

## Cancer Incidence and Prevalence in Isfahan: Application of Mortality Data to Estimates and Projects for the Period 2001-2015

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### ABSTRACT

**Background:** The aim of this study was to show up-to-date estimates of incidence and prevalence in Isfahan for all cancers, except non-melanoma skin cancer over the period 2001-2010 to provide projections up to 2015, based on a statistical method that uses mortality and cancer patients' survival data.

**Methods:** Mortality data in Isfahan province were collected from various sources such as hospitals, medical forensic, cemetery, and health centers. In addition, population data by sex, age, location, and calendar year in the period of 2001-2010 were acquired from the Statistical Center of Iran. Relative survival probabilities for all cancers combined and for selected specific cancers were estimated based on observed cancer death and expected mortality data. Incidence and prevalence estimates were computed with Mortality-incidence Analysis Model (MIAMOD) method.

**Results:** The estimated age-standardized cancer incidence rate had higher increase rate for urban females than for males. Also, the number of prevalent cancers was higher among females, which was mostly due to better cancer survival rates in women. Age-adjusted incidence was estimated to increase by 6.9 and 8.7 per 100000 annually, between 2001 and 2015, in males and females, respectively. The prevalence is to increase by 24 and 40 and mortality by 2.8 and 2.5 per 100000 between 2001 and 2015.

**Conclusion:** The present study does not only show the incidence and prevalence estimates of all cancers combined, but also gives information about cancer burden, which can be used as a bases for planning healthcare management and allocating recourses in public health.

**Key words:** Cancer, incidence, mortality, prevalence, relative survival

### INTRODUCTION

In recent century, chronic diseases including cancers raised as one of the most challenging public health issues in developing countries.<sup>[1]</sup> About half (51%) of cancer incidence worldwide was accounted for developing countries in 1975. This proportion

was increased to 55% in 2007 and is projected to reach 61% by 2050.<sup>[2]</sup> The raising of the global burden of cancer and its disproportionate impact in low-middle-income countries is simultaneous with both demographic changes in high-risk population and by temporal variation in major risk factor.<sup>[3]</sup> According to the national death registry in Iran, cancer is the third cause of death after coronary heart disease, accidents and other phenomena.<sup>[4,5]</sup> It was reported that cancer incidence rate in Iran is 98 to 100 per 100000 population annually.<sup>[4]</sup> Updating cancer burden indicators such as incidence, prevalence, mortality, and survival at a national and regional level is essential both for research purposes and for planning and assessment of programs for cancer control.<sup>[1,6,7]</sup> The knowledge of these indicators is limited to the national level and should also be calculated in a regional scale. As cancer levels and trends are often geographically heterogeneous within countries, appropriate local information for planning care policies and allocating resources are needed increasingly.<sup>[8]</sup> In most countries, only mortality data for whole the population is published systematically from national and regional official statistics with delay of 2-3 years. Other important indicators are collected by population-based cancer registry (PBCRs) that covers only small fraction of the population. Usually, incidence and prevalence are published 4-6 years after primary data gathering.<sup>[1,7]</sup> These population-based cancer statistics are valuable and reliable sources of information. However, because of partial coverage, they don't statistically represent a sample for the total population; they can prepare only partial pictures of risk patterns and trends at a national and regional level.<sup>[6,8]</sup> Unfortunately, there are a few cancer control programs in Iran as PBCRs cover only 16% of the population.<sup>[9]</sup> Isfahan province is the biggest and most important area that is located at a desert border in the center of Iran. Population-based data from Isfahan cancer registry has been collected since 2005. It covers all districts of Isfahan, except 2 cities Kashan and Aran-Bidegol.<sup>[10]</sup> The history of cancer registry in Iran was published previously.<sup>[9,11]</sup> Cancer incidence data in Isfahan registry has been collected according to the Iran ministry of health guideline and published for first time in 2011. It showed a dramatically increase in cancer incidence in Isfahan.<sup>[10]</sup> However, this estimation could be substantially subordinated

to underestimation. It is because registration completeness is imperfect compared with those registries in European countries.<sup>[12]</sup> To access cancer trends and estimations of health care demand in a population which are not covered completely by PBCRs, statistical models could be used.<sup>[8,13]</sup> The statistical model fitted to empirical data could produce epidemiological indicators at a national and regional scale. Moreover, it could be projected them to the near future.<sup>[13-15]</sup> The method was validated and applied for cancer indicator estimation by other researchers in European countries, i.e. Italy and Spain.<sup>[6,7,16-20]</sup>

The aim of this study was to show up-to-date estimates of incidence and prevalence in Isfahan for all cancers combined, except non-melanoma skin cancer over the period 2001-2010. It also provides projections up to 2015, based on a statistical method that uses mortality and cancer patient survival data.

## METHODS

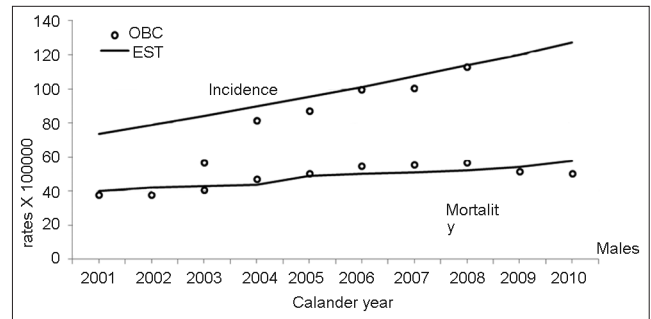
To perform the study, we used mortality data from two sources; ministry of health death registration system and national death registration office. Mortality data in Isfahan province is collected from various sources such as hospitals, medical forensic, cemetery, and health centers. These resources are reliable, and mortality from cancerous disease can be affected only by other non-cancer causes of death. However, this case is negligible in Isfahan. We considered mortality information for all cause, and all cancers combined with the exception of non-melanoma skin cancers (International Classification of Disease for Oncology 3<sup>rd</sup> revision: Cods C00-C80 excluding C44).<sup>[21]</sup> In addition, population data by sex, age, location, and calendar year in the period of 2001-2010 were acquired from the Statistical Center of Iran. Relative survival probabilities for all cancers combined and for selected specific cancers were estimated based on observed cancer death and expected mortality data. Observed cancer survival rate was derived from passive follow-up by comparison of two sources of data, the death certificate of vital statistics and patient registry data from registered cases by the actuarial method.<sup>[22]</sup> This data was stratified by period of diagnosis into two-year interval and following age group diagnosis: 15-44, 45-54, 65-74, and 75-99 years.

Incidence and prevalence estimates were computed with MIAMOD (Mortality-incidence Analysis Model) method. That is a back calculation approach to the estimation and projection of chronic degenerative disease from mortality and survival data. In this method, the registration period must be adequately long (at least 10 years). The disease under survey must be chronic irreversible, such a cancers.<sup>[13,15,17]</sup> Parameters used in the method are mortality by age, period and birth cohort, survival, and mean population. This method is based on the mathematical relationship between mortality, prevalence, incidence, and survival when putative disease is posited to be irreversible. Incidence was modeled as polynomial function of age, period, and birth cohort covariates. The incidence model parameters were back calculated using Poisson maximum likelihood regression based on observed mortality data. Incidence in future years can be projected after last year of observed mortality data, based on age-period-cohort covariate. Furthermore, mortality and prevalence are consequently forward projected by MIAMOD. Ad-hoc software named MIAMOD/PIAMOD (Mortality-incidence Analysis Model/Prevalence-incidence Analysis Model) was developed and used for producing estimation.<sup>[7,8,14]</sup>

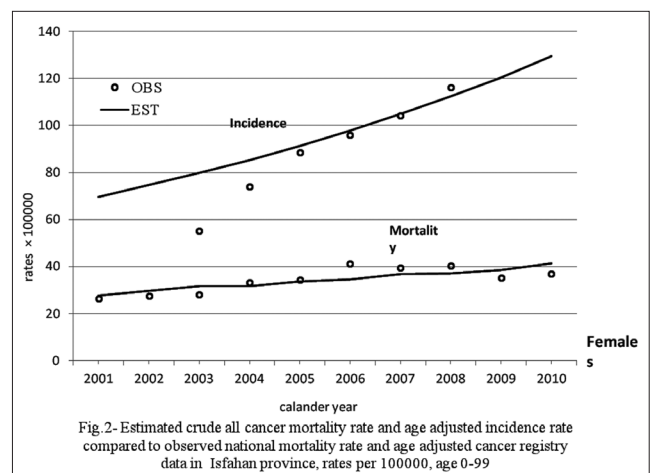
## RESULTS

Incidence and prevalence rates for all cancers combined, except non-melanoma skin cancer was estimated for males and females resident in urban and rural district of Isfahan province using MIAMOD method. Figures 1 and 2 present estimated crude mortality and age-specific incidence rates compared with observed national mortality and empirical incidence data by sex. Residual error is generally low, and goodness of fit obtained by MIAMOD method was acceptable.

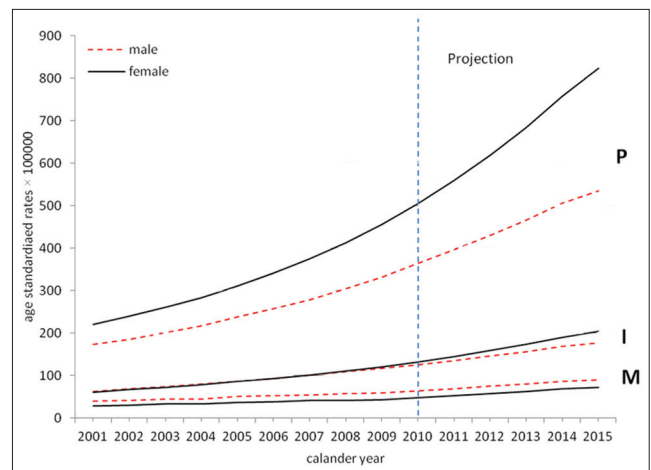
Figure 3 presents trend of standardized morbidity rate in urban area. The estimated age-standardized incidence rate (ASIR) had higher increase rate for urban females than for males. Also, the number of prevalent cancers was higher among females, which was mostly due to better cancer survival rates in women. Estimates show that annual incidence rate among urban males and a female has increased in recent years and will continue in the future. As a consequence, dramatic increase in prevalence over time is expected. However, the cancer trend



**Figure 1:** Estimated crude all cancer mortality rate and age-adjusted incidence rate compared to observed national mortality rate and age-adjusted cancer registry data in Isfahan province, rates per 100000, age 0-99 for females



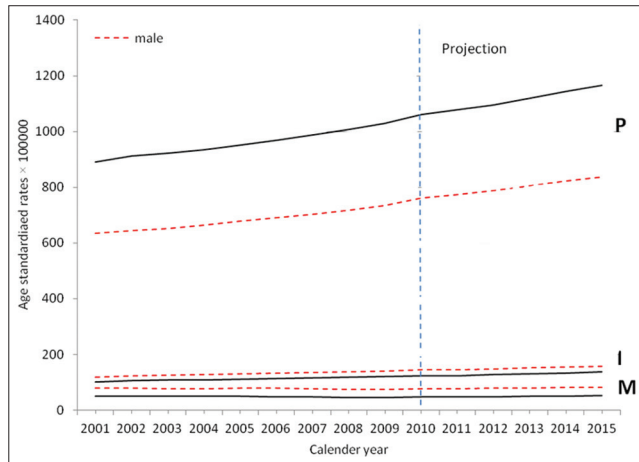
**Figure 2:** Estimated crude all cancer mortality rate and age-adjusted incidence rate compared to observed national mortality rate and age-adjusted cancer registry data in Isfahan province, rates per 100000, age 0-99 for males



**Figure 3:** Estimated mortality (M), Incidence (I) and Prevalence (P) for all cancer in Isfahan Urban area by gender. Age standardized rates (World population) per 100000, 0-99 age

in females has a sharper slope than males, hence ASIR after 2007 in females has passed males. In 2001, ASIR for males was about 3% more than females, whereas in 2015, ASR for females will be about 15% more than males. Unlike urban in rural districts, cancer incidence rate in males is more than in females with a constant rate (about 16%) in the whole study period, but the estimated prevalence rate like in urban areas for females is more than in males [Figure 4]. Generally, in recent years, the estimated incidence in rural district was higher than in urban areas, but in the projection period, the situation will be inverted. Prevalence was estimated in rural areas more than in urban district in whole study period.

Age-adjusted incidence was estimated to increase by 6.9 and 8.7 per 100000 annually between 2001 and 2015 in males and females, respectively, the prevalence is to increase by 24 and 40 and mortality by 2.8 and 2.5 per 100000. Table 1 shows annual percentage change (APC) of incidence, prevalence, and mortality for males and females adjusted for age and corresponding confidence interval for periods 2001-2010 and 2011-2015



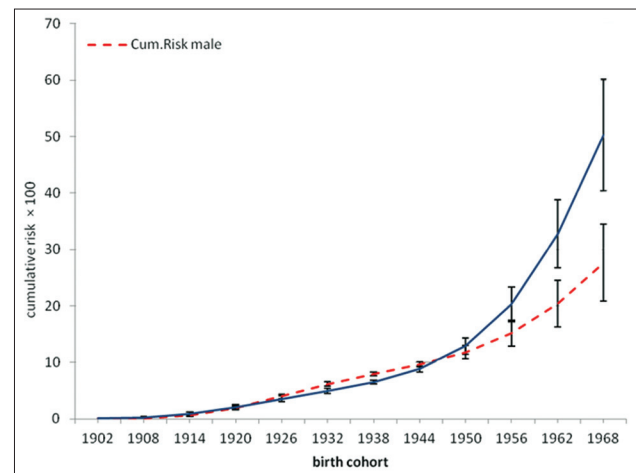
**Figure 4:** Estimated mortality (M), Incidence (I) and Prevalence (P) for all cancer in Isfahan Rural area by gender. Age standardized rates (World population) per 100000, 0-99 age

separately. Overall, 4435 new cancer cases and 2241 cancer deaths in males are estimated to occur in Isfahan province in the year 2015, which will lead to 14912 prevalent cancer cases. In this way, 4703 new cancer incident cases and 1666 cancer deaths for females are estimated to occur, which will lead to 21035 prevalent cancer cases.

The expected cancer prevalence rate for the year 2015 increased 3 times for urban areas in males and about 3.7 times in females with respect to 2001. In rural districts, prevalence also increased in males and females about 1.5 and 1.3 times, respectively. This could be attributed to the population aging and cancer survival promotion.

Table 2 shows age-specific observed mortality, estimated incidence, and prevalence rates for the years 2001, 2005, and 2010. The respective projections are presented for the year 2015. Age-adjusted mortality, incidence, and prevalence increased by 80%, 130%, and 150% for males from 2001 to 2015, respectively. The rate also increased by 100%, 170%, and 190% for females, respectively.

Figure 5 presents lifetime risk for developing all cancers combined with corresponding standard error based on birth cohort until age 74. Cumulative



**Figure 5:** Estimated cumulative risk and correspond standard error of all cancers combined by birth cohort, age 0-74 by gender

**Table 1:** Annual percent change for Incidence (IAPC), Prevalence (PAPC), and Mortality (MAPC) in Isfahan by gender

	Sex	IAPC (95% CI)	PAPC (95% CI)	MAPC (95% CI)
2001-2010	Males	1.056 (1.04, 1.07)	1.063 (1.05, 1.08)	1.034 (1.01, 1.05)
	Females	1.064 (1.05, 1.08)	1.069 (1.05, 1.08)	1.038 (1.02, 1.06)
2011-2015	Males	1.059 (1.05, 1.07)	1.065 (1.06, 1.07)	1.056 (1.05, 1.07)
	Females	1.081 (1.07, 1.09)	1.083 (1.08, 1.09)	1.075 (1.06, 1.08)



**Table 2:** Age-specific observed mortality, estimated incidence, and prevalence rate in Isfahan province by gender, rates×10000

Age (year)	2001			2005			2010			2015		
	Mort	Inc	Prev	Mort	Inc	Prev	Mort	Inc	Prev	Mort	Inc	Prev
Male												
40-44	1.2	3.7	19.3	1.7	4.7	24.8	1.5	6.3	34.7	3.1	8.3	47.8
45-49	4.2	5.6	22.8	4.6	6.8	28.7	5.2	9.0	40.1	6.5	12.2	57.1
50-54	5.9	8.8	29.0	7.6	10.4	35.7	7.3	13.4	48.6	9.7	17.7	68.5
55-59	8.9	14.5	40.7	10.8	16.7	48.5	9.3	20.5	65.2	14.9	26.3	88.6
60-64	18.4	24.0	61.8	14.7	27.5	72.6	18.7	32.7	95.2	23.0	40.2	125.9
65-69	28.7	38.7	94.4	34.5	45.9	118.7	23.0	54.1	155.4	36.7	63.6	190.7
70-74	32.0	56.5	124.6	40.6	72.1	166.8	44.6	89.4	235.0	61.4	105.5	319.0
75-79	49.6	73.1	150.4	78.3	105.8	244.4	65.7	144.4	390.4	91.2	178.2	514.7
80-84	31.9	81.6	151.4	91.7	141.5	292.4	72.7	221.1	545.5	152.7	300.9	892.5
85-89	57.9	81.0	123.3	83.1	172.0	296.3	255.2	341.4	719.9	263.6	513.7	1217.7
90-94	47.4	72.3	86.1	44.8	196.8	267.6	199.4	484.1	823.4	415.8	845.2	1853.9
95-99	74.6	62.4	57.4	47.1	210.5	219.5	88.9	685.7	903.1	510.2	1053.4	351.8
0-99 crude rate	3.8	6.4	21.3	5.0	8.4	27.7	5.1	11.4	39.2	8.9	17.6	59.2
0-99 (world standard population)	4.8	7.4	22.7	5.7	9.5	29.3	6.6	12.7	41.5	8.7	17.0	56.9
0-99 cases	874	1382	4620	1112	1904	6275	1384	2731	9402	2241	4435	14912
Female												
40-44	2.2	5.8	24.0	2.6	8.5	35.6	2.8	13.7	60.4	4.7	21.3	100.0
45-49	2.9	8.0	31.9	4.9	11.5	46.1	5.4	18.6	79.0	8.2	30.0	133.4
50-54	4.4	11.3	43.7	7.4	15.4	60.0	6.3	24.0	100.0	11.3	38.6	172.9
55-59	6.9	15.9	61.8	7.5	20.6	81.1	8.8	30.1	127.9	17.1	46.7	205.2
60-64	9.2	22.3	87.0	12.4	27.5	107.8	13.9	37.8	160.3	21.4	55.2	253.5
65-69	18.4	31.0	125.4	18.8	37.5	156.8	22.3	48.5	213.6	30.6	65.9	295.7
70-74	24.3	41.4	162.6	24.3	50.7	204.1	19.4	64.0	271.8	38.6	82.1	383.5
75-79	26.6	51.4	199.1	42.5	67.3	270.2	47.4	86.7	375.5	55.1	109.0	473.5
80-84	21.9	57.6	192.6	44.8	85.6	288.0	43.8	118.5	426.8	76.5	154.1	650.1
85-89	38.9	57.7	165.1	52.1	103.0	300.6	107.3	172.5	549.4	112.4	234.8	735.1
90-94	37.0	50.2	110.6	11.9	114.4	259.4	61.5	235.9	593.3	169.3	372.4	1108.1
95-99	0.0	34.0	55.2	85.5	112.5	183.4	16.0	310.4	562.2	212.3	468.5	182.9
0-99 crude rate	2.6	6.1	26.9	3.4	8.0	35.4	3.7	11.7	52.9	6.9	19.5	87.1
0-99 (world standard population)	3.3	7.0	29.5	3.9	9.1	38.9	4.7	13.0	57.3	6.8	19.1	85.4
0-99 cases	548	1265	5584	744	1746	7694	846	2661	12082	1666	4703	21035

risk increased significantly in females more than in males.

## DISCUSSION

For validation purposes, we applied age-adjusted cancer incidence from empirical data collected by Isfahan cancer registry. Estimated rate by MIAMOD method for all cancer combined in 2003 was very different from the corresponding observed data. The differences for males and females were respectively 48% and 45% more than the empirical data, which was due to the imperfect data registry.

Until 2008, the discrepancies were descended. In 2008, the difference for men was disappeared, and for women reversed (estimated incidence about 3% less than observed incidence). However, the incidence trends show a continuous improvement in cancer registration as shown in Figures 1 and 2. Interpretation of current trend of all cancers combined is very difficult due to the multiplicity of disease nature altogether. In recent years, great changes in lifestyle such as high-calorie foods consumption and immobility, smoking habits, socio-economic factors, and population aging has increased life-related disease such as cancers.

This study presents no sex-related diversity in the incidence pattern. While rates for females, similar to those in European countries, continue to rise, rates for males continue to rise too. This trend is exactly unlike those for men in European countries.<sup>[23]</sup> Urbanizing and emersion of young workers from rural district and the settlement of old age and patient people are a characteristic of developing countries, which reduced rural population. This is a case for Isfahan province, which should be considered as an agent for the incredible increase in cancer prevalence in the rural area.<sup>[24-27]</sup>

As shown in Figures 3 and 4, estimated age-adjusted prevalence in rural areas was more than in urban areas. However, mortality and incidence rates have a steeper trend in urban areas and surpass rural areas for the projection period. This seems to be related to the poor access of healthcare and screening services in rural areas, lack of insurance for the individual residents in rural areas, lack of basic knowledge about cancers and finally, the physician in the rural area may not encourage to screen as well as the physician, which lived in urban community.<sup>[28-31]</sup>

In some European countries, the cancer trend is decreasing for males and increasing for females; however, cancer's estimation for female is lower than for males in developed countries.<sup>[6-8]</sup> In these studies, trends were completely different from those in high-income countries.

The increased estimated age-adjusted incidence in females than in males in urban areas from 2007 could be attributed to the sex-specific cancer cases such as uterus, ovary, and breast. In recent years, breast cancer has increased extremely and is first leading cancer cause in Isfahan's females. Also, because of the elimination of non-melanoma skin cancer in the present study, ASR of all cancers combined was more declined for men than for women. However, estimated cancer trends were completely compatible with current trend in Isfahan.<sup>[10,32-37]</sup>

Cumulative lifetime risk is an incidence estimate of all ages during life. Thus, reported standard error in Figure 5 was the combination of uncertainty from each age-specific estimate. Although the age-specific standard errors are very small, they become large when aggregated for each person up to the age of 74. Standard error of incidence and prevalence estimates were generally small and

were not reported in the paper. Cumulative risk for younger cohorts was more increased than for older. Albeit the increased risk was more significant for females from cohort of 1958 forward as in cohorts of 1968, cumulative risk in females was about 2 times more than for males. In general, this increased risk in cancer incident is possibly due to the changes in lifestyle and population aging. More increased risk for developing cancer in females may be due to the women's reproductive history and lifestyle factors, which modify the endogenous sex hormone.<sup>[38]</sup> Increasing woman's knowledge about self-examination, haunt to health services and consequently more communions in screening programs and also promotions in diagnostic technique such as mammography and pap smear are other factor contributed to the increase cancer risk in females.

In the year 2015, there will be 9138 new patients with cancer diagnosis for the first time and will requires a treatment and 3907 patients that will die from cancer and, therefore, will require finish surveillance cares. Approximately, 37535 of the cases will be diagnosed with cancer within 5 years up to 2015 and thus require major health care recourses.

The health care system is too faced with expected increases in the cancer burden in the near future. Prevention is the only possible way to limit the occurrence of new cancer cases in the population and to prohibit inducing extra burden of prevalent cases that also causes great deficiency in quality of life plus to the major health care demand.<sup>[17]</sup> Performing prohibitory action against prevalence of risk factors such as cigarette smoking and improving health dietary production plays an important role in reducing the increased number of related cancers i.e. respiratory and digestive cancers. A lot of therapeutic and diagnostic recourses could be saved with respect to the efficient preventive action just like one that occurs in US leading to the decline in lung cancer incidence since 1990.<sup>[39]</sup>

The present study does not only shows the incidence and prevalence estimates of all cancers combined, but also gives information about cancer burden, which can be used as a bases for planning healthcare management and allocating recourses in public health.

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