

Trend of Gastrointestinal and Liver Diseases in Iran: Results of the Global Burden of Disease Study, 2010

Sadaf Ghajarieh Sepanlou^{†1,2}, Fatemeh Malekzadeh^{†1,3}, Mohsen Naghavi⁴, Mohammad Hossein Forouzanfar⁴, Saeid Shahraz⁵, Maziar Moradi-Lakeh^{4,6}, Reza Malekzadeh^{1,2,7,8}, Hossein Poustchi^{1,2,7*}

1. Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
2. Liver and Pancreatobiliary Diseases Research Center, Digestive Diseases Research Institute, Shariati Hospital, Tehran university of Medical Sciences, Tehran, Iran
3. Non-Communicable Disease Research Center, Endocrine and Metabolism Research Institute, Shariati Hospital, Tehran University of medical Sciences, Tehran, Iran
4. Institute for Health Metric and Evolution, Seattle, WA, USA
5. Institute for Clinical Research and Health Policy Studies (ICRHPS) Tufts Medical Center, USA
6. Gastrointestinal and Liver Disease Research Center (GILDRC), Iran University of Medical Sciences, Tehran, Iran
7. Digestive Oncology Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
8. Iranian Association of Gastroenterology and Hepatology

† These two authors contributed equally to this paper

* **Corresponding Author:**
Hossein Poustchi M.D/ Ph.D
Digestive Diseases Research Center, Digestive Disease Research Institute, Shariati Hospital
N. Kargar St. Tehran, Iran
Tel: + 98 21 82415104
Fax: + 98 21 82415400
Email: poustchi@ams.ac.ir
Received: 20 Apr. 2015
Accepted: 10 Jun. 2015

ABSTRACT

BACKGROUND

The general pattern of epidemiologic transition from communicable to non-communicable diseases is also observed for gastrointestinal and liver diseases (GILD), which constitute a heterogeneous array of causes of death and disability. We aimed to describe the trend of GILD in Iran based on the global burden of disease (GBD2010) study from 1990 to 2010.

METHODS

The trend of number of deaths, disability, adjusted life years (DALYs) and their age-standardized rates caused by 5 major GILD have been reported. The change in the rankings of major causes of death and DALY has been described as well.

RESULTS

The age standardized rates of death and DALYs in both sexes have decreased from 1990 to 2010 for most GILD. The most prominent decreases in death rates are observed for diarrheal diseases, gastritis and duodenitis, and peptic ulcer disease. Positive trends are observed for liver cancer, pancreatic cancer, and gall bladder cancer. Diarrheal diseases have retained their 1st rank among children under 5. Among adults, decreased ranks are observed for diarrheal diseases, appendicitis, gastritis and duodenitis, gall bladder diseases, pancreatitis, and all types of cirrhosis. The trends in age standardized rates of DALYs, deaths, and YLLs are negative for almost all GILD, and especially for diarrheal diseases. However, there is no upward or downward trend in rates of years lost due to disability (YLDs) for most diseases. Total numbers of DALYs and deaths due to acute hepatitis C, stomach cancer, and liver cancers are rising. The total DALYs due to overall digestive diseases except cirrhosis and DALYs due to cirrhosis are both somehow stable. No data has been reported for GILD that are mainly diagnosed in outpatient settings, including gastroesophageal reflux disease, irritable bowel syndrome, and non-alcoholic fatty liver disease.

CONCLUSION

The results of GBD 2010 demonstrate that the rates of most GILD are decreasing in Iran but total DALYs are somehow stable. However, as diseases detected in outpatient settings have not been captured, the burden of GILD seems to be underestimated. Population-based studies at national level are required for accurate reports.

KEYWORDS

Mortality; Disability; Burden; Gastrointestinal Diseases

Please cite this paper as:

Sepanlou SG, Malekzadeh F, Naghavi M, Forouzanfar M, Shahraz S, Moradi-Lakeh M, Malekzadeh R, Poustchi H. Trend of Gastrointestinal and Liver Diseases in Iran: Results of the Global Burden of Disease Study, 2010. *Middle East J Dig Dis* 2015;7:121-37.

INTRODUCTION

During last 2 decades, an epidemiologic transition has happened across the world, which is especially noticeable in developing countries, and has resulted in an obvious shift from communicable infectious diseases to chronic non-communicable diseases (NCD).¹⁻³ Similar shift has been observed among GILD.

Study of regional and national disease trend is an important and necessary step for priority setting in health research, and can help the authorities and policy makers to use the evidence based data for appropriate prevention and treatment of diseases. Data on trend of prevalence, incidence and mortality rates remain sparse especially in developing countries. In Iran the trends of infectious diseases have been reported periodically mainly by the Ministry of Health and trends of gastrointestinal cancers have been estimated mostly based on pathology based national cancer registries and a few population-based cancer registries in five provinces in Northern and Southern Iran (Golestan, Mazandaran, Gilan, Ardabil, and Kerman). As for other diseases in the category of GILD, the data are sparse and almost no population-based study at national level has been done on their trend. The Global Burden of Disease (GBD) study has been the first attempt to estimate the levels and trends of diseases at global, regional, and national level using novel and sophisticated statistical methods and unique metrics.⁴⁻¹² Details of methods reported elsewhere.^{13,14} In the present paper, we have investigated the results of GBD 2010 on the trend of GILD in Iran from 1990 to 2010.

MATERIALS AND METHODS

The details of major methods used in GBD for estimating deaths, years of life lost due to premature death (YLLs), years of life lost due to disability (YLDs), and disability adjusted life years (DALYs) have been adequately described elsewhere.¹⁵ In the current paper, we investigated the trend of the above mentioned metrics for major gastrointestinal and hepatic diseases. Total numbers as well

as age-standardized rates have been reported. The diseases studied in this paper included: infections of gastrointestinal tract (diarrhea, typhoid and paratyphoid fevers), acute hepatitis (A, B, C, and E), cancers of digestive system (esophagus, stomach, colon and rectum, liver, gall bladder, biliary tract and pancreas), end stage liver diseases (cirrhosis), and all other digestive diseases including: gastritis and duodenitis, peptic ulcer disease, appendicitis, paralytic ileus and intestinal obstruction without hernia, inguinal and femoral hernia, non-infective inflammatory bowel disease, vascular disorders of intestine, gall bladder and bile duct disease, pancreatitis, and yet other digestive diseases. The changes in ranking of these diseases in terms of their overall number as well as rates from 1990 to 2010 have been illustrated. Line trends of major gastrointestinal and hepatic diseases from 1990 to 1995, 2000, 2005, and 2010 have been presented. Age-standardized rates have been reported to adjust for the effect of ageing and the population growth.

RESULTS

Tables 1 and 2 demonstrate the estimated age standardized rates of deaths and DALYs for 25 gastrointestinal and hepatic diseases in 1990, 2005, and 2010, separately for women and men in Iran. The death and DALY rates for most causes have decreased from 2005 to 2010 in both men and women. Exceptions are acute hepatitis B and C in women and acute hepatitis E and colorectal cancer in men. The percent changes of death rates from 2005 to 2010 range between -24.2% for gastritis and duodenitis and -23.4% for peptic ulcer to 16.0% for acute hepatitis C in women. As for men, the percent changes range from -22.1% for peptic ulcer to 1.6% for hepatitis E. The same pattern is observed for DALY rates. The percent changes of DALY rates from 2005 to 2010 range from -23.0% for peptic ulcer and -15.4% for gastritis and duodenitis to 10.0% for acute hepatitis C in women. As for men, the respective figures are -24.4% for peptic ulcer and 2.3% for acute hepatitis E.

The percent changes from 1990 to 2005 are much more significant. The most substantial decreases in

death rates in both sexes are observed for diarrheal diseases, appendicitis, acute hepatitis A, gastritis and duodenitis, and gall bladder diseases. As for DALYs, diarrheal diseases, appendicitis, acute hepatitis A, gastritis and duodenitis, and cirrhosis due to causes other than hepatitis or alcohol are among the causes of DALYs with highest decrease in rate in both sexes. However, the decrease in acute hepatitis B in women is significant as well as gall bladder diseases in men.

The most substantial positive percent changes from 1990 to 2005 are observed for liver cancer, pancreatic cancer, and gall bladder cancer. The percent changes for both death and DALY rates for liver cancer and pancreatic cancer are over 100% in women. In men as well, the only observed positive percent changes belong to liver cancer, pancreatic cancer, and gall bladder cancer.

Figure 1 demonstrates the ranking of diseases in terms of absolute number of deaths that they cause among females and males under 5 years. Results show that diarrheal diseases are still the main important cause of death in both sexes. The changes in rankings from 2005 to 2010 are not noteworthy. However, decreases are observed for acute hepatitis A and B, appendicitis, gastritis and duodenitis, gall bladder and bile duct diseases, cirrhosis secondary to hepatitis C, and pancreatitis in both sexes.

Figure 2 shows the rankings of causes of death by numbers among women and men between 15 and 49 years of age. Similar to previous figure, changes in ranks are not noteworthy from 2005 to 2010. Stomach cancer, typhoid fevers, esophageal cancer, and colorectal cancer are the top 4 diseases in both years. However, the rankings show significant changes from 1990 to 2010. Increased ranks in terms of deaths numbers are observed for liver cancer secondary to hepatitis B, C and alcohol, as well as secondary to all other causes in women. Among men, increased ranks for liver cancers are less steep. Decreased ranks are observed for diarrheal diseases, appendicitis, gastritis and duodenitis, gall bladder diseases, pancreatitis, and all types of cirrhosis in both sexes.

Figure 3 demonstrates the rankings of diseases

in terms of the number of deaths among women and men aged 50 years and more. Stomach cancer, esophageal cancer, and colorectal cancer are the top 3 in both women and men, unchanged from 1990 to 2010. Similar to previous figures, changes in rankings are not substantial from 2005 to 2010. Again similar to figure 2, liver cancers show increased ranks from 1990 to 2005 in both sexes. Diarrheal diseases, appendicitis, gastritis and duodenitis, gall bladder diseases, pancreatitis, and all types of cirrhosis show decreased ranks in both sexes from 1990 to 2005. Overall, acute hepatitis of all kinds and typhoid fevers have lower ranks in adults aged above 50 compared to adults between 15 to 49 years old.

Figure 4 shows the rankings of diseases in terms of age standardized DALY rates per 100,000 among women and men in 1990, 2005, and 2010. Stomach cancer, esophageal cancer, and colorectal cancer are the top 3 causes of DALY in 2005 and 2010 among both sexes. Liver cancers show increased ranks from 1990 to 2005. Diarrheal diseases and typhoid fevers, cirrhosis of all kinds, appendicitis, gastritis and duodenitis, gall bladder diseases, and pancreatitis have decreased ranks. Acute hepatitis A, B, and E show decreased ranks in oppose to the increased rank of hepatitis C in both sexes. The rank of peptic ulcer has not changed from 1990 to 2005 in men, but has a prominent increased rank in women.

Figures 5, 6, 7, and 8 show the trends of age-standardized rates from 1990 to 2010 for major GILD in both sexes in terms of DALYs, deaths, YLLs, and YLDs per 100,000 respectively. The trends in rates of DALYs, deaths, and YLLs are negative for almost all diseases, and especially for diarrheal diseases. Acute hepatitis B, stomach cancer, appendicitis, and cirrhosis show substantial decline. In spite of decreases in rates of DALYs, deaths, and YLLs, there is no upward or downward trend in rates of YLDs for most of diseases. Exceptions are gastritis and duodenitis, and peptic ulcer disease, which demonstrate a downward trend in terms of YLD rates.

Figures 9 and 10 show the trends of total DALYs and deaths for all ages both sexes. Unlike rates

Table 1: The trend of age-standardized death rates per 100,000 due to gastrointestinal and liver diseases from 1990 to 2010 in Iran

A. Women

	ASR (95% UI) in 1990		ASR (95% UI) in 2005		%change from 1990 to 2005	ASR (95% UI) in 2010		%change from 2005 to 2010		
Stomach cancer	15.5	8.7	23.5	11.1	6.6	17.9	10.1	5.6	15.9	-8.9
Diarrheal diseases	9.1	6.5	12.5	5.0	3.6	7.7	4.2	2.8	6.6	-15.6
Esophageal cancer	7.6	4.6	10.4	3.5	2.9	4.6	3.4	2.6	4.5	-0.6
Colorectal cancer	4.0	2.7	4.8	2.3	0.7	3.4	2.2	0.7	3.5	-6.4
Other digestive diseases										
Cirrhosis hepatitis C	2.6	1.8	3.3	2.1	1.6	2.9	1.7	1.2	2.5	-19.3
Diarrheal diseases										
Cirrhosis other	1.3	1.0	1.7	1.6	1.3	2.4	1.6	1.2	2.3	0.5
Cirrhosis hepatitis C										
Cirrhosis hepatitis B	1.1	0.8	1.4	1.6	0.8	2.1	1.5	0.7	2.1	-7.0
Liver cancer hepatitis C										
Gallbladder cancer	1.1	0.6	1.9	1.1	0.5	1.5	1.0	0.1	2.1	-6.1
Peptic ulcer	1.0	0.4	1.5	1.1	0.1	2.2	0.9	0.5	1.3	-7.3
Typhoid fevers										
Liver cancer hepatitis B	1.0	0.5	1.7	1.0	0.5	1.3	0.9	0.5	1.4	-1.5
Pancreatic cancer	1.0	0.1	2.0	1.0	0.5	1.6	0.9	0.4	1.4	-8.9
Gallbladder cancer										
Pancreatic cancer	0.9	0.5	1.4	0.9	0.6	1.4	0.9	0.4	1.3	-23.4
Peptic ulcer	0.8	0.5	1.2	0.7	0.6	1.0	0.7	0.5	0.9	-4.0
Cirrhosis other										
Liver cancer hepatitis C	0.7	0.5	1.2	0.7	0.5	1.0	0.7	0.5	1.0	0.3
Cirrhosis hepatitis B										
Gastritis & duodenitis	0.7	0.4	1.1	0.5	0.3	0.6	0.5	0.2	0.7	-7.3
Liver cancer other										
Other digestive diseases	0.6	0.3	1.2	0.5	0.4	0.7	0.4	0.2	0.6	-7.5
Gall bladder diseases										
Cirrhosis alcohol	0.5	0.4	0.7	0.5	0.2	0.6	0.4	0.3	0.7	-16.0
Liver cancer alcohol										
Gall bladder diseases	0.5	0.2	0.9	0.4	0.2	0.6	0.3	0.1	0.6	-10.0
Appendicitis										
Liver cancer hepatitis B	0.5	0.3	0.8	0.3	0.3	0.5	0.3	0.2	0.5	0.1
Cirrhosis alcohol										
Acute hepatitis A	0.4	0.1	1.0	0.3	0.2	0.6	0.3	0.2	0.5	6.4
Gastritis & duodenitis										
Acute hepatitis B	0.3	0.1	0.7	0.3	0.2	0.4	0.3	0.1	0.6	16.0
Acute hepatitis C										
Acute hepatitis E	0.3	0.1	0.5	0.2	0.1	0.4	0.2	0.1	0.5	-24.2
Gastritis & duodenitis										
Liver cancer other	0.2	0.1	0.4	0.2	0.1	0.3	0.2	0.1	0.3	-0.1
Acute hepatitis E										
Liver cancer alcohol	0.2	0.1	0.4	0.2	0.1	0.3	0.1	0.1	0.2	-11.8
Pancreatitis										
Acute hepatitis A	0.2	0.1	0.3	0.2	0.1	0.4	0.1	0.1	0.4	-6.3
Acute hepatitis B										
All causes	746.8	670.5	839.1	532.4	489.4	578.2	488.4	421.1	566.6	-8.3
All causes										
All causes										

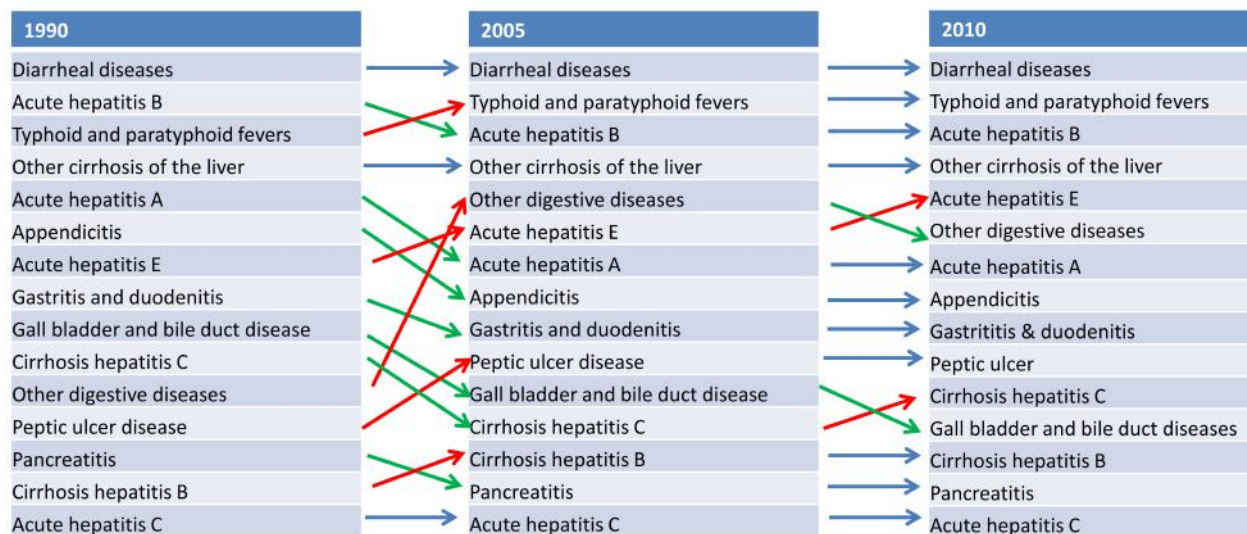
B.Men	ASR (95% UI) in 1990			ASR (95% UI) in 2005			%change from 1990 to 2005			ASR (95% UI) in 2010			%change from 2005 to 2010		
Stomach cancer	32.3	21.4	46.7	24.4	14.6	33.5	22.1	12.0	29.0	-24.5	Stomach cancer	22.1	12.0	29.0	-9.2
Esophageal cancer	11.1	7.3	14.1	7.4	5.9	11.5	7.0	5.1	10.6	-33.1	Esophageal cancer	7.0	5.1	10.6	-6.4
Diarrheal diseases	10.5	8.0	14.0	4.9	4.4	5.9	4.9	3.9	6.2	-26.7	Colorectal cancer	4.9	3.9	6.2	0.3
Colorectal cancer	6.6	4.5	7.7	3.0	0.6	4.0	2.7	0.6	3.7	474.2	Other digestive diseases	2.7	0.6	3.7	-8.5
Cirrhosis hepatitis C	3.5	2.4	4.5	2.5	2.0	3.6	2.5	1.9	3.5	-26.6	Cirrhosis hepatitis C	2.5	1.9	3.5	-0.2
Cirrhosis alcohol	2.6	1.8	3.3	2.4	1.2	2.9	2.2	1.1	3.0	99.2	Liver cancer hepatitis B	2.2	1.1	3.0	-5.7
Cirrhosis hepatitis B	2.0	1.4	2.7	2.3	1.1	2.8	2.1	1.0	2.8	111.2	Liver cancer hepatitis C	2.1	1.0	2.8	-5.8
Cirrhosis other	1.9	1.2	2.4	2.2	1.7	2.8	1.9	1.4	2.6	-79.0	Diarrheal diseases	1.9	1.4	2.6	-14.8
Peptic ulcer	1.6	1.2	2.4	1.8	1.4	2.6	1.8	1.4	2.6	-29.8	Cirrhosis alcohol	1.8	1.4	2.6	-0.2
Appendicitis	1.5	0.6	2.4	1.7	0.7	2.1	1.5	0.9	2.6	3.1	Acute hepatitis B	1.5	0.9	2.6	0.0
Acute hepatitis B	1.4	0.6	2.2	1.5	1.0	2.2	1.5	1.1	2.1	6.0	Cirrhosis hepatitis B	1.5	1.1	2.1	-0.3
Typhoid fevers	1.4	0.2	2.7	1.5	1.1	2.2	1.4	0.9	1.9	-27.3	Pancreatic cancer	1.4	0.9	1.9	0.6
Gastritis & duodenitis	1.3	0.9	1.9	1.4	0.9	1.8	1.3	0.1	2.8	13.9	Typhoid fevers	1.3	0.1	2.8	-2.7
Pancreatic cancer	1.3	0.9	1.8	1.4	0.2	2.8	1.3	0.6	1.8	2.5	Peptic ulcer	1.3	0.6	1.8	-22.1
Liver cancer hepatitis B	1.2	0.9	1.8	1.2	0.9	1.7	1.2	0.9	1.6	-36.2	Cirrhosis other	1.2	0.9	1.6	-2.4
Gall bladder diseases	1.1	0.6	1.8	0.8	0.4	1.0	0.7	0.4	1.0	99.3	Liver cancer alcohol	0.7	0.4	1.0	-5.7
Liver cancer hepatitis C	1.1	0.8	1.7	0.6	0.3	0.8	0.6	0.3	0.8	64.2	Liver cancer other	0.6	0.3	0.8	-4.7
Other digestive diseases	0.5	0.4	0.8	0.6	0.3	1.0	0.5	0.3	0.8	-55.2	Gallbladder cancer	0.5	0.3	0.8	-0.4
Gallbladder cancer	0.4	0.3	0.8	0.5	0.3	0.8	0.5	0.3	0.9	20.1	Gastritis & duodenitis	0.5	0.3	0.9	-15.7
Liver cancer alcohol	0.4	0.3	0.6	0.5	0.2	0.7	0.4	0.1	0.8	-69.8	Appendicitis	0.4	0.1	0.8	-9.2
Liver cancer other	0.4	0.3	0.5	0.4	0.3	0.6	0.4	0.3	0.6	-61.4	Gall bladder diseases	0.4	0.3	0.6	-7.4
Acute hepatitis A	0.3	0.1	1.0	0.3	0.2	0.6	0.3	0.2	0.5	14.0	Acute hepatitis C	0.3	0.2	0.5	-6.6
Acute hepatitis C	0.3	0.1	0.7	0.2	0.1	0.5	0.2	0.1	0.4	-40.9	Acute hepatitis E	0.2	0.1	0.4	1.5
Acute hepatitis E	0.2	0.1	0.5	0.2	0.1	0.3	0.2	0.1	0.6	-20.9	Acute hepatitis A	0.2	0.1	0.6	-5.3
Pancreatitis	0.2	0.1	0.3	0.1	0.1	0.2	0.1	0.1	0.2	-32.0	Pancreatitis	0.1	0.1	0.2	-4.7
All causes	1114.9	1019.0	1258.2	833.4	786.1	899.7	784.1	715.5	905.3	-25.2	All causes	784.1	715.5	905.3	-5.9

Table 2: The trend of age-standardized DALY rates due to gastrointestinal and liver diseases from 1990 to 2010 in Iran
A. Women

	ASR (95% UI) in 1990			ASR (95% UI) in 2005			%change from 1990 to 2005			ASR (95% UI) in 2010			%change from 2005 to 2010		
Diarrheal diseases	725.0	511.0	1027.3	Diarrheal diseases	262.1	187.2	350.9	-63.8	Diarrheal diseases	226.4	158.1	318.4	-13.6		
Stomach cancer	335.9	193.9	502.1	Stomach cancer	234.2	137.0	358.9	-30.3	Stomach cancer	206.4	111.4	309.2	-11.9		
Esophageal cancer	170.3	100.7	232.9	Esophageal cancer	108.9	75.7	170.1	-36.1	Esophageal cancer	89.1	57.8	143.3	-18.2		
Colorectal cancer	96.9	64.6	116.1	Colorectal cancer	82.9	69.1	107.1	-14.4	Colorectal cancer	80.2	57.9	105.1	-3.3		
Cirrhosis hepatitis C	63.6	45.8	80.4	Typhoid fevers	65.6	8.0	134.1	11.4	Typhoid fevers	61.6	8.7	125.8	-6.1		
Typhoid fevers	58.9	7.1	121.1	Other digestive diseases	56.8	17.8	80.7	448.1	Other digestive diseases	49.9	16.7	74.7	-12.1		
Cirrhosis other	57.8	40.4	78.7	Cirrhosis hepatitis C	35.8	28.2	55.4	-43.7	Cirrhosis hepatitis C	35.3	26.5	50.3	-1.5		
Appendicitis	41.3	18.1	61.8	Liver cancer hepatitis C	32.5	16.5	42.1	127.0	Liver cancer hepatitis C	30.2	14.9	42.8	-7.2		
Gastritis & duodenitis	30.5	20.0	47.1	Cirrhosis other	28.2	21.4	39.6	-51.2	Cirrhosis other	25.9	18.9	35.9	-8.3		
Acute hepatitis B	30.1	12.2	58.9	Liver cancer hepatitis B	23.6	11.7	30.4	136.9	Liver cancer hepatitis B	21.8	10.8	31.1	-7.6		
Cirrhosis hepatitis B	28.3	20.8	36.3	Peptic ulcer	23.4	10.8	37.3	12.3	Gallbladder cancer	19.2	9.3	31.4	-10.3		
Gall bladder diseases	27.7	17.8	39.8	Gallbladder cancer	21.4	10.7	35.2	-16.3	Pancreatic cancer	19.1	11.2	29.5	-2.3		
Gallbladder cancer	25.6	13.3	49.6	Pancreatic cancer	19.6	12.3	30.5	4.8	Peptic ulcer	18.0	8.4	32.6	-23.0		
Acute hepatitis A	22.2	6.0	61.1	Liver cancer other	17.0	8.3	22.1	159.9	Liver cancer other	15.9	7.0	24.1	-6.7		
Peptic ulcer	20.9	12.5	44.0	Gall bladder diseases	17.0	11.4	26.1	-38.8	Cirrhosis hepatitis B	15.5	11.6	21.5	-1.8		
Acute hepatitis E	18.8	9.0	33.6	Gastritis & duodenitis	16.1	9.5	29.5	-47.1	Gall bladder diseases	15.3	9.7	23.8	-9.8		
Pancreatic cancer	18.7	11.5	30.8	Cirrhosis hepatitis B	15.8	12.2	24.3	-44.2	Acute hepatitis B	14.3	7.2	28.8	4.2		
Cirrhosis alcohol	15.1	10.8	19.0	Appendicitis	14.0	7.1	19.8	-66.1	Gastritis & duodenitis	13.6	7.9	25.4	-15.4		
Liver cancer hepatitis C	14.3	9.3	26.7	Acute hepatitis B	13.7	8.1	23.9	-54.4	Appendicitis	12.0	5.2	18.8	-14.0		
Other digestive diseases	10.4	6.8	21.7	Acute hepatitis E	11.9	6.8	19.3	-36.8	Acute hepatitis E	11.8	5.4	23.7	-0.7		
Liver cancer hepatitis B	9.9	6.5	19.0	Liver cancer alcohol	11.2	5.5	14.5	141.0	Liver cancer alcohol	10.3	5.1	14.6	-8.1		
Liver cancer other	6.5	3.6	14.8	Acute hepatitis A	8.6	4.1	17.7	-61.2	Acute hepatitis A	8.2	3.9	16.8	-5.3		
Acute hepatitis C	6.4	2.3	13.0	Cirrhosis alcohol	8.2	6.5	12.3	-45.6	Cirrhosis alcohol	8.0	6.1	11.1	-2.0		
Pancreatitis	5.1	2.8	9.6	Acute hepatitis C	5.1	2.4	8.3	-20.0	Acute hepatitis C	5.6	2.3	10.5	10.0		
Liver cancer alcohol	4.7	3.0	9.1	Pancreatitis	3.8	2.5	6.1	-26.5	Pancreatitis	3.4	2.2	5.1	-10.8		
All causes	36910.1	33475.7	40685.6	All causes	27735.3	24936.0	30661.6	-24.9	All causes	25773.8	22728.4	29051.7	-7.1		

B.Men	ASR (95% UI) in 1990			ASR (95% UI) in 2005			%change from 1990 to 2005			ASR (95% UI) in 2010			%change from 2005 to 2010		
Diarrheal diseases	732.4	535.1	1019.4	491.1	288.7	670.0	-28.8	432.7	234.1	563.5	-11.9				
Stomach cancer	690.0	462.9	1010.8	241.7	176.2	323.3	-67.0	211.7	150.2	294.0	-12.4				
Esophageal cancer	238.7	154.8	305.7	151.8	121.0	233.4	-36.4	139.0	100.4	217.6	-8.4				
Colorectal cancer	159.3	103.8	186.9	111.8	99.5	135.1	-29.8	109.2	86.9	139.1	-2.3				
Cirrhosis hepatitis C	89.1	60.9	114.8	85.6	10.6	174.7	2.4	83.2	10.4	173.9	-2.9				
Typhoid fevers	83.6	10.4	167.7	77.0	20.1	100.1	628.0	66.3	20.1	86.5	-14.0				
Cirrhosis alcohol	73.6	48.6	93.9	58.9	45.1	84.7	-33.9	58.2	43.3	83.9	-1.2				
Cirrhosis other	73.2	47.8	97.6	52.6	29.0	64.8	67.0	49.9	27.0	65.9	-5.2				
Acute hepatitis B	55.6	24.1	108.8	48.6	34.4	72.7	-12.6	47.9	28.6	87.5	-1.5				
Appendicitis	54.4	23.1	83.8	46.0	36.5	68.5	-37.6	45.5	34.9	65.6	-1.0				
Cirrhosis hepatitis B	53.0	35.3	70.7	45.1	23.8	56.1	77.8	42.6	22.5	56.2	-5.6				
DPeptic ulcer	46.8	32.6	84.4	42.4	32.4	61.2	-42.2	40.1	29.5	55.4	-5.2				
Gastritis & duodenitis	38.4	27.5	55.2	40.5	17.9	67.2	-13.5	34.3	25.0	50.7	-1.3				
Liver cancer hepatitis B	31.5	23.2	44.2	34.7	26.0	53.5	-34.5	31.1	19.9	41.1	0.9				
Gall bladder diseases	30.0	18.7	45.0	30.8	20.8	40.3	11.7	30.6	14.2	51.8	-24.4				
Pancreatic cancer	27.6	19.9	39.9	19.4	11.2	24.0	43.7	18.7	10.4	25.3	-3.5				
Liver cancer hepatitis C	25.4	18.4	37.4	18.6	11.9	29.7	-51.6	16.5	9.0	21.9	-5.4				
Acute hepatitis A	20.9	4.6	64.1	17.5	9.5	21.6	67.0	16.1	10.0	25.9	-13.6				
Acute hepatitis E	17.9	7.7	37.2	16.3	7.5	24.8	-70.1	14.5	6.0	24.5	-10.7				
Liver cancer other	13.5	9.2	19.8	13.8	9.7	19.8	-54.0	12.9	8.8	18.3	-6.6				
Other digestive diseases	10.6	7.7	17.0	12.4	6.2	21.9	-30.8	12.7	5.3	26.6	2.3				
Liver cancer alcohol	10.5	7.7	14.8	11.7	6.7	17.7	22.8	11.6	6.6	18.6	-0.7				
Gallbladder cancer	9.5	5.8	18.1	10.1	4.1	26.3	-51.6	9.7	3.8	28.1	-4.2				
Acute hepatitis C	7.7	3.1	15.7	9.2	5.4	14.6	20.8	8.4	5.2	13.4	-8.7				
Pancreatitis	5.4	3.3	9.3	3.1	2.1	4.8	-41.9	3.0	2.0	4.6	-3.0				
All causes	47559.6	43630.5	53182.4	35235.4	32538.1	38280.5	-25.9	32919.0	29785.7	37246.7	-6.6				

A Female



B Male

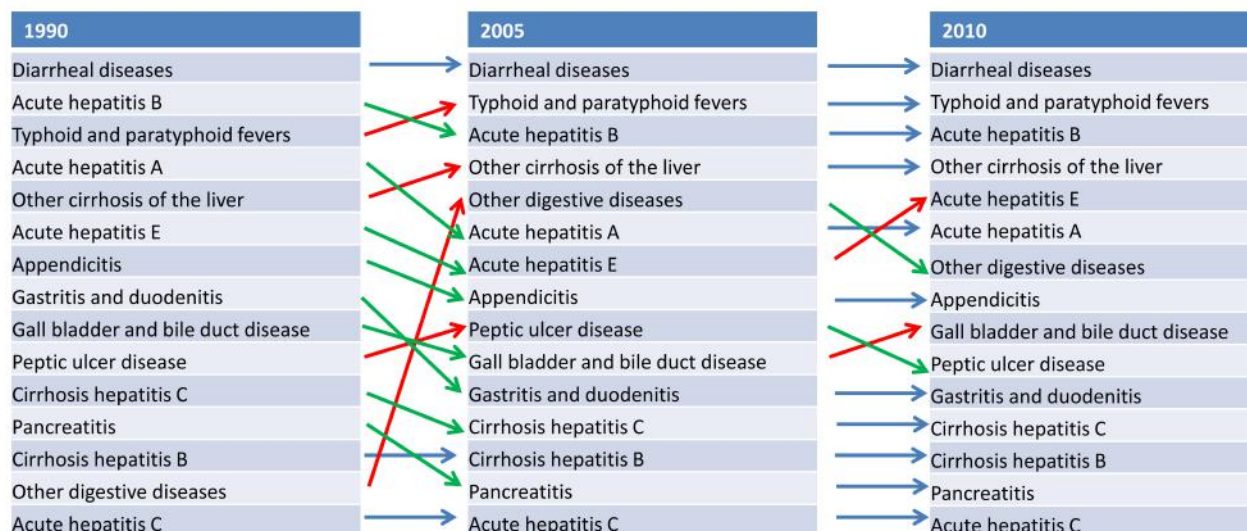


Fig. 1: Ranking of diseases based on death numbers in A) female and B) male under 5 years in 1990, 2005, and 2010

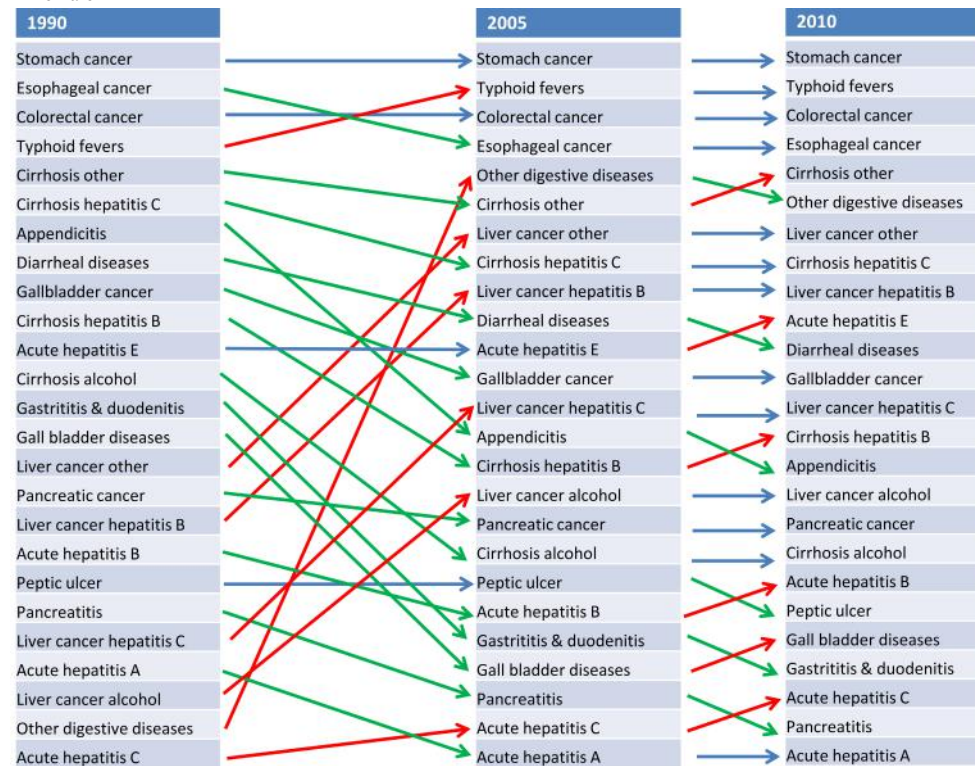
and except for diarrheal diseases and appendicitis, trends are generally not declining. Total numbers of DALYs and deaths due to acute hepatitis C, stomach cancer, and liver cancers are rising. The total DALYs due to overall digestive diseases except cirrhosis and DALYs due to cirrhosis are not increasing and somehow stable.

DISCUSSION

GBD 2010 shows that compared with 1990 - the starting point of the first GBD study - the world's population has grown substantially older; that the

main causes of disease burden have shifted from infectious diseases and childhood and maternal illnesses to non-communicable diseases such as coronary heart diseases and malignancies, and traffic injuries,^{4,9} and that now a significant portion of DALYs are attributed to disability rather than premature death.⁵ Since 1990, the average length of a human life has increased substantially, but many people spend these extra years with chronic disabling diseases such as musculoskeletal disorders, major depression, cancers, or diabetes.^{7,8} In real life, one should consider life as a rectangle instead

A Female



B Male

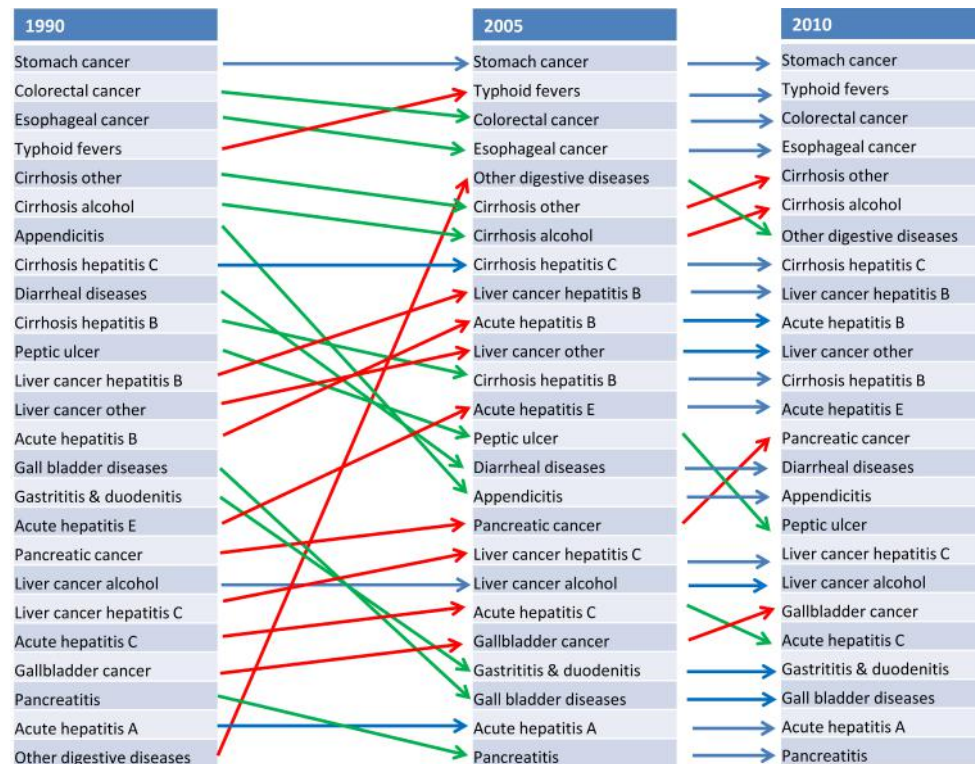


Fig. 2: Ranking of diseases based on death numbers in A) female and B) male 15-49 years in 1990, 2005, and 2010

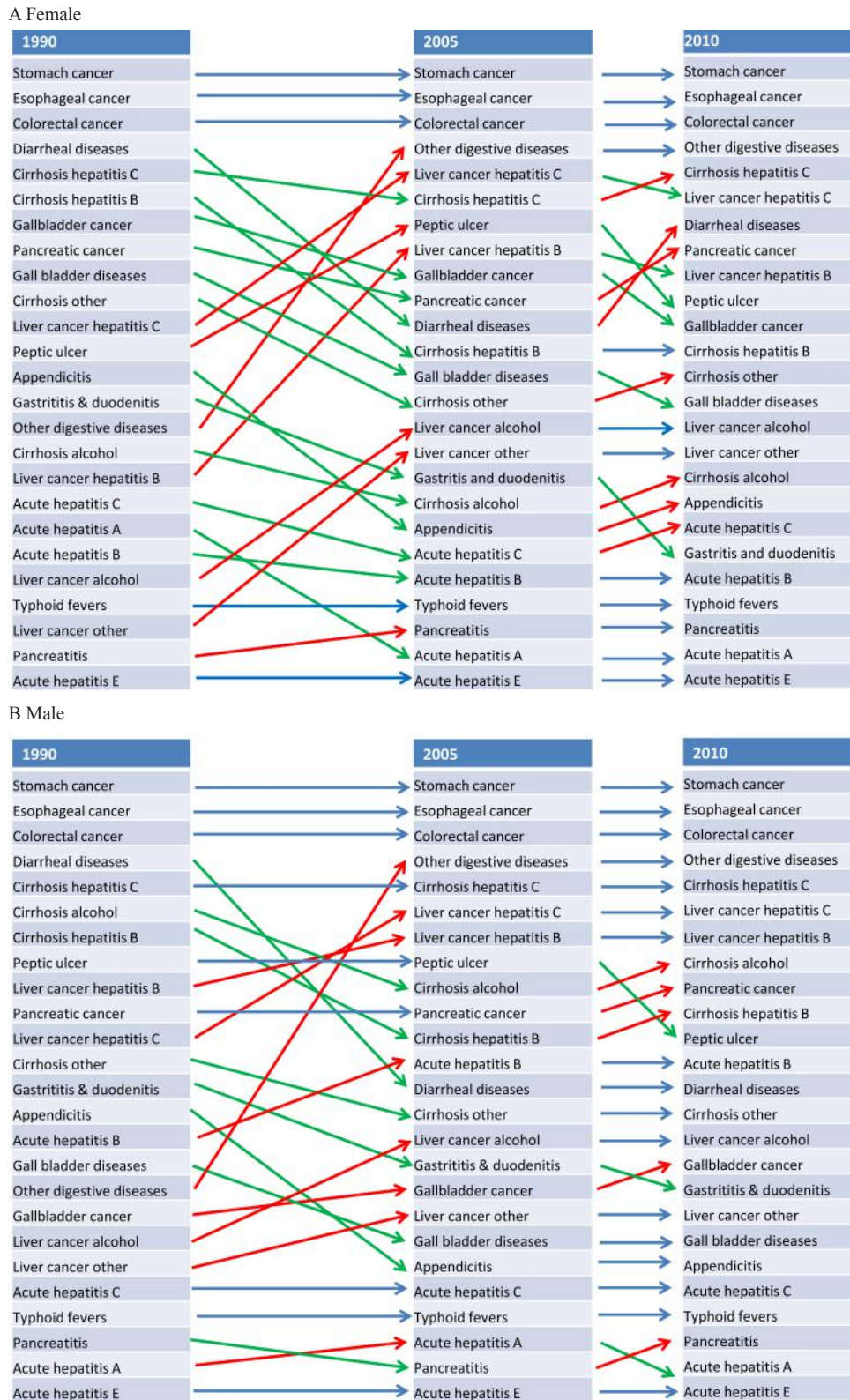
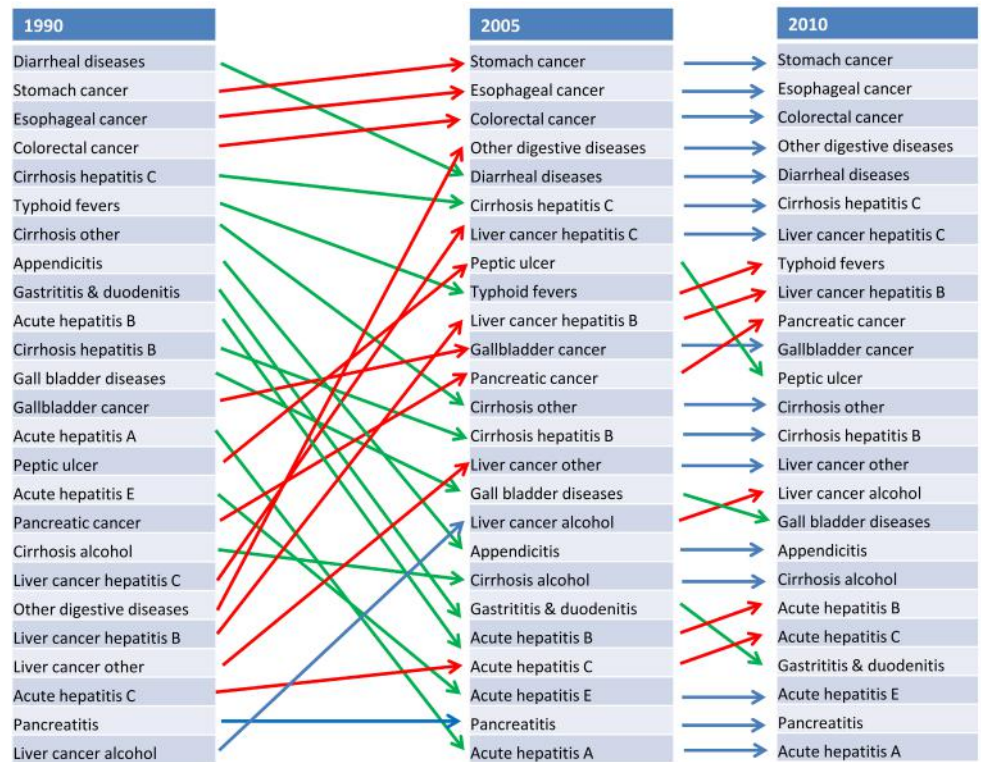


Fig. 3: Ranking of diseases based on death numbers in A) female and B) male 50+ years in 1990, 2005, and 2010

A Female



B Male

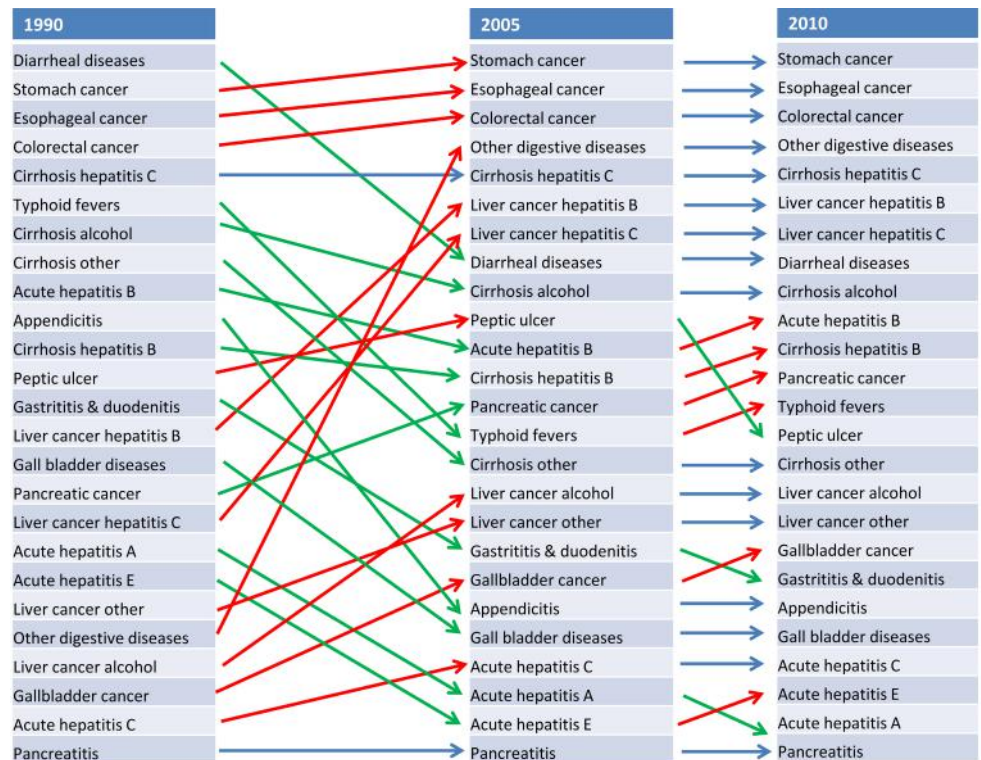


Fig. 4: Age standardized rates of DALYs in A) female and B) male in 1990, 2005, and 2010

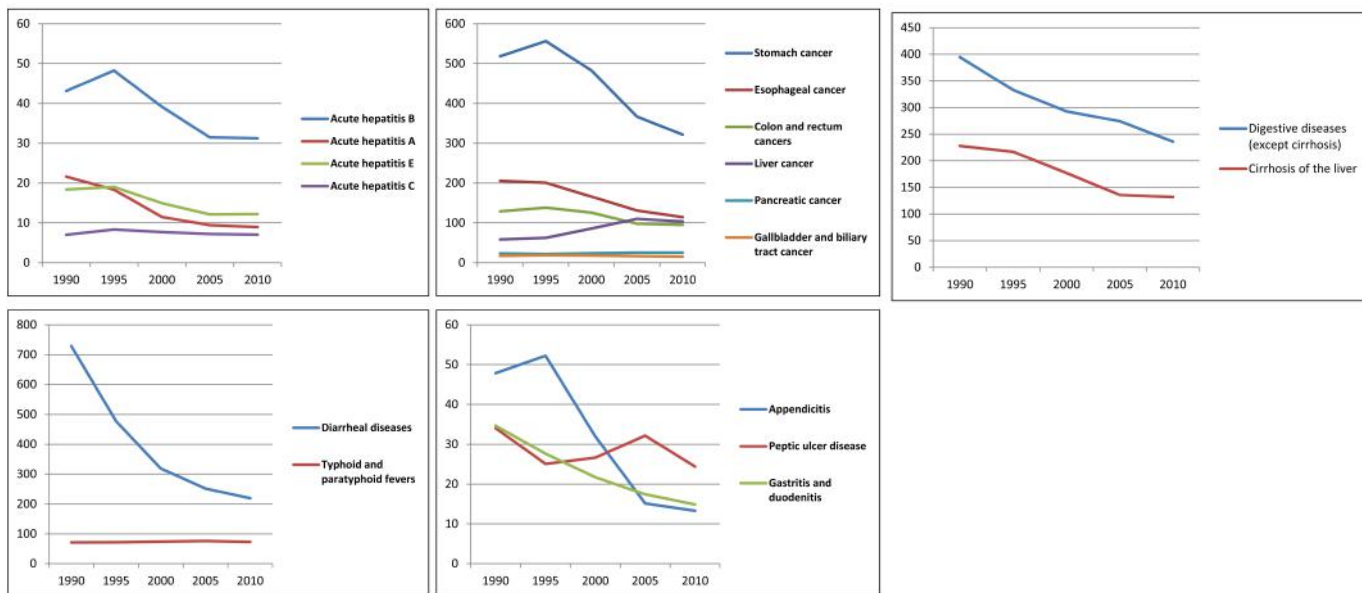


Fig. 5: Trend of DALYs per 100,000 for GILD (GBD 2010)

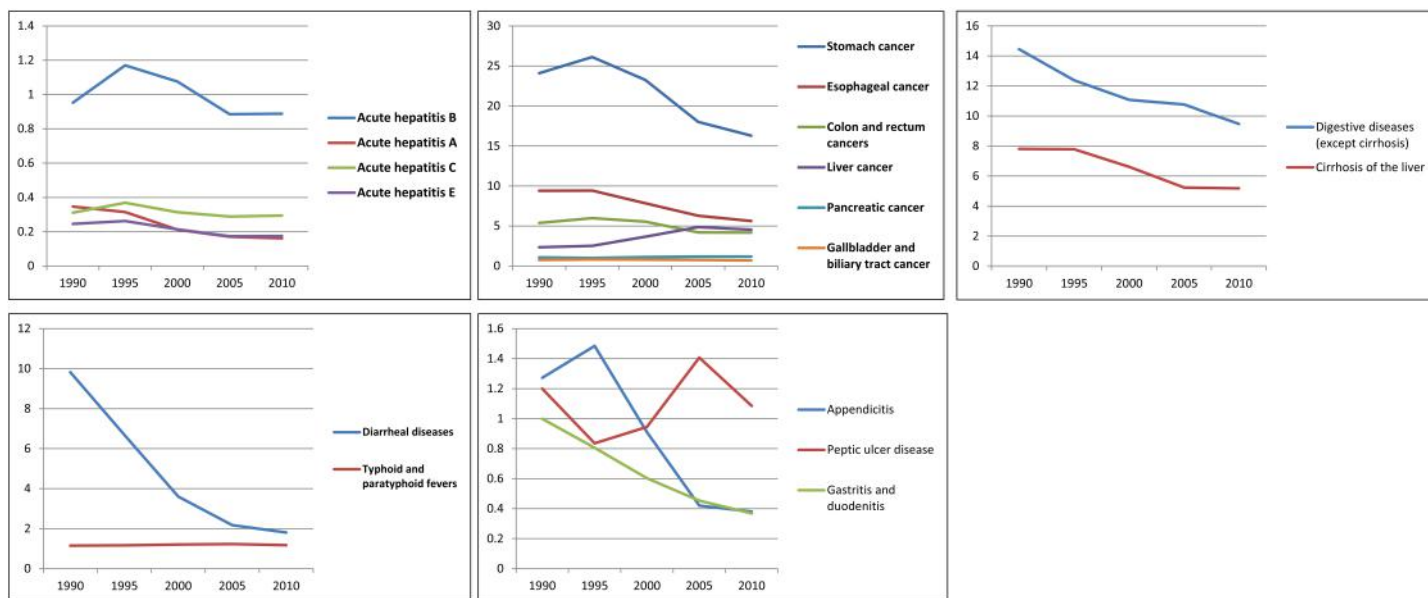


Fig. 6: Trend of deaths per 100,000 for GILD (GBD 2010)

of a line, “length” of life is not the only measure to be considered to determine quality of life; “width” of life should also be considered!

In Iran life expectancy has increased by 22 years for women and 21 years for men during last 45 years.¹¹ The incidence and mortality due to intestinal infections, mainly diarrheal diseases, typhoid and paratyphoid fevers, have decreased both among under 5 year children and adults (-40% decrease in

years of life lost from 2000 to 2012). Similarly, trends of incidence and mortality rates of stomach cancer and esophageal cancer are declining in both men and women from 1975 to 2010. However, trends of colorectal cancer and liver cancer are stable or increasing in many countries during the same time period. All gastrointestinal and liver cancers have higher rates in men compared to women.

GBD 2010 study is a landmark study for assess-

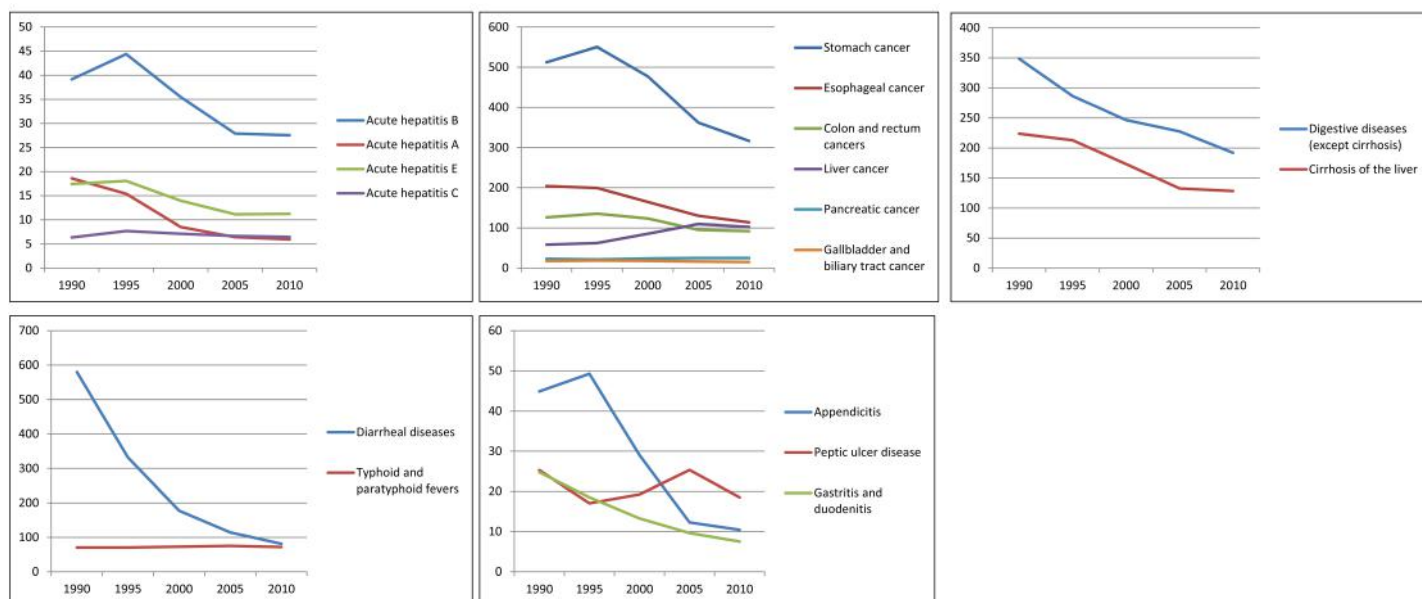


Fig. 7: Trend of YLLs per 100,000 for GILD (GBD 2010)

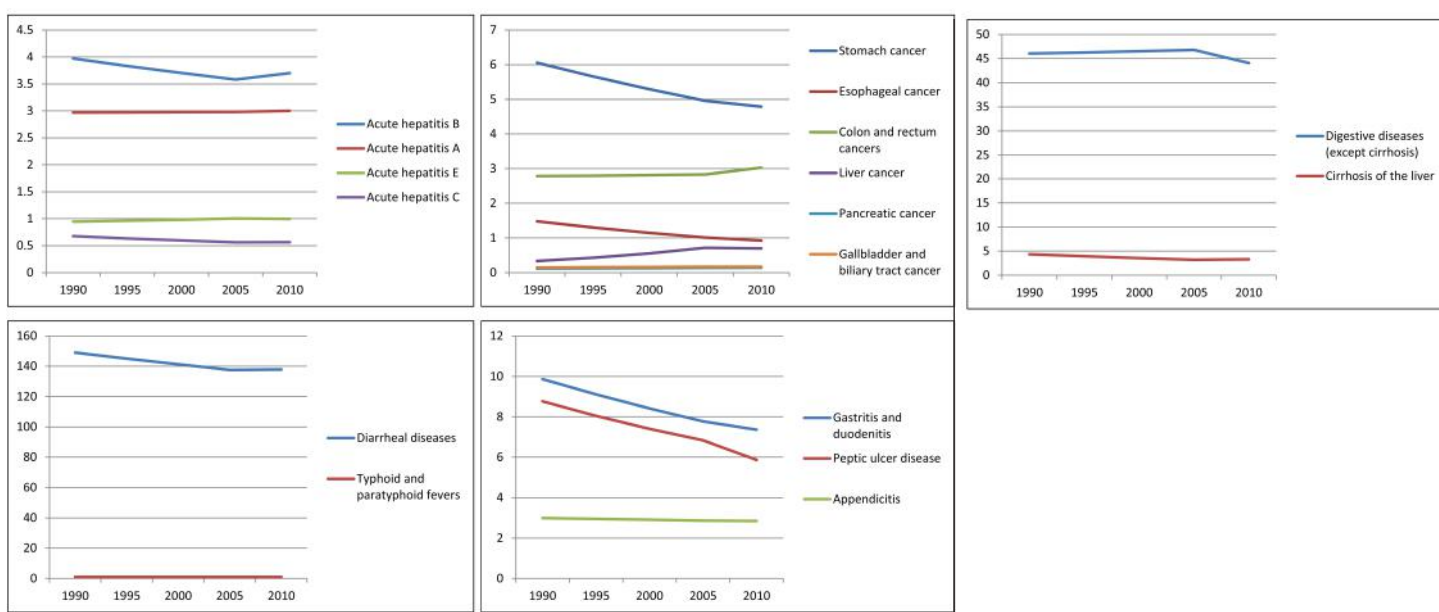


Fig. 8: Trend of YLDs per 100,000 for GILD (GBD 2010)

ing the trend of all diseases including GILD and their mortality and morbidity across the world and is a step forward in understanding changing risk factors of chronic diseases. In spite of being novel and very informative, this study has its own challenges especially in estimating the burden and trend of diseases in developing countries where data are of poor quality. Using population based local data

from Iran, we will try to explain the challenges GBD 2010 faces and suggest strategies to improve the accuracy of future updates in GBD 2015.

Local studies in Iran imply that gastroesophageal reflux disease (GERD) and peptic ulcer disease,¹⁶⁻²² irritable bowel syndrome (IBS),¹⁷ inflammatory bowel diseases (IBD),²³⁻²⁷ chronic nonalcoholic fatty liver disease (NAFLD),^{28,29} and chronic active

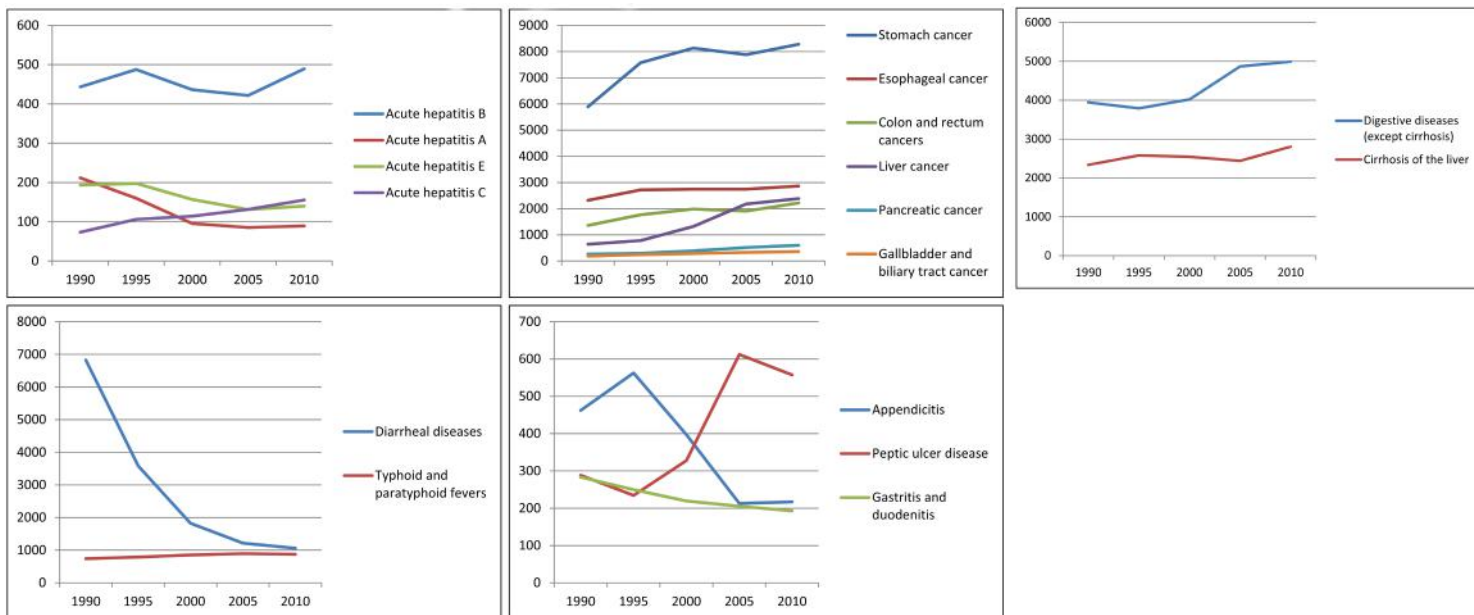


Fig. 9: Trend of total deaths in all ages, both sexes for GILD (GBD 2010)

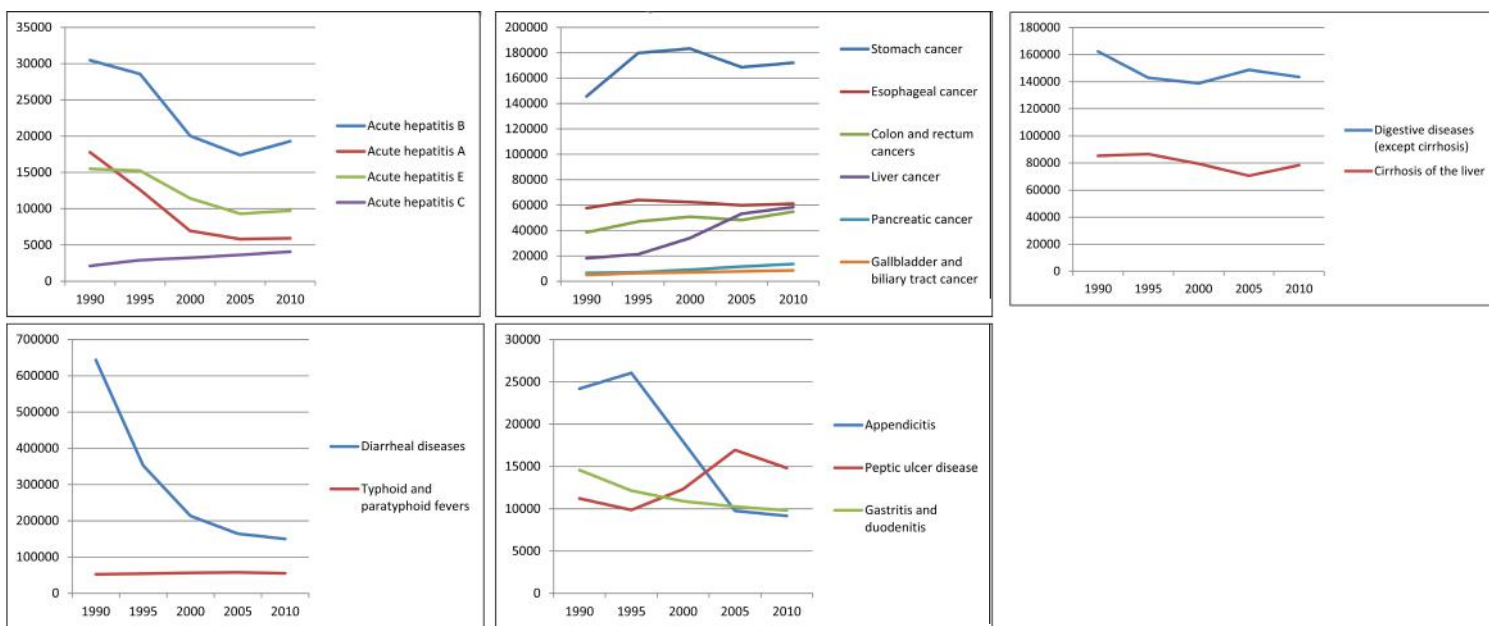


Fig. 10: Trend of total DALYs in all ages, both sexes for GILD (GBD 2010)

and inactive HBV infection³⁰ are amongst the main causes of disability due to GILD in Iran. Among these common diseases, GERD, IBD, and NAFLD show a remarkable increasing trend during the recent decades.^{22,26,29} However, these studies have their own limitations. Some of them are not population-based and others have reported outpatient or inpatient data

of specific referral clinics or hospitals. This is the source of the challenge GBD faces in reporting those GILD that are detected in outpatient settings. This category of GI and hepatic diseases have not been adequately addressed and estimates even do not exist (eg. for the case of GERD and NAFLD) or seem to be lower than existing estimates (eg. for the case of

IBD) in GBD results.

Limited population based cancer registries established in Iran during last 2 decades confirm the findings of GBD 2010 and show an increasing trend for gastric and colorectal cancer and a declining trend of esophageal cancer. The reason for declining trend of squamous cell cancer of esophagus^{31,32} which seems to be paralleled by an increasing incidence of adenocarcinoma of esophagus³³ is most likely due to improvement in socioeconomic status of rural population in Iran and concomitant improvement in quality of nutrition.³⁴ Gastric cancer has remained as the most common cancer in Iran with no declining trend.^{31,35,36} The reason for increasing prevalence of gastric cancer seems to be partly due to high *H.pylori* infection along with several important risk factors specifically common in Iranian population including tobacco, opium, poor oral health, high salt intake, and overweight and obesity.³⁷⁻⁴⁷ A special characteristic of gastric cancer in Iran is the high incidence of proximal or so called cardia gastric cancer.^{48,49} Risk factors for gastric cardia cancer are obesity, overweight, and GERD which is becoming very common in Iran during last two decades.⁴⁹ Therefore, prevailing risk factors for non-cardia cancer along with addition of risk factors for gastric cardia cancer are probably the main reasons for the increasing incidence of gastric cancer in Iran.^{41,48}

Despite the concordance of GBD results with population-based studies regarding gastric, esophageal, and colorectal cancers, the reported increasing trend of liver cancer seems to be overestimated.^{31,36,50,51} Primary liver cancer is not among the 10 most common cancers in Iran and majority of reported cases of liver cancer are actually metastatic secondary liver neoplasia with primary origin mainly from GI tract.^{36,51} HCV infection is very uncommon in Iran⁵² and the HBV infection is of genotype D1 in more than 90% of cases.³⁰ For these reasons, liver cancer has been reported to be uncommon and there is no increasing trend reported from local studies and cancer registries during last 2 decades in Iran.^{53,54}

It is evident that GBD has had numerous achieve-

ments since its establishment, including development of unique metrics for measurement of health across countries. The results have urged policy-makers and other stakeholders especially in developing countries to identify priorities and take action for preventing the prevailing diseases and their risk factors at national level. However, cost-effective interventions may require more detailed and more accurate national and even sub-national estimates. In this regard, we have recently started an important study to especially investigate the trend of national and sub-national burden of gastrointestinal and liver diseases as part of national and sub-national burden of diseases (NASBOD) study in Iran.^{55,56} This study, which contains a comprehensive systematic review can be a reliable source to be used in future updates of GBD studies. Local gray literature, non-English sources of data, access to micro-data of national surveys and specific sub-studies (on hospital data and prescriptions) will enrich the input data of NASBOD compared to GBD. The study can be adopted by other developing countries that are facing similar challenges.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

FUNDING

This study was supported by grants from Iranian association of gastroenterology and Hepatology.

REFERENCES

1. De Maeseneer J, Roberts RG, Demarzo M, Heath I, Sewankambo N, Kidd MR et al. Tackling NCDs: a different approach is needed. *Lancet* 2012;**379**:1860-1.
2. Global Status Report on Noncommunicable Diseases. Geneva. World Health Organization. 2011.
3. Preventing Chronic Diseases: A Vital Investment: WHO Global Report. World Health Organization, Geneva. 2005.
4. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2095-128.
5. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD,

- Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2197-223.
6. Salomon JA, Vos T, Hogan DR, Gagnon M, Naghavi M, Mokdad A, et al. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2129-43.
 7. Salomon JA, Wang H, Freeman MK, Vos T, Flaxman AD, Lopez AD, et al. Healthy life expectancy for 187 countries, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2144-62.
 8. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2163-96.
 9. Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, Levin-Rector A, et al. Age-specific and sex-specific mortality in 187 countries, 1970-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2071-94.
 10. Forouzanfar MH, Sepanlou SG, Shahrz S, Dicker D, Naghavi P, Pourmalek F et al. Evaluating causes of death and morbidity in Iran, global burden of diseases, injuries, and risk factors study 2010. *Arch Iran Med* 2014;**17**:304-20.
 11. Naghavi M, Shahrz S, Sepanlou SG, Dicker D, Naghavi P, Pourmalek F et al. Health transition in Iran toward chronic diseases based on results of Global Burden of Disease 2010. *Arch Iran Med* 2014;**17**:321-35.
 12. Shahrz S, Forouzanfar MH, Sepanlou SG, Dicker D, Naghavi P, Pourmalek F et al. Population health and burden of disease profile of Iran among 20 countries in the region: from Afghanistan to Qatar and Lebanon. *Arch Iran Med* 2014;**17**:336-42.
 13. Mathers CD, Lopez AD, Murray CJL, The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001, in Global Burden of Disease and Risk Factors, A.D. Lopez, et al., Editors. 2006: Washington (DC).
 14. Murray CJ, Ezzati M, Flaxman AD, Lim S, Lozano R, Michaud C et al. GBD 2010: design, definitions, and metrics. *Lancet* 2012;**380**:2063-6.
 15. Malekzadeh F, Sepanlou SG, Malekzadeh R, Poustchi H. Burden of Gastrointestinal and Liver Diseases in Iran from Global burden of disease 2010. *Middle East J Dig Dis* 2015;**7**:138-54.
 16. Barazandeh F, Yazdanbod A, Pourfarzi F, Sepanlou SG, Derakhshan MH, Malekzadeh R. Epidemiology of peptic ulcer disease: endoscopic results of a systematic investigation in Iran. *Middle East J Dig Dis* 2012;**4**:90-6.
 17. Ganji A, Malekzadeh F, Safavi M, Nasserri Moghaddam S, Nourai M, Merat S, et al. Digestive and Liver Disease Statistics in Iran. *Middle East J Dig Dis* 2009;**1**:56-62.
 18. Islami F, Nasserri-Moghaddam S, Pourshams A, Poustchi H, Semnani S, Kamangar F et al. Determinants of gastroesophageal reflux disease, including hookah smoking and opium use- a cross-sectional analysis of 50,000 individuals. *PLoS One* 2014;**9**:e89256.
 19. Islami F, Pourshams A, Nasserri-Moghaddam S, Khademi H, Poutschi H, Khoshnia M et al. Gastroesophageal Reflux Disease and overall and Cause-specific Mortality: A Prospective Study of 50000 Individuals. *Middle East J Dig Dis* 2014;**6**:65-80.
 20. Nourai M, Radmard AR, Zaer-Rezaii H, Razjouyan H, Nasserri-Moghaddam S, Malekzadeh R. Hygiene could affect GERD prevalence independently: a population-based study in Tehran. *Am J Gastroenterol* 2007;**102**:1353-60.
 21. Nourai M, Razjouyan H, Assady M, Malekzadeh R, Nasserri-Moghaddam S. Epidemiology of gastroesophageal reflux symptoms in Tehran, Iran: a population-based telephone survey. *Arch Iran Med* 2007;**10**:289-94.
 22. Sepanlou S, Khademi H, Abdollahzadeh N, Noori F, Malekzadeh F, Malekzadeh R. Time Trends of Gastro-esophageal Reflux Disease (GERD) and Peptic Ulcer Disease (PUD) in Iran. *Middle East J Dig Dis* 2010;**2**:78-83.
 23. Abedian S, Asl Soleimani H, Saberifiroozi M, Malekzadeh R. Common Digestive and Liver Diseases among 5880 Patients Admitted to Shariati Hospital, Tehran, Iran during 2000-2009. *Middle East J Dig Dis* 2012;**4**:28-33.
 24. Aghazadeh R, Zali MR, Bahari A, Amin K, Ghahghaie F, Firouzi F. Inflammatory bowel disease in Iran: a review of 457 cases. *J Gastroenterol Hepatol* 2005;**20**:1691-5.
 25. Malekzadeh R, Varshosaz S, Merat S, Hadidchi S, Mirmajlesi S, Vahedi H et al. Crohn's disease: a review of 140 cases from Iran. *Iran J Med* 2000;**25**:138-43.
 26. Malekzadeh R, Varshosaz S, Mirmajlesi S, Tavakoli H. Rising Incidence of Crohn's disease in Iran over 1989-1999. *Gastroenterology* 2000;**118**:A6172.
 27. Vahedi H, Merat S, Momtahn S, Olfati G, Kazzazi AS, Tabrizian T, et al. Epidemiologic characteristics of 500 patients with inflammatory bowel disease in Iran studied from 2004 through 2007. *Arch Iran Med* 2009;**12**:454-60.
 28. Pourshams A, Malekzadeh R, Monavvari A, Akbari MR, Mohamadkhani A, Yarahmadi S, et al. Prevalence and etiology of persistently elevated alanine aminotransferase levels in healthy Iranian blood donors. *J Gastroenterol Hepatol* 2005;**20**:229-33.
 29. Sohrabpour A, Rezvan H, Amini-Kafiabad S, Dayhim M, Merat S, Pourshams A. Prevalence of Nonalcoholic Steatohepatitis in Iran: A Population based Study. *Middle East J Dig Dis* 2010;**2**:14-9.
 30. Merat S, Rezvan H, Nourai M, Jamali A, Assari S, Abolghasemi H, et al. The prevalence of hepatitis B surface antigen and anti-hepatitis B core antibody in Iran: a population-based study. *Arch Iran Med* 2009;**12**:225-31.
 31. Roshandel G, Sadjadi A, Aarabi M, Keshtkar A, Sedaghat SM, Nourai SM, et al. Cancer incidence in Golestan

- Province: report of an ongoing population-based cancer registry in Iran between 2004 and 2008. *Arch Iran Med* 2012;**15**:196-200.
32. Semnani S, Sadjadi A, Fahimi S, Nouraie M, Naeimi M, Kabir J, et al. Declining incidence of esophageal cancer in the Turkmen Plain, eastern part of the Caspian Littoral of Iran: a retrospective cancer surveillance. *Cancer Detect Prev* 2006;**30**:14-9.
 33. Ghasemi-Kebrja F, Roshandel G, Semnani S, Shakeri R, Khoshnia M, Naeimi-Tabiei M, et al. Marked increase in the incidence rate of esophageal adenocarcinoma in a high-risk area for esophageal cancer. *Arch Iran Med* 2013;**16**:320-3.
 34. Islami F, Kamangar F, Nasrollahzadeh D, Aghcheli K, Sotoudeh M, Abedi-Ardekani B, et al. Socio-economic status and oesophageal cancer: results from a population-based case-control study in a high-risk area. *Int J Epidemiol* 2009;**38**:978-88.
 35. Babaei M, Pourfarzi F, Yazdanbod A, Chiniforush MM, Derakhshan MH, Mousavi SM, et al. Gastric cancer in Ardabil, Iran--a review and update on cancer registry data. *Asian Pac J Cancer Prev* 2010;**11**:595-9.
 36. Sadjadi A, Malekzadeh R, Derakhshan MH, Sepehr A, Nouraie M, Sotoudeh M, et al. Cancer occurrence in Ardabil: results of a population-based cancer registry from Iran. *Int J Cancer* 2003;**107**:113-8.
 37. Hakami R, Etemadi A, Kamangar F, Pourshams A, Mohtadina J, Firoozi MS, et al. Cooking methods and esophageal squamous cell carcinoma in high-risk areas of Iran. *Nutr Cancer* 2014;**66**:500-5.
 38. Kamangar F, Shakeri R, Malekzadeh R, Islami F. Opium use: an emerging risk factor for cancer? *Lancet Oncol* 2014;**15**:e69-77.
 39. Khademi H, Malekzadeh R, Pourshams A, Jafari E, Salahi R, Semnani S, et al. Opium use and mortality in Golestan Cohort Study: prospective cohort study of 50,000 adults in Iran. *BMJ* 2012;**344**:e2502.
 40. Malekzadeh MM, Khademi H, Pourshams A, Etemadi A, Poustchi H, Bagheri M, et al. Opium use and risk of mortality from digestive diseases: a prospective cohort study. *Am J Gastroenterol* 2013;**108**:1757-65.
 41. Malekzadeh R, Derakhshan MH, Malekzadeh Z. Gastric cancer in Iran: epidemiology and risk factors. *Arch Iran Med* 2009;**12**:576-583.
 42. Pakseresht M, Forman D, Malekzadeh R, Yazdanbod A, West RM, Greenwood DC, et al. Dietary habits and gastric cancer risk in north-west Iran. *Cancer Causes Control* 2011;**22**:725-36.
 43. Pourfarzi F, Whelan A, Kaldor J, Malekzadeh R. The role of diet and other environmental factors in the causation of gastric cancer in Iran--a population based study. *Int J Cancer* 2009;**125**:1953-60.
 44. Sadjadi A, Derakhshan MH, Yazdanbod A, Boreiri M, Parsaeian M, Babaei M, et al. Neglected role of hookah and opium in gastric carcinogenesis: a cohort study on risk factors and attributable fractions. *Int J Cancer* 2014;**134**:181-8.
 45. Shakeri R, Malekzadeh R, Etemadi A, Nasrollahzadeh D, Aghcheli K, Sotoudeh M, et al. Opium: an emerging risk factor for gastric adenocarcinoma. *Int J Cancer* 2013;**133**:455-61.
 46. Zamani N, Hajifaraji M, Fazel-tabar Malekshah A, Keshkar AA, Esmailzadeh A, Malekzadeh R. A case-control study of the relationship between gastric cancer and meat consumption in Iran. *Arch Iran Med* 2013;**16**:324-9.
 47. Bashash M, Yavari P, Hislop TG, Shah A, Sadjadi A, Babaei M, et al. Comparison of two diverse populations, British Columbia, Canada, and Ardabil, Iran, indicates several variables associated with gastric and esophageal cancer survival. *J Gastrointest Cancer* 2011;**42**:40-5.
 48. Derakhshan MH, Malekzadeh R, Watabe H, Yazdanbod A, Fyfe V, Kazemi A et al. Combination of gastric atrophy, reflux symptoms and histological subtype indicates two distinct aetiologies of gastric cardia cancer. *Gut* 2008;**57**:298-305.
 49. Derakhshan MH, Yazdanbod A, Sadjadi AR, Shokoohi B, McColl KE, Malekzadeh R. High incidence of adenocarcinoma arising from the right side of the gastric cardia in NW Iran. *Gut* 2004;**53**:1262-6.
 50. Ansari R, Mahdavinia M, Sadjadi A, Nouraie M, Kamangar F, Bishehsari F, et al. Incidence and age distribution of colorectal cancer in Iran: results of a population-based cancer registry. *Cancer Lett* 2006;**240**:143-7.
 51. Sadjadi A, Nouraie M, Mohagheghi MA, Mousavi-Jarrahi A, Malekzadeh R, Parkin DM. Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev* 2005;**6**:359-63.
 52. Merat S, Rezvan H, Nouraie M, Jafari E, Abolghasemi H, Radmard AR, et al. Seroprevalence of hepatitis C virus: the first population-based study from Iran. *Int J Infect Dis* 2010;**14 Suppl3**:e113-6.
 53. Moghaddam SD, Haghdoost AA, Hoseini SH, Ramazani R, Rezazadehkermani M. Incidence of hepatocellular carcinoma in southeast Iran. *Hepat Mon* 2010;**10**:270-4.
 54. Poustchi H, Sepanlou S, Esmaili S, Mehrabi N, Ansary-moghaddam A. Hepatocellular carcinoma in the world and the middle East. *Middle East J Dig Dis* 2010;**2**:31-41.
 55. Farzadfar F, Delavari A, Malekzadeh R, Mesdaghinia A, Jamshidi HR, Sayyari A, et al. NASBOD 2013: design, definitions, and metrics. *Arch Iran Med* 2014;**17**:7-15.
 56. Salimzadeh H, Ardeshtir Larijani F, Abedian S, Kalantar Motamedi SM, Malekzadeh MM, Mohaghegh H, et al. The trend of national and sub-national burden of gastrointestinal and liver diseases in Iran 1990 to 2013; study protocol. *Arch Iran Med* 2014;**17**:33-53.