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Varicella vaccination in the Nordic Countries - pros and cons.

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Varicella vaccine

- Made from live attenuated varicella-zoster virus
- Minimum potency 1350 PFU
- Different manufacturers, different formulations
  - But all vaccines are based on OKA derived strains

Immunogenicity

- Infants below 2 years of age
  - One dose: 90 – 100 % seropositive (most studies 93 – 97 %)
  - Two doses: 99 – 100 % seropositive
- Adolescents and adults
  - 75 – 90 % after one dose
  - 95 – 100 % after two doses

Systemic adverse events

- Vaccine related fever in the second week, 7 – 10 days after vaccination (varicella-like rash 1 – 4 %)
- Febrile convulsions (more common after MMRV than after MMR+V)
- Serious adverse events only reported in immuno-compromised patients

Break through infections

- All studies of vaccinated cohorts in an unvaccinated society register some break through infections
- Incidence varies between 0.2 and 2.3 % per year
- Breakthrough varicella cases are less severe and less contagious than unvaccinated cases

Duration of protection

- Studies of vaccinated groups in unvaccinated populations show stable breakthrough rate and increasing titres through many years
  - Boosting through subclinical infection?

- Very limited (any?) knowledge about long term protection in a fully vaccinated population without circulating varicella

One or two dose program?

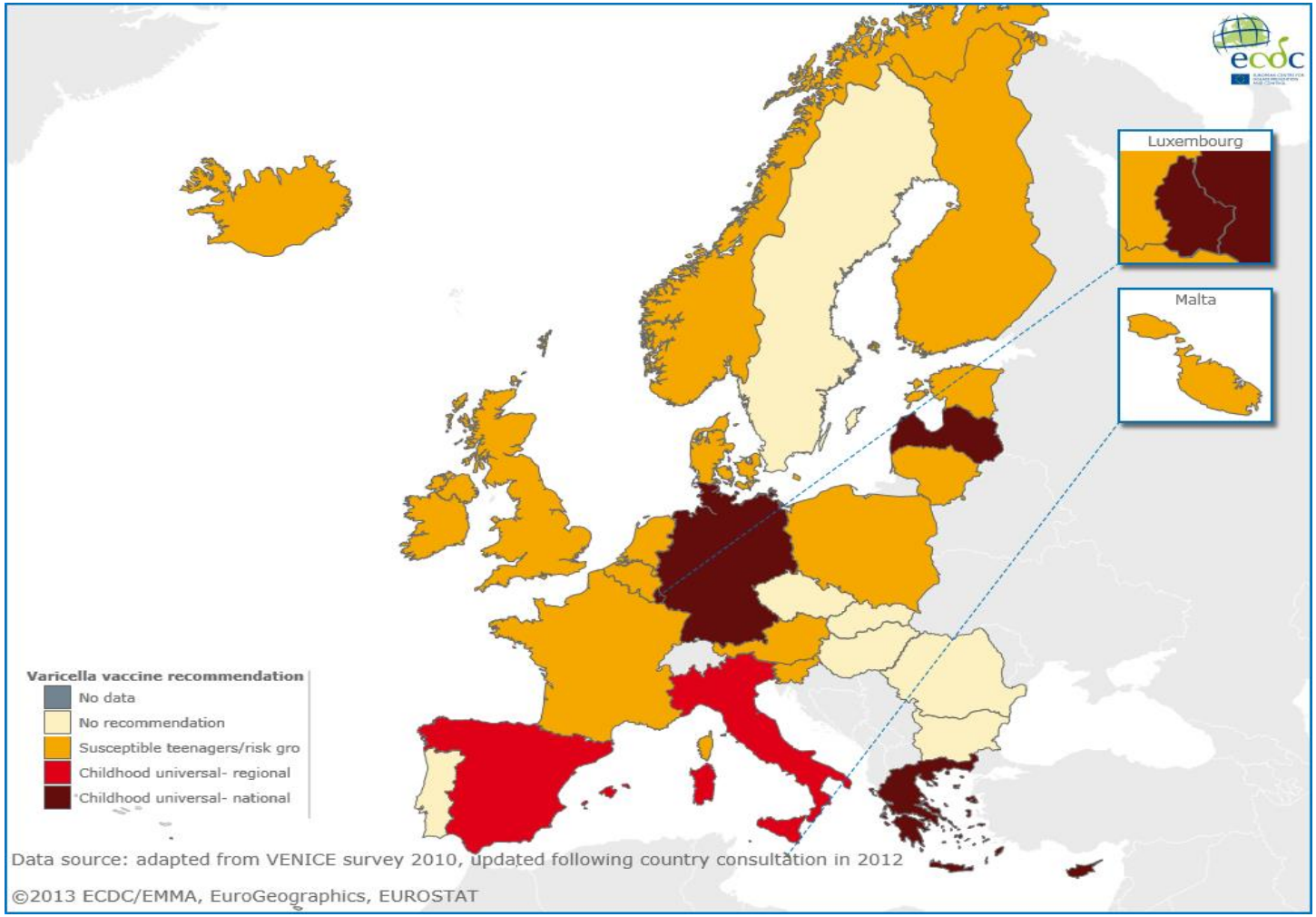
- One dose (US experience):
  - Significant decline in varicella during the first 7-8 years, then stable incidence rates
  - In settings with high transmission potential (schools), varicella outbreaks continued to occur in spite of high vaccination coverage
- Immunogenicity studies indicated that two doses give better protection than one
  - Second dose introduced before school start to stop outbreaks
- Timing of the second dose differs between countries depending on the vaccination schedule for MMR 2 (interval from 6 weeks to 3 – 5 years)

Effectiveness (vaccination programme)

- One dose:
  - 80 – 90 % (higher against severe disease)
- Two doses:
  - 90 – 95 %

Marin M et al. Pediatrics 2016

Use of varicella vaccine in Europe



What happens when the vaccine is introduced?

- Germany:
  - One dose 2004, 2 doses (4 - 6 weeks interval) 2009
  - Coverage around 80 % (higher for first dose)
  - Decrease in incidence 70 – 80 %
  - Decrease in complications 81 %
  - VE (outbreaks) 71 %

- Navarra:
  - 2 doses + catch up in 2007
  - Coverage 95 / 81 %
  - Decrease in incidence 93 %
  - Decrease in hospitalisations 73 %

Risks when introducing infant varicella vaccination program

- Moving varicella to higher age
  - Would increase the number of (severe) complications
  - Only relevant if the coverage is < 80 %
- Increase of herpes zoster in persons who have had varicella before the vaccination program started
  - What is really the relationship between varicella and zoster?

Evolutionary theory

- Latency is the varicella virus's way of survival
  - In small populations varicella would infect everybody and then disappear
  - Through latency, and the ability to be reactivated (zoster), the virus can survive

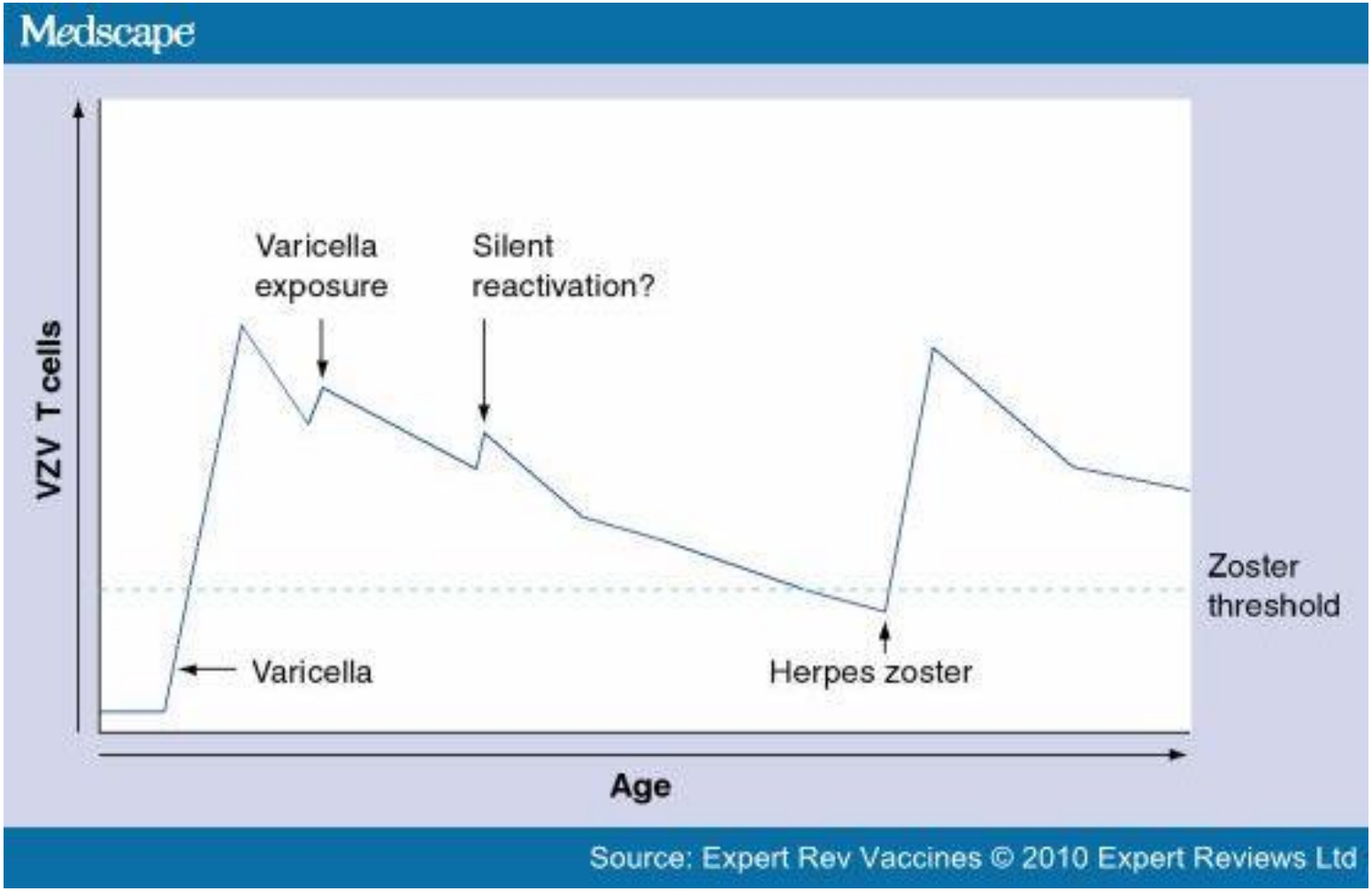
- In large populations, where the virus is continuously circulating, these reactivations are «unnecessary»
  - Contact with persons with varicella boosts the immunity, so zoster won't appear so easily

Hope-Simpson RE Proc R Soc Medicine1964

- Supported by studies of mothers of children with varicella and children with cancer and household exposure to varicella

Thomas SL et al. Lancet 2002

Present understanding of the role of boosting in zoster prevention

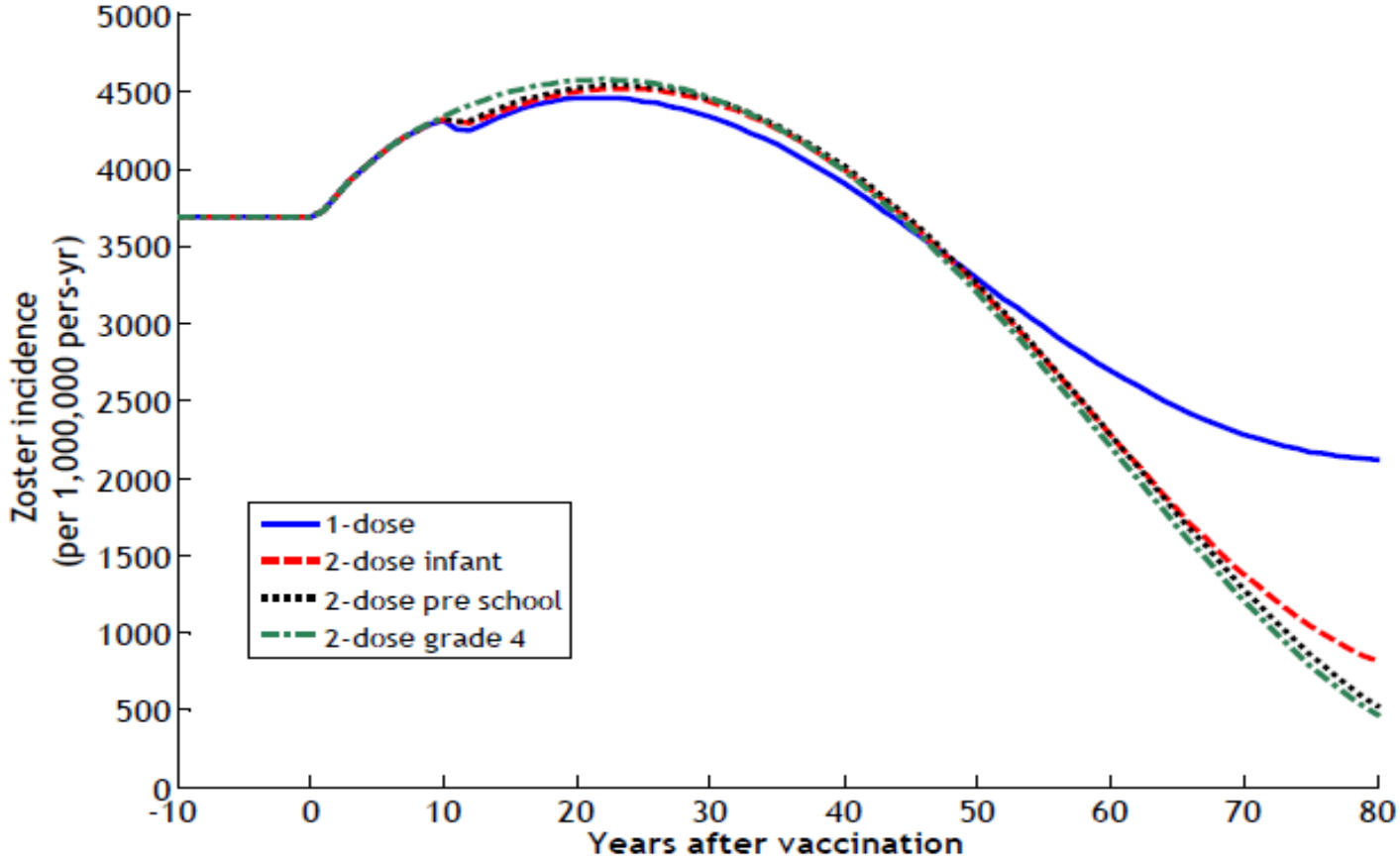


Potential impact of a vaccination program with high coverage (modelling)

- High coverage with varicella vaccine in a 2 dose program would quickly reduce the number of varicella cases
- Reduced boosting would increase the number of zoster cases, starting after 10 – 20 years of vaccination and continuing for at least 50 years (different in different models)
- The total burden of disease caused by VZV would increase, as zoster gives more severe and long-lasting disease than varicella

Impact of varicella vaccination

by efficacy, 90% coverage, Canada



Ref: Brisson *Vaccine*, 2010

Reports from countries with varicella vaccination programs

- USA:
  - Many studies show increase in zoster, but this started before varicella vaccination. Impact of vaccine uncertain
  - Vaccine coverage in the US was low during the first years. A potential effect should really be manifest about now

- Australia:
  - Zoster increasing
  - According to some studies this started before, in others after vaccine introduction
  - Vaccine introduction 2005 – too early to have clear results

Varicella infant vaccination program – pros and cons

PROS:

- Varicella will almost disappear
- Complications and hospitalisations due to varicella will be considerably reduced
- The Nordic countries will reach high coverage, therefore no reason to fear shift of disease to higher age

CONS

- The number of zoster cases and the cases of post herpetic neuralgia may increase considerably after some years
- If so the total burden of disease caused by VZV will increase
- The modifying effect of the present zoster vaccine is uncertain due to short duration of protection