Original article

Epidemiology of chronic liver disease mortality in community population

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Background: Liver disease is an important cause of morbidity and mortality in the United States. Currently, up to 2% of all deaths are attributable to liver disease. The economic burden associated with liver disease is also substantial. There are still significant gaps in the current understanding of the epidemiology and burden of liver disease at the population level.

Materials and Methods: We studied chronic liver disease (CLD) and cirrhosis deaths among a community population of the state of Wisconsin for the duration of 1999-2005 to estimate the mortality and disease burden of CLD. Data information was gathered from the population based public data source; Wisconsin Interactive Statistics on Health.

Results: A total of 3024 deaths were recorded due to CLD the study period of 1999-2005. The mortality rate was 7.92 per 100,000 person-year (95%CI :7.64–8.21). Male had higher mortality compared to female. Though statistically insignificant, a trend of increase in mortality rate was observed from 1999 (4.81, 95%CI:4.17–5.44) to 2005 (6.02, 95%CI:5.33–6.21).

Conclusion: The findings were suggestive that the death due to CLD causes noteworthy burden for the population in terms of years of potential life lost. Prevention programme addressing this very problem should be accentuated.

Key words: chronic liver disease, cirrhosis, mortality, disease-burden.

Introduction

It has been reported that since 1979 the death rate for chronic liver disease and cirrhosis (CLD) has been showing a declining trend in the United States [1-2]. The reason for this declining trend is still unclear; however, some reports have suggested that it may be related to a decline in alcohol use in the United States [3]. Despite this decline, chronic liver disease remains an important cause for both in terms of death and of years of potential life lost [4-6]. According to the national vital statistics report [7] the annual number of deaths attributed to chronic liver disease and cirrhosis has been listed as the tenth leading cause of death as of 1998 in the United States. Cases of newly diagnosed chronic liver disease are defined by persistently elevated liver enzymes, radiological evidence of cirrhosis, pathology consistent with chronic liver disease or primary liver cancer, or a clinical event diagnostic of chronic liver disease. Ascertainment methods vary across the facilities, with some sites identifying cases by surveillance of gastroenterology practices and others using collected medical records, such a disease or death registration system. But whatever the case ascertain method is, a community population based study of liver disease is necessary for accurate information on the burden of disease and the contribution of different factors of the disease to this burden. Four disease groups are coded as the chronic liver disease due to the reason that they may share common characteristics or etiologies. These groups include alcohol related liver disease, cirrhosis without alcohol, chronic hepatitis or liver disease without alcohol, and biliary cirrhosis. In this report, we describe CLD mortality and analyses of recent trends in a community

population in the United States.

Materials and method

Our analysis included all CLD deaths among the population of the state of Wisconsin, USA. The period of the present study covers the duration from the 1st January 1999 to the 31st December 2002. We analyzed the secondary data for the CLD mortality for the study population. Data information was obtained from the public data source of Wisconsin Interactive Statistics on Health (WISH) [8]. This data base gives information about health indicators (measures of health) in Wisconsin. The database contains information from death certificates filed in state vital-statistics offices and includes causes of death reported by attending physicians, medical examiners, and coroners. Population data come from the Bureau of the Census. These data are based on information gathered in censuses and on estimation procedures conducted in non-census years. This allows policy makers, health professionals, and the public to submit requests for data and receive respond. To construct respond to questions, WISH uses protected databases containing Wisconsin birth, death, population and injury data for multiple years and geographic areas. WISH was prepared by the Department of Health and Family Services, Division of Public Health, Bureau of Health Information and Policy [8]. On these files, CLD deaths are coded according to the International Classification of Diseases (ICD-10) [9].

To calculate the age specific pattern of injury death the age was categorized into eighteen groups; 0-17, 18-24, 25-34, 35-44, 45—54, 55—64, 65—74, 75—84 and 85+. To calculate the age adjusted CLD death rate direct method was applied using the US population from 2000 census as the standard population. Death rate for injury deaths per 100,000 person-years was calculated by gender, age group and study years. For all the incidence rates 95% confidence intervals (95%CI) were calculated [10]. To calculate incidence rate the total number of events in the relevant faction was taken as numerator and person-time of each population at risk was taken as the denominator. For example, the CLD death rate for the "Men" was calculated by dividing 'the total number of CLD death events for the group' by 'the person-time for the group'. Person-time of the group was constructed by averaging the four year population in the study area. The eight year population average was calculated by taking the population record of each year for the years of 1999 to 2005 for the relevant group and calculating the average. The result was then multiplied by 100,000 to get the death rate for CLD per 100,000 populations per year (person-year). Years of Potential Life Lost (YPLL) was calculated to identify the disease burden on the population. The population demographic data derived from the routine census and vital statistics system are collected annually for the Wisconsin County for each of the years of the study period. These provide the precise denominator for the calculations of different rates.

Result

In the community of Wisconsin County during the years of 1999 to 2005 a total of 3024 deaths were recorded due to chronic liver disease and cirrhosis. The mortality rate was 7.92 per 100,000 person-year (95% CI: 7.64 – 8.21). Table 1 shows the chronic liver disease and cirrhosis mortality for the entire population for the period 1998–2002 by age specific and age adjusted death rates stratified by gender. In every age group the male population had higher chronic liver disease and cirrhosis death rates in comparison to the corresponding female age group population. Male had higher chronic liver disease and cirrhosis mortality compared to female. Chronic liver disease and cirrhosis mortality for male was 9.71 per 100,000 person-year (95%CI: 9.35 - 10.24), which was higher than the death rate for female (6.1 per 100,000 person-year; 95%CI: 5.75 – 6.44). The age adjusted mortality rate for male was 10.0 per 100,000 person-year (95%CI: 9.56 – 10.46) and for the female was 5.56 per 100,000 person-year (95%CI: 5.22 – 5.89).

Table 1: Age specific and age adjusted death rates of chronic liver disease and cirrthosis (CLD) mortality in Wisconsin, USA. 1998-2002.

Gender	Age group	Number of Deaths	Population	CLD Death Rate*	95% Confidence Interval
Men					
	25 - 34	20	2,484,634	0.8	0.45 - 1.16
	35 - 44	192	3,024,052	6.35	5.45 - 7.25
	45 - 54	490	2,750,421	17.82	16.24 - 19.39
	55 - 64	438	1,743,452	25.12	22.77 - 27.48
	65 - 74	399	1,141,144	34.96	31.53 - 38.40
	75+	306	937,793	32.63	28.97 - 36.29
	All age	1,847	18,860,291	9.79	9.35 - 10.24
	Age adjusted	1,847	18,860,291	10.01	9.56 - 10.46
Women					
	25 - 34	12	2,403,123	0.5	0.22 - 0.78
	35 - 44	145	2,996,732	4.84	4.05 - 5.63
	45 - 54	208	2,729,575	7.62	6.58 - 8.66
	55 - 64	228	1,807,084	12.62	10.98 - 14.25
	65 - 74	260	1,321,839	19.67	17.28 - 22.06
	75+	321	1,578,339	20.34	18.11 - 22.56
	All age	1,177	19,307,397	6.1	5.75 - 6.44
	Age adjusted	1,177	19,307,397	5.56	5.22 - 5.89
All case					
	25 - 34	32	4,887,756	0.65	0.43 - 0.88
	35 - 44	337	6,020,783	5.6	5.00 - 6.19
	45 - 54	698	5,479,996	12.74	11.79 - 13.68
	55 - 64	666	3,550,535	18.76	17.33 - 20.18
	65 - 74	659	2,462,983	26.76	24.71 - 28.80
	75+	627	2,516,132	24.92	22.97 - 26.87
	All age	3,024	38,167,688	7.92	7.64 - 8.21
	Age adjusted	3,024	38,167,688	7.66	7.38 - 7.93

* Death rate in per 100,000 person-year

Table 2 shows the liver disease and cirrhosis mortality across the years of 1999 to 2005. The mortality rate increased from the year 1999 (4.81 per 100,000 person-year; 95%CI: 4.17 – 5.44) to the year 2005 (6.02 per 100,000 person-year; 95%CI:

5.33 – 6.21). Though statistically insignificant but a tendency of increase from the year 1999 to 2005 was observed among both male and female. It was also observed that across the years always the liver disease and cirrhosis mortality was lower for the female in comparison to the male.

Table 2: shows the average age at death for the liver disease

Year	Gender	Number of Deaths	Population	CLD Death Rate*	95% Confidence Interval
1999	All case	221	4,597,884	4.81	4.17 - 5.44
	Male	145	2,312,408	6.27	5.25 - 7.29
	Female	76	2,285,475	3.33	2.58 - 4.07
2000	All case	234	4,661,122	5.02	4.38 - 5.66
	Male	175	2,357,531	7.42	6.32 - 8.52
	Female	59	2,303,591	2.56	1.91 - 3.21
2001	All case	234	4,720,104	4.96	4.32 - 5.59
	Male	156	2,387,852	6.53	5.51 - 7.56
	Female	78	2,332,253	3.34	2.60 - 4.09
2002	All case	256	4,752,645	5.39	4.73 - 6.05
	Male	157	2,404,026	6.53	5.51 - 7.55
	Female	99	2,348,619	4.22	3.38 - 5.05
2003	All case	257	4,782,959	5.37	4.72 - 6.03
	Male	163	2,421,259	6.73	5.70 - 7.77
	Female	94	2,361,700	3.98	3.18 - 4.78
2004	All case	244	4,819,599	5.06	4.43 - 5.70
	Male	155	2,440,034	6.35	5.35 - 7.35
	Female	89	2,379,565	3.74	2.96 - 4.52
2005	All case	292	4,854,260	6.02	5.33 - 6.71
	Male	191	2,458,245	7.77	6.67 - 8.87
	Female	101	2,396,015	4.22	3.39 - 5.04

* Death rate in per 100,000 person-year

Table 3 shows the average age at death for the liver disease and cirrhosis fatalities stratified by gender and age groups. The overall average age at death for the male were 60.15 years (Standard Deviation (SD) ± 0.31) and for female were 63.23 years (SD ± 0.44). The average age at death for female was significantly higher than the average age at death for male.

Table 3: Average age at death for the liver disease and cirrhosis (CLD) fatalities stratified by gender and age groups in Wisconsin, USA. 1998-2002.

Gender	Age group	Total of Ages (years)	Total Number of Deaths	Average Age at Death	SD*	95% Confidence Interval
Men	All ages	111,098	1,847	60.15	0.31	59.54 - 60.76
	25-34	621	20	31.05	0.62	29.83 - 32.27
	35-44	7,794	192	40.59	0.19	40.23 - 40.96
	45-54	24,356	490	49.71	0.13	49.46 - 49.95
	55-64	26,046	438	59.47	0.14	59.19 - 59.74
	65-74	27,648	399	69.29	0.14	69.01 - 69.57
	75+	24,611	306	80.43	0.27	79.90 - 80.96
Women	All ages	74,416	1,177	63.23	0.44	62.37 - 64.08
	18-24	68	3	22.67	1.46	19.80 - 25.54
	25-34	377	12	31.42	0.97	29.51 - 33.32
	35-44	5,869	145	40.48	0.22	40.04 - 40.91
	45-54	10,296	208	49.5	0.20	49.11 - 49.89
	55-64	13,577	228	59.55	0.20	59.16 - 59.94
	65-74	18,140	260	69.77	0.18	69.42 - 70.12
	75+	26,089	321	81.27	0.25	80.78 - 81.77
Both	All ages	185,514	3,024	61.35	0.26	60.85 - 61.85
	18-24	90	4	22.5	0.81	20.91 - 24.09
	25-34	998	32	31.19	0.48	30.25 - 32.13
	35-44	13,663	337	40.54	0.14	40.26 - 40.82
	45-54	34,652	698	49.64	0.10	49.44 - 49.85
	55-64	39,623	666	59.49	0.11	59.27 - 59.72
	65-74	45,788	659	69.48	0.11	69.26 - 69.70
	75+	50,700	627	80.86	0.18	80.50 - 81.22

*SD – Standard deviation.

Table 4 describes the average age at death for the liver disease and cirrhosis fatalities across the years of 1999 to 2005. The average age at death for both men and women remained similar across the study years.

Gender	Year of Death	Total of Ages (years)	Total Number of Deaths	Average Age at Death	SD* (±)	95% Confidence Interval
Men	1999	14,231	236	60.3	0.86	58.63 - 61.97
	2000	17,443	288	60.57	0.82	58.95 - 62.18
	2001	16,020	267	60	0.82	58.39 - 61.61
	2002	16,528	269	61.44	0.84	59.79 - 63.09
	2003	14,960	251	59.6	0.83	57.98 - 61.22
	2004	15,615	260	60.06	0.78	58.53 - 61.59
	2005	16,301	276	59.06	0.79	57.52 - 60.60
	All year	111,098	1,847	60.15	0.31	59.54 - 60.76
Women	1999	10,828	166	65.23	1.15	62.98 - 67.47
	2000	10,057	153	65.73	1.16	63.47 - 68.00
	2001	10,462	163	64.18	1.11	62.01 - 66.36
	2002	10,162	167	60.85	1.16	58.58 - 63.12
	2003	11,523	184	62.63	1.14	60.40 - 64.85
	2004	9,371	154	60.85	1.26	58.39 - 63.31
	2005	12,013	190	63.23	1.09	61.09 - 65.36
	All year	74,416	1,177	63.23	0.44	62.37 - 64.08
All case	1999	25,059	402	62.34	0.70	60.97 - 63.71
	2000	27,500	441	62.36	0.68	61.02 - 63.69
	2001	26,482	430	61.59	0.67	60.28 - 62.89
	2002	26,690	436	61.22	0.68	59.88 - 62.55
	2003	26,483	435	60.88	0.68	59.55 - 62.21
	2004	24,986	414	60.35	0.68	59.03 - 61.68
	2005	28,314	466	60.76	0.65	59.49 - 62.03
	All year	185,514	3,024	61.35	0.26	60.85 - 61.85

*SD – Standard deviation.

Table 4: average age at death for the liver disease

Table 5 shows the Years of Potential Life Lost (YPLL) and YPPL rate in years per 100,000 population with the 95% CI stratified by gender and age group. For all case, YPLL rate was 1147.66 year per 100,000 population (95%CI: 113.59 – 115.74). For men the YPLL rate was 154.23 years per 100,000 population (95%CI: 152.46 – 156.00) and for women the rate was 82.21 years per 100,000 population (95%CI: 80.93 – 83.49). The YPLL rate among men was about two times higher than women. Similar also was observed for the age adjusted YPLL rate among men and women.

Table 5: years of potential life lost (YPLL) and YPLL rate in years per 100,000 population

Gender	Age group	YPLL*	Population	YPLL Rate†	95% Confidence Interval
Men					
	25-34	879	2,484,634	35.38	33.04 - 37.72
	35-44	6,606	3,024,052	218.45	213.19 - 223.71
	45-54	12,394	2,750,421	450.62	442.71 - 458.54
	55-64	6,804	1,743,452	390.26	381.01 - 399.52
	65-74	2,277	1,141,144	199.54	191.35 - 207.72
	All age	29,088	18,860,291	154.23	152.46 - 156.00
	Age adjusted	29,088	18,860,291	148.99	147.25 - 150.73
Women					
	25-34	523	2,403,123	21.76	19.90 - 23.63
	35-44	5,006	2,996,732	167.05	162.42 - 171.67
	45-54	5,304	2,729,575	194.32	189.09 - 199.54
	55-64	3,523	1,807,084	194.96	188.52 - 201.39
	65-74	1,360	1,321,839	102.89	97.42 - 108.35
	All age	15,873	19,307,397	82.21	80.93 - 83.49
	Age adjusted	15,873	19,307,397	80.92	79.65 - 82.18
Both gender					
	25-34	1,402	4,887,756	28.68	27.18 - 30.19
	35-44	11,612	6,020,783	192.87	189.36 - 196.37
	45-54	17,698	5,479,996	322.96	318.21 - 327.71
	55-64	10,327	3,550,535	290.86	285.26 - 296.46
	65-74	3,637	2,462,983	147.67	142.87 - 152.46
	All age	44,961	38,167,688	117.8	116.71 - 118.89
	Age adjusted	44,961	38,167,688	114.66	113.59 - 115.74

*YPPL- Years of Potential Life Lost.

† YPLL Rate - Years of Potential Life Lost rate, rate in per 100,000 person-year.

Discussion

The present study examined the CLD mortality and disease burden in a community based population in the United States. The findings were suggestive that the death due to CLD causes noteworthy burden for the population in terms of years of potential life lost. There was a difference between the mortality among the gender and ages. Though insignificant, but the CLD mortality seemed to have increased across the starting and the end of the study period. The average age at death did not change across the study period indicating that the age distribution regarding the mortality did not have major variation.

Liver disease is an important cause of morbidity and mortality in the United States. Currently, up to 2% of all deaths are attributable to liver disease. The economic burden associated with liver disease is also substantial with approximately 1% of the total national health care expenditure devoted to the care of patients with liver disease [11]. Moreover, the burden of liver disease appears to be on the rise, due in part to the increasing prevalence of hepatitis C and non-alcoholic fatty liver disease (NAFLD). Many liver diseases with relatively low frequency have substantial impact on the longevity or on the quality of life of the population affected by the diseases. The most common etiology of chronic liver disease in the United States is hepatitis C (57%), followed by alcoholic fatty liver disease (24%), and NAFLD (9.1%) [12]. Other etiologies include hepatitis B, primary sclerosing cholangitis, primary biliary cirrhosis, hereditary hemochromatosis, autoimmune hepatitis, alpha 1-antitrypsin deficiency, and liver cancer [12]. These conditions accounted for less than 7% of all newly diagnosed cases of chronic liver disease seen by gastrointestinal specialists [12]. In the report of the American Gastroenterological Association [11], which estimated the prevalence and economic burden of common gastrointestinal and liver disorders, including chronic liver disease and cirrhosis, chronic hepatitis C, liver cancer, and gallbladder disease; these four liver disease categories accounted for approximately one quarter (approximately $9.1 billion) of all direct costs associated with the 17 conditions in the report and also represented approximately 1% of all health care spending in the United States in 1998 [11]. These estimates were derived from publicly available data sets, supplemented by proprietary third-party payer databases.

Third National Health and Nutrition Examination Survey (NHANES III), a nationwide survey in a representative sample of non-institutionalized and civilian citizens, has estimated the prevalence of hepatitis C virus (HCV) infection in the general population of the United States. The prevalence of antibodies against HCV (anti-HCV) was 1.8%, which corresponded to approximately 3.9 million United States populations who have been infected with HCV. Of them, approximately 70% (2.7 million) had evidence of chronic infection [13]. Using mathematical models, Armstrong et al. estimated that the prevalence of HCV in the United States peaked in the mid-1990s at slightly above 2.0% and would slowly decline to 1.0% by 2030 [14]. Furthermore, the model predicted that the proportion of people with infection for 20 years or longer would increase with an anticipated peak in the mid 2010s. Indeed, there is a projected 4-fold increase in the number of persons with long-standing (more than two decades) infection between 1990 and 2015 [14]. The importance of this prediction is that persons with a long duration of infection are at risk to develop serious complications of chronic liver disease such as cirrhosis.

Reliable and accurate estimation for the incidence and prevalence of alcohol-induced liver disease or alcoholic liver disease are scarce. In 1986, over 50% of deaths due to cirrhosis were attributed to alcohol [15]. In 1997, the age-adjusted death rate from alcoholic liver disease was 3.8 per 100,000, which corresponds to 40% of deaths from cirrhosis or 28% of all deaths from liver disease [15]. Every heavy drinker does not develop alcohol-induced liver disease, and the risk factors for alcohol-induced liver disease have not been fully elucidated. Genetic differences are also likely to contribute to the susceptibility to alcoholism and alcohol-induced liver disease. Additionally, alcohol may accelerate the progression of other coexisting liver diseases, such as hepatitis C.

NAFLD includes a spectrum of histological abnormalities [16]. The pathogenesis of NAFLD has not been completely defined, but clinical and biochemical correlates include obesity, hyper-lipidemia, type 2 diabetes mellitus, hyper-insulinemia, and insulin resistance. The clinical importance of NAFLD relates to its high prevalence in the population and the potential of this to progress to cirrhosis. A recent analysis of biochemical data in participants of the NHANES III suggested that the prevalence of liver diseases with enzyme evaluation without evidence of hepatitis B or C and normal iron index among nondrinkers may be as high as 24% in the United States [17]. Although the extent to which NAFLD accounts for these abnormalities remains unknown, but this group of individuals had several of the risk factors for NAFLD including obesity and diabetes. Another prevalence study based on histological sources, such as liver biopsy, autopsy, and post-mortem series, indicate that 10% to 40% of the general population may have NAFLD [18].

There are significant gaps in the current understanding of the epidemiology and burden of liver disease at the

population level. This is partly due to the fact that many studies in hepatology are conducted at referral centers based on selected patients. As most of the liver diseases have a substantial latency period during which patients have mild asymptomatic liver disease, studies based on referral patients only recognize patients with the most severe or advanced disease and thus fail to obtain information on the entire spectrum of disease. Thus there will be a bias towards severity among those study results. Population-based data are especially important for diseases of chronic nature and for those diseases whose prevalence is on the rise. Increasing consciousness of the impact and need for intervention by the public and funding agencies appears to be a prerequisite for a continued expansion of research in the area as it has in other fields such as heart disease, diabetes or stroke. Simultaneously, hepatology specialists also can contribute to a better understanding of the epidemiology of liver disease. Epidemiologic investigation of NAFLD is difficult because of lack of precise diagnostic markers that are applicable to the population. So the hepatologists can attempt to be able to classify diseases by clear-cut diagnostic criteria on the basis of underlying patho-physiological mechanisms. Further more, investigation in many liver diseases that are infrequent will continue to depend on patients seen at referral centers. So, concerted efforts across specialty centers are needed for a meaningful progress to be made. For better understanding of the epidemiology of liver diseases, collaborative studies are in general necessary and systematic efforts supported by private and public research funding are essential to advance the knowledge in the most efficient manner. A growing recognition within the hepatologist society regarding the issue that a well designed and executed epidemiology and health service research in liver disease is as important as, and complementary to, traditional "wet-bench" research needs to continue to gain acceptance within the academic societies. Generally speaking, to improve the understanding of the epidemiology and impact of liver disease and to increase the ability to introduce effective means of diagnosis, therapy, and prevention of liver disease at the population level the key issues are comprehensive data from systematic population based research infrastructure. Results of such comprehensive programs will best inform policy-making decisions for formulating guidelines and resource allocation for the prevention of liver disease in the population level.

References

1. National Center for Health Statistics. Advance report of final mortality statistics, 1991. Month Vital Stat Rep. 1993; 42(2).
2. Hurwitz ES, Homan RC, Strine TW, Chorba TL. Chronic liver disease mortality in the United States, 1979 through 1989. Am J Pub Health 1995;**85:**1256-1260.
3. Williams GD, Stinson FS, Brooks SD, Clem D, Noble J. Apparent per capita consumption: national, state, and regional trends, 1977-1989. Rockville, Md: US Dept of Health and Human Services; 1991. DHHS publication ADM 281-89-0001.
4. Centers for Disease Control and Prevention. Deaths and hospitalizations from chronic liver disease and cirrhosis-United States, 1980-1989. MMWR. 1993;**41:**969-973.
5. Dufour MC. Chronic liver disease and cirrhosis. In: Everhart JE, ed. Digestive Diseases in the United States: Epidemiology and Impact. Washington, DC: US Department of Health and Human Services, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases 1994:615-646.
6. Grant BF, DeBakey S, Zobeck TS. Liver cirrhosis mortality in the United States 1973-1988. In: November Surveillance Report, No. 18. Washington, DC: 1991.
7. Martin JA, Smith BL, Mathews TJ, Ventura SJ. Births and deaths: preliminary data for 1998. In: National Center for Health Statistics. National Vital Statistics Report. Vol. 47, No. 25. Hyattsville, MD: National Center for Health Statistics, 1998.
8. Wisconsin Dept. of Health and Family Services, Divison of Public Health, Bureau of Health Information and Policy. Wisconsin Interactive Statistics on Health (WISH) data query system.
9. World Health Organisation. 1992. International statistical classification of diseases and related health problems—10th revision. Geneva: WHO.
10. Kenneth J. Rothman. 2002. Epidemiology: an introduction. New York: Oxford University Press. 137-139.
11. The burden of gastrointestinal diseases. Bethesda, MD: The American Gastroenterologica Association, 2001;41-60.
12. Murphy S. Deaths: final data for 1998. National vital statistics reports. Hyattsville, MD: National Center for Health Statistics, 2000, Vol. 48.
13. Alter MJ, Kruszon-Moran D, Nainan OV, McQuillan GM, Gao F, Moyer LA, Kaslow RA, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. N Engl J Med 1999;**341:**

556-562.

14. Armstrong GL, Alter MJ, McQuillan GM, Margolis HS. The past incidence of hepatitis C virus infection: implications for the future burden of chronic liver disease in the United States. Hepatology 2000;**31:** 777-782.

15. Greenfield TK, Rogers JD. Who drinks most of the alcohol in the US? The policy implications. J Studies Alcohol 1999;**60:**78-89.

16. Matteoni C, Younossi Z, Gramlich T, Boparai N, Liu Y, McCullough A. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 1999;**116:**1413-1419.

17. Clark JM, Brancati FL, Diehl AM. Nonalcoholic fatty liver disease: the most common cause of abnormal liver enzymes in the US population [Abstract]. Gastroenterology 2001;**120:**A65.

18. Falck-Ytter Y, Younossi Z, Marchesini G, McCullough A. Clinical features and natural history of nonalcoholic steatosis syndromes. Semin Liver Dis 2001;**21:**17-26.