Vaccination against shingles (Herpes Zoster) in England

Dr Mary Ramsay
Vaccines against varicella-zoster virus

Numerous studies have shown the vaccine to be safe and immunogenic.

Efficacy and Effectiveness against severe varicella has been demonstrated.

The varicella vaccines have been introduced in the U.S. and in some European countries.

Varicella OKA vaccine in higher doses (19,400 PFU vs 1350 PFU)

Vaccine reduced the incidence of Herpes Zoster by 51.3% and PHN by 66.5% [Oxman et al. 2005]

Efficacy depends on age and time after vaccination.
UK considerations about mass varicella vaccination

In favour

Preventable deaths and hospitalisations

Large economic cost, particularly through parental work-loss

Against

Increase in average age at infection could lead to more severe disease (particularly if low coverage)

Decrease in incidence of varicella could lead to an increase in the incidence of zoster due to the loss of exogenous boosting
Annual burden of disease varicella & zoster in England

<table>
<thead>
<tr>
<th></th>
<th>Varicella</th>
<th>Zoster</th>
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</thead>
<tbody>
<tr>
<td>Hospitalisations</td>
<td>~2,300</td>
<td>~2,300</td>
</tr>
<tr>
<td>QALYs lost</td>
<td>~3,000</td>
<td>~20,000</td>
</tr>
<tr>
<td>Cost (NHS)</td>
<td>£13m</td>
<td>£22m</td>
</tr>
<tr>
<td>Cost (society)</td>
<td>£54m</td>
<td>£170m</td>
</tr>
</tbody>
</table>

Clinical presentation of shingles

Acute stage

- Rash of fluid filled blisters within the distribution of a dermatome
- Pain, itching or a tingling sensation
- Scab over in 7-10 days and eventually clear within 2-4 weeks
- Can lead to disseminated disease in immunosuppressed

Vaccination against shingles (Herpes Zoster)
Incidence of shingles by age (per 100,000) in patients presenting to general practice, 1967-2007
Estimated incidence of shingles by age, those aged 60 years and over.

Estimated annual age-specific incidence of shingles per 100,000 per year in immunocompetent population. (Data taken from van Hoek et al, 2009).
Complications of shingles

- Post herpetic neuralgia (PHN)
  - Pain persisting after 90 days from onset
  - Persist for 3 to 6 months
  - Sensitive to touch and not relieved by common pain killers
- Secondary bacterial skin infections
- Ophthalmic Zoster
- Peripheral motor neuropathy
- Hospitalisation and death

WebMed
Severity of shingles in England and Wales

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Incidence per 100,000 per year (general)</th>
<th>Percentage developing post herpetic neuralgia after 90 days</th>
<th>Proportion hospitalised first diagnosis (first three diagnosis)</th>
<th>Mean number of days in hospital (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>706</td>
<td>9%</td>
<td>0.8% (1.3%)</td>
<td>9 (4)</td>
</tr>
<tr>
<td>65-69</td>
<td>791</td>
<td>11%</td>
<td>1.0% (1.7%)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>70-74</td>
<td>876</td>
<td>15%</td>
<td>1.5% (2.4%)</td>
<td>11 (5)</td>
</tr>
<tr>
<td>75-79</td>
<td>961</td>
<td>20%</td>
<td>2.2% (3.8%)</td>
<td>14 (7)</td>
</tr>
<tr>
<td>80-84</td>
<td>1046</td>
<td>27%</td>
<td>3.0% (5.2%)</td>
<td>17 (9)</td>
</tr>
<tr>
<td>85+</td>
<td>1216</td>
<td>52%</td>
<td>4.4% (8.1%)</td>
<td>22 (13)</td>
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</table>

Estimated annual age-specific incidence, hospitalisation rate, length of inpatient stay, Burden of disease in the immunocompetent population England and Wales. (Data taken from van Hoek et al, 2009).
A one dose schedule of Zostavax® was assessed in clinical trials using 17,775 adults aged 70 years and over.

The vaccine reduced the incidence of shingles by 38% and provided protection for a minimum of 7 years.

For those vaccinated but who later developed shingles, the vaccine significantly reduced the burden of illness by 55% and significantly reduced the incidence of PHN by 67%.
The Shingles Prevention Study (SPS) demonstrated efficacy of preventing Zoster and post herpetic neuralgia (PHN). 

[Oxman et al. N.Eng.J, 2005]
Zoster vaccination
Cost effectiveness model

Decision analytic cohort model

Epidemiological parameters
- Incidence of zoster and PHN
- Hospitalisations
- Case Fatality Ratio

Cost parameters
- cost of inpatient day
- cost of treatment
- GP consultation
- Cost of vaccine and delivery

Vaccine parameters
- VE against HZ and PHN
- Waning rate
Zoster vaccination
Cost per QALY gained

ICER
Base case  £26,705  £20,412  £15,146  £18,546
No additional efficacy  £28,660  £21,428  £22,406  £24,129
Addtional efficacy against PHN  £6,598  £6,576

<table>
<thead>
<tr>
<th>Age at vaccination</th>
<th>60</th>
<th>65</th>
<th>70</th>
<th>75</th>
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<tbody>
<tr>
<td>Base case</td>
<td>£26,705</td>
<td>£20,412</td>
<td>£15,146</td>
<td>£18,546</td>
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<td>£24,129</td>
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<tr>
<td>Addtional efficacy against PHN</td>
<td>£6,598</td>
<td>£6,576</td>
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Conclusions from CEA

Zoster vaccination is likely to be the most cost effective at an age of 70

Probably still cost-effective up to 79 years

Cost-effectiveness in over 80s uncertain as efficacy is lower

Results are very sensitive to
  • Duration of vaccine protection
  • QALY loss from HZ and PHN

Decision to implement as routine programme in those aged 70 years

Catch up programme in those aged 71-79 years
Shingles programme

Launched in Sept 2013

- Vaccine to be given alongside seasonal flu to those aged 70

Vaccine supply limited

- Unable to vaccinate all aged 70-79 in catch-up

Programme commenced with

- Routine vaccine for those aged 70
- Catch up vaccine in those aged 79 years
Shingles jab campaign for people in their 70s

People in their 70s across the UK will be offered a vaccine against shingles from this week.

The government-backed programme will initially offer the vaccine to those aged 70 and 79.

Shingles, or herpes zoster, is an infection of a nerve and the area of skin around it, and can cause a painful rash.

Around 380,000 people will be eligible for the vaccine in the first year of the programme.

In England, Scotland, Wales and Northern Ireland, those aged 70 and 79 will initially be invited to take up the vaccination.

Over the next few years, the programme will expand to include more of the 70-to-79 age group across the UK until it is fully covered.

After that, the jab should only need to be offered to people as they reach their 70th birthdays.

Flare-up

Shingles is caused by the same virus that causes chickenpox. Around 14,000 people develop it each year.

After someone has had chickenpox most of the virus is destroyed but some survives and lies inactive in the body in the nervous system.

It can then be reactivated later in life when the
Key programme outcome questions

1. Vaccine coverage

2. Impact of vaccination programme
   - Incidence of herpes zoster in primary care
   - Incidence of PHN
   - Hospitalisations, deaths for HZ

3. Long term efficacy of single dose schedule

4. Risk factors for vaccine failure
Measuring vaccine coverage

• For both the routine and Catch up programme
  • Extraction from GP systems
  • Similar to seasonal influenza and PPV programmes
• Automated monthly collections from around 90% of practices collected since December
• Final collection planned for March 2014
  • With semi-automated or manual input from the remaining sites

• But, major disruption to supply in October 2013

Provisional vaccine coverage data: England, September 2013 to January 2014

First five months of the programme:

- 46.6% of the routine cohort
- 45.5% of the catch-up cohort
- not adjusted for those with contra-indications

Programme extended to August 2014 (because of vaccine shortage)
• Primary Care Research Network (PCRN)
  • part of the National Institute for Health Research Clinical Research Networks (funded by the Department of Health

• Royal College General Practitioners (RCGP)
  • Longstanding network of 100 practices undertaking surveillance

• Participating practices: 143
• Population: 1,312,906
• Population 70+ years: 158,157
Primary care sentinel surveillance

Clinical case: defined as a vesicular rash with a dermatomal distribution that may be associated with pain, occurring in skin areas supplied by sensory nerves of the dorsal root ganglia, and includes cases of ophthalmic zoster.

Criteria for sampling

- All clinically diagnosed cases of shingles 70 years and above
- Regardless of vaccine history
- Active lesions or scabs which can be sampled

Participating practices are sent pre-prepared kits from PHE to collect 2 samples:

(i) a vesicle swab
(ii) oral fluid specimen from each of these cases.
Surveillance of Post Herpetic Neuralgia (PHN)

• To capture the severe end of the spectrum, pain clinics have been approached to participate in surveillance.

• Asked to complete a very short question card each quarter asking about new cases of PHN seen.

• When a case is indicated the clinic will then be asked to complete an enhanced questionnaire on each case.

• The aim is to measure the impact the herpes zoster campaign is having on the incidence of PHN in the targeted population.
122 Pain clinics in England were identified and approached

88 have indicated they want to take part.

Shingles surveillance programmes

Participating Pain Clinics

Quarterly return for:

Pain clinic name: ____________________________
Clinician name: ____________________________
Quarter/Year: ________________________________

Please record the ID number of all newly identified cases of post herpetic neuralgia * in patients aged 70 years or older that you have seen in the last quarter.

If no new cases please tick box

<table>
<thead>
<tr>
<th>Hospital number</th>
<th>** Full name code (see below)</th>
<th>Age</th>
<th>Gender</th>
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* Case definition: Nerve pain which persists for 3 months following the resolution of the shingles cutaneous eruption.

** Full name code is the first two letters of the first name and the first two letters of the surname i.e. John Smith is JOSM and Ian de Souza is IADE.
UK reluctant to introduce varicella vaccine
Shingles prevention identified as higher priority
Analysis identified that elderly programme could be cost-effective
Optimal age chosen to balance increasing risk against declining protection
  highly dependent on protection against PHN
Vaccine has been highly acceptable – despite vaccine shortage
Surveillance programme now in place
Acknowledgements

Albert Jan Van Hoek, Edna Kara, Philip Keel, Gayatri Amirthalingam
Kevin Brown, Joanne White, Iain Kennedy
References


