



Non-specific effects of routine immunisations in Denmark

Signe Sørup, MSc, PhD, postdoc
Research Center for Vitamins and Vaccines,
Bandim Health Project,
Statens Serum Institut
Copenhagen, Denmark

Non-specific effects of vaccines

**Health effects not related to
the protection against the
targeted diseases**

Non-specific effects of vaccines: Hypotheses generated in low- income countries

- Most recent vaccine
 - *Live* vaccines are associated with decreased mortality
 - *Inactivated* vaccines are associated with increased childhood mortality
 - Simultaneous administration of *live* and *inactivated* vaccines are associated with increased childhood mortality

SAGE review of non-specific effects of vaccines

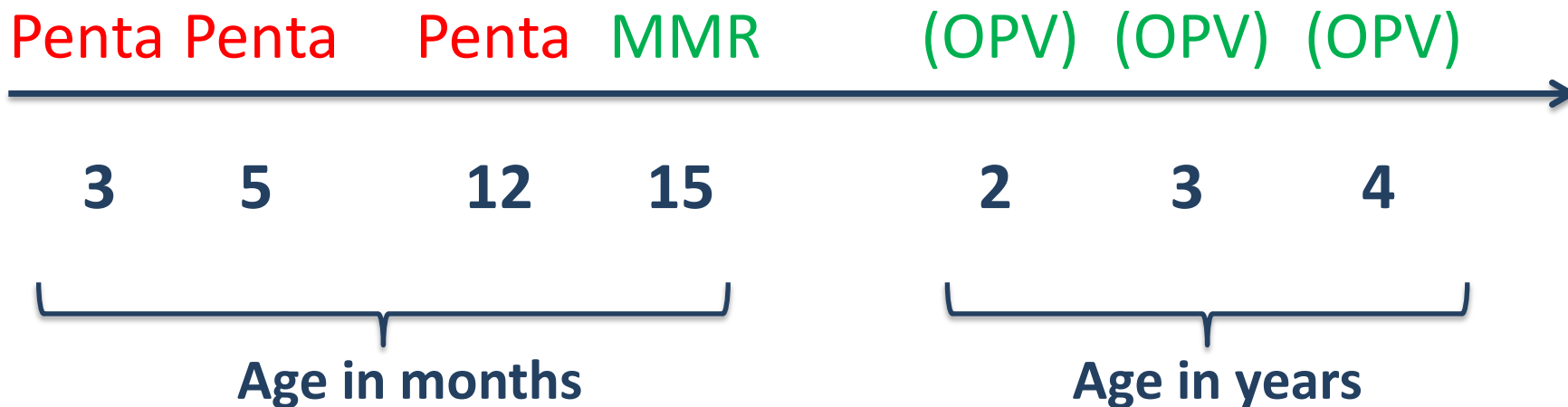
- *Live* Bacille Calmette-Guérin (BCG) and *live* measles containing vaccines: “The review suggested possible beneficial effects on all-cause mortality”
- *Inactivated* diphtheria, tetanus and pertussis vaccine (DTP): “The available data neither exclude nor confirm the possibility of beneficial or deleterious non-specific effects”
- Further research is warranted

Objective

To examine the potential non-specific effects of routine childhood vaccines on infectious disease hospital admissions among Danish Children.

Danish vaccination schedule

Jan 1997- Oct 2007



Penta = Diphtheria, tetanus, pertussis, polio, and *Haemophilus influenzae* type b

MMR = Measles, mumps, and rubella

OPV = Oral polio vaccine

DESIGN

Design: Nationwide retrospective cohort studies

Vaccinations



Hospital admissions due to infections

Admission with laboratory-confirmed RSV

“Vulnerability” factors

Age, maternal smoking during pregnancy, birth weight, prematurity, caesarean section, chronic diseases, previous admissions with infections, recent admissions

Socioeconomic factors

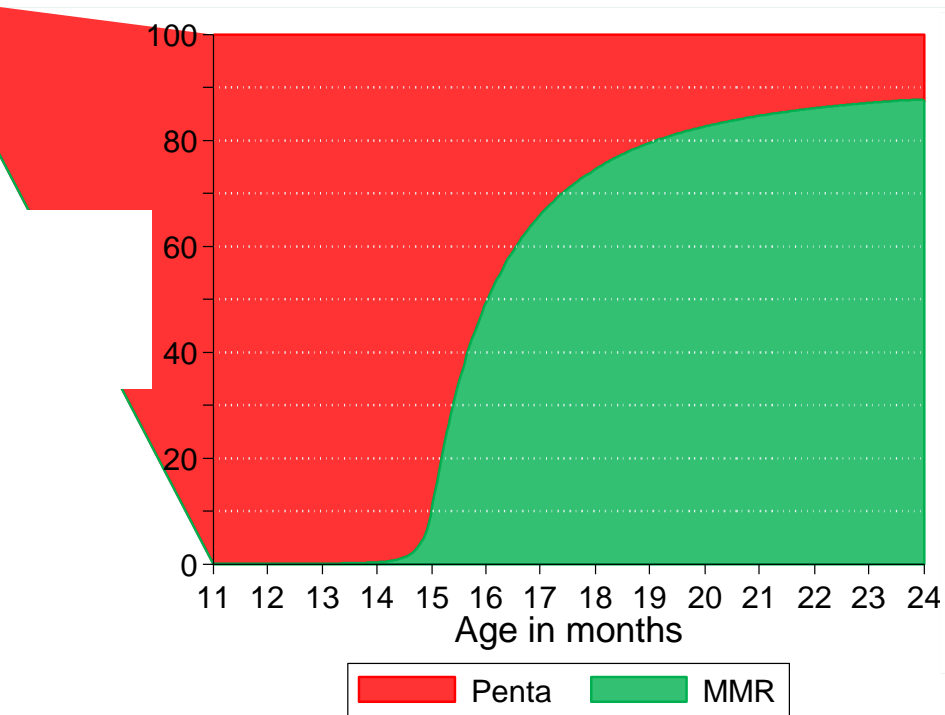
Maternal age, single parenthood, other children in the household, parental origin, household income and maternal education

External factors

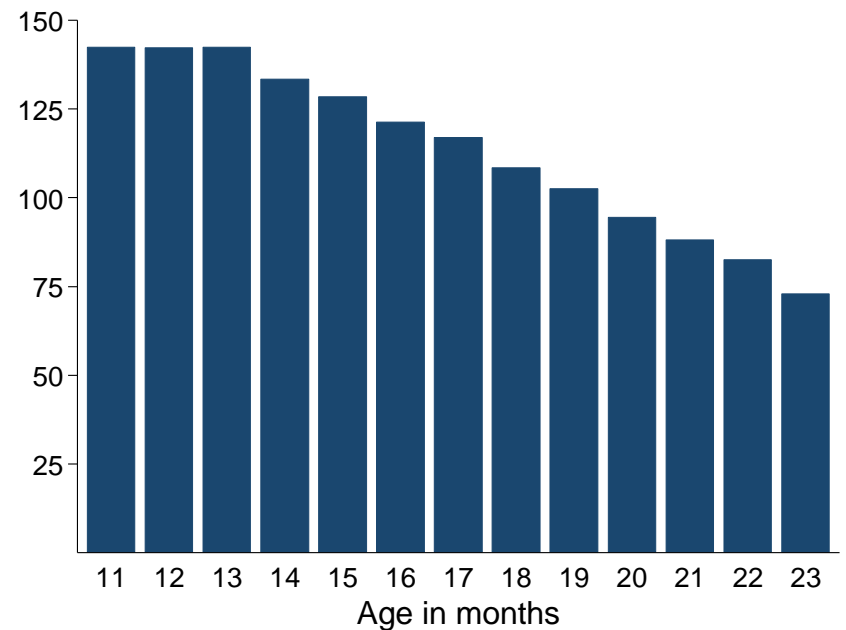
Season and calendar year

The importance of age

Distribution of vaccinations

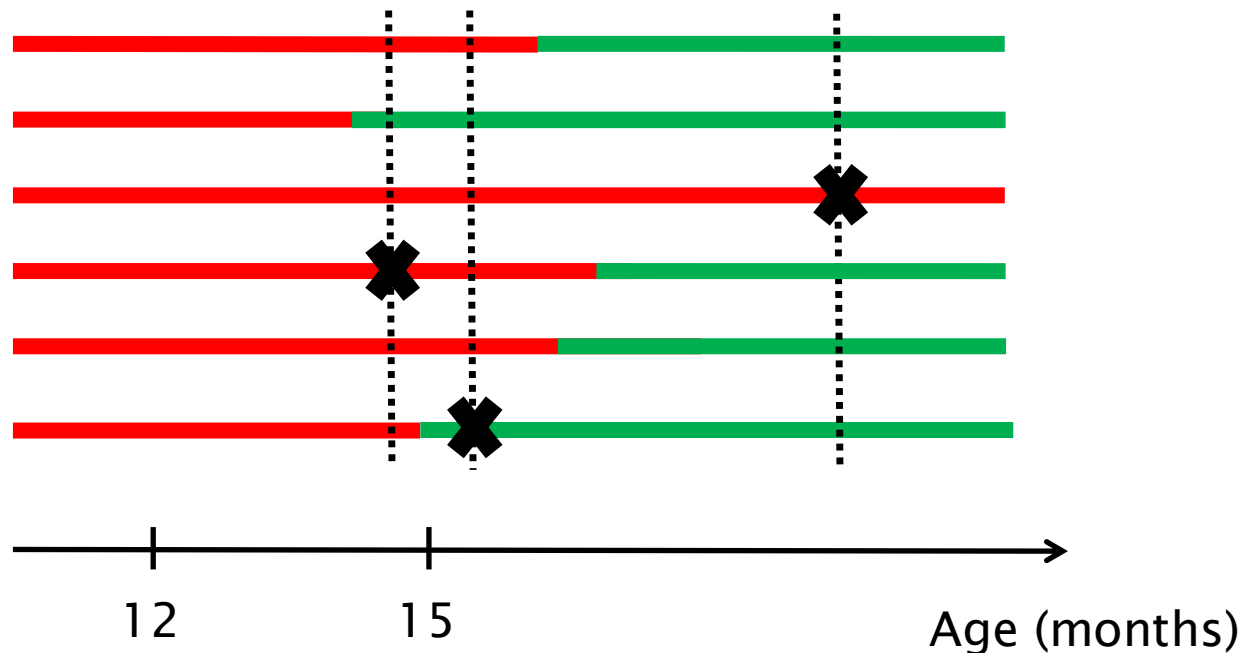


Admissions by age



Statistical analysis

- Cox proportional hazards model
 - Time scale: age

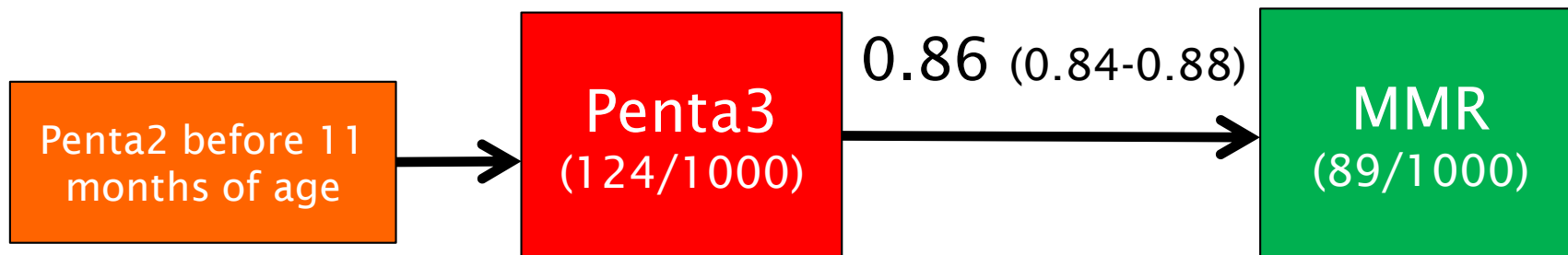


STUDIES OF MMR AND PENTA

MMR vs. Penta3

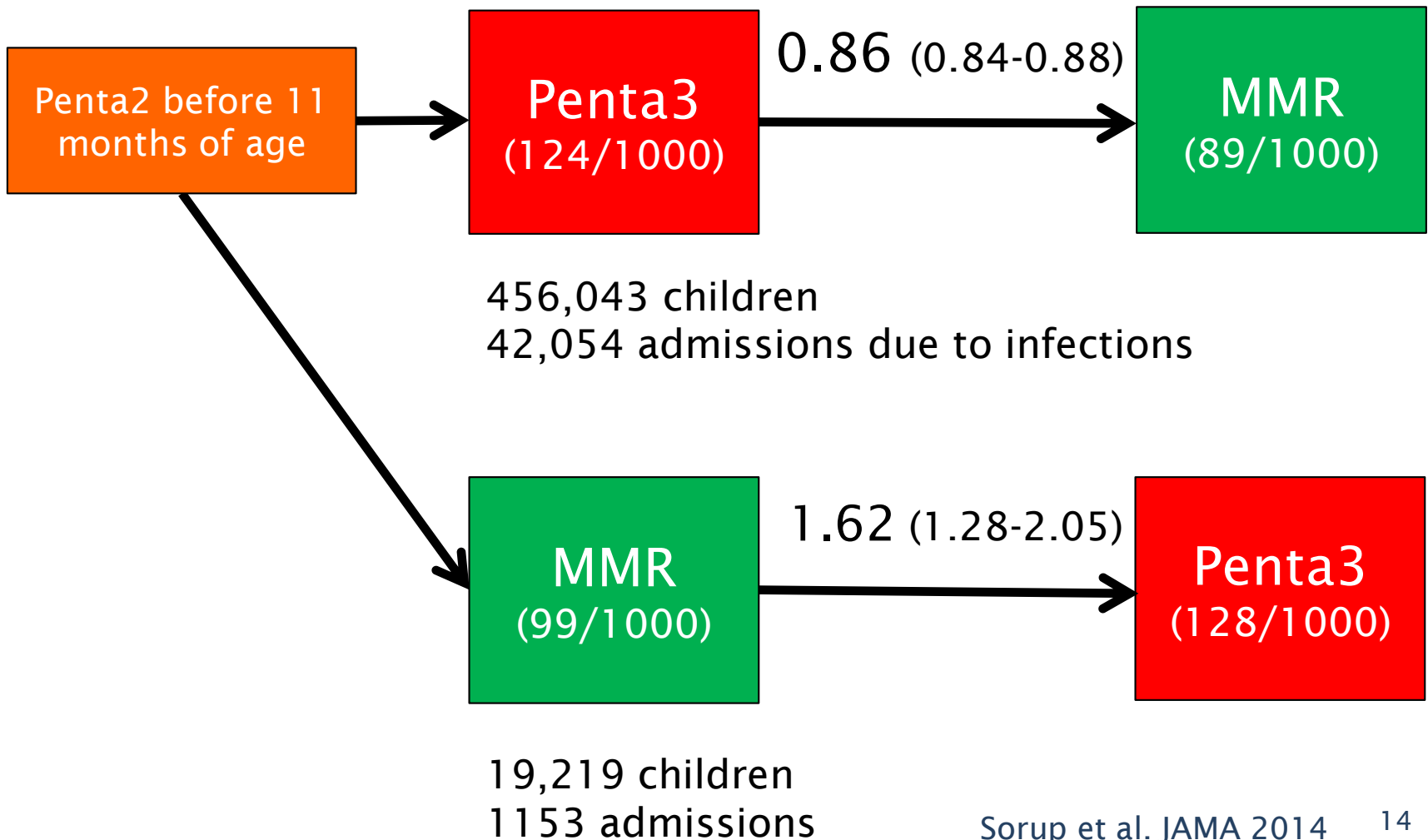
- Birth cohort 1997-2006
- **Penta2** before 11 months of age
- ~ 480,000 children
- Follow-up to 2 years of age (or other vaccines (OPV))

Results: All-cause infections

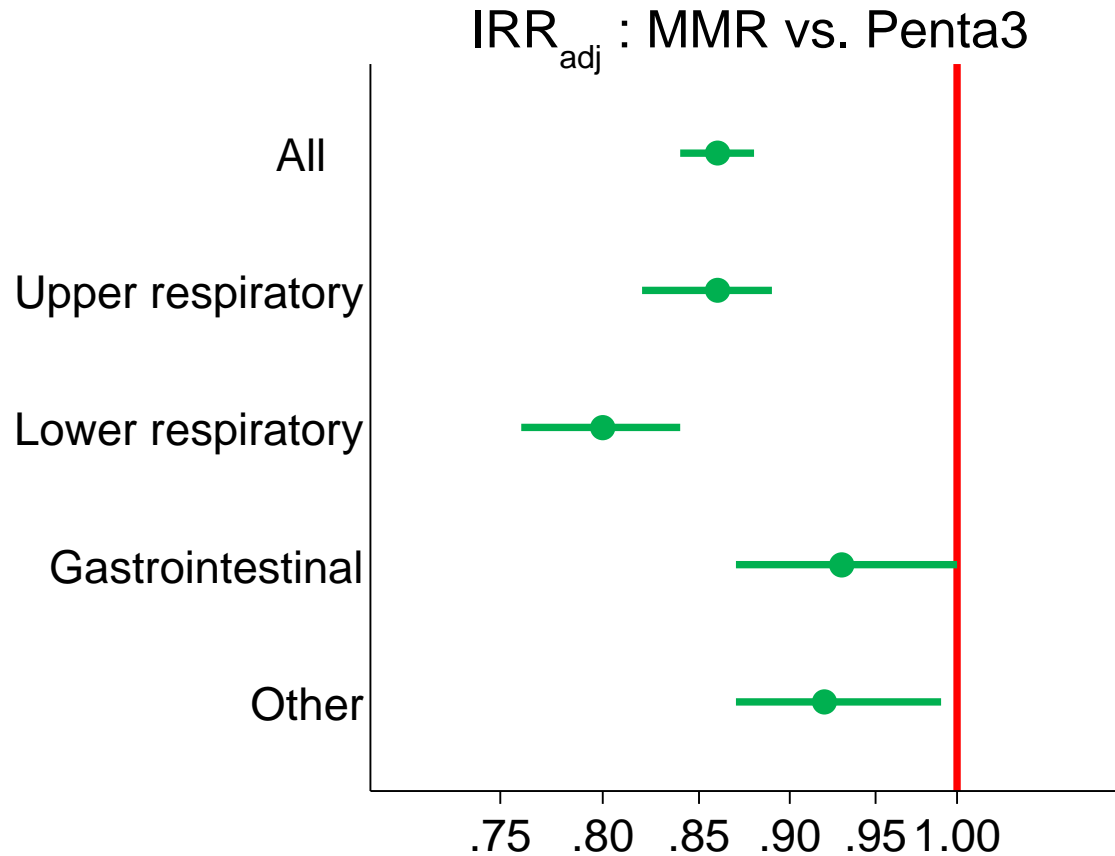


456,043 children
42,054 admissions due to infections

Results: All-cause infections



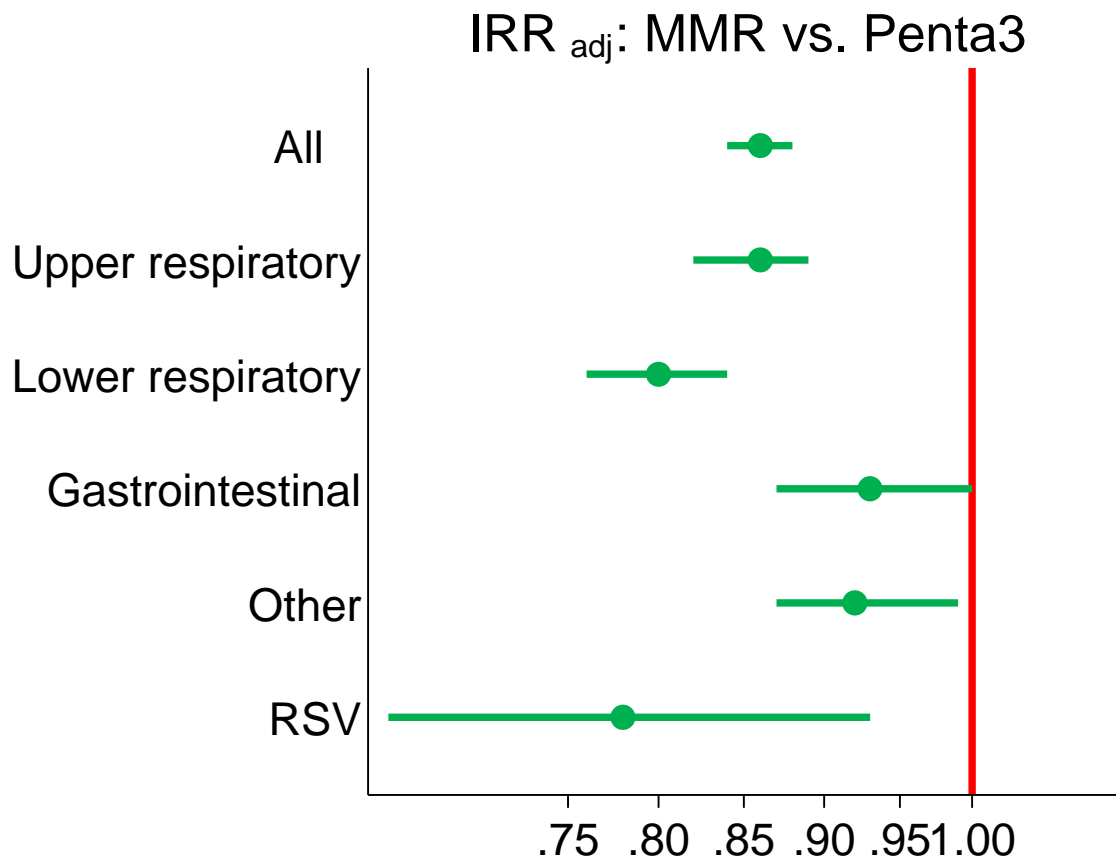
Results: Type of infection



MMR vs. Penta3 on RSV admissions

- Birth cohort 1997-2002
- Penta1, 2 and 3 at recommended ages (3, 5, and 12 months, respectively)
- ~ 170,000 children
- Follow-up to 2 years of age (or other vaccines (OPV))

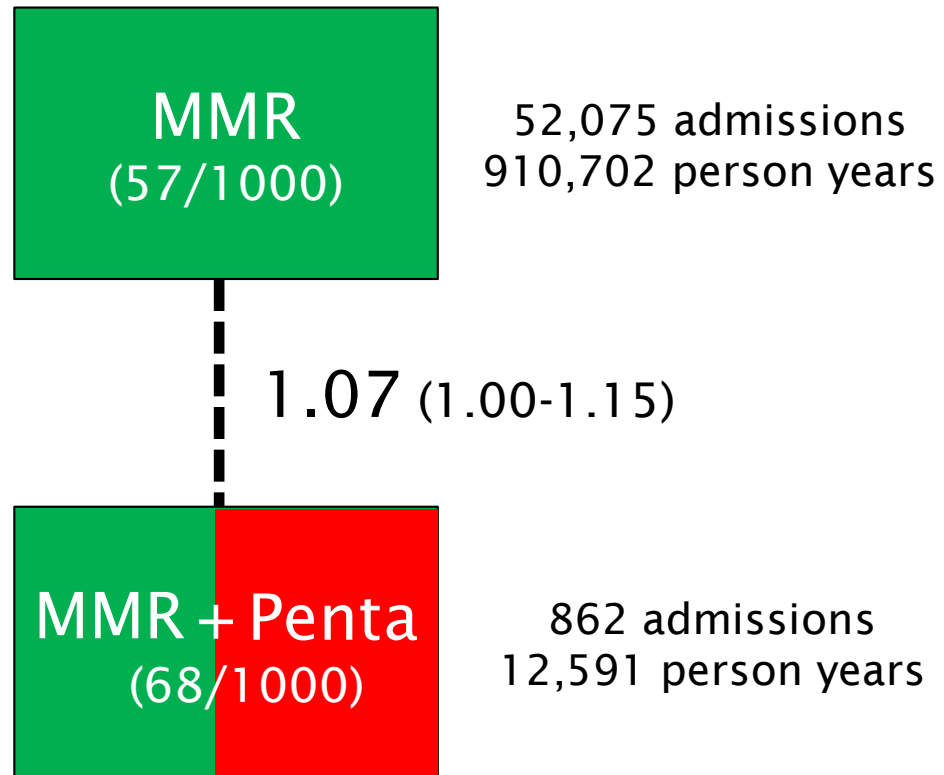
Results: Type of infection including RSV



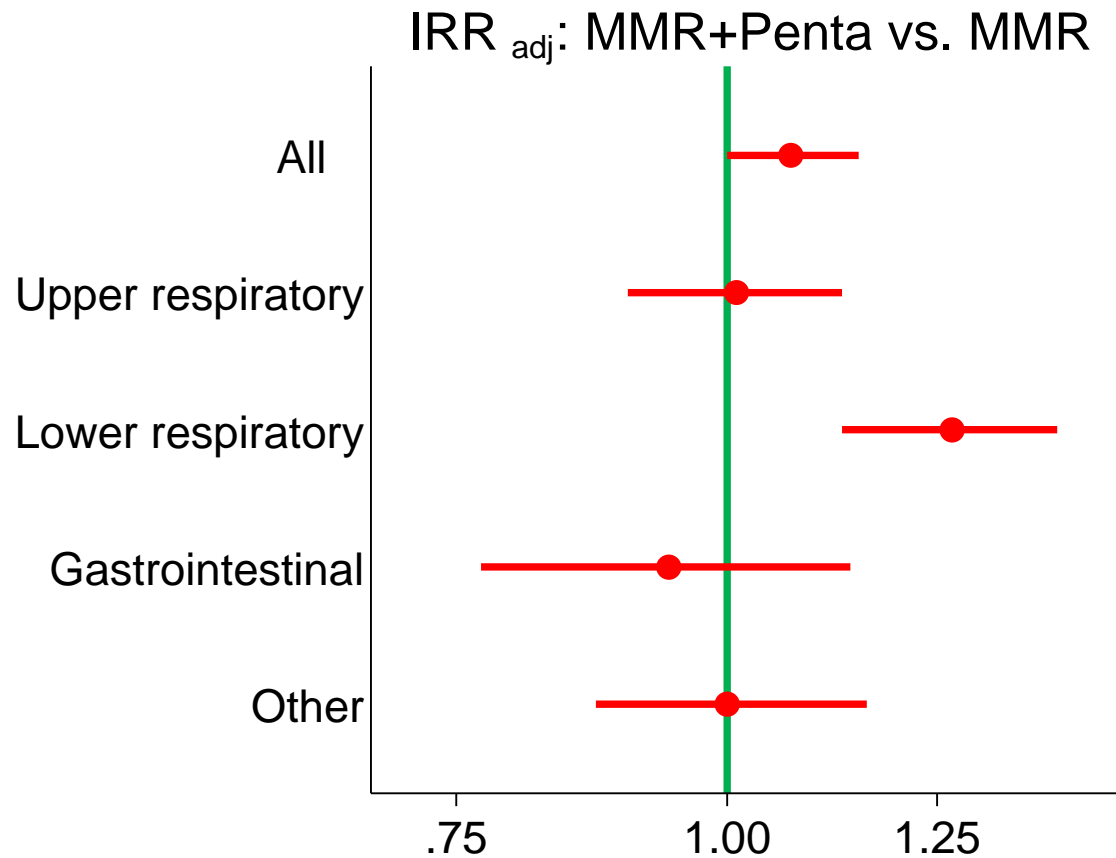
MMR+Penta vs. MMR

- Birth cohort 1997-2006
- Have received at least one dose of either Penta or MMR
- ~ 560,000 children
- Follow-up to 4 years of age (or other vaccines (OPV))

Results: All-cause infections



Results: Type of infection

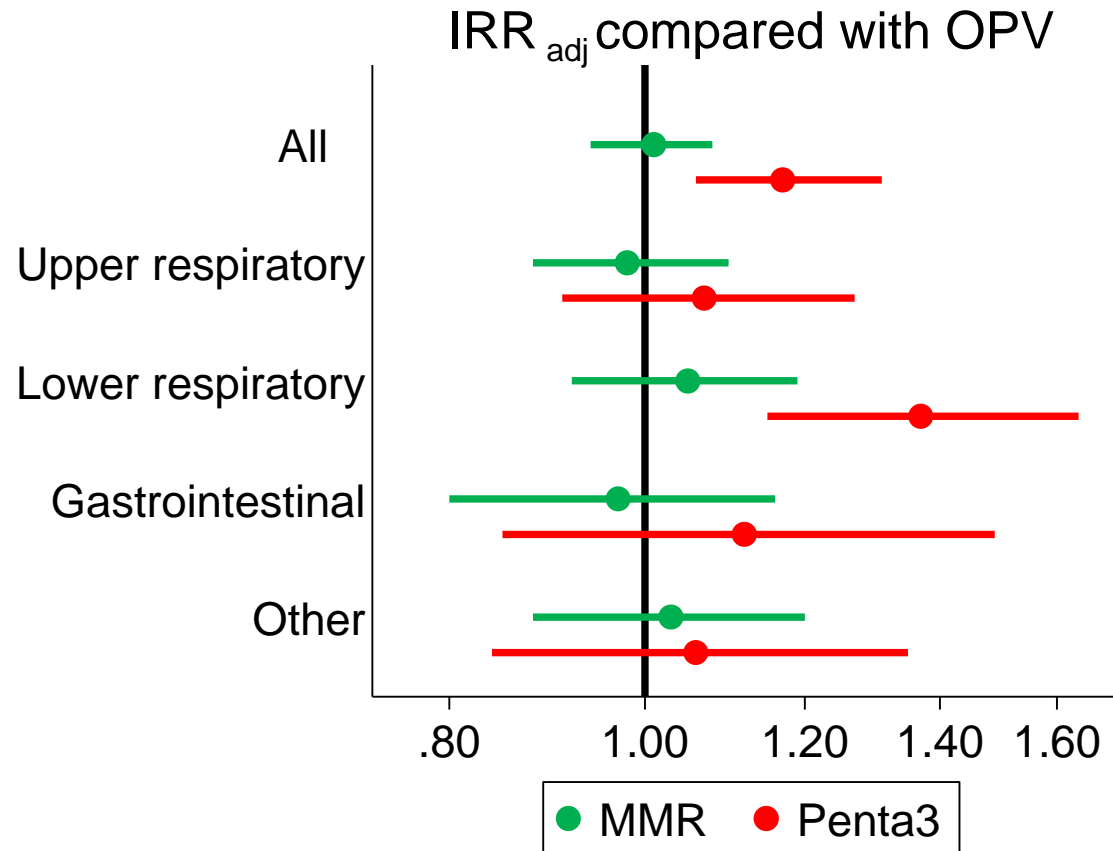


STUDY OF OPV

MMR and Penta3 vs. OPV

- Birth cohort 1997-1999
- Have received Penta3 before 2 years of age
- ~ 137,000 children
- Follow-up to 3 years of age

Results: Type of infection



CONCLUSIONS

- **MMR** as the most recent vaccine is associated with 14 % (12%-16%) lower rate of infectious disease admission compared with **Penta3**
 - Stronger for
 - lower respiratory infections: 20% (16%-24%)
 - Including laboratory-verified RSV: 22% (7%-34%)
- Simultaneous administration of **MMR** and **Penta** is associated with 27% (13%-42%) higher rate of admission for lower respiratory infections compared with **MMR** alone

- **Penta3** is associated with 37% (15%-64%) higher rate of admission for lower respiratory infections compared with **OPV**
- No difference between **MMR** and **OPV**

Acknowledgements

Christine S. Benn,^{1, 2, 3} Peter Aaby,^{1, 3} and
Henrik Ravn^{1, 3}

Anja Poulsen,⁴ and Lone Graff Stensballe⁴

Tyra G. Krause⁵

¹ Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Copenhagen, Denmark

² Institute of Clinical Research, University of Southern Denmark and Odense University Hospital, Denmark

³ Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau

⁴ The Child & Adolescent Clinic, Rigshospitalet, Copenhagen, Denmark

⁵ Department of Infectious Disease Epidemiology, Statens Serum Institut, Copenhagen, Denmark

Thank you! Any questions?



E-mail: sgs@ssi.dk