



A Comparison of Epidemiologic Patterns of Primary Liver and Intrahepatic Bile Duct Cancer in Massachusetts and Israel, 2002-2012

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OBJECTIVE: To compare the epidemiology of primary invasive liver cancer in Massachusetts with Israel, 2002-2012

What is Primary Liver and Intrahepatic Bile Duct Cancer?

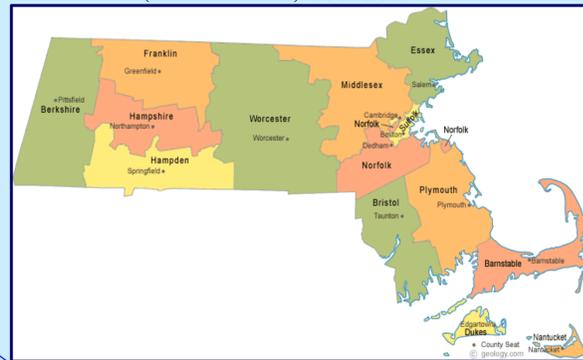
(American Cancer Society's Liver Cancer Overview)

- The liver is the largest organ in the body and performs many functions including: breakdown and storage of nutrients absorbed from the intestine, clotting factor production, bile production to help absorb nutrients from the intestine, and toxic waste breakdown from the body. The liver is a common metastatic site for cancers originating elsewhere (colorectal, breast, pancreas). These are secondary liver cancers.
- Primary liver cancer originates in the liver in the hepatocyte cells and is known as hepatocellular carcinoma. Intrahepatic bile duct cancer, accounting for 10-20% of liver cancers originate in the ducts that carry bile from the liver to the gallbladder and intestines.
- Risk factors include being male, being infected with hepatitis B and C, heavy alcohol use, and liver cirrhosis.
- There are areas of the world such as Southeast Asia, sub-Saharan Africa, and the Middle East where hepatitis B is endemic and there is a greater incidence of maternal transmission of the virus. These ethnic groups have higher rates of hepatitis B infection at birth and subsequently higher rates of liver cancer.

Background:

- While geographically distant, Israel and Massachusetts are similar in size and population.
- By state ranking, Massachusetts has the 3rd highest Jewish population in the United States (4.0%)¹ and, like Israel, has a growing immigrant population.
- The Massachusetts Cancer Registry in collaboration with the Israel Cancer Registry examined patterns of liver and intrahepatic cancer from 2002-2012 as well as patterns of risk factors, such as hepatitis B and C infection and injection drug use.

(Massachusetts) מדינת מסצ'וסטס



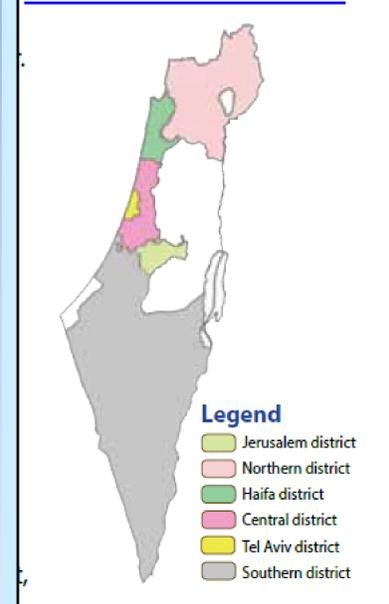
Demographics – Israel and Massachusetts, 2013

	ISRAEL	MASSACHUSETTS
Population	8,134,500	6,646,144
Area	8,356 square miles	10,555 square miles
Race/Ethnicity	Jews 75.0%	White, non-Hispanic 75.7%
	Arab 20.7%	Black, non-Hispanic 6.3%
	Other 5.4%	Asian, non-Hispanic 5.5%
		Hispanic 9.9%
		Other/Unknown 2.6%
Gender	Male 49.5%	Male 49.5%
	Female 51.5%	Female 51.5%
Age Groups	0-18 34.5%	0-18 20.8%
	19-64 54.9%	19-64 64.4%
	65+ 10.6%	65+ 14.8%

- While Massachusetts specific population data were not available, the 2012 estimated racial/ethnic breakdown for the Jewish population in US was 89.1% white, non-Hispanic, 5.5% Hispanic, 1.7% black, non-Hispanic, and 3.8% other, non-Hispanic.¹
- In Israel among the Jewish population, 41% have American/European ancestry, 14% have Asian ancestry, 16% have African ancestry, and 29% have native Israeli ancestry. The Arab population is nearly 85% Muslim and of Middle Eastern (Palestinian) ancestry.² With the exception of the Israelis of sub-Saharan African ancestry and those of Asian ancestry outside of the Middle East, all would be classified as white, non-Hispanic in Massachusetts

(Israel) מדינת ישראל

The State of Israel, by District



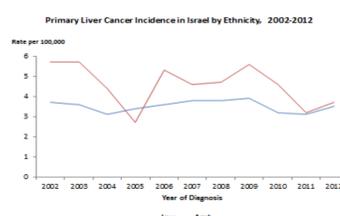
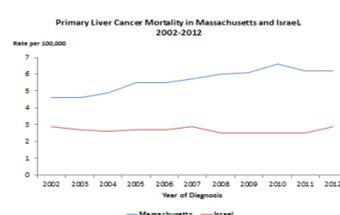
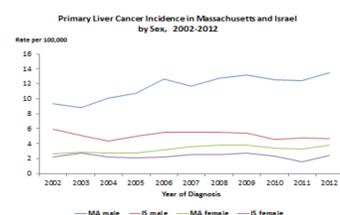
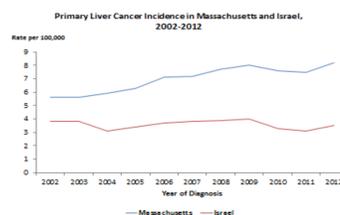
Hepatitis B & C Chronic Infection in Israel & Massachusetts

ISRAEL (2000-2010)	MASSACHUSETTS
HEPATITIS B Prevalence:	
Total Chronic Infection – 1.7%*	223.55/100,000 (2000-2012)**
Male – 59.6% of chronic cases*	Male – 55% of chronic cases (2000-2013)**
Female – 40.4% of chronic cases	Female – 45% of chronic cases (2000-2013)
Total Cases: Jew – 59.2% Arab – 40.8% ³	Total Cases: Asian-42.4%, White-21.5%, Black-18.9%, Other-6.8%, Unknown (10.4%)**
HEPATITIS C Prevalence:	
Total Chronic Infection – approx. 2.0%*	estimated to be at least 100,000 or 1.6% of the population ⁴
Male – 61% of chronic cases*	Male – 61% of chronic cases (2007-2013)**
Female – 39% of chronic cases	Female – 39% of chronic cases (2007-2013)
Injection Drug Users – 55.5% are positive ⁵	Injection Drug Users (U.S. estimates) – 75% are positive ⁶

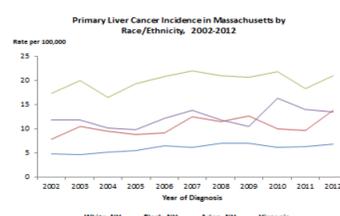
*Data Source: HBV and HCV Epidemiology in Israel; Eli Zuckerman, Hedy S. Rennett, Gad Rennett, Carmel Medical Center, Haifa, Israel (Data are from Clalit Health Services Patients and not from a population based registry)
 **Data Source: Massachusetts Department of Public Health

INCIDENCE AND MORTALITY TRENDS IN MASSACHUSETTS AND ISRAEL

- While there was no significant change in liver cancer rates among the total population in Israel, the incidence increased significantly in Massachusetts from 2002-2008 (annual percent change (APC)=6.2) and remained stable from 2008-2012 (APC=0.2).
- The incidence rates for both males and females in Massachusetts increased significantly from 2002-2012 (APC=3.9 and APC=3.6, respectively). There were no changes in Israel.
- While there were significant increases in trends for 2 of the 4 main racial/ethnic groups in Massachusetts (white, non-Hispanic (APC=6.5) and black, non-Hispanic (APC=3.3), there were no significant changes in trends for the 2 main racial/ethnic groups in Israel (Jews and Arabs).
- While mortality rates increased significantly in Massachusetts from 2002-2010 (APC=4.6) and then remained stable from 2010-2012 (APC=3.1), the mortality rates remained stable in Israel (APC=0.9).

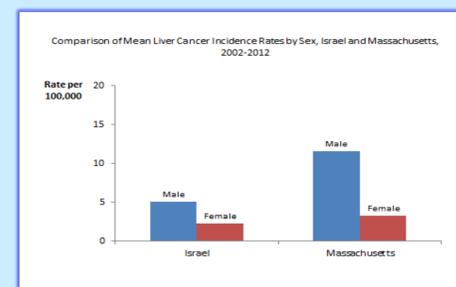
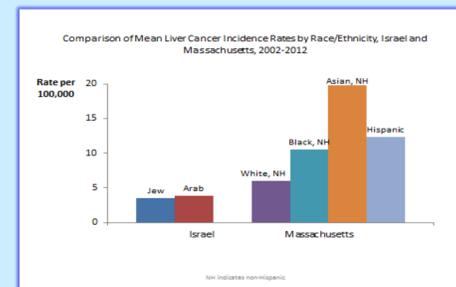


Note: While all the Massachusetts incidence and mortality rates and the Israeli incidence rates used the US standard 2000 population, the Israeli rates were calculated by combining the three 75+ groups into one. The mortality rates were calculated with different standards, with Israel using the world standard population.



COMPARISON OF OVERALL RATES, 2002-2012

- There were differences in the mean incidence rates from 2002-2012 among the four racial/ethnic groups in Massachusetts, with Asian, non-Hispanics having the highest rates followed by Hispanics, black, non-Hispanics, and white, non-Hispanics.
- While there were differences by race/ethnicity in the mean incidence rate in Israel from 2002-2012, they were not very pronounced.
- In both Israel and Massachusetts, the mean incidence rate from 2002-2012 among males was two to three times the rate among females. When comparing the two areas by sex, Massachusetts males and females had higher incidence rates compared to Israeli males and females.



Hepatitis B & C Risk Factors in Israel & Massachusetts

ISRAEL	MASSACHUSETTS
Injection Drug Use (IDU):	
Heroin users from the former Soviet Union reported significantly more injection use than native born Israeli heroin users. ⁷	National survey data (2000-2002) suggests a decrease in IDU among younger black, non-Hispanics and an increase among younger white, non-Hispanics. ⁸
1.0% of surveyed adults in 2008 aged 18-40 reported IDU. ⁷	40,743 admissions related to IDU in 2012 (crude rate – 614.4/100,000 or approximately 0.6% of the population) ⁹
Chronic Hepatitis B Infection Prevalence Estimates in Immigrant Groups⁸:	
Eastern Europe & Central Asia – 5.8% (former USSR immigrants) Sub Saharan Africa – 10.3% (Ethiopian immigrants)	East Asia – 11.3% (Chinese, Vietnamese, Cambodian immigrants) Sub Saharan Africa – 10.3% (West African immigrants)

These chronic infections are due to maternal transmission of the virus in those countries.
 *Data Source: Massachusetts Department of Public Health

Conclusions:

- The incidence of liver cancer is higher in Massachusetts than in Israel.
- While there were significantly increasing trends in liver cancer incidence and mortality during 2002-2012 in Massachusetts, there were none in Israel.
- Hepatitis B and C infections are contributing factors to liver cancer and the prevalence of infections in each country is related to the incidence of liver cancer.
- In both countries, males have a higher incidence of injection drug use, higher rates of hepatitis B and C and higher rates of liver cancer.

These prevention strategies are already in place in Massachusetts and Israel:

- needle exchange to stop infection;
- screening of immigrants from high prevalence countries;
- prompt treatment of infections once they are detected;
- prompt treatment of newborns born to hepatitis B infected mothers through immune globulin and hepatitis B vaccinations; and
- hepatitis B vaccinations of all newborns.

Current Projects:

- Massachusetts linked the entire registry database from 2002-2012 with the hepatitis B and C registry for the same time period. The association between all types of cancer and hepatitis B and C will be analyzed.

References:

¹ Steinhilber Institute American Jewish Population Estimates: 2012.
² Statistical Abstract of 2010, Israeli Central Bureau of Statistics.
³ Zamir, D, Zamir, C, and Rishpon, S, 'Epidemiology of Chronic Hepatitis B Infection among Family Members of Chronic Carriers in Israel', Israel Medical Association Journal, Volume 3, May 2011.
⁴ Shifting Epidemics: HIV and Hepatitis C Infection among Injection Drug Users in Massachusetts, Massachusetts Department of Public Health, 2012.
⁵ Israelowitz, R. et al. 'Severity of heroin use in Israel: comparisons between native Israelis and former Soviet Union immigrants', Addiction, 102:630-637, February 2007.
⁶ Armstrong, G., 'Injection Drug Users in the United States, 1979-2002: An Aging Population', Archives of Internal Medicine, 2007; 167(2):166-173.
⁷ Ben-Hamburger, R. et al., Israeli Anti-Drug Authority, 'Illegal Use of Drugs and Alcohol: Israel, 2009, Seventh National Epidemiological Survey'.
⁸ Rossi, C. et al. 'Seroprevalence of Chronic Hepatitis B Virus Infection and Prior Immunity in Immigrants and Refugees: A Systemic Review and Meta-Analysis', PLoS ONE, Volume 7 (9), September 2012.