The changing epidemiology of upper gastrointestinal cancers in Israel: clinical and screening implications

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Western countries and now developing countries have noted a decreasing incidence of upper gastrointestinal (UGI) (esophageal and gastric) cancers, but increasing distal esophageal adenocarcinoma and a shift to fundal-sited gastric cancer. We examined these trends in Israeli Jewish and nonJewish populations, drawing conclusions on the need to promote prevention and/or screening. Israel Cancer Registry UGI cancer data were computed by ethnicity, immigration after 1990, sex, sites and histology, examining age-standardized rates (ASR)/10^5 for 2000–2005 and incidence trends during 1980–2005. In Jews, male esophageal cancer incidence has increased ($P<0.01$) and is highest in European-American-born males (ASR/10^5, 1.98), but decreasing in the upper two-thirds of esophagus so that in men 89% now occur in the lower one-third. In both sexes this was associated with decreasing squamous cell carcinoma ($P<0.01$) but increased adenocarcinoma to cause 72.6% of esophageal cancers in men. Gastric cancer incidence is highest in European-American-born males (ASR/10^5, 11.75); there is a decreasing incidence in both sexes ($P<0.01$) and gastric site trends are stable. In nonJews, esophageal cancer incidence is three times higher in men (ASR/10^5, 0.82); they are only squamous cell cancers and incidence trends are stable. Gastric cancer incidence is twice as high in men (ASR/10^5, 8.45) and gastric site trends are stable. UGI cancer incidence in Jews and nonJews, men and women, is low as compared with most developing countries. The important findings are the low but prominent incidence of distal esophageal and gastric adenocarcinoma in male immigrants. This requires attention to possible preventive measures in at-risk groups. *European Journal of Cancer Prevention* 18:191–198 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: adenocarcinoma of esophagus, cancer site, esophagus, immigrants, Israel, Jews, nonJews, stomach cancer, squamous cell esophageal cancer

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Introduction

Western countries and now developing countries, have noted a change in their upper gastrointestinal (UGI) cancer epidemiology. Namely, a decreasing incidence of esophageal and gastric cancers, but increasing esophageal adenocarcinoma, and also fundal rather than distal gastric cancer (Devesa *et al.*, 1998; Kamangar *et al.*, 2006; He *et al.*, 2008).

In Israel, approximately 633 new cases of gastric cancer and 100 esophageal cancers are being diagnosed annually; during the period 2000–2005 these UGI cancers, together, represented only 3.3% of all new cancer cases. In 2005, the prevalence of esophageal cancer was 164 Jewish and five nonJewish patients, whereas for gastric cancer there were 1511 Jewish and 128 nonJewish patients.

The aims of this study were to follow long-term UGI cancer incidence trends in Israeli Jews and nonJews by: continent of birth and date of immigration for immigrants, sex, anatomic site, and histology and to compare them with the international data (Israel National Cancer Registry). The goals were to evaluate clinical implications of the findings and to consider the need to address possible preventable and treatable risk factors.

Materials and methods

Cancer patients and data

This included all cancers that were diagnosed in Jews and nonJewish citizens (about 18.5% of the population) (Statistical Abstract of Israel, 2007) from 1980 to 2005. The data source is the Israel National Cancer Registry (INCR) and its description has been published in detail (Barchana *et al.*, 2004). In summary, the INCR is a population-based central tumor registry established in 1960 and since 1982 reporting to the registry is mandatory. All medical facilities, both public and private, and pathology laboratories that are diagnosing or treating cancer patients send a copy of their medical summary to the registry. The INCR also collects data on cancer deaths from District Health Authorities and the Central Population Registry (Israel National Cancer Registry).

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In Israel, everyone receives at birth, or immigrants upon getting citizenship, a personal identification number. This number identifies an individual in all his/her contacts with all organizations in the country, including the health system. All demographic data, including place of birth and immigration date, as well as residential and other personal data (including religion) are stored in the Central Population Registry. The INCR is linked to this registry and each cancer patient's personal data are then retrieved and validated. The last audit of data completeness concluded that registration was above 95% (Fishler *et al.*, 2003).

In the INCR, in addition to demographic data, all data available on cancers are registered including date of diagnosis and tumor location using the International Classification of Diseases, Oncology (ICD-O) version-3 codes (SEER Program, 1999).

Statistical methods

Age-standardized cancer incidence rates (ASR) were computed per 10^5 populations standardized to 'World Standard Population'. Rates were computed for UGI cancer in Jews and nonJews for each UGI site by sex and histology. Israeli population data, by age group, continent of birth for immigrant Jews and sex, were retrieved from the Central Bureau of Statistics (Statistical Abstract of Israel, 2007). Owing to small numbers, the Jewish patients were grouped as European–American or non-European born (the latter included Israel, Asia or Africa born). From 1990, there was a large immigration of Jews from the former Soviet Union, so we also analyzed the occurrence of UGI cancer in these immigrants.

For sites, we used ICD-O codes and analyzed separately and/or combined: esophageal cancer, upper two-thirds esophagus, lower one-third, lower one-third and gastroesophageal junction and cardia, gastroesophageal junction and cardia, esophageal squamous cell cancer, esophageal adenocarcinoma, all stomach, gastric body and antrum.

Trends were computed by joint point analysis. Tests of significance used confidence intervals of 95% and a significant result was when the *P* value was less than 0.05.

Results

Population studied

During the period studied there were 2382 patients with esophageal cancer; 2.8% occurred in nonJews. Patients with gastric cancer numbered 14 983 and 4.8% occurred in nonJews.

Incidence of upper gastrointestinal cancers during years 2000–2005 and trends 1980–2005, by ethnic group, sex, continent of birth, and date of immigration

Esophagus

In the period 2000–2005, the incidence in the Jewish male population was more than twice that occurring in women (Table 1). The incidence in male Jews of European–American origin, but not females, was significantly higher ($P < 0.01$) than in nonEuropean–American born males (Table 2).

During 1980–2005, the incidence trends were of a significant increase in men ($P < 0.01$) and decrease in women ($P = 0.05$) (Table 1, Fig. 1). This was true for

Table 1 Esophageal cancer; age-standardized incidence rates/10^5 for 5-year periods, 1980–2005, for all Jews, by sex and the changing RR of cancer site and histology, with time

	Site							Cancer histology		
	All esophagus	Upper 2/3	Lower 1/3	RR	Upper 2/3	Lower 1/3 + GE junction	RR	Squamous cell	Adenocarcinoma	RR
Period	ASR	ASR	ASR		ASR	ASR		ASR	ASR	
Males										
1980–1984	1.59	0.49	1.10	0.43	0.49	3.96	0.12	1.20	0.02	60.50
1985–1989	1.57	0.52	1.05	0.45	0.52	3.72	0.13	1.12	0.12	10.25
1990–1994	2.07	0.29	1.78	0.15	0.29	3.39	0.08	0.97	0.61	1.68
1995–1999	2.32	0.15	2.16	0.08	0.15	3.39	0.05	0.77	1.05	0.80
2000–2005	1.98	0.22	1.76	0.13	0.22	3.55	0.06	0.75	0.79	1.03
Rate ratio										
1980–1989 vs. 1995–2005	1.3	0.41	1.68		0.41	0.9		0.68	12.44	
P value	<0.01	<0.01	<0.01		<0.01	NS		<0.01	<0.01	
Females										
1980–1984	1.23	0.32	0.91	0.30	0.32	1.93	0.15	0.90	0.01	104.00
1985–1989	1.00	0.35	0.65	0.53	0.35	1.38	0.25	0.78	0.02	34.67
1990–1994	1.02	0.18	0.84	0.19	0.18	1.38	0.12	0.68	0.09	7.00
1995–1999	1.06	0.19	0.87	0.20	0.19	1.23	0.15	0.68	0.19	3.59
2000–2005	0.87	0.16	0.72	0.20	0.16	1.36	0.11	0.49	0.19	2.53
Rate ratio										
1980–1989 vs. 1995–2005	0.85	0.5	0.98		0.5	0.79		0.7	9.84	
P value	0.05	<0.01	NS		<0.01	<0.01		<0.01	<0.01	

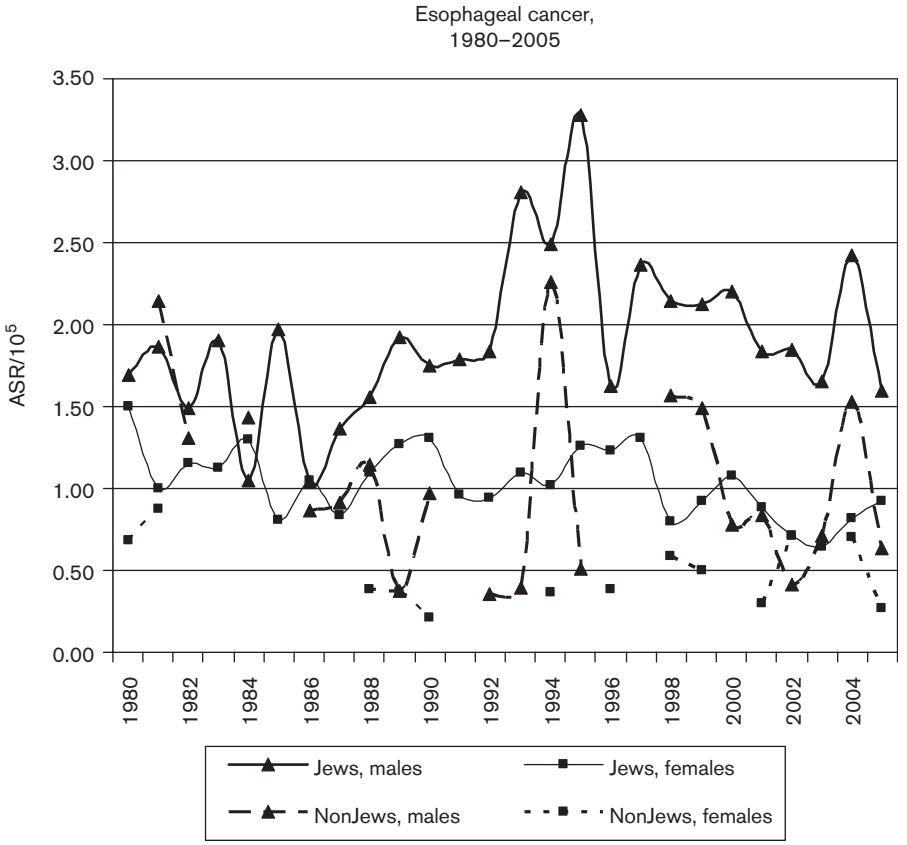
ASR, age-standardized cancer incidence rates; RR, rate ratio.

Table 2 Esophageal cancer by continent of birth: age-standardized incidence rates/10^5 for 5-year periods, 1980–2005, for all Jews by sex and the changing RR of cancer with time

	Males: ASR				Females: ASR			
Period	European born	NonEuropean born	RR	*P*	European born	NonEuropean born	RR	*P*
1980–1984	1.82	1.22	1.49	<0.01	1.05	1.58	0.71	<0.01
1985–1989	1.64	1.40	1.20	0.03	1.03	0.93	1.08	NS
1990–1994	2.20	1.85	1.27	<0.01	0.78	1.37	0.59	<0.01
1995–1999	2.47	1.99	1.32	<0.01	1.02	1.07	1.00	NS
2000–2005	1.95	1.78	1.26	<0.01	0.72	0.94	0.93	NS
Rate ratio								
1980–1989 vs. 1995–2005	1.23	1.39			0.83	0.80		
P	*P*<0.01	*P*<0.01			*P*<0.01	*P*<0.01		

ASR, age-standardized cancer incidence rates; RR, rate ratio.

Fig. 1

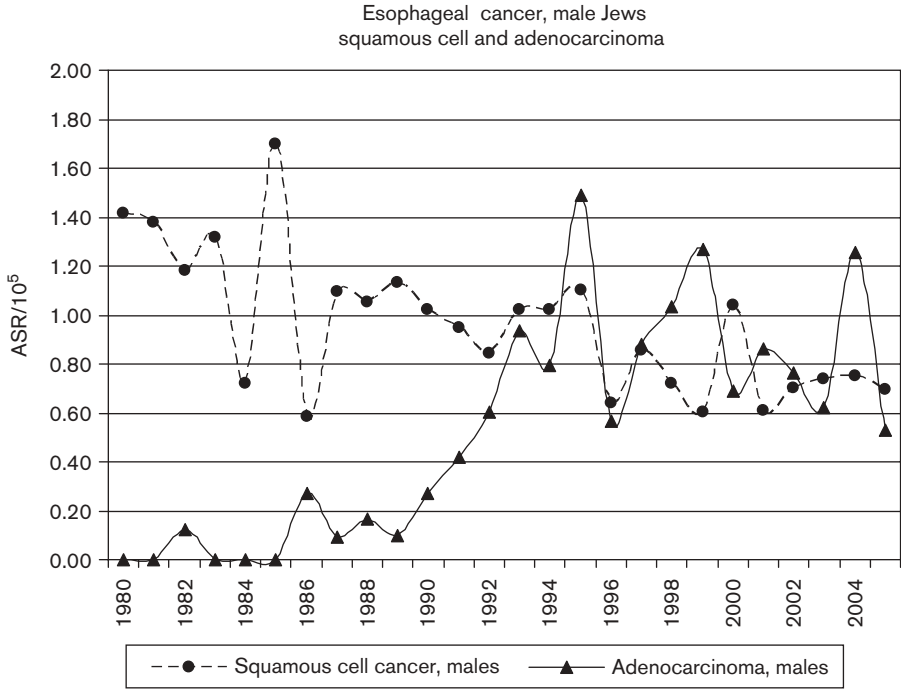


Incidence trends of esophageal cancer from 1980 to 2005 in male and female Jews and nonJews. Note the rising trends in Jewish men. ASR, age-standardized rates.

both European–American and nonEuropean–American-born males (Table 2). Conversely, in women the incidence and trends were similar in both European–American and nonEuropean–American born women and were significantly decreased ($P < 0.01$) (Table 2).

However, in both men and women during the last 15 years there had been a significant decrease in cancer of the upper two-thirds of the esophagus ($P < 0.01$) (Table 1). During this time, in men there was a significantly increased trend and shift in site so, that during the years 2000–2005, 89% of cancers occurred in the lower one-third of the esophagus ($P < 0.01$). In both men and women, this change was associated with decreased squamous cell carcinoma but increased adenocarcinoma ($P < 0.01$ for both) so that, during 2000–2005,

Fig. 2



Incidence trends of esophageal cancer by histology from 1980 to 2005 in male Jews. A decrease in squamous cell cancer and marked rise in adenocarcinoma in the last 15 years was observed ($P<0.01$ for both). ASR, age-standardized rates.

it was 39.5% of the esophageal cancers in men ($P = 0.04$), about four times that occurring in women (Table 1, Fig. 2). However, when also including the gastroesophageal junction and cardia in the analysis for adenocarcinoma it was 72.6% of the cancers occurring in this site in men (not shown) (Israel National Cancer Registry). It also became apparent that the trend for adenocarcinoma in the esophagus was almost unchanged during 1980–2005 (and this was despite a falling incidence at the gastroesophageal junction and cardia, not shown, $P < 0.01$) (Fig. 3). During the period 1995–2005, 24.1% of male adenocarcinoma occurred in recent immigrants, slightly more than expected.

During the period 2000–2005, the incidence in nonJews was almost four times higher in men (ASR/10^5, 0.82) than in women (ASR/10^5, 0.24), but lower than that in Jewish men and women of Asian or African origin (not shown) (Israel National Cancer Registry). The incidence trends in men and women during 1980–2005 were stable and they were only squamous cell cancers (not shown) (Fig. 1 (Israel National Cancer Registry).

Stomach

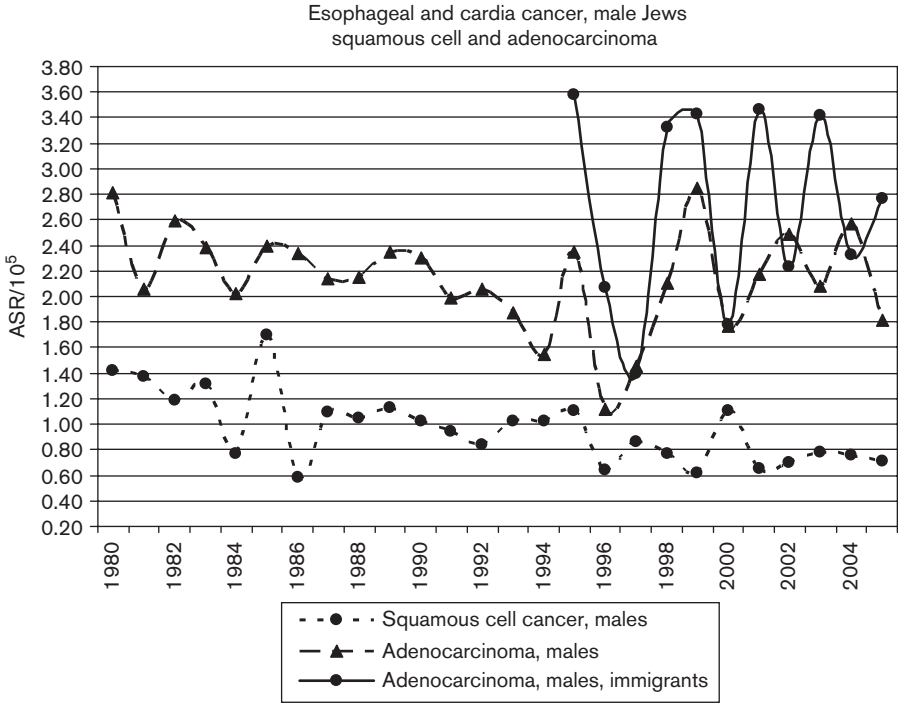
During 2000–2005, the incidence in the Jewish male population was almost twice that occurring in women (Table 3, Fig. 4). The incidence in both male and female Jews of European–American origin was significantly higher than that occurring in Jews of Asian or African origin or Israel born ($P < 0.01$) (Table 4).

During 1980–2005, the incidence was consistently higher (almost double) in male Jews and the trends were of a consistent significant decrease in both men and women ($P < 0.01$) (Table 3, Fig. 4). The incidence in male European–American-born Jews was consistently and significantly higher than in nonEuropean–American born. The trends were of a consistent decrease in both men and women of European–American and non-European–American birth ($P < 0.01$) (Table 4). During the period 1995–2005, 34% of male gastric cancer occurred in immigrants, which was more than expected (Fig. 5).

The decrease occurred in all gastric sites; esophagogastric junction and fundus, body, and antrum ($P < 0.01$ for all) (Table 3). During the period 2000–2005, cancer of the body and antrum in men represented 72.4% of the cases of gastric cancer (not shown) (Israel National Cancer Registry).

During the period 2000–2005, the incidence in nonJews was less than that occurring in the Jewish population. It was almost twice as high in men (ASR/10^5, 8.45) as in women (ASR/10^5, 4.59). The incidence trends during 1980–2005, in men and women, were stable (Fig. 4).

Fig. 3



Incidence trends of esophageal cancer by histology (also including the gastroesophageal junction and cardia) from 1980 to 2005 in male Jews. Note the decrease in squamous cell cancer ($P<0.01$) and markedly higher and increasing incidence of adenocarcinoma ($P<0.01$) because of the contribution of cancer occurring in immigrants. ASR, age-standardized rates.

Table 3 Gastric cancer: age-standardized incidence rates/10^5, for 5-year periods, 1980–2005, for all Jews, by sex and the changing RR of cancer site with time

	Site			
	All stomach	GE junction + fundus	Body + antrum	RR
Period	ASR	ASR	ASR	
Males				
1980–1984	15.97	3.03	12.94	0.24
1985–1989	14.73	2.92	11.82	0.25
1990–1994	13.97	1.86	12.12	0.15
1995–1999	13.13	1.38	11.75	0.12
2000–2005	11.75	1.92	9.82	0.20
Rate ratio				
1980–1989 vs. 1995–2005	0.80	0.58	0.85	
P value	<0.01	<0.01	<0.01	
Females				
1980–1984	8.91	1.08	7.83	0.14
1985–1989	7.38	0.80	6.58	0.13
1990–1994	7.55	0.65	6.90	0.09
1995–1999	6.97	0.46	6.51	0.07
2000–2005	6.68	0.71	5.97	0.12
Rate ratio				
1980–1989 vs. 1995–2005	0.83	0.61	0.87	
P value	<0.01	<0.01	<0.01	

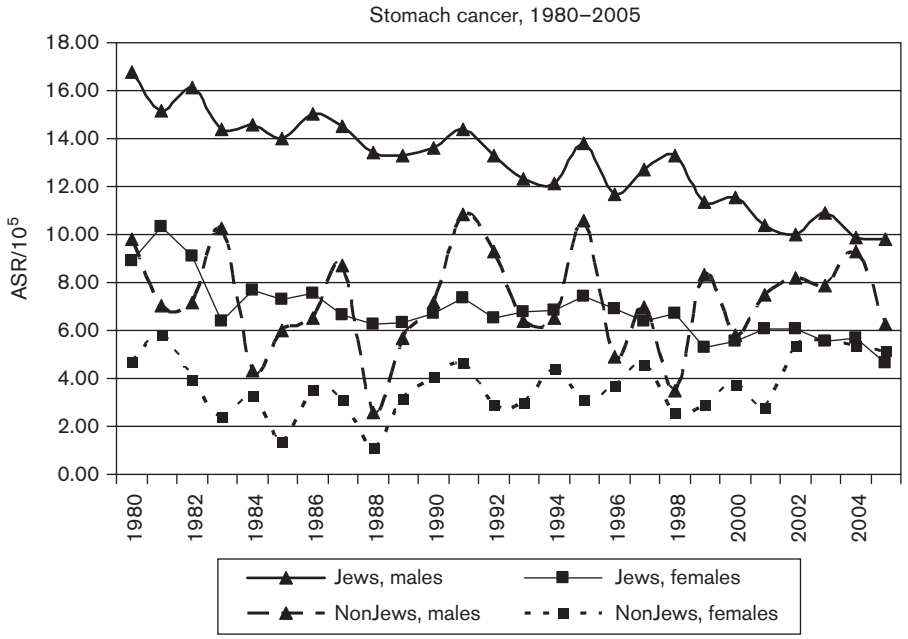
ASR, age-standardized cancer incidence rates; GE, gastroesophageal junction; RR, rate ratio.

Discussion

Both our Jewish and nonJewish populations have a low incidence of esophageal and gastric cancers as compared with rates reported in many 'more-developed or less-developed' countries (Kamangar *et al.*, 2006). The incidence of both malignancies is higher in Jews than in nonJews and in men of both ethnic groups, and is highest in European–American-born Jews and recent immigrants from the former Soviet Union. In the Jewish population, other than male esophageal cancer, there has been a continuous fall in the incidence of all UGI cancers, but what is now prominent is the significant decrease in esophageal squamous cell cancer and rise in distal esophageal adenocarcinoma in men, especially in recent European immigrants. Similarly, the incidence of male gastric cancer is twice as high in immigrants.

The temporal pattern of UGI cancer incidence trends in 'westernizing' countries is that of a decreasing incidence of esophageal squamous cell cancer and increasing adenocarcinoma of the distal esophagus. This has been associated with a decreasing incidence of gastric cancer and shift in cancer site from the distal to proximal stomach (Devesa *et al.*, 1998; Kamangar *et al.*, 2006). This was noted worldwide in diverse populations (Kamangar *et al.*, 2006; He *et al.*, 2008). In our Jewish population, over the last two decades we observed this pattern in the esophagus, but not in nonJews. In Jews the decreased incidence of stomach cancer has been gradual over the

Fig. 4



Incidence trends of gastric cancer from 1980 to 2005 in male and female Jews and nonJews. Note the higher incidence in Jews, decreasing with time, in both men ($P<0.01$) and women ($P<0.04$), more markedly in the former. Trends in nonJews are stable. ASR, age-standardized rates.

Table 4 Gastric cancer by continent of birth: age-standardized incidence rates/10^5 for 5-year periods, 1980–2005, for all Jews by sex and the changing RR of cancer with time

	Males: ASR				Females: ASR			
Period	European born	NonEuropean born	RR	*P*	European born	NonEuropean born	RR	*P*
1980–1984	17.80	12.66	1.50	<0.01	9.75	7.69	1.26	<0.01
1985–1989	16.97	11.92	1.45	<0.01	7.97	6.68	1.14	<0.01
1990–1994	16.83	10.26	1.65	<0.01	8.30	6.51	1.29	<0.01
1995–1999	16.77	9.19	1.81	<0.01	8.41	5.22	1.57	<0.01
2000–2005	13.47	9.67	1.35	<0.01	7.12	5.56	1.33	<0.01
Rate ratio								
1980–1989 vs. 1995–2005	0.83	0.77			0.86	0.75		
P	*P*<0.01	*P*<0.01			*P*<0.01	*P*<0.01		

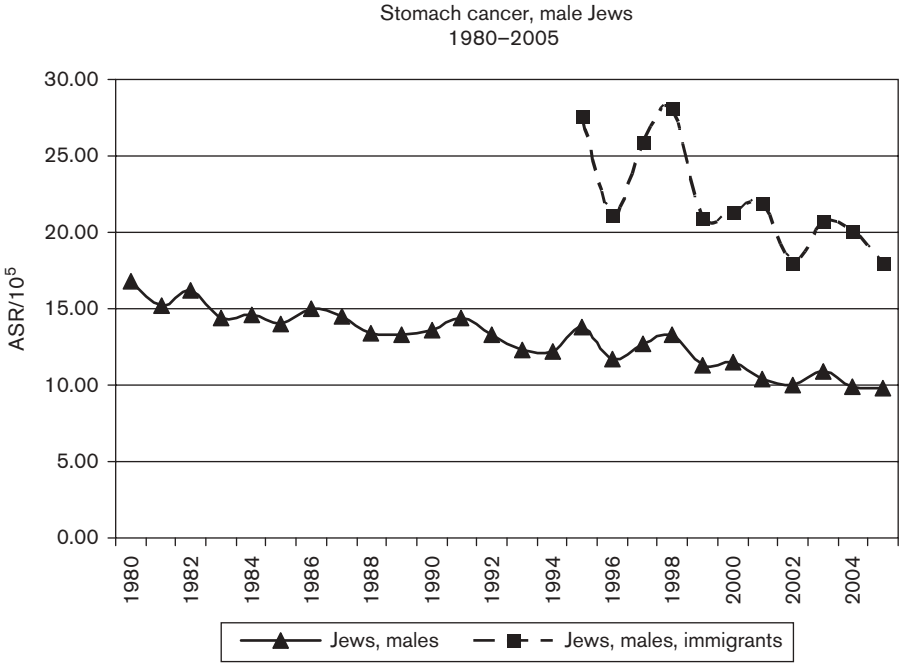
ASR, age-standardized cancer incidence rates; RR, rate ratio.

years of data collection and includes all sites, while remaining low and stable in nonJews.

The recently published Middle East Consortium data provided comparative information on UGI cancer in the USA, Israel and neighboring countries. The US SEER male world age-standardized incidence rates/10^5 for esophageal cancer in 1999–2001, were $5.1/10^5$, twice that of Israeli Jews and even more as compared with those reported in Israeli nonJews (Ergör, 2006b). The rates in females were only slightly higher. The incidence in male Jews is about double that reported from adjacent countries such as Cyprus, Egypt, or Jordan. These differences were attributed, in part, to differences in alcohol drinking (Ergör, 2006b).

During the last half decade, together with the increase in esophageal adenocarcinoma in Israeli men, there was a shift in site with 89% of cancers occurring in the lower one-third of the esophagus. This was even more than the 58.2% reported during 1999–2001 in the US SEER data (Ergör, 2006b). In the United States, adenocarcinoma is the most common histology, 57.1% in men, whereas squamous cell carcinoma is still the predominant histology in US women, Israeli Jewish women and even more so in the other Middle Eastern populations including Israeli nonJews (Ergör, 2006b). As we have shown, this has recently changed in Israeli men, with squamous cell carcinoma decreasing and adenocarcinoma becoming the predominant histological type when the gastroesophageal junction and cardia are also included in

Fig. 5



Incidence trends of gastric cancer from 1980 to 2005 in male Jews. Note the decreasing trend ($P<0.01$) and markedly higher (double) and also decreasing incidence occurring in recent immigrants. ASR, age-standardized rates.

the analysis. We did this because the anatomic classification is dependent on the clinical information provided. The possibility that the sharp rise in adenocarcinoma was because of a change in diagnosis and/or registration has been evaluated in the US (Pohl and Welch, 2005). Over the years there have been changes in diagnostic methodologies, improvements in endoscopes, and recognition of anatomic landmarks. The endoscopic identification and classification of the gastroesophageal junction was made clearer and previous registration of adenocarcinoma in this area as being always of gastric origin was reassessed in the US (Pohl and Welch, 2005).

During this period, the INCR staff had not made changes in coding esophageal site or histology. These above issues, however, may have played a role in the marked changes seen in Israeli data from 1990. This period corresponds to the ever-increasing availability of flexible UGI endoscopy. Therefore, when including cancers of the gastroesophageal junction and cardia in the analysis, the adenocarcinoma incidence trends seem relatively high and stable. Even so, both in Israeli Jewish men and women there has been a fall in the incidence of adenocarcinoma in the gastroesophageal junction and cardia and therefore we cannot explain these findings. In addition, the similar changes seen in Jewish females and lack of similar changes in nonJewish data make it most likely that this is a true observation.

The incidence of gastric cancer in Israeli Jews is not high on a world scale, but is higher than the World Standardized US SEER data 1999–2001 of $7.4/10^5$ in men and $3.6/10^5$ in women. It is also higher than the Israeli nonJewish population and that reported from other adjacent countries (Ergör, 2006a). We did not find the proximal cancer shift described to occur in other nonMediterranean populations (Ergör, 2006a; Ji *et al.*, 1997; Devesa *et al.*, 1998).

Known preventable risk factors for esophageal cancer include chronic alcohol intake, tobacco smoking, nutritional deficiencies, dietary nitrates, and obesity (assumed to lead to chronic reflux, Barrett's esophagus and dysplasia) (Ji *et al.*, 1997; van Soest *et al.*, 2005; Cook *et al.*, 2007; Rastogi *et al.*, 2008). Chronic alcohol intake has not been an issue in our Jewish populations and especially Moslem populations, nor is a nutritional deficiency. However, tobacco smoking is common and there is a clinical impression that obesity is becoming so. This was confirmed by a limited survey of obesity (body mass index ≥ 30.0) in Jewish and Arab men and women in 1999–2000 (Keinan-Boker *et al.*, 2005). Arab men smoke more tobacco than Jewish men; diabetes and obesity are more common than in Jews, myocardial infarction is almost twice as common. Obesity was recorded in 19.4% of Arab men and 21.4% of Jewish men. Arab women were more likely to be obese (33.2%)

than Jewish women (23.6%) (Keinan-Boker *et al.*, 2005; Tarabeia, 2006; Statistical Abstract of Israel, 2007). These are all risk factors associated with westernized lifestyle. Even so, esophageal cancer and esophageal adenocarcinoma are uncommon in the nonJewish population and rarer in Jewish women than in men.

However, distal esophageal adenocarcinoma has become predominant in the Israeli men and this is assumed to be a result of obesity, tobacco smoking, and chronic reflux. We have no information on the epidemiology of Barrett's esophagus in the Israeli population. Therefore, we do not have supporting evidence to explain the occurrence of adenocarcinoma in men. The only information on risk factors that might explain the high incidence occurring in recent immigrants from the former Soviet Union is that they had the highest prevalence of overweight and obesity (Keinan-Boker *et al.*, 2005). These perturbations of lifestyle are also risk factors for the metabolic syndrome, especially cardiovascular disease and this is another reason for the promotion of preventive treatment (Cook *et al.*, 2007).

A high prevalence of *Helicobacter pylori* infection is an important risk factor for gastric cancer. There are no definitive population surveys in the Mediterranean populations. However, the prevalence in selected Jewish groups ranges from 54 to 38% in young males of nonEuropean and European origin, respectively, to 72% in kibbutz members (having a high health standard) (Gilboa *et al.*, 1995; Gdalevich *et al.*, 2000; Kelley and Duggan, 2003; Ergör, 2006a). No definitive information is available from our nonJewish population or recent immigrants. This risk factor is offset by the high intake of protective fruits and vegetables that is typical of the diet in Mediterranean countries. The higher incidence of gastric cancer seen initially in Israeli Jews of European origin and recent immigrants could reflect their earlier dietary habits which were not typically rich in fresh fruits and vegetables (Ergör, 2006a).

What we do need is more systematic information on the prevalence of obesity, Barrett's esophagus, and *H. pylori* infection in our populations. In conclusion, although UGI cancer is not common in the Israeli population and other than male esophageal cancer, seems to be decreasing and, or, at a low plateau level, distal esophageal adenocarcinoma has now become predominant. Immigrants from the former Soviet Union are a high-risk group and should receive specific attention. A healthy lifestyle, namely avoiding alcohol, tobacco smoking and obesity, diagnosing and treating *H. pylori* and having a Mediterranean-type diet could be both cancer and cardiovascular disease preventive.

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References

Barchana M, Liphshitz I, Rozen P (2004). Trends in colorectal cancer incidence and mortality in the Israeli Jewish ethnic populations. *Fam Cancer* **3**:207–214.

Cook MB, Wild CP, Everett SM, Hardie LJ, Bani-Hani KE, Martin IG, Forman D (2007). Risk of mortality and cancer incidence in Barrett's esophagus. *Cancer Epidemiol Biomarkers Prev* **16**:2090–2096.

Devesa SS, Blot WJ, Fraumeni JF Jr (1998). Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer* **83**:2049–2053.

Ergör G (2006a). Stomach cancer. In: Freedman LS, Edwards BK, Reis LAG, Young JL, editors. *Cancer incidence in four member countries (Cyprus, Egypt, Israel and Jordan) of the Middle East Cancer Consortium (MECC) compared with US SEER; National Cancer Institute*. Bethesda, MD: NIH Pub. No. 06-5873. pp. 35–39.

Ergör G (2006b). Esophageal cancer. In: Freedman LS, Edwards BK, Reis LAG, Young JL, editors. *Cancer incidence in four member countries (Cyprus, Egypt, Israel and Jordan) of the Middle East Cancer Consortium (MECC) compared with US SEER; National Cancer Institute*. Bethesda, MD: NIH Pub. No. 06-5873. pp. 29–33.

Fishler Y, Chitrit A, Barchana M, Modan B (2003). *Examination of Israel national cancer data accumulation completeness for 1991*. Tel Hashomer, Israel: The National Center for Disease Control, Publication No. 230. (in Hebrew)

Gdalevich M, Cohen D, Ashkenazi I, Mimouni D, Shpilberg O, Kark JD (2000). Helicobacter pylori infection and subsequent peptic duodenal disease among young adults. *Int J Epidemiol* **29**:592–595.

Gilboa S, Gabay G, Zamir D, Zeev A, Novis B (1995). Helicobacter pylori infection in rural settlements (Kibbutzim) in Israel. *Int J Epidemiol* **24**:232–237.

He Y-T, Hou J, Chen Z-F, Qiao C-Y, Song G-H, Meng F-S, *et al.* (2008). Trends in incidence of esophageal and gastric cardia cancer in high-risk areas in China. *Eur J Cancer Prev* **17**:71–76.

Israel National Cancer Registry: (www.health.gov.il/icr) accessed 2008.

Ji B-T, Chow W-H, Yang G, McLaughlin JK, Gao R-N, Zheng W, *et al.* (1997). Body mass index and the risk of cancers of the gastric cardia and distal stomach in Shanghai, China. *Cancer Epidemiol Biomarkers Prev* **6**:481–485.

Kamangar F, Dores GM, Anderson WF (2006). Patterns of cancer incidence, mortality, and prevalence across five continents: Defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol* **24**:2137–2150.

Keinan-Boker L, Noyman N, Chinich A, Green MS, Nitzan Kaluski D (2005). Overweight and obesity prevalence in Israel: Findings of the First National Health and Nutrition Survey (MABAT). *Isr Med Assoc J* **7**:219–223.

Kelley JR, Duggan JM (2003). Gastric cancer epidemiology and risk factors. *J Clin Epidemiol* **56**:1–9.

Pohl H, Welch HG (2005). The role of over diagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. *J Natl Cancer Institute* **97**:142–146.

Rastogi A, Puli S, El-Serag HB, Bansal A, Wani S, Sharma P (2008). Incidence of esophageal adenocarcinoma in patients with Barrett's esophagus and high-grade dysplasia: a meta-analysis. *Gastrointest Endosc* **67**:394–398.

SEER Program. National Cancer Institute (1999). *Self-instructional manual for cancer registrars*. 3rd ed. USA: National Institutes of Health.

Statistical Abstract of Israel (2007). Number 58, Central Bureau of Statistics Publication. Government Press, Jerusalem. (*www1.cbs.gov.il/reader/shnatonenewsite.htm*).

Tarabeia J (2006). *Health status of the Arab population in Israel*. Israel: Center for Disease Control, Ministry of Health Publication No. 247.

Van Soest EM, Dieleman JP, Siersema PD, Sturkenboom MCJM, Kuipers EJ (2005). Increasing incidence of Barrett's oesophagus in the general population. *Gut* **54**:1062–1066.