

Universal Vaccination Against Hepatitis A

Lessons From the Experience in Immunization of Toddlers in Israel

Daniel Shouval

Liver Unit

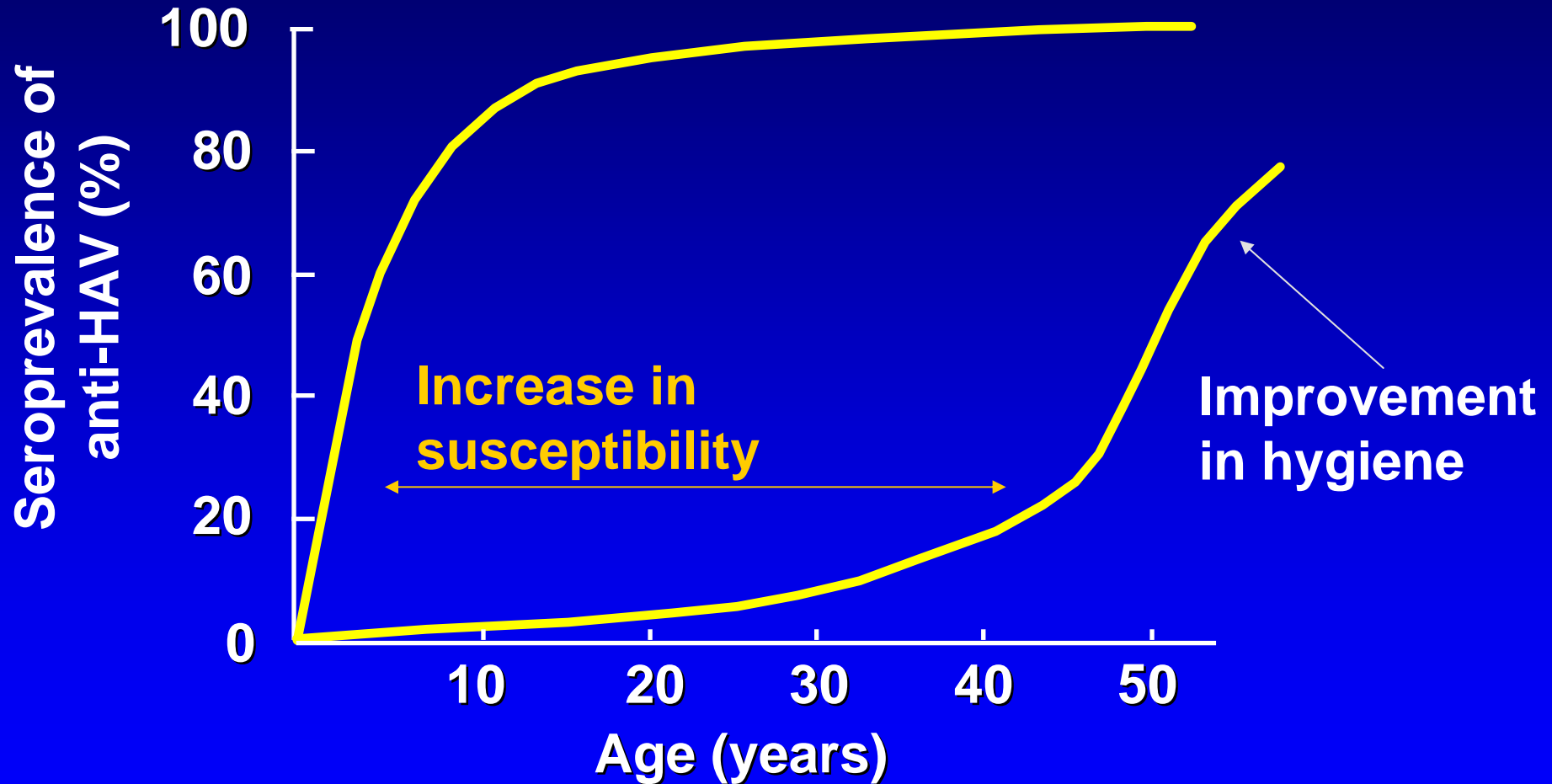
Hadassah-Hebrew University Hospital

Jerusalem, Israel

**Participating Investigators: Yaffa Ashur, Nili Daudi, Emilia Anis,
Alex Leventhal, Guo-liang Xia, Omana Nainan, Beth Bell, Harold Margolis,
Ron Dagan**

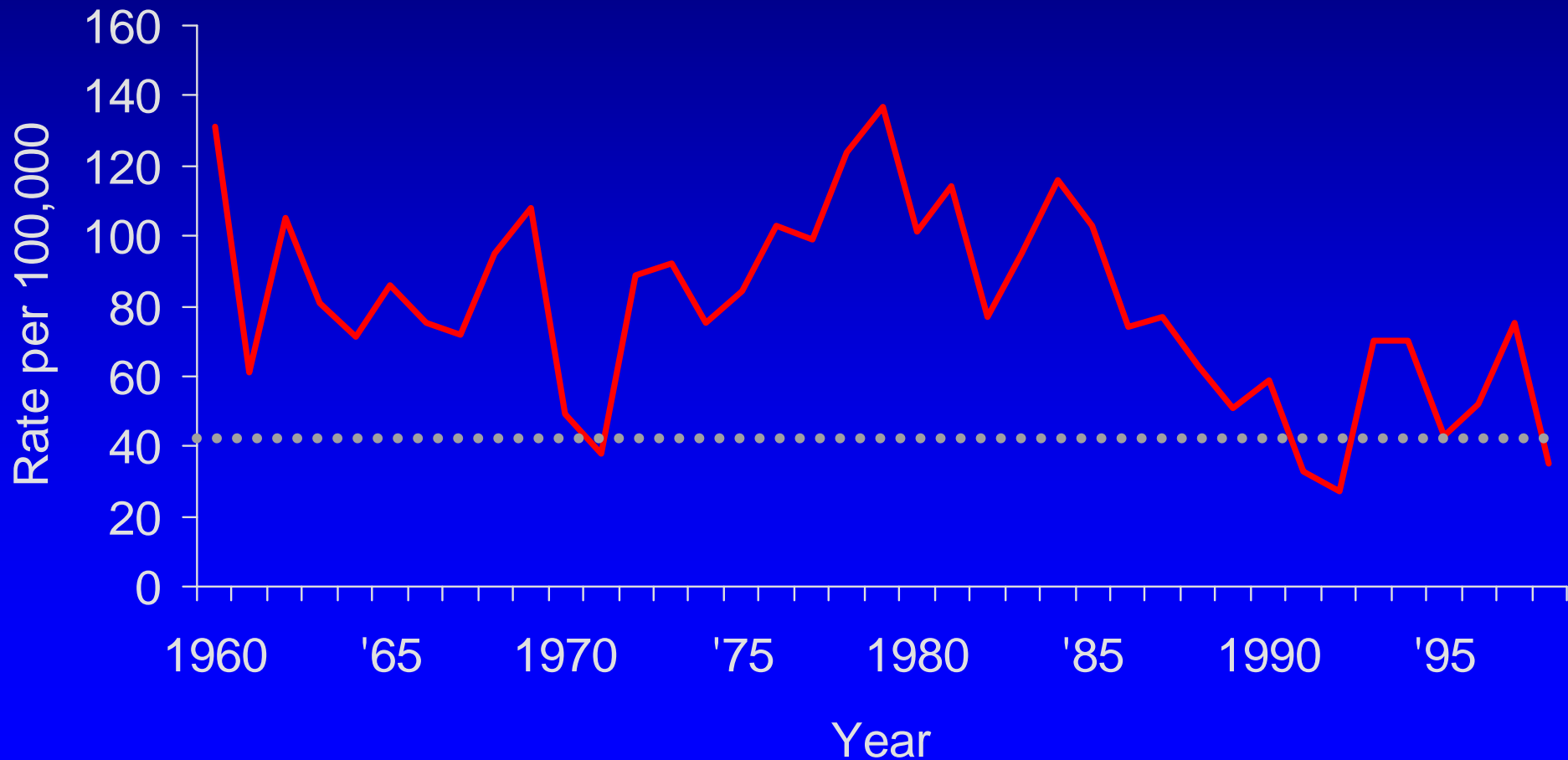
VHPB, Athens -16.11.2007

Hepatitis A epidemiology shifts with improving hygiene



Reported Acute Viral Hepatitis Through Passive Surveillance

Incidence - Israel, 1960-1998

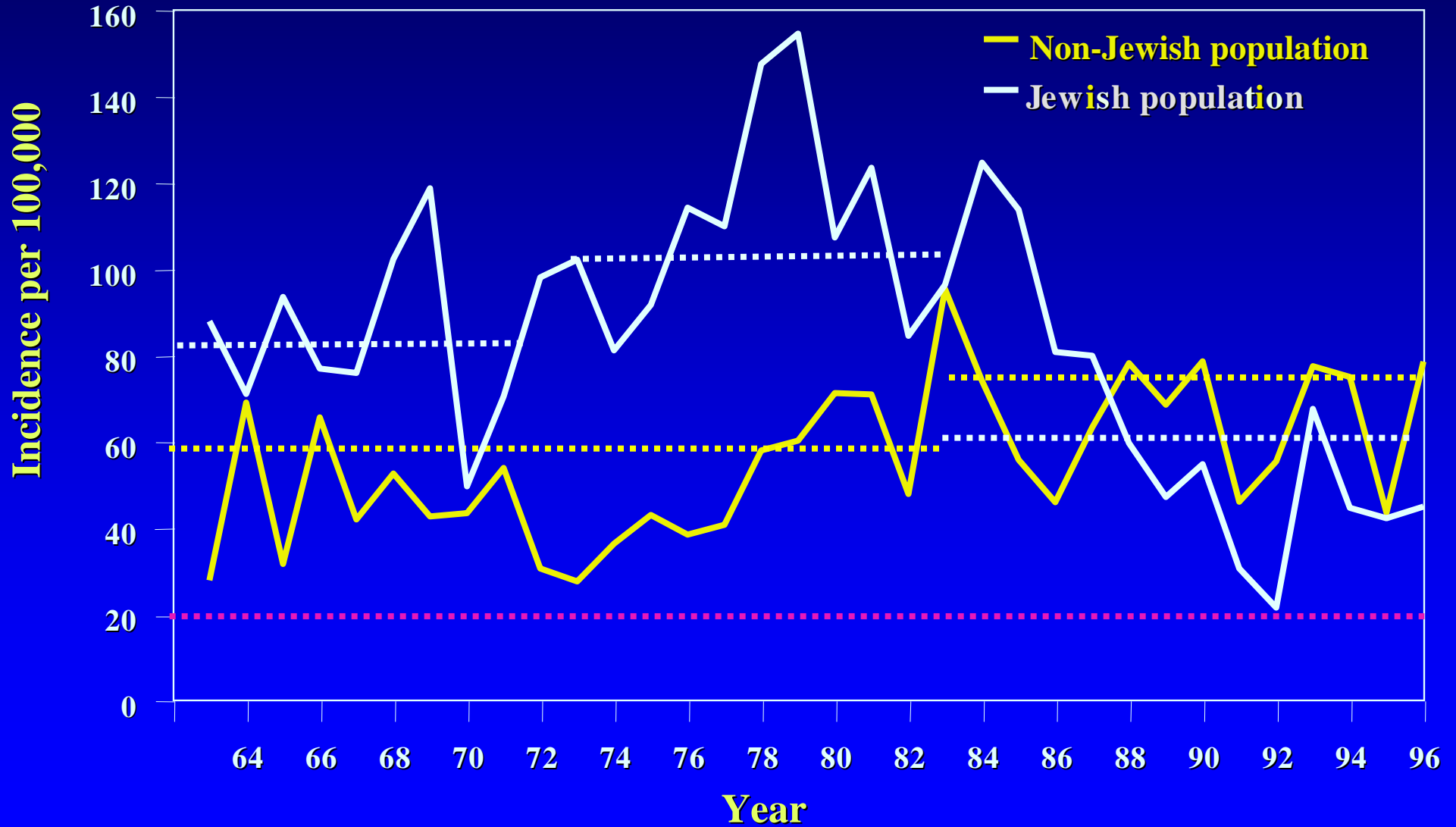


Demographics

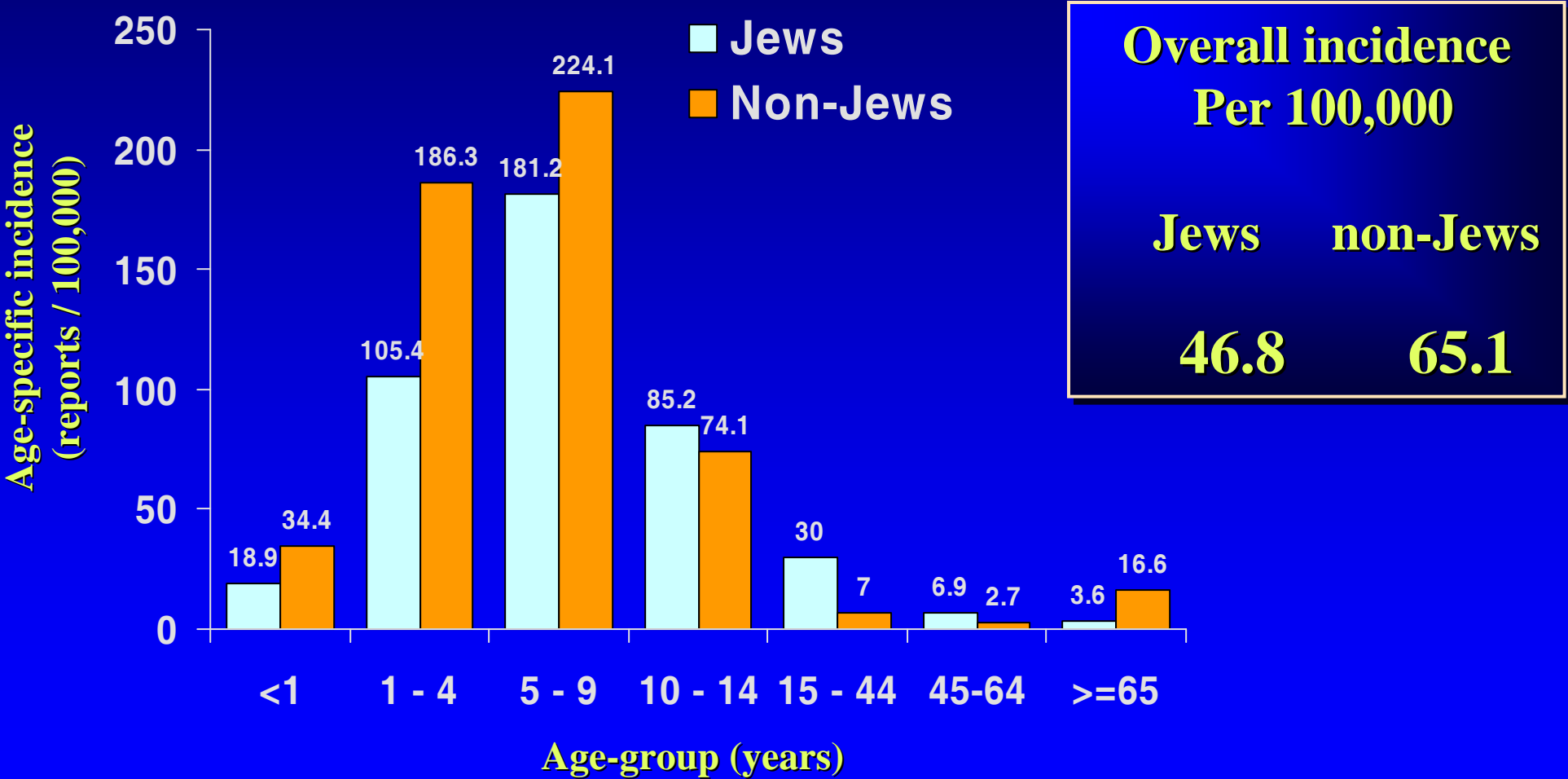
Israel's population: 6.3 million in 2000

- **Jewish population - 78%**
- **Non-Jewish population - 22%, of whom**
 - **82% Moslems**
 - **9% Christians**
 - **8.8% others**

Incidence of Viral Hepatitis A per 100,000 in Israel During 1963-1996 by Population



Age-Specific Incidence of Reported HAV in Israel during 1993-8



Highlights of HAV Epidemiology in Israel

Background information:

- Heterogeneous population (contact between high and low socioeconomic risk groups)
- Highest attack rate in children 5-9 years old
- Maternal anti-HAV IgG is usually cleared in babies by the age of 18 months
- Hepatitis A is rarely observed < age of 18m
- Toddlers seem to be the main vehicle for HAV transmission (pilot study results)

Hepatitis A Surveillance Systems in Israel

Passive surveillance:

National

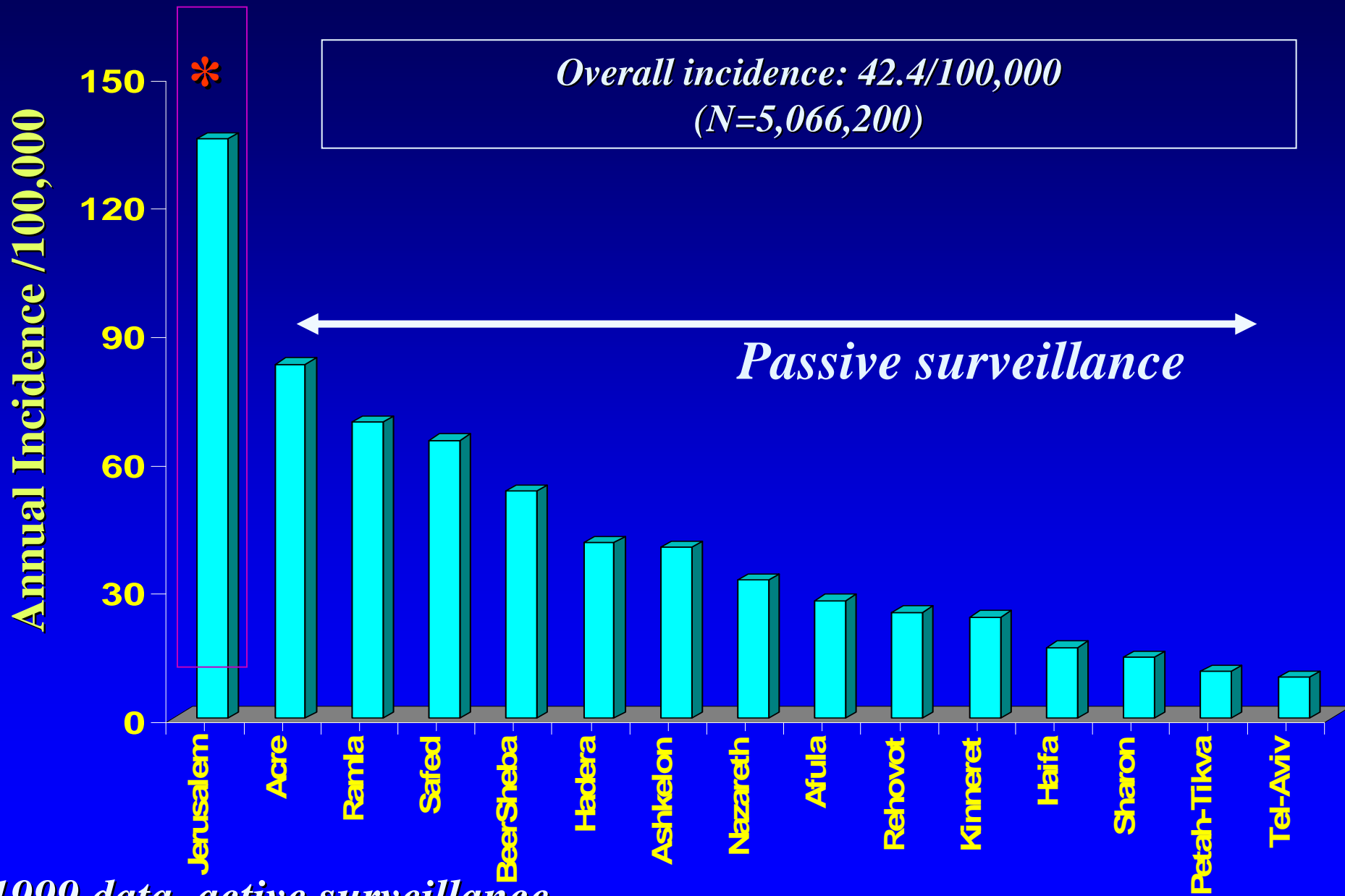
Through notifications to the Ministry of Health
(HAV committee: coordinator - Ron Dagan)

Active Surveillance:

Only in Jerusalem

(coordinator - Daniel Shouval)

Annual Incidence of Acute HAV per District



There are two major ethnic populations residing in Jerusalem:

❑ The Jewish population comprises of various ethnic and socioeconomic subgroups (secular, religious and orthodox).
N=732,163*

❑ The non-Jewish population is mostly of Arab origin (Moslems and Christians) . N=205,000*

Sub- populations differ in:

- Socioeconomic status
- Different birthrate
- Living conditions
- Hygienic infra-structure

Active Surveillance in the Jerusalem District 1999-2004

- Contact with all HMO labs and hospitals in the Jerusalem district twice a week**
- Established contact with family physician or pediatrician**
- Obtained informed consent**
- Recruit index cases (or their custodians) and their household contacts for serologic survey**
- Anti-HAV IgM+ samples re-tested and checked for HAV-RNA by PCR followed by sequencing**

Universal Vaccination Against Hepatitis A

Pros:

- Area of intermediate endemicity in transition
- Contact between populations with high and low risk
- True incidence $>5x$ of reported cases/year through passive surveillance
- Increased incidence of fulminant hepatitis A
- Favorable cost/benefit analysis*
- High acceptance rate by population

* *Ginsberg GM, Shouval D. Cost-benefit analysis of a nationwide neonatal inoculation programme against hepatitis B in an area of intermediate endemicity.*

The Israeli Project: Toddler-only 2-dose vaccination

Ron Dagan, MD

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Daniel Shouval, MD

Introduction of Universal Vaccination Against Hepatitis A in Israel

- Universal vaccination started July 1, 1999 in babies immunized at age 18 and 24 months
- Vaccine: HAVRIX^R- Pediatric dose of 720EU x2
- The vaccine is provided free of charge, as a part of the regular immunization program
- ~ 90% received 1 dose; > 80% received 2 doses
- No catch-up program beyond toddlers was introduced

It is estimated that <10% of children <18y and <4% of adults >18y received at least one dose of HAVRIX or Vaqta through non-governmental initiatives

Number of HAV Vaccine Doses Delivered to the Jerusalem District

● 1999 19,000

● 2000 36,520


● 2001 59,130

● 2002 43,986

Total: 158,636

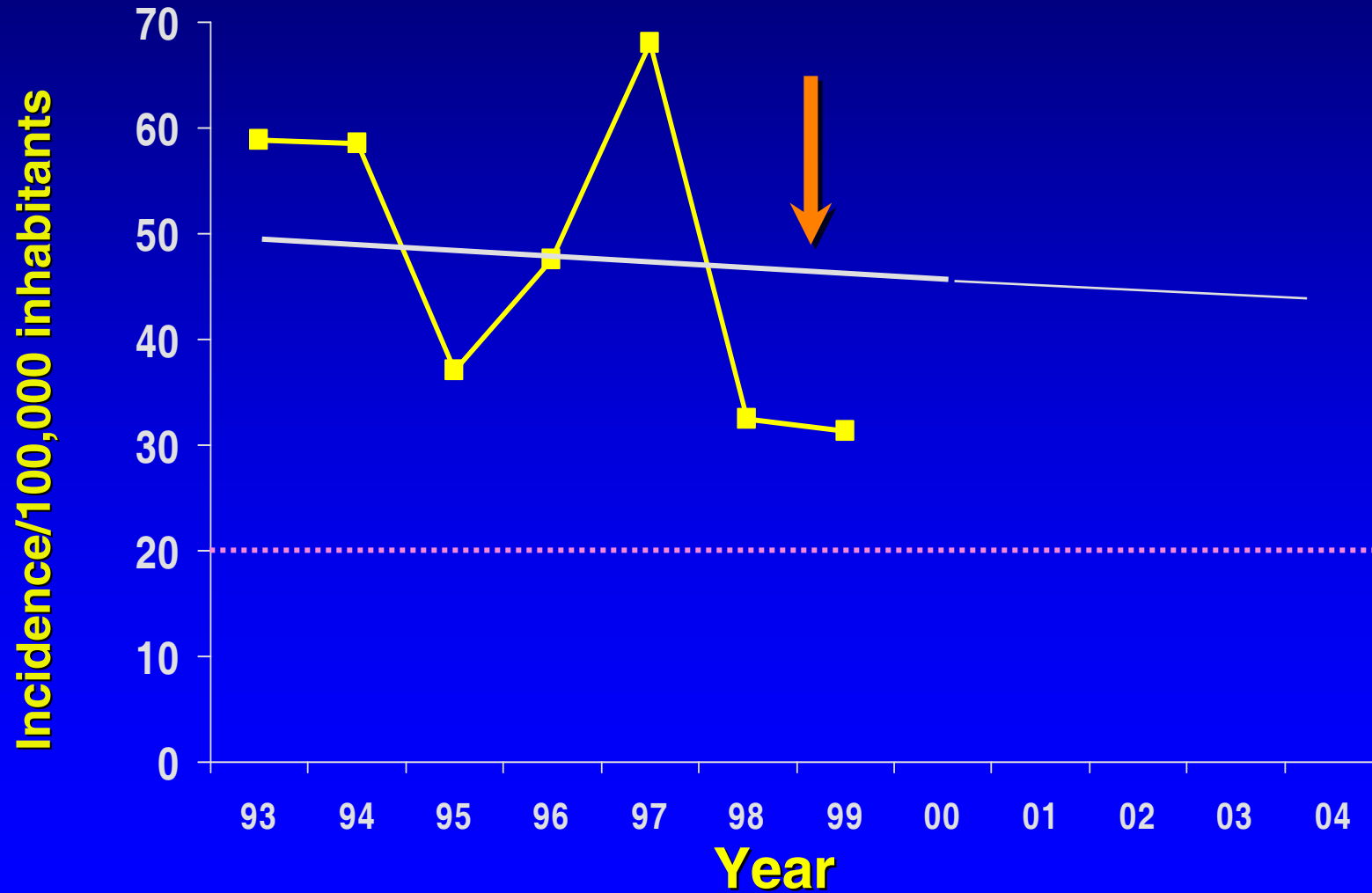
Reduction in the Number of Reported Acute HAV Cases Following Introduction of Universal Vaccination

Year	Passive Surveillance*	Active Surveillance**
1999	1246	671
2000	501	654
2001	336	420
2002	90	46
2003	72	67
2004	193	105
2005	137	57
Total	2575	2020

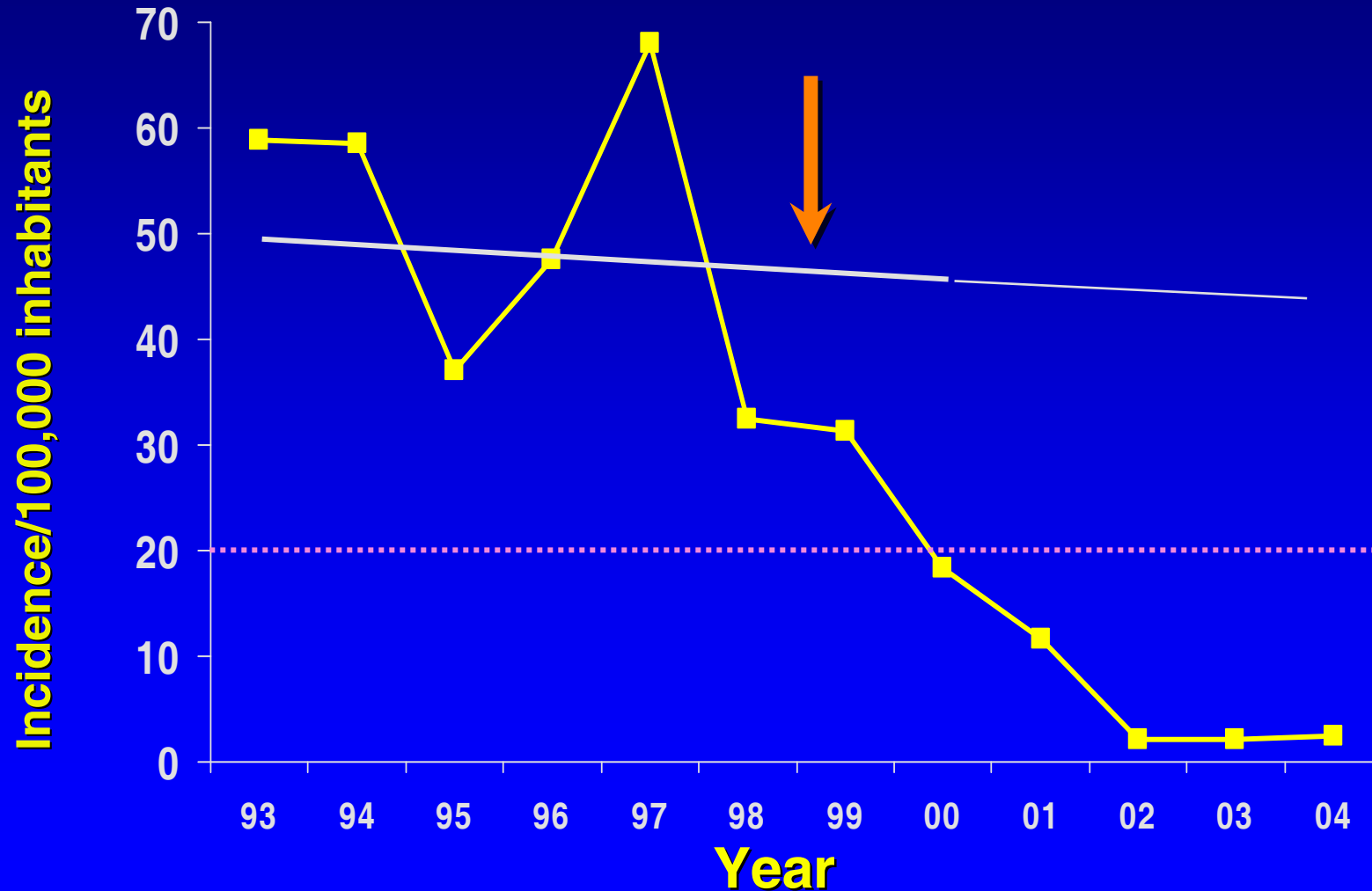


* $N = \sim 6,300,000$ ** $N = \sim 900,000$

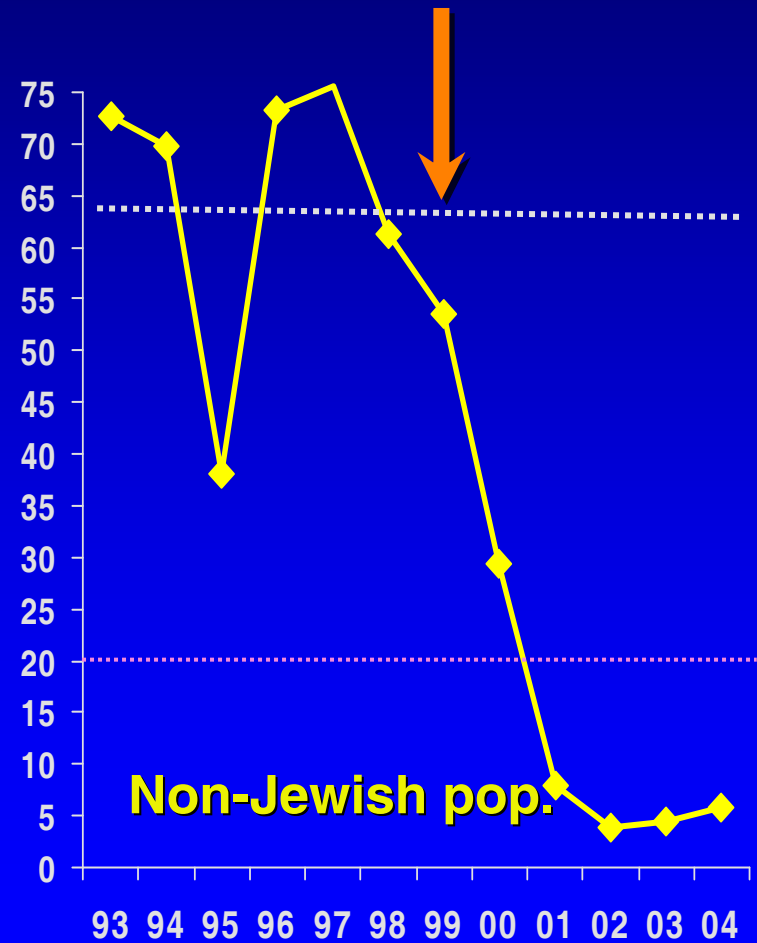
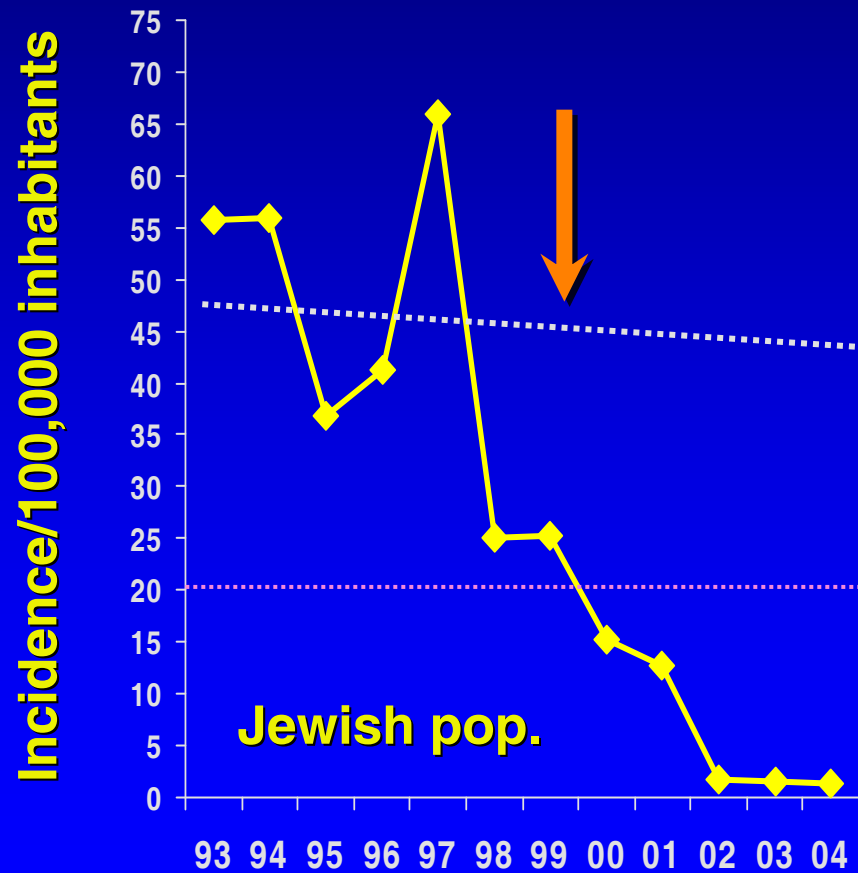
Reporting of HAV Cases in Israel: 1993 Through 2004



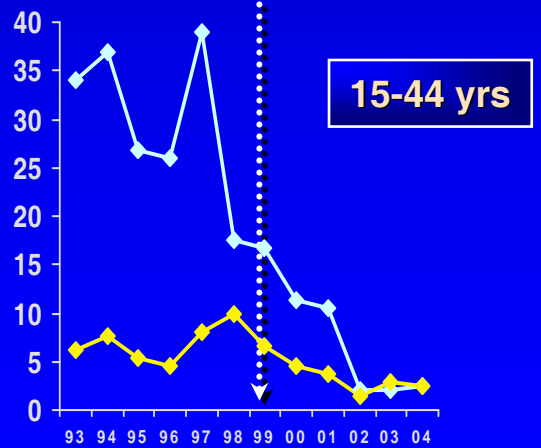
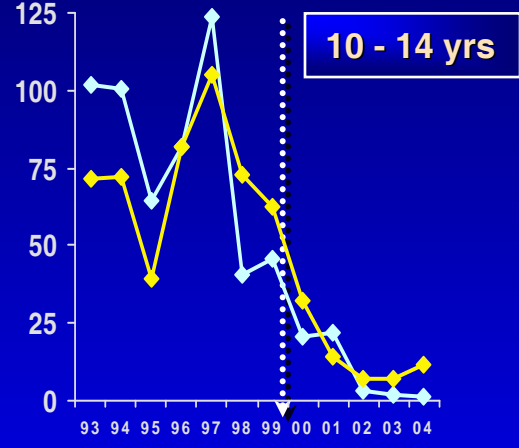
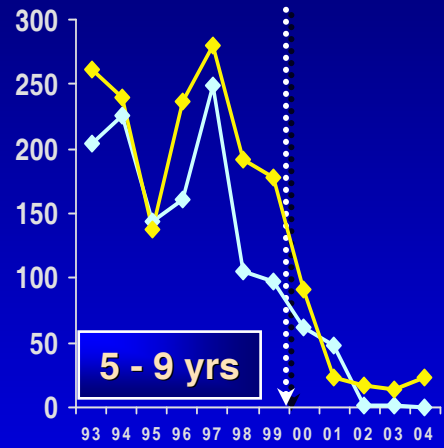
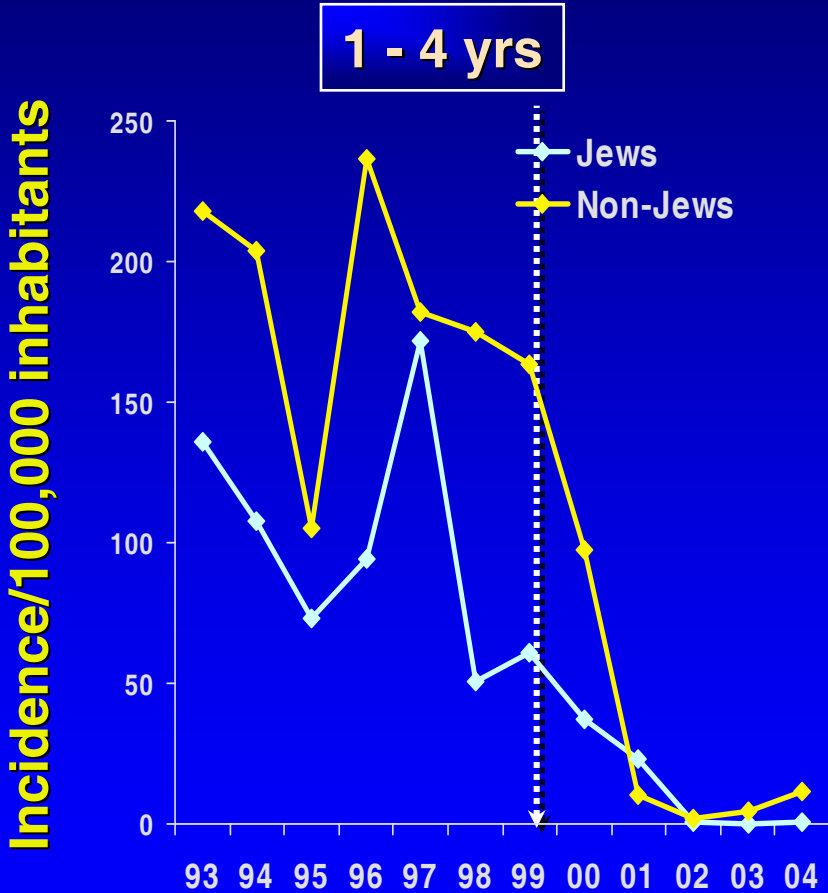
Reporting of HAV Cases in Israel: Passive Surveillance 1993 - 2004



Reporting of HAV Cases in Israel by Ethnic Groups: 1993 Through 2004

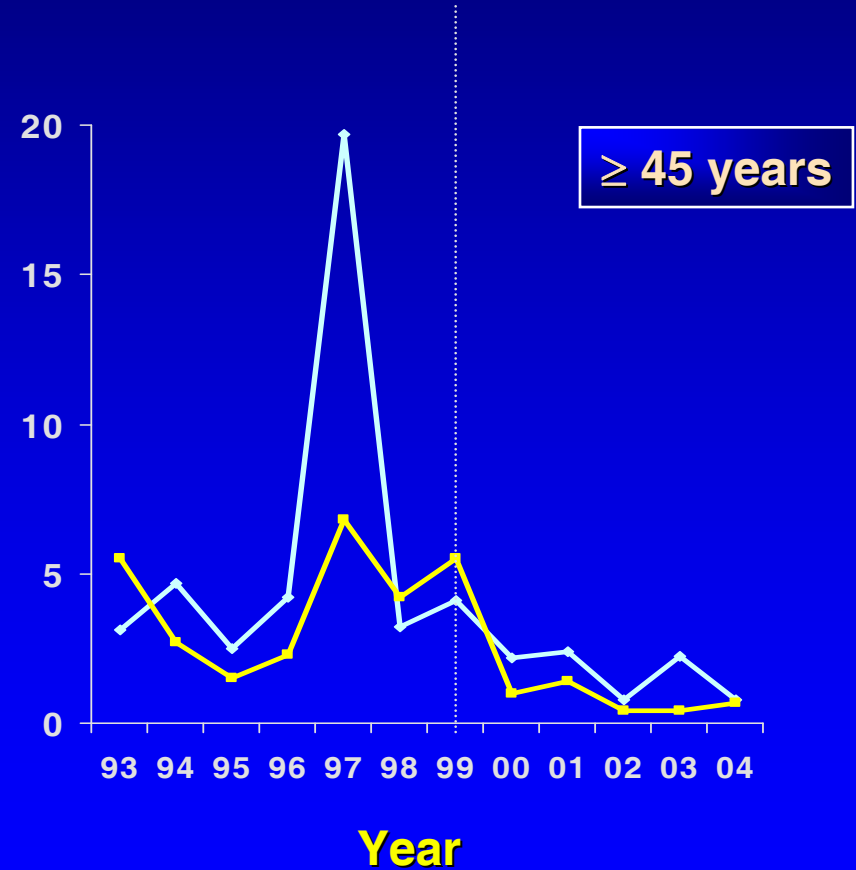
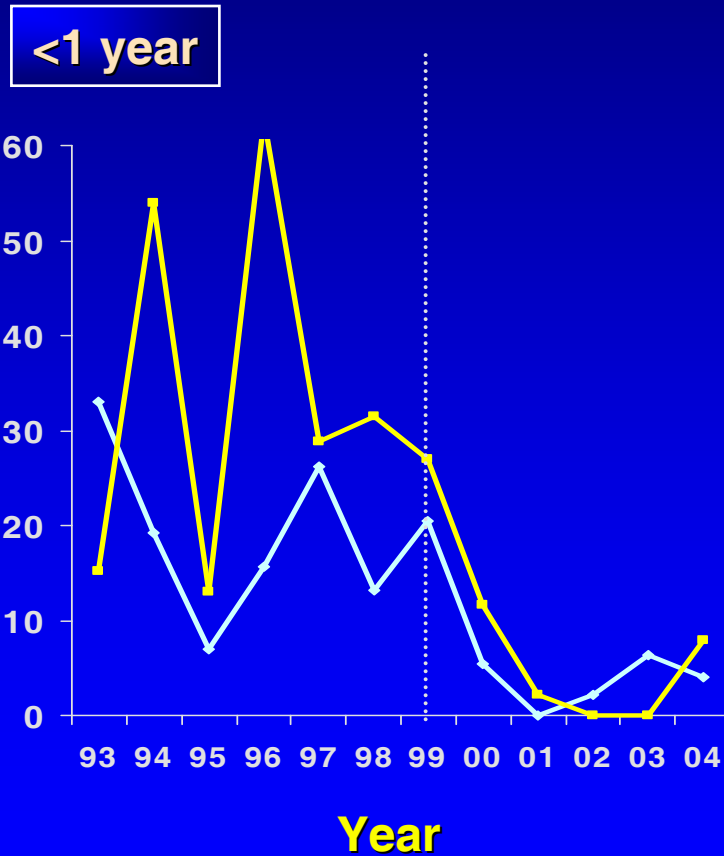


Reporting of HAV Cases in Israel : 1993 Through 2004 by Age-Group and Ethnic Population

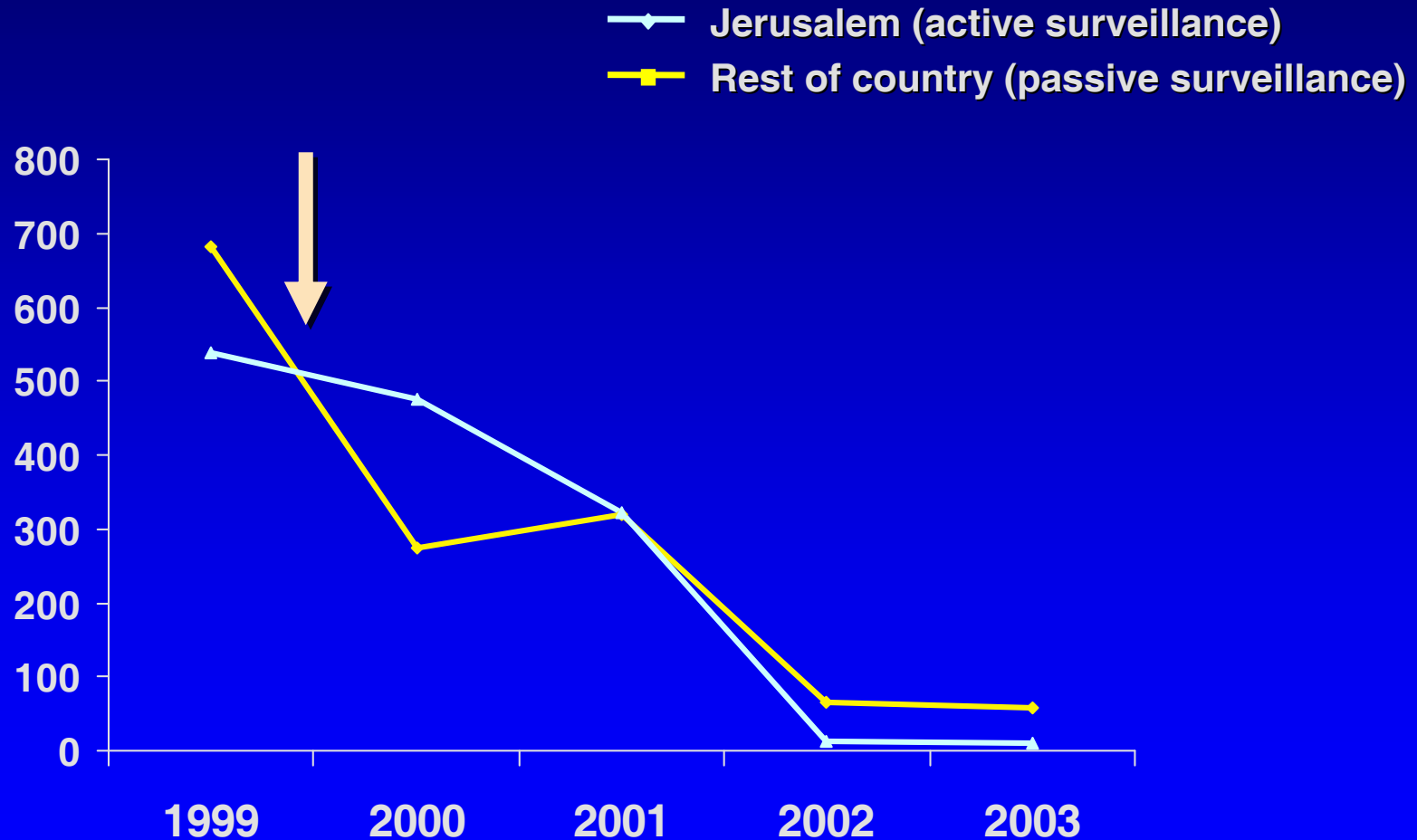


Reporting of HAV Cases, Extremes of Life in Israel: 1993 Through 2004

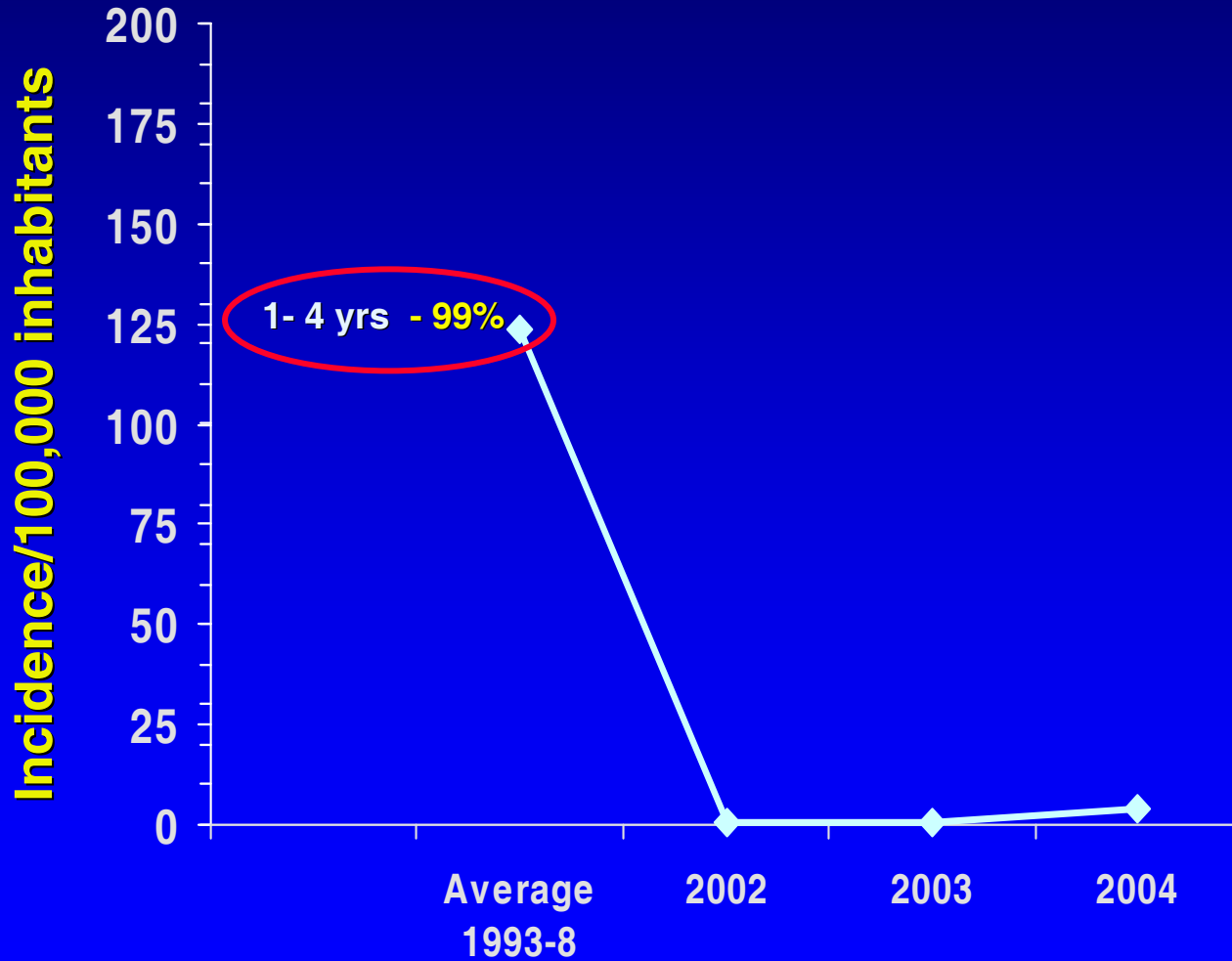
Incidence/100,000 inhabitants



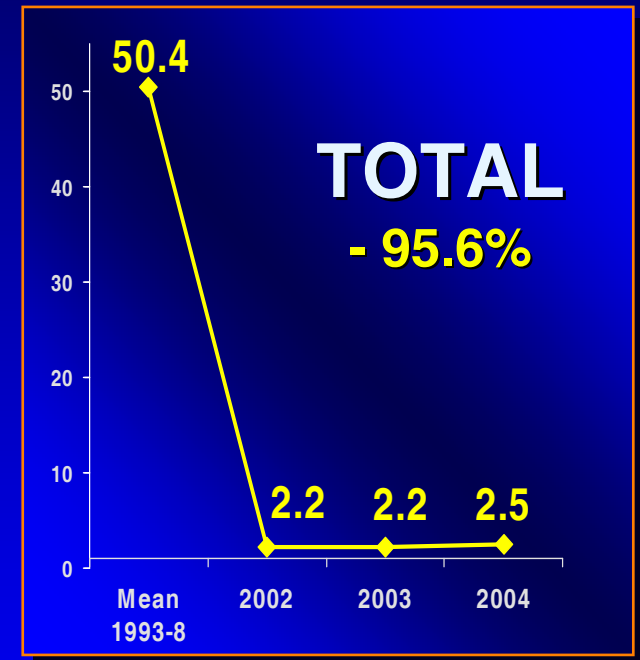
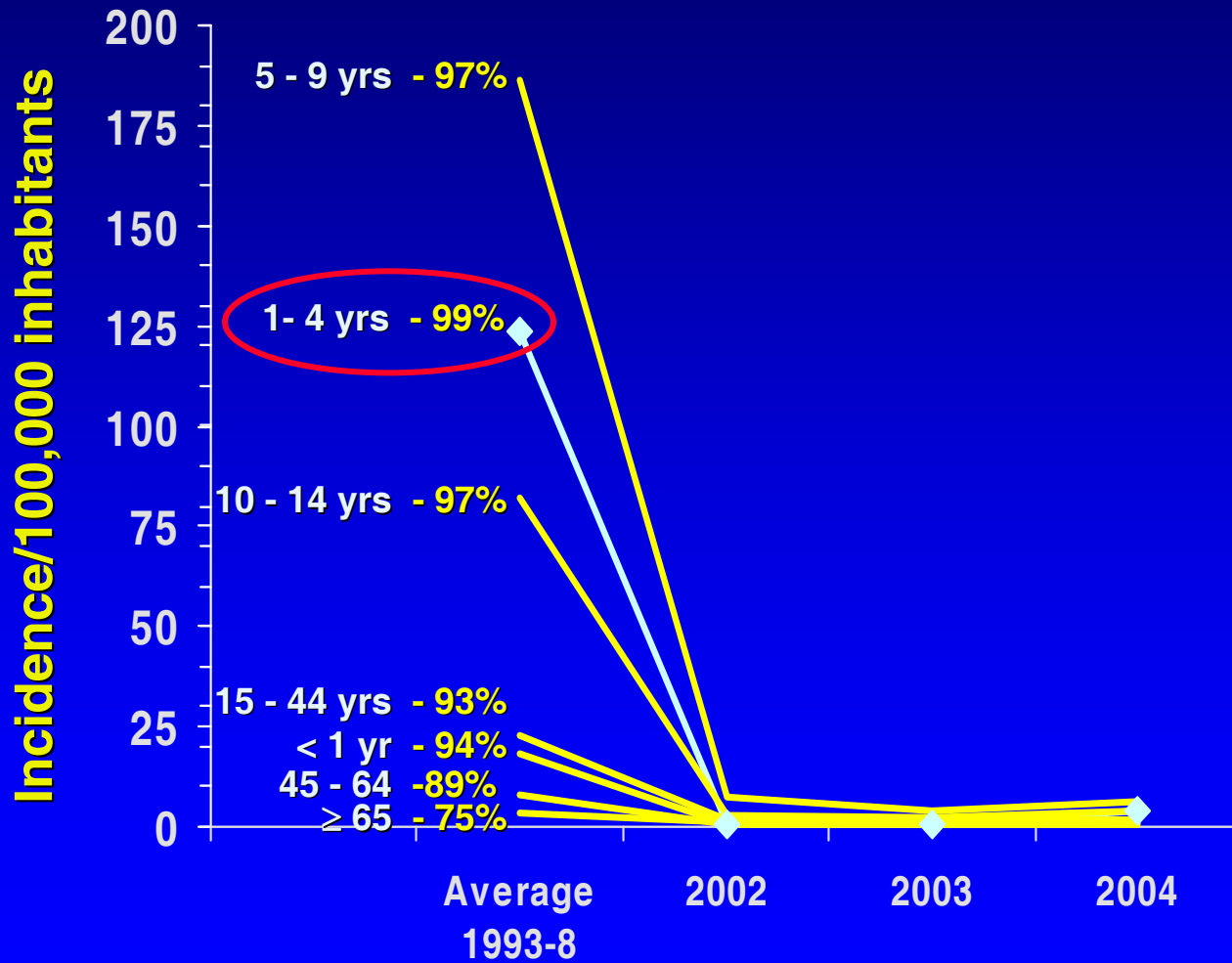
Cases of HAV Reported Since 1999: Jerusalem County vs the Rest of Israel

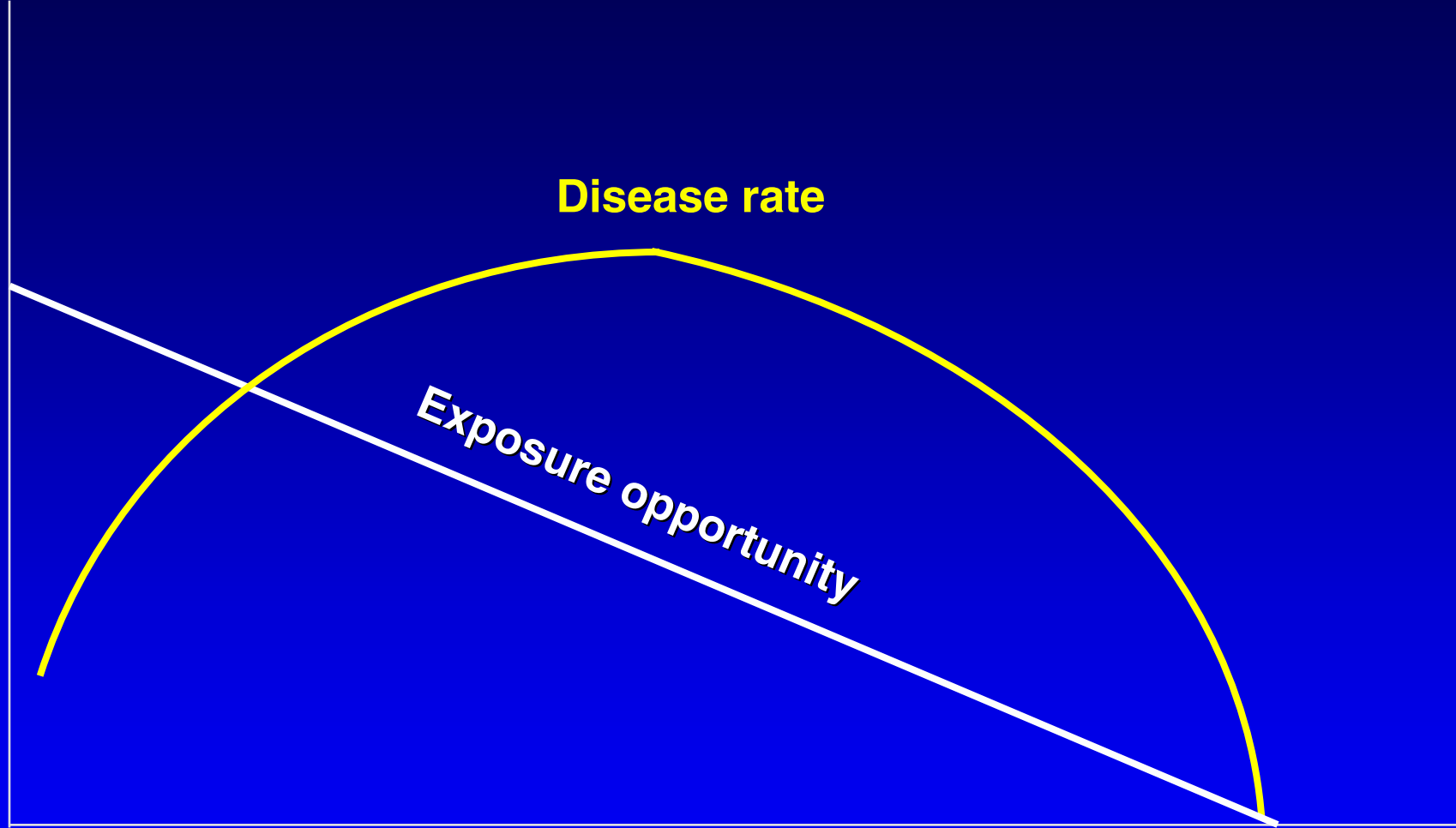


Summary of National Age-Specific Reduction in Reported HAV Disease 1993-8 vs 2002-4



Summary of Age-Specific Reduction in Reported HAV Disease 1993-8 vs 2002-4





Disease rate

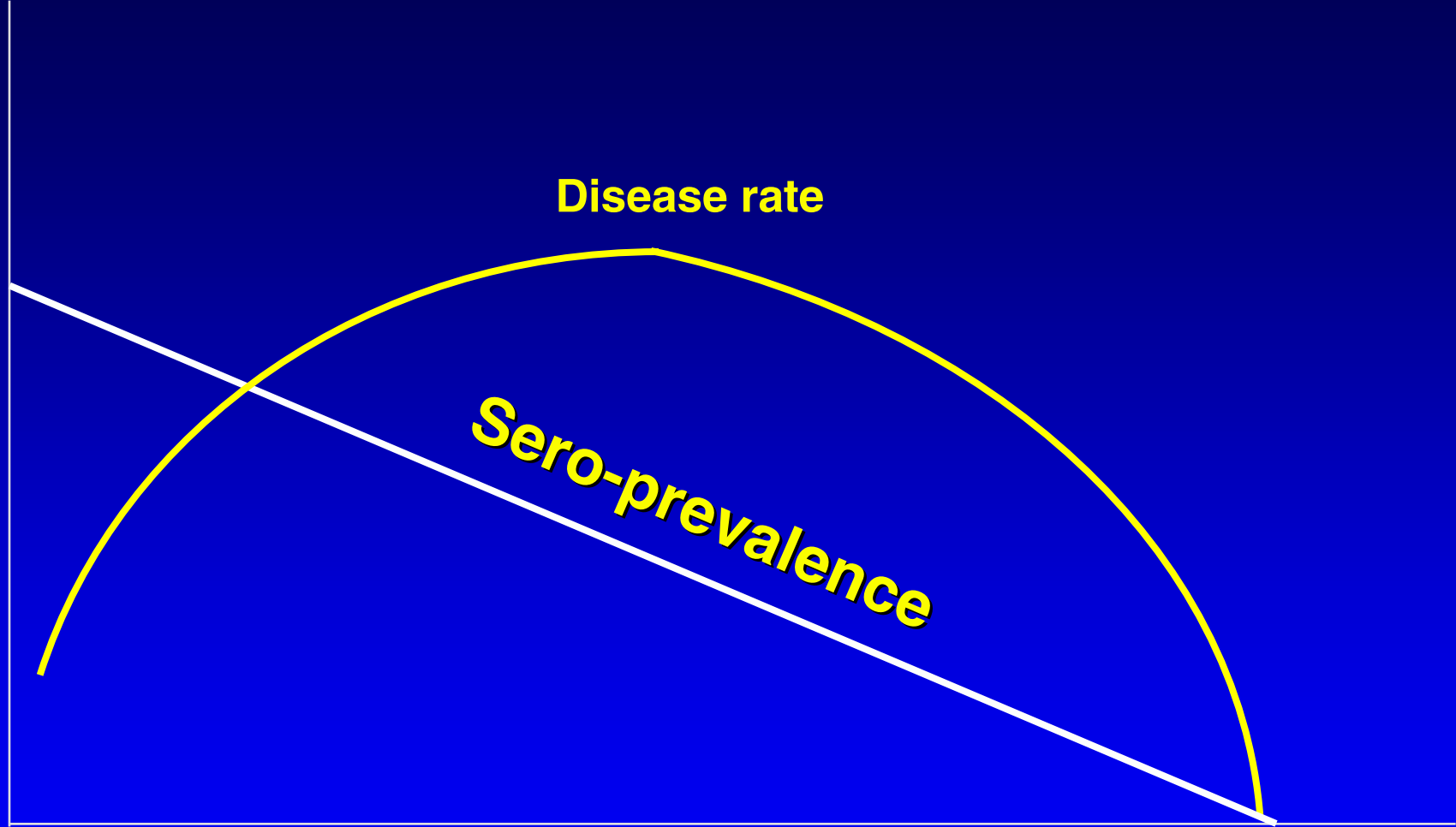
Exposure opportunity

Time

High endemicity

Intermediate endemicity

Low endemicity



Disease rate

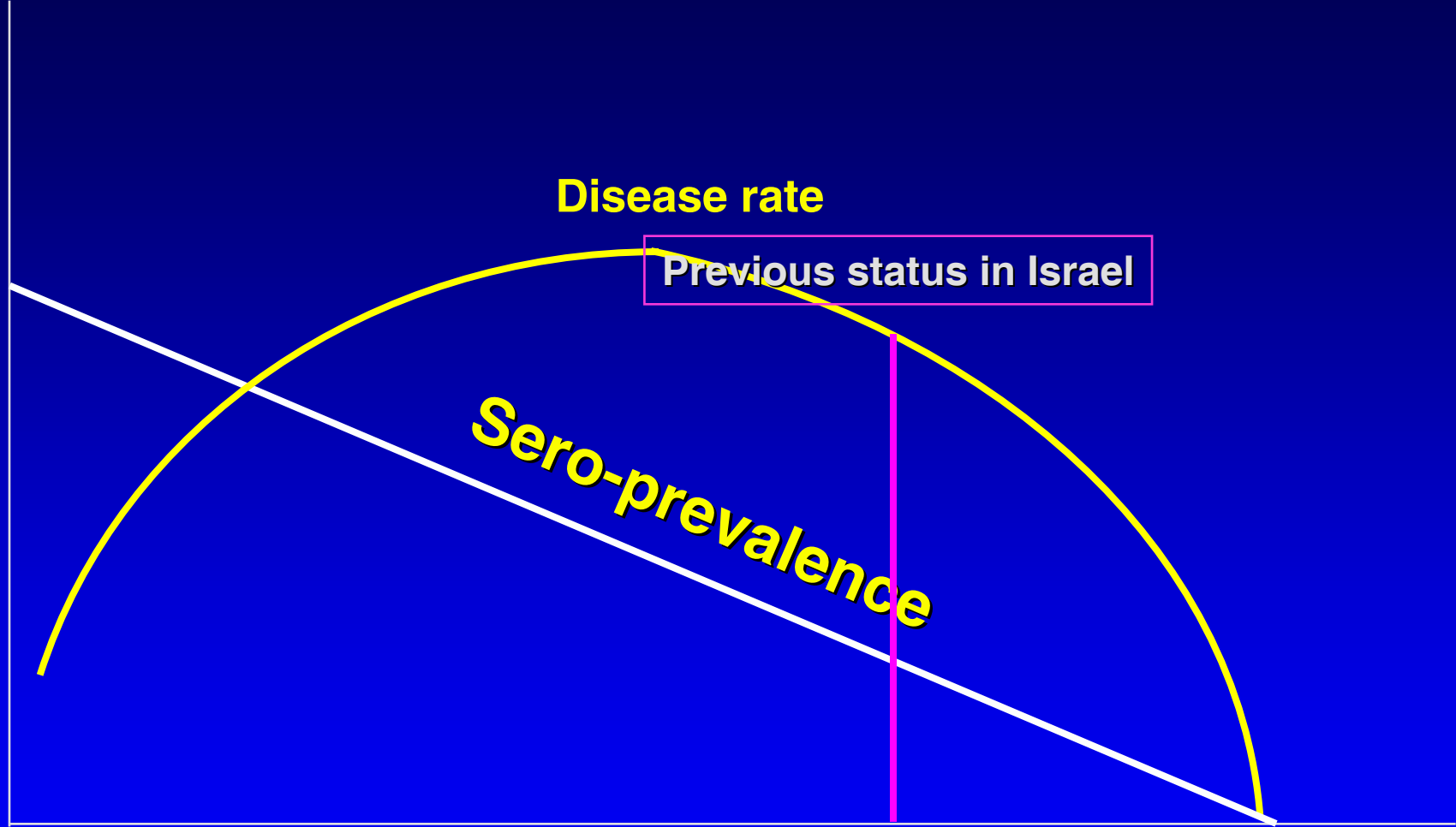
Sero-prevalence

Time

**High
endemicity**

**Intermediate
endemicity**

**Low
endemicity**



Disease rate

Previous status in Israel

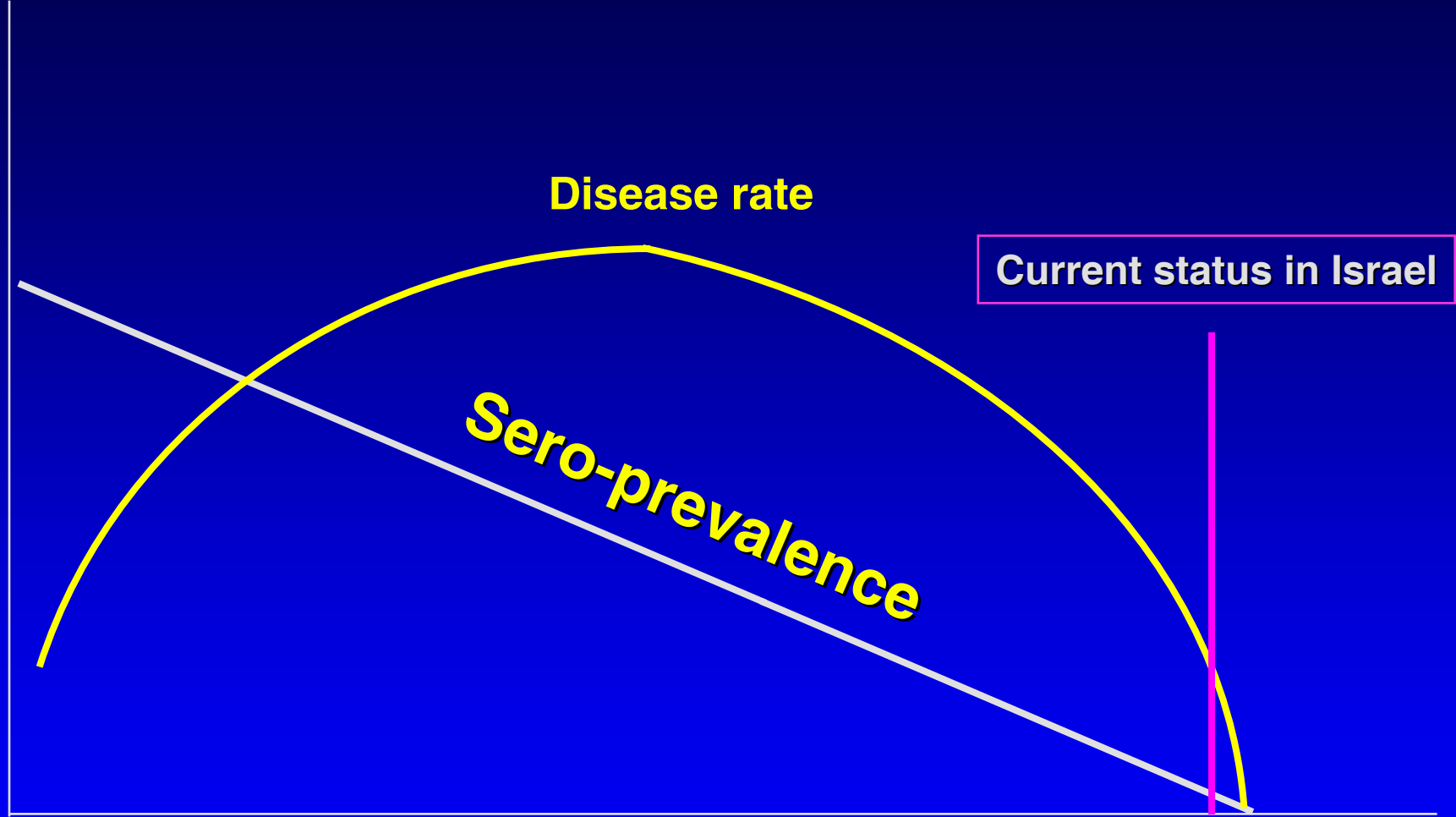
Sero-prevalence

Time

High endemicity

Intermediate endemicity

Low endemicity



Disease rate

Current status in Israel

Sero-prevalence

Time

High endemicity

Intermediate endemicity

Low endemicity

Conclusions

- **The universal toddler-only immunization program in Israel is leading to:**
 - **a dramatic reduction of HAV circulation and disease in all ages**
 - **a marked herd protection**
- **regional HAV universal vaccination programs in other countries demonstrate a marked decline in incidence of HAV infection**

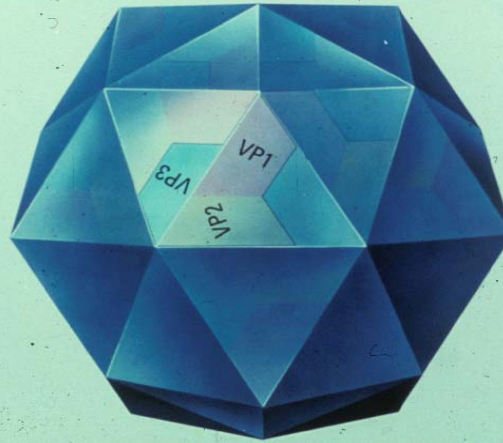
The experience gained in Israel raises two important issues:

- *The need to plan for catch-up programs is questioned, if the toddlers-only approach is adopted*
- *Cost-benefit studies must take in account that vaccination programs aimed at only a small fraction of the population (in the present case < 3%) can reduce profoundly disease in the entire population*

Summary

- ✓ **Universal vaccination against hepatitis A in toddlers is leading to disappearance of HAV infection in the entire population in Israel**

The Hepatitis A Virus



Hepatitis A Virus Infection in Israel

An End to an Era ?

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