Bristol Children's Vaccine Centre

Vaccination – room for more?

Adam Finn

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8th May 2014

Vaccines Sympo, ESPID, Dublin

University of BRISTOL

Interests statement

- Adam Finn does research, consultancy and talks, funded by industry
- Income is paid to his employers not him
- He does not receive benefits (travel, hotels, registration etc.) from industry except when on their business
- He & his family own no pharma shares or intellectual property

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Acknowledgements

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Valtyr Thors

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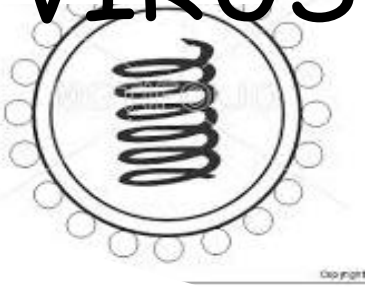
Assertion

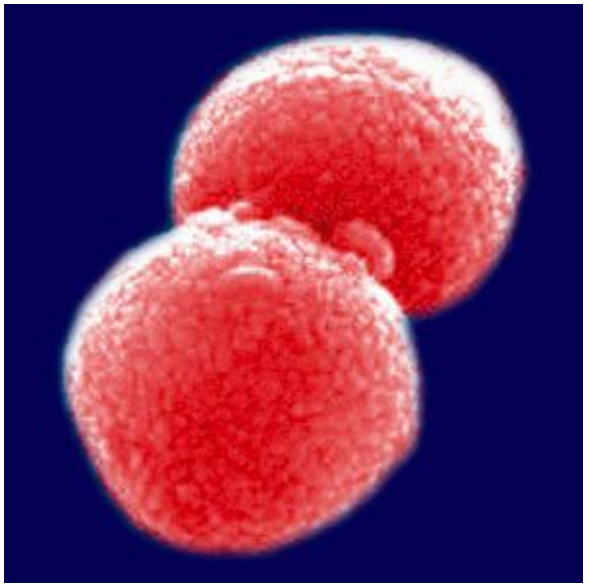
- All universal high-uptake vaccine programmes (apart from tetanus) work largely or entirely through **indirect effects** (i.e. by **reducing or eliminating transmission of infection**) rather than through the direct effects ("immunise your child and s/he won't get sick") which usually drive development and licensure"

Transmission

VIRUS

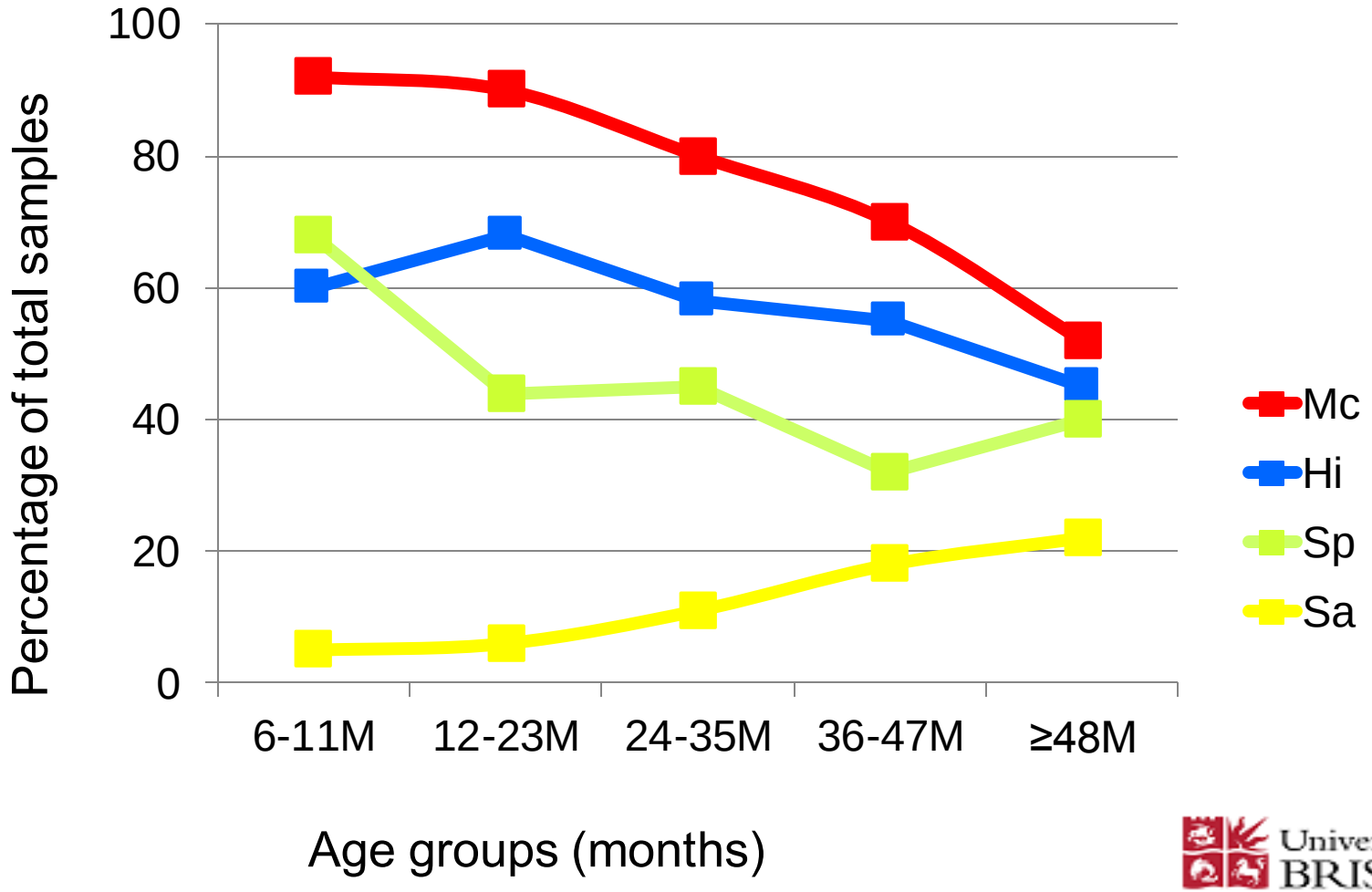


BACTERIA



SNOT score = 3

n= 586 (326 boys, 56%)
Mean age= 41.5 months (6-75)
Colonisation rates: Mc= 68.7%, Hi= 51.7%, Sp= 45.7% , Sa=15.5%



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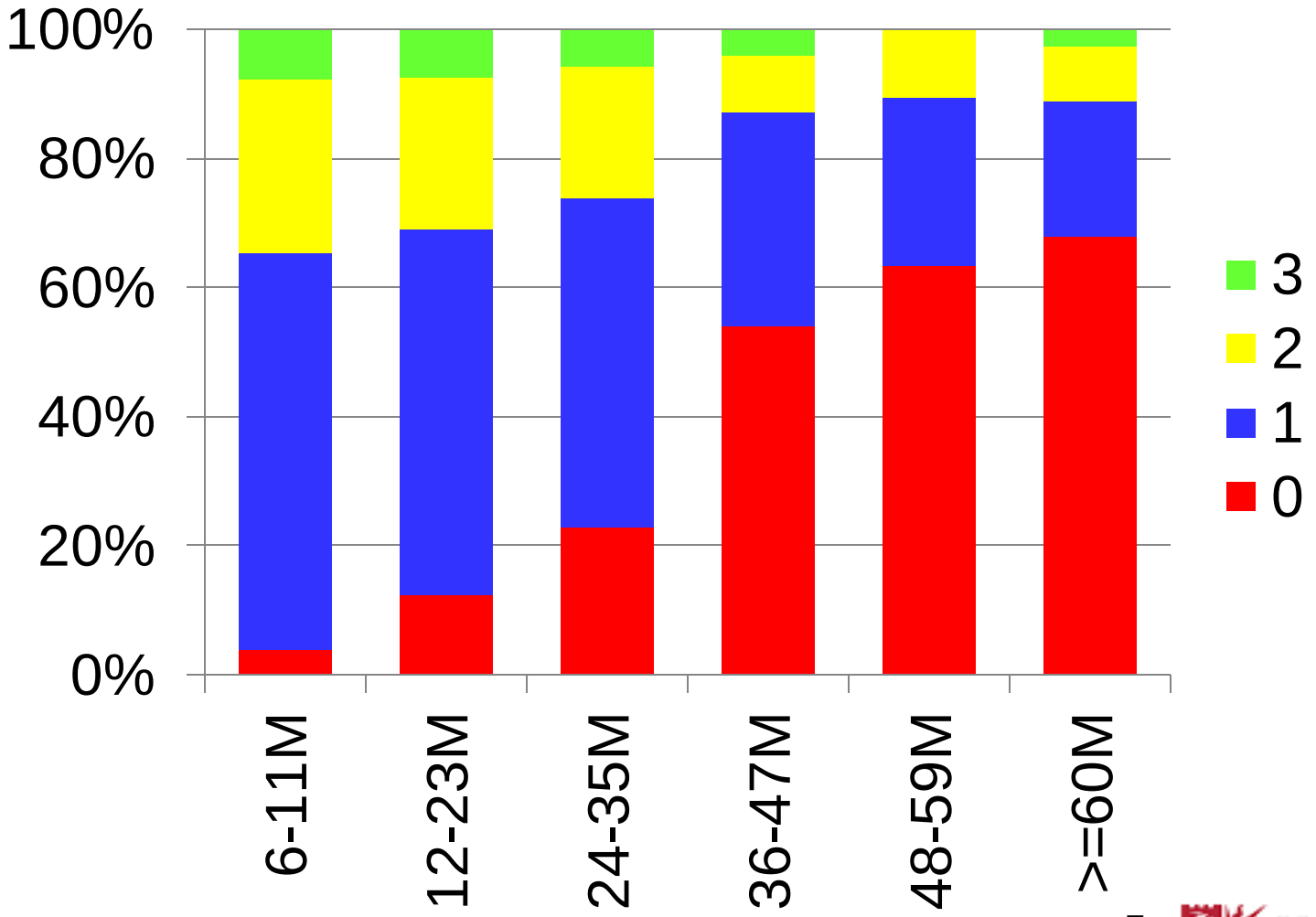
SNOT score by age

Rodrigues Poster PW05 Abstract 0067



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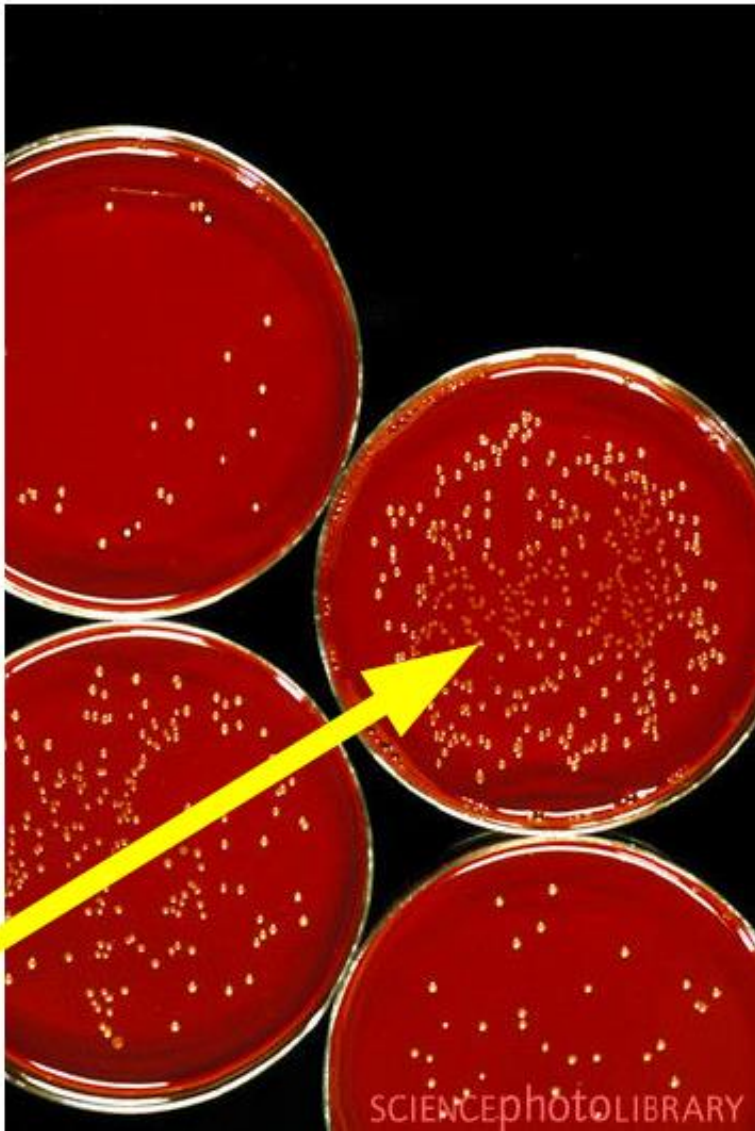
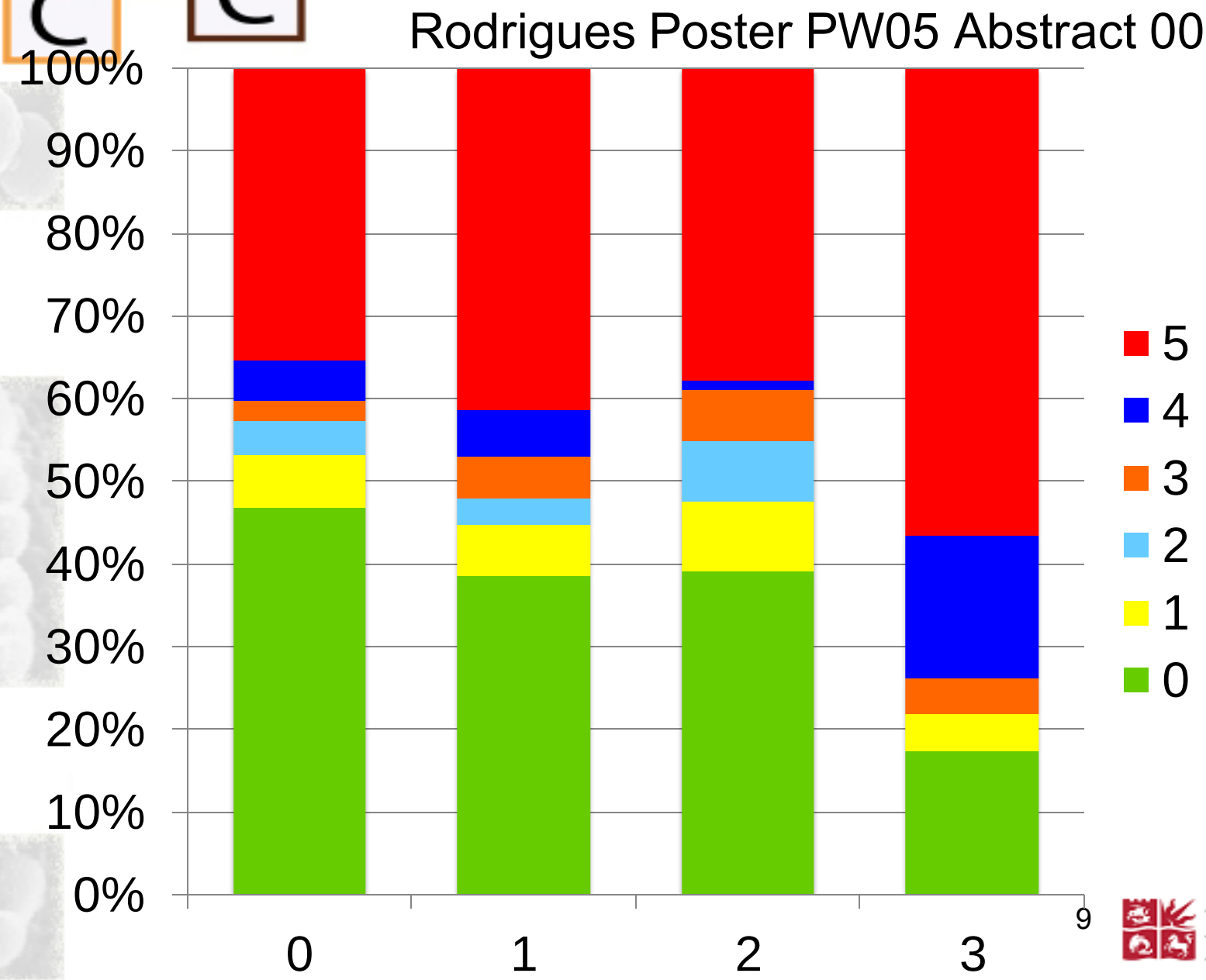
Density scoring

- Different colony types were identified visually and their respective densities over the plate scored using the following system:
  - 0 = no colonies
  - 1= 1- 5 colonies
  - 2= >5 – 20 colonies
  - 3= >20– 50 colonies
  - 4= >50 – 100 colonies
  - 5= >100 colonies/50µl broth



Density by rhinitis score



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Rhinitis and…

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Presence	F-stat	P-value
S. pneumoniae	3.99	0.046
H. influenzae	2.78	0.096
M. catarrhalis	1.64	0.200
S. aureus	0.19	0.664
Any virus	4.89	0.027

Density	F-stat	P-value
S. pneumoniae	2.34	0.040
H. influenzae	3.73	0.003
M. catarrhalis	1.45	0.204
S. aureus	0.26	0.936

Bug to bug..

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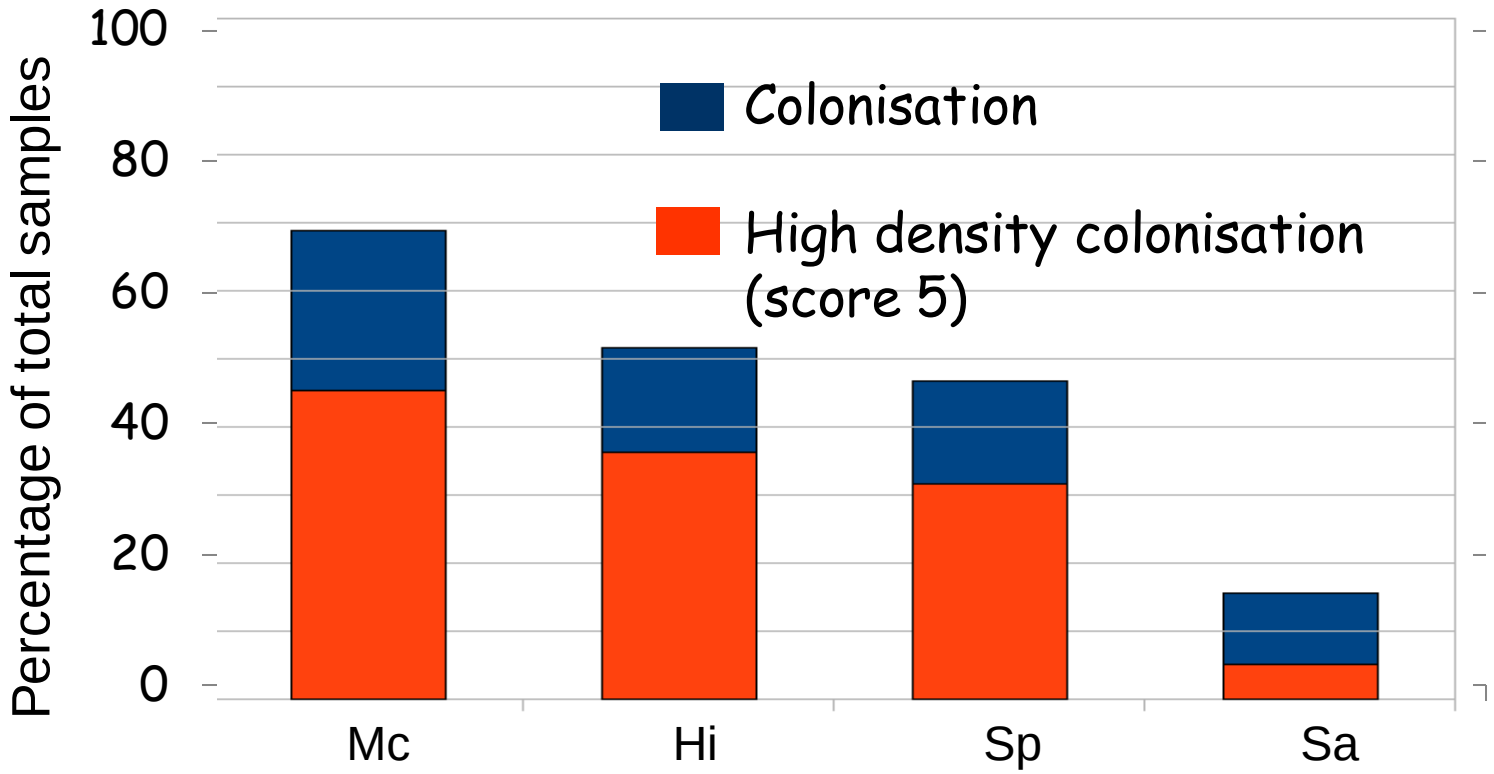
	S. pneumoniae		
H. influenzae	***8.99***		
	<0.01	*H. influenzae*	
S. aureus	***0.47***	***0.69***	
	0.8	0.63	***S. aureus***
M. catarrhalis	***2.52***	***0.51***	***9.36***
	0.03	0.77	<0.01

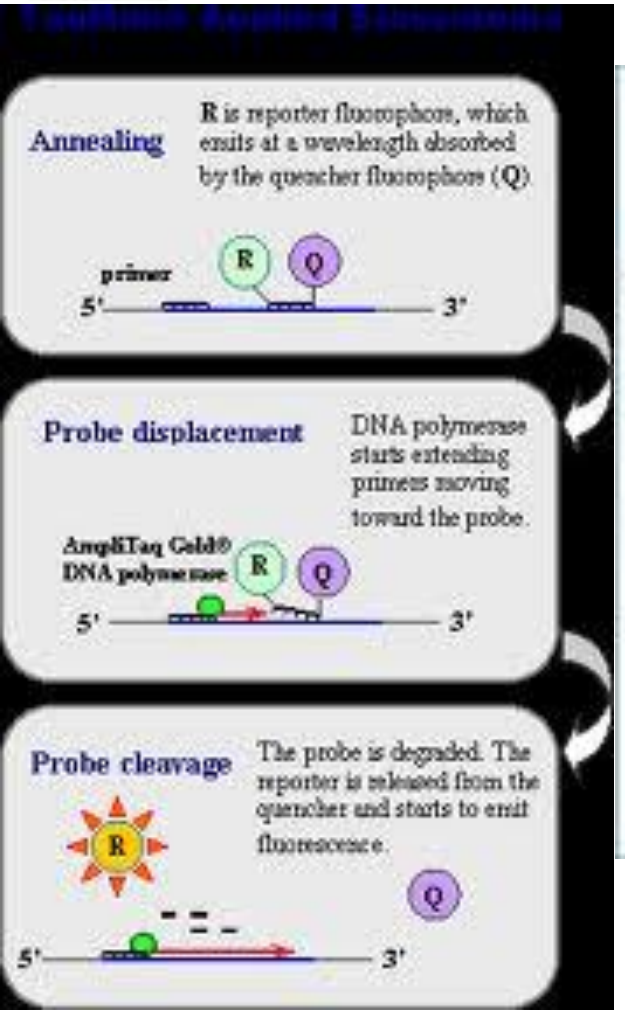
Why study density?

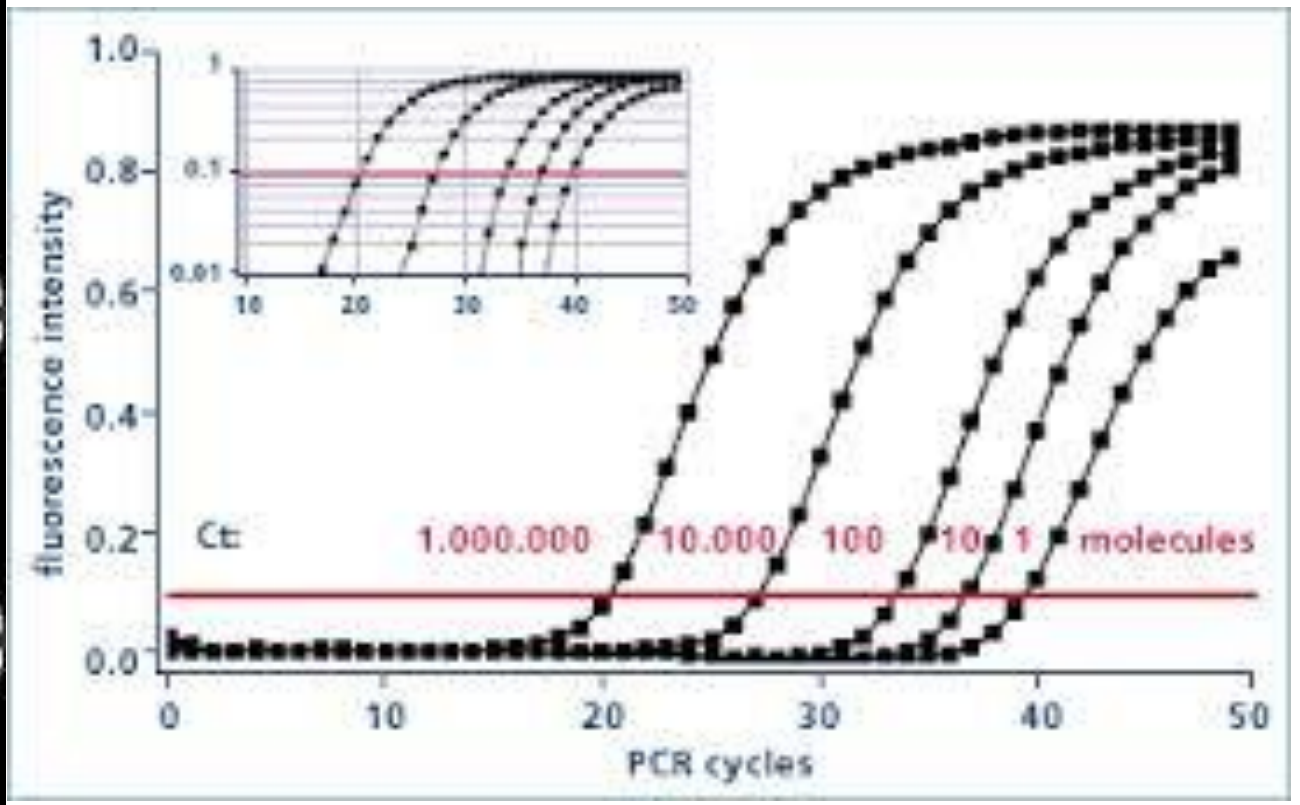
Some elephants are bigger than others…

Most colonisation is "high density"



qRT-PCR discrimination at much higher concentrations





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"Bacterial PCR..." vs Broth culture

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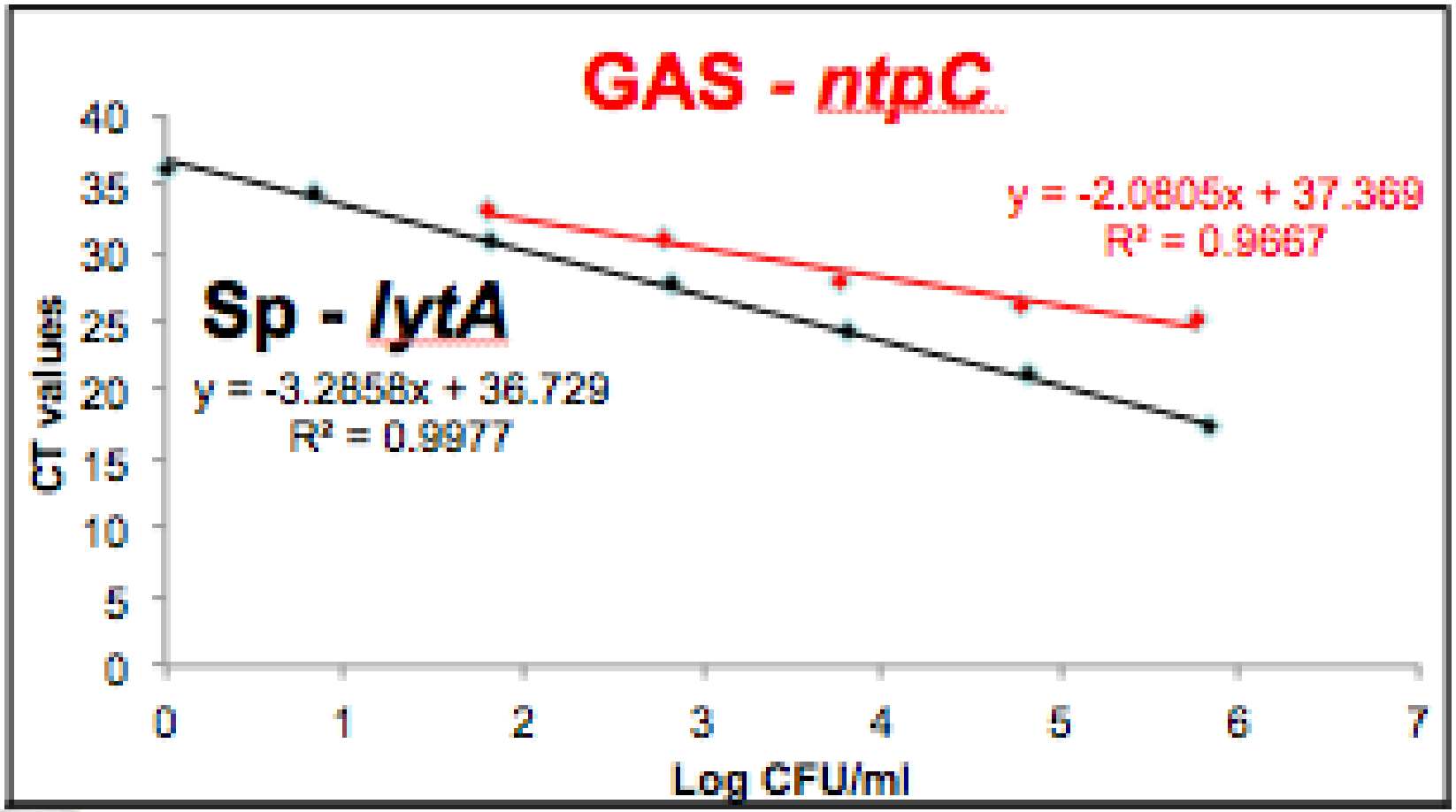

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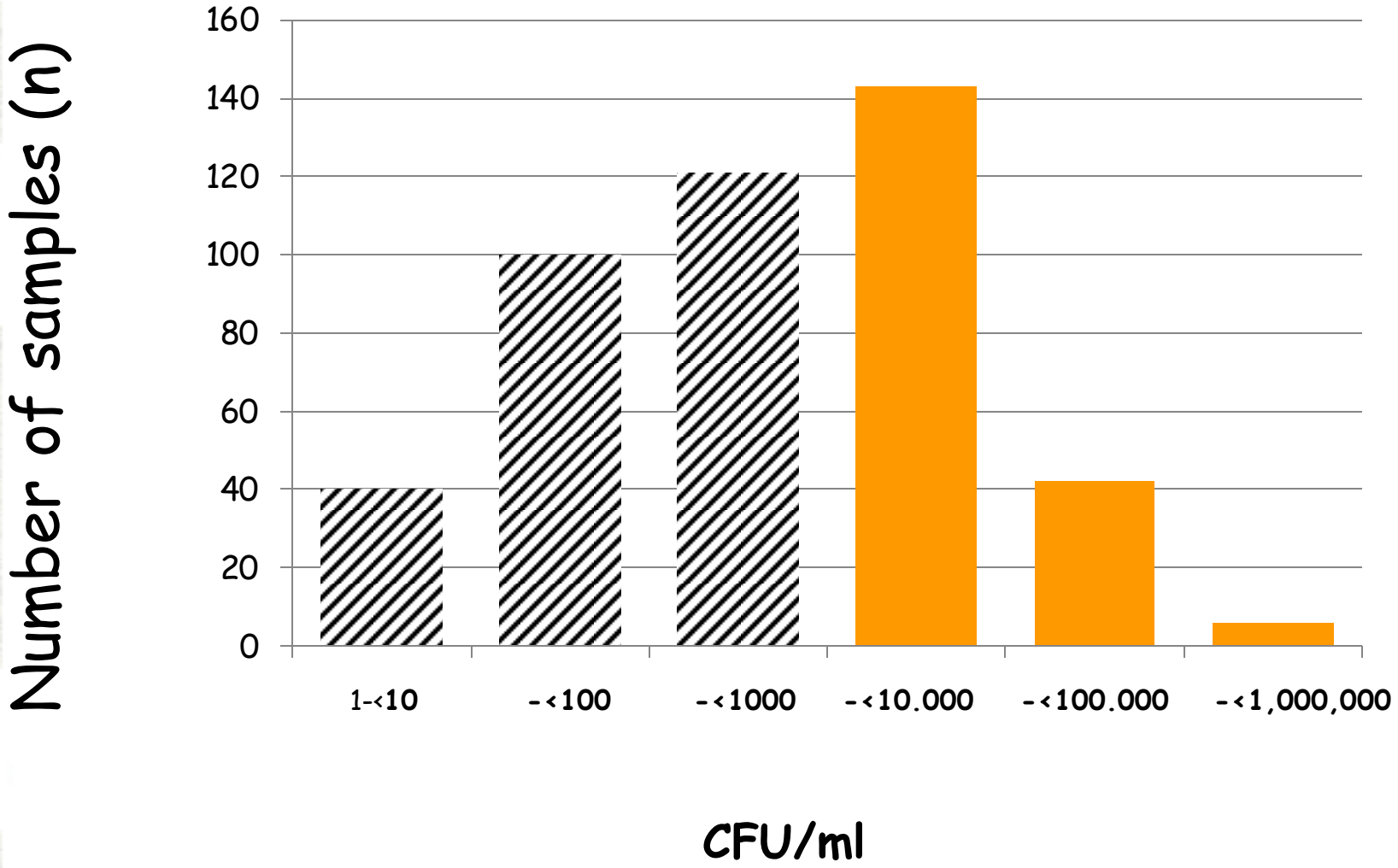
Sp density distribution



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Detection Cx vs qPCR

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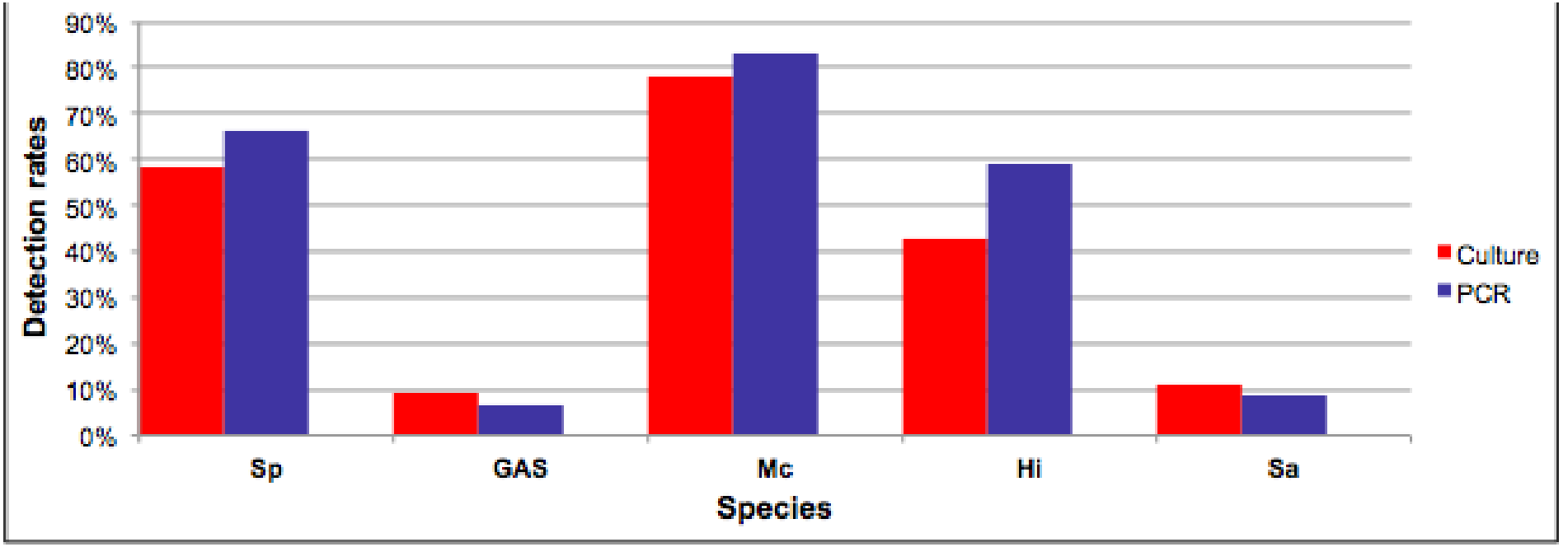

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Do results match?

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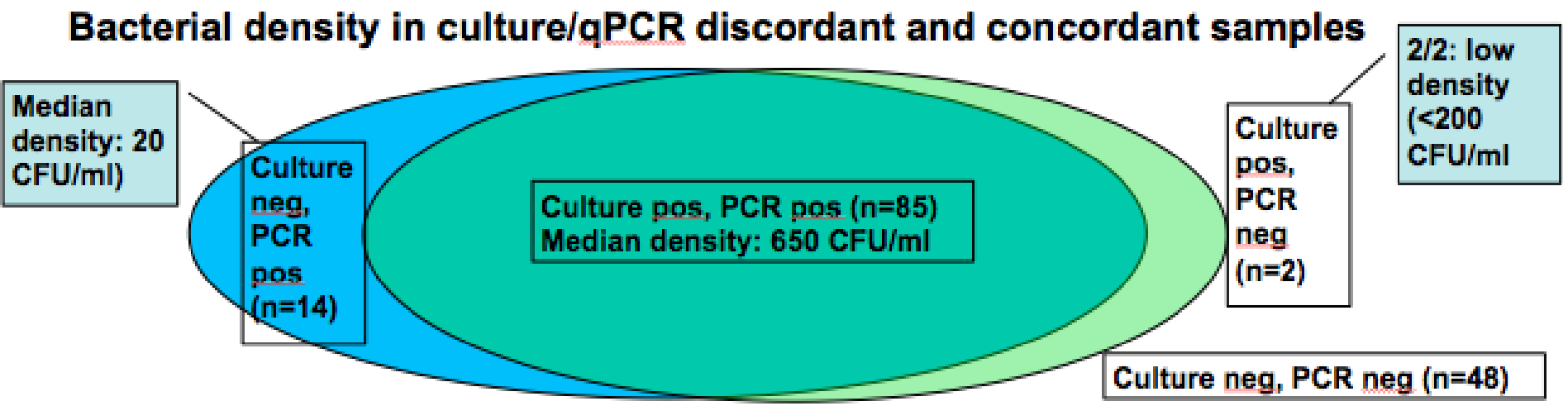

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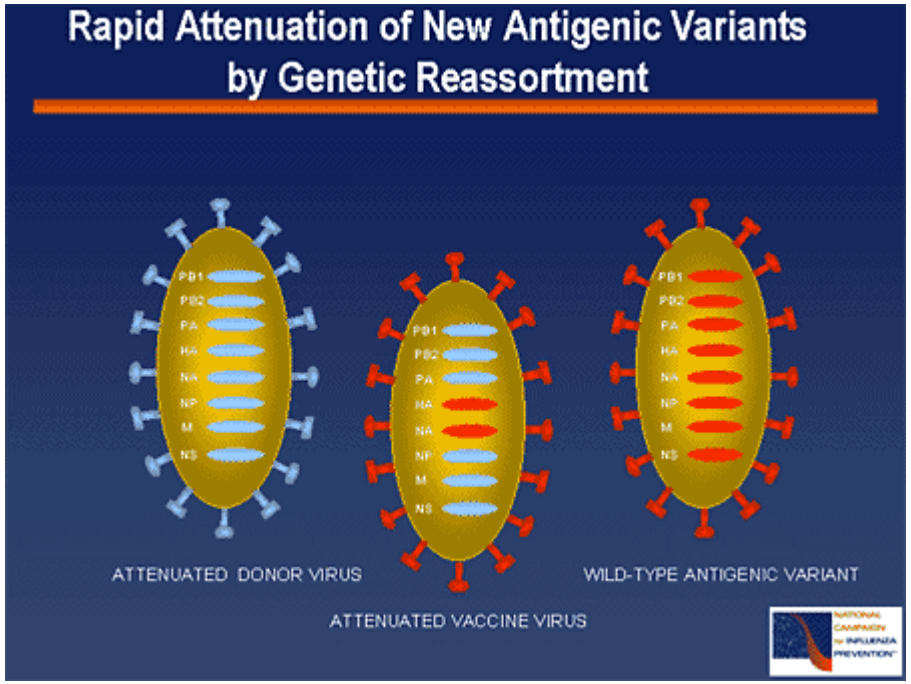
How do you prove cause and effect?

Live attenuated intranasal flu vaccine LAIV

Cold adapted, attenuated trivalent



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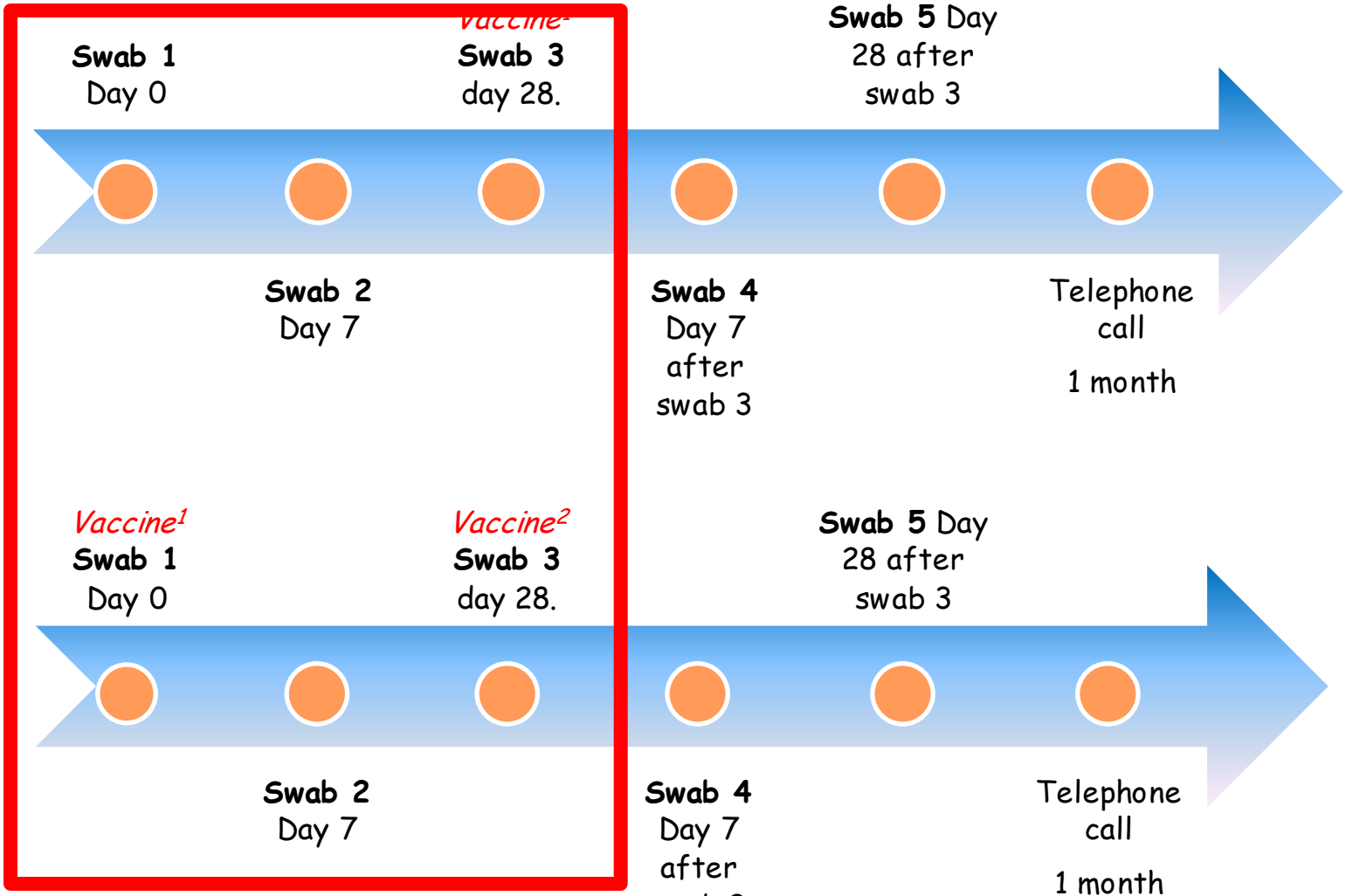
Visits



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Carriage rates don't change

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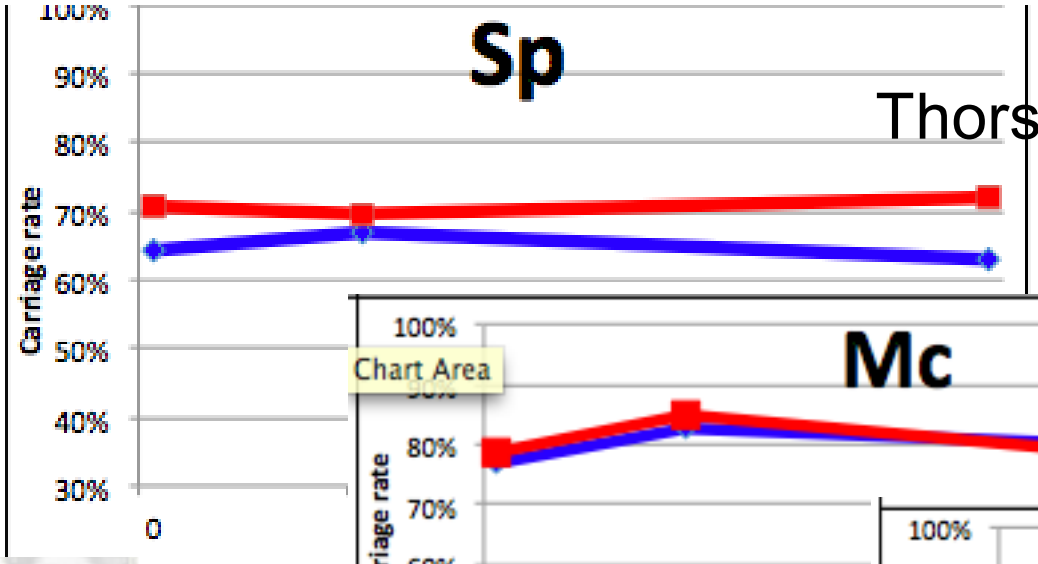

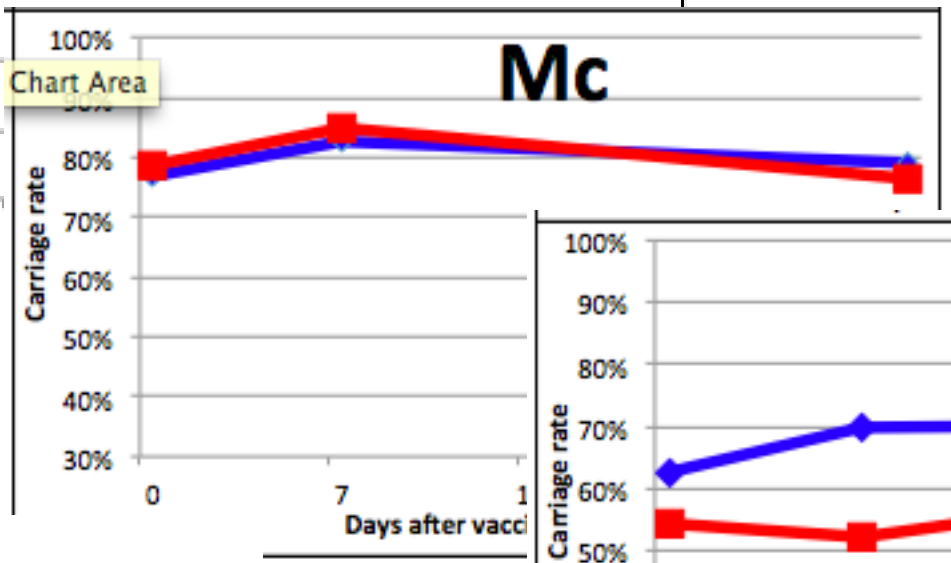

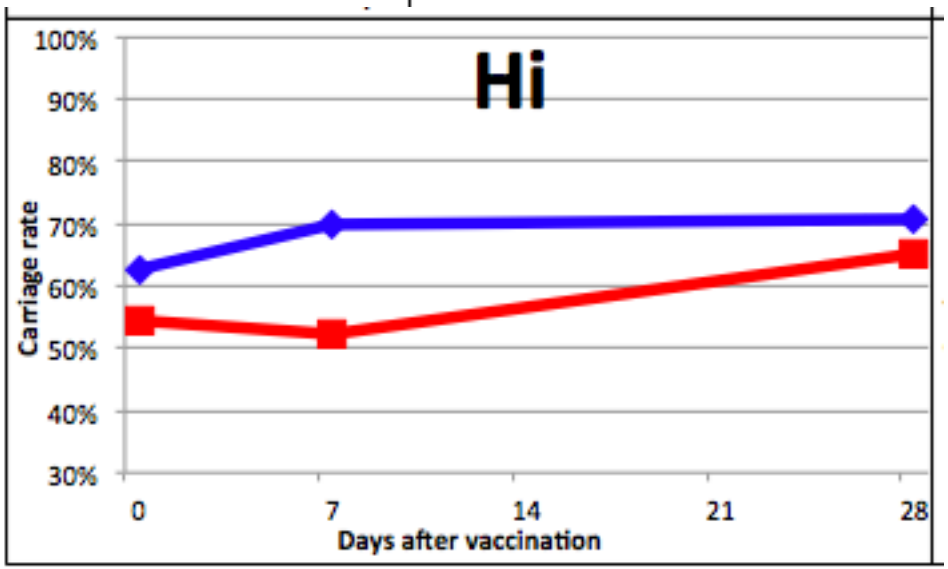

- LAIV group
- Control group

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But density does..

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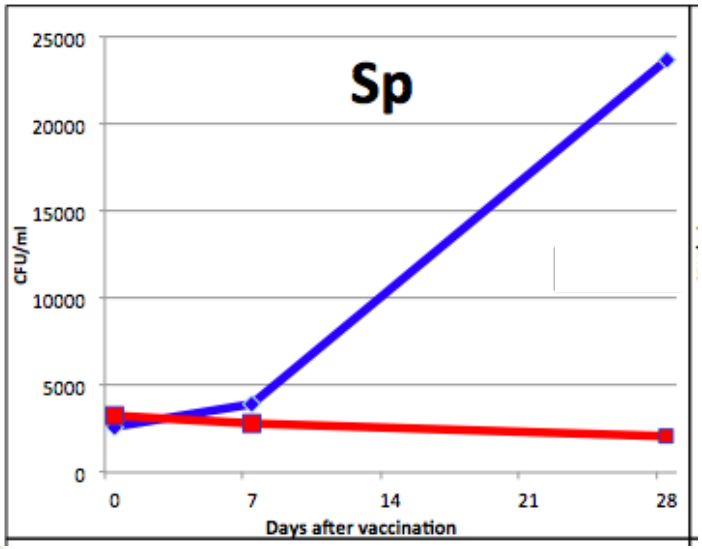

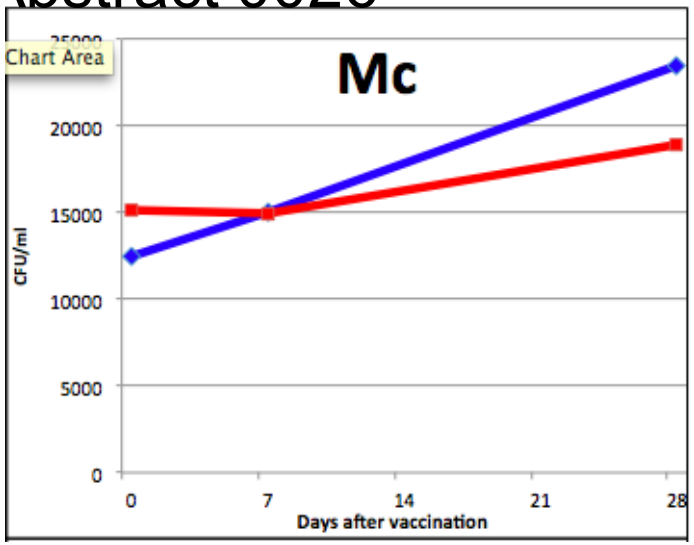

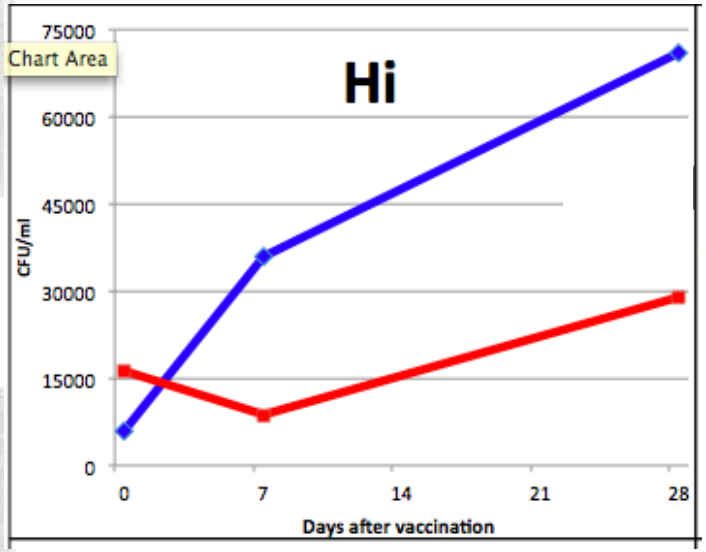

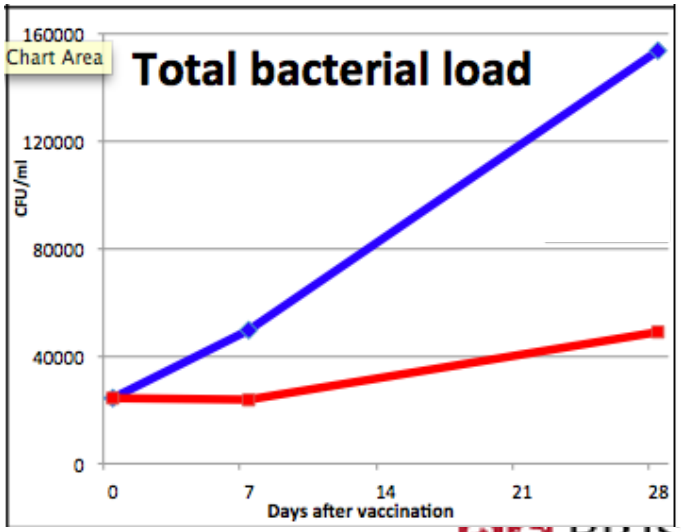

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Implications

- LAIV – no known safety risks in 2-4year old children despite millions of doses given
- This suggests increased bacterial colonisation density NOT cause of disease
- But COULD increase transmission rates
- And effects of wild type infection could be bigger/different

What about meningococcus?

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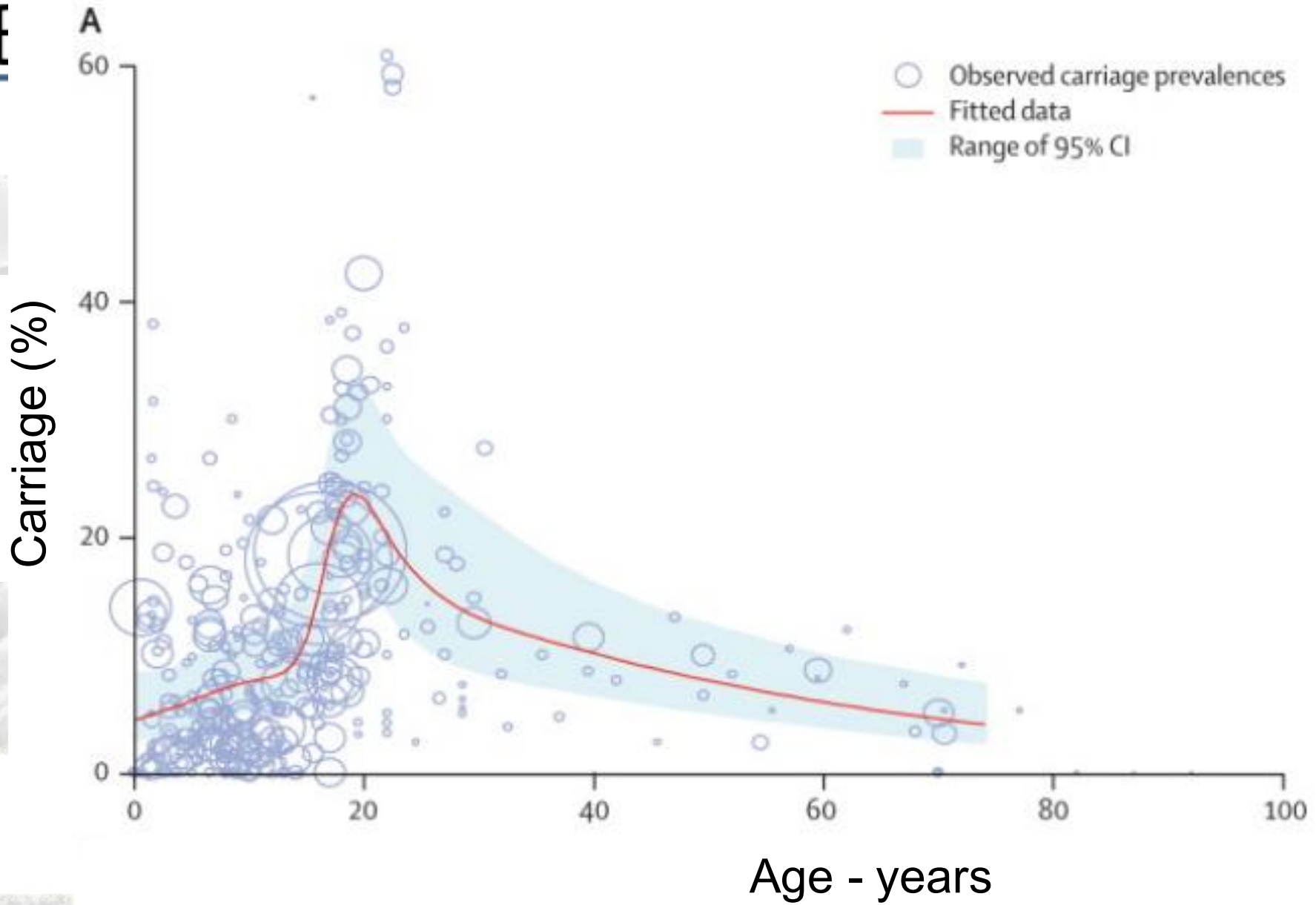

Hannah Christensen et al Lancet ID 2010

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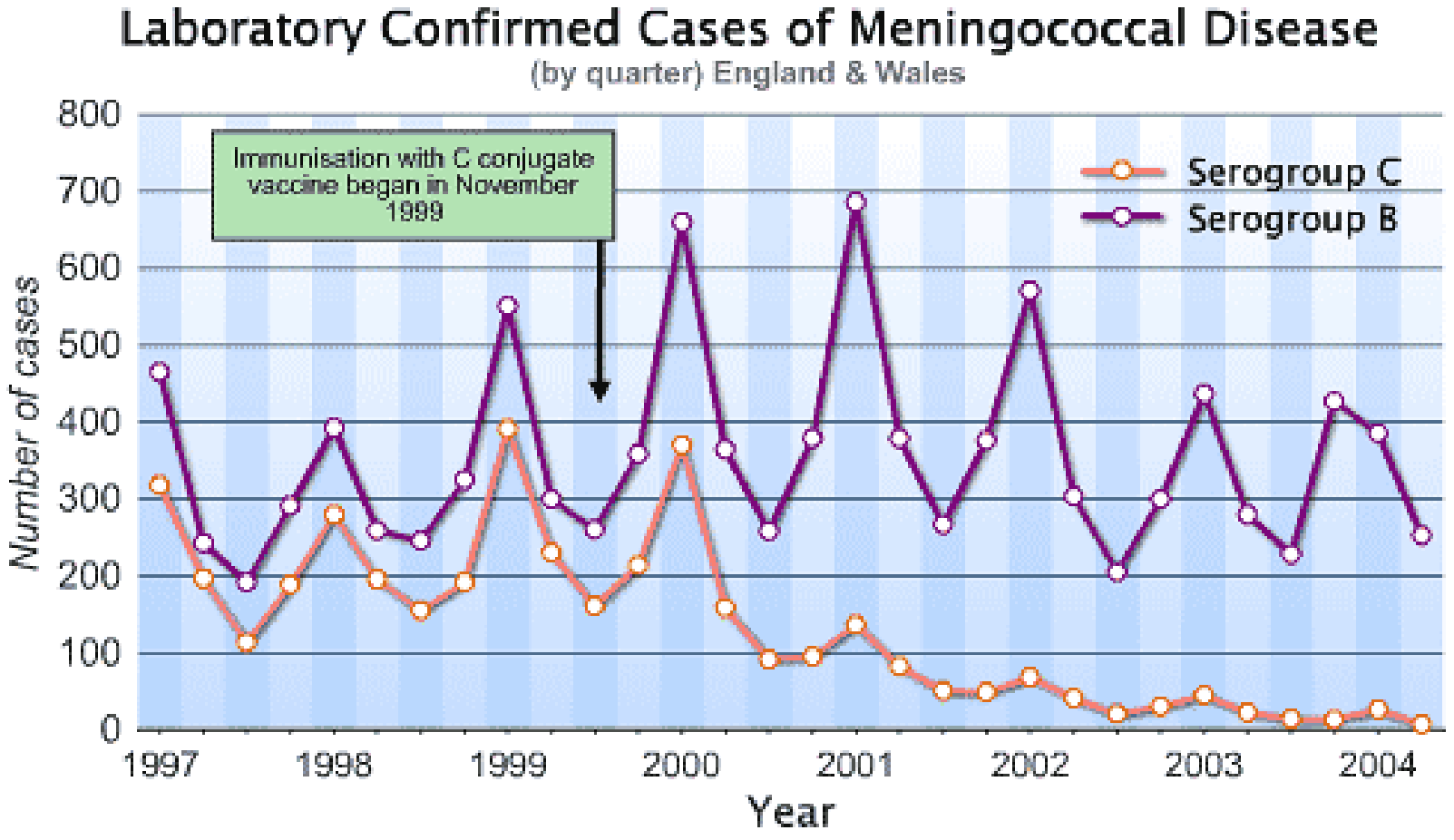
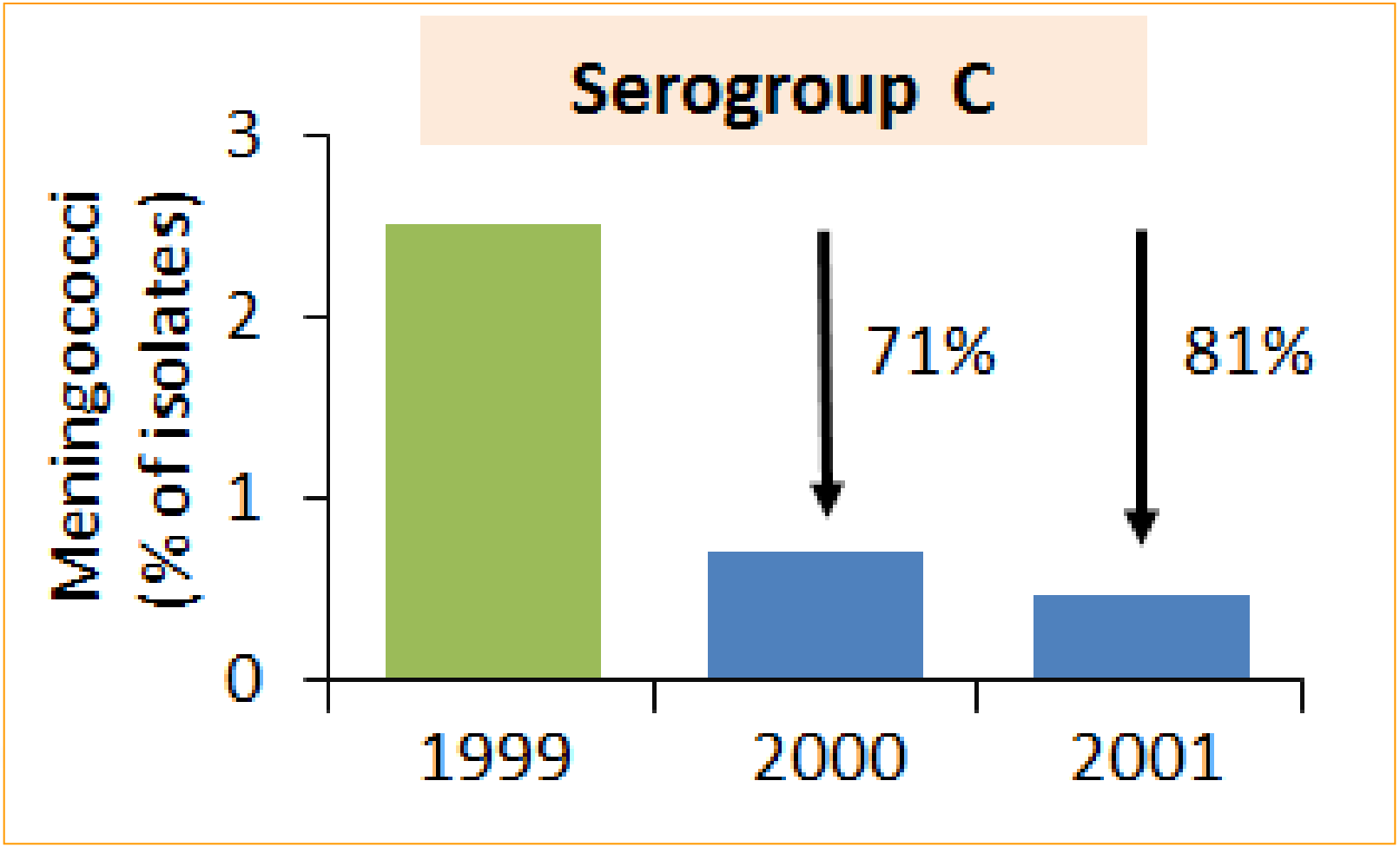
HPA surveillance



UK Students - carriage



Maiden MC, et al. *J Infect Dis. 2008;197:737-743*

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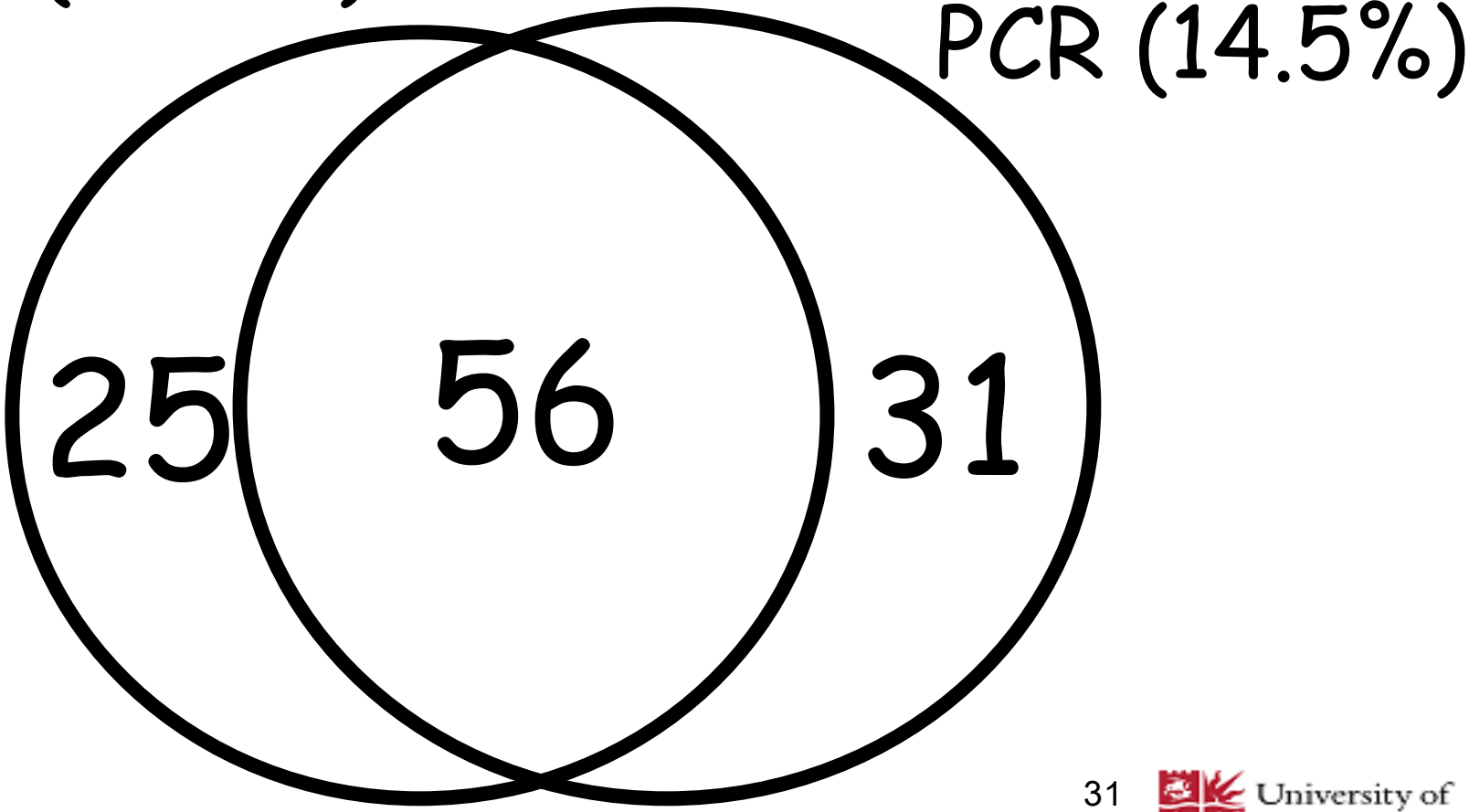
Birth
10 years
20 years

Bristol/Coimbra 601 Student Cx vs PCR results



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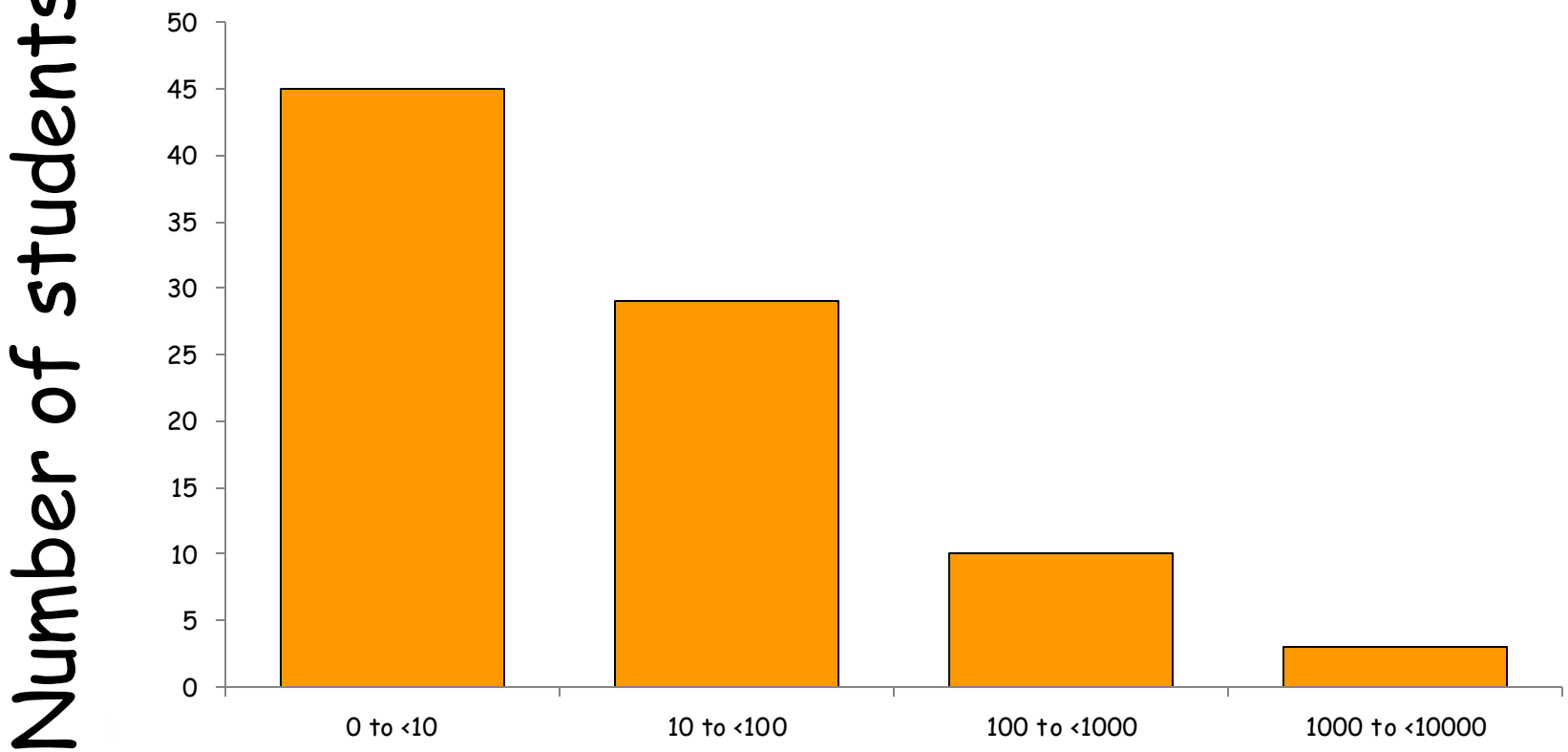
Meningococcal carriage density in 87 young adults



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Transmission