Zoster Vaccines Session: Burden of Herpes Zoster in Immunocompromised Adults

ACIP Meeting
June 25, 2021

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CDC Lead, Herpes Zoster Work Group
Current ACIP Recommendations

- ACIP recommended recombinant zoster vaccine (RZV, Shingrix) in Oct 2017 for use in immunocompetent adults age ≥50 years

- ACIP recommendations include use of RZV in persons
  - Taking low-dose immunosuppressive therapy
  - Anticipating immunosuppression or who have recovered from an immunocompromising illness

Risk of herpes zoster (HZ), severe disease, and complications generally higher in immunocompromised (IC) populations

IC populations are very heterogeneous, both within and across groups

Zostavax, a live, attenuated HZ vaccine, was contraindicated for persons with IC conditions

RZV can potentially address an unmet need for HZ prevention in IC populations
How many IC persons in the United States?*

- ~7 million IC adults\textsuperscript{1}

- ~3 million among:
  - Hematopoietic stem cell transplant recipients\textsuperscript{2}
  - Patients with hematologic malignancies\textsuperscript{3}
  - Renal or other solid organ transplant recipients\textsuperscript{4}
  - Patients with solid tumor malignancies\textsuperscript{3,5}
  - People living with HIV\textsuperscript{6}

- ~22 million with autoimmune and/or inflammatory (AI) conditions\textsuperscript{7}
  - >80 diverse conditions (e.g., systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease)
  - Often have underlying immune dysfunction, but generally not considered frankly IC unless iatrogenic (i.e., on IC treatments)

*References on slide 20
IC Populations under Consideration

1. Hematopoietic stem cell transplant (HCT) recipients
2. Patients with hematologic malignancies (HM)
3. Renal or other solid organ transplant (SOT) recipients
4. Patients with solid tumor malignancies (STM)
5. People living with HIV
6. IC populations at increased risk of HZ not covered in groups 1 through 5 (i.e., patients with primary immunodeficiencies, patients with autoimmune conditions, patients taking immunosuppressive medications)
## Evidence to Recommendations (EtR) Framework

<table>
<thead>
<tr>
<th>EtR Domain</th>
<th>Question</th>
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<tbody>
<tr>
<td><strong>Public Health Problem</strong></td>
<td>Is the problem of public health importance?</td>
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<tr>
<td><strong>Benefits and Harms</strong></td>
<td>How substantial are the desirable anticipated effects?</td>
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<td>Do the desirable effects outweigh the undesirable effects?</td>
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<td><strong>Values</strong></td>
<td>Does the target population feel the desirable effects are large relative to the undesirable effects?</td>
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<td>Is there important variability in how patients value the outcomes?</td>
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<td><strong>Acceptability</strong></td>
<td>Is the intervention acceptable to key stakeholders?</td>
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<td><strong>Feasibility</strong></td>
<td>Is the intervention feasible to implement?</td>
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<td><strong>Resource Use</strong></td>
<td>Is the intervention a reasonable and efficient allocation of resources?</td>
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<tr>
<td><strong>Equity</strong></td>
<td>What would be the impact of the intervention on health equity?</td>
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Clinical Presentations of Herpes Zoster

Courtesy of NIAID

Courtesy of MN Oxman UCSD/San Diego VAMC

Courtesy of CDC/Robert Sumpter
“Five years later, I still take prescription medication for pain. My shingles rash quickly developed into open, oozing sores that in only a few days required me to be hospitalized. I could not eat, sleep, or perform even the most minor tasks. It was totally debilitating. The pain still limits my activity levels to this day.”

—A 63-year-old harpist who was unable to continue playing due to shingles
https://www.cdc.gov/shingles/about/complications.html
HZ Incidence Common in Adults and Increases with Age

~1 million HZ cases per year in U.S. during pre- HZ vaccine era¹

Public Health Importance
Risk of HZ in IC Groups 1–5

- Median HZ incidence estimates for these IC groups exceeded those reported for immunocompetent adults >50 years.


Figure 3. Herpes zoster incidence rates among patients with selected immunocompromising conditions. *Studies with low or medium risk of bias.
Public Health Importance
Severity of HZ in IC Groups 1–5

- **Postherpetic neuralgia (PHN)**
  - ~6–10% vs ~4% overall in administrative claims databases\(^1\)
  - Between 6% and 45% across IC conditions and studies\(^2\)

- **Disseminated HZ:**
  - ~3%\(^2\) of IC, but exceedingly uncommon in healthy persons
  - 10–17% mortality associated with disseminated HZ among renal transplant recipients\(^3,4\)

- **Hospitalization:** 8% of HCT recipients with HZ\(^5\) vs ~<1% of overall Medicare beneficiaries with HZ\(^6\)

Antiviral Prophylaxis

- Antiviral prophylaxis is recommended post-transplant
  - No universal standard prophylactic regimen for transplant recipients, and antiviral drug, duration, and dosage vary
  - Studies of patients post HCT with follow up >2 years revealed that HZ incidence increases once prophylaxis is discontinued

- ACIP General Best Practice Guidelines, Altered Immunocompetence
  - Most inactivated vaccines should be initiated 6 months after HCT

https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html
IC Populations under Consideration

1. Hematopoietic stem cell transplant (HCT) recipients
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6. **IC populations at increased risk of HZ not covered in groups 1 through 5**
   - Patients with primary immunodeficiencies
   - Patients with autoimmune (AI) conditions
   - Patients taking immunosuppressive medications
Public Health Importance
Risk of HZ in IC Group 6

▪ ~2 to 4-fold higher risk in patients with AI conditions than in healthy individuals¹

▪ ~1.5-fold higher risk for unvaccinated Medicare beneficiaries with AI conditions vs not IC²

2. Izurieta et al. Recombinant Zoster Vaccine (Shingrix) real-world effectiveness in the first two years post-licensure. Clinical Infectious Diseases, 2021;, ciab125, https://doi.org/10.1093/cid/ciab125

Age and sex-standardized HZ incidence rates, among adults ≥20 years with selected autoimmune diseases

Figure adapted from Yun et al. Bars show the IRs of HZ with 95% confidence intervals. Cohorts of healthy adults without autoimmune diseases or diabetic conditions and adult patients with diabetes were used as controls. SLE=systemic lupus erythematosus; IBD=inflammatory bowel disease; RA=rheumatoid arthritis; PsA=psoriatic arthritis; PsO=psoriasis; AS=ankylosing spondylitis.
Group 6 Examples: SLE, IBD, and RA

- **Disease burden**
  - HZ risk ~2 to 4-fold higher
  - Age-specific incidence rates among 21–50-year-olds comparable or substantially higher than corresponding rates in healthy adults >60 years

- **Impact of immunosuppressive treatments**
  - Standard of care for patients to be on ≥1 IC drugs
  - Not possible to define high risk subgroups based on anticipated drugs
    - Disease modifying antirheumatic drugs, or DMARDs (e.g., methotrexate)
    - Glucocorticoids
    - Biologics (e.g., Janus Kinase inhibitors)
Work Group Interpretation

- Are HZ and HZ complications in IC adults ≥19 years of public health importance?
  - Yes

- Summary of work group discussions
  - IC populations are very heterogeneous, both across and within groups and among individuals over time
  - Risk of HZ and HZ complications generally higher in IC populations, although there is variability across and within IC groups
  - Not feasible to define every possible IC condition/medication combination
  - Important to consider broad recommendations and appropriate guidance for IC populations
EtR Framework
Next Steps

- GRADE analysis of existing evidence of RZV benefits and harms
- Review knowledge, attitudes, and current practices for RZV in IC populations
- Cost effectiveness analyses of use of RZV in IC populations

Public Health Importance
- Benefits and Harms
- Values
- Acceptability
- Feasibility
- Resource Use
- Equity
Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Backup Slides
## IC Populations: Groups 1–5

<table>
<thead>
<tr>
<th>IC Condition</th>
<th>Incident Cases (New cases per year)</th>
<th>Prevalent Cases</th>
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<tbody>
<tr>
<td>Hematopoietic stem cell transplant&lt;sup&gt;1&lt;/sup&gt;</td>
<td>23,379</td>
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<tr>
<td>Hematologic malignancy&lt;sup&gt;2&lt;/sup&gt;</td>
<td>~176,200</td>
<td></td>
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<tr>
<td>Solid organ (including renal) transplant&lt;sup&gt;3&lt;/sup&gt;</td>
<td>58,532</td>
<td>~591,000</td>
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<tr>
<td>Solid tumor on chemotherapy&lt;sup&gt;2,4&lt;/sup&gt;</td>
<td>~1,200,000</td>
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<tr>
<td>HIV infection&lt;sup&gt;5&lt;/sup&gt;</td>
<td>38,739</td>
<td>1,008,929</td>
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<td><strong>Total</strong></td>
<td>~1,496,850</td>
<td>~1,599,929</td>
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Policy question: “Should vaccination with RZV be recommended for immunocompromised adults 19 years of age and older?”

- **Population**: IC adults ≥19 years of age; split into two parts (19–49 years, ≥50 years)
- **Intervention**: RZV, 2 doses at least 4 weeks apart
- **Comparison**: No vaccine
- **Outcomes**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Harms</th>
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<tr>
<td><strong>Critical</strong></td>
<td>Prevent HZ</td>
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<tr>
<td><strong>Important</strong></td>
<td>Prevent PHN</td>
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<td>Prevent HZ-related hospitalization</td>
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