ORIGINAL ARTICLE

Received: May 2014
Accepted: August 2014

Cancer Incidence Rates among Iranian immigrants in Sweden, a Population-Based Retrospective Cohort Study

Omid Beiki[1,2,†], Kazem Zendehdel[3,4,*,†], Shahram Bahmanyar[5,6]
Mohammad Ali Mohagheghi[3], Par Sparen[4], Alireza Mousavi Jarrahi[3,7]
Sara Keshtkari[3], Azin Nahvijou[3], Zahra Sedighi[3], Leila Shademan[3]
Olof Nyren[4], Tahereh Moradi[8]

ABSTRACT

Introduction: Migrant studies may provide valuable clues to the etiology of chronic diseases such as cancer. We conducted a migrant study to examine cancer incidence among Iranian immigrants in Sweden.

Methods: A cohort of Iranian immigrants in Sweden in 1960-2004 was followed through record linkages with Swedish registers of cancer, death, and migration. We compared Age-Standardized Incidence Rates (ASRs) with corresponding ASRs in Tehran and Sweden and estimated Standard Rate Ratios with 95% confidence intervals (CI). In addition, ASRs were stratified by follow-up time.

Results: In total 1,041 cancers occurred among 60,718 Iranian immigrants. The ASRs for all cancers combined were 182.3 and 175.5 per 100,000 person-years among men and women, respectively. For men, this rate was slightly and non-significantly higher than in Iran, while for women the excess (24%) was statistically significant. However, their ASRs were significantly lower than those for native Swedes: men had 37% (95% CI 27-47%) and women 35% (95% CI 33-37%) lower ASRs. Compared to male Iranians living in Tehran, ASRs of esophageal and gastric cancer were lower while ASRs of colorectal and prostate cancer were higher, and both of the latter increased with time since immigration. In women, the ASR of non-melanoma skin cancer was lower and that of breast cancer higher and increasing.

Conclusion: In male first-generation immigrants, incidence rates of esophageal, gastric, colorectal, and prostate cancer change in the direction of prevailing rates in Sweden, likely due to changes in exposure to environmental risk factors. A similar adjustment occurs for breast and non-melanoma skin cancer among female immigrants.

Keywords: Cancer, Immigrants, Sweden, Register-based study, Iran.

1. Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
2. Kermanshah University of Medical Sciences, Kermanshah, Iran.
3. Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran.
4. Department of Medical Epidemiology and Biostatistics (MEB), Karolinska Institutet, Stockholm, Sweden.
5. Unite of Clinical Epidemiology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden.
6. Department of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
7. Faculty of Social Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
8. Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden.
† Kazem Zendehdel and Omid Beiki contributed equally to this work

***Corresponding Author:**
Kazem Zendehdel
Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences End Keshavarz Boulevard, Tehran, 1419733141, Iran.
Email: Kzendeh@tums.ac.ir

BCCR
2014; 6(4): 2-13
www.bccrjournal.com

Introduction

Migrant studies offer an opportunity to study changes in disease occurrence among people who move between areas with different patterns of disease incidence and risk factor profile. Through such studies our understanding of cancer etiology and potentials for cancer control may be broadened.[1-2] The information may provide clues to the nature and timing of factor(s) that determine the differences in risks, and hence to the etiology of the disease. Little change in risk is expected by changing the environment if risk is predominantly determined by genetic factors. If an excess is caused mainly by early stage environmental carcinogens, a gradual change will be observed in the adopted country, but less so among first-generation immigrants, particularly those who immigrate as older adults. However, if the etiologic factors are mainly late stage carcinogens, a more rapid change in incidence is anticipated already in the first-generation immigrants.

Sweden has assimilated more than 1.2 million immigrants from the entire world in the last decades. Iranians, adding up to more than 57,000 (5% of all immigrants), constitute one of the largest groups of non-European immigrants living in Sweden.[3] The efficient and complete population administration and cancer registration in Sweden provides an almost unique opportunity to perform a valid migrant study of Iranians, coming from an area with a distinctive pattern of cancer incidence. For instance, while stomach cancer is the most common cancer among Iranian men,[4] it ranks number 11 in Sweden, where the highest incidence rate is reported for prostate cancer.[5]

In this cohort study we explored the possible changes in incidence of site-specific cancers in Iranian who immigrated to Sweden between 1960 and 2004. Further we examined the speed of changes in cancer incidence since immigration as well as the influence of the age at migration on the risk. Finally, we compared the rates among Iranian immigrants in Sweden with native Swedes and with the rates in Iran.

Material and Methods

This study was approved by the Regional Ethics Committee at Karolinska Institutet in Sweden and the Regional Ethics Committee at Tehran University of Medical Sciences in Iran.

Cohort and follow-up

We defined cohort of Iranian immigrants who settled in Sweden between 1960 and 2004 based on information from the total Swedish population register. A unique 10-digits personal identification number is assigned to every Swedish resident. This personal identification number was used for record linkages to the Swedish cancer, death, and migration registers. The cohort members were followed from the date of first registration in the Swedish population register until cancer, death, emigration out from Sweden, or December 31st, 2004, whichever occurred first. Those who re-immigrated into Sweden were not included in the cohort for the second time.

Cancers have been coded according to the seventh revision of the International Classification of Diseases (ICD-7) in the Swedish Cancer Register which is 96-98% complete.[6-7] We counted primary, secondary and multiple tumors in this study. However, as recommended by International Agency for Research on Cancer (IARC), only the first records of cancer were used for patients with Leukemia, Lymphoma, and Kaposi Sarcoma to estimate Age Standardized Incidence Rate (ASR).[8] We excluded cancers found incidentally at autopsy.

In order to compare with incidence rates in Iran, we used data from Tehran Cancer Registry (TCR). Cancer registration in Iran is in its infancy and the validity and completeness of TCR is not fully known. Therefore, we conducted a validation study to address this issue and make appropriate inference from our comparison.

Tehran Cancer Register (TCR)

Approximately eight million inhabitants, corresponding to more than 10% of the country's population and representing all ethnicities, are living in the greater city of Tehran. Trained registrars from TCR actively travel and abstract cancer data from hospitals, pathology laboratories, and radiotherapy centers in the Tehran metropolitan area. In addition, data from death certificates with cancer coded as the underlying or contributory cause of death are obtained from the central office of the city cemetery (Behesht-Zahra). The first report of TCR, estimating cancer incidence in Tehran based on data collected in 1998-

2001, was published recently.[4] Due to a continuous influx of all ethnic and socio-cultural groups from the entire country, Tehran resembles a cross-section of the total Iranian population and estimates for cancer incidence in Tehran could be viewed as a proper approximation of the average rate for the entire Iranian population. The proportion of cases ascertained only through death certificates (death certificate only cases – DCO%), is an indicator for the completeness of a cancer registry.[8] Overall, 24.2 percent DCO% was reported by the Tehran Cancer Register. The highest DCO% was observed for highly fatal cancers including pancreas (51%), trachea and lung (45.5%), and stomach (36.8%). We included DCO cases in the estimation of incidence rates in TCR.

In contrast to Swedish Cancer Register, TCR is in the early stage and the validity and completeness of this data is not fully known. Therefore, we conducted a validation study to address this issue and make appropriate inference from our comparison. In this validation survey, we re-abstracted cancer data for two specified months of the year 2001 and compared the yield with the routinely collected data in the TCR. We estimated the total number of cancer cases using capture-recapture methodology.[8]

Statistical analyses

In order to compare incidence rates of cancer among Iranian immigrants in Sweden with those in Tehran and Sweden, we age-standardized the rates (ASRs) using standard world population. We used the methods suggested by Armitage and Berry (1987) to compute standard errors of ASRs.[9] Because the number of cancer cases among Iranian immigrants in Sweden was limited, we present ASRs for all cancer sites combined and results for site-specific cancers only if at least five cancers had been observed. Corresponding ASRs were estimated for the Tehrani and native Swedish populations. We used Standard Rate Ratios (SRRs) to compare the standardized incidence rates and the method proposed by Boyle and Parkin[9] was used to compute 95% confidence intervals for these ratios and corresponding 95% confidence intervals.

We performed stratified analyses by follow-up time (10 year strata) and age at immigration (20-40 and >40 years). The number of events was too small to allow meaningful estimations of incidence rates among those who immigrated when they were younger than 20 years old.

About 90 percent of the Iranian immigrants arrived in Sweden after 1985. Therefore, we restricted the analyses to 1985 through 2004 when we compared incidence rates in immigrants and the native Swedish population. Cancer incidence in TCR was based on data from 1997 through 2001. All the Swedish Cancer register data from 1960 through 2004 were used when we studied the incidence among immigrants by follow-up time and age at migration.

Results

In total, 60,718 Iranian immigrants were registered in 1960 through 2004; 51% of them arrived between 1985 and 1989. Average age at immigration was 26 years and average duration of follow-up 14 years (**Table 1**).

Male Iranian immigrants compared to men in Tehran

ASR of total cancer (all types combined) among male Iranian immigrants was 182.3 per 100,000 person-years. This represented a statistically non-significant 12 percent excess compared to the rate among men living in Tehran (SRR=1.12, 95% CI 0.90-1.39) (**Table 2**). While prostate was the most common cancer site in male Iranian immigrants in Sweden (ASR=38.6 per 100,000 person-years) and native Swedish men (ASR=77.6 per 100,000 person-years), stomach was the most common site in Tehrani men (ASR=19.7 per 100,000 person-years) (**Table 2**). The excess of prostate cancer among male Iranian immigrants, compared to their peers living in Tehran, was 2.6-fold (95% CI of SRR 1.3-5.2). We also found a more than 2-fold increase in ASRs of colorectal cancer (SRR=2.2, 95% CI 1.0-4.9). On the other hand, SRRs for stomach and esophageal cancer were 0.3 (95% CI 0.2-0.5) and 0.4 (95% CI 0.1-0.9), respectively.

Male Iranian immigrants compared to native Swedish men

ASR of any cancer (regardless of site and type) among male immigrants was 38 percent lower than that in the Swedish male population (SRR=0.62, 95% CI 0.53-0.73). The immigrants had significantly lower ASRs for trachea and lung (SRR=0.5, 95% CI 0.3-0.9), prostate (SRR=0.5;

Table 1. Descriptive statistics for Iranian men and women who immigrants to Sweden from 1960 through 2004.			
	Women	**Men**	**Overall**
Number of Iranian immigrants in Sweden (%)	27603 (45.5)	33115 (54.5)	60718
Total number of cancer	556	491	1047
Year of immigration (%)			
<1985	14.3	7.5	11.2
1985 - 1989	54.1	47.0	50.9
1990 - 1994	21.1	26.4	23.5
>=1995 - 2000	10.6	18.2	8.5
Age at migration (year) (%)			
<20	29.7	30.5	30.1
20 - 39	57.7	52.2	55.2
40 - 59	9.7	11.4	10.5
>=60	2.9	5.9	4.2
Average age at migration (year) (+-SD)	25.3 (14.2)	26.9 (16.7)	26.0 (15.5)
Mean age at cancer diagnosis (year) (+-SD)	58.9 (16.9)	57.7 (15.8)	58.2 (16.4)
Total person time (year)	365281	483456	848737
Mean follow - up time (year) (+-SD)	13 (7)	15 (6)	14 (6)
SD: Standard deviation			

95% CI 0.4-0.7), and testicular (SRR=0.3; 95% CI 0.1-0.5) cancers and borderline significant lower rate for non-melanoma skin cancer (SRR=0.5; 95% CI 0.2-1.0).

Female Iranian immigrants compared to women in Tehran

ASR of total cancer was 24 percent higher among female Iranian immigrants than among Tehrani women (SRR=1.24, 95% CI 1.01-1.54). Breast cancer was the most common cancer in both groups, but the ASR was 90 percent higher (SSR=1.9, 95% CI 1.3-2.8) among the immigrants than among Tehrani women (ASR among the former 60.7 vs. 31.5 per 100,000 person-years among the latter), (**Table 3**). On the other hand, ASR of stomach cancer (4.7 per 100,000 person-years) among immigrant women was only half of the ASR among Tehrani women (10 per 100,000 person-years), albeit SRR was no more than borderline significant (SRR=0.5; 95% CI 0.2-1.0).

Female Iranian immigrants compared to native Swedish women

Although higher than in the country of origin, ASR of total cancer among female immigrants was 35 percent lower than the corresponding ASR among Swedish women (SSR=0.65, 95% CI 0.56-0.75). ASR of breast cancer did not quite reach the rate among native Swedish women (SRR=0.7, 95% CI 0.6-0.9), but ASRs of stomach cancer were similar. The immigrants had significantly lower rates of colorectal (SRR=0.5), pancreatic (SRR=0.4), trachea and lung (SRR=0.4), non-melanoma skin (SRR=0.2), breast (SRR=0.7), corpus uteri (SRR=0.4), and ovarian (SRR=0.5) cancers. In addition, there was a deficit of cervical cancer that was statistically borderline significant (SRR=0.4, 95% CI 0.2-1.0).

Table 2. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years among male Iranian immigrants in Sweden (1985-2004) in comparison with Tehrani and Swedish male population using Standard Rate Ratio (SRR).

ICD7	Site	Iranian Immigrants	
		n	ASR1 (SE)
140-144	Oral cavity	7	2,6 (1,10)
150	Esophagus	6	2,4 (1,0)
151	Stomach	14	5,6 (1,72)
153-4	Colon and rectum	60	24,2 (3,5)
155-6	Liver and gall bladder	6	3,3 (1,4)
162-163	Trachea/bronchus/lung	24	11,8 (2,6)
196	Bone	8	2,0 (0,9)
191	Non-melanoma of skin	18	7,9 (2,1)
177	Prostate	76	39,6 (4,7)
178	Testis	11	1,5 (0,5)
180	Kidney	17	5,2 (1,5)
181	Bladder and urinary tract	54	20,3 (3,2)
193	Brain	41	9,1 (1,8)
194	Thyroid	13	3,9 (1,4)
201	Hodgkin's lymphoma	15	3,2 (1,0)
200-202	Non-Hodgkin's lymphoma	34	10,6 (2,2)
203	Multiple Myeloma	6	2,3 (1,1)
204-207, 209	Leukemia	26	10,4 (2,3)
140-209 (not 191)	All sites excluding 191	473	174,2 (9,3)
140-209	All sites	491	182,1 (9,5)

Importance of time since arrival and age at arrival among male Iranian immigrants

Analysis by follow-up time revealed that ASR of all cancer combined among male immigrants increased from 159.9 per 100,000 person-years in the first 10 years to 205 per 100,000 person-years ten years or more after immigration (SRR=1.28, 95% CI 0.85-1.91) (**Table 4**). Site-specific data were generally too sparse for meaningful statistical analyses, but ASR of stomach cancer decreased by 30 percent across these follow-up periods, and there were trends for increases in colorectal (from 14.6 to 34.3 per 100,000 person-years) and prostate cancer (from 25.8 to 53.7 per 100,000 person-years). Although statistically non-significant, there was a strong trend for decreasing incidence of stomach cancer with increasing age at arrival (SRR=0.3, among male immigrated at age 20-39 years relative to those who immigrated at age more than 40 years), while likewise non-significant trends for increasing rates with increasing age at arrival were observed for cancer of trachea and lung (SRR=4.4), non-melanoma skin (SRR=13.5), and thyroid (SRR=2.4) (**Table 4**).

Importance of time since arrival and age at arrival among female Iranian immigrants

ASR of all cancer combined among female immigrants were not modified by time (Table 5). In site specific cancers, we found that stomach (SRR=0.6 after more than 10 years in Sweden, relative to less than 10 years), thyroid (SRR=0.4), and brain (SRR=0.7) showed trends towards lower ASRs with increasing duration of stay, as did non-Hodgkin lymphoma (SRR=0.6), but most of other cancers exhibited trends in the opposite direc-

Continue Table 2. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years among male Iranian immigrants in Sweden (1985-2004) in comparison with Tehrani and Swedish male population using Standard Rate Ratio (SRR).

ICD7	Site	Tehran			Sweden		
		n	ASR2 (SE)	SRR ASR1/ASR2	n	ASR3 (SE)	SRR ASR1/ASR3
140-144	Oral cavity	299	2,4 (0,17)	1.1 (0.2-5.6)	4371	4,8 (0,08)	0.5 (0.2-1.8)
150	Esophagus	729	6,8 (0,24)	0.4 (0.1-0.9)	3265	3,4 (0,06)	0.7 (0.2-2.7)
151	Stomach	2119	19,7 (0,45)	0.3 (0.2-0.5)	9567	9,1 (0,10)	0.6 (0.2-1.5)
153-4	Colon and rectum	1258	11,0 (0,32)	2.2 (1.0-4.9)	33021	32,5 (0,19)	0.7 (0.5-1.2)
155-6	Liver and gall bladder	538	5,0 (0,22)	0.7 (0.2-2.5)	6473	6,4 (0,09)	0.5 (0.2-1.6)
162-163	Trachea/bronchus/lung	1644	15,2 (0,37)	0.8 (0.4-1.6)	22976	23,9 (0,16)	0.5 (0.3-0.9)
196	Bone	364	2,5 (0,10)	0.8 (0.2-3.8)	498	0,9 (0,04)	2.2 (0.2-27.4)
191	Non-melanoma of skin	1138	10,4 (0,32)	0.8 (0.3-1.9)	18356	15,9 (0,13)	0.5 (0.2-1.0)
177	Prostate	1570	15,5 (0,39)	2.6 (1.3-5.2)	82814	77,6 (0,29)	0.5 (0.4-0.7)
178	Testis	284	1,8 (0,10)	0.8 (0.2-2.8)	2874	5,3 (0,10)	0.3 (0.1-0.5)
180	Kidney	347	3,1 (0,17)	1.7 (0.4-7.0)	8140	9,0 (0,10)	0.6 (0.3-1.3)
181	Bladder and urinary tract	1423	13,3 (0,36)	1.5 (0.7-3.2)	19757	19,5 (0,15)	1.0 (0.6-1.9)
193	Brain	807	5,9 (0,22)	1.5 (0.6-3.9)	7556	11,3 (0,14)	0.8 (0.4-1.6)
194	Thyroid	134	1,0 (0,10)	3.9 (0.3-50.0)	1071	1,4 (0,05)	2.8 (0.4-25.3)
201	Hodgkin's lymphoma	312	2,1 (0,10)	1.5 (0.3-6.6)	1255	2,1 (0,06)	1.5 (0.3-6.7)
200-202	Non-Hodgkin's lymphoma	900	7,1 (0,24)	1.5 (0.6-3.9)	9701	11,1 (1,20)	1.0 (0.4-2.3)
203	Multiple Myeloma	191	1,7 (0,14)	1.3 (0.2-11.4)	3898	3,9 (0,07)	0.6 (0.1-2.4)
204-207, 209	Leukemia	1098	8,5 (0,26)	1.2 (0.5-3.1)	7652	9,4 (1,20)	1.1 (0.4-3.0)
140-209 (not 191)	All sites excluding 191	17407	152,6 (1,10)	1.14 (0.91-1.41)	263543	275,6 (0,50)	0.63 (0.53-0.74)
140-209	All sites	18545	163,0 (1,10)	1.12 (0.90-1.39)	281899	291,5 (0,60)	0.62 (0.53-0.73)

tion, notably breast cancer (SRR=1.2, 95% CI 0.7-2.3). Female immigrants who arrived at age 40 years or later had lower ASRs for breast (SRR=0.4), ovary (SRR=0.7), and thyroid (SRR=0.8) cancer compared to women who immigrated at younger ages, but had higher ASRs for the rest of selected cancers. Due to small number of events, observed relative differences were not statistically significant.

Noteworthy, ASRs of leukemia remained stable by follow-up time among both male and female Iranian immigrants in Sweden (**Table 4**, and **Table 5**).

Validation study

We abstracted 3,154 cancer cases in the validation study. Linkage of these data with TCR revealed that while 1,045 cancer cases (24.9%) were apparent only in the TCR, 2,645 (63%) cases were abstracted both in the survey and the TCR, and 509 (12.1%) of the cases were abstracted only by the survey (new cases). Using capture-recapture methods, we found that 15% of the cases were not abstracted from the pathology centers and TCR faces 15% under-reporting of the cases diagnosed in pathology centers.

Discussion

In this study we observed higher incidence rates for all cancer combined among more than 60,000 Iranian immigrants in Sweden compared to Iranian residents living in the capital city of Tehran, but lower rates compared to the Swedish population. We also demonstrated that the incidence of several of the dominating cancers in either

Table 3. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years among male Iranian immigrants in Sweden (1985-2004) in comparison with Tehrani and Swedish male population using Standard Rate Ratio (SRR).

ICD7	Site	Iranian Immigrants	
		n	ASR1 (SE)
140-144	Oral cavity	8	2,4 (0,9)
150	Esophagus	6	2,5 (1,1)
151	Stomach	13	4,7 (1,3)
153-4	Colon and rectum	41	13,5 (2,2)
155-6	Liver and gall bladder	6	2,4 (1,0)
157	Pancreas	6	2,2 (0,9)
162-163	Trachea/bronchus/lung	17	5,4 (1,4)
196	Bone	4	1,4 (0,6)
191	Non-melanoma of skin	6	1,7 (0,7)
170	Breast	205	60,7 (4,6)
171	Cervix Uteri	9	3,3 (1,1)
172	Corpus Uteri	14	5,5 (1,5)
175	Ovary	23	6,3 (1,4)
181	Bladder and urinary tract	11	4,0 (1,3)
193	Brain	36	11,5 (2,1)
194	Thyroid	31	7,2 (1,5)
201	Hodgkin's lymphoma	10	3,1 (1,0)
200-202	Non-Hodgkin's lymphoma	22	6,5 (1,5)
203	Multiple Myeloma	5	1,7 (0,8)
204-207, 209	Leukemia	15	4,8 (1,3)
140-209 (not 191)	All sites excluding 191	550	174,1 (8,4)
140-209	All sites	556	175,8 (8,5)

country changes rapidly in the direction of the existing pattern in the population at the destination: among men the ASRs of stomach and esophageal cancers fell rapidly while prostate and colorectal cancer increased. Among women, the incidence of stomach cancer fell while that of breast cancer rose.

Strengths of our study include appropriate definition of the immigrant cohort from the Total Swedish Population register, availability of data on date of immigration, complete follow-up through precise linkages with high quality registers of cancer, migration, and death. This international collaborative study allowed us to compare the rates among the immigrants with the rates in their countries of origin and destination.

Notwithstanding several strengths, we faced some limitations. We had insufficient statistical power to evaluate changes in the occurrence of less common site-specific cancers, especially when we stratified for follow-up time and age at migration. Evaluation of cancer incidence among immigrants who were younger than 20 years at arrival could potentially provide important insights into etiology of cancers that are linked to early life exposures, but since migration from Iran to Sweden has occurred predominantly in the three most recent decades most young immigrants have not yet reached the cancer ages. Thus, several hypotheses cannot be addressed until the cohort grows older.

While cancer registration in Sweden is generally con-

Continue Table 3. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years among male Iranian immigrants in Sweden (1985-2004) in comparison with Tehrani and Swedish male population using Standard Rate Ratio (SRR).

ICD7	Site	Tehran			Sweden		
		n	ASR2 (SE)	SRR ASR1/ASR2	n	ASR3 (SE)	SRR ASR1/ASR3
140-144	Oral cavity	270	2,4 (0,02)	1.0 (0.2-4.2)	2903	2,7 (0,06)	0.9 (0.2-3.4)
150	Esophagus	541	5,3 (0,05)	0.5 (0.2-1.5)	1315	1,0 (0,03)	2.5 (0.2-33.1)
151	Stomach	1033	10,0 (0,10)	0.5 (0.2-1.0)	6173	4,6 (0,07)	1.0 (0.4-2.7)
153-4	Colon and rectum	1070	9,9 (0,04)	1.4 (0.7-2.8)	32361	26,3 (0,17)	0.5 (0.3-0.8)
155-6	Liver and gall bladder	501	4,8 (0,05)	0.5 (0.2-1.5)	7526	6,0 (0,08)	0.4 (0.1-1.1)
157	Pancreas	263	2,6 (0,03)	0.8 (0.2-3.6)	6894	5,7 (0,08)	0.4 (0.2-1.0)
162-163	Trachea/bronchus/lung	776	7,4 (0,07)	0.7 (0.3-1.7)	13607	14,1 (0,13)	0.4 (0.2-0.7)
196	Bone	271	2,0 (0,02)	0.7 (0.2-2.8)	373	0,6 (0,04)	2.3 (0.2-26.8)
191	Non-melanoma of skin	619	6,0 (0,06)	0.3 (0.1-0.6)	11761	7,6 (0,09)	0.2 (0.1-0.4)
170	Breast	3579	31,5 (0,30)	1.9 (1.3-2.9)	72403	83,3 (0,34)	0.7 (0.6-0.9)
171	Cervix Uteri	514	4,8 (0,05)	0.7 (0.2-2.0)	5657	7,7 (0,11)	0.4 (0.2-1.0)
172	Corpus Uteri	262	2,5 (0,02)	2.2 (0.5-10.0)	14622	15,0 (0,14)	0.4 (0.2-0.7)
175	Ovary	731	6,5 (0,06)	1.0 (0.3-3.6)	11536	13,3 (0,14)	0.5 (0.3-0.8)
181	Bladder and urinary tract	393	3,9 (0,04)	1.2 (0.3-3.6)	6961	5,7 (0,08)	0.7 (0.2-2.0)
193	Brain	577	4,5 (0,04)	2.6 (0.9-7.5)	8358	11,7 (0,09)	1.0 (0.4-2.2)
194	Thyroid	361	2,8 (0,02)	2.6 (0.7-8.9)	2586	3,4 (0,08)	2.1 (0.7-6.6)
201	Hodgkin's lymphoma	179	1,2 (0,01)	2.6 (0.4-17.6)	971	1,6 (0,06)	1.9 (0.4-10.6)
200-202	Non-Hodgkin's lymphoma	574	4,9 (0,04)	1.3 (0.5-3.7)	7897	7,5 (0,10)	0.9 (0.4-1.9)
203	Multiple Myeloma	138	1,3 (0,01)	1.3 (0.2-10.3)	3289	2,7 (0,05)	0.6 (0.2-2.6)
204-207, 209	Leukemia	768	6,1 (0,05)	0.8 (0.3-2.0)	5947	6,7 (0,10)	0.7 (0.3-1.7)
140-209 (not 191)	All sites excluding 191	15154	135,8 (1,28)	1.29 (1.04-1.59)	254605	264,7 (0,5)	0.66 (0.57-0.77)
140-209	All sites	15773	141,8 (1,34)	1.24 (1.01-1.54)	266366	272,3 (0,6)	0.65 (0.56-0.75)

sidered to be of high quality and estimated to be 96-98 percent complete,[6] there is no nationwide cancer registration in Iran. Therefore, we used estimates provided from the Tehran Cancer Register as a reasonable representation of cancer incidence in the entire Iran, in part because the Tehran metropolitan area accommodates almost 20 percent of the Iranian population, and in part since these residents constitute a mix of essentially all ethnic groups with roots in all parts of the country. A high prevalence of DCO cases (25%) in the TCR indicates that it is still far from reaching complete coverage. Our validation study showed that about 15 percent of the pathology data were not collected in TCR. Therefore, a large part of the DCO problem in TCR could be eliminated just by improving the standards of data collection from pathology departments. We have included 25 percent DCOs in the estimation of overall cancer incidence in TCR. Therefore, we believe that the results pertaining to total cancer are close to reality. Recently a paper was published in parallel to this work in which results of the nationwide pathology-based cancer registry was used as the reference rate in Iran.[10] We believe that the inference made in that study about the differences between the cancer risk among Iranian immigrants and Iranian residents is biased because in overall about 40 percent and for some cancers such as lung, esophageal and stomach cancers more than 50% of

Table 4. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years and corresponding rate ratios for male Iranian immigrants followed from 1960 through 2004, stratified by follow-up time and age at migration and after excluding the first year of follow-up.

ICD7	Site	Follow-up time				SRR (95%CI)
		2-9 Years		≥10 Years		
		n	ASR (SE)	n	ASR (SE)	
Men						
151	Stomach	7	6,5 (2,6)	7	4,3 (1,9)	0.7 (0.1-6.8)
153-4	Colon and rectum	19	14,6 (3,7)	41	34,3 (6,2)	2.4 (0.7-7.8)
162-163	Trachea/bronchus/lung	12	12,3 (3,7)	12	11,3 (3,7)	0.9 (0.2-4.9)
191	Non-melanoma of skin	13	10,4 (3,2)	5	5,5 (2,7)	0.5 (0.1-4.3)
177	Prostate	23	25,8 (5,4)	53	53,7 (7,9)	2.1 (0.8-5.5)
178	Testis	6	1,4 (0,6)	5	2,1 (1,1)	1.5 (0.1-24.4)
180	Kidney	6	3,6 (1,8)	11	6,4 (2,4)	1.8 (0.2-19.1)
181	Bladder and urinary tract	30	21,2 (4,4)	24	20,5 (5,0)	1.0 (0.3-3.0)
193	Brain	12	9,0 (2,3)	19	8,8 (2,3)	1.0 (0.3-3.5)
194	Thyroid	5	3,2 (1,8)	8	4,2 (1,9)	1.3 (0.1-19.8)
201	Hodgkin's lymphoma	8	3,3 (1,5)	7	3,1 (1,3)	0.9 (0.1-9.9)
200-202	Non-Hodgkin's lymphoma	18	10,6 (3,0)	16	10,7 (3,4)	1.0 (0.2-5.7)
204-207, 209	Leukemia	14	10,2 (3,2)	12	10,1 (3,4)	1.0 (0.2-6.0)
	All sites	225	159,5 (12,3)	266	204,9 (14,9)	1.28 (0.85-1.91)

Continue Table 4. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years and corresponding rate ratios for male Iranian immigrants followed from 1960 through 2004, stratified by follow-up time and age at migration and after excluding the first year of follow-up

ICD7	Site	Age at migration				SRR (95%CI)
		20 - 39 year old		>40 year old		
		n	ASR (SE)	n	ASR (SE)	
Men						
151	Stomach	6	19,1 (17,6)	8	5,0 (1,8)	0.3 (0.0-172.8)
153-4	Colon and rectum	23	35,2(19,9)	37	24,7 (4,3)	0.7 (0.2-2.9)
162-163	Trachea/bronchus/lung	6	2,6 (1,2)	18	11,3 (2,7)	4.4 (0.6-29.6)
191	Non-melanoma of skin	4	0,6 (0,3)	13	8,1 (2,3)	13.5 (0.6-297.3)
177	Prostate	16	48,6 (22,0)	59	36,1 (4,7)	0.7 (0.1-5.9)
178	Testis	6	0,8 (0,4)	0	-	-
180	Kidney	10	2,2 (0,9)	7	4,0 (1,5)	1.8 (0.2-17.0)
181	Bladder and urinary tract	21	13,4(8,7)	32	22,4 (4,4)	1.7 (0.2-14.1)
193	Brain	26	14,8 (9,0)	11	6,6 (2,0)	0.5 (0.0-14.2)
194	Thyroid	7	1,1 (0,4)	4	2,6 (1,3)	2.4 (0.1-47.0)
201	Hodgkin's lymphoma	8	1,9 (0,9)	2	1,2 (0,8)	0.6 (0.0-13.3)
200-202	Non-Hodgkin's lymphoma	17	4,2 (1,4)	14	8,7 (2,3)	2.1 (0.4-11.0)
204-207, 209	Leukemia	8	9,6 (8,6)	12	7,6 (2,2)	0.8 (0.0-44.0)
	All sites	197	172,2 (38,6)	256	162,4 (10,4)	0.9 (0.4-2.5)

Table 5. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years and corresponding rate ratios for female Iranian immigrants followed from 1960 through 2004, stratified by follow-up time and age at migration and after excluding the first year of follow-up.

ICD7	Site	Follow-up time				SRR (95%CI)
		2-9 Years		≥10 Years		
		n	ASR (SE)	n	ASR (SE)	
Men						
151	Stomach	4	5.3 (1.9)	8	2.9 (1.4)	0.6 (0.1-5.3)
153-4	Colon and rectum	20	12.4 (2.9)	21	14.5 (3.4)	1.2 (0.3-4.2)
162-163	Trachea/bronchus/lung	8	5.0 (1.9)	8	6.0 (2.2)	1.2 (0.2-9.9)
191	Breast	110	54.9 (5.8)	66	66.8 (7.6)	1.2 (0.7-2.3)
177	Corpus Uteri	7	5.6 (2.1)	7	6.6 (2.6)	1.2 (0.1-9.8)
178	Ovary	10	5.7 (1.8)	11	7.8 (2.7)	1.4 (0.2-8.9)
180	Bladder and urinary tract	6	3.9 (1.6)	5	4.6 (2.2)	1.2 (0.1-14.0)
181	Brain	24	13.3 (3.0)	12	9.9 (3.3)	0.7 (0.2-3.4)
193	Thyroid	22	9.4 (2.3)	9	4.0 (1.5)	0.4 (0.8-2.2)
201	Hodgkin's lymphoma	5	2.8 (1.3)	5	2.9 (1.3)	1.0 (0.1-16.6)
200-202	Non-Hodgkin's lymphoma	15	8.5 (2.3)	7	4.8 (2.0)	0.6 (0.1-3.5)
204-207. 209	Leukemia	7	4.3 (1.7)	8	4.8 (1.8)	1.1 (0.1-9.6)
	All sites	316	176.9 (11.0)	240	172.4 (12.3)	1.0 (0.6-1.5)

Continue Table 5. Age-standardized incidence rates (ASRs) for cancer in overall and site specific rates per 100 000 person-years and corresponding rate ratios for female Iranian immigrants followed from 1960 through 2004, stratified by follow-up time and age at migration and after excluding the first year of follow-up.

ICD7	Site	Age at migration				SRR (95%CI)
		20 - 39 year old		>40 year old		
		n	ASR (SE)	n	ASR (SE)	
Men						
151	Stomach	3	1.6 (1.1)	10	3.9 (1.3)	2.4 (0.2-30.9)
153-4	Colon and rectum	11	4.1 (1.7)	30	13.2 (2.6)	3.2 (0.7-14.9)
162-163	Trachea/bronchus/lung	4	1.7 (1.1)	12	5.5 (1.7)	3.2 (0.3-35.9)
191	Breast	116	121.3 (41.1)	50	50.9 (6.5)	0.4 (0.1-3.0)
177	Corpus Uteri	1	0.4 (0.4)	13	6.6 (1.9)	16.5 (0.6-481)
178	Ovary	6	8.2 (5.9)	10	5.6 (2.0)	0.7 (0.0-23.7)
180	Bladder and urinary tract	0	0	10	4.7 (1.6)	-
181	Brain	14	4.4 (1.6)	17	10.4 (3.1)	2..4 (0.3-16.1)
193	Thyroid	21	10.1 (5.8)	9	7.7 (3.1)	0.8 (0.0-13.7)
201	Hodgkin's lymphoma	1	0.4 (0.4)	2	0.8 (0.6)	2.0 (0.0-243.1)
200-202	Non-Hodgkin's lymphoma	7	1.4 (0.6)	13	5.8 (1.7)	4.1 (0.4-38.7)
204-207. 209	Leukemia	3	0.5 (0.3)	10	4.1 (1.3)	8.2 (0.4-163)
	All sites	227	206.4 (61.7)	296	157.5 (10.7)	0.76 (0.19-2.96)

the cases were not counted in this registry. (This manuscript is under review by another Journal, but we can provide the data on request). In this study we selected a more appropriate comparison data from Iran and a performed more detailed statistical analyses. However, as coding of site is generally unreliable or lacking in Iranian death registers, site-specific data may be less trustworthy. Although some underestimation of the Iranian incidence rates for specific cancers is to be expected, the gradual change among immigrants being subjected to more valid cancer reporting in Sweden strongly suggests that the incidence disparities between Iran and Sweden cannot be entirely attributed to incomplete registration. Consequently, it is unlikely that the marked changes observed for some specific cancers including stomach, colorectal, and non-melanoma skin cancers in both sexes, prostate cancer among men and breast cancer among women is explained only by differences in cancer registration standard.

Selection bias commonly referred to as 'migrant effect' is a concern in migrant studies.[1,11] It arises because migrants are generally not representative of their population of origin. We did not have information about the exact origin and background of the migrants in this study, and even if we had, we would not have had access to cancer incidence data specific for their population strata. Since it is conceivable that migrants would prefer destinations with a lifestyle that resembles their own, both the differences in cancer incidence vis-à-vis their source population and their adaptation to the rates at the destination might be partly artifactual. The gradual adaptation with time since arrival somewhat allays concerns that our observations would be entirely attributable to this migrant effect.

Various pieces of evidence suggest that the incidence of stomach cancer is very high in Iran; rates of up to 50 per 100,000 person-years have been reported in northwestern Iran.[12-13] Therefore, we expected to find a high incidence rate of this cancer also among the Iranian immigrants, at least in the first few years after arrival to Sweden. However, it appears that the selection bias discussed above led to considerably lower rates. Notwithstanding this contrast, ASR of stomach cancer was halved in both men and women after 10 years or more in Sweden. Unfortunately we did not have sufficient statistical power to fully evaluate the importance of age at immigration.

The increase in incidence of colorectal cancer among men and women, breast and corpus uteri cancers among women and prostate cancer among men seemingly provides support for the importance of environmental risk factors in these diseases. However, screening activities in Sweden may have inflated the incidence of breast cancer. An ASR of breast cancer among female Iranian immigrants greatly exceeding the corresponding ASR among Tehrani women already in the first 10 years after migration suggests that screening (and possibly selection bias) might have been the cause rather than changes in the risk factor profile. While organized screening for colorectal prostate cancer was not widely implemented during the time period covered by this study, some opportunistic screening may still have occurred. An observed ASR of prostate cancer close to that among Tehrani men in the first few years, followed by a more than doubled incidence after more than 10 years in Sweden, is more consistent with a change in exposure to etiologic factors, although a recent upsurge in opportunistic PSA screening may also have contributed. Nonetheless, it is plausible that nutritional factors, reproductive factors, and body composition – more or less established risk factors for one or more of these cancers – may have gradually changed with improved socioeconomic status. If so, our findings support the importance of environmental factors acting relatively late in life, as has been proposed for prostate cancer.[14]

The higher incidence of thyroid cancer among immigrants in Sweden compared to Swedish people in this study is consistent with the results of previous studies conducted among Iranian immigrants in Sweden,[15] and among Middle Eastern immigrants in Australia and California.[16-17] One explanation might be improvement in the iodine intake in the previously iodine-deficient individuals. Iodine deficiency has been implicated as a risk factor for thyroid cancer.[18] Thyroid cancer has a good prognosis and due to higher standards in the Swedish health care system detection of prevalent cases may have led to an artificially high incidence among immigrant women.[14] The rapid decrease after arrival to Sweden supports this hypothesis: further stratification of the first 10 years revealed a quickly decreasing trend (ASRyear0-.1 =33.5; ASRyear2-.4=13; ASRyear5-.7=7.9; ASR year8-.10

=7.0).

Finally, stable ASRs of leukemia among both male and female immigrants, distinct from the rates in the new population suggest that genetic components may play a more important role than environmental risk factors for the development of leukemia.

In conclusion, the age-standardized incidence of several common cancers changed among first-generation migrants from Iran, away from the rates in the country of origin and in the direction of the existing rates in the population at the destination. This was statistically confirmed for stomach and esophageal cancers, which fell rapidly, and for colorectal, prostate, and breast cancer, which increased. Although differences in the completeness of cancer registration may explain some, but not all, of the discrepancies between Iranian and Swedish incidence rates, and selection bias and increased detection might have inflated differences between Iranian immigrants and their peers in Iran, our data provide support for the importance of environmental risk factors acting in adult life.

Acknowledgement

This study was funded by grants from Swedish-Research link in Sweden and Cancer Research Center, Tehran University of Medical Sciences in Iran

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