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# **Sero-prevalence of HBs antibodies 19 years after introduction of universal vaccination**

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# Introduction

- **Hepatitis B is a reportable disease in Israel since 1992.**
- **Case definition:**
  - **Clinical:** Acute illness with discrete onset of symptoms and jaundice.
  - **Laboratory confirmation:**
    - IgM Ab to Hepatitis B core antigen or HBsAg positive

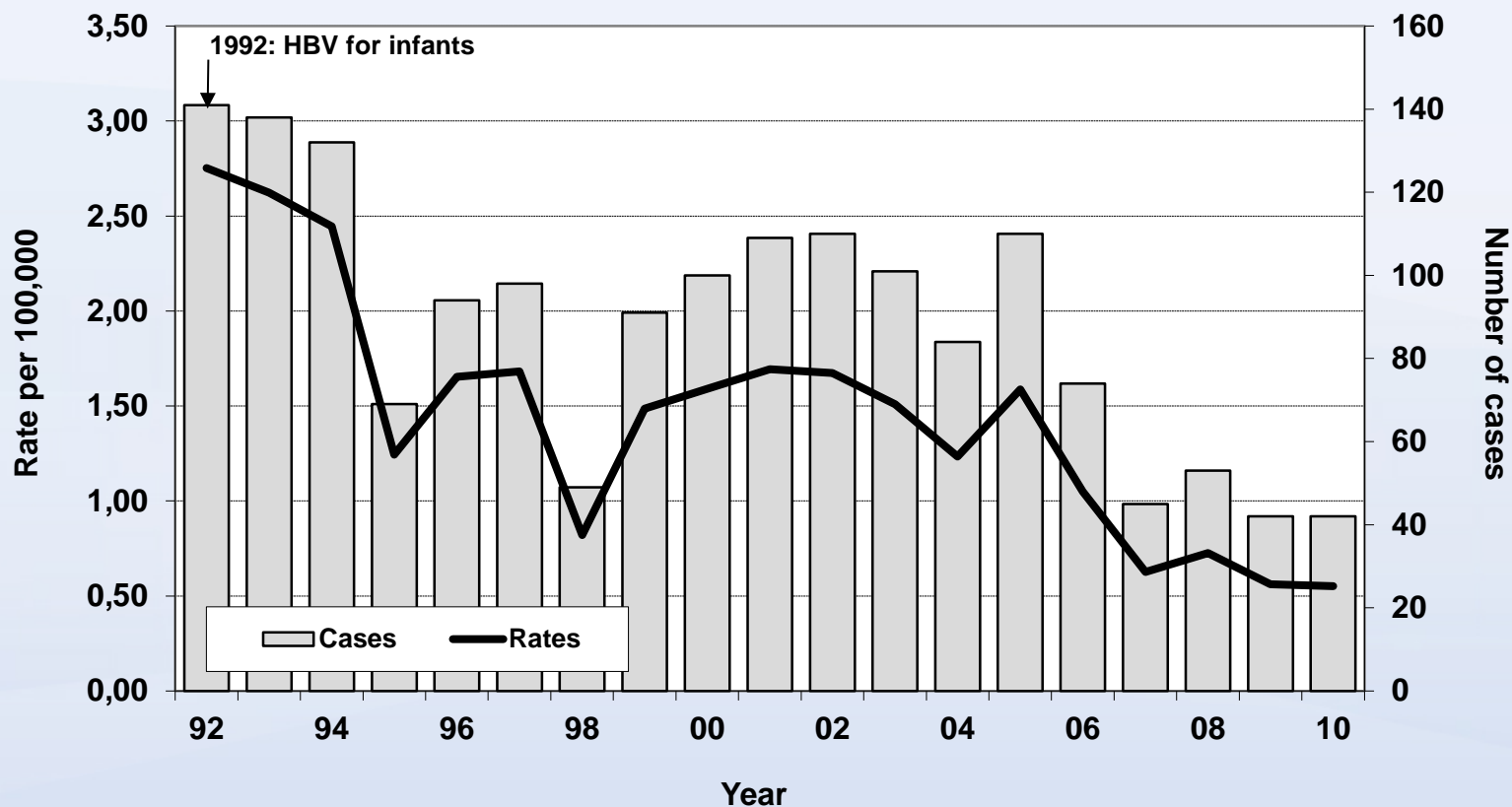


## **Surveillance of Hepatitis B in Israel**

- **In 1992:**
  - 141 reported cases
  - Rate of 2.75 per 100,000
  - HBsAg carrier rate in 1988: 1.01% - blood donors
  - Differences between ethnic groups
  - Low endemicity



## Reported cases of acute Hepatitis B in Israel, 1992-2010





# Hepatitis B vaccination policy in Israel

- Prior to universal vaccination (1985-1991).
  - Vaccination of immigrants from Ethiopia aged 0-2 years.
  - 1985-1989: Plasma derived vaccine.
  - 1990-1991: Recombinant HBV vaccine.



# Hepatitis B vaccination policy in Israel

- Universal vaccination
  - Implemented in 1992
  - Schedule: 0, 1, 6 months. 1<sup>st</sup> dose at birth
  - Catch up for those born after 1.1.92, through age 17ys
  - Vaccines in use:
    - Engerix B (GSK)
    - SciBVac (SciGen IL) - since 2011, 55% of vaccines in use.



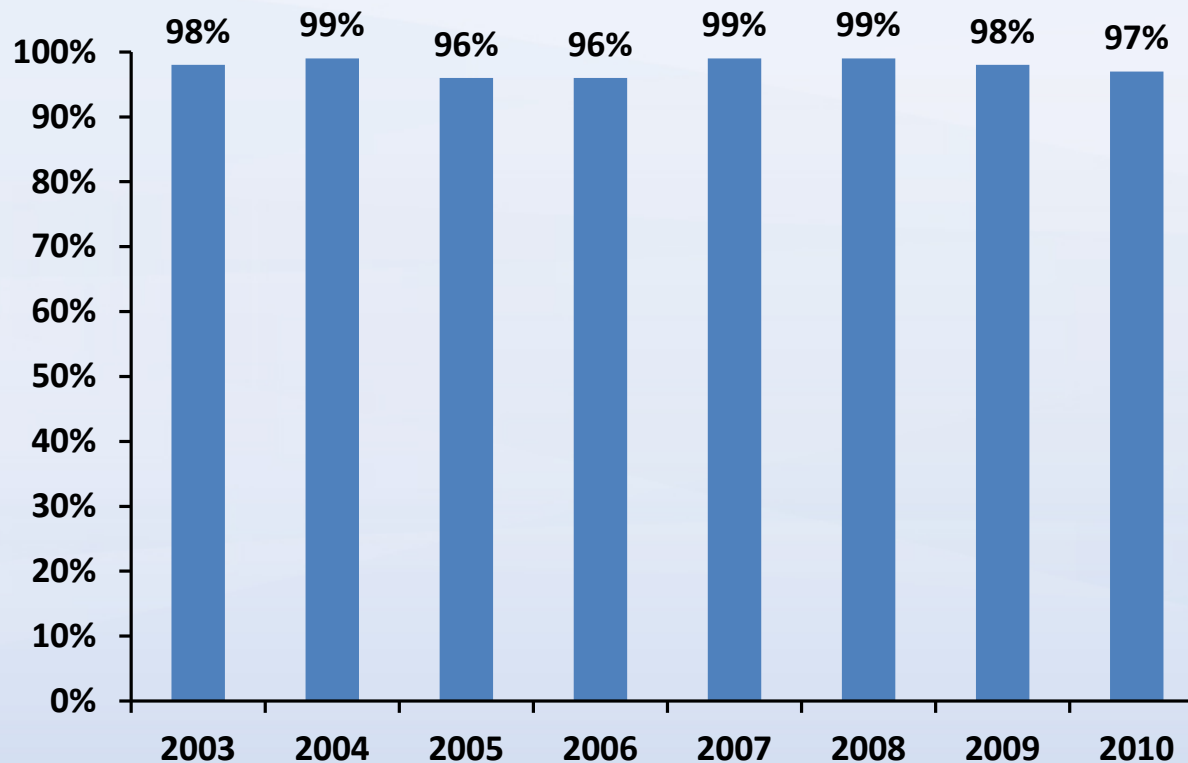
## **Hepatitis B vaccination policy in Israel**

- High risk groups: People with possible work exposure
  - Health-care workers, policemen, prison guards, mental institutes employees.
    - Dialysis patients, Hemophilic patients, HIV.
    - Drug users.
    - MSM.
    - Travelers to hyper-endemic countries.



## Vaccine coverage

completed 3 doses at 2 years of age







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- The concentration of antibodies to hepatitis B surface antigen (anti HBs) decline with time.



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## **Study Aim**

To evaluate the prevalence of anti-HBs in the Israeli population 19 years following hepatitis B vaccine introduction at birth



## Methods

- Cross sectional sero-survey.
- Samples were randomly selected from the ICDC sera bank using an age- and sex- stratified. sampling design.
- Samples collected during 2011.



## **ICDC Sera bank**

- Established in 1997.
- Samples collected from all regions of Israel throughout the year.
- Residual sera from diagnostic laboratories or from blood donors.
- Representative of the Israeli population - age groups, gender, major population groups.
- Information collected : age, gender, place of residence, country of birth, population group.



## **ICDC Sera bank**

- Samples from subjects with confirmed or suspected immunological disorders are discarded.
- Sera are stored at  $-80^{\circ}\text{C}$ .



## **Laboratory analysis**

- Analysis was done with “Vitek Immuno Diagnostic Assay System (VIDAS)” automated system according to manufacturer instructions.
- Validation done with fresh sera and frozen sera.
- Central virology laboratory at Sheba Med. Center



Validation on fresh sera

		Axsym system	
		HBVs+	HBVs-
Vidas system	HBVs+	10	0
	HBVs-	0	10
		10	10

Validation on thawed sera

		Axsym system	
		HBVs+	HBVs-
Vidas system	HBVs+	18	0
	HBVs-	0	2*
		18	2

\* The 2 thawed samples were previously positive Axsym system



# Definitions

Titer (mIU/ml)	VIDAS interpretation
<8	Negative
$8 \leq \text{titer} \leq 12$	Intermediate
>12	Positive





## **Analysis**

- Seroprevalence by age, gender and population group.
- Geometric mean titer was calculated by age, gender and population group.



## Samples tested by age and population group

	<b>Total</b>	<b>Jews and others</b>	<b>Arabs</b>
<b>Age (years)</b>	<b>N</b>	<b>N</b>	<b>N</b>
0.5-1	128	93	35
2-4	229	148	81
5-9	257	190	67
10-14	276	184	92
15-19	354	246	108

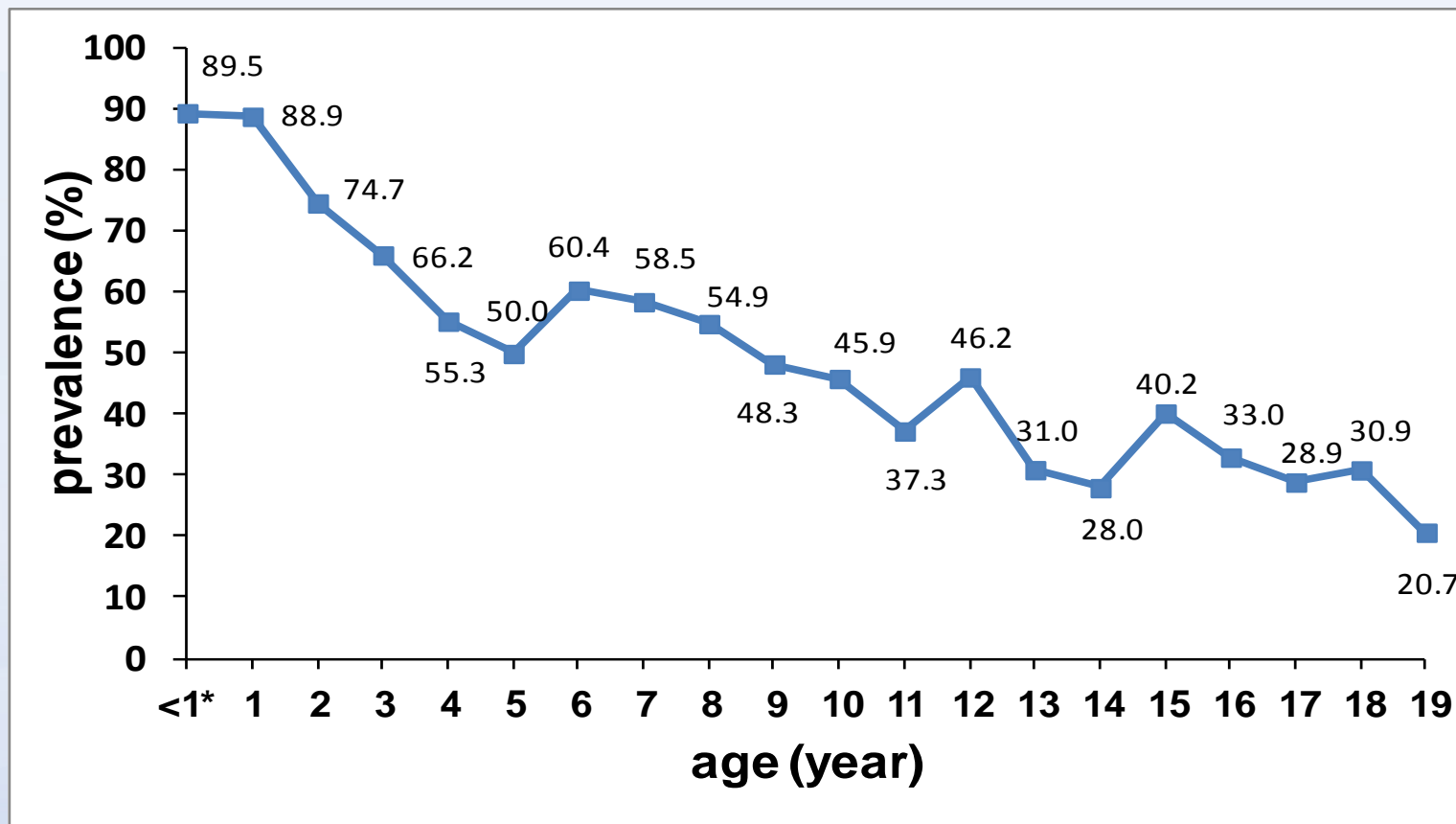


## Results

- Of the 1,273 samples, 49.6% (95% CI: 46.8-52.3%) were positive.
- Among seropositive subjects: GMT was 89.9mIU/ml (95% CI:81.7-99.0 mIU/ml).
- **At age1: 88.9% positive.**
- **At age 2: 74.7% positive.**



## Seropositivity by age



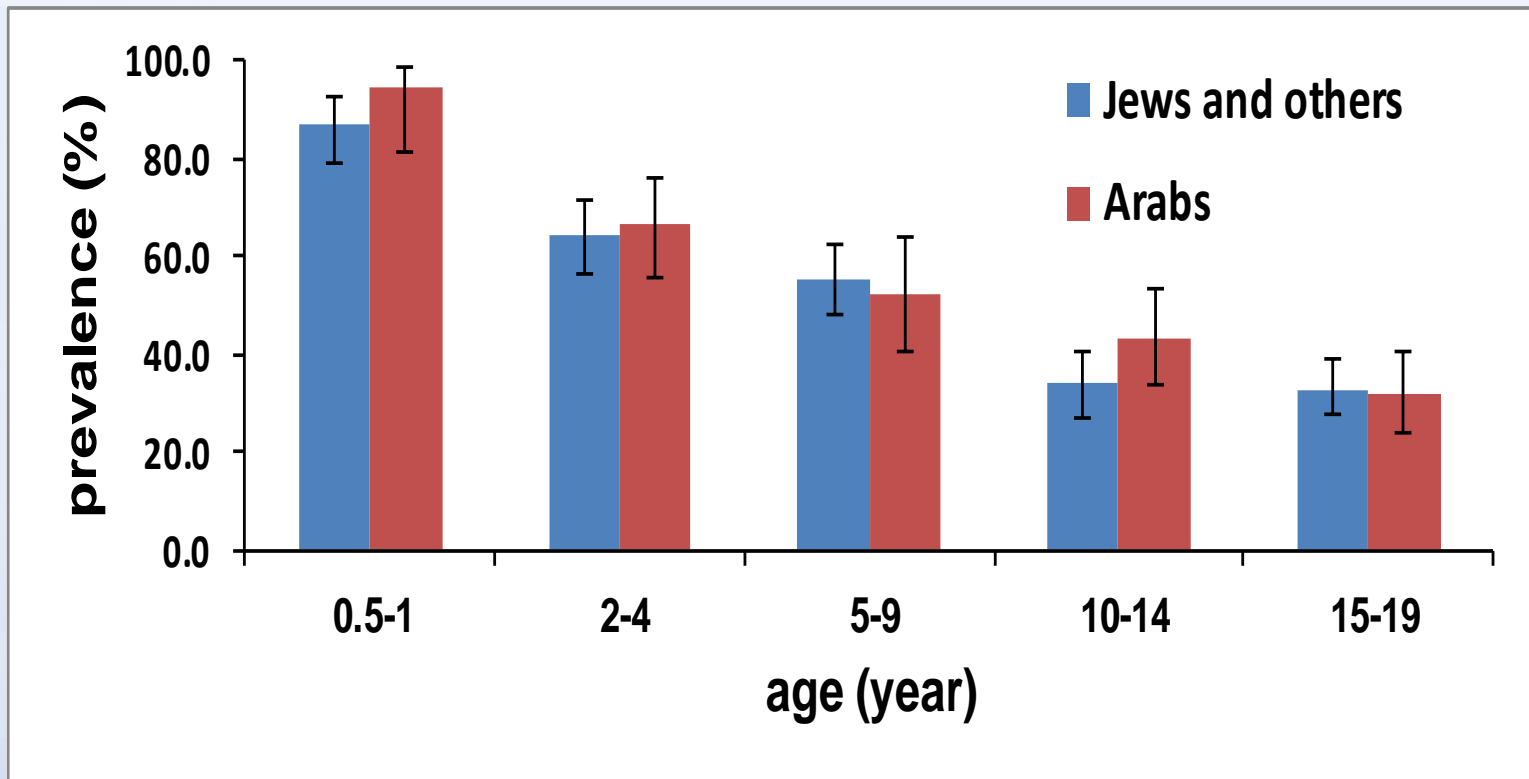


## Results

- There were no significant differences between population groups.
- There were no significant differences between genders.

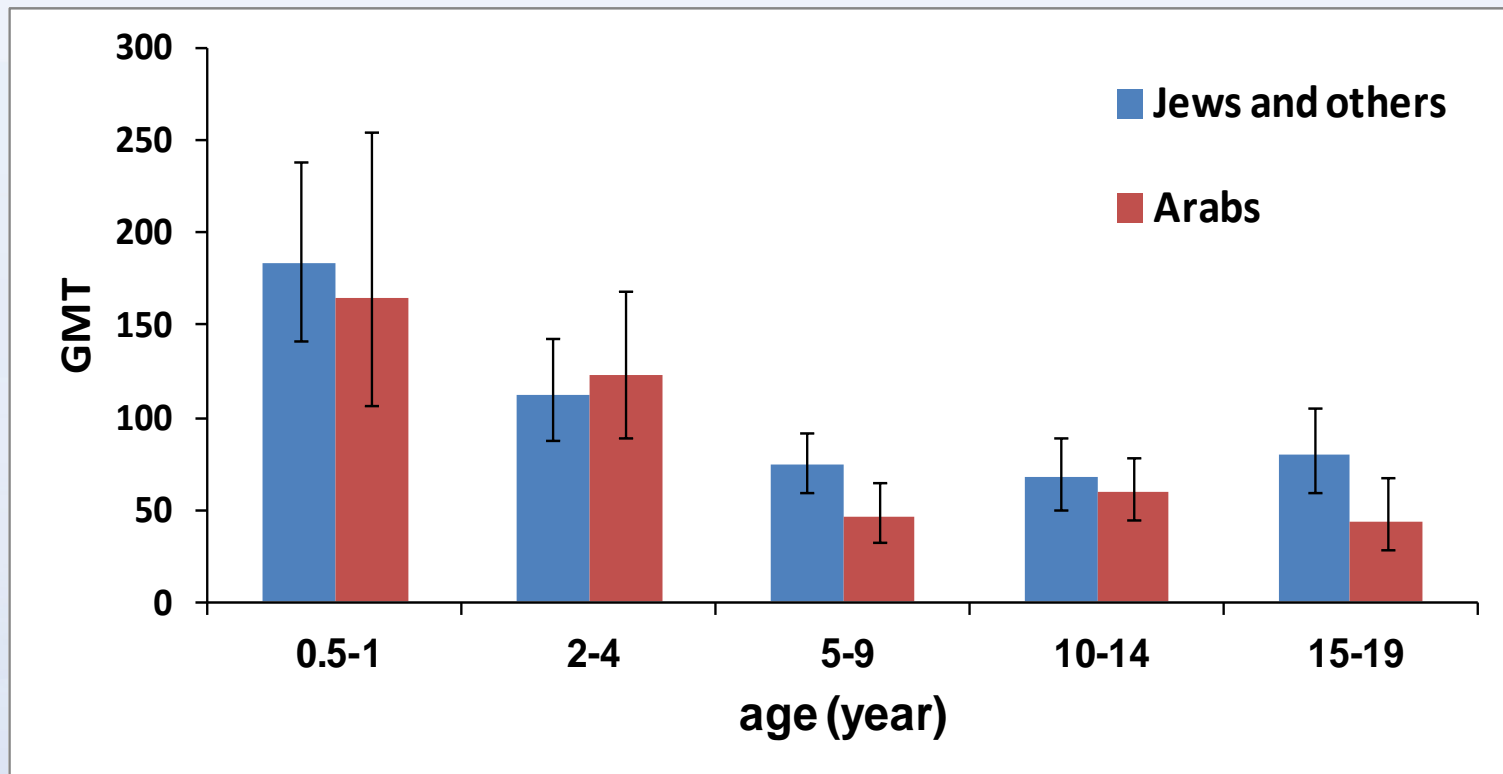


## Seroprevalence by age and population group



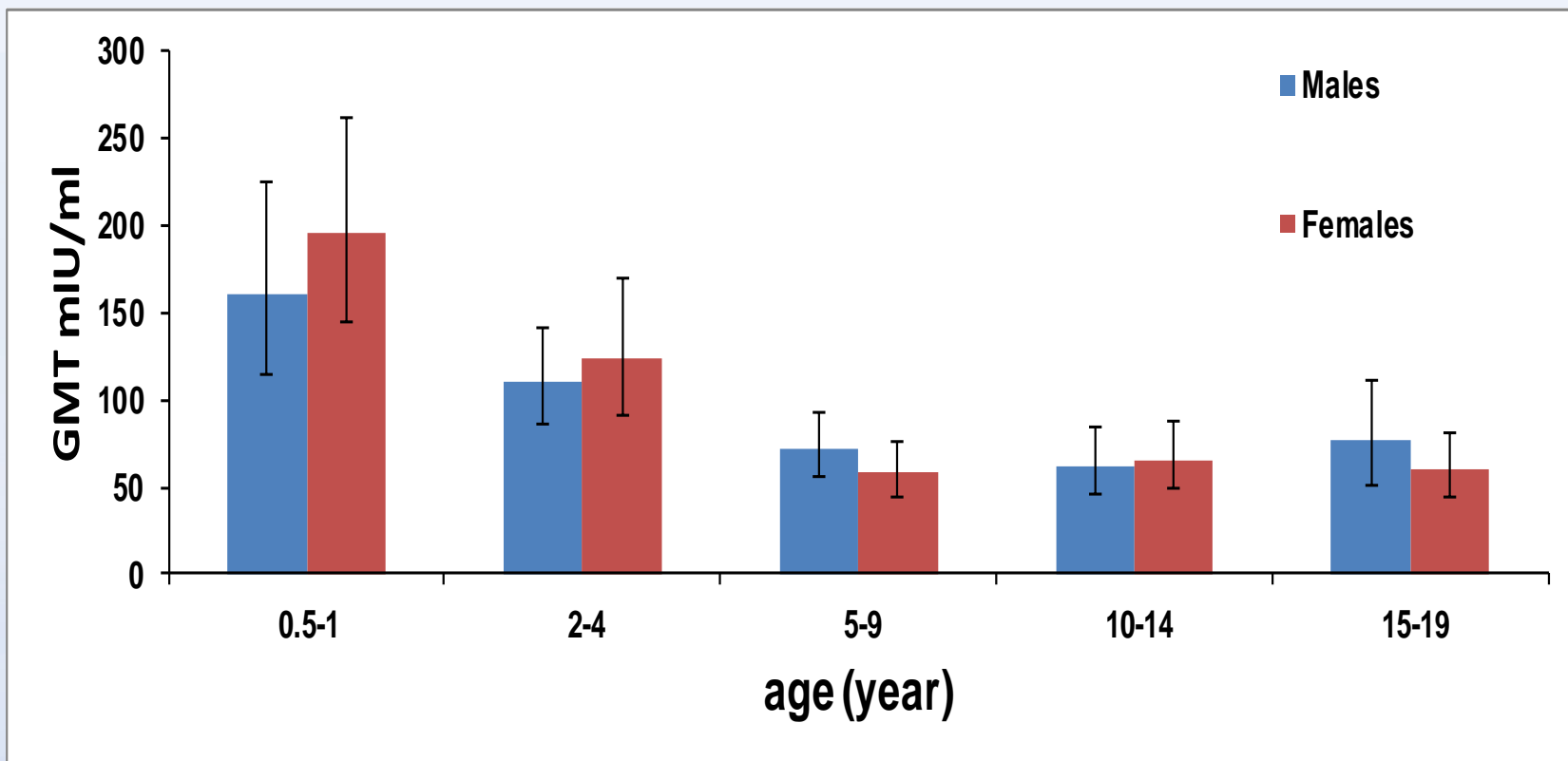


## GMT by age and population group





## GMT by age group and gender







## Results

Age (years)	Total population			Jews and others			Arabs		
	N	Positive %	95% CI	N	Positive %	95% CI	N	Positive %	95% CI
0.5-1	128	89.1	82.5-93.4	93	87.1	78.8-92.5	35	94.3	81.4-98.4
2-4	229	65.1	58.7-70.9	148	64.2	56.2-71.5	81	66.7	55.9-76.0
5-9	257	54.5	48.4-60.5	190	55.3	48.2-62.2	67	52.2	40.5-63.7
10-14	276	37.0	31.5-42.8	184	33.7	27.3-40.8	92	43.5	33.8-53.7
15-19	354	32.5	27.8-37.5	246	32.9	27.4-39.0	108	31.5	23.5-40.7



## Results – GMT values in seroprotected

Age (years)	Total population			Jews and others			Arabs		
	N	GMT	95% CI	N	GMT	95% CI	N	GMT	95% CI
0.5-1	128	122.6	93.7-160.4	93	117.2	84.5-162.5	35	138.3	86.9-220.0
2-4	229	40.1	32.0-50.2	148	38.2	29.0-50.4	81	43.7	29.8-64.1
5-9	257	21.6	18.1-25.9	190	23.5	18.9-29.2	67	17.2	12.6-23.3
10-14	276	13.6	11.6-15.9	184	12.9	10.5-15.7	92	15.2	11.5-20.0
15-19	354	12.5	10.8-14.4	246	13.3	11.1-16.0	108	10.9	8.6-13.6

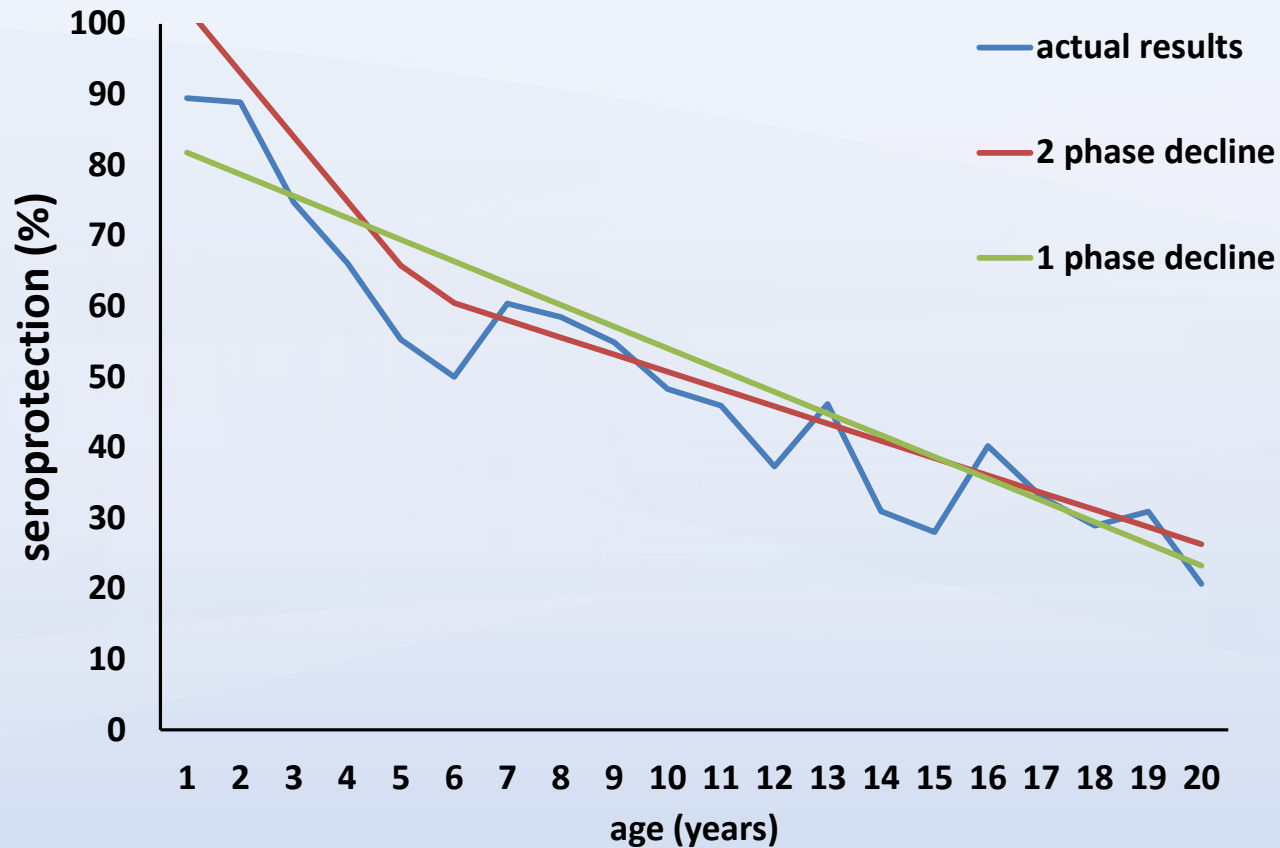


## Results - high responders

Age (years)	Total population			Jews and others			Arabs		
	N	>100 %	95% CI	N	>100 %	95% CI	N	>100 %	95% CI
0.5-1	128	58.6	49.9-66.8	93	58.1	47.9-67.6	35	60.0	43.6-74.4
2-4	229	36.7	30.7-43.1	148	35.1	27.9-43.1	81	39.5	29.6-50.4
5-9	257	17.9	13.7-23.0	190	20.0	14.9-26.3	67	11.9	6.2-21.8
10-14	276	11.2	8.0-15.5	184	10.9	7.1-16.2	92	12.0	6.8-20.2
15-19	354	11.0	8.2-14.7	246	12.6	9.0-17.3	108	7.4	3.8-13.9



## Seroprevalence by age





## Discussion

- Anti HBs antibodies decline with time.
- Over 46 studies reporting on anti HBs $\geq$ 10, 5-20 years after primary immunization (+ meta analysis).
- Few from non endemic countries.
- 29 studies on booster response.
- Seropositivity in Israel: relatively low.



Author, year, country	Type of vaccine	Vaccine schedule	Years from vaccination	Seropositivity rate %
<b>Present study</b>	<b>10µg recombinant</b>	<b>0, 1, 6 mo</b>	<b>5</b>	<b>50-60</b>
Belloni, 2000 Italy	recombinant	0, 1, 6 mo	5	<b>66, 74</b>
<b>Present study</b>	<b>10µg recombinant</b>	<b>0, 1, 6 mo</b>	<b>10</b>	<b>45.9</b>
Zanetti, 2005, Italy	10µg recombinant	3, 5, 11 mo	10	64
Aghakhani 2011 Iran	10µg recombinant	0, 2, 6	15	24
<b>Present study</b>	<b>10µg recombinant</b>	<b>0, 1, 6 mo</b>	<b>19</b>	<b>20.7</b>



Author, year, country	Type of vaccine	Vaccine schedule	Years from vaccination	Seropositivity rate %
Poovorawan, 2010, Thailand	10µg recombinant	0, 1, 2, 12 mo	20	60.5
Chinchai, 2009, Thailand	10µg recombinant	0, 1, 2, 12 mo	18-20	69.9
AlFaleh, 2008, Saudi Arabia	10µg SKF or 5µg MSD	0, 1, 5 mo	16-18	38.0
Poovorawan, 2010, Thailand	10µg recombinant	0, 1, 2, 12 mo	20	60.5



## **Study limitations**

- No documented history of immunization.
- No data on Anti HBV core antibodies and HBsAg.
- No data on antibody level shortly after vaccination.
- Third generation vaccines are more immunogenic.
- SciBVac in use for routine children vaccination since mid March 2011.
- The use of a more immunogenic vaccine may alter the results in the long run.





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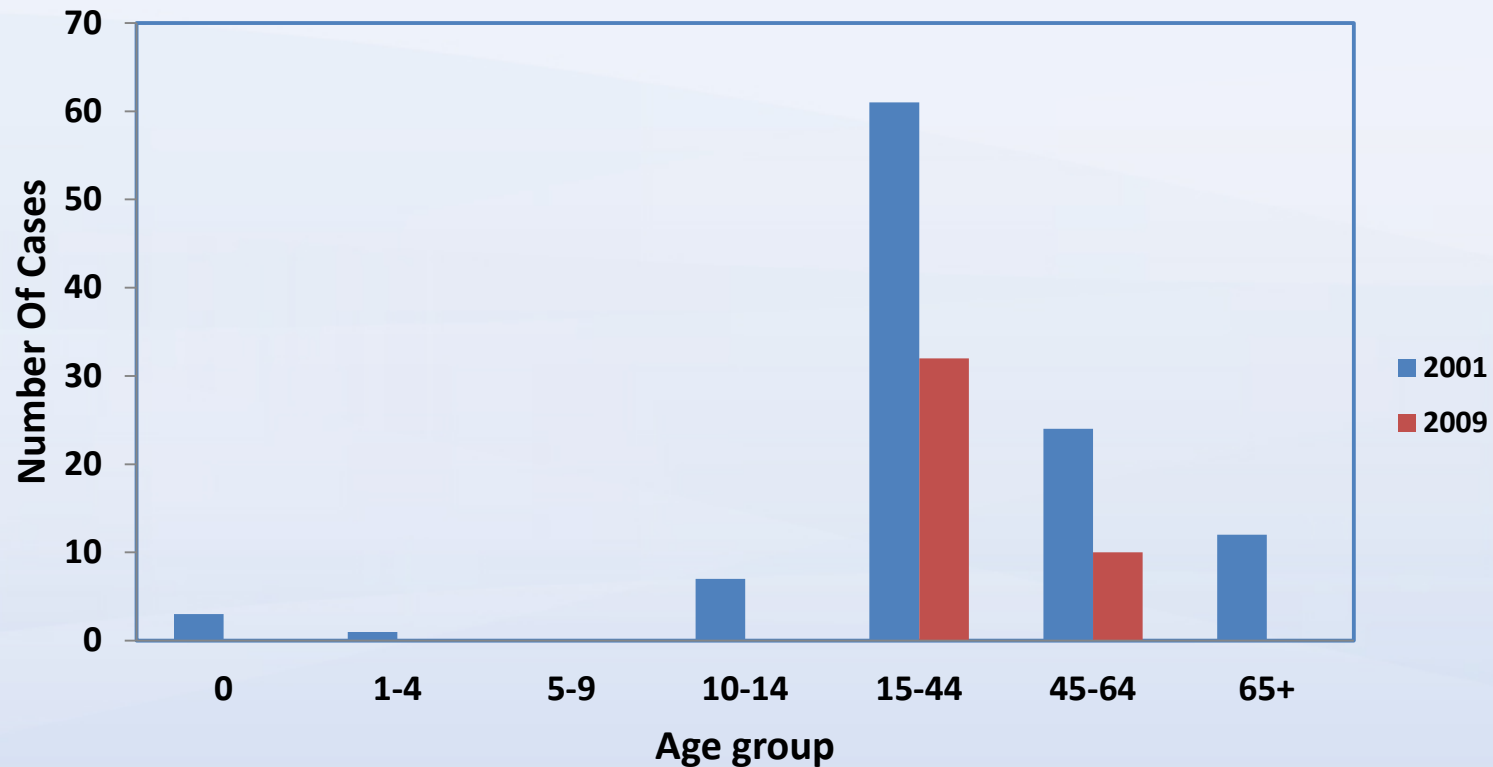
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## **For Discussion**

- Is a booster dose required?

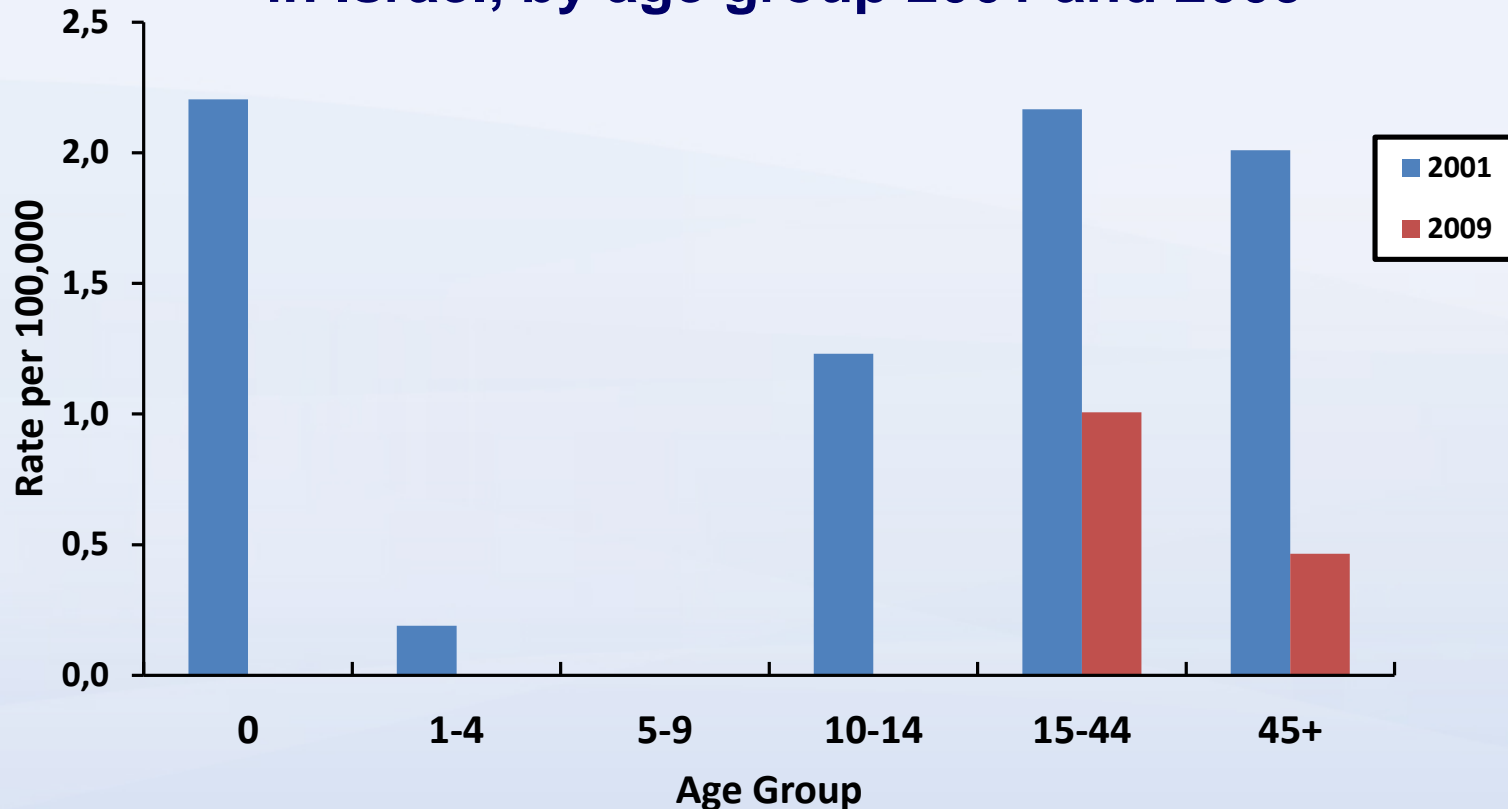


## Reported cases of acute Hepatitis B in Israel, by age group 2001 and 2009





## Reported rates of acute Hepatitis B Cases in Israel, by age group 2001 and 2009



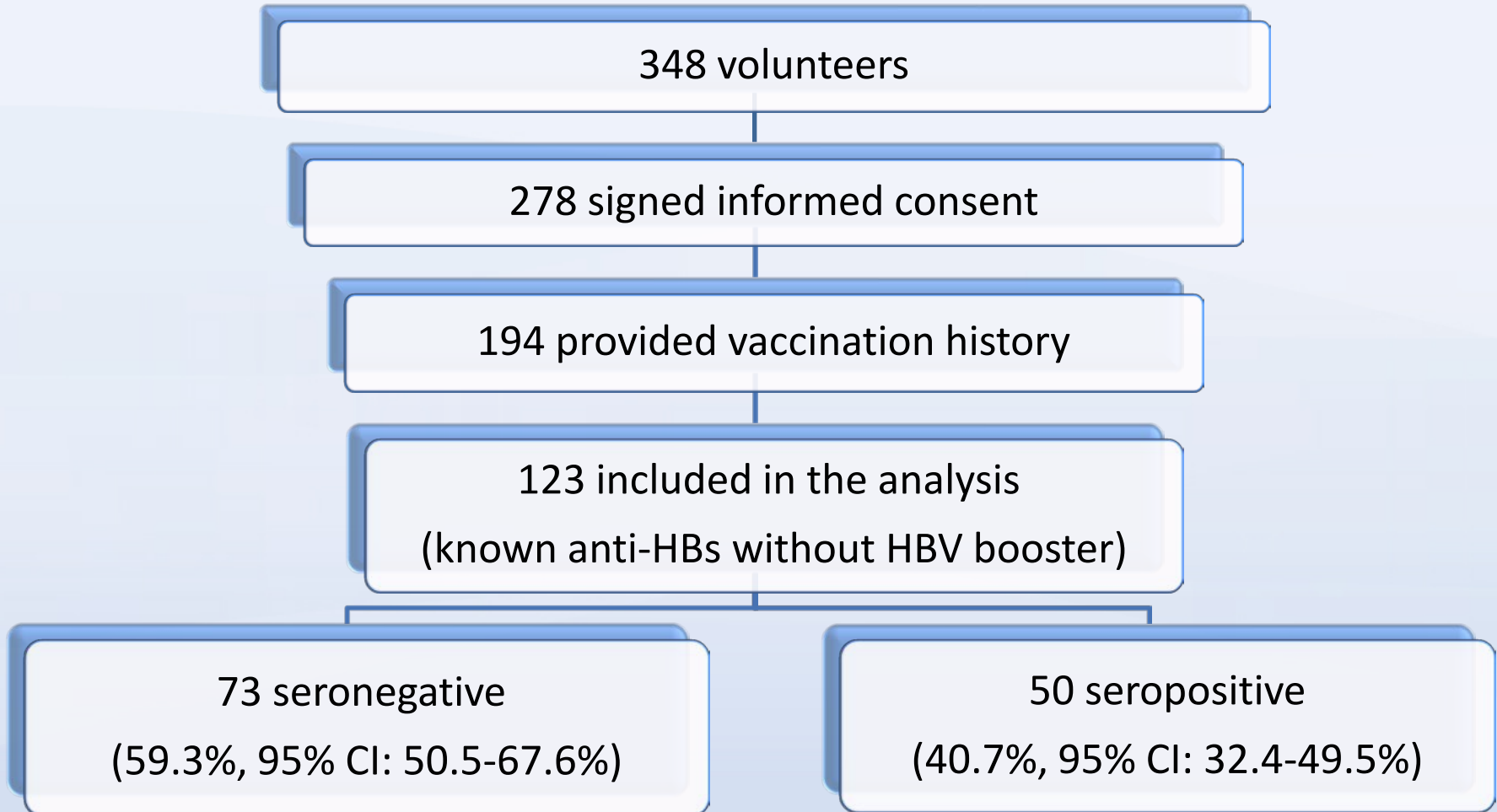


## **Future studies**

- The prevalence of HBc antibodies
- The prevalence of HBsAg among vaccinated
- The effect of booster dose in negatives

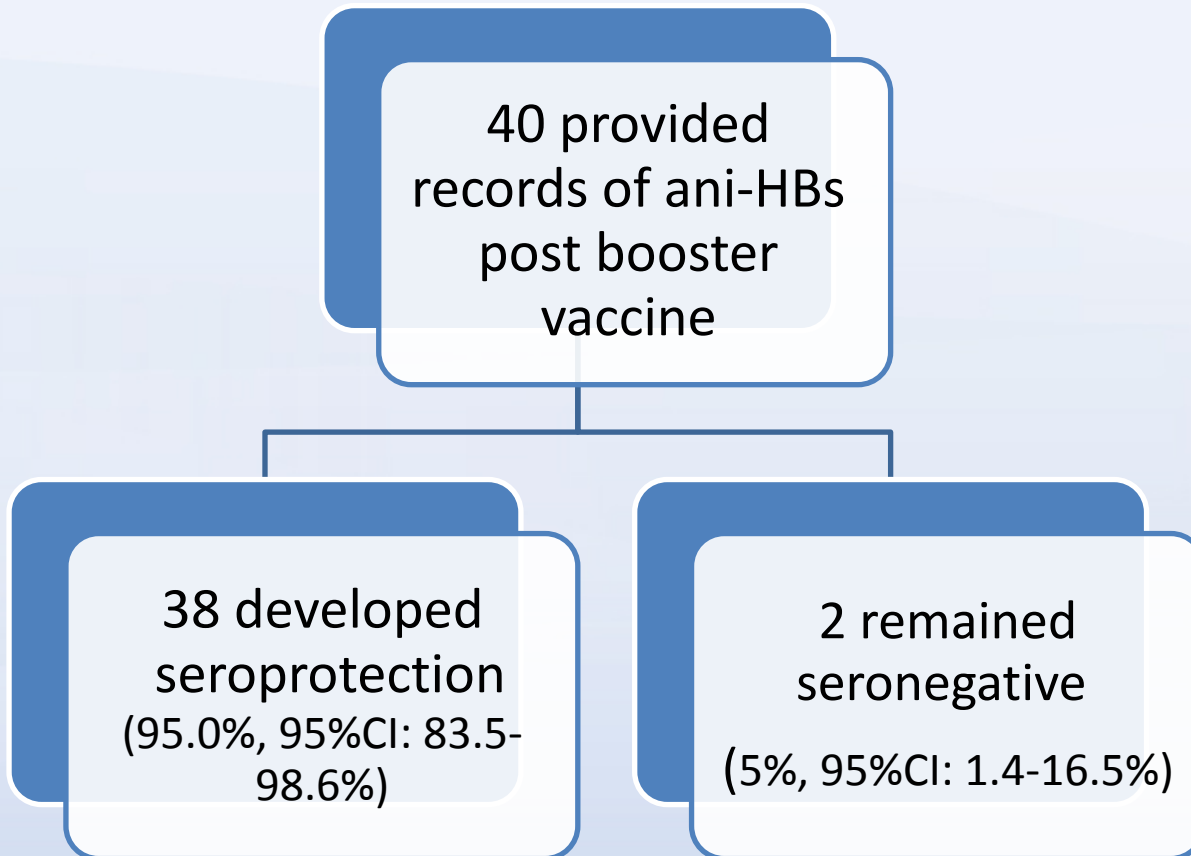


## The effect of a booster dose





## The effect of a booster dose





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## **Acknowledge**

### **ICDC**

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Prof. Ella Mendelson

Dr. Merav Weil



Age (years)	No of Samples	Jews	Arabs
6-11 months	38	32	6
1	90	61	29
2	79	52	27
3	65	40	25
4	85	56	29
5	42	30	12
6	53	41	12
7	53	36	17
8	51	37	14
9	58	46	12
10	61	39	22
11	59	37	22
12	39	26	13
13	42	28	14
14	75	54	21
15	87	65	22
16	100	60	40
17	83	54	29
18	55	43	12
19	29	24	5
Total	1,244	861	383

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Age (years)	No of Samples	Positive	Seroprotected %
6-11 months	38	34	89.5
1	90	80	88.9
2	79	59	74.7
3	65	43	66.2
4	85	47	55.3
5	42	21	50.0
6	53	32	60.4
7	53	31	58.5
8	51	28	54.9
9	58	28	48.3
10	61	28	45.9
11	59	22	37.3
12	39	18	46.2
13	42	13	31.0
14	75	21	28.0
15	87	35	40.2
16	100	33	33.0
17	83	24	28.9
18	55	17	30.9
19	29	6	20.7
Total	1,244	620	49.8

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Age (years)	No of Samples	Positive	Seroprotected %
6-11 months	38	34	89.5
1	90	80	88.9
2	79	59	74.7
3	65	43	66.2
4	85	47	55.3
5	42	21	50.0
6	53	32	60.4
7	53	31	58.5
8	51	28	54.9
9	58	28	48.3
10	61	28	45.9
11	59	22	37.3
12	39	18	46.2
13	42	13	31.0
14	75	21	28.0
15	87	35	40.2
16	100	33	33.0
17	83	24	28.9
18	55	17	30.9
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Total	1,244	620	49.8

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