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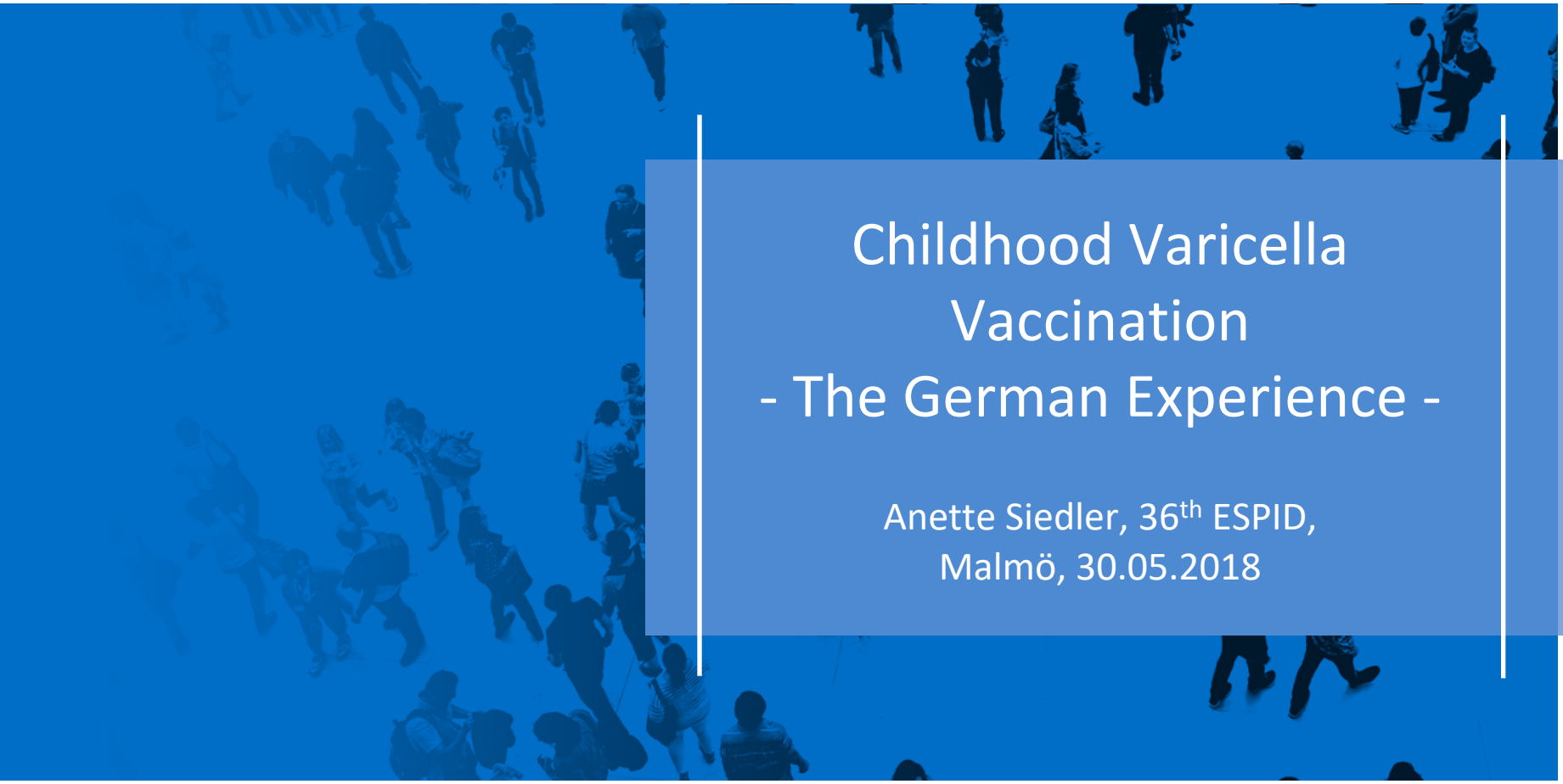


Childhood Varicella Vaccination
- The German Experience -

Anette Siedler, 36th ESPID,
Malmö, 30.05.2018

Experience of 14 years with childhood varicella vaccination

1. Why and how varicella vaccination?
2. What were the concerns?
3. What are the results?

   Vaccination coverage / acceptance

   Incidences

   Vaccine Effectiveness

   Effects on Herpes zoster
4. Conclusion

Vaccination system in Germany

Standing committee on vaccination (STIKO) develops evidence-based recommendations

Recommendations consider antigens rather than specific vaccines

Costs of vaccination are covered by statutory health insurances based on STIKO-recommendations (private insurances cover costs voluntarily)

85% of population statutory health insured,
15% in private insurances

De-centralised health care system:

Vaccines are administered mainly by physicians in private practices

Free vaccine market - physicians can choose from available vaccines

Pre-vaccination situation

Substantial disease burden due to varicella

- ~735,000 cases per year (one birth cohort)
- 2,000 hospitalized cases <16 yrs., majority in former healthy children [1]
- 1,600 cases in pregnancy, resulting in ~9 CVS cases [2]
- Sero-prevalence: 12% (age 1 yr.) and >90% (age 9+ yrs.) seropositive [3]

Risk of complications highest in infants, adults, pregnant women

- Secondary bacterial infections, i.e. superinfections of the skin, pneumonia
- CNS-involvement, i.e. meningo-encephalitis

Aim of vaccination:
Reduction of the burden of disease
Reduction of hospitalization and complications associated with varicella

1 Liese et al. Pediatr Infect Dis J (2008)27: 119
2 Enders, Miller. Cambridge University press (2000): 327
3 Wiese-Posselt et al. BMC Infectious Diseases (2017)17: 356

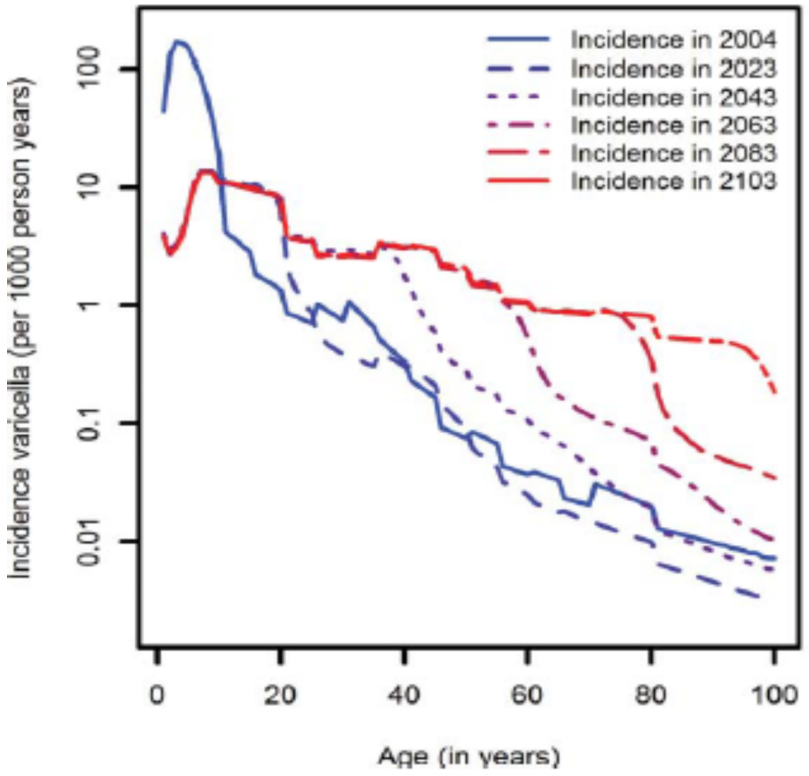
Recommendation of varicella vaccination in Germany

- **2004** - 1 dose for all children at 11-14 months (same time as MMR)
- **2006** - MMR-V available → 2 doses (according to product information)
- **2009** - 2nd dose for all children at 15-23 months (same time as MMR)
- **2011** - preference for separate 1st dose MMR + V
- **Individual catch-up**: unvaccinated children/adolescents <18 years without previous varicella → 2 doses

What may happen after introduction of vaccination against varicella?

- Low acceptance / low vaccine uptake
- Negative impact on MMR uptake
- Coverage rates are insufficient for herd protection (<80%)
- Disease-shift to older ages
- Higher burden of disease by more complicated cases
- Higher risk of infection for vulnerable groups
- Less opportunities to booster immunity
- More Herpes zoster

Modelled age-specific varicella incidence over 100 years:



Horn et al. Hum Vacc Immun (2016)12:1766

Varicella surveillance in Germany

2005-2017: Physician based countrywide Sentinel
(since 2011 funded by MoH)

- About 700 participating practices per month
- Aggregated monthly reports on all varicella (and herpes zoster) cases by age group (incl. zero)
- Case based: vaccinated cases, varicella associated complications

Since 2013: Statutory case based reporting by doctors and laboratories

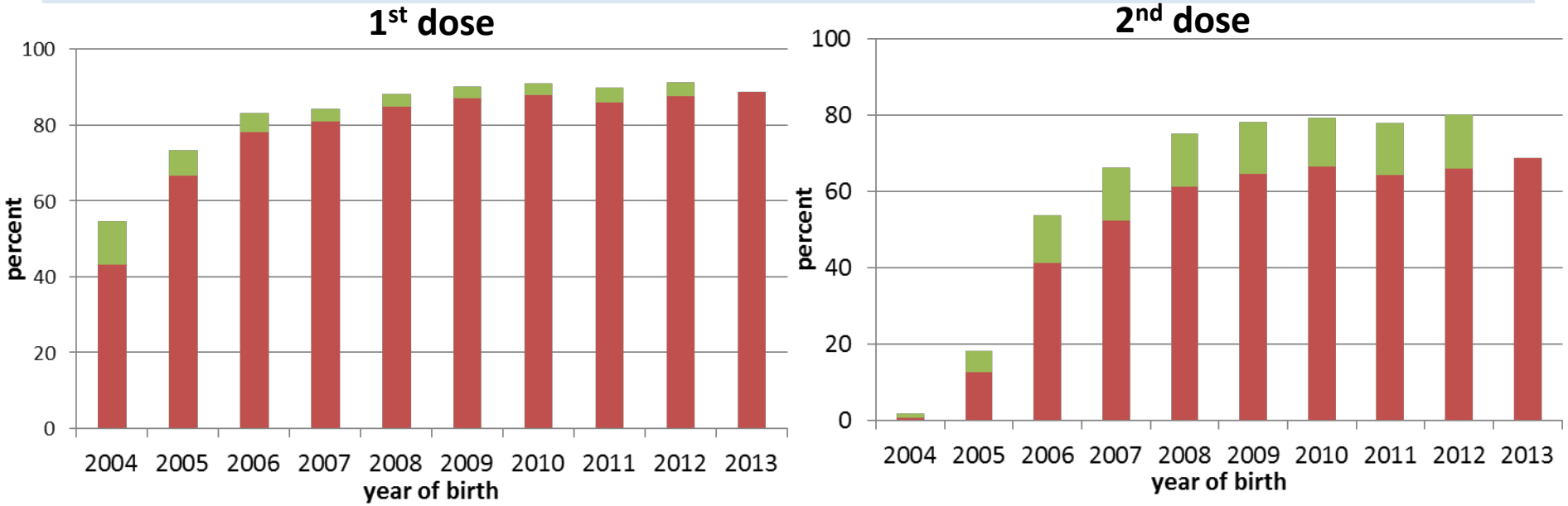
Since 1995: Federal Statistics on hospitalized cases by respective ICD-10 codes

Since 2004: Secondary data
billing data of physicians for statutory health insured patients

Monitor Vaccination coverage:
school entrance examination and billing data

Vaccine uptake (billing data) (1)

Countrywide varicella vaccination coverage at age 24 and 36 month by year of birth

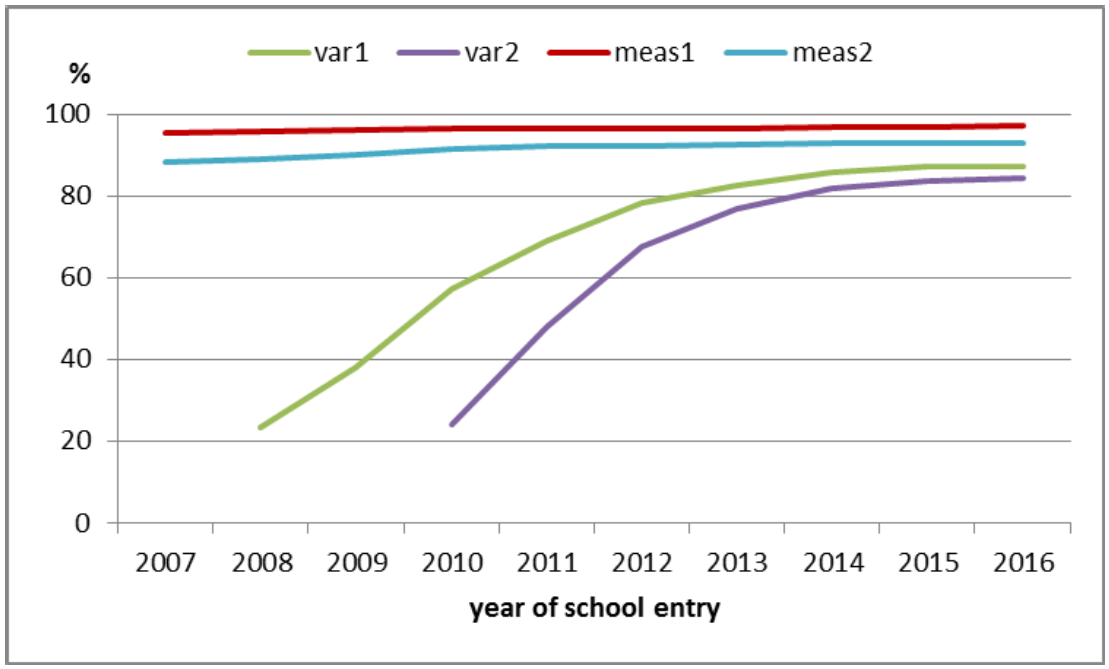


Rieck et al. Hum Vacc Immun(2014)10:476; Siedler, Rieck. Monatsschr Kinderheilkd(2018)

- Varicella vaccination successfully introduced and accepted
- However: later in age than recommended

Vaccine uptake (2) – school entry

Measles and varicella vaccination coverage at school entry (5-6 yrs.)



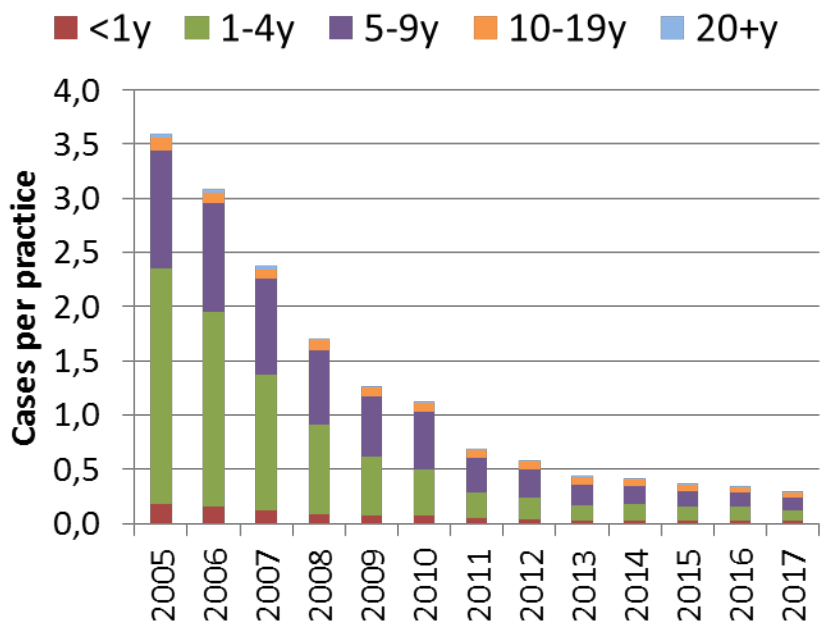
Varicella uptake 2016 - range by Federal state:
1st dose 75.9% - 94.7%
2nd dose 70.9% - 91.7%

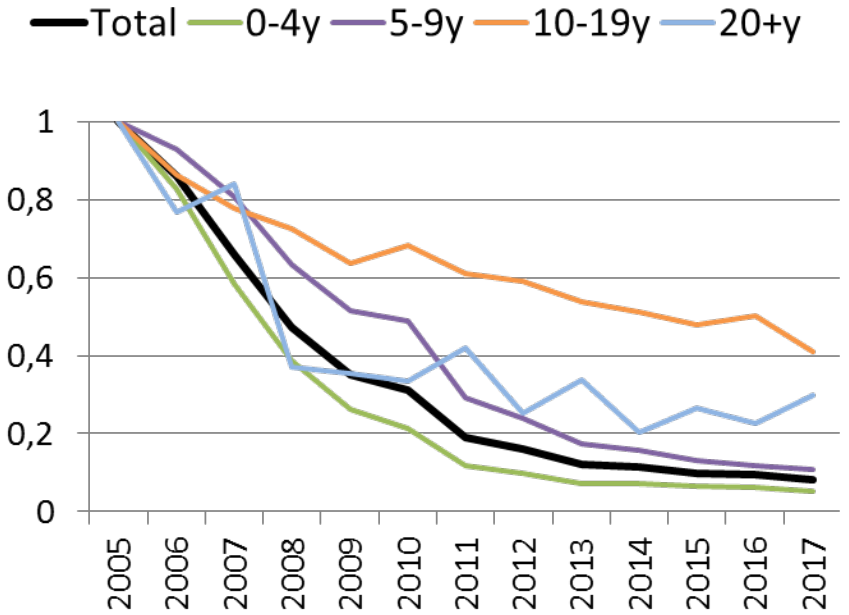
- Measles uptake >95% / >90% for 1st and 2nd dose – not impacted by varicella vaccination
- Varicella uptake in children >80% for 2 doses
- However: large regional differences

Epid Bull 16/2018

Incidences: Total and by age (sentinel data)

Varicella cases per practice by age group and by year and compared to 2005

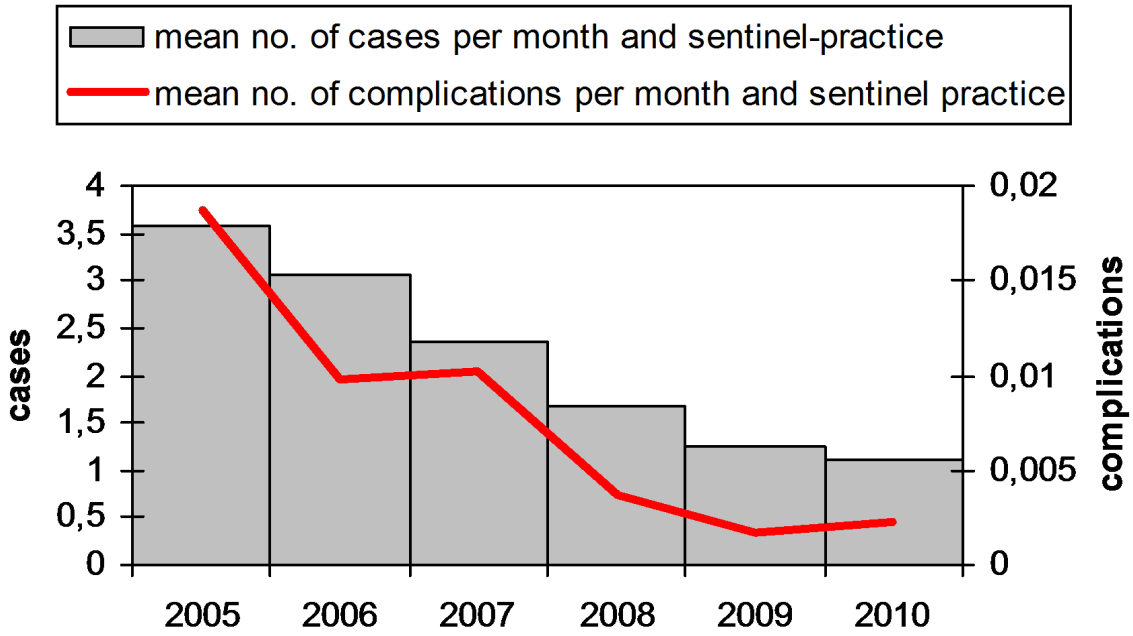




Source: RKI, unpublished

- 2005- 2017: Decrease of varicella incidence by ≥90% in total
- Strongest decrease in age groups <10 years
- However: decrease of varicella incidence also in age groups not eligible for vaccination → herd protection?

Incidences: Complications (sentinel data)



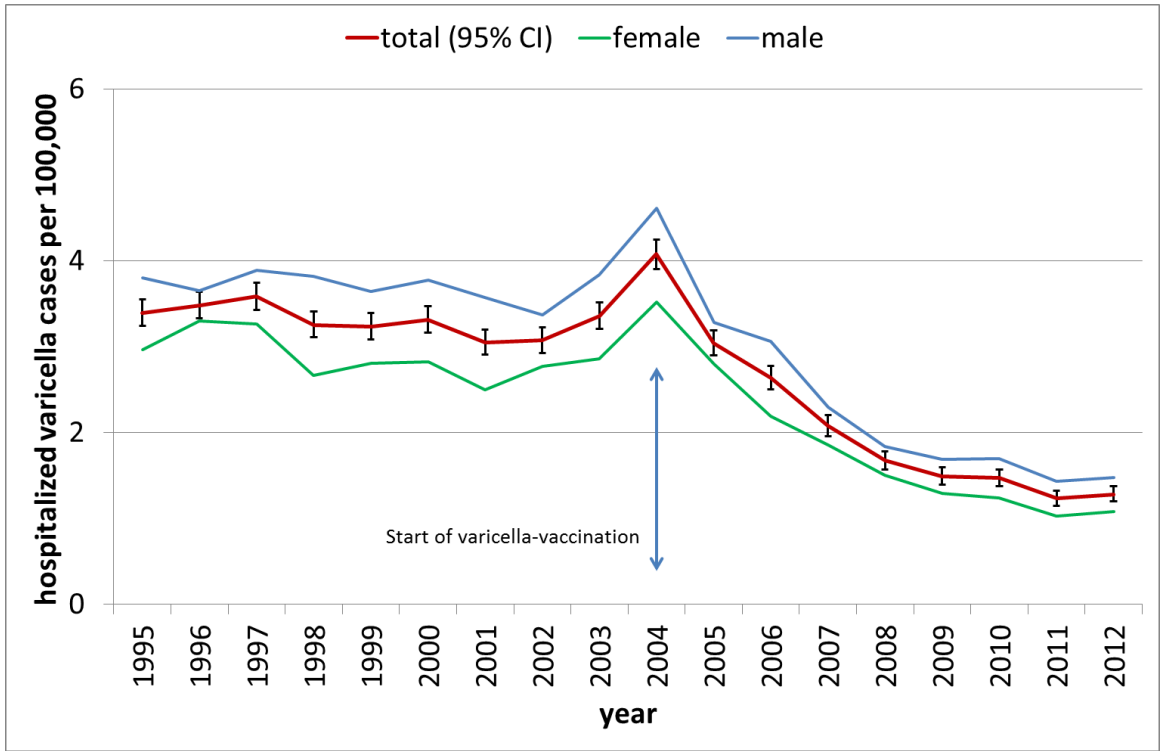
PIDJ 2010 (29) 9: 884-6

- 2005 - 2010: decrease of complications by 88%
- decrease of proportion of complications on all varicella cases

from 0.6 to 0.2%

Varicella Hospitalizations (Federal statistics)

Countrywide age-standardized varicella hospitalization incidence



- 2005-2012: Decrease of hospitalized cases by 42% in total
- Decrease of hospitalized cases by 62% in 1-4 years aged children

Siedler et al. Human Vacc Immun (2014)10: 3594

Vaccine Effectiveness (VE)

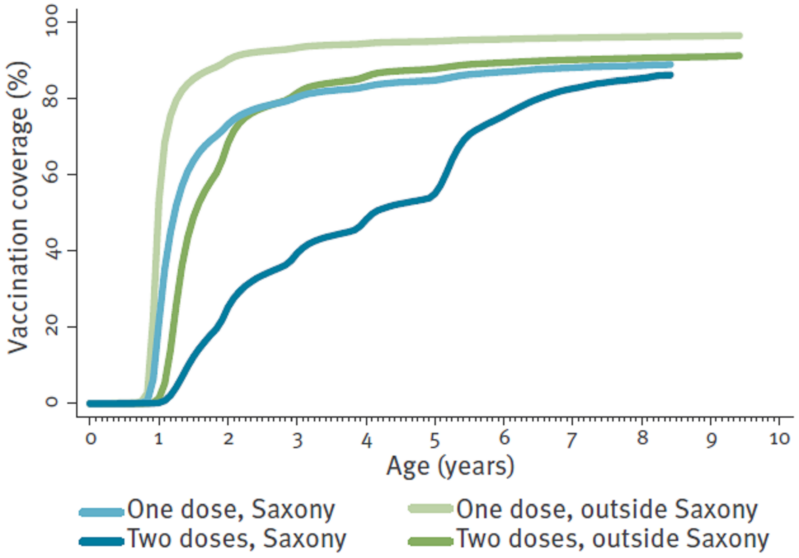
1. Outbreak investigation in 7 day-care-centers, 2008 [1] (n=1084 pre-school children; coverage 62% with ≥1 dose)	
Overall VE	**71%** (95% CI 57-81)
differed significantly → by severity **→ by vaccine brand (1 dose)** **→ by no. of doses**	**53%** (mild) ←→ **89%** (moderate disease) **56%** ←→ **86%** (not significant) **62%** (one dose) ←→ **94%** (2 doses)
2. Sentinel data 2009-2014 (screening method) [2]	
VE after 1 dose **VE after 2 doses** **Incremental VE of 2 doses**	**86.6%** (95% CI 85.2-87.9) **97.3%** (95% CI 97.0-97.6) **84.6%** → high additional effect of 2nd dose
3. Billing data 2006-2014 (time series analysis) [3]	
VE after 1 dose **VE after 2 doses**	**81.9%** (95%CI 81.4-82.5) **94.4%** (95%CI 94.2-94.6) → remained unchanged over observation period

1 Spackova et al. Vaccine (2011)28:686 .
2 Siedler et al. JPed(2016) 173: 202
3 Rieck et al. Eurosurv(2017)22(17)

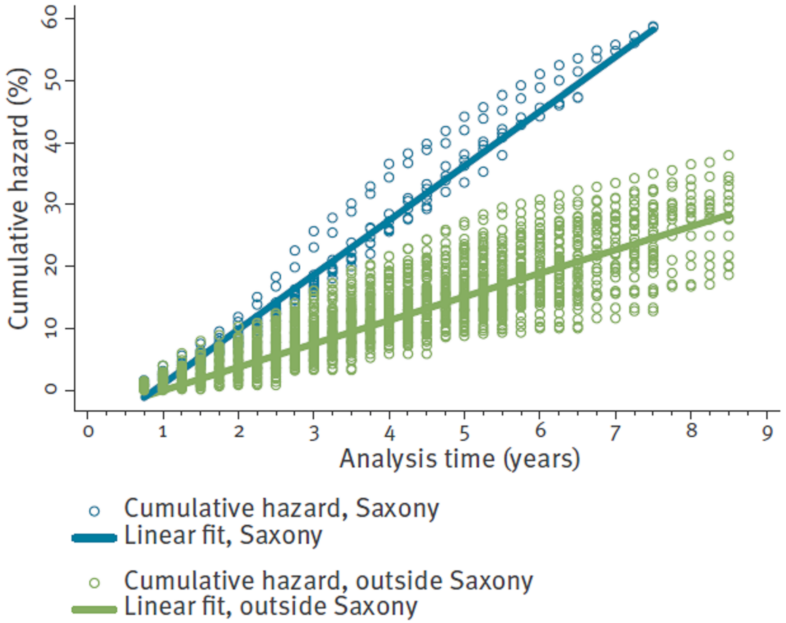
Indirect effects of vaccination (billing data)

Unvaccinated children had a twofold higher risk of acquiring varicella in regions with low vaccination coverage

Varicella Vaccination coverage in 2 regions



Cumulative hazard for varicella



Rieck et al. Eurosurv(2017)22(17)

Together with the results from sentinel-surveillance (decrease of age specific incidences): → strong indication for the presence of herd effects

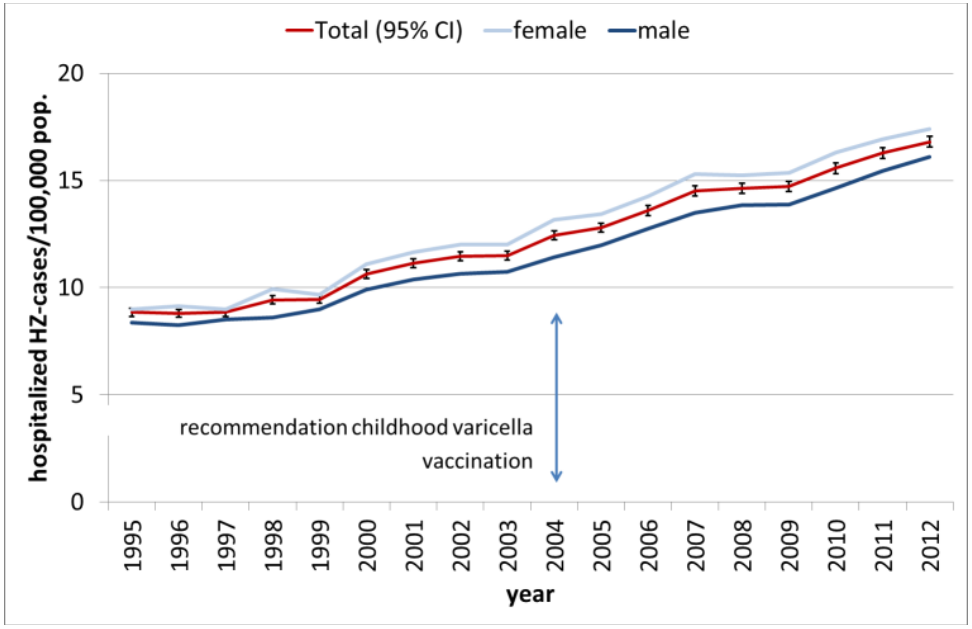
Impact of varicella vaccination on herpes zoster (HZ)

Sentinel data

- Increase of age-standardized consultation incidences since 2006
- Increase of age-specific consultation incidence in almost all age groups 20 years and older since 2012
- Decrease in age groups eligible for childhood varicella vaccination since 2006

Zoch et al. Hum Vacc Immun (2018)

Federal statistics on hospitalization

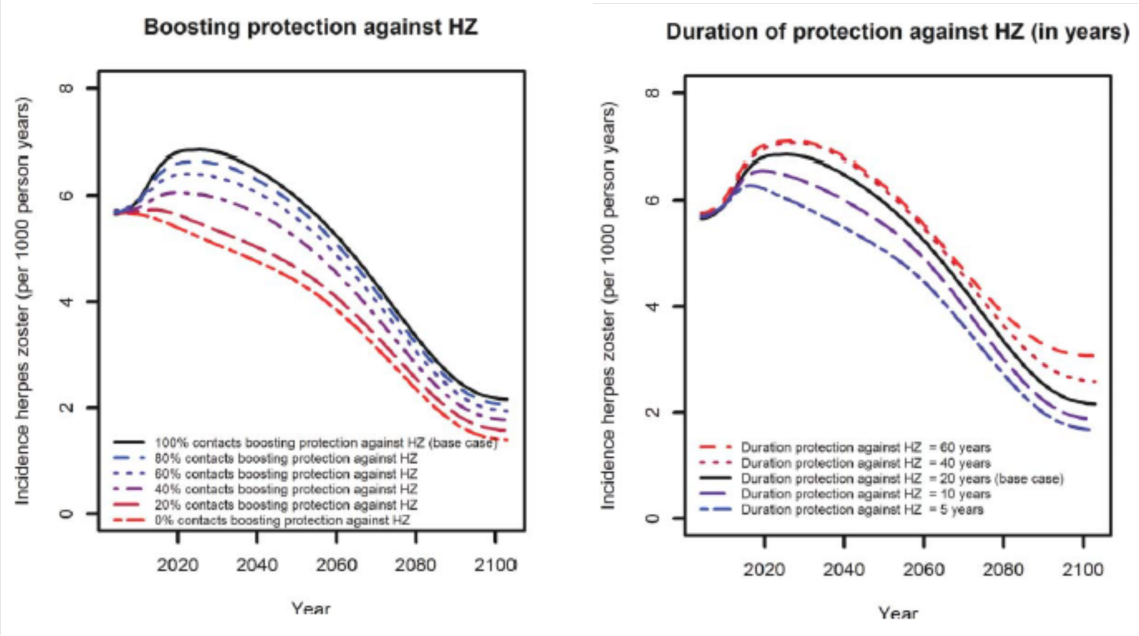


Age-standardized HZ- (hospitalization) incindence:

- started before introduction of childhood varicella vaccination
- continued steadily thereafter

Siedler et al. Hum Vacc Immun (2014)10: 3594

Impact of varicella vaccination on HZ (2)

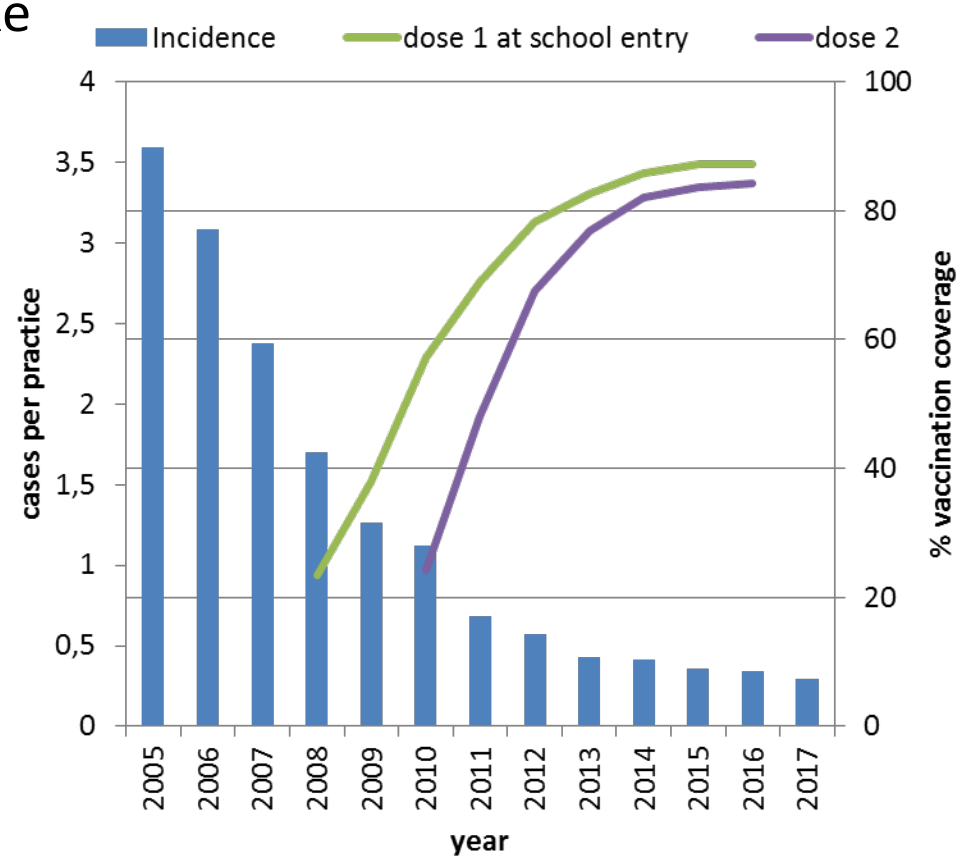


Horn et al. Hum Vacc Immun (2016)12:1766

- **Modelling:** Contact to varicella cases may or may not influence incidence of HZ, depending on assumptions on proportion of necessary contacts and on duration of protection
- **Systematic Review:** No consistent effects of varicella vaccination on zoster in meta-analysis (interrupted time-series) of epidemiological studies with at least 3 measure points before and after varicella vaccine introduction (unpublished data)

What did happen after introduction of vaccination against varicella?

- Good acceptance: vaccine uptake steadily increased
- Coverage rates sufficient for herd protection (>80%)
- Burden of disease decreased significantly
- No disease-shift to older ages
- Lower risk of infection for vulnerable groups
- Still opportunities to booster immunity
- Low incidence of breakthrough disease
- Herpes zoster less in children, more in adults (effect of vaccination?)



Conclusion

Varicella childhood vaccination – successful in Germany

Aims of vaccination achieved

No negative effects of the vaccination were observed

Coverage >= 80% has to be sustained

Continuous monitoring has to be ensured

Laboratory surveillance will play a greater role

Thank you for your attention