Herpes zoster vaccination
The Netherlands

Hester de Melker

Department NIP/Epidemiology and Surveillance unit (EPI)
Center of Infectious Disease Control, RIVM, The Netherlands
Varicella zoster virus (VZV)

- Herpes virus (HHV3 or VZV)
- Primary infection: varicella
- Latency in trigeminal and spinal ganglia
- After reactivation: herpes zoster
Herpes zoster – clinical manifestations

› Life-time risk 23-30% in Europe
  - 50% of ≥85-year-old people

› Symptoms:
  - Pre-eruptive stage: pain (+/- headache, general malaise, photophobia)
  - Eruptive stage: painful rash (2-4 weeks)
  - Chronic HZ infection: herpetic neuralgia (>4 weeks – years)

Herpes zoster

Possible complications

- Postherpetic neuralgia
- Bell's palsy
- Ramsay-Hunt syndrome
- Eye involvement
- Meningitis
- Deafness
- Encephalitis
- Transverse myelitis

Health Council

• Disease burden
• Effectiveness
• Safety
• Acceptability
• Cost-effectiveness
Estimated incidence per 100,000 population of episodes of varicella and herpes zoster in 2020 versus mean 2010–2019 by age group GP consultations
## Epidemiology (Netherlands)

<table>
<thead>
<tr>
<th>Period</th>
<th>Incidence per 100,000</th>
<th>Absolute number per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2021</td>
<td>0.1</td>
<td>25</td>
</tr>
<tr>
<td>2000-2020</td>
<td>2.5</td>
<td>400</td>
</tr>
<tr>
<td>2010-2020</td>
<td>520</td>
<td>88,000</td>
</tr>
</tbody>
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Sources: Nivel Primary Care data, Dutch Hospital Data, Statistics Netherlands (Primary cause of death)
Disease burden VZV and herpes zoster in DALYs (Netherlands)

Fig. 2. Ranking of the four diseases by estimated burden at population level (DALYs/year) and individual level (DALYs per 100 cases) in the period 2010–2013, comparing the two disease burden calculation methods (GPM/OAM).


Vaccines

› Recombinant zoster vaccine: RZV
  – Recombinant vaccine, adjuvanted
  – 2 doses
  – FDA approval: 2017

› Zoster vaccine live: ZVL
  – Live-attenuated vaccine
  – 1 dose
  – FDA approval: 2006

Health Council 2016:
“Currently only one vaccine available which provides insufficient protection”
RZV- Efficacy

- Two large trials: ZOE-50 and ZOE-70
  - In total, almost 28,000 participants
  - Pooled analysis of adults ≥70 years (n=16,596)
  - Efficacy against herpes zoster in adults ≥70 years: 91.3% (95%CI 86.0-94.9)

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  - Efficacy against postherpetic neuralgia: 88.8% (95%CI 68.7-97.1)

RZV – Efficacy

Information after Health Council advice

› Long-term follow-up
   - 7413 participants aged ≥50 years
   - Efficacy against herpes zoster: >84% between 5-7 years after 2-dose vaccination

RZV – Effectiveness

Information after Health Council advice

- Cohort study among vaccinated and unvaccinated Medicare beneficiaries ≥65 years (n=15,589,546) (1)
  - VE for incidence of HZ was 56.9% and 70.1% for 1 and 2 doses of RZV
  - VE for PHN was 76.0% and 66.8% for ophthalmic HZ after 2 doses of RZV
  - The 2-dose VE in patients with immunocompromising chronic conditions was 64.1% versus 70.9% in immunocompetent patients

- Cohort study in 4,769,819 patients >50 years (2)
  - VE for incidence of HZ was 85.5% in RZV recipients 50–79 years and 80.2% in RZV recipients ≥80 years

RZV - Safety

› ZOE-50

- Reactogenicity subgroup (n=8926)
  - Solicited or unsolicited symptoms within 7 days after vaccination: 84.4% of vaccine group vs 37.8% of placebo group
  - Grade 3 symptoms (preventing normal everyday activities) in 17.0% of vaccine group vs 3.2% of placebo group
    - Most common symptoms: pain at injection site, myalgia
  - Median duration of symptoms: 1-3 days
  - Serious adverse events within 3.5 years after vaccination: 9% of vaccine group vs 8.9% of placebo group (most unrelated to vaccine)

RZV - Safety

- **ZOE-70**
  - Reactogenicity subgroup (n=1025)
    - Solicited or unsolicited symptoms within 7 days after vaccination: 79.0% of vaccine group vs 29.5% of placebo group
    - Grade 3 symptoms (preventing normal everyday activities) in 8.5% of vaccine group vs 0.2% of placebo group
      - Most common symptoms: pain at injection site, fatigue
      - Median duration of symptoms: 1-3 days
    - Serious adverse events within 4 years after vaccination: 16.6% of vaccine group vs 17.5% of placebo group
RZV - Safety

› ZOE-70 + ZOE-50 (1)
  - Long-term follow-up (5-7 years)
  - N=7413
  - No deaths or other SAEs causally related to vaccination

› Several trials in immunocompromised people
  - RZV is safe and effective (2)

› Postlicensure safety monitoring in VAERS during the first 8 months of use (3.2 million RZV doses distributed), showed a safety profile consistent with prelicensure efficacy trials (3)

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RZV - Acceptability

- Dutch Health Council judges benefits greater than risks
  - Also in immunocompromised people
Cost-effectiveness analysis (The Netherlands)

Interventions

- Intervention strategies:
  - No vaccination
  - Shingrix® (2 doses within 2 months)
  - Zostavax® (single dose)
  - Zostavax® (single dose with booster after 10 years)

- Population:
  - Cohorts of 50, 60, 70, 80 year-olds
  - Vaccination coverage of 50% (restricted to immunocompetent individuals)

Model overview

- Model structure: Markov model with decision tree, using annual cycles
- Time horizon: 15 years
- Discount rates: 4% for costs, 1.5% for QALYs
- Perspective: societal
- Model inputs herpes zoster:
  - Clinical outcomes: national registries (GP sentinel surveillance NIVEL, DHD, Statistics Netherlands)
  - Vaccine efficacy: randomized clinical trials
  - QALY loss and costs: Dutch prospective cohort study
  - Vaccine administration costs: Dutch flu tariff of €11,79 per dose

Effects and cost-effectiveness

Shingrix® superior in reducing HZ burden

Cost-effectiveness depends on age (vaccine price at 50% of list price)

Gained QALYs per 100,000 persons

- 50 years
- 60 years
- 70 years
- 80 years

Recent review (2023) of publications of past 5 years

Conclusions:

- Out of 18 selected studies, RZV vaccination against herpes zoster and post-herpetic neuralgia is cost-effective in 15.
- In the 15 studies establishing RZV cost-effectiveness, RZV is always cost-effective or frequently cost-saving in direct comparisons to ZVL.
- RZV was found cost-saving in several immune-compromised populations.

Nikolaos Giannelos, Cheryl Ng & Desmond Curran (2023) Cost-effectiveness of the recombinant zoster vaccine (RZV) against herpes zoster: An updated critical review, Human Vaccines & Immunotherapeutics, 19:1, 2168952, DOI: 10.1080/21645515.2023.2168952
Health Council advice (2019)

› Positive advice regarding vaccination of elderly
  - Disease burden
    ▪ Postherpes neuralgia
    ▪ But disease burden lower compared to e.g. pneumococcal disease
  - High vaccine effectivity
  - Cost-effectiveness
    ▪ Vaccinate 60-year olds (health benefits and cost-effectiveness)
    ▪ Catch-up campaign
  - Troublesome but shortterm side effects -> give communication
Acknowledgement

Alies van Lier, Pieter de Boer, Caren van Roekel