

FINDINGS of the “HEPATITIS B VACCINATION FOR INJECTION DRUG USERS” STUDY

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CASE



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Hepatitis B information

- ◆ Hepatitis B virus (HBV) is a DNA virus which infects the liver and is transmitted by body fluids
- ◆ Fulminant disease occurs in 1-2% of acute infections with about 60-90% mortality.
- ◆ In adults, 95% of those infected clear the virus. The remaining 5% develop chronic infection (carriers)
- ◆ A safe and effective vaccine was introduced in 1981.
- ◆ Universal protection in the US is expected by 2015.
- ◆ Yet an estimated 72,000 annual infections continue to be concentrated in high risk groups such as IDUs.

HBV Infection among IDUs

- ◆ At least 25% of all new HBV infections are among IDUs.
- ◆ Prevalence among IDUs ranges from 40% - 80%. Annual incidence rates of 10% - 12% have been reported among susceptible IDUs.
- ◆ <10% of those never infected have been immunized although vaccination of IDUs has been strongly recommended by the Immunization Practices Advisory Committee since 1991.

Treatment Costs for Hepatitis B Infections & Associated Illnesses

Illness	Annual treatment costs (per person)
Acute infection	
Non-hospitalized	\$309
Hospitalized	\$9,173
Fulminant hepatitis B	\$17,407
Chronic carrier	\$1,003
Compensated Cirrhosis	\$5,666
Decompensated Cirrhosis	\$29,800
Hepatocellular carcinoma	\$26,425
Liver transplantation	
First year	\$328,407
Follow-up years	\$31,681



Note: the information are from literature review

Hepatitis Vaccine Study (HVS) Aims

- ◆ Determine the optimal strategies of vaccinating IDUs. We examined venue and dosing schedule.
- ◆ Determine whether hepatitis B vaccination campaigns targeting IDUs through SEPs economically desirable for the healthcare system. We examined costs and benefits.
- ◆ Determine the epidemiological impact of scaling up the optimal hepatitis B vaccination strategy among IDUs and the needed duration of such a program.

Hepatitis B Vaccination Study

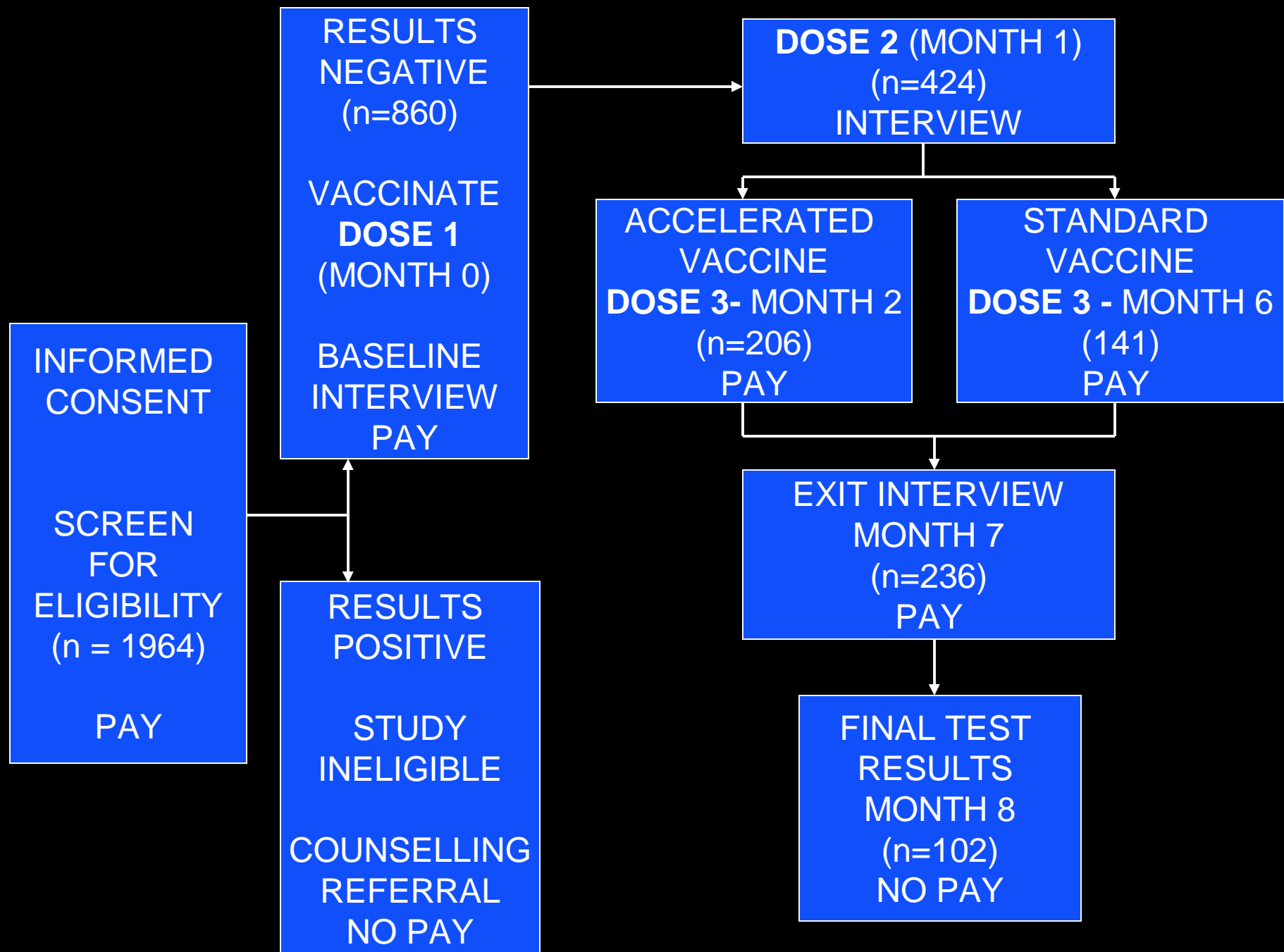
◆ SEP study sites:

- Chicago IL (Oct 2003 – Mar 2006)
- Hartford CT (Oct 2003 – Mar 2006)
- Bridgeport CT (Dec 2004 – Mar 2006)

◆ Inclusion criteria

- ≥ 18 years old
- capable of giving informed consent
- ≥ 1 illicit drug injection (past 30 days)
- evidence of injection stigmata





Participant Characteristics

	Chicago (n=1333)	Hartford (n=478)	Bridgeport (n=153)	Total (n=1964)	p-value
Sex (male)	69%	83%	76%	73%	<.0001
Age* in years	41 (10.1)	39 (8.8)	36 (9.1)	40 (9.8)	<.0001
Race/ethnicity					<.0001
White	23%	20%	22%	22%	
African American	59%	16%	12%	45%	
Hispanic	15%	64%	66%	31%	
Other	3%	1%	1%	2%	
Education level (< hs)	38%	44%	51%	40%	NS
Income* in US\$	852 (1001)	435 (649)	897 (901)	808 (969)	<.01
SEP customer	81%	70%	78%	78%	<.0001

* mean (SD)

Screening Results

	Chicago (n=1333)	Hartford (n=478)	Bridgeport (n=153)	Total (n=1964)
Never Infected/Not Vaccinated	684 51%	116 24%	60 40%	860 44%
Previously Infected	582 44%	295 62%	72 47%	949 48%
Carriers	3 <1%	17 4%	3 2%	23 1%
Already Vaccinated	48 4%	48 10%	18 12%	114 6%
Missing	16 1%	2 <1%	0	18 <1%

Participants in the accelerated schedule were significantly more likely to complete the vaccination series

Total number of accepting Dose 1	Receive Dose 2	Vaccination Schedule	Receive Dose 3	p-value
595	424 (77.3%)	Accelerated (n=253)	206 (81.4%)	0.001
		Standard (n=171)	141 (68.1%)	

Successful Immunization Rates (HBsAb Response Rates)

- ◆ Immunization rates were lower than expected in both schedules
 - Not correlated with age, HIV or HCV status, or type or amount of drug injected.
 - Similar low rates were observed in three other studies with injection drug users.

Returning at Month 7	HBsAb \geq 10mIU/ml	HBsAb $<$ 10mIU/ml	p-value
Accelerated (n=116)	78.3%	21.7%	NS
Standard (n=120)	85.7%	14.3%	

Vaccine Efficacy

- ◆ Efficacy is the product of the vaccination completion rate and the successful immunization rates (after receiving either two doses or three doses)
- ◆ The vaccine efficacy (proportions of those who received the first dose who are successfully immunized) in the accelerated schedule (60.0%) was significantly higher than that in the standard schedule (51.1%)

Cost-effectiveness Analysis

- ◆ The perspective: health care sector

Only direct costs (i.e., all elements of the vaccination campaign) and costs directly related to medical treatment of hepatitis B associated illnesses were considered in the model

- ◆ Net cost = costs of vaccination program — medical costs saved from averted hepatitis B infections

If net cost is negative, the vaccination program is cost-saving

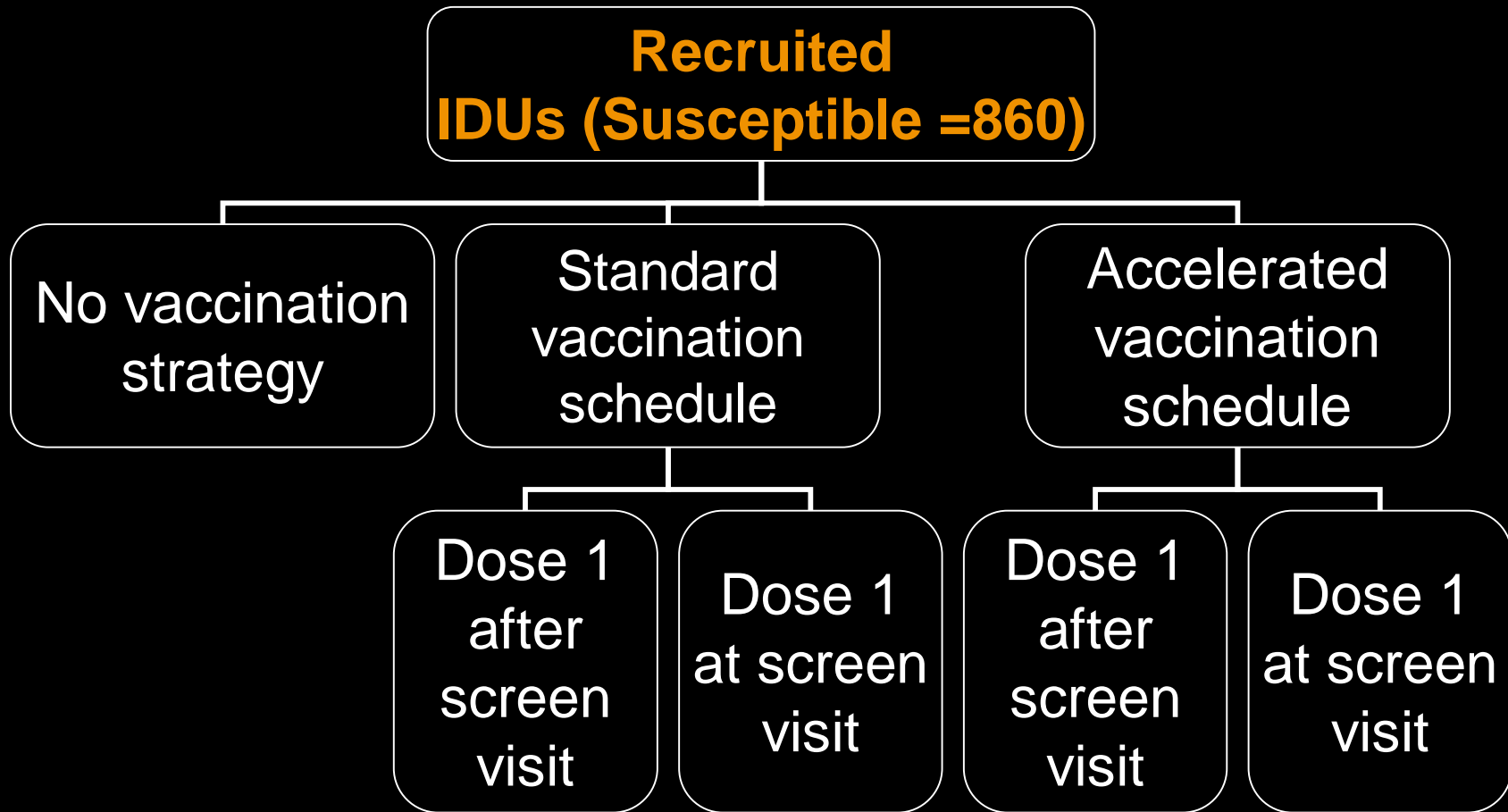
- ◆ Health benefits:

Prevented infections and quality-adjusted life years (QALYs)

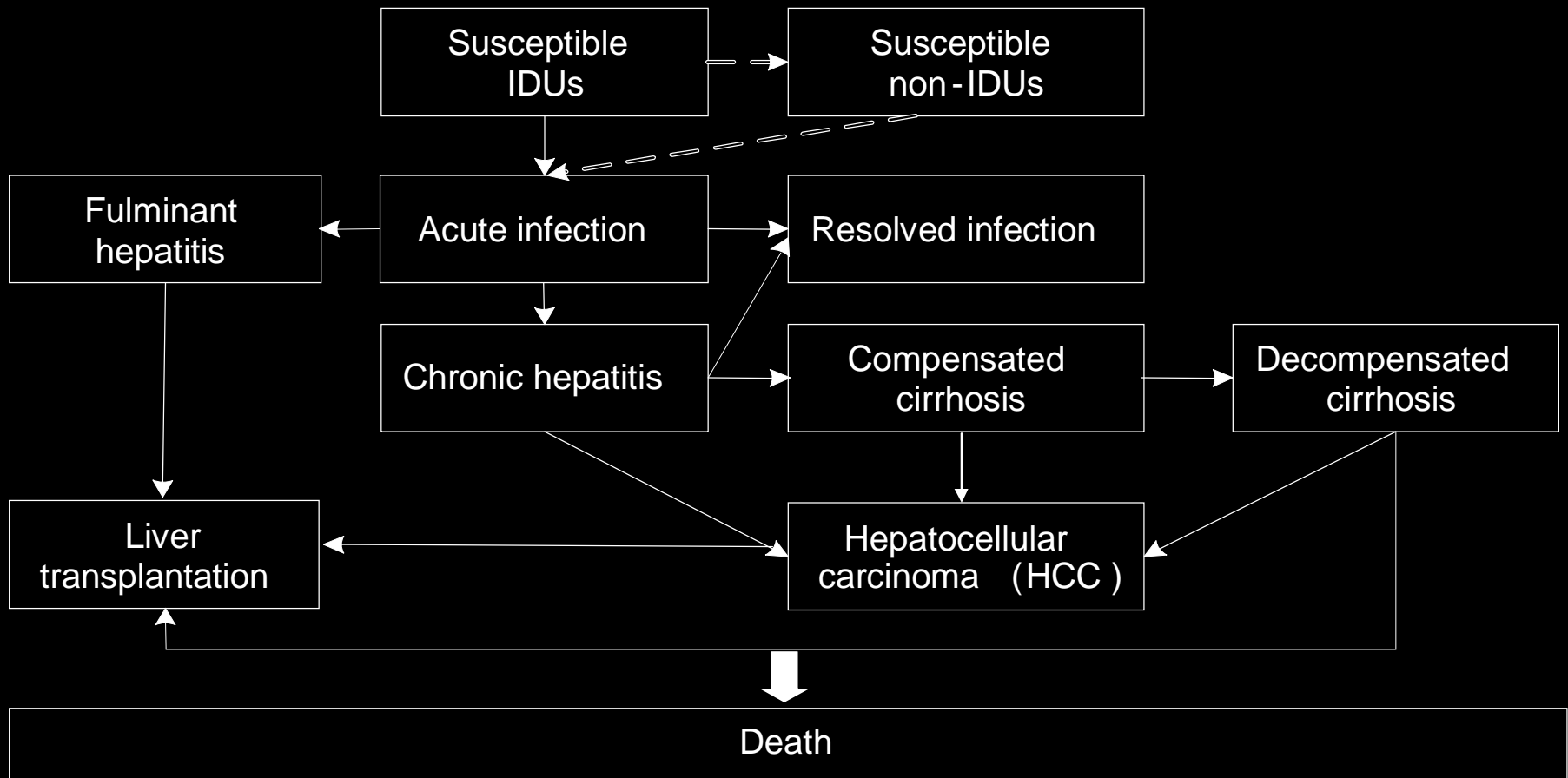
- ◆ The discounted rate:

Future medical costs of hepatitis B illnesses is discounted at an annual rate of 3%

Comparison of five strategies



Markov model—Natural History of HBV Infection



Per-person Cost of the HVS

Costs*	US\$ per person
Recruiting	42
Blood drawing	15
Vaccine administering (per shot)	13
Serologic test	34
Supplies	8
Payment per visit	15
Vaccine	10-55

* Vaccination program costs only (i.e., no costs directly related to program evaluation were included)

Baseline Results

Strategy	Acute infections prevented	Discounted QALYs gained	Discounted HBV-related medical costs (\$)	Program cost (\$)		Net cost (\$)	
				\$10 vaccine	\$55 vaccine	\$10 vaccine	\$55 vaccine
No vaccination	0	0	1,414,526	0	0	/	/
Standard with Dose 1 after screen	225	0.07	914,508	342,052	403,207	-157,967	-96,812
Accelerated with Dose 1 after screen	264	0.08	827,333	348,926	413,636	-238,267	-173,557
Standard with Dose 1 at screen	326	0.10	690,815	364,783	503,129	-358,928	-220,582
Accelerated with Dose 1 at screen	382	0.12	565,811	374,717	518,192	-473,999	-330,524

Sensitivity Analysis Results

- ◆ The results were more sensitive to the vaccine completion rates rather than the successful immunization rates.
- ◆ When the susceptibility was less than 17% or the annual incidence of acute infection was lower than 2.5%, all four vaccination were no longer cost-saving.
- ◆ When less than 46% of IDUs had access to medical care, all four vaccination strategies were no longer cost-saving.
 - 79.7% active IDUs in Connecticut are insured.

Epidemiological Impact of Hepatitis B Vaccination Campaigns through SEPs

- ◆ **What is the potential impact of scaling up the optimal vaccination regimen in a hypothetical IDU population using data from the HVS (n=14,435)?**

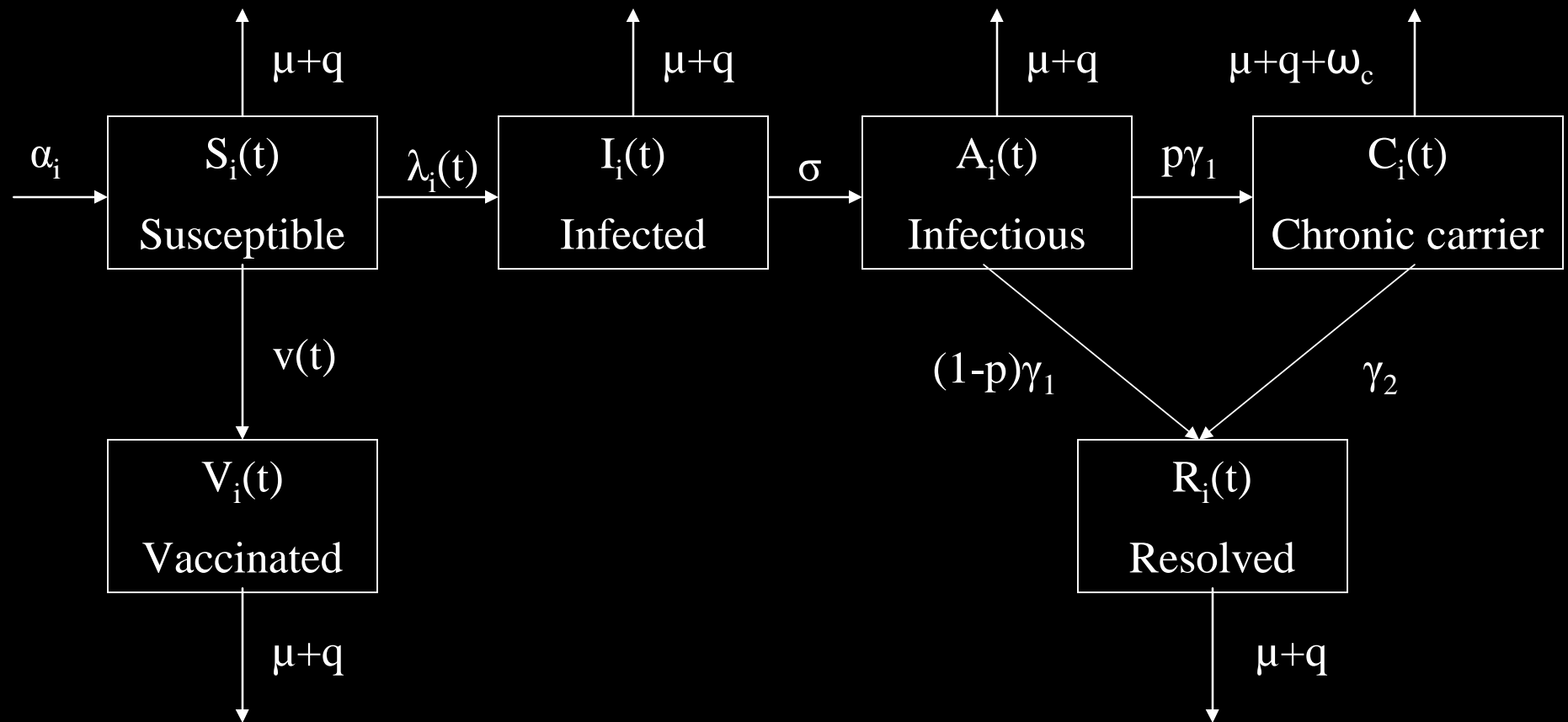
Study Assumptions

- ◆ **IDUs visit SEPs randomly and accept the vaccine at a constant rate.**
- ◆ **A series of annual acceptance (vaccination) rates - 20%, 40%, 60%, 80%, and 100% - were tested in the model. Among those accepting the vaccine, 60% will be successfully immunized.**

Study Assumptions (continued)

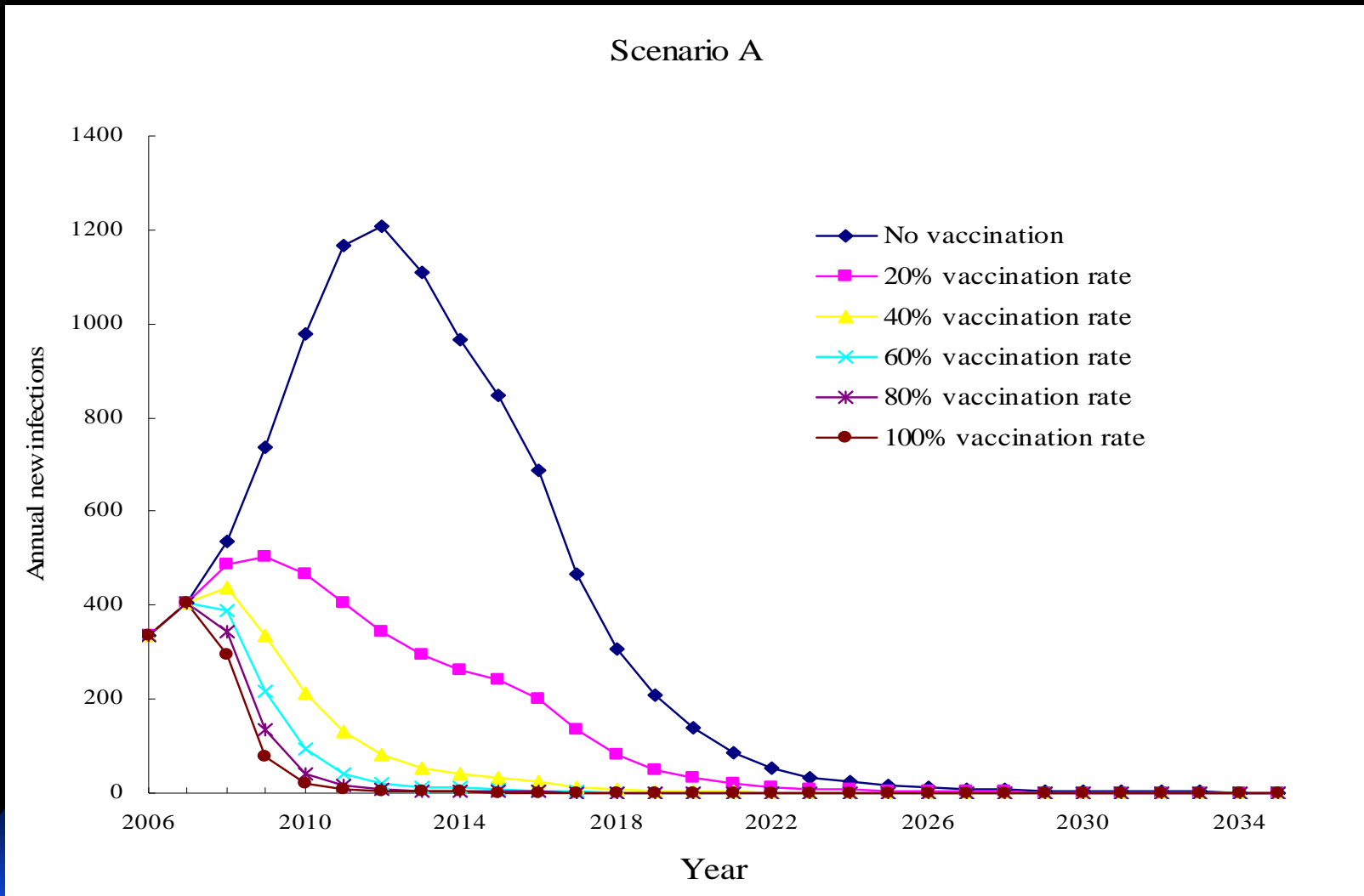
- ◆ All newly initiating IDUs from 2003 - 2016 are susceptible to HBV infection.
- ◆ Susceptibility of newly initiating IDUs declines to 40% in 2016 - 2019 and 10% in 2020.
- ◆ SEP-based vaccination campaigns are introduced at the beginning of 2008. Two vaccination scenarios are considered:
 - **Scenario A:** vaccination program runs for 12 years (2008 – 2019).
 - **Scenario B:** vaccination program runs 8 years (2008 – 2015).
- ◆ The force of infection has two components: transmission through unsafe injection and heterosexual transmission.

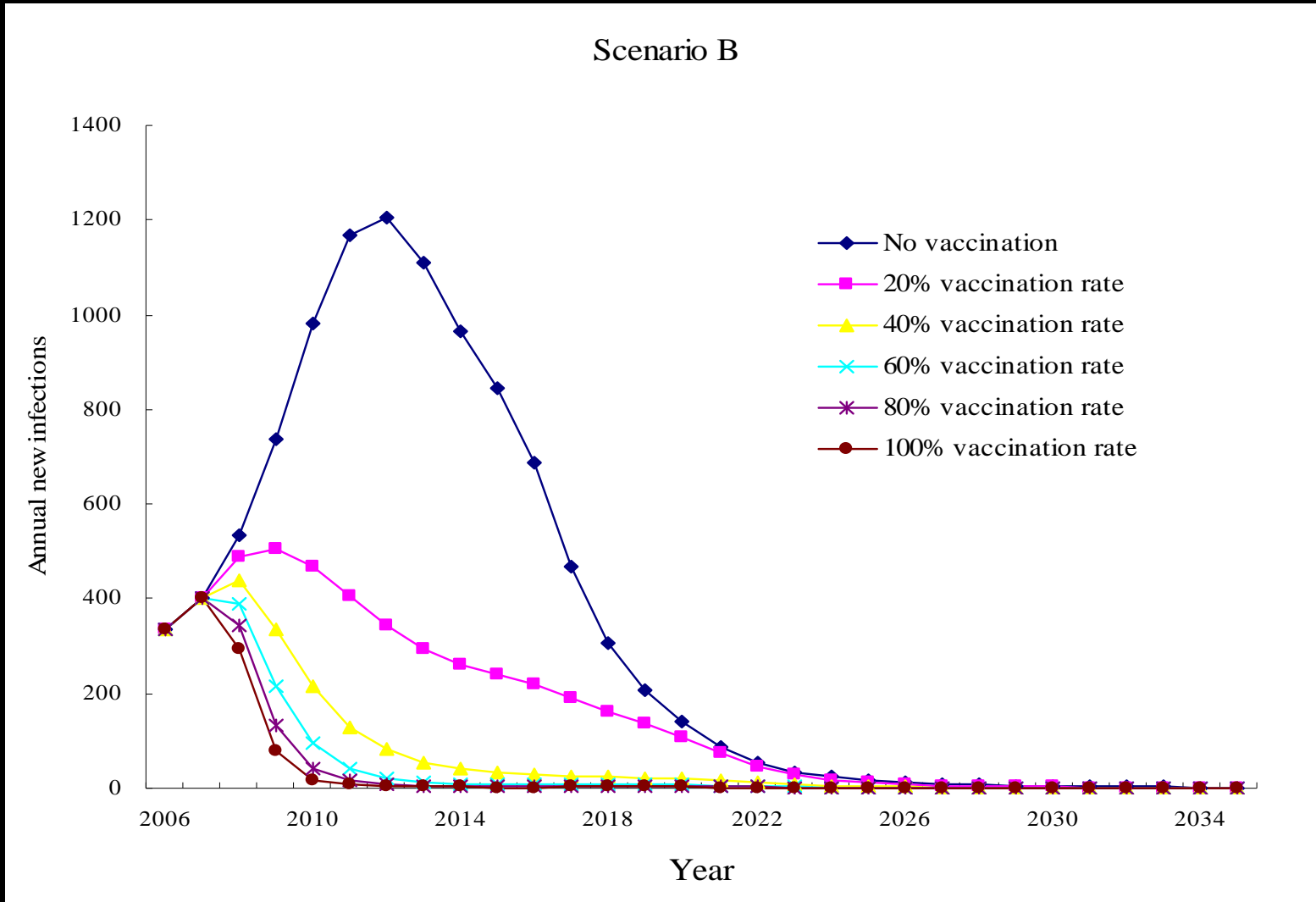
Disease Transmission Model



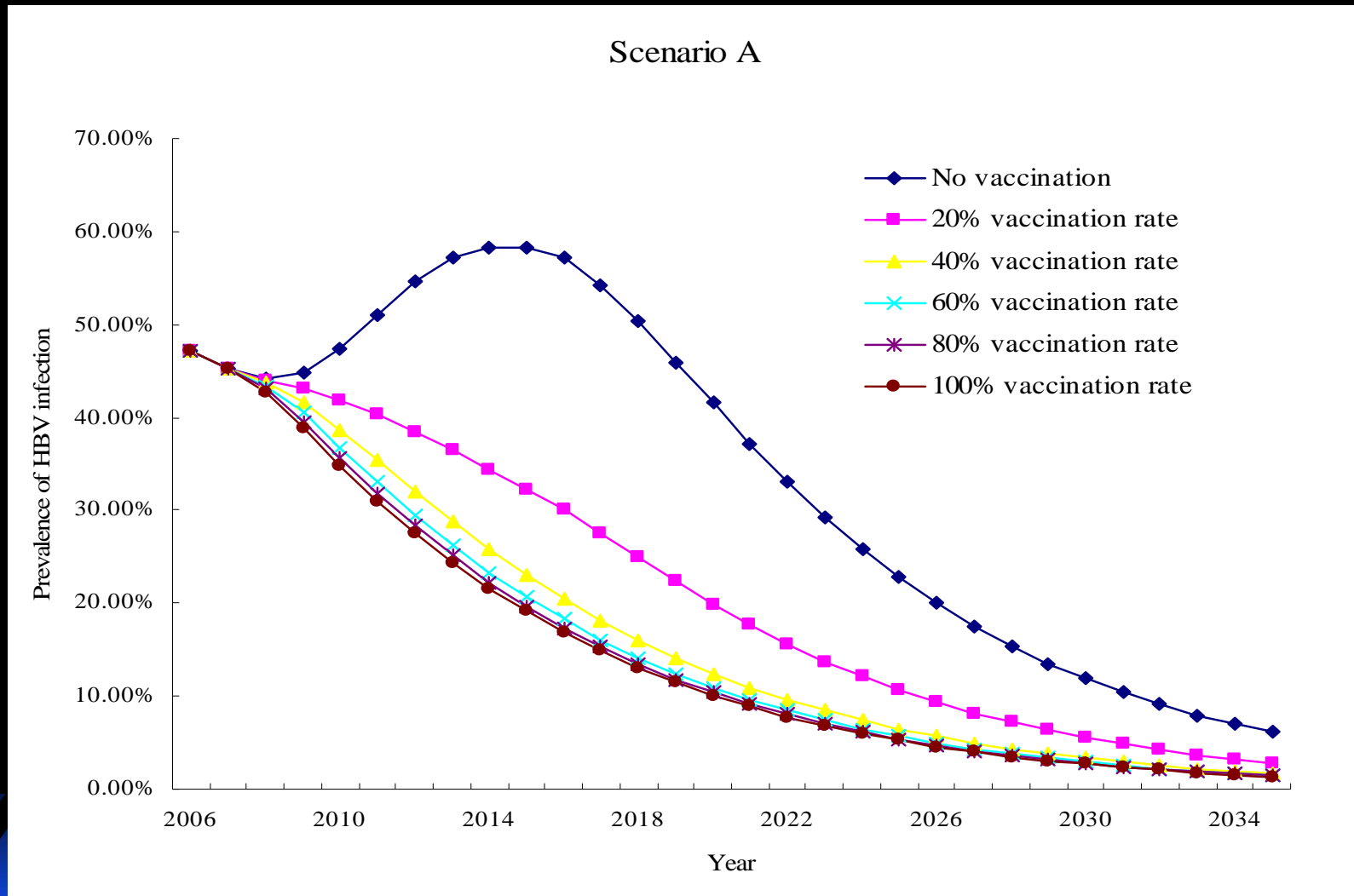
The IDU population was divided into three groups, male, female, and female commercial sex workers.

Annual New Acute HBV Infections

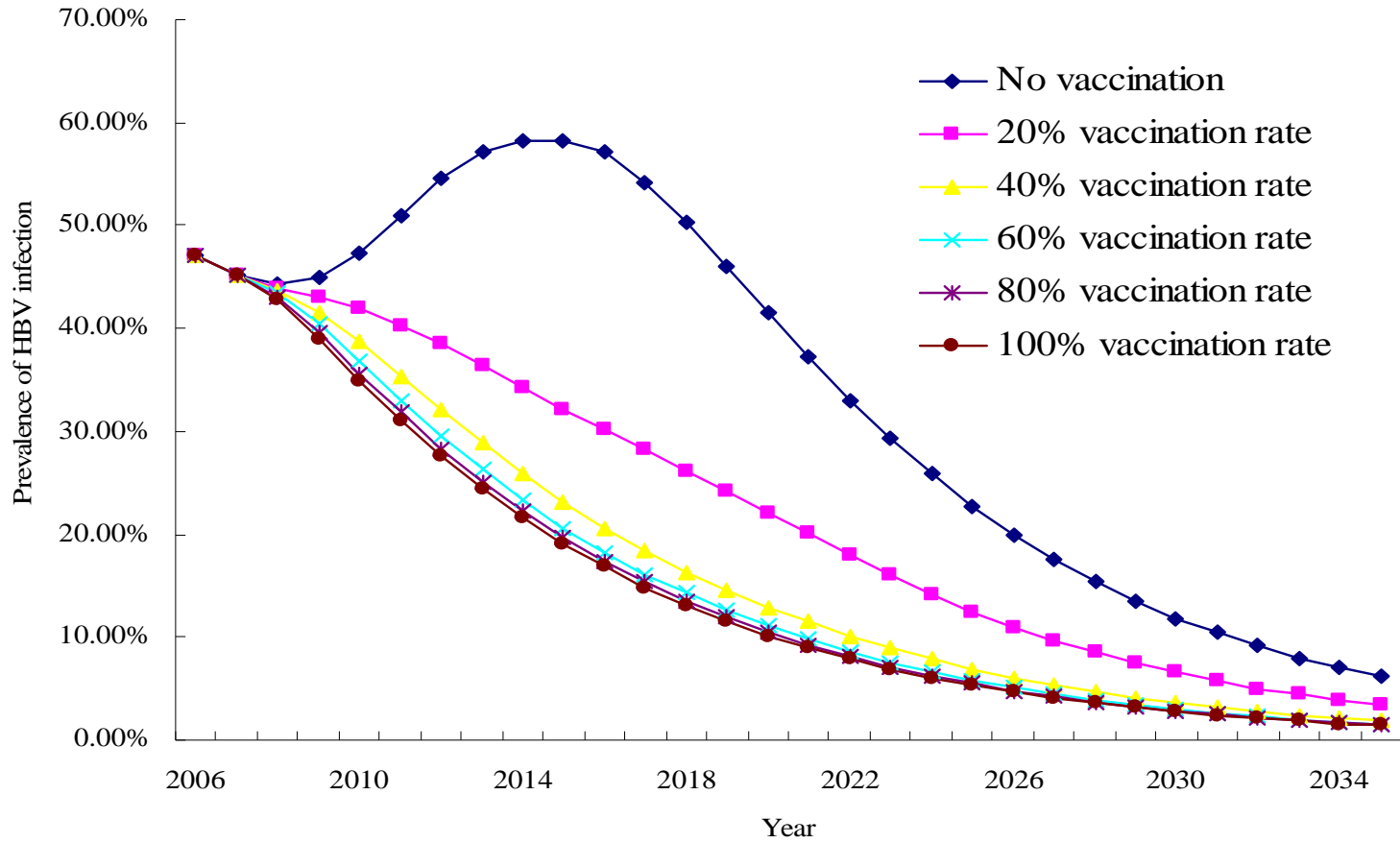




Prevalence of HBV Infection



Scenario B



Study Limitations

- ◆ Study population was a convenience sample.
- ◆ Data collection at screening was limited due to time constraints and response burden. Factors associated with failure to return cannot be assessed in order to improve follow-up rates.
- ◆ The results of the economic models are conservative and likely underestimate the benefits of a hepatitis B vaccination program for IDUs.
- ◆ Estimates used in the economic models are based on current available data.
- ◆ The epidemiological impact models does not consider non-injection risk of transmission or trend in immigration.

Recommendations from the HVS

- ◆ SEPs are effective and cost-saving venues for implementing HBV vaccination programs for IDUs.
- ◆ First dose should be administered at screening.
- ◆ Accelerated schedule recommended for SEP-based HBV vaccination programs .
- ◆ SEP-delivered vaccination campaigns are needed for the coming 8-12 years in the US.
- ◆ Unsafe injection practice was the major transmission route of HBV infection in the current IDU population. Injection hygiene programs are recommended in addition to implementing vaccination campaigns.

Practical Lessons Learned

- ◆ **Regular meetings of all participating organizations.**
- ◆ **Confusion of HBV and HCV information: IDUs need to understand the distinction and the efficacy of vaccination against HBV infection.**

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