REGIONAL REVIEW

Cancer Epidemiology and Control in North-Western and Central Asia - Past, Present and Future

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Abstract

The North-Western and Central region of Asia stretches from Turkey through Armenia, Georgia and Azerbaijan, to Iran and Turkmenistan, Uzbekistan, Kazakhstan, Kyrgyzstan, Tadjikistan and Afghanistan. These countries in the main share Turkic, Iranian or Caucasus ethnicity and culture and can be considered as a regional entity for cooperation in control of cancer. The present review of cancer registry and other epidemiological data was undertaken to provide an evidence base for cancer control programs and pointers to possible research collaboration. The most prevalent cancer site in males is the lung in the Western part of the region and the stomach in most of Iran and Central Asia, followed by the oesophagus in the latter two. Bladder cancer is comparatively frequent throughout. In females breast cancer is number one, generally followed by gastric, oesophageal or cervical lesions. However, there are interesting differences between countries or regions, particularly regarding the stomach. General tendencies for increase in adenocarcinomas but decrease in squamous cell carcinomas and gastric cancer point to change in environmental influence over time. Variation in risk factors depends to some extent on the level of economic development but overall the countries of the region face similar challenges in achieving effective cancer control, underlying the necessity for cooperation.

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Introduction

The countries of the North-Western Asia, whether Turkic, Iranian or Caucasian, share a great deal in terms of culture as well as geographical proximity. The included population is approximately 250 million, the same size as the United States, but the level of economic development is varied and this is reflected in the infrastructure for cancer control. Given the increasing importance of neoplastic diseases, as well as the other chronic medical conditions like diabetes and circulatory problems, cooperation across the region to best marshal the available resources is a high priority. A comprehensive understanding of the present situation is therefore necessary.

There is a general awareness of the scope of the cancer problem faced by North-West and Central Asia and efforts are increasing to develop and expand cancer control programs incorporating registration and screening or dearly detection. The present review was conducted to assess the state of cancer registration and research into underlying risk and protective factors, taking advantage of all of the Pubmed references covering the area, as well as the CancerMondial website of the International Agency for Research on Cancer (IARC) (www-dep.iarc.fr/).

Cancer Registration in North Western and Central Asia

Although cancer registries have been active in the region for many years, Kyrgyzstan being listed in Cancer Incidence in Five Continents in 1992, only two registries, Izmir and Antalya in Turkey, are presently regarded as having sufficiently accurate data to be included in the International Agency for Research on Cancer publication. Therefore recourse has been made in the present case to Globocan 2002 for comparisons. However, Iranian registry data are also available in the Pubmed cited literature for the country as a whole (Sadjadi et al., 2005; Yavari et al., 2008), and for Ardabil (Sadjadi et al., 2003), East Azerbaijan (Somi et al., 2006; 2008), Tehran (Larijani et al., 2004), and Semnan (Babaei et al., 2005; 2006). Findings from the Commonwealth of Independent States and Kyrgyzstan have also been published (Igisinov et al., 2002; 2005; Davydov and Aksel, 2007).

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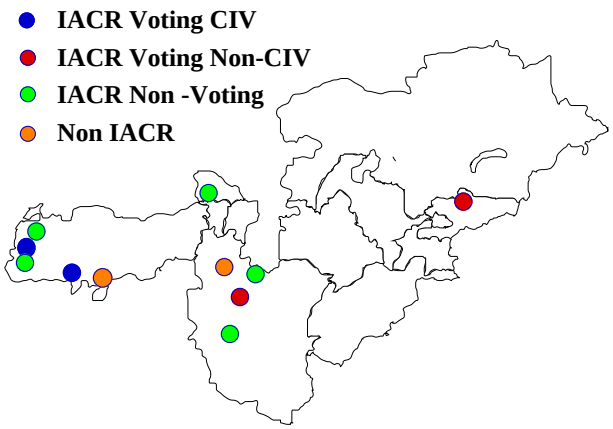

Figure 1. Cancer Registries in North-Western and Central Asia

Members of the International Association for Cancer Registries are indicated in Figure 1. Unfortunately, many countries do not have any representation.

The available population-based data have been summarized in Tables 1 and 2, for males and females, respectively, and the overall picture in terms of the most prevalent cancers is illustrated in Figure 2. In males, lung cancer is number one in the Westernmost area, also with relatively high laryngeal cancer incidences, then stomach cancer takes over in countries, stretching into Central Asia, that also have relatively high incidences of oesophageal cancer. In Tehran, the relative rates of cancer increase from the upper oesophagus to the distal stomach. In Golestan, Iran, the reverse pattern is observed, while in Ardabil, the mid portion (distal esophagus and proximal stomach) is involved most frequently (Taghavi et al., 2007). Bladder cancer features in the first five most frequent cancers in males throughout the region. In females, breast cancer predominates in all but two cases, with cervical, stomach and/or oesophageal lesions often as the second most frequent. A striking feature is the inclusion of ovarian and/or endometrial cancer in the first five.

With regard to trends over time, data are very limited although over the last 30 years in Shiraz and Tehran there has been a sharp increase in colon cancer, slight to moderate increase in stomach cancer and sharp decrease in esophageal cancer (Yazdizadeh et al., 2005). In Semnan Province of Iran, gastric cancer alone constitutes one-sixth of all cancers, (47.2%), followed by colon malignancies (8.1%) and esophageal lesions (6.8%) (Babaei et al., 2005). Gastrointestinal tract cancers exhibit significant spatial clustering of risk in northern Iran, pointing to potential life-style and environmental factors (Mohebbi et al., 2008)

Table 1. Population-based Cancer Registry Data for Turkey and Iran - Males

	Turkey			Iran			
	I*	A*	C^{+}	Ar$^{\#}$	EA^{++}	S$^{\#\#}$	T$^{\#\#\#}$
Buccal	1.4	1.5	-	1.7	2.8	3.4	2.4
Pharynx	0.3	0.1	-	0.7	1.0	-	10.9
Buccal	2.9	4.1	-	3.8	3.6	0.2	2.6
Pharynx	0.7	0.0	-	0.9	1.8	-	1.7
Nasopharynx	1.3	1.3	-	0.8	-	-	-
Oesophagus	2.3	1.6	-	15.4	12.4	11.7	6.8
Stomach	11.0	10.6	22.1	49.1	26.0	36.9	19.7
Colon	7.8	7.6	38.7	7.9	11.6	11.4	6.7
Rectum	6.3	5.1	-	-	-	-	4.3
Liver	3.2	3.8	12.4	1.6	2.2	5.8	3.8
Gallbladder	1.5	1.4	-	0.7	1.2	0.4	1.1
Pancreas	4.1	4.2	-	0.7	1.9	1.6	3.3
Larynx	11.0	7.2	-	0.3	2.1	3.0	5.3
Trachea, lung	74.5	37.5	81.0	7.9	9.6	9.2	14.9
Prostate	13.7	19.1	23.2	3.4	7.3	10.1	15.6
Kidney	3.3	2.9	-	1.1	3.4	2.3	3.2
Bladder	17.6	15.8	13.2	7.6	15.7	7.2	13.3
Brain	5.3	6.0	8.6	4.4	5.0	7.0	6.0
Thyroid	1.1	1.1	-	0.7	1.4	2.2	1.0
Non-Hodgkin	5.0	5.3	-	2.6	5.2	5.4	7.1
Leukemia	5.1	5.7	-	1.4	-	4.2	8.4
Total	125	126	249	96	164	136	163

*Curado et al., 2007; $^{+}$Hinçal et al., 2008; $^{\#}$Sadjadi et al., 2003; $^{++}$Babaei et al., 2005; $^{\#\#}$Somi et al., 2008; $^{\#\#\#}$Larijani et al., 2004; A, Antalya; Ar, Ardabil; C, Cyprus; EA, East Azerbaijan; I, Izmir, S, Semnan; T, Tehran

Organ Specific Epidemiology

Skin Cancer

Skin cancers are relatively rare, except in some particular areas, for example in central Iran (Mohagheghi et al., 2009), with male melanoma rates below 2/100,000 except in Kazakhstan and Turkmenistan. However, rates may be increasing (Eser, personal comunication), and there is some interest in sun exposure of Turkish high school students and their sun bathing habits (Dalli et al., 2004).

Table 2. Population-based Cancer Registry Data for Turkey and Iran - Females

	Turkey			Iran			
	I*	A*	C^{+}	Ar$^{\#}$	EA^{++}	S$^{\#\#}$	T$^{\#\#\#}$
Buccal	1.4	1.5	-	1.7	2.8	3.4	2.4
Pharynx	0.3	0.1	-	0.7	1.0	-	10.9
Nasopharynx	0.5	0.5	-	0.7	-	-	-
Oesophagus	1.1	0.6	-	14.4	11.7	8.8	5.3
Stomach	5.1	5.5	8.3	25.4	11.6	14.8	10.0
Colon	5.3	5.6	30.8	5.9	9.7	10.5	6.1
Rectum	4.2	3.5	-	-	-	-	3.4
Liver	1.3	1.2	4.7	2.3	2.0	3.5	3.2
Gallbladder	2.0	1.8	-	0.7	1.7	2.1	1.6
Pancreas	2.7	2.6	-	0.2	1.3	2.8	2.6
Larynx	0.5	0.6	-	0.2	0.3	1.1	0.9
Lung	5.9	4.8	15.5	3.6	3.7	4.8	7.0
Breast	34.8	29.1	72.5	7.6	23.5	21.3	31.4
Ovary	4.9	6.1	10.5	0.8	5.3	17.0	6.5
Corpus uteri	6.5	7.2	12.6	0.5	2.2	-	3.8
Cervix uteri	5.4	4.4	9.5	0.7	1.9	1.1	4.8
Kidney	1.6	1.6	-	1.3	1.8	0.7	1.7
Bladder	2.1	2.5	5.9	1.8	3.7	3.0	3.8
Brain	3.1	4.4	5.6	3.1	5.5	6.3	4.5
Thyroid	3.6	4.5	-	1.0	4.9	4.5	2.8
Non-Hodgkin	4.1	3.9	-	1.4	2.9	4.5	4.8
Leukemia	4.0	3.8	-	1.3	-	3.1	6.1
Total	125	126	212	96	131	136	136

*Curado et al., 2007; $^{+}$Hinçal et al., 2008; $^{\#}$Sadjadi et al., 2003; $^{++}$Babaei et al., 2005; $^{\#\#}$Somi et al., 2008; $^{\#\#\#}$Larijani et al., 2004; A, Antalya; Ar, Ardabil; C, Cyprus; EA, East Azerbaijan; I, Izmir, S, Semnan; T, Tehran

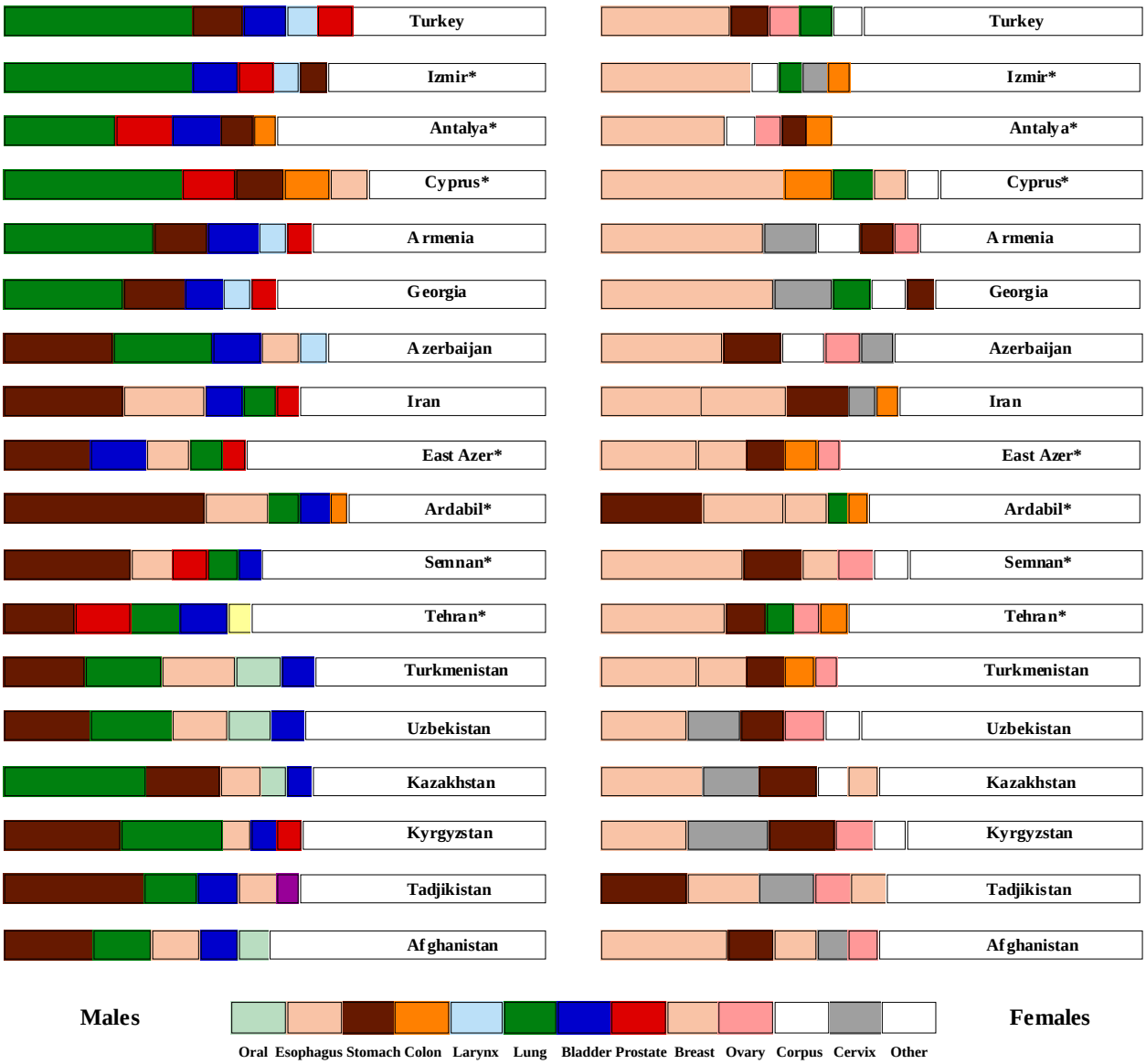

Figure 2. Percentage Data for the Five Most Prevalent Cancers in Countries/Registries of North-Western and Central Asia (from Globocan, 2002: Ferlay et al., 2004 and the references listed for Tables 1 and 2)

Oral Cancer

Oral cancers are rare except in some of the Central Asian Republics and Iran (see Figure 3). Clearly smoking is one risk factor, as evidenced by an additive interaction with the GSTM1-null genotype (Suzen et al., 2007) but recent research within the area has been very limited.

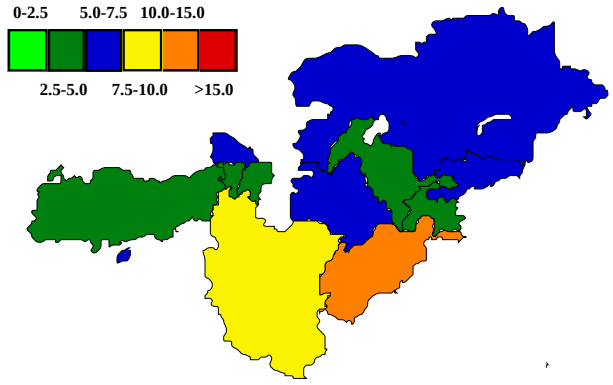

Figure 3.Male Oral Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

During the Soviet era, a series of studies were carried out and Nass use and cigarette smoking emerging as independent risk factors for oral leukoplakia (Zaridze et al., 1985; Zaridze et al., 1987; Evstifeeva and Zaridze, 1992). Alcohol intake was not found to be independently associated with the presence of oral precancerous lesions (Evstifeeva and Zaridze, 1992)

Oesophageal Cancer

Through Iran and all of Central Asia, oesophageal cancer is of major importance and has attracted a great deal of research interest, with setting up a cohort in Golestan (Pourshams et al., 2005). Intriguingly, rates appear very low in Western Turkey and the Caucasus. However, in Van close to the Iranian border the sitatuion is clearly different (http://www.ukdk.org/pdf/kitap/en/51.pdf). In Turkish population-based registries, the percentages of SCCs and ACs of the esophagus are reported to be 72.5 and 20.5 in Antalya and 71.7 and 18.7 in Izmir males, respectively, and 58.8/35.3 and 82.0/6.7 in females (Curado et al., 2007).

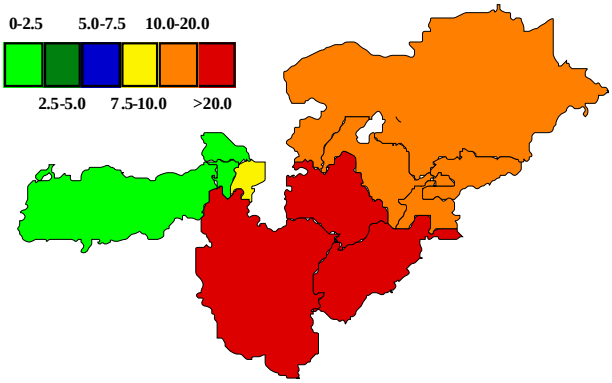

Figure 4. Male Oesophageal Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

Thermal irritation and coarse food (physical damage to the mucosal lining of the esophagus) are risk factors, presumably interacting with low socioeconomic status and poor nutritional diet (Mosavi-Jarrahi and Mohagheghi, 2006). Drinking of hot tea 'kitlama'and low fruit diet are the most common risk factors for oesophageal cancer in high risk area in Eastern Turkey (Onuk et al., 2002). Consumption of smoked, salted, hot, fatty foods, and well water, cigarette smoking, poor intake of fresh fruits and vegetables and poor hygienic conditions are also probable culprit factors (Turkdogan et al., 2005).

A traditional diet rich in nitrate and nitrite is significant in the development of endemic upper gastrointestinal (esophageal and gastric) cancers in the Van region of Turkey (Turkdogan et al., 2003). Low zinc and molybdenum levels (Nouri et al., 2008) and riboflavin deficiency (Siassi and Ghadirian, 2005) are prevalent in high-incidence areas and nutrients such as phosphorus and niacin confer play protection (Siassi et al., 2000). Risk is increased in those who use tobacco only, in those who used opium only, and in those who used both tobacco and opium (Nasrollahzadeh et al., 2008). Smoking is an independent risk factor for oesophageal lesions and significantly associated with chronic oesophagitis (Zaridze et al., 1985; Zaridze et al., 1987; Evstifeeva and Zaridze, 1992). Alcohol intake was not found to be independently associated with the presence of oral and oesophageal precancerous lesions (Evstifeeva and Zaridze, 1992) Polycyclic aromatic hydrocarbons might also contribute to the high risk (Hakami et al., 2008). However, variations in CYP1A1 m1, CYP1A1 m2, CYP2A6*9 polymorphic genes were not found to be major contributors to the high incidence among Turkomans (Sepehr et al., 2004).

Familial heritable factors could be significant (Akbari et al., 2006), although the dramatic decrease in incidence found in Iranian immigrants in Canada suggest that the genetic influence must be limited (Yavari et al., 2006). In addition, the human papilloma virus may play a role in Iran (Farhadi et al., 2005). In a recent study 23.6% of tumour specimens and 8.6% of non-involved tumour margins were found to be HPV positive (Far et al., 2007).

Data on relative incidences of squamous cell carcinomas and adenocarcinomas are limited, but in Turkish males the latter account for about 20%. In northwest Iran there appears to be a relatively low incidence of adenocarcinomas, but the situation is complicated by gastric involvement (Bafandeh et al., 2006). In one series in Northeast Iran, there were ten times as many SCCs as ACs (Islami et al., 2004), while in Eastern Azerbaijan, they accounted for 86.9% and 12.8% of cases, respectively, although many tumors were in the lower third of the esophagus (Gholipour et al., 2008). The oesophageal cancer incidence rate in the Turkmen Plain, eastern part of the Caspian Littoral of Iran is decreasing (Semnani et al., 2006) and similar data have been published by other authors (Sadjadi et al., 2003; 2005). In Kerman, the South-east of Iran, risk of SCCs appears to have remained more or less constant over time, while that of ACs has increased around 11% annually (Haghdoost et al., 2008).

The control of esophageal cancer is also a top priority in Kazakhstan (Sharmanov et al., 1996). Regarding traditional analytical epidemiology one group have evaluated variation between plain (Kzyl-Orda Region) and mountainous (Alma-Ata Region) areas, finding an inverse association with altitude for this cancer (Akhtiamov and Kairakbaev, 1983). There are much higher rates in Kyrgyz than in Russians in Kyrgyzstan, with an altitude link (Igisinov et al., 2002).

Of men from whom blood was drawn for analysis, 4%, 66%, and 86% had low levels of retinol, carotene, and riboflavin, respectively, providing an opportunity and a justification for chemopreventive trials focused on precancerous lesions as end points (Zaridze et al., 1985b). Differential evaluation of different pathologies of the esophageal mucosa suggested a link between catarrhal and erosive esophagitis and vitamin B2 deficiency and atrophic esophagitis and vitamin A deficit (Zaridze et al.,1989). Furthermore, a significant decrease in the prevalence odds ratio (OR) of oral leukoplakia was observed after 6 months of treatment in men receiving retinol, beta-carotene, and vitamin E, and of risk of progression of chronic esophagitis (Zaridze et al., 1993).

Stomach Cancer

Stomach cancer is relatively prevalent throughout the region, especially in parts of Iran and the Central Asian republics (see Figure 5). Particularly high rates are evident in Ardabil (Sadjadi et al., 2003), and incidences may be increasing (Semnani et al., 2006). In NW Iran the great majority of tumours originate from the right side of the

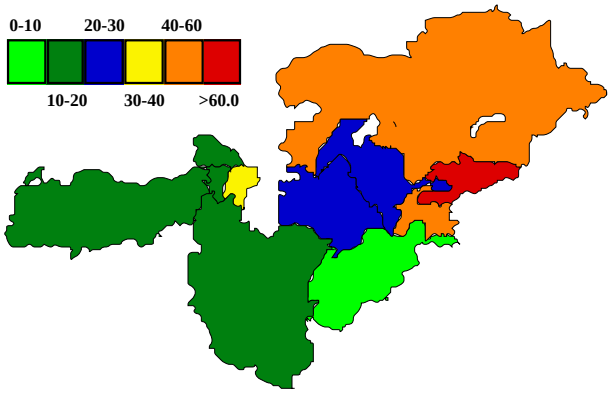

Figure 5. Male Stomach Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

cardia (Derakhshan et al., 2004). Over 36 years, the prevalence of cancers in the upper and middle third of the stomach in Tehran have increased and that of the lower third has decreased, especially in younger patients (Abdi-Rad et al., 2006). Proximal lesions also predominate in the eastern part of Turkey, contrasting with the distal tumours found in the western region (Bor et al., 2007).

In Ardibil, atrophic gastritis, reactive atypia, and intestinal metaplasia are reported to be common in antrum, corpus, and cardia subsites, with most subjects positive for *H. pylori* infection (Malekzadeh et al., 2004). The bacterium is the main risk factor for gastritis in all stomach sites, but the relationship is stronger for the antrum and cardia than for the body (Ghadimi et al., 2007; Sotoudeh et al., 2008). The role of intestinal metaplasia is open (Dincer et al., 2002). The Epstein-Barr virus is only found in a very small number of cases (~3%) (Abdirad et al., 2007). Gastric cancer risk is statistically increased by the GSTM1 null genotype (Saadat and Saadat, 2001) and possibly also the GSTT1 null genotype (Saadat, 2006), pointing to tobacco as a risk factor. Selenium deficiency may play a role in the high incidence of gastric cancer in Ardabil Province (Nouarie et al., 2004). The incidence of gastric cancer also appears to reflect the climatic-geographical zone (Saenko, 1979).

Gastric cancer history in parents and familial clustering of the disease have been reproted (Bakir et al., 2003). Gastric cancer patients in Iran have a low 5-year survival rate due to delayed consultation and diagnosis (Sadighi et al., 2005; Zeraati et al., 2005).

Colorectal Cancer

Colorectal cancers are still very infrequent in North-Western and Central Asia, although there are signs of increase (Semnani et al., 2006). There is a slight predomination of colon over rectum in both sexes and males have slightly higher incidences. A marked increase has been reported for Shiraz, with no alteration in the ratio of right to left sides (Hosseini et al., 2004), whereas in Tabriz, a left shift of both colorectal adenomas and cancers has been described (Bafandeh et al., 2005; 2006). On the basis of more left lesions, screening with fecal occult blood testing and sigmoidoscopy have ben recommended as most appropriate for screening (Erkek et al., 2007). In Turkey, colon cancers slightly outnumber those in the rectum but the situation in Iran is unclear. Synchronous colon and rectum lesions may not be rare (Yalcinkaya et al., 2008).

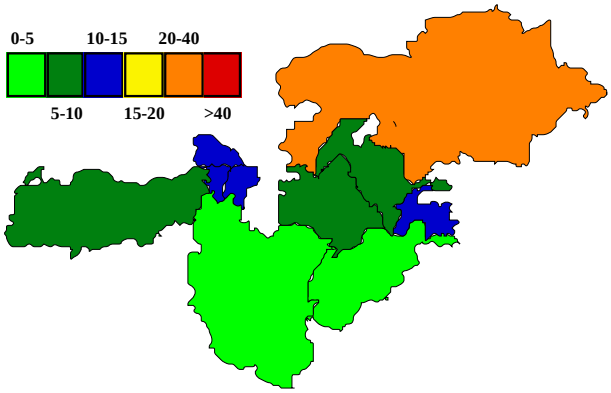

Figure 6. Male Colorectal Cancer Incidences /100,000
(Globocan, 2002: Ferlay et al., 2004)

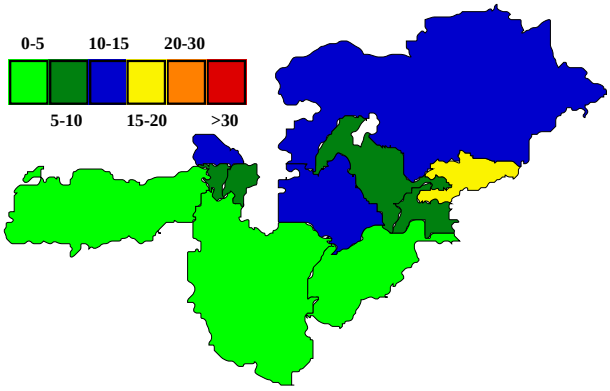

Figure 7. Male Liver Cancer Incidences/100,000
(Globocan, 2002: Ferlay et al., 2004)

In Turkey, the young age group colorectal cancers appear more common than in Western communities so that genetic or cohort effects have been surmised (Zorluoglu et al., 2004). Almost half of cases in Iran may also be below the age of 50 years, with a family history in one third of cases, again suggestive of genetic factors (Azadeh et al., 2008). However, the high proportions of young cases could also be at least partly due to the young age-structure of these countries (Ansari et al., 2006).

The Turkish version of the Champion's Health Belief Model Scales is a reliable and valid instrument that can be used for measuring beliefs related to colorectal cancer (Ozsoy et al., 2007). Stage of tumor, distant metastasis, grade of tumor, and tumor size arethe most important prognostic factors (Moghimi-Dehkordi et al., 2008).

Liver Cancer

Liver cancer is not a major problem in the region, except possibly in Kyrgyzstan (see Figure 7). In Southern Iran, the predominant etiology of hepatocellular carcinoma is hepatitis B and hepatitis C, whereas alcohol and metabolic diseases are only found in rare cases (Hajiani et al., 2005). Expression of p53, RB1 and c-fos genes appears to have a key role in the pathogenesis (Moghaddam et al., 2007).

Pancreatic Cancer

Pancreatic cancer rates are moderately high in the 'European' area of the former Soviet Union, but otherwise they are very low, especially in Iran (see Figure 8). In

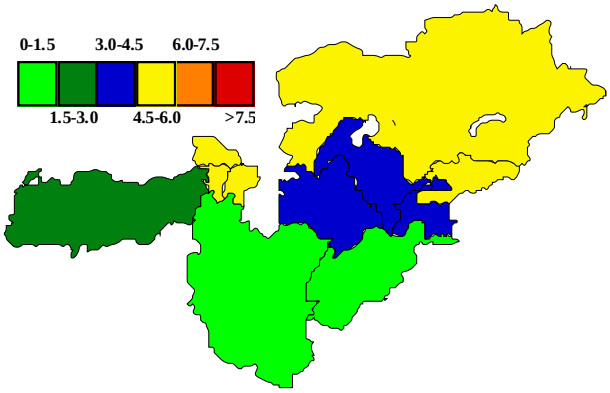

Figure 8. Male Pancreatic Cancer Incidences/100,000
(Globocan, 2002: Ferlay et al., 2004)

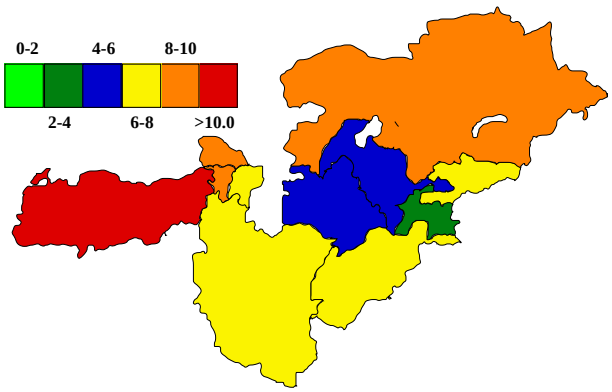

Figure 9. Male Laryngeal Cancer Incidences (Globocan 2002)

Turkey, links with high insulin and C-peptide levels suggest that insulin resistance may be a risk factor (Cetin et al., 2002).

NAT2 slow acetylators have a higher risk of developing pancreatic cancer than fast acetylators, in line with the well established tobacco etiology (Ayaz et al., 2007).

Laryngeal Cancer

Turkey and the countries of the Caucasus have exceedingly high rates of laryngeal cancer (see Figure 9). In a series of papers, Elci et al demonstrated diesel exhaust, silica and cotton dust exposure, also together with lung smoking and alcohol use, to be major risk factors (Elci et al., 2002; 2003). Opium dependency has not only been established as an independent possible risk factor for laryngeal cancer but also significantly increases the likelihood of developing of the disease at a younger age (Mousavi et al., 2003).

Lung Cancer

Lung cancers account for a large proportion of male neoplasms in the region, except intriguingly in Iran (see Figure 10), but rates in females are very low other than in Western Turkey and Georgia. The histology is largely SCC in males in Turkey, with late stage presentation (Goksel et al., 2002), but in females thereare twice as many ACs. In Istanbul, the AC is the most common lung cancer (Okutan et al., 2005), but in Thrace SCCs predominate, even in females (Karlikaya and Cakir Edis, 2005). In Turkish population-based registries, the percentages of SCCs and ACs of the lung were found to be 42.1 and 15.5 in Antalya and 29.2 and 15.6 in Izmir males, respectively, and 19.8/39.7 and 13.0/33.4 in females (Curado et al., 2007). In line with the expected tobacco etiology, the null GSTM1 genotype is an independent risk factor (Pinarbasi et al., 2003), although no link overall was found for CYP1A1 Msp1 (Demir et al., 2005). HPV has also been suggested to be a risk factor in Mazandaran, Iran (Nadji et al., 2007).

Different types of lung cancer are associated with several occupations (Elci et al., 2003) and Turkey includes areas with exceedingly high incidences of asbestos- and erionite-induced mesotheliomas (Emri and Demir AU (2004). In 11 villages around Eskisehir in central Anatolia, the risk of mesothelioma is 88.3 times greater in men and 799 times greater in women, respectively, in comparison to world background incidence rates, due to asbestos-contaminated soil (Metintas et al., 2002). Environmental exposure to asbestos begins at birth and this may be important in the age of disease onset, with no apparent familial genetic influence (Metintas et al., 2008).

Kidney Cancer

Low rates prevail, as compared with the Western world, with highest incidences in the former Soviet Union countries (see Figure 11). Slight increase was recently noted in Izmir (Eser et al., 2009).

Urinary Bladder Cancer

Appreciable rates for bladder cancer are consistently seen in the region, with highest rates in Kazakhstan and Iran (see Figure 12), but limited to males, the most important risk factors being smoking and occupation (Yaris

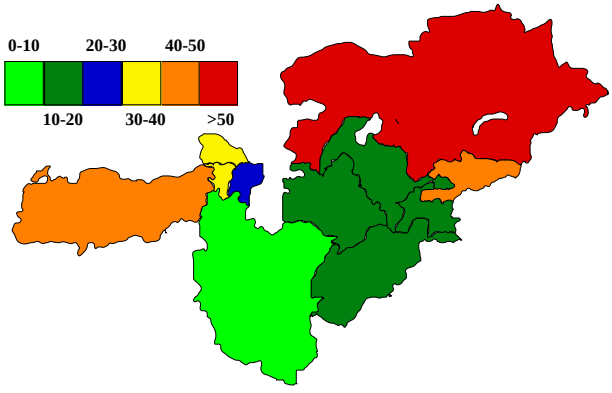

Figure 10. Male Lung Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

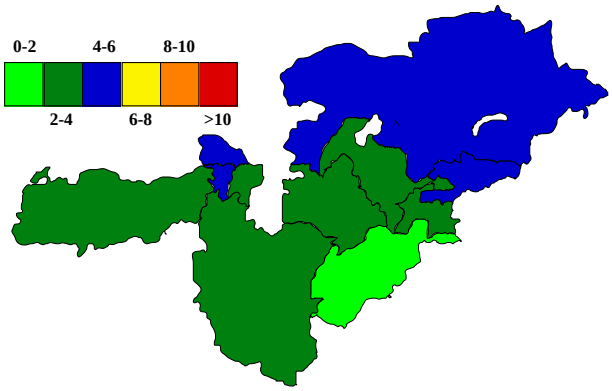

Figure 11. Kidney Cancer Incidences ((Globocan, 2002: Ferlay et al., 2004)

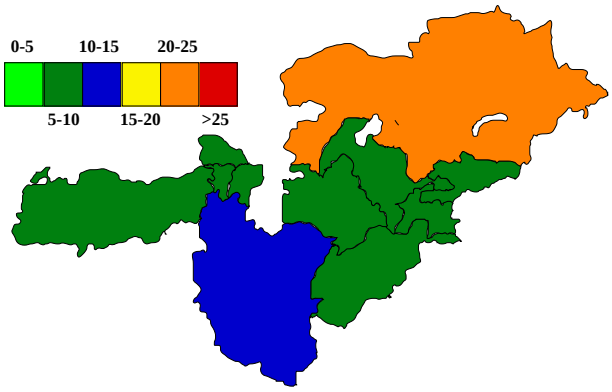

Figure 12. Male Urinary Bladder Cancer Incidences/ 100,000 (Globocan, 2002: Ferlay et al., 2004)

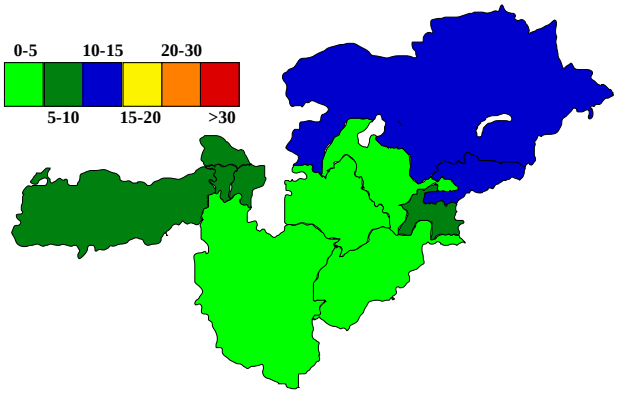

Figure 13. Prostate Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

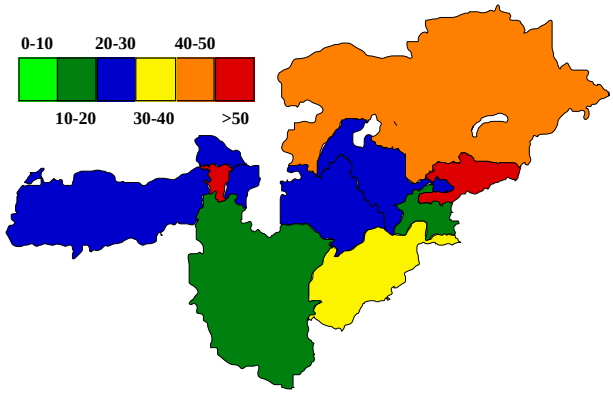

Figure 14. Female Breast Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

et al., 2006; Mohseni et al., 2004; Demirel et al., 2008). Opium consuming smokers exhibit higher incidences than those who were only smokers (Aliasgari et al., 2004). Roles for the GSTM1 null and specific GSTP1 genotypes have been proposed in the development of bladder cancer in Turkey (Toruner et al., 2001) and there are also links with industrial agents and agricultural chemicals (Gumus et al., 1999). Slight increase was recently noted in Izmir (Eser et al., 2009).

Prostate Cancer

In some parts of Turkey, the Caucasus and Iran, prostate cancer has become notable (see Figure 13), although at levels much lower than in the Western world. However, marked increase over time was recently noted in Izmir (Eser et al., 2009) and the lack of nationwide screening programs, younger age structures and limited quality cancer registration systems also needs to be taken into account (Sadjadi et al., 2007). Patients diagnosed with prostate cancer have low levels of serum testosterone and high levels of serum FSH compared with patients with BPH (Sofikerim et al., 2007).

Risk is reported to increase with aging, the frequency of sexual intercourse, fat intake and elevated serum estradiol, while high testosterone concentrations, a history of diabetes and dietary consumption of lycopene are protective (Pourmand et al., 2007). Other factors including educational level, marriage status, dietary meat consumption, vasectomy and smoking have not been shown to affect risk in the Iranian population (Pourmand et al., 2007).

Prostate specific antigen (PSA) gene promoter variation may play a significant role in the development of cancer and benign prostate hyperplasia, and a CYP17 gene polymorphism was found associated with BPH in a Turkish population (Gunes et al., 2007). Patients with PTEN mutations have a poorer prognosis (Pourmand et al., 2007).

Screening is opportunistic on a voluntary basis for men above 50 years (Razi, 2007). Normal PSA levels appear lower than in the US, Europe and Japan (Mehrabi et al., 2007).

Breast Cancer

The region is no exception to the world trend in having breast cancer as number one in frequency, with particularly large proportions in Armenia and Georgia (see Figure 14). Change over time has also been described, dependent on the region and ethnic make up (Igisinov, 2005)

Risk factors in one Turkish study were found to be long-term lactation young age at menarche, late age at first full-term pregnancy, oral contraceptive use, positive family history and menstrual irregularity (Kurur et al. 2002). A history of diabetes or hypertension, use of alcohol, oral contraceptives and hormone replacement therapy, never having breastfed and delayed age at first birth were significant factors in other studies (Oran et al., 2004; Ceber et al., 2005; Beji and Reis; 2007). Smoking also apparently increases the likelihood of developing breast cancer (Ceber et al., 2005), possibly linked to GSTT1 but not CYP1A2, CYP2D6, NAT2, GSTM1, and GSTP1 gene polymorphisms (Kocabas et al., 2004; Altayli et al., 2008). With MnSOD Ala combined with either cytochrome P450 1B1 CYP1B1*1 or catechol O-methyltransferase COMT-L (V158M) genotypes, risk was significantly increased in patients with a body mass index (BMI) greater than 24 (Kocabas et al., 2005). Elevated BMI might be particularly a risk factor for breast cancer in postmenopausal women (Yumuk et al., 2008). A close relation between exposure to electromagnetic fields and light at night with male breast carcinoma has been reported in eastern Turkey (Cok and Polat, 2001).

In Iran, family history of breast cancer in a first-degree relative, younger age at menarche, never married, first full-term pregnancy age>5 full-term pregnancies, and a negative history of breastfeeding have been found to be significant risk factors (Ebrahimi et al., 2003 Mahouri et al., 2007; Pourhoseingholi et al., 2008). In one study, high education, early age at menarche, abortion, breast feeding and its duration were not significant (Yavari et al., 2005). Variables such as obesity in postmenopausal women could increase risk (Montazeri et al., 2008) Both passive and active smoking equally increase the risk of female breast cancer (Sadri and Mahjub, 2007). Psychological determinants such as depressed mood may play an important role in etiology of breast cancer and deserve further investigation (Montazeri et al., 2004).

The IFN-gamma and interleukin genotypes may influence the risk of breast cancer development (Kamali-Sarvestani et al., 2005; Gonullu et al., 2007). There is also evidence of roles for polymorphisms in DNA repair genes (Saadat et al., 2007) and the GST gene family (Unlü et al.,

2008), although no predominant mutations in the BRCA1 and BRCA2 genes were found in Turkish high risk families (Manguoglu et al., 2003)

Breast cancer affects women in the region at least one decade younger than their counterparts in developed countries, with approximately one third of cases under 40 years old (Mousavi et al., 2006; 2008). Considerable proportions are stage II or III at diagnosis (Harirchi et al., 2004; Kermani, 2004; Mousavi et al., 2007), with an overall relative 5-year survival rate of 62% (Vahdaninia and Montazeri, 2004).

Most Muslim women do not perceive breast self-examination as being against their Islamic beliefs (Montazeri et al., 2003). Therefore attention needs to be focused on education programmes and encouraging women to self-examine with positive health beliefs (Hadi et al., 2002; Canbulat et al., 2008), especially those with a lower level of education (Parsa et al., 2006; Budakoglu et al., 2007; Yavari and Pourhoseingholi, 2007; Avci, 2008; Avci and Kurt, 2008). BSE training is necessary for nursing and midwifery students but should be repeated periodically for better efficacy (Haji-Mahmoodi et al., 2002; Balkaya et al., 2007; Yaren et al., 2008). Use of training guides may be recommended (Sevil et al., 2005), also for teachers (Jarvandi et al., 2002; Nahcivan and Secginli, 2007). Cultural attitudes toward breast cancer screening tests, modesty, lack of encouragement by family members and physicians are the major inhibitors to women's participation in breast cancer screening. Facilitating factors are self-care, proactive coping, state of mind and advocacy. Barriers are negligence, cancer-related fear, low self-efficacy, fatalism, misinformation, ineffective health communication and competing priorities (Lamyian et al., 2007). Poster displays may be useful for awareness campaigns but need to be designed to prevent anxiety (Montazeri and Sajadian, 2004).

Replacement of general surgeons by midwives in the health care system as the first examiner for clinical breast screening may not be recommended (Kaviani et al., 2006). Women experience a high level of needs associated with a diagnosis of breast cancer (Erci and Karabulut, 2007) but levels of satisfaction are reasonable (Sadjadian et al., 2004).

Ovarian Cancer

While ovarian cancers are relatively prevalent, especially in Georgia (see Figure 15), very little information is available on risk factors. In Kyrgyzstan, clear increase over time has been documented for Kyrgyz but not Russian communities, but in the latter case data are complicated by extensive emigration (Igisinov and Umaralieva, 2008). Low concentrations of IGF-I and IGFBP-3 could be a reliable pointer to differentiate benign from malignant ovarian tumors (Serin et al., 2008).

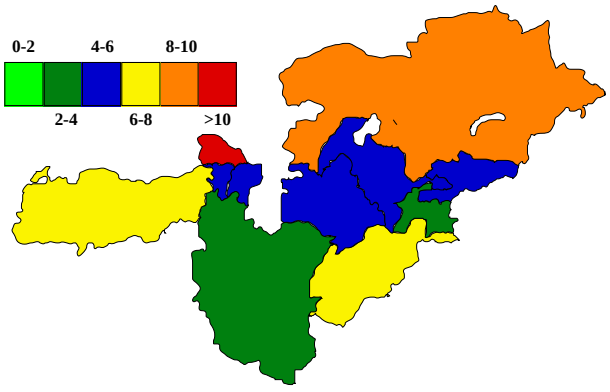

Figure 15. Ovarian Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

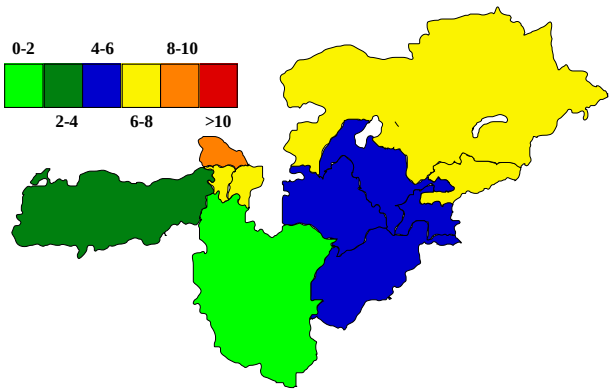

Figure 16. Endometrial Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

Corpus uteri

Similarly, the reason for the comparatively high incidences of endometrial cancers, again particularly in the Caucasus and countries of Central Asia with large Russian minorities (see Figure 16) is unclear.

Cervix uteri

In most of Central Asia and the 'European' parts of the region, cervical cancer accounts for an appreciable proportion of the total burden (see Figure 17). In Turkey, the overall frequency rate of HPV infection was demonstrated to be 6.1% (Ozcelik et al., 2003). Among HPV-positive dysplasia and metaplasia cases, 55.6% had HPV16 and 18 (Hamkar et al., 2002). In another series, 64% of lesion samples proved positive, mostly for 16, 31 or 18 (Esmaeili et al., 2008). High rates of infection with HPV genotypes have also been reported in sexually active Iranian women, again with HPV16 and 18 (Ghaffari et al., 2006).

Public education is necessary for cervical cancer prevention with population-based cancer screening programs (Turkistanli et al., 2003). Among married women

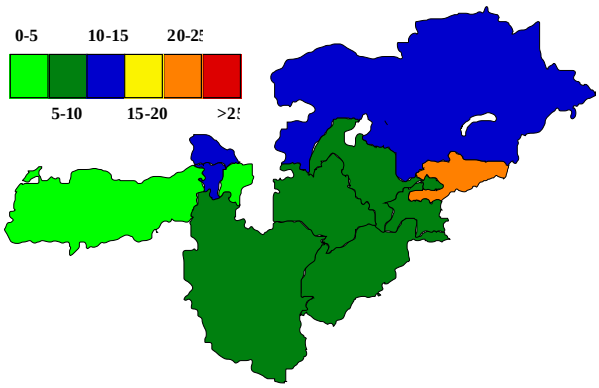

Figure 17. Cervical Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

of childbearing age, 68.5% reported having undergone at least one Pap test, correlating with knowledge about screening (Allahverdipour and Emami, 2008). Visual inspection with acetic acid has also been explored as a feasible method (Ghaemmaghami et al., 2004), although best used along with Pap smears (Eftekhar et al., 2005). The quality of the Papanicolaou smear can be improved by using the Ayre spatula first followed by the endocervical brush (Rahnama et al., 2005). It has been reported that women in Turkey would be willing to have themselves and their children receive HPV vaccine against cervical cancer and related diseases (Baykal et al., 2008).

Education by lecture and flash cards was more effective than by pamphlets for knowledge, attitude, and practice of women high school teachers in prevention of cervical cancer (Rezaei et al., 2004). One major problem is that cervical cancer patients do not pay enough attention to disease follow-up (Farnaz et al., 2008).

Brain and Nervous Tissue Cancer

Relatively high rates are seen in Turkey, Armenia, Georgia and Kazakhstan but there is no information on risk factors in the literature (see Figure 18).

Thyroid cancer

Thyroid cancer is prevalent in Iran and Kazakhstan (see Figure 19), and there are some very high risk areas. For example a high incidence of papillary tumours among ethnic Farsis has been described in Iran (Larijani et al., 2004). Kazakh and Japanese scientists have reported on risk associated with the Semipalatinsk Nuclear Testing Site. In the period 1982-96, there was a noticeable increase in the number of cases of Hashimoto's thyroiditis and thyroid cancer (Zhumadilov et al., 2000). However, another study found no evidence of radiation risk for thyroid gland among local schoolchildren (Hamada et al., 2003).

Leukemias and Lymphomas

Unlike the Arab world, incidences of NHL and leukemia are relatively low (see Figures 19 and 20). Data do not support any association between HCV infection and NHL in southeastern Anatolia region of Turkey (Isikdogan et al., 2003). Findings of collaboration with an American group suggested an increased risk of leukemia among those exposed to high irradiation, but this could have been a chance finding (Abylkassimova et al., 2000).

Childhood cancers

In Iran, childhood leukemias have been linked to high voltage overhead lines (Feizi and Arabi, 2007), with clustering in the inner city of Tehran metropolitan area (Mosavi-Jarrahi et al., 2007).

In central ASia the incidence of acute leukaemia was also found to significantly increase with increasing proximity of residence to nuclear testing areas, with some evidence of elevated numbers of brain tumours (Zaridze et al., 1994).

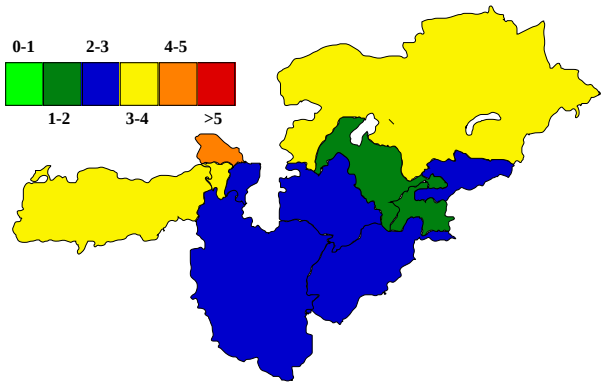

Figure 18. Male Brain and Nervous Tissue Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

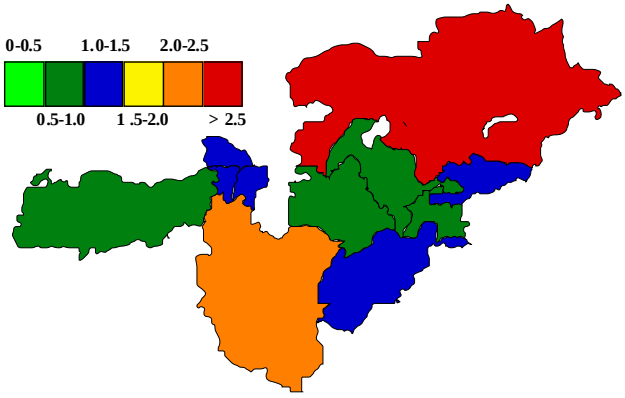

Figure 19. Male Thyroid Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

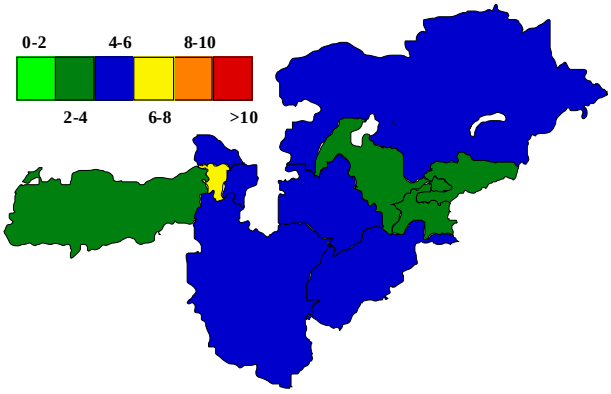

Figure 20. Male Non-Hodgkins Lymphoma Incidences/ 100,000 (Globocan, 2002: Ferlay et al., 2004)

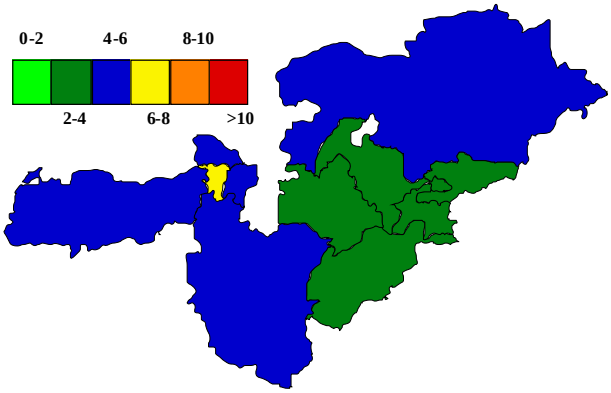

Figure 21. Male Leukemia Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

Future Perspectives

Within the region of North-West and central Asia there are high rates of obesity-related diabetes and other chronic diseases (Abdullakhodzhaeva and Utepov, 1990; Meimanaliev et al., 1991a; 1991b; Onat, 2001; King et al., 2002; Satman et al., 2002; Erem et al., 2004; Kausova, 2004), also in children (Kocaoglu et al., 2005; Sur et al., 2005). Therefore, primary prevention needs to focus on lifestyle modifications (Gokcel et al., 2003).

Furthermore, smoking prevalence among adolescents is alarmingly high and the gender gap is closing (Erguder et al., 2006; Uysal et al., 2007). Physicians have insufficient knowledge on smoking cessation therapies and the law regarding the use of tobacco and that smoking cessation techniques should be incorporated in the curriculum of the faculties and post graduation training programs. The level of general knowledge about cancer is also poor (Eftekhar and Yarandi, 2004).

Therefore, given the high rates for chronic diseases overall, many related to particular types of neoplasm, and also continued tobacco consumption, there are good grounds for believing that the burden of cancer will also become progressively heavier in the future, underlining the need for collaborative efforts for control.

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Denizli province, Turkeyurinary cancers at 26.4%, gastrointestinal cancers at 19.2% and respiratory cancers at 18.9%; there was a significant increase in gastrointestinal, blood and skin cancers over the years. Lung (14.9%), breast (14.1%), bladder (8.0%), prostate (5.3%), and lymphatic (4.8%) cancer cases were the most common (Köksal et al., 2009)

The rate of prostate cancer incidence in Iran is significantly less than those in developed countries and similar to Eastern Mediterranean Regions. However, it is expected to rise dramatically in the future because of the anticipated increase in life expectancy and percentage of old age groups. Therefore, prostate cancer control should be integrated into the National Cancer Control Program focusing on prevention and early detection in men over 40 years old or with symptomatic BPH (Mousavi, 2009)

incidence rate of adenocarcinoma of the most proximal cardia region and adjacent gastro-oesophageal junction has increased (Mousavi and Somi, 2009).

Smoking, bu also ccupational exposures to inorganic dusts chemical compounds and heavy metals were also independent risk factors for lung cancer (Hosseini et al., 2009)
Helicobacter pylori infection as measured by serum IgG as well as the consumption of red meat and dairy products increases the risk of GC in Ardabil, while the intake of fresh fruit and fresh fish decrease the risk (Pourfarzi et al., 2009). gastric cardia was involved in 40.3% of patients with gastric adenocarcinoma, while the gastric fundus was involved in 3.7%, the gastric body in 49.1%, and the gastric antrum in 24.1%(Bafandeh and Farhang, 2009).
low level of awareness, lack of screening programs and subsequent late access to treatment, associated with poor survival of breast (Rezaianzadeh et al., 2009). obesity in postmenopausal women could increase risk of breast cancer (Montazeri et al., 2008)

the viral etiology (hepatitis B and C infections) in Turkish population is found to be an important factor in HCC development (Alacacioglu et al., 2008)
prostate cancer among our population was dramatically higher than in other countries of Asia (Akbari et al., 2008)

lower parity, early menarche and use of HRT were increased-risk factors but negative family history of cancer