Postherpetic neuralgia: an update

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Promotor Dr. A Kumar
Human Herpesviruses (HHV)

HHV family

Alpha-HHV
- HSV* (HHV-1, -2)
- Primary infection: varicella (chickenpox)*

Beta-HHV
- VZV† (HHV-3)
- Reactivation: herpes zoster (shingles)*
- (HHV-6A, -6B)
- (HHV-7)

Gamma-HHV
- EBV‡ (HHV-4)
- CMV§ (HHV-5)
- KSHV¶ (HHV-8)

*HSV = herpes simplex virus
†VZV = varicella-zoster virus
‡EBV = Epstein-Barr virus
§CMV = cytomegalovirus
¶KSHV = Kaposi’s sarcoma-associated herpesvirus

Postherpetic neuralgia

- Most frequent chronic complication of herpes zoster
- Most common neuropathic pain resulting from infection

- Definitions
  - pain > 90 days after appearance zoster rash
  - pain after resolution rash
  - pain > 30 days appearance zoster rash

- “Pain” = neuropathic → burning, allodynia, hyperesthesia

- Reduced quality of life, physical functioning, psychological well-being → drug dependency, depression, suicide
Epidemiology

Annual age-specific number of HZ patients with at least one GP consultation per 100 000.

Fig. 2. Annual age-specific number of herpes zoster (HZ) patients with at least one general practitioner (GP) consultation per 100 000 (Scientific Institute of Public Health data, 2006–2008). As the observed rates for ages 102 and 103 are very high (8402 and 15248/100 000, respectively), these points are not presented in this plot because it would make the plot less informative. Only patients for whom information on age and/or gender was available, are included (97.8%).

Age-specific incidence rate of herpes zoster in North America, Europe and Asia-Pacific.
Incidence of pain over time after the onset of herpes zoster.

Incidence of Pain over Time after the Onset of Herpes Zoster. Shown are the proportions of patients with any pain, clinically significant pain, and severe pain in a study involving 566 patients with a mean age of 66 years (range, 58 to 75). Clinically significant pain was defined by a score of more than 30 on a visual-analogue scale that ranged from 0 to 100, with 100 indicating maximal pain. Severe pain was defined by a score of more than 70 on the same scale. I bars denote 95% confidence intervals. Data are from van Wijck.

Independent risk factors HZ

- **VZV-specific cell-mediated immunity ↓**
  - Older age (> 50y)
  - Chronic lung disease, renal failure, and liver disease
  - Suppressed immune systems
    - malignancy
    - HIV
    - bone marrow or solid organ transplantation
    - immunosuppressive medications

Independent risk factors PHN

- Older age
- Presence of severe rash
- Rash duration before consultation
- Greater acute pain severity
- Limitation in performing usual activities prior to HZ


Pathophysiology PHN

- Two pathophysiologic mechanisms contribute to the development of PHN.
  - Sensitization
    - peripheral: acute injury leads to ongoing discharge and hyperexcitability of nociceptor
    - central: prolonged nociceptor discharge leads to enhanced dorsal horn response to afferent neurones with expansion of receptive field
    - Explains allodynia and hyperesthesia in presence of minimal sensory loss
  - Deafferentation
Pathophysiology PHN

• Two pathophysiologic mechanisms contribute to the development of PHN.
  o Sensitization
  o Deafferentation
    • VZV reactivation in dorsal root ganglia leads to inflammation and neural damage. This loss of afferent neurones leads to spontaneous activity in deafferenated central neurones.
    • Autopsy studies by Watson et al.
      • We report here 5 cases, 3 with severe post-herpetic neuralgia (PHN) and 2 with no persistent pain. The findings of dorsal horn atrophy and cell, axon and myelin loss with fibrosis in the sensory ganglion were found only in patients with persistent pain. Marked loss of myelin and axons in the nerve and/or sensory root were found in cases with and without pain.
Fig. 1. Case 1. This demonstrates atrophy of the dorsal horn of the spinal cord on the affected side (left side of photograph). This loss is due in part to loss of myelin as evidenced by the reduced darker staining of the central area of the dorsal horn compared with the control (unaffected side). MBP, × 2.5.
Fig. 2. Case 1. Marked loss of myelinated nerve fibers in left T6 sensory root (picture on left), compared with the opposite (control) side. MBP, ×10.

Treatment herpes zoster

• Antivirals
  o no effect on incidence of PHN

• Corticosteroids (oral)
  o no effect on incidence of PHN

• Standard analgesia

• Epidural corticosteroids?
The PINE study of epidural steroids and local anaesthetics to prevent PHN

Proportion of patients with pain over time

Treatment PHN

- Currently no disease-modifying therapy for PHN, thus treatment is based on symptom control
- Elderly population → polypharmacy, comorbidity
- First line
  - topical lidocaine
  - voltage-gated calcium channel blockers: gabapentin, pregabalin
- Second/Third line:
  - tricyclic antidepressants: amitriptyline, nortriptyline, desipramine
  - opioids: tramadol, morphine, oxycodone
  - topical capsaicin

<table>
<thead>
<tr>
<th>Agent</th>
<th>Average Effective Dose in Clinical Trials</th>
<th>Starting Dose</th>
<th>Dose Adjustment</th>
<th>Number Needed to Treat (95% CI)†</th>
<th>Side Effects</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical treatments</strong></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Lidocaine patch</td>
<td>5%; up to 3 patches/day</td>
<td>Maximum of 3 patches/day for a maximum of 12 hr</td>
<td>2.0 (1.4–3.3)²⁰</td>
<td>Local erythema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capsaicin cream</td>
<td>0.075%; 4 applications/day</td>
<td>NA</td>
<td>3.3 (2.3–5.8)²⁰</td>
<td>Pain on application, local erythema, rash</td>
<td>Avoid eyes and nose</td>
<td></td>
</tr>
<tr>
<td>Capsaicin patch</td>
<td>8%; application time of 30–90 min</td>
<td>NA</td>
<td>11.0 (6.1–62.0)²²</td>
<td>Pain on application, local erythema, rash; systemic adverse events in &lt;5% of study participants‡</td>
<td></td>
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<tr>
<td><strong>Oral treatments</strong></td>
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<tr>
<td>Gabapentin</td>
<td>2572 mg/day</td>
<td>100 mg 3 times daily</td>
<td>Increase each of the 3 daily doses by 100–300 mg every 3–7 days as tolerated; maximum dose is 1800 mg/day, but unlicensed dose of up to 3600 mg/day is used by some clinicians</td>
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<td>Pregabalin</td>
<td>398 mg/day</td>
<td>50–75 mg twice daily</td>
<td>Increase to 300 mg daily after 3–7 days, then by an additional 150 mg daily every 3–7 days as tolerated, to a maximum dose of 600 mg daily</td>
<td>4.2 (3.4–5.4)²⁰,²³</td>
<td>Same as with gabapentin</td>
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<td>Tricyclic antidepressants (off-label use)</td>
<td>Amitriptyline, 95 mg/day; nortriptyline, 122 mg/day</td>
<td>10–25 mg at bedtime</td>
<td>Increase by 10–25 mg every 3–7 days as tolerated to 75–150 mg/day with caution as side effects permit; if blood level of active drug and its metabolite is &gt;100 ng/mL, continue dose adjustment very cautiously</td>
<td>2.6 (2.1–3.5)²⁰</td>
<td>Sedation, dry mouth, blurred vision, weight gain, urinary retention</td>
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<td>Morphea and oxycodone</td>
<td>Morphine, 90 mg/day; oxycodone, 45 mg/day</td>
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<td>Morphea, 2.8 (2.0–4.6), oxycodone, 2.5 (1.7–4.4)²⁰</td>
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<td>There is risk of abuse and uncertainty over long-term effectiveness and safety§</td>
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<td>Tramadol</td>
<td>298 mg/day</td>
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<td>Increase by 50–100 mg/day in divided doses every 3–7 days as tolerated, to maximum dose of 400 mg/day (300 mg/day in patients &gt;75 yr of age)</td>
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<td>Same as with morphea and oxycodone; also, avoid concomitant use of SSRIs, SSNRI, tricyclic antidepressants</td>
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* Data are primarily from Hempenstall et al.²⁰ and Dworkin et al.²¹ NA denotes not available, SSNRI selective serotonin- and norepinephrine-reuptake inhibitors, and SSRI selective serotonin-reuptake inhibitors.
† This is the number needed to treat for one person to have at least 50% pain relief.
‡ Systemic adverse events include diarrhea, nausea, vomiting, fatigue, infections, musculoskeletal disorders, hypertension, dizziness, and headache.
§ See also national guidelines on opioid use for chronic pain²⁴,²⁵
## Topical therapy

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Topical therapy

• **Lidocaine patch**
  - No evidence from good quality randomised controlled studies
  - Individual studies indicated that it was effective for relief of pain

• **Capsaicin patch**
  - High-concentration topical capsaicin generates more participants with high levels of pain relief than does control treatment with low-concentration capsaicin
  - High cost, unknown risks, application in hospital
# Voltage-gated calcium channel blockers

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Avoid in patients with renal insufficiency |
| Pregabalin  | 398 mg/day                             | 50–75 mg twice daily | Increase to 300 mg daily after 3–7 days, then by an additional 150 mg daily every 3–7 days as tolerated, to a maximum dose of 600 mg daily | 4.2 (3.4–5.4)$^{20,23}$ | Same as with gabapentin |
Voltage-gated calcium channel blockers

- Gabapentin, pregabalin
  - Clinical trial evidence supports the use
  - Still only a minority of people achieved acceptably good pain relief, but it is known that quality of life and function improved markedly with the outcome of at least 50% pain intensity reduction
# Tricyclic antidepressants

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Tricyclic antidepressants

- Amitriptyline
  - Has been first-line treatment for many years
  - Fact that there is no supportive unbiased evidence for a beneficial effect is disappointing, but has to be balanced against decades of successful treatment

- Nortriptyline and Desipramine
  - Little evidence to support use of nortriptyline
  - Studies were methodologically flawed, largely due to small size, and potentially subject to major bias
## Opioids

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† This is the number needed to treat for one person to have at least 50% pain relief.

‡ Systemic adverse events include diarrhea, nausea, vomiting, fatigue, infections, musculoskeletal disorders, hypertension, dizziness, and headache.

§ See also national guidelines on opioid use for chronic pain.²⁴,²³
Opioids


- Short-term studies provide only equivocal evidence
- Intermediate-term studies demonstrate significant efficacy of opioids over placebo, but these results are likely to be subject to significant bias
Miscellaneous

- **Intrathecal glucocorticoids**

- **New drug targets**
  - TRPV1 receptor (cfr capsaicin)
  - NMDA receptor; drugs targeting this receptor have not been found to be effective in the treatment of PHN
  - Cannabinoids
  - Calcium channels (other subunits than those targeted by pregabalin and gabapentin)
  - The norepinephrine (NE) transporter is a new target, and drugs that interact with this molecule are still at Phase I of development
  - Drugs that target the aminopeptidase N (APN) and neutral endopeptidase (NEP) are still in early phases of research
  - Neurotrophic factors and growth factors are potentially interesting targets because it is thought that the loss of nerve fibres plays an important role in the pathogenesis of PHN.
Conclusion

• Need for more randomized, controlled trials!
• In general, effects of treatment tend to be suboptimal; even the most effective treatment results in clinically significant analgesia (e.g., ≥50% pain relief) in fewer than half of patients.
• Assessing different pain phenotypes?
Prevention PHN

- Varicella vaccine?
- Zoster vaccine?
Does varicella vaccination prevent herpes zoster?

Following a successful vaccination programme, the incidence of varicella in Australia was modelled to decrease and the incidence of zoster to increase, based on a theoretical decrease in boosting of zoster immunity following a decrease in wild varicella virus circulation due to vaccination.


**Decreased varicella and increased herpes zoster incidence at a sentinel medical deputising service in a setting of increasing varicella vaccine coverage in Victoria, Australia, 1998 to 2012.**
Kelly HA¹, Grant KA, Gidding H, Carville KS.
Deputising service consultations for varicella, age standardised and by age group, Victoria, Australia, 1998–2012

Herpes zoster vaccination

• Hypothesis: if the increased incidence of herpes zoster that accompanies aging results from the natural waning of immunity, active immunization may prevent or attenuate zoster in the elderly.

The Shingles Prevention Study (1998 – 2001)

- Randomized, double-blind, placebo-controlled trial of an investigational live attenuated Oka/Merck VZV vaccine ("zoster vaccine", number of plaque-forming units 14 times that of the varicella vaccine)
- 38,546 adults 60 years of age or older
- Primary end point: burden of illness due to herpes zoster
- Secondary end point: incidence of postherpetic neuralgia

The Shingles Prevention Study (1998 – 2001)

Table 2. Effect of Zoster Vaccine on the Burden of Illness in Herpes Zoster in the Modified Intention-to-Treat Population. *

| Group of Subjects | Vaccine Group | Placebo Group | VE_{BOI} (95% CI) \$ \%
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of Confirmed Cases/No. of Subjects</td>
<td>BOI Score$</td>
<td>Incidence per 1000 Person-Yr$</td>
</tr>
<tr>
<td>All subjects</td>
<td>315/19,254</td>
<td>2.21</td>
<td>5.42</td>
</tr>
</tbody>
</table>

The zoster vaccine reduced the burden of illness due to herpes zoster by 61.1 percent (P<0.001)

| Sex     | Vaccine Group | Placebo Group | VE_{BOI} (95% CI) \$ \%
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>181/11,390</td>
<td>2.09</td>
<td>5.30</td>
</tr>
<tr>
<td>Female</td>
<td>134/7864</td>
<td>2.34</td>
<td>5.58</td>
</tr>
</tbody>
</table>
The Shingles Prevention Study (1998 – 2001)

The zoster vaccine reduced the incidence of postherpetic neuralgia by 66.5 percent (P<0.001)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Vaccine Group</th>
<th>Placebo Group</th>
<th>VEPHN (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>No. of Confirmed Cases of Herpes Zoster with PHN</td>
<td>Incidence per 1000 Person-Yr</td>
<td>No. of Confirmed Cases of Herpes Zoster with PHN</td>
</tr>
<tr>
<td>All subjects</td>
<td>27</td>
<td>0.46</td>
<td>80</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>0.33</td>
<td>29</td>
</tr>
<tr>
<td>Persistence of PHN among all subjects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 days</td>
<td>81</td>
<td>1.39</td>
<td>196</td>
</tr>
<tr>
<td>60 days</td>
<td>45</td>
<td>0.77</td>
<td>113</td>
</tr>
<tr>
<td>90 days</td>
<td>27</td>
<td>0.46</td>
<td>80</td>
</tr>
<tr>
<td>120 days</td>
<td>17</td>
<td>0.29</td>
<td>54</td>
</tr>
<tr>
<td>182 days</td>
<td>9</td>
<td>0.16</td>
<td>33</td>
</tr>
</tbody>
</table>
Long-term Persistence Substudy

- Data concerning zoster vaccine efficacy were collected from year 7 through to year 10 following vaccination in the Shingles Prevention Study, with a median duration of follow-up of 3.9 years.
- Estimated $\text{VE}_{\text{BOI}}$ was 37% (95% CI 27-46) and $\text{VE}_{\text{PHN}}$ was 35% (95% CI 11-30).
- The decline in efficacy suggests that the clinical efficacy of zoster vaccine becomes increasingly limited beyond 5–8 years postvaccination.

Vaccine efficacy for study outcomes by year postvaccination: HZ BOI

Vaccine efficacy for study outcomes by year postvaccination: incidence PHN

Retrospective Cohort Studies

• Large retrospective cohort studies have been conducted in the USA to examine the protective efficacy of zoster vaccine in various populations in real-world settings.

• The risk of herpes zoster was significantly reduced in adults aged ≥60 or ≥65 years who received zoster vaccine, compared with those who did not.

• There was no evidence of a safety concern.
<table>
<thead>
<tr>
<th>Study(^a)</th>
<th>Subject characteristics</th>
<th>Study group (no. of subjects)</th>
<th>Herpes zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Langan et al. [31]</strong></td>
<td>Aged ≥65 years, immunocompetent or immunosuppressed(^e)</td>
<td>Zoster vaccine (29,785) &amp; Unvaccinated (736,545)</td>
<td>5.4 &amp; 10.0</td>
</tr>
<tr>
<td><strong>Tseng et al. [32]</strong></td>
<td>Aged ≥60 years, immunocompetent</td>
<td>Zoster vaccine (75,761) &amp; Unvaccinated (227,283)</td>
<td>6.4 &amp; 13.0</td>
</tr>
<tr>
<td><strong>Tseng et al. [33]</strong></td>
<td>Aged ≥60 and &lt;70 years, recent episode of herpes zoster, immunocompetent</td>
<td>Zoster vaccine (533) &amp; Unvaccinated (2,665)</td>
<td>0.99 &amp; 2.20</td>
</tr>
<tr>
<td><strong>Tseng et al. [34](^d)</strong></td>
<td>Aged ≥60 years, also receiving pneumococcal vaccine</td>
<td>Concomitant vaccination (7,187) &amp; Nonconcomitant vaccination (7,179)</td>
<td>4.54 &amp; 4.51</td>
</tr>
<tr>
<td><strong>Zhang et al. [35]</strong></td>
<td>Aged ≥50 years with immunemediated diseases(^g)</td>
<td>Zoster vaccine (551) &amp; Unvaccinated (43,564)</td>
<td>9.97 &amp; 8.61</td>
</tr>
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<td><strong>Zhang et al. [36]</strong></td>
<td>Aged ≥60 years with immunemediated diseases(^g)</td>
<td>Zoster vaccine (18,683) &amp; Unvaccinated (444,858)</td>
<td>6.7(^g) &amp; 11.6</td>
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\(HR\) hazard ratio

- \(^a\) Studies used data from Medicare [31, 36], the Kaiser Permanente Southern California health plan [32-34], or the Aetna health plan [35]
- \(^b\) No. of cases per 1,000 person-years
- \(^c\) Immunosuppression was defined as leukaemia, lymphoma or HIV infection, or use of an immunosuppressant (including corticosteroids) in the prior 6 months
- \(^d\) Participants in this study received zoster vaccine and 23-valent pneumococcal polysaccharide vaccine (Pneumovax\(^\circ\), 23) on the same day, or zoster vaccine 30–365 days after administration of pneumococcal vaccine
- \(^e\) Participants had rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis and/or inflammatory bowel disease
- \(^f\) Standardized incidence rate ratio
- \(^g\) Incidence ≥42 days after vaccination

Keating GM. Shingles (herpes zoster) vaccine (zostavax\(^\circ\)): a review of its use in the prevention of herpes zoster and postherpetic neuralgia in adults aged ≥50 years. Drugs. 2013 Jul;73(11):1227-44
Should Zostavax be administered to an individual due to receive immunosuppressive therapy in the near future?

- The risk and severity of shingles is considerably higher amongst immunosuppressed individuals (e.g. chemotherapy)

- Is zoster vaccine effective in patients who subsequently undergo chemotherapy?
  - There were 4710 vaccinated members and 16,766 unvaccinated members included in the study. Among the vaccinated cohort, 74 (1.6%), 78 (1.6%), 326 (6.9%), 584 (12.4%), and 3,648 (77.5%) members were vaccinated in ≤30 days, 31–59 days, 60–180 days, 181–365 days, and >365 days, respectively, before initiation of chemotherapy.
  - The incidence rate was 12.87 (95% CI, 10.48–15.80) per 1000 person-years in the vaccinated cohort vs 22.05 (95% CI, 20.33–23.92) in the unvaccinated cohort.
  - The 30-month cumulative incidence of HZ after chemotherapy was 3.28% in the vaccinated group and 5.34% in the unvaccinated group (P < 0.05)
### Table 2.
Comparison of Herpes Zoster Incidence in Study Cohorts by Herpes Zoster Vaccination Status

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Vaccinated (n = 4710)</th>
<th>Unvaccinated (n = 16 766)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Total No. of PY</td>
</tr>
<tr>
<td>All</td>
<td>4710</td>
<td>7071.82</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>1410</td>
<td>2245.96</td>
</tr>
<tr>
<td>≥70</td>
<td>3300</td>
<td>4825.86</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2783</td>
<td>4278.34</td>
</tr>
<tr>
<td>Male</td>
<td>1927</td>
<td>2793.48</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3612</td>
<td>5519.64</td>
</tr>
<tr>
<td>Black</td>
<td>235</td>
<td>327.56</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>311</td>
<td>446.85</td>
</tr>
<tr>
<td>Hispanic</td>
<td>462</td>
<td>660.29</td>
</tr>
<tr>
<td>Other/multiple/unknown</td>
<td>90</td>
<td>117.47</td>
</tr>
</tbody>
</table>

**Abbreviations:** CI, confidence interval; PY, person-years.

Should Zostavax be administered to an individual due to receive immunosuppressive therapy in the near future?

• Is zoster vaccine effective in patients who subsequently undergo chemotherapy?
  o Our data suggest that VZV-specific immunity is well maintained in the presence of chemotherapy-induced immunosuppression.
  o By preventing HZ-associated hospitalizations, the vaccine also appeared to prevent the severe disease manifestations that often occur in the immunocompromised population.
  o Additional studies are needed to provide reassurance that this practice would be safe.

• The ACIP (Advisory Committee on Immunization Practices) currently recommends that zoster vaccine be specifically offered to patients at least 14–30 days before they undergo immunocompromising treatments in order to obtain the benefits of vaccine protection without the risks of dissemination of this live attenuated vaccine. However, this recommendation has never been formally evaluated for safety and efficacy.
So it’s effective, but is it also cost-effective?

- Zostavax available in Belgium since 10/2014, but is expensive (€ 137,40 for a single dose vaccine)
- Bilcke et al aimed to assess the cost-effectiveness of vaccinating all or subgroups of adults aged 60 to 85 years against herpes zoster in Belgium
- Two possible scenarios: one least in favour of vaccination and one most in favour of vaccination

Table 1
Uncertainties and the choices most and least in favour of vaccination against herpes zoster (HZ) for each of these uncertainties.

<table>
<thead>
<tr>
<th>Uncertainties</th>
<th>Choice most in favour of vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population that can benefit from the vaccine</td>
<td>Everybody</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>Highest estimate</td>
</tr>
<tr>
<td>Severity-of-illness (SOI) score ambulatory HZ episode</td>
<td>Based on Drolet et al. data</td>
</tr>
<tr>
<td>Endpoint for vaccine efficacy</td>
<td>Burden of illness due to herpes zoster</td>
</tr>
<tr>
<td>Vaccine efficacy by age at vaccination and time since vaccination</td>
<td>See Fig. 1 and Appendix Table A7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uncertainties</th>
<th>Choice least in favour of vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population that can benefit from the vaccine</td>
<td>According to inclusion criteria Shingles Prevention Study [5]</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>No deaths</td>
</tr>
<tr>
<td>Severity-of-illness (SOI) score ambulatory HZ episode</td>
<td>Based on Scott et al. data</td>
</tr>
<tr>
<td>Endpoint for vaccine efficacy</td>
<td>Number of herpes zoster cases</td>
</tr>
<tr>
<td>Vaccine efficacy by age at vaccination and time since vaccination</td>
<td>See Fig. 1 and Appendix Table A7</td>
</tr>
</tbody>
</table>

At a vaccine price of about €45 per dose, vaccination would likely be considered cost-effective (i.e. incremental cost per QALY gained <€30,000) in Belgium for age cohorts 60–64, under a scenario least in favour of vaccination.

this is how I finish a presentation:

Soo...
Uhh
...yeah.

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Thank you for your attention