RESEARCH COMMUNICATION

Iran Cancer Incidence should be Corrected for Under-Ascertainment in Cancer Cases in the Elderly (Aged 65+)

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Abstract

Objective: This article is to calculate corrected Iran cancer incidence by a novel method to compensate under-ascertainment of cancer cases in the very elderly (aged 65+). Study Design and Setting: Corrected age-specific rate for a certain cancer in age group 65+ was calculated from the age-specific rate of that cancer in age group 55-64 multiplied by the corresponding coefficient from reference cancer registry (sex- and age-specific coefficients from Finnish Cancer Registry, a nation-wide registry with high validity of data). All cancer data were obtained from GLOBOCAN 2002. Results: The crude rate (and number of new cases) for "All sites excluding skin" was 13.6% (men 18.7%; women 8.1%) under-estimated. The under-enumeration was 18.9% for the age-standardized rate (men 25.4%; women 11.8%). This means there were 58,000 new cancer cases (about 7,000 more than original) in 2002. Corrected incidence for the year 2050 was 26.1% higher (men 32.8%; women 17.3%) than the original estimate (49,000 more). Depending on cancer site and sex, percentage under-estimation varied remarkably. Conclusion: After correction, the estimates of number of new cases and incidence rates of Iran increase substantially. Without correction, cancer occurrence measures can be remarkably under-estimated which may lead to inadequate resource allocation for control measures.

Key Words: Neoplasms - incidence - rate - bias - under-ascertainment - old age - Iran

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Introduction

For most of the epithelial cancers, incidence rate increases as a power of age, and since most cancers are epithelial in origin, this pattern should be observed for "All sites" (at least after the age of 15). It is usual to see some decline in the oldest age groups (over 70). This is partly due to less efficient case ascertainment, some of which is a consequence of competing causes of mortality in the elderly (so that cancer is not recorded on death certificate), partly because of a decrease in the proportion of the population who have some predisposition to cancer (so that those who make it to old age are genuinely lower risk). Under-ascertainment must always be considered if there is an actual decline in rates (Parkin et al., 1994). Age-specific incidence curve is often used as an indicator of quality of cancer registry data in order to detect abnormal fluctuations in the anticipated patterns, including any fall-off in the incidence rate in older subjects (suggestive of under-ascertainment in oldest age groups) (Parkin et al., 2002). When the age-specific rates of elderly ages is combined and presented as only age group 65+, the decline due to under-registration cannot be seen. However, this may present as a failure to logarithmic increase in the age group 65+ compared to age group 55-64.

So far the under-registration for elderly ages has only been reported or disregarded by presenting age-specific curves only up to age 65 or 75 and there is no method available to correct this lacuna in the cancer registry data. This article is to use a novel method to compensate the defect in age-specific curve and try to estimate corrected crude incidence rate and number of new cases in Iran with less under-ascertainment bias. With respect to preparing future projections of incidence, when the effects of an aging population need to be taken into account, accurate age-specific rates in the upper age groups are important. This increases the significance of this correction method in the context of aging in the Iran population.

It seems cancer registries with higher percentage of microscopic verification (MV%, as an indicator of higher quality of cancer registry data) tend to have lower degree of under-registration in the oldest age groups (Figure 1). In other words, under-ascertainment in elderly seems to be inversely associated with quality and validity of cancer registry data. Therefore, different age-specific incidence pattern among registries with different quality of data may be mostly due to under-enumeration in the registries with lower quality of data, so role of birth cohort effect and other reasons of fall-off in the age-specific curve cannot completely justify this substantial difference in all cancer sites.

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Table 1. Iran Cancer Incidence before and after Correction for Under-Ascertainment, Male, 2002 and 2050

		2002									2050							
	Correction coefficient (k65+)[a]	Before correction			After correction			Increase due to correction			Before correction				After correction			Increase due to correction in cases or rate
Cancer site		Cases n	Rate[b] /10^5	ASR[c] /10^5	Cases n	Rate[b] /10^5	ASR[b] /10^5	In rate[b] %	In ASR[c] %		Cases n	Increase[d] %	Rate[b] /10^5	Increase[e] %	Cases n	Increase[f] %	Rate[b] /10^5	%
Oral cavity	2.74	665	1.8	2.9	793	2.2	3.7	19.2	25.4		2714	308.1	5.4	84.6	3583	351.8	7.2	32.0
Esophagus	2.31	3683	10.0	17.5	3949	10.7	19.1	7.2	8.8		16920	359.4	33.8	92.7	18724	374.2	37.4	10.7
Stomach	2.76	5393	14.6	26.1	6243	16.9	31.0	15.8	19.0		25704	376.6	51.4	97.1	31471	404.1	62.9	22.4
Colon/rectum	3.01	2046	5.5	8.3	2616	7.1	11.6	27.8	40.2		6956	240.0	13.9	68.3	10822	313.8	21.6	55.6
Liver	2.86	322	0.9	1.4	356	1.0	1.6	10.5	14.1		1264	292.5	2.5	80.5	1494	319.8	3.0	18.2
Pancreas	2.35	288	0.8	1.3	287	0.8	1.3	-0.3	-0.4		1254	335.5	2.5	90.0	1248	334.7	2.5	-0.5
Larynx	1.79	691	1.9	3.1	703	1.9	3.2	1.8	2.3		2873	315.8	5.7	83.7	2957	320.5	5.9	2.9
Lung	3.02	1502	4.1	7.2	1761	4.8	8.7	17.3	20.9		7096	372.4	14.2	96.1	8856	402.8	17.7	24.8
Melanoma	1.75	187	0.5	0.8	200	0.5	0.8	7.1	10.1		668	257.2	1.3	73.6	758	278.5	1.5	13.5
Prostate	3.56	1066	2.9	5.4	935	2.5	4.6	-12.3	-14.2		5634	428.5	11.3	109.3	4746	407.5	9.5	-15.8
Kidney	2.40	361	1.0	1.5	442	1.2	1.9	22.5	32.6		1193	230.5	2.4	64.1	1745	294.5	3.5	46.2
Bladder	3.70	1677	4.5	8.0	1904	5.2	9.3	13.5	16.6		7777	363.8	15.5	95.1	9316	389.4	18.6	19.8
Brain	1.29	1091	3.0	3.7	1099	3.0	3.7	0.8	1.3		2522	131.2	5.0	37.2	2579	134.6	5.2	2.3
Thyroid	1.19	364	1.0	1.2	349	0.9	1.1	-4.2	-7.2		881	141.9	1.8	42.3	777	122.8	1.6	-11.8
Non-Hodgkin's	2.35	1228	3.3	4.2	1324	3.6	4.8	7.8	13.2		3094	151.9	6.2	46.1	3746	182.9	7.5	21.1
Hodgkin's	1.74	662	1.8	2.2	739	2.0	2.6	11.6	20.8		1405	112.2	2.8	30.2	1927	160.8	3.9	37.2
Multiple myeloma	3.55	54	0.1	0.2	82	0.2	0.4	51.0	68.6		202	273.2	0.4	71.8	389	376.5	0.8	92.8
Leukemia	2.89	1540	4.2	4.8	1674	4.5	5.6	8.7	16.4		2989	94.1	6.0	25.2	3900	133.0	7.8	30.5
All sites but skin	2.97	27263	73.9	116.8	32353	87.7	146.5	18.7	25.4		105329	286.3	210.5	80.3	139882	332.4	279.6	32.8

a = Correction coefficient from Finnish male site-specific incidence rates 2002 (Finnish rate for age group 65+ divided by Finnish rate for age group 55-64). b = Crude incidence rate. c = Age-standardized rate usingWorld Standard Population. d = Increase in uncorrected number of new cases due to population growth in Iran, 2002-2050. e = Increase in crude incidence rate due to change in the age structure of Iran population, 2002-2050. f = Increase in corrected number of new cases, 2002-2050

Materials and Methods

The elderly under-registration appears mostly after age 75 years (Figure 1) but when only age group 65+ is presented (like what is presented in GLOBOCAN 2002), this may not be seen easily, however it may appear as failure to logarithmic increase in the age group 65+ compared to age group 55-64 (Figure 2).

To correct for under-ascertainment of age group 65+ for a certain cancer, age-specific rate of the same cancer in the same registry in the lower age groups (55-64) is multiplied by a corresponding coefficient from a reference high quality cancer registry (second columns in Tables 1 and 2). For this purpose, sex- and age-specific coefficients from the Finnish Cancer Registry are used since this registry is a well-known nation-wide population-based registry with high validity of data (Teppo et al., 1994). Moreover, Finns have rather high life expectancy so that proportion of elderly people in the Finnish population is quite remarkable, thus the random variation due to low number of cases in the oldest age groups does not affect Finnish data significantly. Moreover, data on vital status and cause-specific death are registered accurately in Finland.

The general formula for the calculation of corrected age-specific incidence rate is as follows:Corrected incidence rate for age group 65+ (CIR65+i) = k65i _ (IR55–64i), where k65i is the coefficient calculated by the rate of a specific cancer (i) in the reference (Finnish) high quality cancer registry in the age group 65+ divided

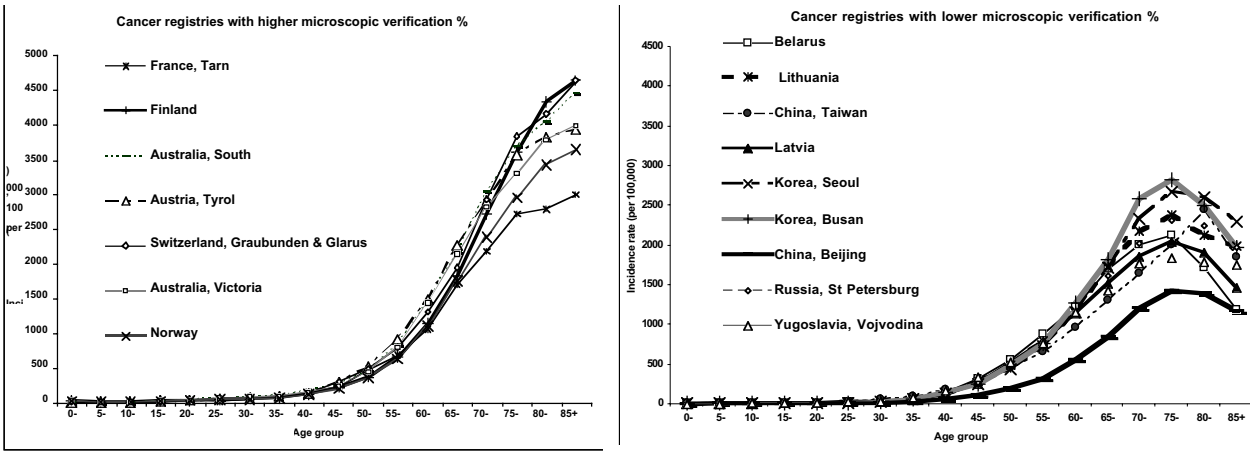

Figure 1. Age-specific Incidence Curves of "All Sites but Skin" Cancer in Some Cancer Registries with Microscopic Verification (MV) more than 90% and less than 75%, Male, 1993-97

Table 2. Iran Cancer Incidence before and after Correction for Under-Ascertainment, Female, 2002 and 2050

	2002									2050							
	Correction coefficient (k65+)[a]	Before correction			After correction			Increase due to correction		Before correction				After correction			Increase due to correction in cases or rate
Cancer site		Cases n	Rate[b] /10^5	ASR[c] /10^5	Cases n	Rate[b] /10^5	ASR[b] /10^5	In rate[b] %	In ASR[c] %	Cases n	Increase[d] %	Rate[b] /10^5	Increase[e] %	Cases n	Increase[f] %	Rate[b] /10^5	%
Oral cavity	2.17	398	1.1	1.7	414	1.2	1.8	4.1	5.1	1737	336.5	3.5	101.6	1858	348.3	3.7	7.0
Esophagus	3.23	3163	9.0	14.4	4805	13.6	23.1	51.9	60.2	14636	362.7	29.3	102.8	26667	455.0	53.3	82.2
Stomach	4.14	2450	6.9	11.1	3868	11.0	18.5	57.9	67.8	11402	365.4	22.8	106.2	21793	463.4	43.6	91.1
Colon and rectum	3.10	1595	4.5	6.5	2340	6.6	10.4	46.7	60.7	5663	255.0	11.3	74.5	11118	375.2	22.2	96.3
Liver	3.86	431	1.2	1.9	1063	3.0	5.3	146.6	173.1	1812	320.4	3.6	87.7	6440	506.0	12.9	255.4
Pancreas	3.49	181	0.5	0.8	169	0.5	0.8	-6.7	-7.8	886	389.4	1.8	115.9	797	371.9	1.6	-10.0
Larynx	2.88	124	0.4	0.5	163	0.5	0.7	31.4	37.9	523	321.8	1.0	92.3	808	396.1	1.6	54.6
Lung	2.33	506	1.4	2.2	499	1.4	2.2	-1.4	-1.7	2267	348.1	4.5	103.5	2216	344.1	4.4	-2.3
Melanoma of skin	1.67	168	0.5	0.6	185	0.5	0.7	10.2	14.2	560	233.4	1.1	75.2	686	270.5	1.4	22.5
Breast	1.01	4742	13.5	17.1	4814	13.7	17.4	1.5	2.2	12221	157.7	24.4	43.2	12751	164.8	25.5	4.3
Cervix uteri	1.70	1118	3.2	4.4	1285	3.6	5.3	15.0	20.0	3665	227.8	7.3	65.1	4891	280.5	9.8	33.5
Corpus uteri	1.29	244	0.7	0.9	250	0.7	0.9	2.4	3.6	611	150.5	1.2	38.4	655	162.0	1.3	7.2
Ovary etc.	1.43	638	1.8	2.3	777	2.2	3.0	21.8	31.8	1651	158.7	3.3	42.7	2668	243.5	5.3	61.7
Kidney etc.	2.72	258	0.7	0.9	316	0.9	1.3	22.4	32.4	734	184.4	1.5	55.2	1158	266.5	2.3	57.8
Bladder	3.09	406	1.2	1.9	574	1.6	2.8	41.5	47.8	1980	387.6	4.0	112.3	3213	459.4	6.4	62.3
Brain	1.07	776	2.2	2.6	824	2.3	2.9	6.2	9.8	1755	126.1	3.5	34.9	2109	155.8	4.2	20.2
Thyroid	0.72	721	2.0	2.4	709	2.0	2.3	-1.6	-2.6	1581	119.2	3.2	32.9	1494	110.6	3.0	-5.5
Non-Hodgkin's	1.81	633	1.8	2.3	658	1.9	2.4	3.9	5.8	1791	182.9	3.6	58.5	1971	199.7	3.9	10.1
Hodgkin's	9.42	272	0.8	0.8	458	1.3	1.8	68.5	122.6	453	66.5	0.9	12.8	1818	296.6	3.6	301.3
Multiple myeloma	3.55	29	0.1	0.1	51	0.1	0.2	76.1	89.7	130	347.0	0.3	99.2	291	470.5	0.6	124.8
Leukemia	3.29	1002	2.8	3.3	1116	3.2	3.9	11.4	18.1	2303	129.8	4.6	38.6	3137	181.1	6.3	36.2
All sites but skin	1.76	23557	66.8	93.1	25461	72.2	103.2	8.1	10.8	80800	243.0	161.5	73.5	94751	272.1	189.4	17.3

a = Correction coefficient from Finnish male site-specific incidence rates 2002 (Finnish rate for age group 65+ divided by Finnish rate for age group 55-64). b = Crude incidence rate. c = Age-standardized rate using World Standard Population. d = Increase in uncorrected number of new cases due to population growth in Iran, 2002-2050. e = Increase in crude incidence rate due to change in the age structure of Iran population, 2002-2050. f = Increase in corrected number of new cases, 2002-2050

by the reference (Finnish) rate in the age group 55-64 for the same cancer. IR55–64i is the age-specific incidence rate of the same cancer in the age groups 55-64 in the registry with under-ascertainment.

The first idea of this correction method was introduced by the author in his doctoral dissertation which was approved by the Faculty of Medicine, University of Tampere, Finland (Fallah, 2007). Elderly people aged 65 or more constituted 3.5% of Iran population in 2002, but according to prediction by United Nation (2006 revision), this proportion will increase to 17.8% in 2050. To calculate the crude rate for the year 2050, the age-specific rates in 2002 were weighted by the proportion of each corresponding age group in the predicted population for 2050 and weighted age-specific rates were summed exactly similar to direct method of standardization (Jensen et al., 1991) with this difference that instead of world standard population, predicted population age structure of Iran in 2050 was used. Crude rates for 2050 multiplied by the population of Iran in 2050 give the estimates of number of new cancer cases in 2050 accounting for change in the age structure of population and population growth rate (Tables 1 and 2). For simplicity and understanding of only the effect of correction on the future estimates, future cancer rates (2050) were not adjusted for change in the cancer incidence due to risk factors other than age. This means the cancer incidence trends had no role in the calculation of future estimates. All cancer data used in this article (Finland and Iran) were obtained from GLOBOCAN 2002 (Ferlay et al., 2004).

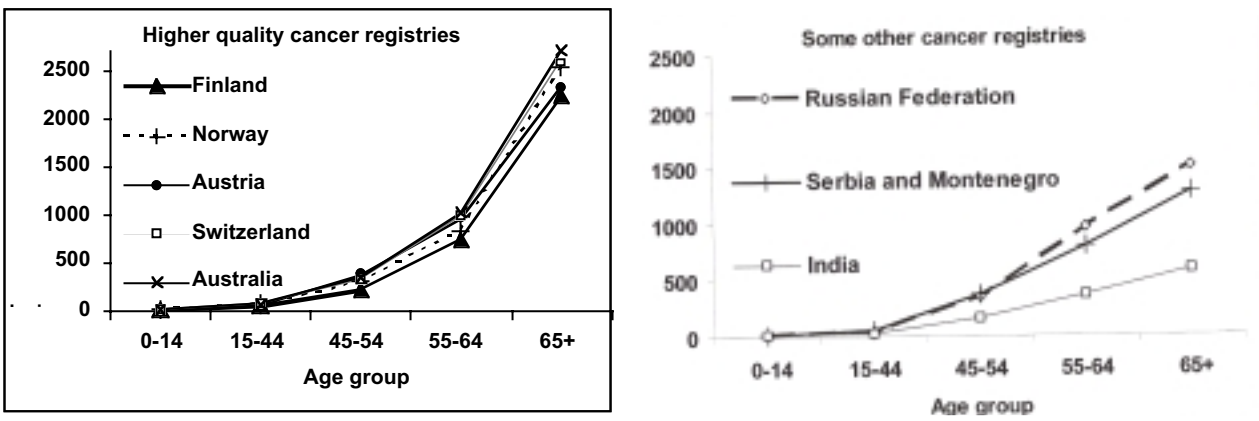

Figure 2. Age-specific Incidence Curves of "All Sites but Skin" Cancer in Some Higher Quality and Some Other Cancer Registries, Male, GLOBOCAN 2002

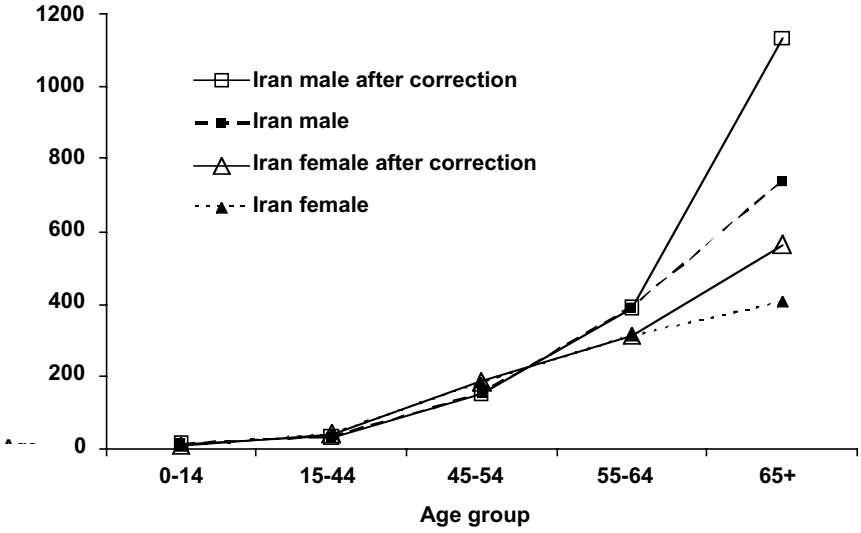

Figure 3. Age-specific Incidence Curves of "All Sites but Skin" Cancer in Iran before and after Correction for Under-ascertainment in the Elderly, 2002

Results

The age-specific incidence curves of cancers in both sexes and almost all the cancer sites in Iran demonstrated presence of under-ascertainment in the oldest age groups (Figure 3, Tables 1 and 2). The corrected age-specific rates were also calculated and corrected curves seemed more acceptable than the original curves with defect in logarithmic increase of incidences by age.

Comparing the corrected incidence rates for 2002 with the original ones showed that without correction, crude rates (and consequently number of new cases) for "All sites excluding skin" were around 13.6% (men 18.7%; women 8.1%) under-estimated. The increase was 18.9% for age-standardized rate (men 25.4%; women 11.8%). This means there were 58,000 new cancer cases [about 7000 (5000 men; 2000 women) more than the original estimation (Sadjadi et al., 2005)] in the year 2002. Corrected incidence for the year 2050 was approximately 26.1% higher (men 32.8%; women 17.3%) than the original estimate (49000 cases more). Depending on cancer site and sex, percentage of under-estimation varied remarkably. For instance, incidence rate of brain cancer in men and breast cancer in women did not substantially vary by correction while multiple myeloma increased about 51% in men and 76% in women in the year 2002 and around 92% and 125% in 2050 respectively. Liver cancer in women increased 147% in 2002 and 255% in 2050. Negative numbers in the column "Increase due to correction" in Table 1 and Table 2 show decrease by correction which should be ignored and considered as zero.

Discussion

Many cancers demonstrate fairly characteristic patterns of incidence with age. Of course, age-specific incidence curve for a single time period comprise data from many birth cohorts, and if there are changes in risk for specific cancers in different cohorts, these will be reflected in the shape of the age-specific curve. Such cohort effects can only be detected when data are available from several time periods (a minimum period of 15 years is a realistic goal). With this important reservation in mind, the shape of the curve of incidence with age is an important indicator of possible under-ascertainment (Parkin et al., 1994).

Using the abovementioned correction method on Iran cancer data showed that cancer occurrence measures of Iran, such as crude rate, age-standardized rate and annual number of new cases are obviously under-estimated and magnitude of this under-estimation varies by cancer site and sex. Rates in women were less under-estimated than men perhaps due to the health seeking behavior in them which leads to more cancer diagnosis of women in the health care facilities that are sources of cancer registry data. The amount of under-estimation is associated with proportion of elderly population so that the higher life expectancy, the higher level of under-registration in incomplete cancer registries and the more biased results in those registries.

Cancer rates in Iran were in average 8-19% under-estimated which is quite substantial. Given no change in the other risk factors of cancer than age and no population growth, number of new cancer cases will be more under-estimated when the future burden of cancer is calculated based on current under-estimated rates by only taking the change in the population age structure into account (like what is done for the calculation of cancer rates in 2050, Table 1 and Table 2). Significance of this correction increases when under-estimated information on cancer burden leads to allocation of resources to cancer control less than needed and it in turn may result in failure to reach expected goals. In addition, providing corrected estimates for each cancer site may help cancer registries in Iran to look for possible sources of defect in their case-finding. Correction for under-ascertainment is not recommended for cancers with unspecified code such as pharynx unspecified, other endocrine, and leukemia unspecified because proportion of unspecified cancers is usually different between cancer registries so that higher

quality registries have less unspecified cancers. Combining specified and unspecified leukemias allows correcting for under-ascertainment in this particular case so that corrected incidence rate can be calculated for leukemia (all leukemia subtypes together) instead. Due to high random variation, correction for under-ascertainment is also not recommended for very rare cancers like placenta or immunoproliferative disorders.

There are some conditions behind use of this correction method; first assumption is the birth cohort effect for some particular cancers such as lung or breast cancer in Iran is supposed to be similar to the reference high quality (Finnish) cancer registry. Second, if the corrected incidence rates are less than the original ones, it means the original rates are not under-registered and the corrected rates should not be preferred in this case (e.g. pancreas and thyroid cancer in both sexes, prostate cancer in men, and lung cancer in women, Table 1 and Table 2). In general, the correction is not recommended for very rare cancer sites but is highly recommended for the leading sites particularly for "All cancer sites".

For the correction, Finnish data was used as a high quality reference registry; however, there are some other high quality registries that can be used such as Switzerland (Basel) and Australia, (Western and South). A comparison was made between coefficients k65+, for "All site cancer" among these four potential reference registries, results were quite convincing that they are similar and Finland was a good choice among them with coefficients at the average level of these four registries.

The Iran cancer data was used for this study, however, application of this correction method is not limited to Iran or similar countries to Iran and it can be used in any registry with under-registration in older ages which may result in different percentage of increase in rates depending on the proportion of older people in the population and the magnitude of under-ascertainment in the original data. Even some registries with very high level of microscopic verification (such as French registries with MV=99%) or US cancer registries (SEER program with MV=94%) may benefit from this method.

The correction for under-ascertainment is neither using Finnish rates for another registry nor age-standardization by Finnish age-structure. It is simply the answer to the question that what would be the estimate of cancer incidence if the registry data had the same completeness as Finnish data using age-specific incidence rates of a younger age group (55 to 64 years) in the incomplete registry multiplied by a sex- and site-specific coefficient from Finnish data to predict the rate in oldest age group (65+).

In conclusion, after correction for under-ascertainment in elderly age groups, the estimates of number of new cases and incidence rates of Iran increase substantially especially in men. With respect to preparing future projections of incidence, when the effects of an aging population need to be taken into account, accurate age-specific rates in the upper age groups are important. Without correction, cancer occurrence measures can be remarkably under-estimated which may lead to inadequate resource allocation for control measures.

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