RESEARCH ARTICLE

Can We Rely on GLOBOCAN and GBD Cancer Estimates? Case Study of Lung Cancer Incidence and Mortality Rates and Trends in Iran

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Abstract

Background: Around half of input data in the global burden of disease cancer collaboration (GBD-CC) and GLOBOCAN projects come from low quality sources, mainly from developing countries. This may lead to loss of precision in estimates. Our question was: Are the absolute values and trends of the GBD-CC and GLOBOCAN estimates for lung cancer (LC) in Iran consistent with available statistics?. Materials and Methods: Incidence and mortality statistics were extracted from national reports (N.IRs & N.MRs) and GBD-CC (GBD-incidence & mortality) and GLOBOCAN databases for 1990-2013 where available. Trends were analyzed and absolute values and annual percentage changes (APCs) were estimated and compared. Incompleteness of case ascertainment at the Iranian national cancer registry and Iranian national civil registration was assessed for better understanding. Results: Trends of N.IRs were significantly rising for males (APC: 19.4; 95% CI: 12.5-26.7) and females (23.2; 16.0-30.8). Trends of GBD-incidence were stable for males (-0.2; -1.5-1.1) and females (-1.0; -2.3-0.4). Absolute N.IRs were less than GBD-incidence steadily except for 2009. Trend of N.MRs was increasing up to 2004, but stable thereafter. Trends of GBD-mortality were also stable. Absolute N.MRs were less than GBD-mortality for years up to 2003 and more than GBD-mortality since 2005. The estimates of GLOBOCAN were more than N.IRs and N.MRs. Conclusions: The GBD-CC and GLOBOCAN values for LC in Iran are underestimates. Generation of data quality indices to present along with country specific estimates is highly recommended.

Keywords: GBD-CC - GLOBOCAN - cancer - incidence- mortality - data quality - lung cancer - Iran

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Introduction

The GLOBOCAN and Global Burden of Disease-Cancer Collaboration (GBD- CC) are the first two major efforts to measure global burden of cancer. Both of them have used cancer incidence and mortality statistics from different sources including published data in the Cancer Incidence in Five Continents (CI5) reports, mainly for developed countries, and also other national or subnational reports, mainly for developing countries (GLOBOCAN 2012, 2013a; Fitzmaurice et al., 2015). However, most data which are not eligible to publish in CI5, suffer from serious data quality shortages.

As a reality, low qualified input data, which is not avoidable in global scope, may leads to lose of precision of output estimates. Considering questionable quality of around half of data which has been used by the GBD-CC and GLOBOCAN, a debate arises: "May the GBD-CC and GLOBOCAN estimates have been affected by low qualified input data?" The debate continues after surprising estimates presented in "The global burden of cancer 2013" regarding cancer incidence and mortality in Iran. It reports the highest decrease in cancer incidence and also one of the highest decease rate in cancer mortality for Iran during recent decades (Fitzmaurice et al., 2015). How is it possible? Iran is experiencing rising trends of incidence and mortality for the most of common cancers (Farahmand et al., 2009; Pourhoseingholi et al., 2011; Haidari et al., 2012; Rahimi and Heidari, 2012; Fazeli et al., 2013; Safavi et al., 2015), population ageing (Pourmalek et al., 2009; Noroozian, 2012) and rising prevalence of unhealthy lifestyle (Mohammad et al., 2001; Kelishadi et al., 2008; Farzadfar et al., 2011), and also absence of an strong long-term cancer control program.

We believe that this inconsistency may be a result of lack of a reliable population- based representative cancer registry in Iran and consequently, imprecise data which has been used by GBD-CC. Herein, the GLOBOCAN and GBD-CC estimates of lung cancer incidence and mortality in Iran were compared with available national and local data from Iran, to answer if the estimates are consistent with actual data?

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Materials and Methods

Data sources

Incidence rates (IRs) for LC were extracted from 1) the Iranian national cancer registry (IR.NCR) reports for 2003- 2009 (2004; 2008; Mousavi et al., 2009; 2010; Khosravi A et al., 2013; Vahedi et al., 2013); 2) the official annual reports by known ongoing regional population-based cancer registries including Golestan, Ardabil and Tehran (Sadjadi et al., 2003; Semnani et al., 2007; Semnani et al., 2008; Babaei et al., 2009; Mohagheghi et al., 2009; Semnani et al., 2010; Roshandel et al., 2012); and 3) Published articles from population-based cancer surveys conducted at Semnan, Kerman and East Azerbaijan (Babaei et al., 2005; Somi et al., 2008; Sajdiadi A, 2007). Estimated age- standardized incidence rates (ASIRs) by the GLOBOCAN 2002, 2008, 2012 were also extracted (2012, 2013c).

Mortality rates of LC were extracted from the Iranian national civil registration (IR.NDR) reports for 1995- 2010 and official reports by the Golestan and Ardabil population based cancer registries if were available (2004; 2008; Mousavi et al., 2009; 2010; Khosravi et al., 2013; Vahedi et al., 2013). Estimated mortality rates for Iran were also extracted from the GBD database for 1990- 2013 and also the GLOBOCAN for 2002, 2008, 2012 (2012, 2013c).

Data manipulation and analysis

Data were manipulated in three main sections. In first section, IRs and crude mortality rates (MRs) (hereafter: N.IRs and N.MRs) were retrieved by year and gender from IR.NCR and IR.NDR reports and entered into the Joinpoint regression program 4.0.1. Possible change points were identified and annual percent changes (APC) were estimated after removing the effect of the major registration improvements (at 2007-2009 for N.IRs and at 2004-2005 for N.MRs). Observed and predicted N.IRs and N.MRs were graphed using MS Excel software.

In second section, estimated MRs of LC in Iran were also retrieved in MS Excel software from the GBD database. These MRs (hereafter: GBD-mortality) were used to calculate IRs by year (hereafter: GBD-incidence), using following equation (Parkin and Bray, 2009):

GBD-Incidence=GBD-mortality/(1- survival) Equation 1

Five-year survival rate of the LC in Iran was assumed 1% at 1990, with a 0.5% increase per year, up to 12.5% at 2013 (Zahir and Mirtalebi, 2012; Gelband et al., 2015). Trends of the GBD-incidence and mortality rates were analyzed using logarithmic Poisson Joinpoint regression and APCs were estimated by genders.

In last section, the extracted data from the GLOBOCAN and regional registries or surveys were tabulated, in three time periods. Mortality: Incidence (M:I) ratios for regional and national registries and completeness of case ascertainment at the IR.NCR were estimated based on the following equation, if applicable:

C= N.ASIRs/ Average of reported local ASIRs Equation 2

Results

Trends of N.IRs were significantly rising for males (APC: 19.4; 95% CI: 12.5, 26.7) and females (APC: 23.2; 95% CI: 16.0, 30.8), even after exclusion of effect of registration improvement. There was a significant change point in trend of N.IRs in males at 2007. Trends of GBD-incidence were stable for males (APC: -0.2; 95% CI: -1.5, 1.1) and females (APC: -1.0; 95% CI: -2.3, 0.4) (Fig 1, A). Trend line of N.IRs caught the trend line of GBD- incidence at 2009. Accordingly, absolute N.IRs were steadily less than GBD-incidence up to 2009.

There was a significant change point in trends of N.MRs of LC at 2004. Trends of LC mortality in males and females were increasing up to this point, but trends were stable for males (APC: 0.06; 95% CI: -4.0, 3.3) and females (APC: -0.09; 95% CI: -3.2, 3.4) since 2004. Trends of GBD-mortality were stable for males (APC: -0.7; 95% CI: -2.0, 0.5) and decreasing for females (APC: -1.5; 95% CI: -2.8, -0.2) (Figure 1B).

Trend lines of N.MRs and GBD- mortality crossed each other at 2004. Accordingly, absolute N.MRs were less than GBD-mortality for years up to 2003 and more than GBD-mortality since 2005.

The GLOBOCAN estimates for ASIRs increased slowly in males and females from 2002 to 2012 (Table 1). There was no local report for 2008 and thereafter, but in earlier years, each of the Golestan and Ardabil registries reported slightly increasing trends of ASIRs, up to 2008 (Table 1). Based on the Golestan registry for 2004- 2007, trend of MRs had been decreasing in males, and increasing in females.

Maximum M:I ratios were 0.47 in Golestan registry;

Table 1. Available data on Lung Cancer Incidence and Mortality in Iran

Registry	Male						Female					
	1996-2004		2005- 2008		2009-2013		1996-2004		2005- 2008		2009- 2013	
	I	M	I	M	I	M	I	M	I	M	I	M
Ardabil	7.95	-	10.8	6.7	-	-	3.59	-	4.8	3	-	-
Kerman	7.1	-	-	-	-	-	2.4	-	-	-	-	-
Golestan	10.7	5	17.1	4.4	-	-	5.3	1.4	7.2	1.6	-	-
Semnan	9.19	-	-	-	-	-	4.57	-	-	-	-	-
Tehran	8.1	-	-	-	-	-	3.6	-	-	-	-	-
East Azerbaijan	-	-	9.58	-	-	-	-	-	3.7	-	-	-
National	3.28	7.49	4.63	9.4	11.3	-	1.23	3.33	2.04	3.7	4.37	-
GLOBOCAN	7.2	-	9.1	-	10.3	7.7	2.2	-	3.5	-	5	3.8
Completeness*	0.38		0.37		-	-	0.315		0.39		-	-

*Completeness= N.ASIRs/ Average of ASIRs by local population- based reports

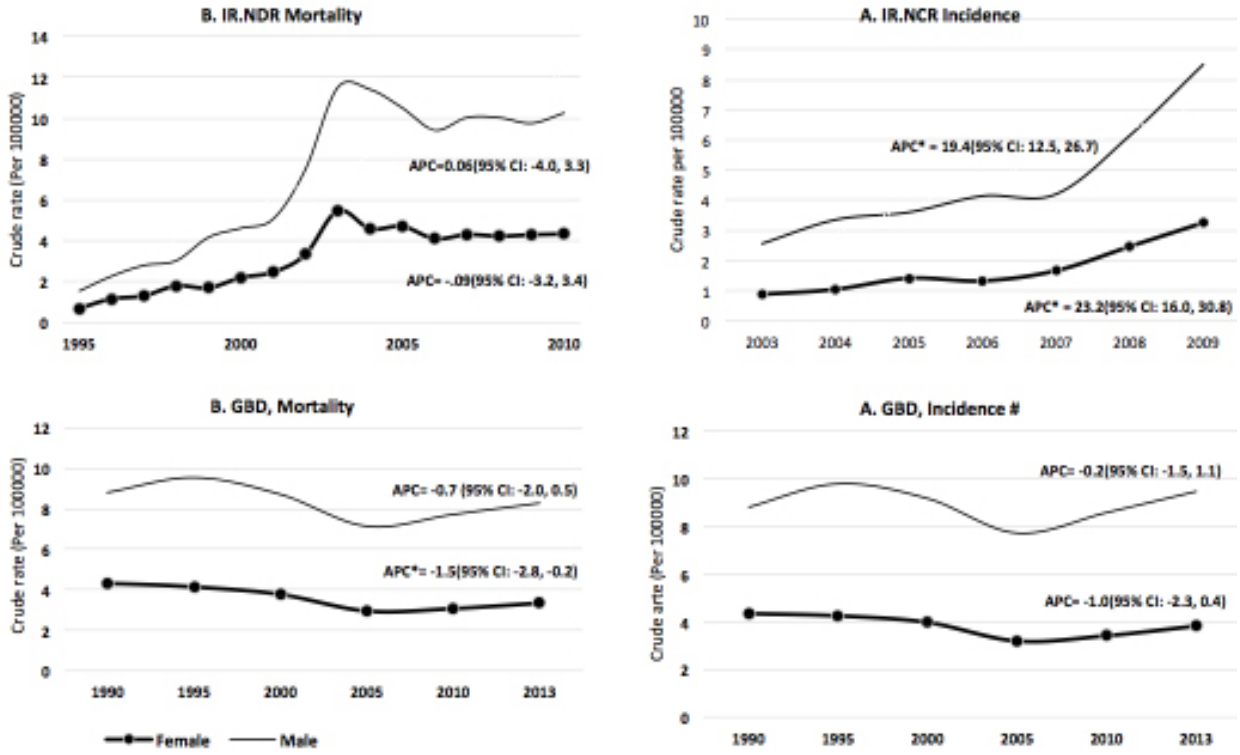

Figure 1. Trends of lung Cancer Incidence and Mortality in Iran According to the National and Global Burden of Disease Cancer Collaboration Estimates. A, Incidence; B, Mortality; IR.NDR, the Iranian National Civil Registration; IR.NCR, the Iranian National Cancer Registry; *significantly different from zero (P-value<0.05); #calculated according to GBD-mortality and survival rates for LC patients

and 0.62 in Ardabil registry. However, for the GLOBOCAN estimates, M:I ratios was 0.76. According to the national reports, M:I ratio was more than 1 and exceed 2.28 (Table 1).

Discussion

We presented an updated overview of incidence and mortality rates of LC in Iran, using available data from the IR.NCR, IR.NDR and GBD-CC estimates. In opposite of stability of GBD- incidence, gender-specific trends of N.IRs of LC were increasing. Despite of increasing trends of N.MRs up to 2004, trends of N.MRs and GBD-mortality were stable and similar since 2004. Absolute values of N.MRs were more than the GBD-CC estimates since 2004. Absolute N.IRs were steadily less than GBD-incidence except for 2009, when the N.IRs and GBD-CC were equal.

Trend line of N.IRs caught the trend line of the GBD-incidences at 2009, due to a positive shift in N.IRs at that point of time. This shift is a result of improvement of completeness of case ascertainment at IR.NCR in 2008 (Lankarani et al., 2013). In addition to this shift, it seems that increasing trends of N.IRs could be justified by slight improvements in IR.NCR coverage and accessibility of diagnostic methods (2004; 2008; Mousavi et al., 2009; 2010).

Increasing trend of N.MRs may be partly because of improvement of death registration at IR.NDR up to 2004 (Khosravi et al., 2007a; Khosravi A et al., 2013). However, sudden stability of this trend since 2004, may be not a real pattern, as LC is a non-communicable disease with a long time induction period.

According to a previous study by a well- known team of Iranian cancer researcher, completeness of cases ascertainment at IR.NCD had been 26% for LC in years up to 2007 (Zendehdel et al., 2011). Therefore, with a rough estimate, if reported N.IR had been 4.2 (per 100000; for males in 2007), its real estimate would be around 16 per 100000. Now consider reported N.IR at 2009 (8.5 per 100000 in males), after the major improvement of IR.NCR. It is equal with 53% of expected real IR (16 per 100000). If this justification be true or relatively true, then the GBD- incidence and GLOBOCAN estimates would be less than 50% of the true value of LC incidence in Iran.

In support of high incompleteness at IR.NCR, Our results show that, if one could assume a 100% completeness of case ascertainment in regional population-based reports, then completeness of IR.NCR may be less than 40%, in case of LC registration. However, based on the study results, assuming a 100% completeness in regional registries may not be a reasonable assumption, As estimated M:I ratios at the Golestan registry were implausibly lower than 0.3. This surprisingly means a 70% survival rate for LC patients in Golestan, while maximum survival rates of LC have been reported in high income countries as 30% and 10-20% in developing countries (Gelband et al., 2015). The M:I ratio was 2.28 for the IR.NCR, which could interpret as an strong evidence of incompleteness of case ascertainment at this registry (Parkin and Bray, 2009).

A similar justification is defensible, regarding

comparison of the absolute values of N.MRs and GBD-mortality and GLOBOCAN estimates, considering previously reported underestimation or misclassifications at IR.NDR in several reports (Mathers et al., 2005; Naghavi, 2005; Khosravi et al., 2007a; 2007b; 2013).

Therefore, if one wants to use LC incidence and mortality estimates, reported by IR.NCR and IR.NDR, she inevitably needs to consider a 60-70% of incompleteness in LC incidence estimates (Zendehdel et al., 2011; Maryam et al., 2015) and also at least 20-40% of underreporting or misclassification of cause of death in LC mortality estimates (Khosravi et al., 2007a; Maryam et al., 2015).

As we showed, the GBD-CC and GLOBOCAN estimates are meaningfully less than expected LC incidence and mortality in Iran. This underestimation is mainly due to lack of a representative national cancer registry in Iran and perhaps simplistic methodology, mainly because of their global scope, which have been adopted by the GBD-CC and GLOBOCAN to generate final input data in case of Iran.

In GLOBOCAN project, data provided by the IR.NCR, Golestan, Ardabil, East Azerbaijan and Tehran registries were used for estimation. Then, final incidence rates have been generated by population weighted averaging on abovementioned data. Then, estimated incidences have been used for estimation of mortality rates (2012, 2013b). We believe that, this procedure in not the best, because of presence of a serious incompleteness in national and may be in other regional registries (Zendehdel et al., 2011; Maryam et al., 2015).

In GBD-CC project, the IR.NDR data (1980 to 2010) have been used in addition of the input data by GLOBOCAN, except for data reported by Tehran and east Azerbaijan, to generate estimations for Iran. Then, incidence based mortality rates were estimated. We could not find any procedure in the GBD-CC methodology regarding correction for incompleteness of input data, except for a weighted averaging procedure in which IR.NCR get a full weight (2015; Fitzmaurice et al., 2015), by this incompleteness of IR.NCR has been ignored. In an e-mail conversation with GBD-CC team, they explained that the observed decreases in the cancer incidence and mortality estimates for Iran are due to an age standardization. Thus we used crude rates in our study.

Accordingly, we believe that providing alarming data quality indices is essential, to kept in mind by users of the GLOBOCAN and GBD databases. Such indices are generated and available along with the GLOBOCAN estimates. In addition, GLOBOCAN readers are able to see how country specific final data have been generated (Mathers et al., 2005; 2012, 2013a). As we know, no data quality index has been presented in GBD-CC reports regarding final country specific estimates (2015; Fitzmaurice et al., 2015).

We compared LC statistics in a country without a national population based cancer registry with respective estimated statistics by two global projects. Therefore, our conclusion may be only generalizable to the GBD-CC and GLOBOCAN estimates for countries without a representative cancer data. This study is not to criticize the value of the GBD-CC or GLOBOCAN projects, but only a call for reporting data quality indices along with cancer estimates in developing world, as a short time action.

In conclusion, absolute values of the GBD-CC and GLOBOCAN estimates of lung cancer incidence and mortality in Iran are underestimated. Trends of these values are inconsistent with those drown from national or subnational available data. Accordingly, it is most probable that the GLOBOCAN and GBD-CC estimates were affected by low qualified data from developing countries, generation of data quality indices which presented along with country specific estimates is recommended.

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