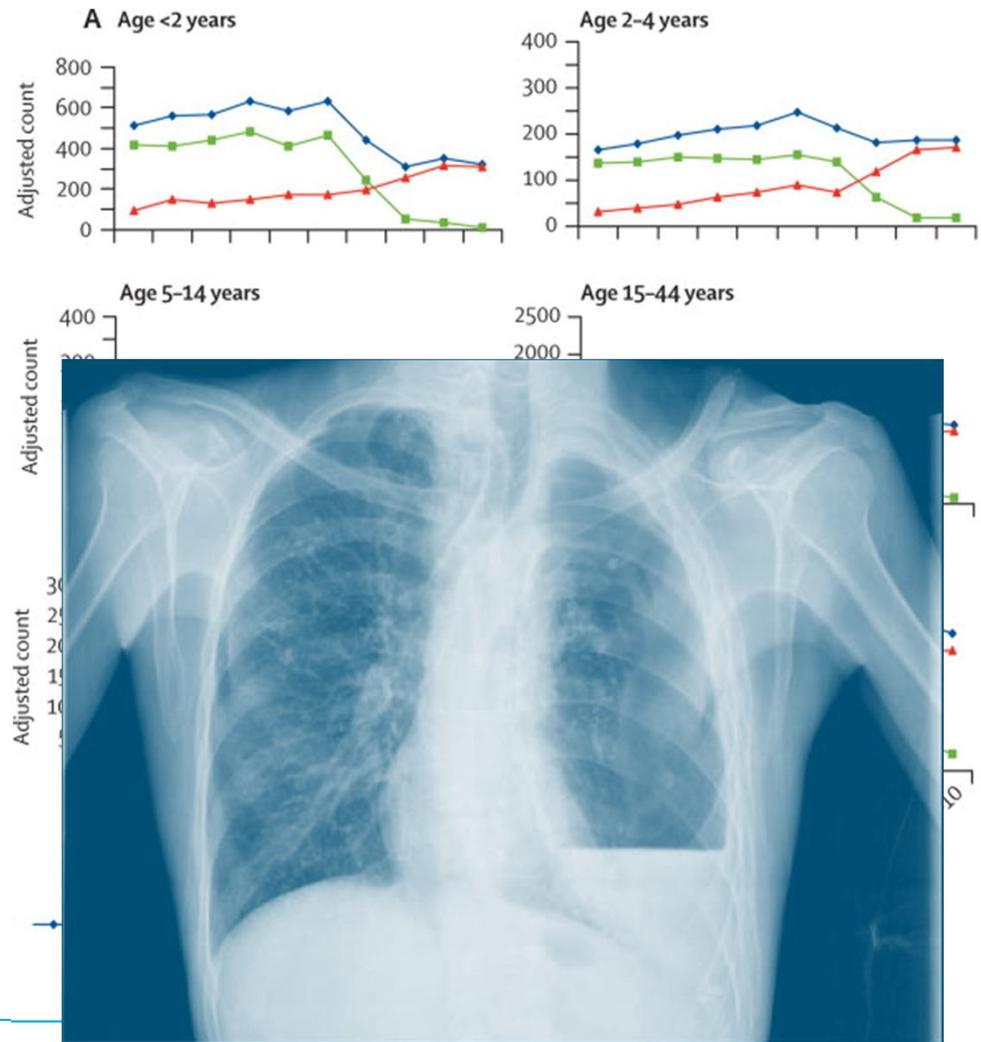
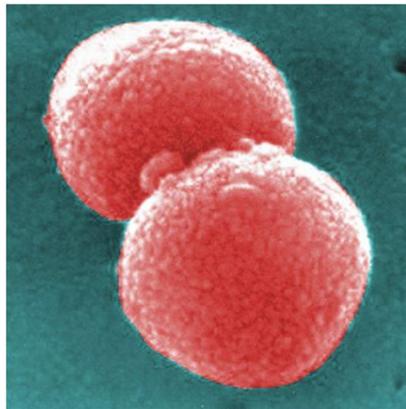
Streptococcus pneumoniae

Serotype – replacement



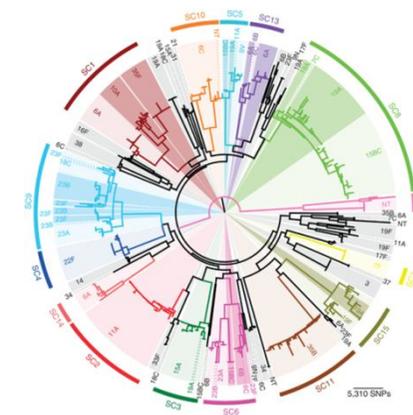
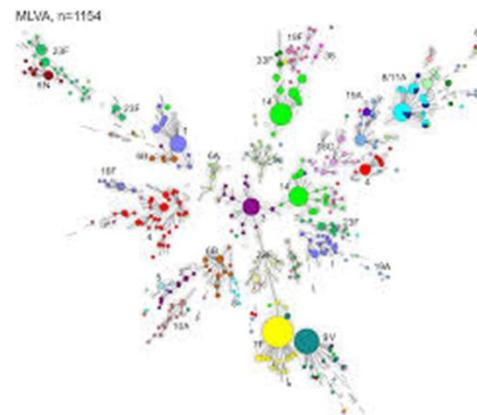
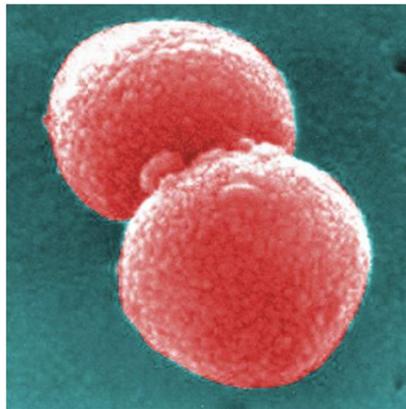
Streptococcus pneumoniae

Serotype – clinical image



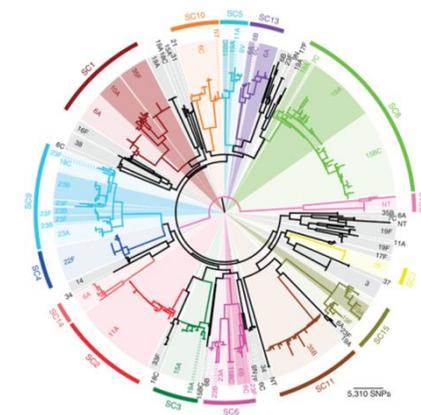
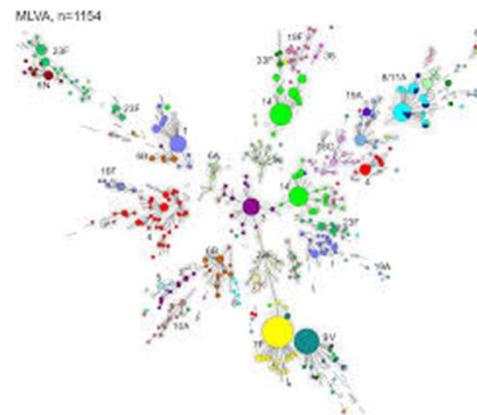
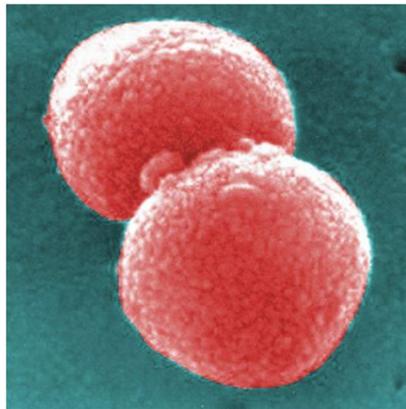
Radboudumc

Streptococcus pneumoniae



Streptococcus pneumoniae

Does clinical diversity among pneumococcal infections originate from the pneumococcal genome?



ZmpC

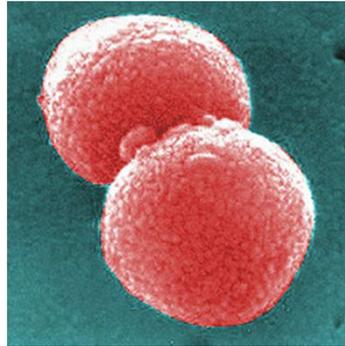
- Present in part of the pneumococcal population
- Large secreted pneumococcal protein
- Sequence highly conserved
- Activates degradation of extracellular matrix, MMP-9
- Inhibits innate host defense, syndecan-1 ectodomain shedding
- Inhibits neutrophil influx, PSGL-1
- More severe disease in animal studies

Its role in different aspects of IPD?

Methods – cohort study



Blood culture +

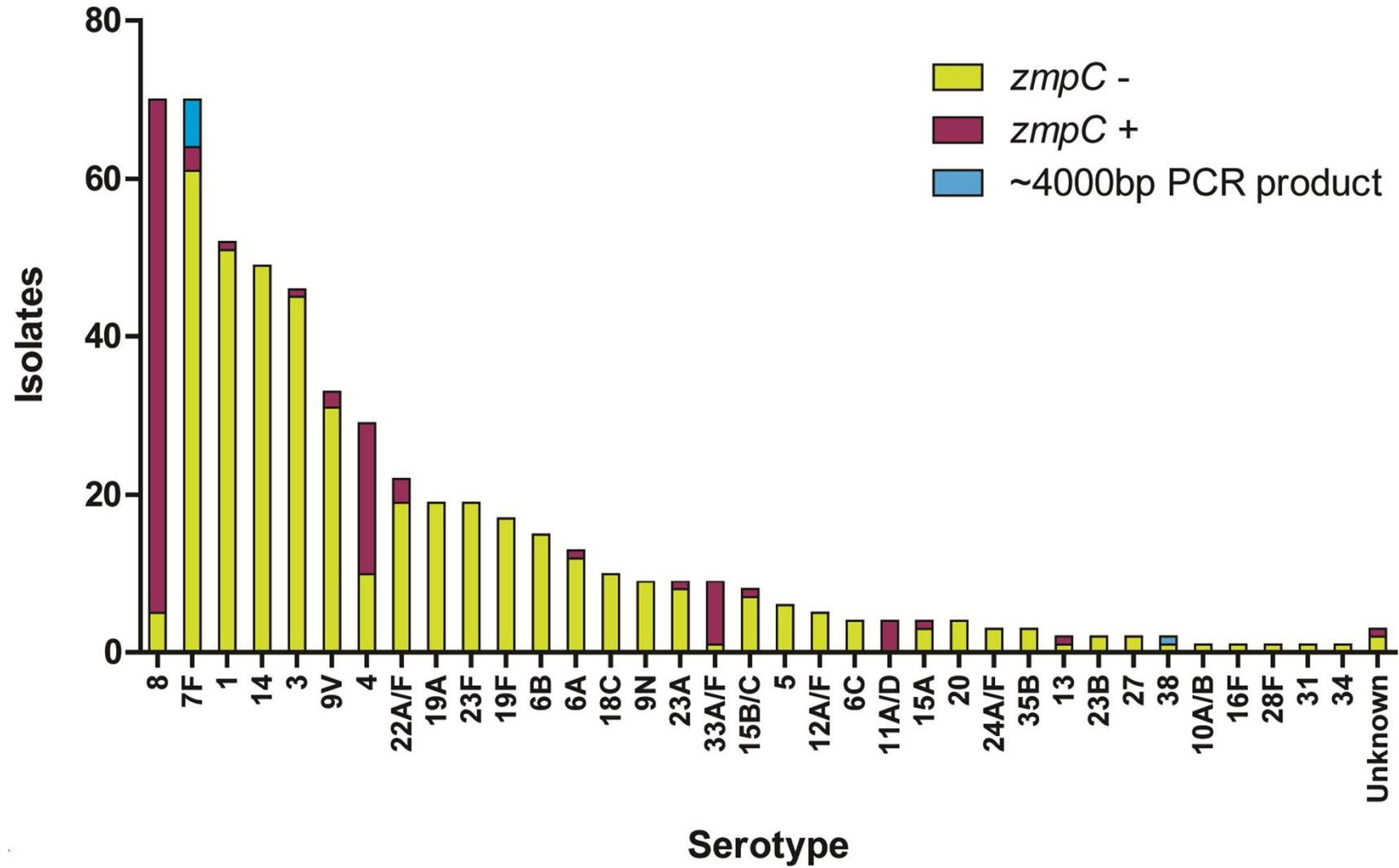


S.pneumoniae

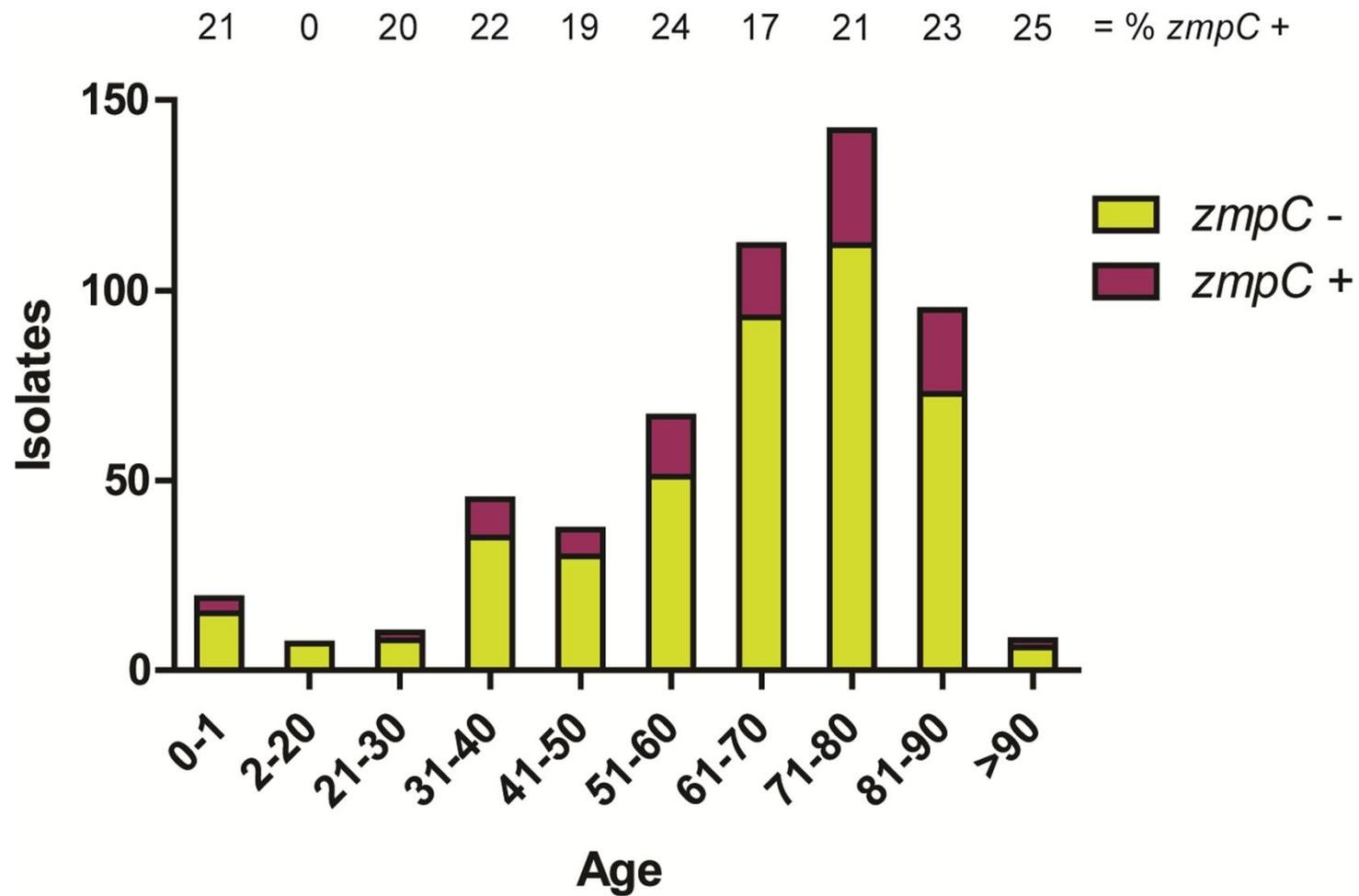


Two Dutch hospitals '01-'13

Serotype (n=549)



Age

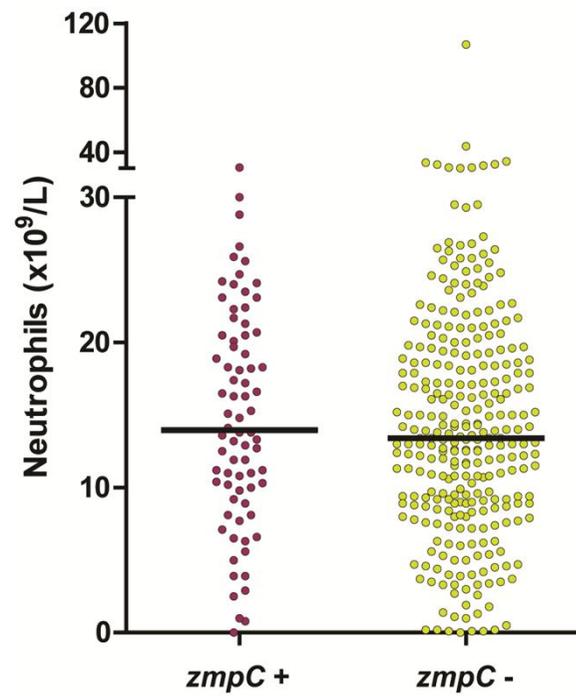
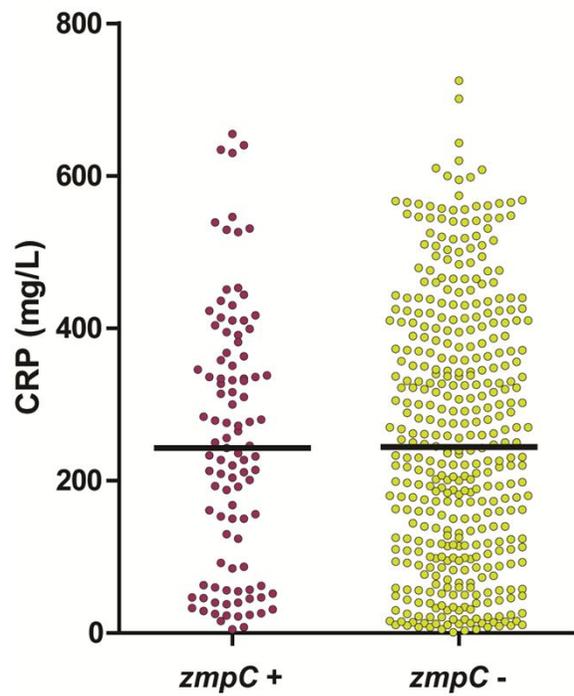
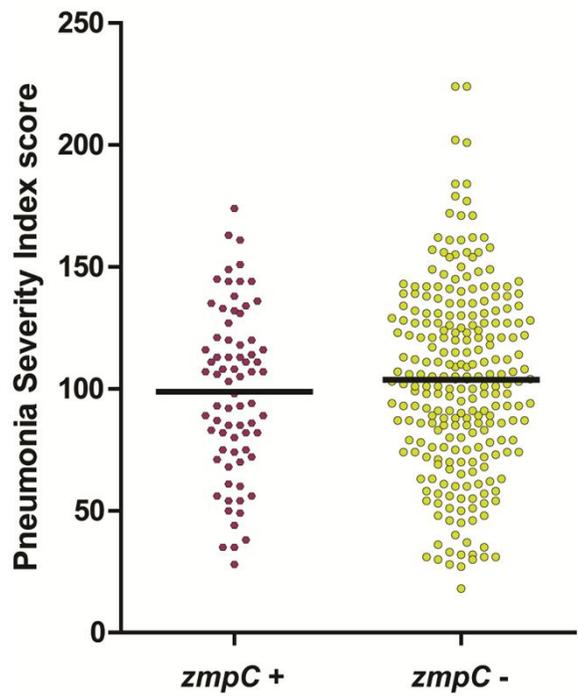


Patient characteristics

	All	<i>zmpC+</i>	<i>zmpC-</i>	<i>p</i> -Value
Subjects	542	112	430	
Age	68 (55-78)	70 (57-78)	68 (54-78)	0.649
Males	47.6 (258/542)	39.3 (44/112)	49.8 (214/430)	0.048*
Comorbidities				
Cancer	21.8 (114/522)	18.5 (20/108)	22.7 (94/414)	0.348
Liver disease	6.9 (36/521)	4.7 (5/107)	7.5 (31/414)	0.395
Renal disease	6.2 (32/519)	6.5 (7/107)	6.1 (25/412)	0.823
COPD	21.0 (114/542)	26.8 (30/112)	19.5 (84/430)	0.094
Diabetes mellitus	17.5 (95/542)	12.5 (14/112)	18.8 (81/430)	0.116
Charlson Comorbidity Score	4.4 ± 2.7	4.3 ± 2.4	4.4 ± 2.7	0.079
Immunocompromising therapy	7.4 (40/538)	8.2 (9/110)	7.2 (31/428)	0.688
Smoking	62.4 (204/327)	73.2 (52/71)	59.4 (152/256)	0.033*
Treated at hospital A	83.4 (441/529)	88.8 (95/107)	82.0 (346/422)	0.092

Clinical syndrome

	All	<i>zmpC</i> +	<i>zmpC</i> -	<i>p</i> -Value
Pneumonia	79.0 (387/490)	85.0 (85/100)	77.4 (302/390)	0.098
Pleural empyema	7.5 (29/387)	5.9 (5/85)	7.7 (24/302)	0.645
Meningitis	9.2 (45/490)	8.0 (8/100)	9.5 (37/390)	0.846
Arthritis	1.0 (5/490)	1.0 (1/100)	1.0 (4/390)	1.000
Endocarditis	1.0 (5/490)	2.0 (2/100)	0.8 (3/390)	0.271
Peritonitis	1.0 (5/490)	1.0 (1/100)	1.0 (4/390)	1.000
Sinusitis	0.6 (3/490)	0.0 (0/100)	0.8 (3/390)	1.000
Unknown focus of infection	8.2 (40/490)	4.0 (4/100)	9.2 (36/390)	0.102
Not retrieved	9.6 (52/542)	10.7 (12/112)	9.3 (40/430)	0.651

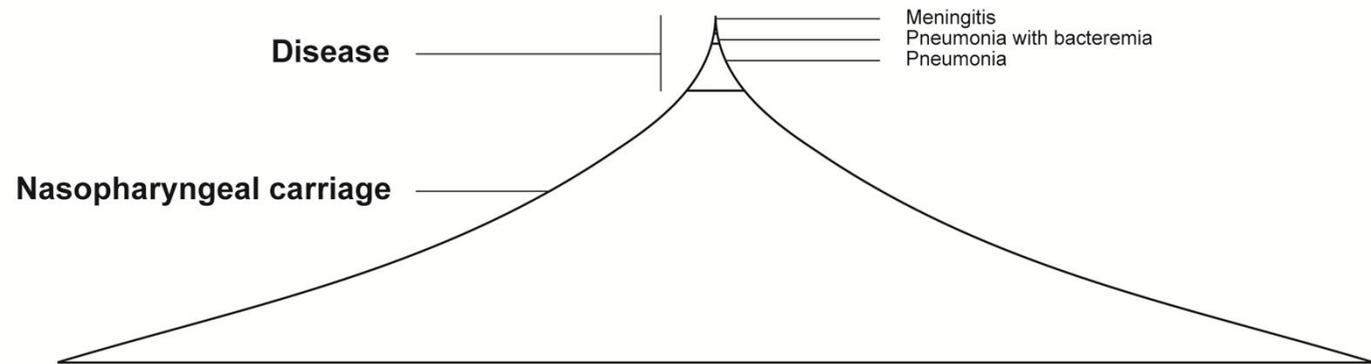


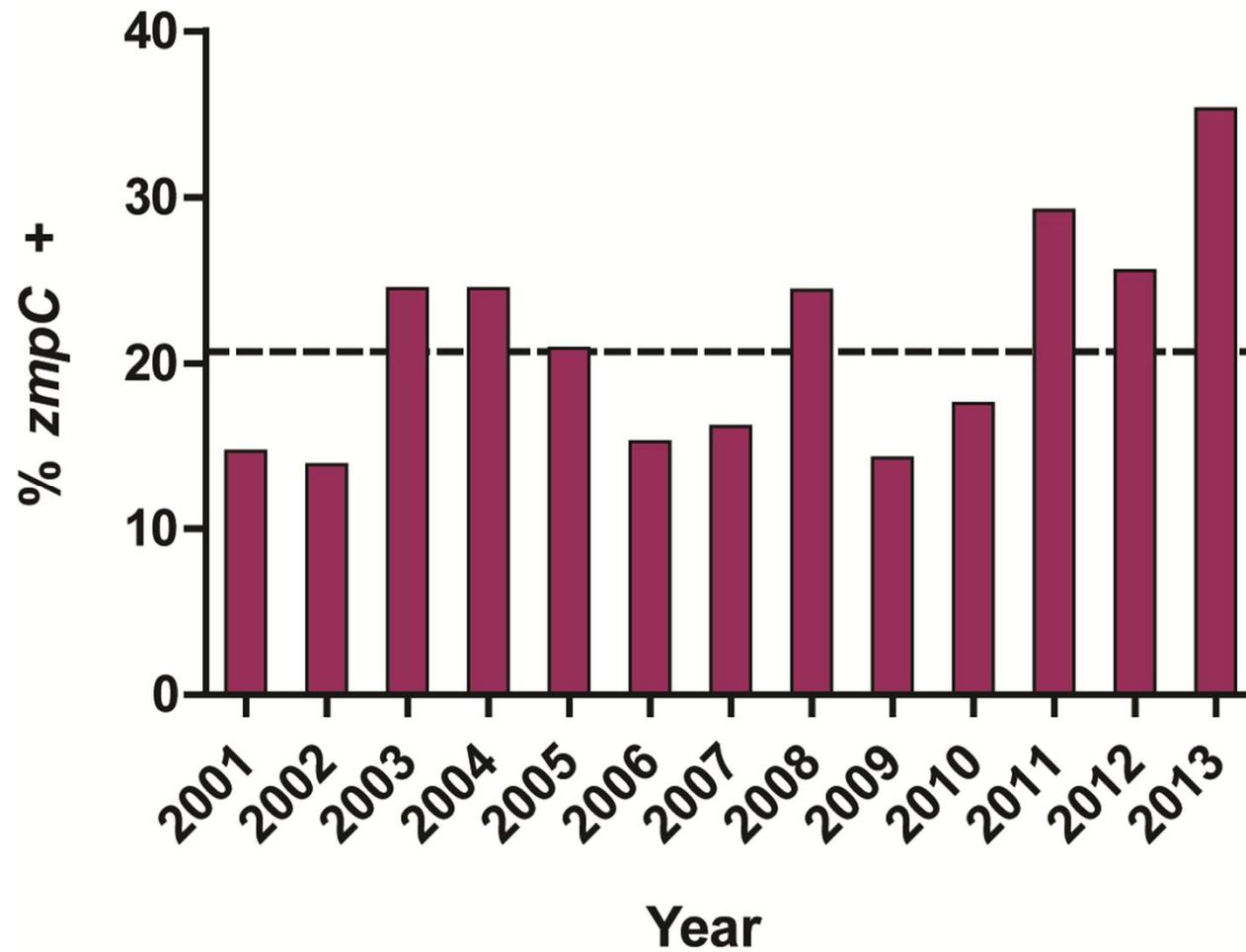
Severity and course of disease

	All	zmpC+	zmpC-	p-Value
Severity at admission				
Start symptoms (days)	2 (1-4)	2 (1-3)	2 (1-4)	0.433
Thoracic pain	45.3 (192/424)	48.2 (40/83)	44.6 (152/341)	0.553
Cough	65.0 (282/434)	75.3 (64/85)	62.5 (218/349)	0.026*
Dyspnea	61.6 (270/438)	76.4 (68/89)	57.9 (202/349)	0.001*
Confusion	27.0 (93/344)	29.3 (17/58)	26.6 (76/286)	0.669
Temperature (°C)	38.6 (37.8-39.3)	38.6 (37.8-39.35)	38.6 (37.8-39.2)	0.949
Hemoglobin (mmol/L)	7.9 (7.1-8.6)	8.2 (7.3-9.1)	7.9 (6.9-8.5)	0.002*
Leukocytes (x10 ⁹ /L)	15.8 (10.7-21.8)	16.0 (12.0-22.4)	15.7 (10.4-21.7)	0.524
Proportion neutrophils (%)	89 (84-93)	91 (84-93)	89 (85-92)	0.382
pH	7.46 (7.41-7.49)	7.45 (7.42-7.48)	7.46 (7.41-7.49)	0.757
Infiltrate on chest X-ray	79.5 (379/477)	81.8 (81/99)	78.8 (298/378)	0.513
Pleural effusion on chest X-ray	41.4 (127/307)	48.4 (31/64)	39.5 (96/243)	0.197
SIRS	89.4 (389/435)	96.6 (84/87)	87.6 (305/348)	0.018*
Course of hospital stay				
ICU admission	23.5 (110/468)	33.3 (32/96)	21.0 (78/372)	0.011*
Mechanical ventilation	9.5 (42/442)	15.1 (13/86)	8.1 (29/356)	0.048
Hospital stay survivors (days)	10 (6-16)	10 (6-16)	10 (6-16)	0.786
Death	14.5 (71/491)	14.4 (15/104)	14.5 (56/387)	0.990
Time to death (days)	5 (1-17)	5 (1-23)	5 (1-17)	0.669

Spread at the risk of...?

...
Cough
Dyspnea
Confusion





Conclusion

The presence of *zmpC* was associated with a more severe clinical manifestation of IPD

Information on pneumococcal genetic background may be useful

- To identify vulnerable individuals
- To predict clinical presentation, severity and course of disease

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→ Provide additional value to rapid diagnostics

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→ Provide rationale for more tailored prevention of IPD

Is it ZmpC to be targeted?

Why not....?

Start from clinically relevant phenotype
→ explore pneumococcal origin

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Start from clinically relevant phenotype
→ explore pneumococcal origin



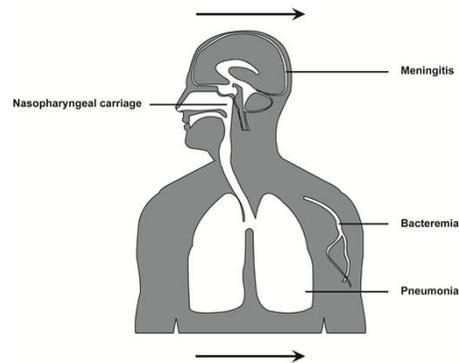
Pre vs post

Why not....?

Start from clinically relevant phenotype
→ explore pneumococcal origin



Pre vs post



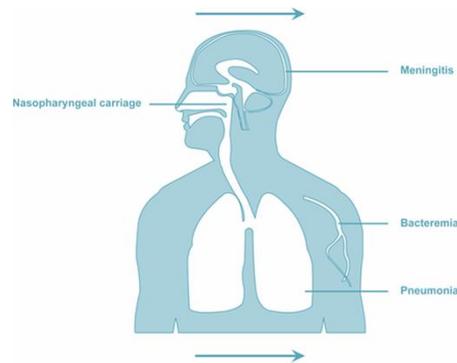
Carriage vs IPD

Why not....?

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→ explore pneumococcal origin



Pre vs post



Carriage vs IPD



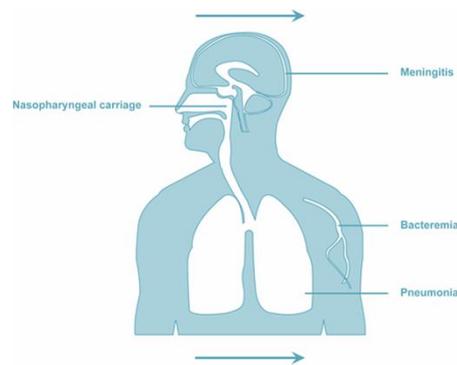
Survivors vs deaths

Why not....?

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→ explore pneumococcal origin



Pre vs post



Carriage vs IPD



Survivors vs deaths



Susceptible vs resistant

Acknowledgements

Canisius-Wilhelmina Ziekenhuis, Nijmegen

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Radboudumc

Thank you for your attention!

Questions?

