

Do Ashkenazi Jews have a Higher than expected Cancer Burden? Implications for Cancer Control Prioritization Efforts*

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Abstract

Background: Recent genetic susceptibility findings in Jews of Eastern European descent, commonly called Ashkenazi Jews, have led to concerns that they may be stigmatized as being more cancer prone than other groups.

Objective: To examine the hypothesis that site-specific or all-cancer incidence and mortality rates are higher than expected in Ashkenazi Jews worldwide when compared with referent populations.

Methods: A MEDLINE search was performed using keywords “Jews,” “cancer,” “incidence” and “mortality” to identify studies directly relevant to the primary study question.

Results: Little evidence suggested that all-cancer incidence or mortality is higher in Ashkenazi Jews than in North American non-Hispanic whites. Ashkenazi Jewish men appear to have relatively low cancer rates, which may be due to lower tobacco use. Colorectal cancer was shown to disproportionately overburden Ashkenazi Jews, who may also be at increased risk for ovarian, pancreatic and stomach cancer, and non-Hodgkin’s lymphoma. Little evidence was found supporting an elevated risk of breast cancer in Ashkenazi Jewish women. Rates of lung, cervical, penile and prostate cancers appear low in this population. Rate disparities were generally attributed to lifestyle differences, particularly diet and tobacco use, rather than to genetic predisposition.

Conclusions: Ashkenazi Jews do not appear to have a higher total cancer burden than comparable North American populations. Any cancer rate differentials in this group are more likely to be related to lifestyle and dietary factors than to genetics. However, colorectal cancer rates in Ashkenazi Jews may be the highest of any ethnic group in the world and cancer controllers should consider this when developing future screening, diagnostic and policy strategies.

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There are about 13 million Jews worldwide and about 80% have ancestral roots in Central and Eastern Europe [1]. This subgroup of world Jewry has traditionally been called “Ashkenazi,” a term that derives from a Biblical name and

later adapted by medieval rabbis to refer to Jews of German or Eastern European descent [2]. It should be noted that this categorization is far from precise [3].

It is estimated that there are 5–6 million Ashkenazi Jews in the U.S., 3–4 million in Israel, and a million or more mostly scattered throughout Western Europe, the former Soviet Union, Canada, Great Britain, Australia, South Africa and Argentina [1,3,4]. Prior to World War II there were approximately 13 million Ashkenazi Jews worldwide [1,4]; it is well known that the total population of this group was truncated by the Holocaust [4]. The balance of world Jewry claims its roots in North Africa and predominantly Arab or Oriental countries, and is generally known as “Sephardi” [1,4].

The study of disease patterns in U.S. Jews has been of great interest to epidemiologists because geographic and cultural circumstances have led to relatively homogeneous genetic patterns in U.S. Jews [3–6]. Up to 95% of U.S. Jews are believed to be of Ashkenazi heritage [5]. Although most of the world’s Ashkenazi Jews live in North America, Jews constitute only about 2% of North America’s total population, and due to the increasing intermarriage rates the study of disease rates in American Ashkenazi Jews is made more difficult [1].

Much has been published recently about the genetic as opposed to lifestyle susceptibilities to cancer – particularly breast, ovarian and colon – in this group [3–7]. Although they constitute an extremely small percentage of the world’s population, the impact of genetic studies in Ashkenazi Jews has led to a sweeping debate about cancer risk, genetic screening, insurability issues and the specter of stigmatization [7]. To date, no analysis has been published on the question of whether or not Ashkenazi Jews worldwide have a higher than expected overall cancer burden compared to other general western populations, specifically North America. In this paper, I have attempted to assess whether there is, in fact, clear and convincing evidence in the literature indicating a higher than expected overall, or site-specific, cancer burden in Ashkenazi Jews.

Methods

A MEDLINE search was performed using the keywords “Jews,” “cancer,” “incidence” and “mortality.” Of the 105

* This article is dedicated to the memory of Rabbi Irwin Feldman.

English-language articles identified, 13 directly or indirectly compared overall cancer rate estimates or proportionate cancer ratios in Jews and other groups. Half of the remaining studies were rejected for not addressing, either directly or indirectly, overall or major site-specific cancer incidence or mortality rate estimates in Jews.

Results

Jewish mortality and cancer rates before World War II

From ancient times right through the Second World War, the major causes of death among Ashkenazi Jews were almost certainly infectious or violent in nature, with tuberculosis and influenza being the most common [8]. It has been inherently difficult to collect data on causes of death in Jewish populations, including Ashkenazi Jews, as religion is usually not noted during census and other vital statistic recordings. Since the overwhelming majority of North American Jewry is of Ashkenazi heritage, studies using only Jewish religion as a demographic characteristic might be reasonably presumed to be reflective of rates in Ashkenazi Jews.

As early as 1911, U.S. Jewish and Canadian Jewish mortality rates were reported to be lower than that of the general population [8–10]. This was confirmed in subsequent studies through 1969, with the data showing that the Jews' mortality advantage was usually more prominent in those under the age of 50, while excess mortality was noted in Jews above age 50. The longevity disparity later in life was attributed to imprudent diet and lack of exercise. Disproportionate death rates from cancer were not noted before the First World War [9,10].

Eastern European Jews were noted to have lower overall mortality rates than their non-Jewish counterparts in the 1920s. This finding was attributed to their conscientiousness in seeking medical care and to their stable nutritional and housing conditions. The first data suggesting higher than expected rates of cancer in this group came after the First World War, when New York City Jews, predominantly immigrants from Eastern Europe, were noted to have higher rates of cancer of several sites. These studies linked these disparities to this group's greater meat intake [8]. Data from 1925, however, showed that the overall death rates from cancer in both Eastern European and New York City Jews were in fact lower than that of non-Jews. Researchers of the day attributed this to "social causes" and not to "racial peculiarities" [8].

Total mortality and cancer-specific mortality in U.S. Ashkenazi Jews after World War II

Cancer mortality data and health behaviors in U.S. Jews born in New York City or Russia were first comprehensively reviewed during the 1970s [11,12]. Smoking and alcohol usage rates in U.S. Jews were noted then to be substantially lower than in other groups, though precise figures as always could not be obtained. Jewish women were noted to have a higher socio-

economic status, lower fertility rates, and less premarital intercourse than Catholics or Protestants.

Compared to non-Jews, U.S. Jews had relative "deficits" in cancer mortality rates from lung, prostate, cervical and bladder cancer, and relative "excesses" of colon, esophageal, stomach, pancreatic, ovarian cancer and all lymphomas. The data published were conflicting regarding breast cancer rates in Jews relative to non-Jews. The higher rate of colon cancer was attributed to a possibly increased consumption of beef or animal fat. The studies presented no evidence to suggest that the Jewish groups studied, mostly Ashkenazi, had higher overall rates of cancer death than white Americans [11,12].

A 1981 study of Rhode Island Jews again confirmed that U.S. Ashkenazi Jews likely smoked fewer cigarettes than other religious groups. A higher percentage of Jewish men than non-Jewish men were noted to have died of gastrointestinal cancers, while a smaller portion died of lung cancer. There was no difference in the percentage of Jewish women who died of breast cancer compared with the non-Jewish group. No evidence was offered to suggest that the proportion of Jewish cancer deaths differed significantly from that of the local white population [13].

Research from 1981 showed that New York City Jews had lower proportionate mortality ratios for lung and prostate cancers compared with other ethnic groups in New York. In this study no differences were reported for breast, ovarian and gastrointestinal cancers. New York City Jews aged 65–84 were found to have substantially lower overall death rates from cancer when compared to the total white New York City population. While Jewish men were noted to have "relatively low" death rates from cancer, rates in Jewish women were noted to be similar to New York's total white population. The studies also noted that New York City had the highest population of Jews of any American city and would be most likely to estimate "trends in the mortality of America's Jews" [14,15].

A 1985 study in Los Angeles found that when compared to other religious groups, Jewish men had a substantially lower proportionate incidence ratio of lung, laryngeal, esophageal and prostate cancer and a statistically significant higher risk of bladder, colon, pancreatic and stomach cancer. Jews were again noted to smoke less, be relatively better educated and more likely to access a high level of medical care [16].

A relatively high PIR was also noted in both Jewish males and females for lymphomas, including non-Hodgkin's lymphoma, and for thyroid cancer. The study did not confirm any substantial excess PIR for ovarian or breast cancer in American Ashkenazi Jewish women. No evidence was presented to suggest that Jews had higher overall rates of cancer compared with the other religious groups studied or to a "standardized" rate ascribed to the general North American white Protestant population [16].

Rhode Island data of 1987 confirmed that overall mortality

PIR = proportional incidence ratio

rates were substantially lower for Jewish men compared with the overall local white population, while Jewish female life expectancy was similar to the referent local white population. Explanations offered to explain the differences in mortality rates included the traditional Jewish emphasis on the “sanctity of the body and the need to care of it.” Specific factors mentioned to explain the differences included lifestyle, diet and the Jews’ higher socioeconomic status [17].

Cancer rates in Israeli Ashkenazi Jews

Israel’s population is 80% Jewish. Since Ashkenazi Jews comprise the majority of the Israeli Jewish population [18], Israeli cancer rates provide the best estimates of rates in this group. Although precise conclusions cannot be drawn, it is worth noting that in a recent evaluation of 46 developed and developing countries, the only cancer sites where Israeli rates ranked among the 10 highest countries were for female rates of leukemia, breast and colorectal cancer. Rates in Israeli males were relatively low for all smoking-related sites compared to other countries [19].

Studies within Israel have shown that adult cancer mortality rates in Jews are substantially higher than those in the Arab and Druze populations. However, the gap between the Jews and the non-Jews has been steadily narrowing since 1970 [18]. As of 1980, the cancer death rate of Israeli Jewish men was similar to that of all U.S. males; and by the end of the 1980s any rate differential between Israeli Jewish and non-Jewish women was projected to reach zero [18–20].

Elevated rates of certain urologic cancers in Israeli Jews compared to non-Jews have been attributed in part to lower intakes of olive oil, cumin and daily fluids in Israeli Jews, particularly Ashkenazi [21]. Data from 1996 noted that Israeli Jews have higher mortality rates from breast and colon cancer than their Arab counterparts. Diet was again presumed to be the most likely explanation [22].

It was recently suggested that a high intake of linoleic acid, an omega-6 polyunsaturated fatty acid, contributes strongly to higher rates of some cancers in Jews. The authors noted that Israeli Ashkenazi Jewish women have a very high intake of linoleic acid. Israeli Jews have relatively low intakes of olive oil, high rates of hyperinsulinemia and obesity, and an extremely high dietary intake ratio of omega-6 to omega-3 PUFA. The study suggested that these dietary factors account for much of the excess risk of breast, colon and urologic cancers in Israeli Jews compared with Israeli non-Jews [23]. This same study reported that the overall cancer death rate for all Israeli Jews was indeed higher than for some “western” countries [19,23]. However, this noted excess was completely accounted for by higher rates in Israeli Jewish women. Israeli Jewish men had relatively lower cancer rates than men in many western countries [19,23]. The authors

made no direct comparison of estimated total cancer mortality rates in Ashkenazi Jews with rates in North American populations.

All-cancer rate estimates in worldwide Ashkenazi Jews and rates in North Americans

Most Ashkenazi Jews live in North America, Israel or the former Soviet Union; thus a reasonable referent population to use in comparison may be that of non-Hispanic whites in North America, or more specifically, U.S. and Canadian whites. It should be noted that total cancer incidence rates in North America are the highest in the world [19,24]. Given the difficulties in assessing actual cancer rates in Ashkenazi Jews and in characterizing their true ethnic background, precise assessment of relative risk is impossible.

In the U.S. and Israel, the vast majority of cancer deaths are likely due to cancers of the lung, breast, prostate, colorectum, pancreas, ovary, leukemia and non-Hodgkin’s lymphoma. In general, cancer rates in North America are substantially higher in males than in females [19,24]. It is believed that about 30% of all cancer deaths in developed countries are attributable to tobacco use [19,24].

As was suggested previously, there are no published population-based estimates of overall cancer incidence rates in Ashkenazi Jews. An estimate of current cancer rates in all Ashkenazi Jews might be made by looking at cancer rates in Israeli Jews born in Europe or America [1,4,5,7,24]. The 1988–92 age-standardized incidence rates for all cancers in Israeli Jewish males and females born in Europe or America are in fact slightly lower than the rates found in U.S. white males and females respectively, based on local registries and National Cancer Institute SEER data from that period [24]. These data also suggest that Ashkenazi Jews may be one of only a few ethnic groups in the world in which the incidence of cancer is higher in females than in males [24].

It should of course be noted that the surrogate use of cancer rates in Israelis born in Europe or America to estimate global rates in Ashkenazi Jews is highly speculative. Comparison of these surrogate rates with those of other groups worldwide should be done with great caution, and firm conclusions cannot be drawn. Table 1 lists, for reference only, a selected sample of western localities with their registry-based cancer incidence data from 1988 to 1992. Among the available localities listed, these appeared to be the areas most likely to include substantial populations of Ashkenazi Jews based on the demographics discussion earlier.

Estimating site-specific relative cancer risks in Ashkenazi Jews

• Lung

Lung cancer is the leading cause of cancer death in the world, with rates of the disease paralleling population smoking rates [12,16,19,24]. Lung cancer death rates for the overall U.S. male and female populations are twice and three times those for

PUFA = polyunsaturated fatty acid.

Table 1. Reference sample of age-standardized incidence rates (per 100,000) of most cancer sites combined, in selected western populations or countries that are likely to include substantial Ashkenazi Jewish populations [24]

	Males	Females	Males + Females
Israeli Jews born in U.S./Europe	255.5	268.3	523.8
Los Angeles, non-Hispanic whites	373.4	303.5	676.9
Connecticut, whites	365.7	289.4	646.1
U.S. SEER data, whites	370.9	280.9	651.8
Ontario, Canada	325.7	261.5	586.8
Calvados, France	335.8	195.9	531.7
UK (England and Wales)	261.1	225.5	486.6
Germany (eastern states)	249.3	197.4	446.7

Israeli males and females, respectively [19,24]. Recent studies confirm that lung cancer incidence rates are lower among both male and female Israeli Ashkenazi Jews than in most developed countries [25]. Smoking rate differentials did not fully explain the incidence rates in the major ethnic Jewish groups studied in Israel, suggesting that there may be varying levels of susceptibility to lung cancer among Jews, influenced by either genetic or lifestyle factors. As previously discussed, low lung cancer rates in U.S. Ashkenazi Jews have been attributed to their well-described lower rates of cigarette smoking [12,13,16,17,24].

• Breast

The BRCA1 and BRCA2 mutations discovered recently strongly predispose a small number (3% or less) of Ashkenazi Jews to breast, ovarian, prostate cancer, and possibly pancreatic cancer and lymphoma [3]. Ashkenazi Jews who carry these mutations are more likely than others to have a family history of early-onset cancers, and family history has been shown to be more predictive of various cancer risks in Jews than in other religious groups [4,26]. While some studies have suggested that Israeli Jewish women may have higher rates of breast cancer than women from other western countries, rates in Israeli Jewish women born in Europe or America are similar to white women in the U.S. [24]. Recent evidence in North America does not support Jewish religion or Ashkenazi Jewish heritage, by itself, as being a significant risk factor for breast cancer [4,5,7,27].

• Prostate

Incidence and mortality rates of prostate cancer have been consistently reported to be substantially lower in U.S. Ashkenazi Jews and very low in all Israelis [12,24,28].

• Colorectum

Colorectal cancer affects both men and women and is the second leading cancer killer in the U.S. and Israel [19,24]. Using population-based data, reports from all over the world have consistently confirmed that the lifetime incidence of colon cancer in Ashkenazi Jews is as high as 15%, or as much as 2–3 times that of the general populations of developed countries

[24,29–32]. About 6% of Ashkenazi Jews carry at least one mutation that would substantially increase their risk for colon cancer even further [7]. In Israel, Ashkenazi Jews have been noted to have higher rates of colorectal cancer than Israeli Jews of other backgrounds. The reasons for the rate differential are presumed to be predominantly environmental and not genetic [32]. General colorectal cancer incidence rates in North America are nearly double the rates in Eastern Europe and second only to those in Australia [19,24]. Recent colorectal cancer rates are higher in Israeli Jews born in Europe or America than in U.S. whites and are among the highest rates reported in the world [19,24].

• Ovary

Prior studies suggested an excess risk of ovarian cancer in Ashkenazi Jews [4,11,12]. Moreover, Israeli Ashkenazi Jewish women appear to have the highest rates of ovarian cancer in the world [4,11,12,24], and the BRCA1 mutation in these patients is quite common [4]. However, as previously mentioned regarding breast cancer, U.S. evidence in the 1980s did not suggest an excess burden of ovarian cancer in a sample of predominantly Ashkenazi Jewish women when compared to other local referent religious groups [16].

• Other sites

At least one textbook has noted that Jews are more prone to pancreatic cancer and certain lymphomas than other groups, while being less prone to penile cancer [33]. However, compared with other developed countries or U.S. whites, rates of pancreatic cancer in Jews born in Europe or America in the 1990s appear to be similar for both men and women [24].

Rates of stomach cancer are relatively high in Israeli Jews born in Europe or America [24]. Jewish women have been consistently reported to have a relatively low incidence of cervical cancer [11,12,24]. Israeli Jews born in Europe or America have similar rates of melanoma when compared to U.S. whites [24]. Cancer of the esophagus is particularly uncommon in Ashkenazi Jews [24].

Non-Hodgkin's lymphoma rates have been shown to be higher in Jews [16,19], but no disparity is found when one compares disease rates in Israelis born in Europe or America to rates in U.S. whites [24].

Discussion

There is little evidence published to date that directly supports the contention that worldwide rates of all-site cancer incidence and mortality are higher in Ashkenazi Jews than in relevant populations in North America. In fact, some of the evidence suggests that they may have lower overall cancer rates because they use less tobacco. Currently, about 25% of them are smokers (G. Rennert, personal communication). There are no recently published studies on the smoking or dietary habits of U.S. Ashkenazi Jews.

Ashkenazi Jews may be more likely than North American whites to have non-Hodgkin's lymphoma and pancreatic,

stomach and ovarian cancer. There is no clear evidence to suggest that they have higher than expected rates of breast cancer worldwide when compared to North American non-Hispanic white women. However, a small number of genetically predisposed Ashkenazi Jewish women, especially in Israel, are indeed at greatly elevated risk for breast and/or ovarian cancer. Total cancer rates in Israeli Ashkenazi Jewish women do appear to be higher than those in women in other western countries. Some evidence suggests that dietary factors play an important role. Future dietary research should examine the impact of meat, omega-3 to omega-6 PUFA intake ratio and olive and cumin products on cancer risk.

At present, uncertainties and controversies still revolve around genetic testing [7]. For most of the cancer sites that may overburden Ashkenazi Jews (i.e., ovary, non-Hodgkin's lymphoma, pancreas), there are currently no practical or validated routine screening tests. Promising early detection protocols in ovarian cancer may be emerging [34] and, if prove effective in the future, would likely be of particular benefit to Ashkenazi Jewish women, especially those in Israel.

A key finding of this review is that the most important worldwide cancer killer proven to disproportionately overburden Ashkenazi Jews appears to be colorectal cancer. Given the relatively low rates of tobacco use and prostate cancer in Ashkenazi Jewish men, colorectal cancer could be the major cause of premature cancer death threatening most of this subpopulation. Colorectal cancer is almost totally preventable and highly curable if current screening guidelines are followed [35,36]. Family history of any of a number of cancers is crucial in addressing risk stratification for this disease. Ashkenazi Jews would likely benefit from intensive counseling regarding their increased risk for this disease and the proven life-saving potential of routine screening [35]. Other behaviors currently believed to be associated with lowered colorectal cancer risk include increased physical activity; avoiding obesity, simple sugars, alcohol, red meat and tobacco; and the long-term use of a daily multivitamin containing folic acid [36]. Future research questions regarding Ashkenazi Jews and colorectal cancer control may focus on physician attention to family history, current symptoms and the question of screening this group prior to the usually advised age of 50 [35,37,38]. Based on emerging evidence on across-site family history associations [3,7,24,31,38] and genetic susceptibilities in this community, Ashkenazi Jewish ethnicity alone may be an absolute indication for total colonic examination by age 60 or earlier.

The totality of evidence discussed supports the conclusion that others have drawn from migrant and gene studies [38–40], namely that higher site-specific cancer incidence rates (especially colorectal and ovarian cancer rates) in Ashkenazi Jews when compared to other groups are probably largely due to differences in diet and exercise and not to genetic susceptibility.

The most obvious limitation of this survey is that many of the studies reviewed do not make clear distinctions between Ashkenazi and non-Ashkenazi Jews. True worldwide rates in Ashkenazi Jews cannot be calculated based on available data,

which are mostly indirect in nature, rarely population-based and resort to proportionate ratio methods. However, given the consistency of the articles studied regarding the major cancers and the virtual absence of any data to accept the null hypothesis, the limitations of the extant data argue for the rejection of the notion that proof exists that Ashkenazi Jews are cancer prone.

Finally, it is interesting to note the great disparity in apparent risk of prostate and colorectal cancer in Ashkenazi Jewish men in comparison to other ethnic groups. Mormons, for example, have relatively low incidence rates of colorectal cancer, and while African-Americans have rates that seem to be near those of Ashkenazi Jews, they also have very high rates of prostate cancer [24]. A case-control study examining dietary and lifestyle factors and overall risk for these cancers in Ashkenazi Jews, African-Americans and Utahn Mormons may be warranted.

Summary and Recommendations

The limited evidence published to date is inadequate to support the assertion that Ashkenazi Jews have a higher than expected cancer burden, or that worldwide they are at higher overall risk for cancer than other comparable North American populations. Nonetheless, Ashkenazi Jews should not construe this report to mean that they should neglect the pursuit of a cancer risk-reducing lifestyle, attention to appropriate screening tests, or the use of the healthcare system for routine complaints that could potentially represent early cancer symptoms. They should know their family history in detail and continue to avoid tobacco. Should ovarian cancer screening become practical, females in this subpopulation might be especially good candidates for such protocols.

Ashkenazi Jews, particularly females, should consider incorporating more olive oil and fish and fewer omega-6 fatty acids into their diet. This review's findings are consistent with the assertion that diet, tobacco use and lifestyle factors are more determinative of overall cancer risk in Ashkenazi Jews than is innate genetic predisposition. Future case-control studies comparing this and other defined ethnic groups may be helpful in clarifying specific lifestyle risk factors.

Finally, cancer control planners should make colorectal cancer a clear priority when addressing communities with large populations of Ashkenazi Jews, since even those without any family history of cancer have been reported to be at least two to three times more likely than western populations to develop colorectal cancer. Early detection tests are proven to save lives. Ashkenazi Jews should be advised aggressively about screening options and primary prevention interventions for colorectal cancer, the disease that probably represents their community's greatest single overall risk from cancer.

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Washington Irving, American writer (1783-1859)