Decision and Cost-Effectiveness Analyses of Herpes Zoster Vaccination in Adults 50 Years of Age and Older

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DISCLAIMER

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Outline

- Policy Questions
- Decision and Cost Effectiveness Model
- Selected parameters and assumptions
- Base case results
- Sensitivity and Scenario analyses
- Discussion

Policy Questions

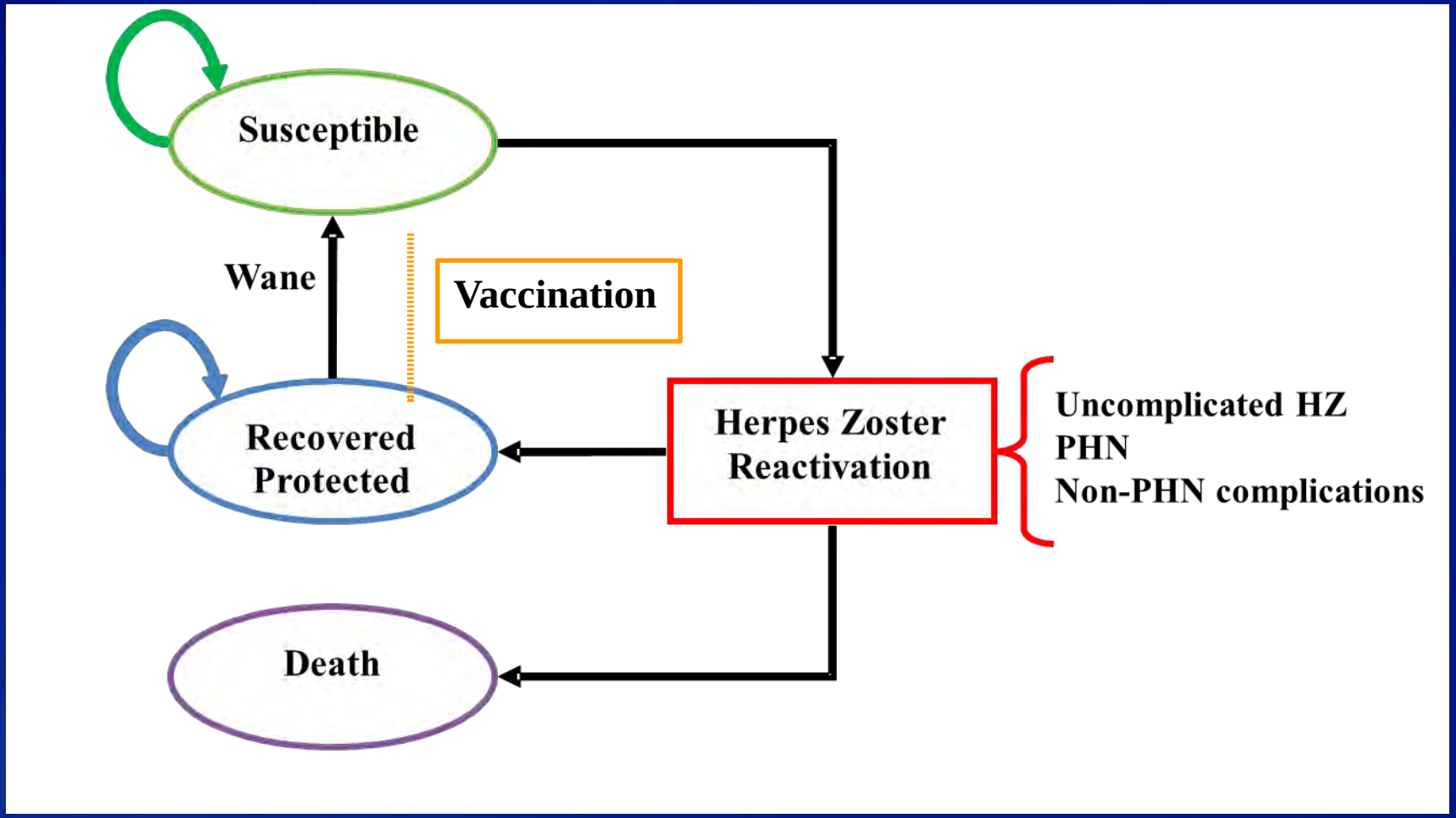
What is the optimal age to recommend a single dose of zoster vaccine in adults 50 or older?

1. From a public health perspective: at what age would vaccination have the greatest population impact?
2. From an economic perspective: at what age would vaccination produce the greatest value?

Decision and Cost Effectiveness Model Overview

- **Objective:**
  - To evaluate the cost effectiveness of one dose of zoster vaccine administered at age 50, 60, or 70 vs. no vaccination
- **Approach:** *Cohort-based decision analysis model*
- **Population:** *Immunocompetent 50+ years of age*
- **Analytic horizon:** *Followed to mean life expectancy*
- **Perspective:** *Societal*

Decision Analysis



Primary Outcomes

- Quality Adjusted Life Years (QALYs) gained
- Cost per QALY saved

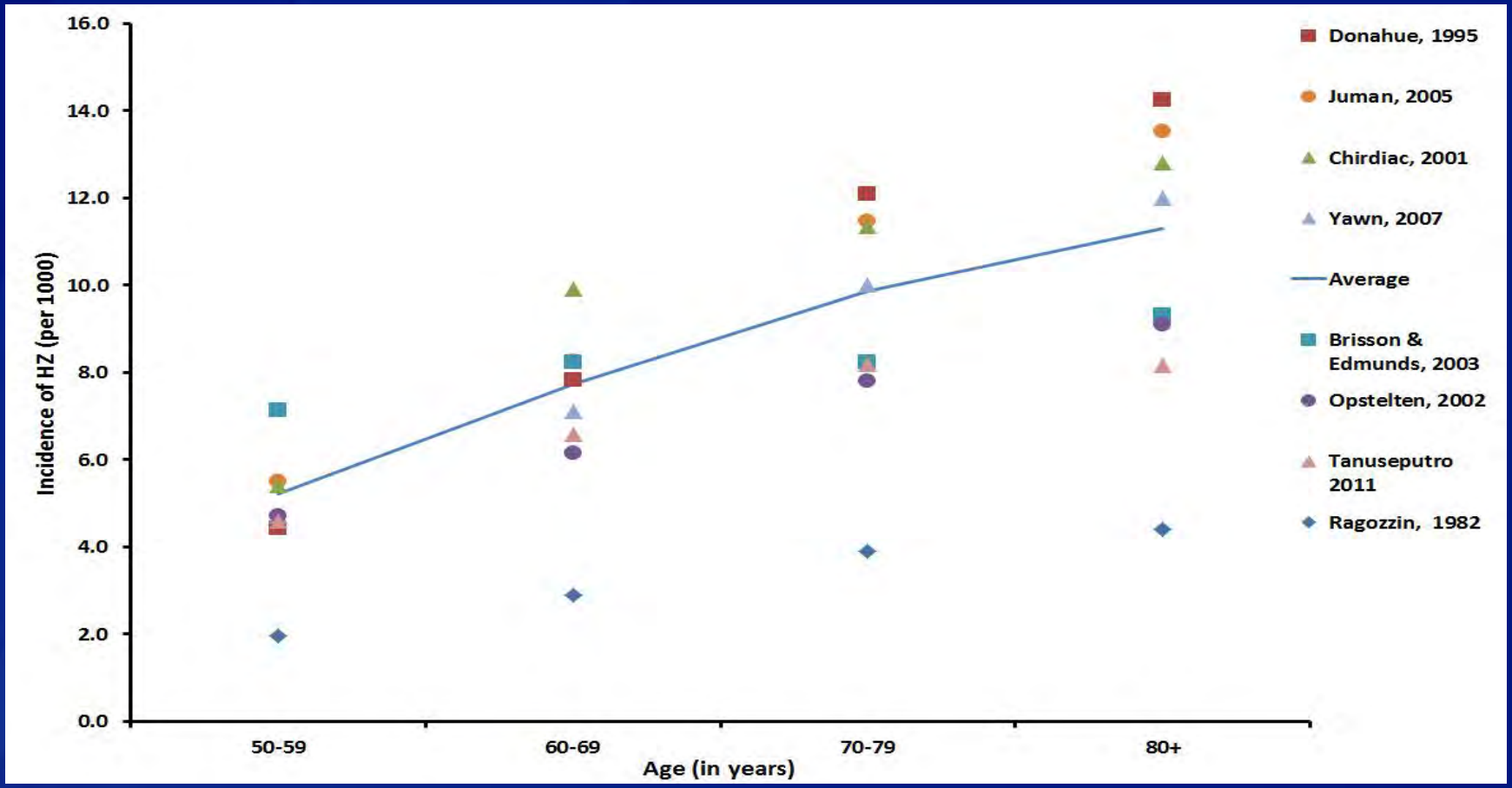
Secondary Outcomes

- **Cost per outcome averted:**
  - Cost per case of HZ
  - Cost per case of PHN
- **Number needed to vaccinate in order to avert:**
  - One case of HZ
  - One case of PHN

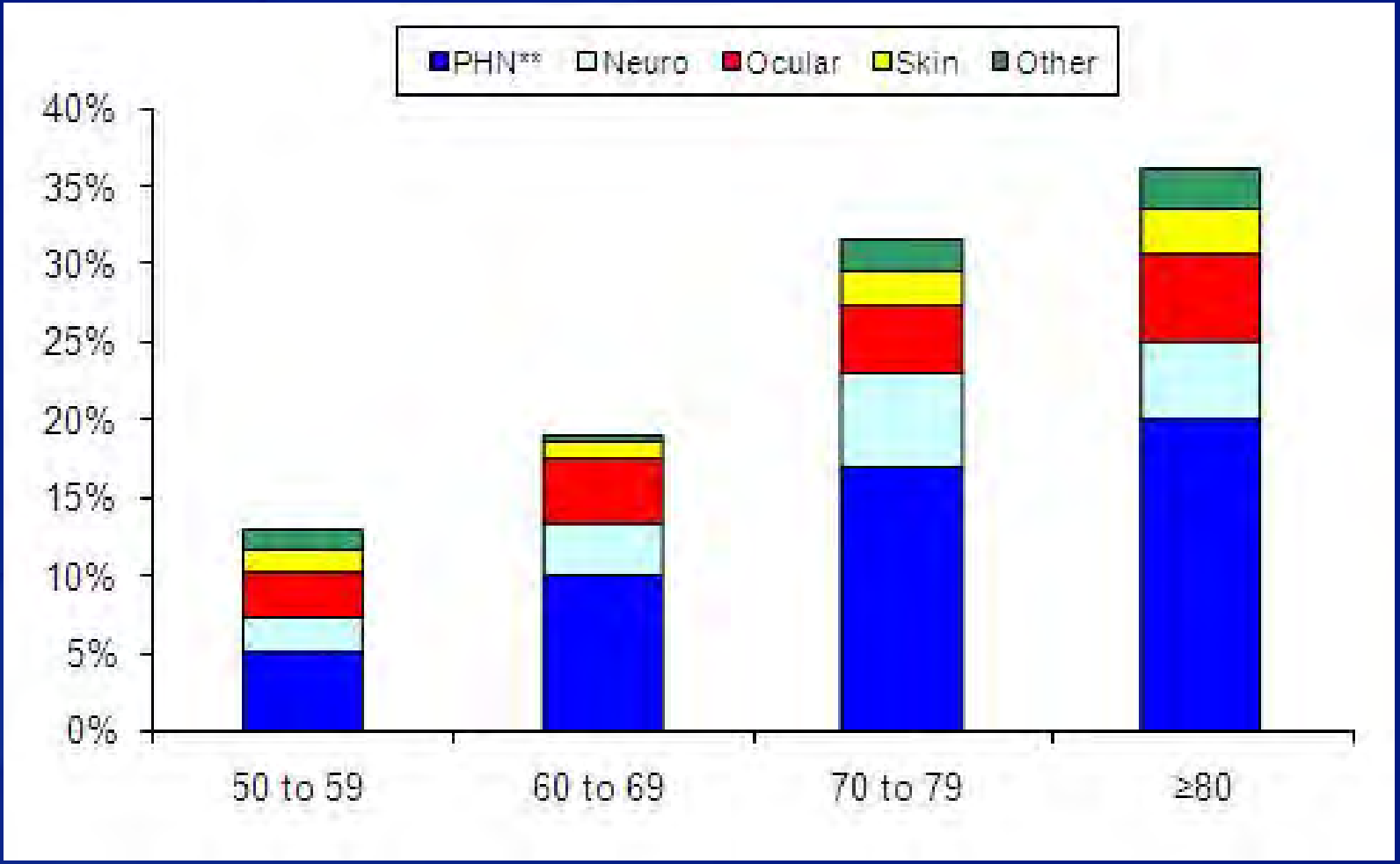
SELECTED PARAMETERS AND ASSUMPTIONS

Herpes Zoster Incidence

- Based on various sources, 1982-2011



Proportion of HZ with PHN and Non-Pain Complications



Source: Yawn 2007

Vaccine Characteristics by Age Group Mean (95% CI)

- **Efficacy for prevention of HZ**

For age 50-59yrs	69.8% (54.1% 80.6%)
For age 60-69yrs	63.9% (44.2% 75.0%)
For age 70+ yrs	37.6% (22.1% 57.6%)

- **Efficacy for prevention of PHN** (≥ 90 days)

For age 60-69yrs	64.9% (20.4% 86.7%)
For age 70+ yrs	66.7% (43.3% 81.3%)

- **Vaccine AEs**

	Local reactions	**Fever/Systemic**
50-59yrs	49.5% (48%-50%)	2.0% (0.7%-3.2%)
60+ yrs	31.7% (28%-33%)	1.4% (0.3%-2.5%)

Sources: Schmader *et al.* CID 2012 & Oxman *et al.* NEJM 2005

Other Assumptions

- **QALY loss calculated from**
  - Duration of pain
  - Pain intensity
  - Health utility from various health states
- **No recurrent HZ**
- **Age-specific health-related quality of life correction used (HUI-III)**
- **Direct and Indirect costs of HZ and PHN**
  - Costs for acute phase of HZ
  - Costs for non-pain complications
  - Long-term costs for PHN
  - Work loss to pain and productivity loss to death
- **Discount rate for all costs (and health outcomes in ratios), 3%**

Cost of Vaccination

- **Vaccination coverage assumed 100%**
- **Vaccine cost based on 2013 private sector prices**
  - **$165/dose*** + $AEs** + $20 Adm*** (≈$190 per vaccinee)

* CDC Vaccine Price List (June 2013) http://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html

** Cost of AE's used age-specific rates multiplied by direct medical cost for AE ($11 per Dr phone call for locals reactions or $115 per medical visit for systemic reactions)

*** Cost of vaccine administration $20 (range $15-$50)

AE = Adverse Event

BASE CASE RESULTS

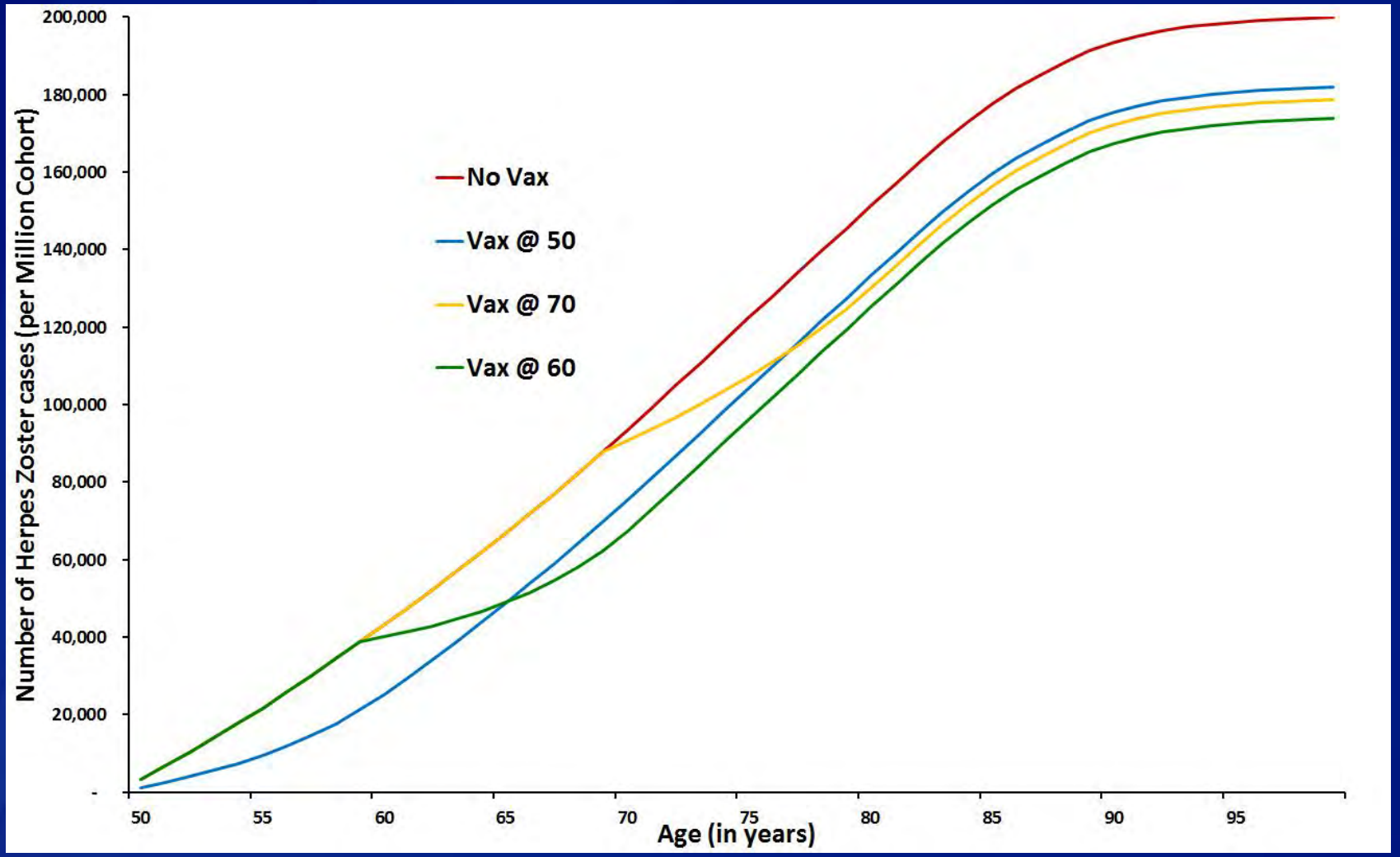
Preliminary

Analytic Approach (1)

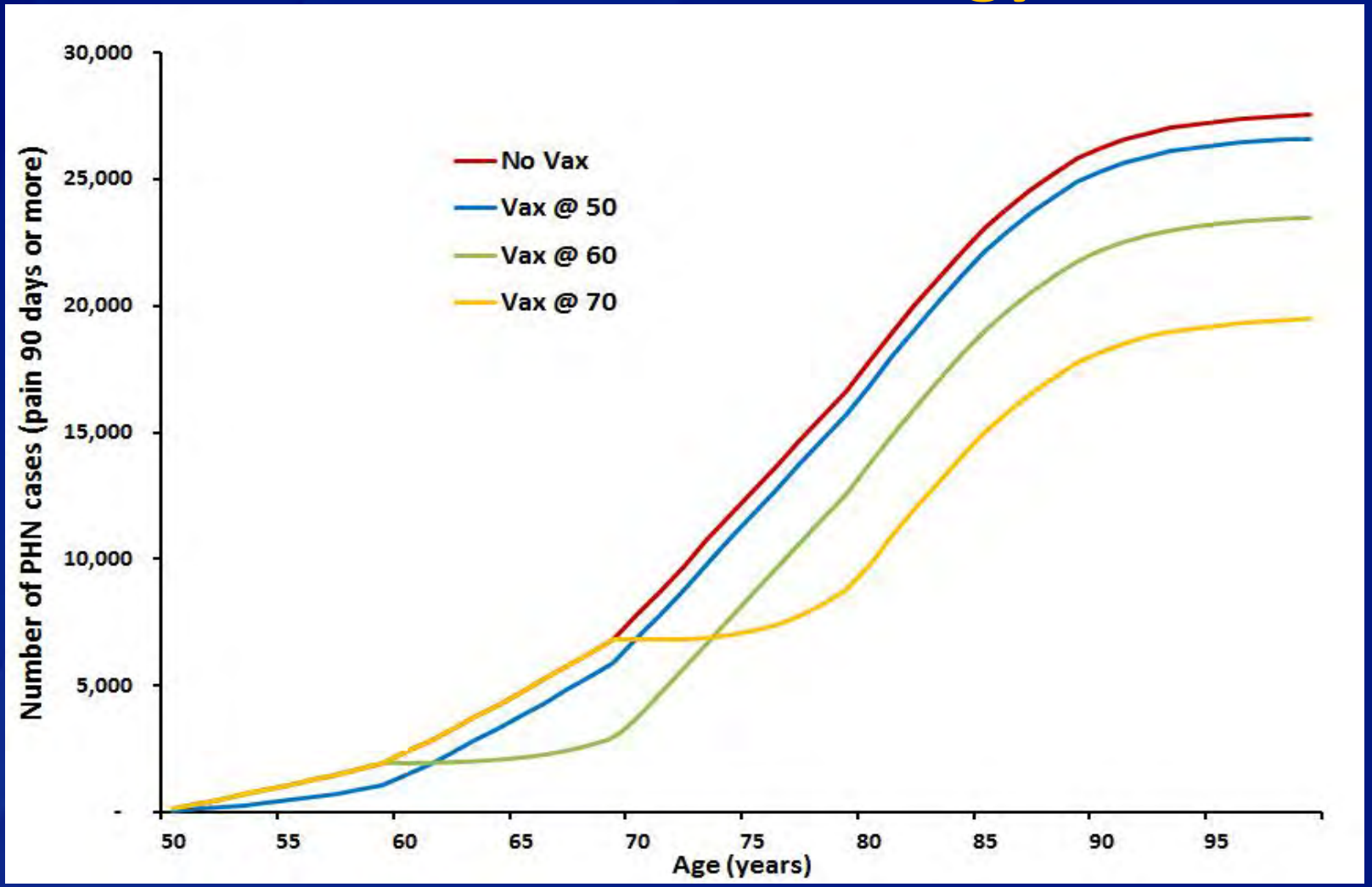
At what age would vaccination have the greatest population impact?

- **4 cohorts of 1M people, all followed from the age 50 years**
  - **Not vaccinated at all**
  - **Vaccinated at age 50**
  - **Vaccinated at age 60**
  - **Vaccinated at age 70**

Cumulative Number of HZ Cases by Vaccination Strategy



Cumulative Number of PHN* Cases by Vaccination Strategy



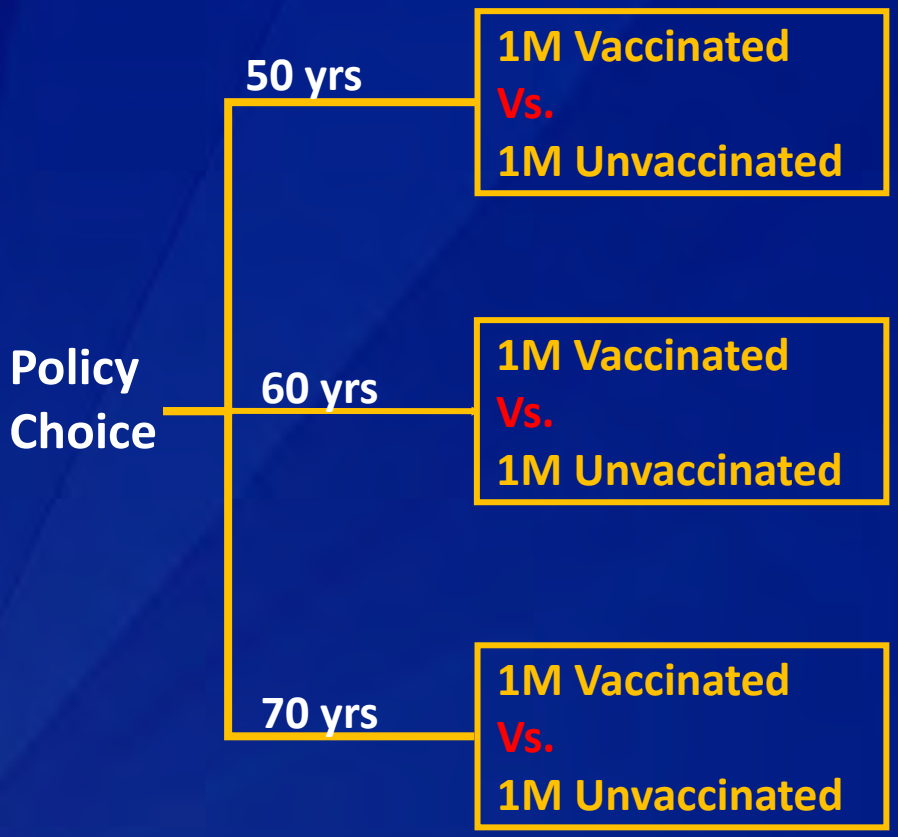
* PHN = moderate to severe pain lasting more than 90 days

Outcomes *Prevented* Compared to No Vaccination Program

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
# HZ cases	19,765 (9.9%)	26,147 (15.0%)	21,269 (15.2%)
# PHN cases	1,012 (3.7%)	4,045 (15.0%)	8,055 (31.4%)
# Deaths	0.2 (0.3%)	0.7 (1.0%)	2 (2.2%)
Ambulatory Visits	37,839	89,169	133,128
ED Visits	8,940	8,193	12,317
Hospitalizations	435	1,492	2,535
# Days in hospital	678	6,693	10,666
# Prescriptions	46,516	90,964	126,357
Lost work (hours)	625,817	506,110	413,058

Analytic Approach (2)

At what age would vaccination produce the greatest value?



- What is the cost-effectiveness of vaccinating a cohort of adults 50 years old ***versus*** a cohort of adults 60 years old ***versus*** a cohort of adults 70 years old compared to ***no*** vaccination in these cohorts?

Savings in Costs and QALYs from Vaccination Compared to No Vaccination Program

(All costs in *thousands and discounted at 3%*)

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
Direct medical costs	$7,307	$15,858	$23,726
Direct non-medical costs	$319	$1,188	$1,909
Indirect costs	$9,241	$7,274	$6,329
Total costs	**$16,867**	**$24,319**	**$31,964**
QALYs saved*	948	2,609	4,780

* Discounted at 3%

Costs of Vaccination Program by Strategy
(All costs in *thousands and discounted at 3%*)

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
Dose + Adm	$185,000	$185,000	$185,000
Local reaction	$5,898	$3,694	$3,694
Fever/systemic	$2,300	$1,610	$1,610
TOTAL	**$193,198**	**$190,304**	**$190,304**

Cost-Effectiveness Summary by Strategy (Societal Perspective)

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
Net cost*	**$178.5 Million**	**$169.0 Million**	**$162.9 Million**
Cost per HZ prevented	$11,255	$8,455	$9,989
Cost per PHN prevented	$61,084	$19,761	$9,607
Cost per QALY saved **	**$271,713**	**$79,967**	**$38,191**

* *NC = Cost of Vaccination Program - Savings in Cost-of-Illness from Vaccination*

** Does not including indirect cost savings

Average Number Needed to Vaccinate by Strategy

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
One HZ case	51	**38**	47
One non-PHN complication	632	**425**	321
One PHN case	988	**247**	124
One QALY	938	**339**	187

SENSITIVITY & SCENARIO ANALYSES

Preliminary

Selected Parameters for Scenario Analyses

- **Duration of vaccine efficacy**
  - Upper and lower 95% CI from SPS, STPS & LTPS data
- **Vaccine efficacy for PHN in 50-59 year olds**
  - Assuming same efficacy reported for PHN in 60-69 year olds
- **Patient perspective for QALYs**
  - Patient responses on health state evaluations from Zoster Utility Evaluation project
- **Vaccine effectiveness for prevention of HZ**
  - Observational study in a HMO (Tseng et al. JAMA 2011)

Cost-Effectiveness
Selected Scenario Analyses

	Vaccinate at 50	Vaccinate at 60	Vaccinate at 70
Base-case	**$271,713**	**$79,967**	**$38,191**
Duration of Vaccine Efficacy - *Lower 95%CI*	$802,356	$215,034	$103,886
Duration of Vaccine Efficacy – *Upper 95%CI*	$227,168	$69,113	$32,864
Vaccine Efficacy for PHN in 50-59 year olds	$226,186	$80,005	$38,210
Patient perspective for QALYs	$222,380	$66,906	$31,991
Vaccine *Effectiveness* for HZ	$336,073	$95,349	$34,739

Study Limitations

- **Uncertain duration of vaccine protection against HZ and PHN**
  - Limitations in LTPS results due to lack of concurrent control group
  - Longer protection against PHN could increase attractiveness of earlier vaccination
  - Duration of protection in ≥60 year olds assumed for all ages
- **QALY-loss due to mild, moderate, and severe adverse events among vaccine recipients not included**
  - Including this could increase attractiveness of later vaccination
- **HZ incidence rates may be increasing over time**
  - This may increase attractiveness of later vaccination
- **Uncertainty in QALY loss due to HZ and its complications**
  - Can affect results for our policy question in any direction
  - Results of scenario analysis increase confidence somewhat

Study Strengths

- Includes data on duration of protection through 11 years after vaccination
- Updated assumption of key parameters based on recent studies relating to zoster and zoster vaccine

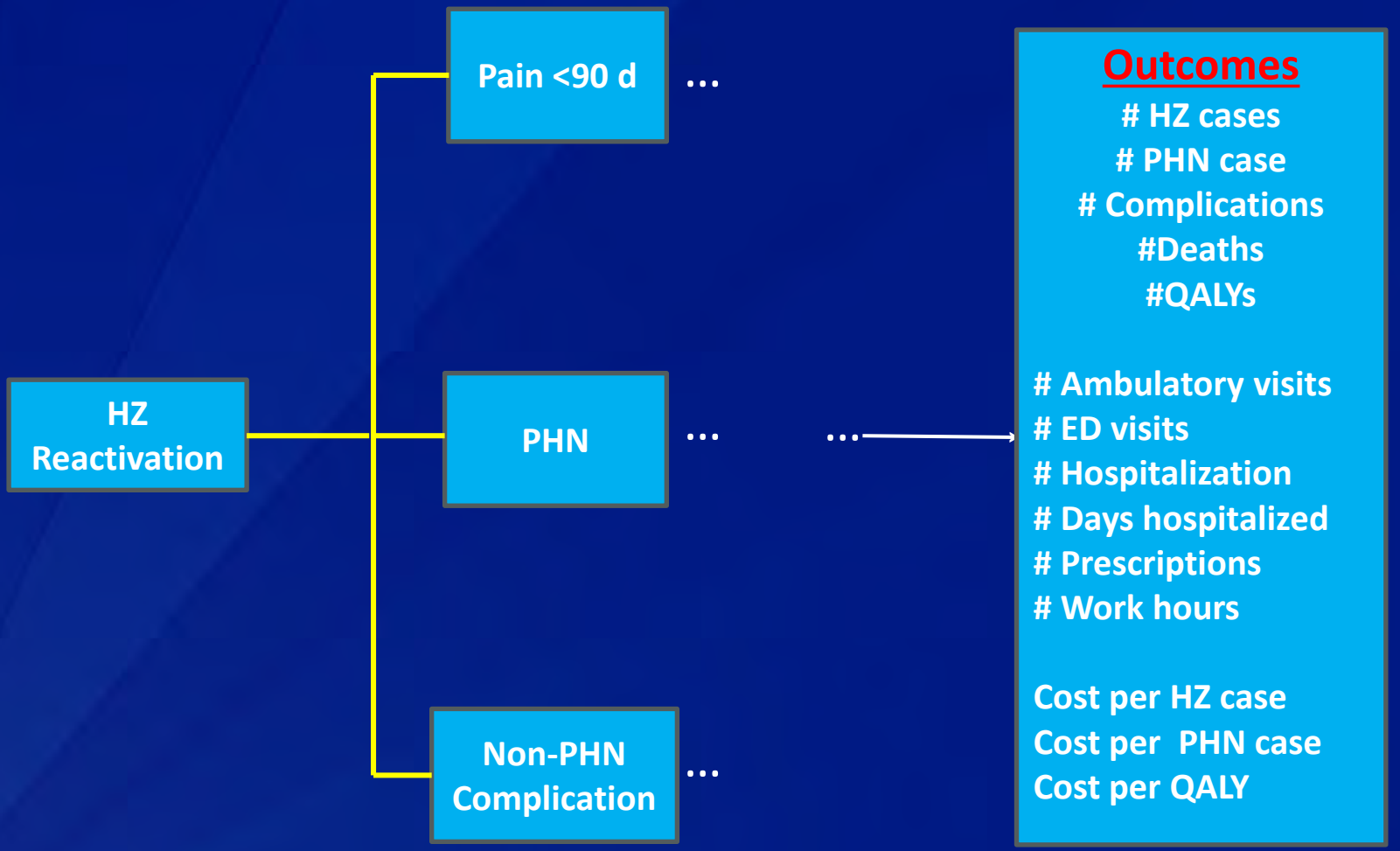
Conclusions

- Substantially greater reduction of disease burden, healthcare utilization, and costs are achieved with vaccination at age 70 or 60 compared to vaccination at age 50
- Results were robust, based on:
  - Magnitude of the differences among vaccination strategies
  - Consistency of public health & economic perspectives
  - Consistency of results from scenario analyses
- These conclusions are consistent with those found in other published analyses

DISCUSSION

Extra Slides

Health and Healthcare Utilization Outcomes



QALYs Estimation by Pain Duration and Intensity

QALYs lost per episode:

$$QALYs_{shingles} = (t/365) * [1 - Pain\ Score_{(t,i)}] * Shingles_{(t,i)}$$

$$QALYs_{PHN} = (t/365) * [1 - Pain\ Score_{(t,i)}] * PHN_{(t,i)} \quad .$$

Where:

- ***t/365 = Time lasting of episode as*** **fraction of time of a year (*time in days divided by 365)***
- ***Pain*** **Score (*t, i*) = Score observed for pain lasting *t* days and with intensity *i*, (*i*= 0 , …, 10; where 0 no pain and 10 worst pain)***
- ***Shingles*** **(*t, i*) = Percent of shingles cases with pain duration *t (in days*) and with intensity *i*.**
- **PHN (*t,i*) = Percent of PHN cases with pain duration *t (in days*) and pain intensity *i*.**

* ZUE project (Lieu et al Pharmacoeconomics 2008)

HZ Incidence for Vaccinated Cohort

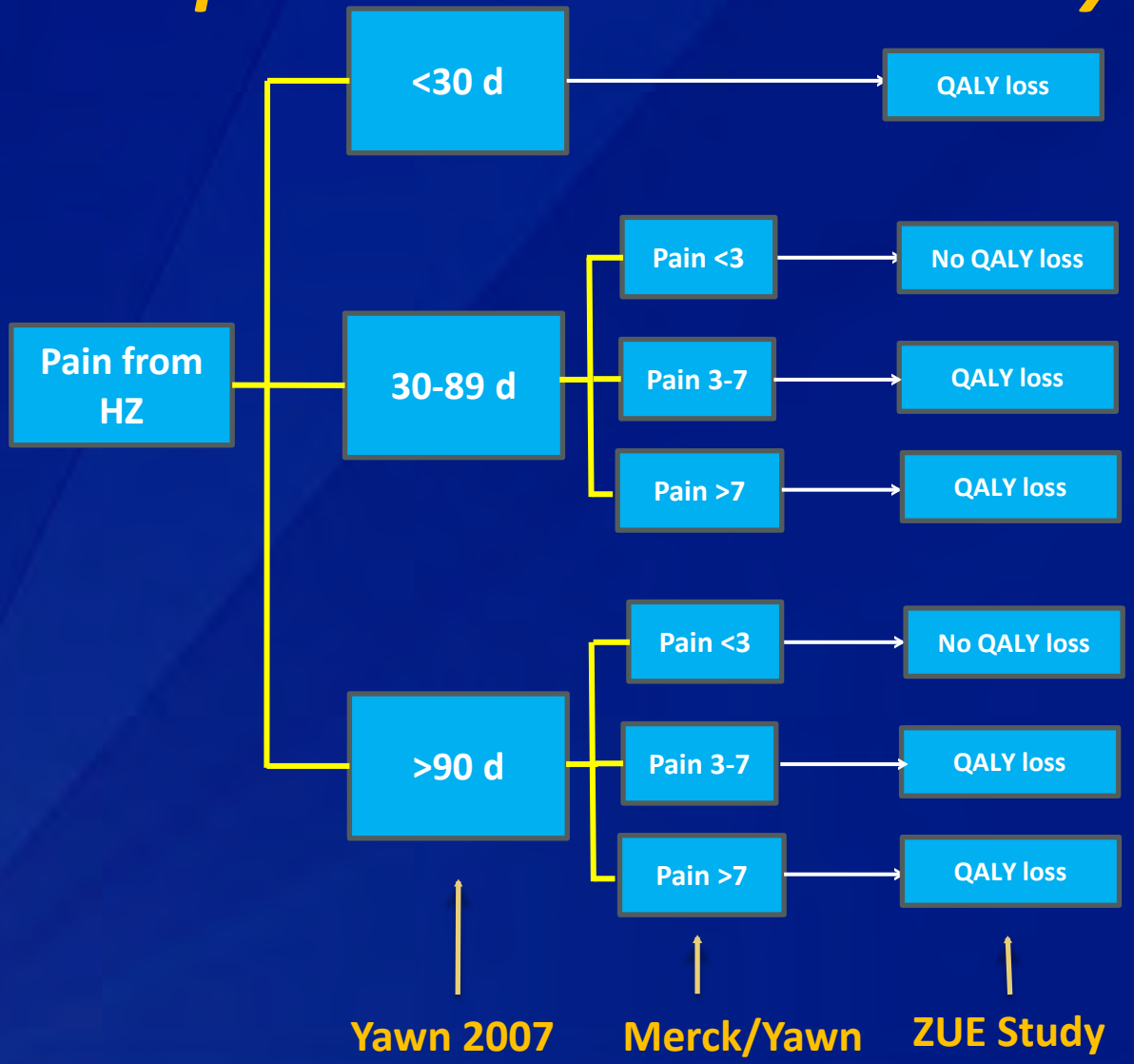
For each age group:

$$HZDI_{vacc} = HZDI_{no\ vacc} * [1-(Residual_t * VEff_{age})]$$

Where:

- $HZDI_{vacc}$ = HZ incidence in vaccinated cohort
- $HZDI_{no\ vacc}$ = HZ incidence in non-vaccinated cohort
- $Residual_t$ = Residual vaccine efficacy (0-100%) *t* years after vaccination *t*=0,…,T
- $VEff_{age}$ = Age-specific vaccine efficacy

QALY Calculations: *pain duration x intensity*



Economic Analysis: Net Cost

- We calculated net cost (*NC*) for vaccinated and unvaccinated cohorts according to the following formula:

$$NC = \sum_{t=0}^{T} \frac{C_t - B_t}{(1+r)^t}$$

Where:

- *C* = cost of the vaccination program (including cost of adverse events)
- *B* = benefits (savings in cost of illness prevented with vaccination program)
- *t* = time in years after immunization (*t*=0, 1, 2,…*T*)
- *r* = discount rate (3%)
- *T*= Analytical horizon (age-specific, in years)

Economic Analysis: Cost-Effectiveness

- We calculated cost-effectiveness ratios (*CE*) according to the following formula:

$$CE = \frac{NC_{vacc} - NC_{unvacc}}{\sum_{t=0}^{T} \frac{(HO_{vacc} - HO_{unvacc})}{(1+r)^t}}$$

Where:

- *NCvacc* = Net cost of vaccination strategy
- *NCunvacc* = Net cost of baseline (no vaccination) strategy
- *HOvacc* = Health outcome of vaccination (ex., QALYs, LYs)
- *HOunvacc* = Health outcome of baseline (no vaccination)
- *t* = time in years after immunization *(t=0, 1, 2,…, T)*
- *r* = discount rate (3%)
- *T*= Analytical horizon (age-specific, in years)