Resource Pack:
CEA Herpes Zoster Vaccine

Overview

This resource pack on the cost-effectiveness of herpes zoster vaccination was curated to support Dr. Lisa Prosser’s seminar on November 9, 2017 at the Center for Health Decision Science. Dr. Prosser discussed an economic evaluation of vaccination against herpes zoster.

Herpes zoster—more commonly known as shingles—presents a major burden for older Americans but, until recently, the only available vaccine (Zoster Vaccine Live, ZVL) was relatively ineffective past 10 years. A recently approved vaccine—herpes zoster subunit (HZ/su)—has shown efficacy at preventing shingles for significantly longer duration than ZVL.

Dr. Prosser’s team conducted a cost-effectiveness analysis to answer three questions: (1) is the new vaccine cost-effective compared to no vaccination; (2) is it cost-effective in those who have already received the old vaccine (ZVL); and (3) is it cost-effective when compared to ZVL (i.e., is it preferred to ZVL). They found that vaccination with the new vaccine provided good value, and would be considered to be cost-effective using standard benchmarks in the U.S. The findings were presented to the Advisory Committee on Immunization Practices (ACIP), whose recommendations are generally followed by the Centers for Disease Control and Prevention to issue guidelines. Learn more about the seminar here.

The resource pack contains selected news, editorials, and articles on vaccine efficacy, cost-effectiveness, and patient preferences. It is not intended to be a comprehensive review, but an opportunity for educators and students to learn more about the potential role of decision science to influence contemporary policy issues.
## Selected Resources – At a Glance

### ARTICLES

**Measuring Health Preferences for Use in Analyses of Interventions in Children**  
Not open access.

**Community and Patient Values for Preventing Herpes Zoster**  
Not open access.

**The Potential Cost-Effectiveness of Vaccination against Herpes Zoster and Post-Herpetic Neuralgia**  
Not open access.

**Vaccination against Herpes Zoster and Postherpetic Neuralgia in France: a Cost-Effectiveness Analysis**  

**Distribution of Health Effects and Cost-Effectiveness of Varicella Vaccination**  

**Cost-Effectiveness of Herpes Zoster Vaccine for Persons Aged 50 Years**  
Not open access.

**Cost-Effectiveness of a Herpes Zoster Vaccination Program among the French Elderly People**  

**Analysis of Real-World Health Care Costs among Patients Aged 50 Years or Older with Herpes Zoster**  

**Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated**  
Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine Co-Administered with Influenza Vaccine in Adults

GUIDELINES, REVIEWS, AND WORKING PAPERS

Decision Models in Clinical Preventive Services Recommendations

A Systematic Review of the Cost Effectiveness of Herpes Zoster Vaccination
Not open access.

The Humanistic, Economic and Societal Burden of Herpes Zoster in Europe

Cost-Effectiveness Analysis of Adjuvanted Subunit Vaccine for Prevention of Herpes Zoster

NEWS

FDA Advisers Recommend Approval of New Shingles Vaccine

C.D.C. Panel Recommends a New Shingles Vaccine
Annotated Bibliography

ARTICLES

Measuring Health Preferences for Use in Analyses of Interventions in Children
Not open access.
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2754
Valuing the health of children for cost-utility or cost-benefit analysis is more challenging than valuing adult health. Young children cannot conceptualize value, they are not responsible for their own decision making, and proxies may not fully understand the child perspective. Moreover illness in children may affect parent/caregiver health and quality of life, further complicating the measurement of value associated with a change in a child’s health status.

This paper reviews the most common approaches (QALYs and willingness-to-pay) for valuing health in economic evaluations and considers the methodological and practical issues associated with measuring child health using each framework. Recommendations acknowledge that valuations will vary by age: the currently recommended approach for infants and preschoolers is direct valuation by a proxy respondent; for school-age children and adolescents, existing multi-attribute instruments can be applied in some situations but direct valuation may be required for others. Future research should focus on minimizing bias from proxy respondents, consideration of a family- or household-based approach to valuing health effects, and development of generic instruments with domains that are appropriate to children and that vary with age.

Community and Patient Values for Preventing Herpes Zoster
Not open access.
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2752
In this 2008 article, the authors report on a survey to assess the value individuals place on preventing herpes zoster. The Zoster Vaccine Live (ZVL) was recommended for routine use in adults aged ≥60 years. Members of the population (“community members”, n = 527), patients with shingles (n = 382) or post-herpetic neuralgia (PHN, n = 137) completed an internet or telephone survey to assess the value they place on preventing herpes zoster. The authors used standard economic valuation techniques—the time trade off and contingent valuation (willingness to pay). In time trade-off questions, community members would give up a mean of 89 days to avoid a case of a mild herpes zoster and a mean of 162 days to avoid a very severe case. In willingness-to-pay questions, community members would pay a mean of $450 to avoid a mild case and $1,384 to avoid a very severe case (2005 US dollars). When patients were asked to assign a value to avoiding their own case of herpes zoster, those with shingles would give up a mean of 67 days or $2319, while those with PHN would give up a mean of 206 days or $18,184. The authors conclude that community members would trade substantial amounts of time or money to avoid herpes zoster, even in the least severe scenarios.

Note: This article was published before the release of the newer herpes zoster subunit (HZ/su) vaccine.

The Potential Cost-Effectiveness of Vaccination against Herpes Zoster and Post-Herpetic Neuralgia
Not open access.
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2755

This resource pack was developed the Center for Health Decision Science at the Harvard T.H. Chan School of Public Health. All materials produced by the Center for Health Decision Science are free and publicly accessible for educational use.

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chds.hsph.harvard.edu
This 2008 Canadian study assessed the cost effectiveness of the Zoster Vaccine Live (ZVL) vaccine against herpes zoster (HZ) and post-herpetic neuralgia (PHN). The authors used a cohort model to estimate the burden of HZ and the cost-effectiveness of HZ vaccination from a ministry of health perspective using Canadian population-based data. They examined different ages at vaccination and conducted probabilistic sensitivity analysis.

There are about 130,000 new cases of HZ, 17,000 cases of PHN and 20 deaths in Canada annually. Most of the pain and suffering is borne by adults over the age of 60 years and is due to PHN. Vaccinating 65-year-olds is estimated to cost $33,000 per QALY-gained. Probabilistic sensitivity analysis suggest that vaccinating between 65 and 75 years of age will likely yield cost-effectiveness ratios below $40,000 per QALY-gained, while vaccinating adults older than 75 years will yield ratios less than $70,000 per QALY-gained. These results are most sensitive to the duration of vaccine protection and the cost of vaccination.

Note: This article was published before the release of the newer herpes zoster subunit (HZ/su) vaccine.

Vaccination against Herpes Zoster and Postherpetic Neuralgia in France: a Cost-Effectiveness Analysis
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2759
This article reports on a cost-effectiveness analysis of the original herpes zoster vaccine (ZVL) for the 65 year + population in France. The authors compared vaccinating all adults over 65 years versus adults from 70-79 years, over their lifetimes, from a third-party payer perspective. French-specific data were combined with results from clinical studies and international quality-of-life-based (EuroQol 5D) utilities from the literature.

Results showed incremental cost-effective ratios between €9513 and €12,304 per quality-adjusted life year gained, corresponding to €2240-€2651 per HZ case avoided and €3539-€4395 per postherpetic neuralgia case avoided. The authors concluded that in addition to epidemiological and clinical evidence, economic evidence supported the implementation of ZVL vaccination in France.

Note: This article was published before the release of the newer herpes zoster subunit (HZ/su) vaccine.

Distribution of Health Effects and Cost-Effectiveness of Varicella Vaccination
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2756
This article reports on an analysis of the impact of universal childhood varicella vaccination on the incidence of herpes zoster (HZ) using dynamic transmission modelling and cost-effectiveness analyses. Scenarios that are considered differ by whether or not immune boosting is included, and whether or not reactivation of vaccine virus is possible.

The authors report that health effects of varicella vaccination in scenarios with immune boosting are unevenly distributed: cohorts born just before introduction of vaccination and persons who refuse vaccination face an increased lifetime risk of herpes zoster while vaccinated cohorts see health gains. Cost-effectiveness of varicella vaccination depends strongly on the impact on herpes zoster and the economic time horizon.

The authors conclude that varicella vaccination may result in trans-generational differences in distribution of health benefits and losses; unvaccinated groups may be exposed to a substantially increased health hazard.
Cost-Effectiveness of Herpes Zoster Vaccine for Persons Aged 50 Years
Not open access.
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2758
This article reports on a cost-effectiveness analysis of the original herpes zoster (HZ) vaccine (ZVL) that at the time of this study was approved for persons age 50+. The authors used a Markov model to simulate adults aged 50 years over a lifetime from a societal perspective; outcomes included the number of HZ and postherpetic neuralgia (PHN) cases prevented and the incremental cost per quality-adjusted life-year (QALY) saved. Their focus was on the cost effectiveness of vaccination for the 50-59 year age group.

For every 1000 persons receiving the vaccine at age 50 years, 25 HZ cases and 1 PHN case could be prevented. The incremental cost-effectiveness ratio (ICER) for HZ vaccine versus no vaccine was $323,456 per QALY. In sensitivity analyses, the only variables that produced an ICER less than $100 000 per QALY were vaccine cost (at a value of $80) and the rate at which efficacy wanes.

The authors concluded that herpes zoster vaccine for persons aged 50 years does not seem to represent good value according to generally accepted standards. This supported the decision of the Advisory Committee on Immunization Practices not to recommend the vaccine for adults in this age group at the time the paper was published.

Note: This article was published before the release of the newer herpes zoster subunit (HZ/su) vaccine.

Cost-Effectiveness of a Herpes Zoster Vaccination Program among the French Elderly People
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2757
This study reports on a cost-effectiveness analysis of herpes zoster (HZ) vaccines among the elderly in France. Starting vaccination in individuals aged 65, 70 and 75 years old appears more cost-effective than vaccination for beginning vaccination at age 60, with a cost-effectiveness ratio between 30,000 and 35,000 euros per quality-adjusted-life year (QALY) gained for the 65 and 70 year age groups versus 54,500 euros for the age 75 group. These results largely contributed to the recommendation to include the HZ vaccination in the French immunization schedule for people aged between 65 and 74 years in France.

Note: This article was published before the release of the newer herpes zoster subunit (HZ/su) vaccine.

Analysis of Real-World Health Care Costs among Patients Aged 50 Years or Older with Herpes Zoster
CHDS repository link: http://repository.chds.hsph.harvard.edu/repository/2748
This article reports on the direct costs associated with herpes zoster (HZ) and postherpetic neuralgia (PHN) in the U.S. The authors use a retrospective managed care insurance claims database of 142,519 patients with herpes zoster (9,470 patients [6.6%] had postherpetic neuralgia) and 357,907 matched controls. They found that resource utilization was greater among patients with herpes zoster: after adjusting for demographic and clinical characteristics, annual incremental health care costs for herpes zoster patients vs. controls were $1,210 for patients aged 50-59 years, $1,629 for those 60-64 years, $1,876 for those 65-69 years, $2,643 for those 70-79 years, and $3,804 for those 80+ years; adjusted annual incremental costs among postherpetic neuralgia patients vs. controls were $4,670 for patients 50-59 years.
years, $6,133 for those 60-64 years, $6,451 for those 65-69 years, $8,548 for those 70-79 years, and $11,147 for those 80+ years.

The authors conclude that that HZ is associated with a significant cost burden, which increases with advancing patient age.

**Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated**


CHDS repository link: [http://repository.chds.hsph.harvard.edu/repository/2761](http://repository.chds.hsph.harvard.edu/repository/2761)

This article reports on a clinical trial of the new herpes zoster vaccine (HZ subunit vaccine, HZ/su) among individuals previously vaccinated with the live-attenuated zoster vaccine Zostavax (ZVL; immunity known to wane within 3-7 years) and previously unvaccinated individuals (multicenter study (NCT02581410)).

Among a sample of 430 adults age 65+ years, HZ/su induces a strong immune response irrespective of prior vaccination with ZVL. They conclude that HZ/su may be an attractive option to re-vaccinate prior ZVL-recipients and for ZVL naïve individuals over age 65.

**Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine Co-Administered with Influenza Vaccine in Adults**


CHDS repository link: [http://repository.chds.hsph.harvard.edu/repository/2762](http://repository.chds.hsph.harvard.edu/repository/2762)

This article reports on a clinical trial (NCT01954251) of herpes zoster subunit vaccine (HZ/su) co-administered with a quadrivalent seasonal inactivated influenza vaccine (IIV4) in adults age 50 years and older. Outcome measures were vaccine response rate and antibody response in the intervention compared to control groups.

There were 413 subjects in the intervention group and 415 in the control.

Antibody response was within statistical limits for similarity between the two groups; no safety concerns were raised.

The authors conclude that there was no interference in the immune response to either vaccine when they are co-administered.

**GUIDELINES, REVIEWS, AND WORKING PAPERS**

**Decision Models in Clinical Preventive Services Recommendations**


CHDS repository link: [http://repository.chds.hsph.harvard.edu/repository/2404](http://repository.chds.hsph.harvard.edu/repository/2404)

The U.S. Preventive Services Task Force (USPSTF) develops evidence-based recommendations about preventive care based on comprehensive systematic reviews of the best available evidence. Decision models provide a complementary, quantitative approach to support the USPSTF as it deliberates about the evidence and develops recommendations for clinical and policy use. This article describes the rationale for using modeling, an approach to selecting topics for modeling, and how modeling may inform recommendations about clinical preventive services.
**A Systematic Review of the Cost Effectiveness of Herpes Zoster Vaccination**


This review summarized the herpes zoster (HZ) vaccination cost effectiveness literature, consisting of 11 studies. Most studies evaluated the cost effectiveness of universal HZ vaccination in adults aged 50 years or 60 years and older and all studies calculated costs per QALY.

The costs per QALY gained and the incremental cost-effectiveness ratio (ICER) differed depending on the age at vaccination, duration of vaccine efficacy, cost of vaccine course, and economic perspective. All but one of the studies concluded that most vaccination scenarios are cost effective and the vaccination of the older age group is most cost effective. Age at vaccination, vaccine costs, HZ incidence, postherpetic neuralgia duration, and duration of vaccine efficacy all affected the estimated cost effectiveness of HZ vaccination.

**The Humanistic, Economic and Societal Burden of Herpes Zoster in Europe**


This review provides documentation and critical appraisal of published data concerning the humanistic, economic and societal burden of herpes zoster (HZ) in Europe. From a review of 1619 abstracts, 53 eligible articles, were identified which reported data concerning healthcare resource use (n = 38), direct costs (n = 20), indirect costs (n = 16), total costs (n = 10) and impact on health-related quality of life (HRQoL) (n = 21).

The findings indicate that postherpetic neuralgia (PHN) is associated with greater impairments in HRQoL and higher costs of management than HZ. For both HZ and PHN, pain severity is a significant predictor of impact on individuals, healthcare systems and society. While the incidence of HZ and PHN increase with age, age is not a predictor overall: direct costs are higher for older patients and indirect costs are higher for younger patients. Of note, informal care costs and social care costs are not captured in this analysis, and may be substantial—leading to an underestimation of the true burden of disease.

**Cost-Effectiveness Analysis of Adjuvanted Subunit Vaccine for Prevention of Herpes Zoster**


Herpes zoster (HZ) develops in up to 50% of unvaccinated individuals who live to 85 years of age, accounting for more than 1 million cases of HZ annually in the United States. A live attenuated vaccine (LAV) for HZ is U.S. FDA approved for persons 50 years or older, though CDC Advisory Committee on Immunization Practices (ACIP) recommendations are only for persons beginning at age 60 years. LAV efficacy at preventing HZ is ~70% for persons 50–59 years of age, with lower efficacy in older adults, and it is efficacious in preventing post-herpetic neuralgia (PHN) beyond the HZ prevention. The efficacy of LAV after vaccination wanes over time. A new adjuvanted HZ subunit vaccine (SUV), administered as a two-dose series, has greater than 95% efficacy against HZ in persons 50–69 years of age. SUV efficacy remains greater than 90% in persons vaccinated at age 70 years and older, including the subgroup older than 80 years of age. Overall efficacy of SUV against PHN approaches 90%. The waning rate of efficacy after SUV vaccination is unknown.

This article reports on a cost-effectiveness analysis of the herpes zoster live attenuated vaccine (LAV—also known as Zoster Vaccine Live, ZVL) compared to the newly approved adjuvanted HZ subunit vaccine (SUV—also known as HZ/su) and to no vaccination. The authors used a Markov model with a US societal perspective. Based on these authors...
assumptions, individuals vaccinated at age 50 years had an incremental cost-effectiveness ratio (ICER) for LAV vs. no vaccination of $142,811 per quality-adjusted life-year (QALY); at age 60 years the ICER dropped to $59,482 per QALY. The cost-effectiveness ratio of SUV approached that of LAV when the SUV cost approached $500 for persons vaccinated at age 50 and when the cost was $400 for persons vaccinated at age 60. The SUV cost that would result in achieving an ICER target of $100,000 per QALY for SUV vaccination vs. no vaccination at age 50 years was $316; at age 60 years the cost was $638.

The authors conclude that vaccination at age 60 years with SUV was more cost-effective than LAV when SUV cost was ~$450 or less. Vaccination with SUV at age 50 years was cost-effective if SUV cost was ~$315 or less.

**NEWS**

**FDA Advisers Recommend Approval of New Shingles Vaccine**


CHDS repository link: [http://repository.chds.hsph.harvard.edu/repository/2764](http://repository.chds.hsph.harvard.edu/repository/2764)

An FDA advisory panel voted 11-0 on Wednesday in favor of approving the Shingrix herpes zoster vaccine for adults aged 50 and older, Reuters reports. In clinical trials, the new vaccine conferred greater protection against herpes zoster among older adults, relative to the currently marketed zoster vaccine, Zostavax. In particular, 4 years after immunization, Shingrix was about 90% effective in adults older than 70, while the efficacy of Zostavax waned with time, according to Reuters. The FDA is not required to follow the advice of its advisers, but it usually does.

**C.D.C. Panel Recommends a New Shingles Vaccine**


CHDS repository link: [http://repository.chds.hsph.harvard.edu/repository/2760](http://repository.chds.hsph.harvard.edu/repository/2760)

In a New York Times report, the Centers for Disease Control and Prevention recommended the use of a new vaccine to prevent herpes zoster (“shingles”) among adults in the US. “In an unusually close vote, an advisory panel to the Centers for Disease Control and Prevention on Wednesday recommended the use of a new vaccine to prevent shingles over an older one that was considered less effective.

"The decision was made just days after the Food and Drug Administration announced approval of the new vaccine, called Shingrix and manufactured by GlaxoSmithKline, for adults ages 50 and older. The panel's recommendation gives preference to the new vaccine over Merck's Zostavax, which has been the only shingles vaccine on the market for over a decade and was recommended for people ages 60 and older."

"The Advisory Committee on Immunization Practices also recommended that adults who have received the older vaccine get the new one. Even with the committee vote, this recommendation still awaits formal endorsement by the head of the C.D.C., which usually takes a couple of months. Insurance companies must also agree to cover the cost of the vaccine, which GSK estimates to be $280 for two doses.