Published in final edited form as:

Hepatology. 2012 February ; 55(2): 447–454. doi:10.1002/hep.24725.

Upper Limits of Normal for Alanine Aminotransferase Activity in the United States Population

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Abstract

Background & Rationale—Alanine aminotransferase (ALT) is an important test for liver disease, yet there is no generally accepted upper limit of normal (ULN) in the United States. Furthermore, the ability of ALT to differentiate persons with and without liver disease is uncertain. We examined cut-offs for ALT for their ability to discriminate between persons with positive hepatitis C virus (HCV) RNA and those at low risk for liver injury in the U.S. population.

Methods—Among adult participants in the 1999–2008 U.S. National Health and Nutrition Examination Survey, 259 were positive for serum HCV RNA and 3,747 were at low risk for liver injury (negative HCV RNA and hepatitis B surface antigen, low alcohol consumption, no evidence of diabetes, normal body mass index and waist circumference). Serum ALT activity was measured centrally.

Results—Maximum correct classification was achieved at ALT=29 IU/L for men (88% sensitivity, 83% specificity) and 22 (89% sensitivity, 82% specificity) for women. The cut-off for 95% sensitivity was an ALT=24 IU/L (70% specificity) for men and 18 (63% specificity) for women. The cut-off for 95% specificity was an ALT=44 IU/L (64% sensitivity) for men and 32 (59% sensitivity) for women. The area under the curve was 0.929 for men and 0.915 for women. If the cut-offs with the best correct classification were applied to the entire population, 36.4% of men and 28.3% of women would have had abnormal ALT.

Conclusion—ALT discriminates persons infected with HCV from those at low risk of liver disease, but would be considered elevated in a large proportion of the U.S. population.

Keywords

liver enzymes; reference range; National Health and Nutrition Examination Survey; epidemiology; population-based

Alanine aminotransferase (ALT) activity is an important screening, diagnostic, and monitoring test for liver disease.(1) As such, there is a need to have uniform measurement and definitions of normal range. However, there is no generally accepted upper limit of normal (ULN) in the United States (U.S.) and reference standards vary 2-fold.(2, 3) While

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The authors have no conflicts of interest.

absolute values vary somewhat across laboratories, the principal reason for the wide range in ULNs is the use of markedly different or undefined reference populations.

As a screening test, ALT activity should differentiate between persons in an asymptomatic population who have liver disease and those who do not. In the current study, we evaluated ALT ULN as a screening test for liver disease in a large sample representative of the U.S. population. This evaluation was accomplished by determining the sensitivity and specificity of ALT cut-offs for ULN among participants at low risk of liver disease and participants infected with viral hepatitis C. We also sought to demonstrate the consequences of using various cut-points for the general U.S. population.

METHODS

The National Health and Nutrition Examination Survey (NHANES) is conducted in the U.S. by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) and since 1999 has been a continuous annual survey.⁽⁴⁾ It consists of cross-sectional interview, examination, and laboratory data collected from a complex multistage, stratified, clustered probability sample representative of the civilian, non-institutionalized population with oversampling of persons aged 60 years and older, African Americans, and Mexican Americans. The survey was approved by the CDC Institutional Review Board, and all participants provided written informed consent to participate. The current analysis utilized data collected from 1999 through 2002 and 2005 through 2008, the years for which HCV RNA was measured.

Serum samples were processed within one hour, frozen, and shipped weekly to testing laboratories. Specimens were screened for HCV by the Ortho HCV enzyme-linked immunosorbent assay (ELISA), version 3.0 (Ortho-Clinical Diagnostics, Raritan, NJ) and positives tested with recombinant immunoblot assay (RIBA) (Chiron RIBA HCV Strip Immunoblot Assay, version 3.0, Chiron Corporation, Emeryville, CA) at the CDC.^(5–8) Specimens classified as positive or indeterminate by RIBA were tested for HCV RNA with a quantitative nucleic acid amplification test (Roche Cobas7 (Amplicor HCV Monitor Test, version 2.0, or Ampliprep TNAI/ TaqMan7 48 RUO Assay), Roche Molecular Diagnostics, Pleasanton, CA). If the result was below the level of detection, a qualitative assay (Amplicor HCV Test, version 2.0, Roche Molecular Diagnostics) was performed.^(9–11) Participants with samples positive by quantitative or qualitative tests were considered to be infected with HCV.

Serum ALT activity was measured centrally based on an indicator reaction that utilized pyruvate for kinetic determination of NADP consumption. From 1999 to 2001, serum ALT activity was assayed by a Hitachi model 917 multichannel analyzer (Roche Diagnostics, Indianapolis, IN) at the Coulston Foundation, Alamogordo, NM and in 2002 and from 2005 to 2008 by a Beckman Synchron (LX20 and DxC800) (Beckman Coulter Inc., Fullerton, CA) at Collaborative Laboratory Services, LLC, Ottumwa, IA.^(12–17) ALT activity distributions did not differ between the Coulston Foundation Laboratory and Collaborative Laboratory Services when the means were compared using a weighted t-test.⁽¹⁸⁾ However, the dispersion of ALT values was wider for 1999–2002 (mean (standard deviation (SD)), 26.0(32.5) compared with 2005–2008 (mean (SD), 25.8(19.0), $p=0.72$).

Of 28,113 sampled persons age 20 years and older, 21,205 were interviewed, 19,951 (71%) attended an examination at a mobile examination center, and 18,518 participants had an ALT measurement. Of these, 259 (1.3%) were positive for serum HCV RNA. To derive a group at low risk for liver disease, we excluded participants who were positive ($n=366$) or indeterminate ($n=69$) (by RIBA) for HCV antibody; and those with hepatitis B (serum

hepatitis B surface antigen positive ($n=57$)), alcohol intake > 2 drinks per day for men or > 1 drink per day for women ($n=1,105$), BMI ≥ 25 kg/m² ($n=11,566$), waist circumference > 102 cm for men or > 88 cm for women ($n=533$), a doctor diagnosis of diabetes ($n=276$) or borderline diabetes ($n=36$), or hemoglobin A_{1C} $\geq 6.0\%$ ($n=176$)(19). We also excluded persons with missing data on any of the factors used for exclusion criteria ($n=587$). Remaining were 3,747 (23%) participants considered to be at low risk for liver disease. For a secondary analysis, we also excluded 1,720 persons taking one or more prescription medications and two with missing medication data, leaving 2,025 at low risk for liver injury. To compare the prevalence of elevated ALT using various ALT ULN or among age, race-ethnicity and BMI subgroups, we used the entire population with an ALT measurement ($N=18,518$).

Data were collected on sex, ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other), age (years), and factors used to define the subgroup at low risk for liver disease. Participants were asked about frequency and quantity of alcohol drinking from which drinks per day were calculated; and about doctor-diagnosed diabetes and use of prescription medications. Height was measured by using a stadiometer and weight by using a self-zeroing weight scale with the participant wearing foam slippers and a paper shirt and pants.(20) Body mass index (BMI) was calculated as weight (kg)/height (m²). Standing waist circumference was measured at the high point of the iliac crest. Hepatitis B surface antigen was measured by using a solid-phase “sandwich” enzyme immunoassay (AUSZYME Monoclonal test, Abbott Diagnostics, Chicago, IL).(21) Hemoglobin A_{1C} was assayed by using high performance liquid chromatography (HPLC) (22–25) and a value of $\geq 6.0\%$ was considered elevated.

Statistical Analysis

Characteristics of participants at low risk for liver disease and positive for HCV RNA were compared using a t-test for continuous factors and a Chi squared test for categorical factors. Sensitivity was calculated as the number of persons who were positive for HCV RNA and had an ALT activity above a given cut-point divided by the total number who were HCV RNA positive. Specificity was calculated as the number of persons at low risk for liver disease with an ALT activity less than or equal to a given cut-point divided by the total number at low risk for liver disease. Receiver operating characteristic (ROC) curves were generated (SAS, PROC LOGISTIC, SAS/STAT® 9.2 User’s Guide, 2008, SAS Institute, Inc., Cary NC) and the area under the curve (AUC), a measure of the overall accuracy of a screening test, was calculated. Five potential ALT ULN and associated sensitivities and specificities were identified from the ROC curves at the points associated with: 1) 95% sensitivity, 2) 90% sensitivity, 3) maximum accuracy (i.e. maximum value of the sum of sensitivity and specificity at the point closest to the upper left-hand corner), 4) 90% specificity, and 5) 95% specificity. Men and women were analyzed separately because of differences in ALT distributions.

RESULTS

The group at low risk of liver disease consisted of 3,747 men and women (Table 1). Relative to the 259 participants positive for HCV RNA, they were more likely to be younger, female, have an ethnic identification other than non-Hispanic black, and by design have lower BMI, waist circumference, diabetes, hemoglobin A_{1C}, and alcohol consumption. These differences were also found in sex-specific comparisons of the two groups (data not shown). ALT distributions for men and women at low risk for liver disease or HCV RNA positive are shown in Figure 1. For men, the median (interquartile range) was 21 (17–27) IU/L for those at low risk and 53 (37–83) IU/L for those HCV RNA positive. For women, the

corresponding levels were 17 (14–21) IU/L for those at low risk and 36 (26–53) IU/L for those HCV RNA positive.

ROC curves for men and women are shown in Figures 2a and 2b and sensitivities and specificities associated with five potential ALT ULN displayed on the ROC curves are presented in Table 2. At the end of the spectrum favoring sensitivity (point #1 on the curve), 95% sensitivity was obtained at ALT=24 IU/L (70% specificity) for men and 18 (63% specificity) for women. The long horizontal portion of the curves indicates that at a lower ALT, specificity would be compromised with minimal improvement in sensitivity. At the end of the spectrum favoring specificity (point #5), 95% specificity occurred at ALT=44 IU/L (64% sensitivity) for men and 32 (59% sensitivity) for women. ULN associated with 90% sensitivity and 90% specificity fell within this range. Maximum correct classification (point #3) was achieved using ALT=29 IU/L for men (88% sensitivity, 83% specificity) and 22 (89% sensitivity, 82% specificity) for women. The AUC was 0.929 for men and 0.915 for women. In an analysis not stratified by sex, the point of greatest accuracy was at ALT=28 IU/L, with a sensitivity of 83% and specificity of 87%. The AUC was 0.926 when men and women were combined. Excluding participants who took prescription medications from the group at low risk for liver disease had minimal effects. For example, maximum correct classification was achieved at ALT=30 IU/L for men (86% sensitivity, 84% specificity) and 22 (89% sensitivity, 83% specificity) for women. The AUC was 0.926 for men and 0.919 for women.

We next calculated the percentage of the U.S. population with an elevated ALT by applying the ULN associated with the five points on the ROC curves for men and women to the entire NHANES population with an ALT measurement (n=18,518) (Table 2). Using the ULN associated with 90% sensitivity, 36% of the total U.S. population would have an elevated ALT. At the point associated with maximum accuracy, 32% would have an elevated ALT, and at 95% specificity, 11% would have an elevated ALT. The ability of ALT to discriminate persons positive for HCV RNA was further tested against the U.S. population without regard to risk factors for liver injury. For men and women combined, the point of greatest accuracy was at ALT=28 IU/L with AUC of 0.878 and specificity of 76%. For all men the maximum correct classification was achieved at ALT=35 IU/L with AUC of 0.870 and specificity of 80%. For all women the maximum correct classification was achieved at ALT=22 IU/L with AUC of 0.876 specificity of 72%.

We also compared the percentage of the U.S. population with an elevated ALT using the ULN from the current study with the percentages with an elevated ALT using selected previously published ULN. Applying the ULN of Italian blood donors(26) of 30 IU/L for men and 19 IU/L for women to the U.S. population would result in 38% with elevated ALT (34% of men and 42% of women). Using the much higher ULN based primarily on manufacturers' recommendations from a U.S. study(2) of 54.2 IU for men and 49.9 IU/L for women would result in only 4.7% of the U.S. population with ALT elevation (6.8% of men and 2.7% of women).

We compared the percentage with elevated ALT by race-ethnicity, age and BMI subgroups among the total U.S. population and by race-ethnicity and age subgroups among persons at low risk for liver injury. An elevated ALT was defined using the points associated with greatest accuracy (29 IU/L for men and 22 IU/L for women). There was considerable demographic variation in the proportion of the total U.S. population with elevated ALT (Table 3). Compared with non-Hispanic white men and women, ALT elevation was more prevalent among Mexican-Americans and less prevalent among non-Hispanic blacks. ALT elevation was more common among young and middle-aged men, but peaked in middle age among women. The prevalence of ALT elevation increased with increasing BMI. In

contrast, among persons at low risk for liver disease, ALT elevation did not differ by race-ethnicity or age, with the exception of a higher prevalence among Mexican American men and a lower prevalence among young women. Finally, we examined participants with elevated ALT (using ULN of 29 IU/L for men and 22 IU/L for women) from the total population to determine the percentages with risk factors for liver disease. One or more liver disease risk factors was present among over two-thirds of men using a BMI of ≥ 30 kg/m² and among almost 90% using a BMI of ≥ 25 kg/m² (Table 4). The corresponding percentages among women were 77% using a BMI of ≥ 30 kg/m² and 83% using a BMI of ≥ 25 kg/m².

DISCUSSION

To our knowledge, this is the first major U.S. study that has examined upper limits of normal for ALT, a critical test for detection and monitoring of liver disease. The broad range across laboratories in ULN for ALT has been a vexing issue. Studies that have addressed the ULN of ALT have been concerned primarily with either the unfortunate variation across laboratories(2, 3) or have attempted to define and apply ULN to defined populations.(26–33) Among the former, it is clear that there is more variation across laboratories than across analyzers, and that the reference populations from which ULN are defined have often been poorly characterized and may have included persons with liver disease. Variation among analyzers exists and may limit the application of an ALT ULN to the US population. However, among 11 clinical laboratories used by the Nonalcoholic Steatohepatitis (NASH) Clinical Research network (CRN), most of the variability in ALT ULN was attributed to differences in reference populations rather than to inter-analyzer variation.(3) Among laboratories in the state of Indiana, the ALT ULN varied more than two-fold (range 31–72 IU/L); however, using standardized samples, variation among analyzers was statistically, but not clinically significant.(2) Differences in manufacturer's recommendations, the most common method for establishing ALT ULN, may have contributed to inter-laboratory variation. A multinational evaluation found very minor differences across three models of autoanalyzers for a reference sample with ALT activity of 39.7 U/L, which is within the range of activity that is of greatest interest for seeking inter-laboratory agreement.(34) Although greater variation across analyzers is to be expected for enzyme activities than for chemical analytes, it should be possible to achieve greater harmonization of analytic approaches and reference ranges for ALT.

Most papers that have addressed the definition of ULN examined a low risk population only, (28–30, 32, 33, 35, 36) while a few also considered the effect of hepatitis C.(26, 31) These studies were conducted in Europe and Asia, usually at a single center. The study cited most often and whose design was similar to the current study was performed on first-time blood donors in Milan, Italy.(26) ALT discriminated asymptomatic donors harboring HCV from a low risk group who were not overweight or taking medication and who had normal blood glucose, triglyceride, and cholesterol concentrations. The 95th percentile cut-offs for the low risk group (30 IU/L for men and 19 IU/L for women) were substantially lower than those for the low risk group in the current study (44 IU/L for men and 32 IU/L for women). Because of the lower cut-offs, sensitivity for detection of hepatitis C of 76% in the Italian study was higher than in the current study (64% for men, 59% for women). In contrast, a study of French blood donors with BMI ≤ 23 kg/m² reported 95th percentiles of 42 IU/L for men and 31 IU/L for women, quite similar to the 95th percentiles of the current study.(31) An alternative approach was taken in a longitudinal study of a South Korean cohort of more than 90,000 men, who were followed for liver disease deaths over 8 years, a cut-off of 30 IU/L classified correctly the most men. (There were too few liver disease deaths among women to analyze.) While applicable to South Korea, such results would not necessarily apply to other countries, where different causes of liver disease predominate.

As a screening test for liver disease, a relatively low ULN for ALT may be limited practically by the large proportion of the general population that would have abnormal values, primarily due to the epidemic of overweight and obesity in the U.S. For example, applying the Italian blood donor cut-offs(26) to the U.S. would have resulted in abnormal ALT in almost 40% of the population. Nevertheless, normal ranges for a marker of liver disease, such as ALT, must be developed from a reference population without liver disease. If the goal were to identify a high proportion of persons with HCV infection, then the ALT activity cut-off of 29 IU/L among men and 22 IU/L among women should be considered, as it classified correctly the highest proportions of persons at low liver disease risk or with hepatitis C. However, if these cut-offs were applied across the U.S., then nearly a third of the adult population would have abnormal ALT (Table 2). It remains to be established the relative utility of labeling a large minority of the population as having liver injury when the cost of evaluation would be high and its value uncertain. If direct virological testing were applied to screening for HCV, and ALT activity was not important for case identification, then the 95th percentiles of 44 IU/L for low risk men and 32 IU/L for low risk women would be preferable. Even at these higher ALT activities, 11% of the U.S. population would be considered abnormal. We were not able to determine the causes of elevated ALT, which is the task of smaller studies that perform a thorough clinical evaluation. Nevertheless, given the phenotype of those participants with elevated ALT (Table 4), we would anticipate that the large majority would have fatty liver, primarily related to overweight and obesity.

While one can question ALT as a practical screening test for liver disease, ALT is quite helpful for the diagnosis and monitoring of liver disease. Therefore, knowledge of the distribution of ALT in persons at low risk of liver injury is important. Furthermore, it would be preferable that clinical trial requirements and drug labels that currently refer to some multiple of the ULN for exclusion or for discontinuation of therapy (such as 3 times the ULN) were instead based on a fixed ALT activity derived from populations without liver disease.(37)

For both the low risk and HCV infected participants, women tended to have lower ALT than men, similar to findings in many other studies. For this reason, we presented separately results for men and women. However, the AUC was essentially the same for sexes combined as when analyzed separately. For screening, it may therefore not be absolutely necessary to use sex-specific cut-offs. Also, there was considerable racial-ethnic variation in the proportion of the total U.S. population with elevated ALT, raising the question of whether ALT ULN should also be specific to racial-ethnic groups. However, among persons at low risk for liver disease, racial-ethnic differences disappeared (Table 3), with the exception of a higher proportion of elevated ALT among Mexican-American men, suggesting that ethnic differences in the total population may be at least partially explained by racial-ethnic variation in liver disease risk factors.

A limitation of using NHANES was reliance on a single ALT measurement. Furthermore, two different autoanalyzers were used during the study period and the machine employed for the first three years generated a wider dispersion of ALT values. In addition, in clinical settings, ALT would be used in combination with other tests, rather than in isolation. Another limitation of the study was the lack of iron studies on some NHANES participants, therefore, persons with iron overload could not be excluded from the subgroup at low risk for liver disease; nor could those with rare causes of liver disease. The inclusion of a small number of participants with undetected liver diseases who had disease-related elevated ALT would have falsely lowered specificity. The choice of HCV infection as the sole reference disease could be considered a study limitation. However, HCV is an important cause of liver disease in the U.S., is transmissible and treatable, and is therefore the liver disease most important to detect. These study limitations are balanced by the benefits of a large, national,

population-based sample, particularly the avoidance of ascertainment bias that can occur in clinical studies of selected patients, and the ability to generalize the results to the U.S. population. In addition, this may be the only study that has considered the effect of cut-offs on the likelihood of detection of a serious liver disease in the general population.

Ultimately, an effective laboratory test should reduce the morbidity and mortality from the diseases associated with the test. In the current study, the implications were demonstrated of the application of various cut-offs of ALT to the identification of an important liver disease, hepatitis C, and the proportion of the population that would be considered abnormal. Based on results from this national sample, a high proportion of the U.S. population would have elevated ALT at a level necessary to detect a high proportion of persons with HCV. We believe that defining the “diseased” group as persons positive for HCV or other liver disease, as done in the current study, is a useful approach. However, evaluation of ALT ULN requires further testing in multiple populations and settings.

Abbreviations

ALT	alanine aminotransferase
ULN	upper limit of normal
HCV	hepatitis C virus
NHANES	National Health and Nutrition Examination Survey
NCHS	National Center for Health Statistics
CDC	Centers for Disease Control and Prevention
ELISA	enzyme-linked immunosorbent assay
RIBA	recombinant immunoblot assay
SD	standard deviation
BMI	body mass index
HPLC	high performance liquid chromatography
ROC	Receiver operating characteristic
AUC	Area under the curve

Acknowledgments

The authors thank Zhongyu Fang for assistance with creation of the box and whiskers plot.

This work was supported by a contract from the National Institute of Diabetes and Digestive and Kidney Diseases (HHSN267200700001G).

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Figure 1. Alanine aminotransferase (ALT) activity (IU/L) distributions among men at low risk of liver disease (n=1,749), men infected with HCV (n=176), women at low risk of liver disease (n=1,998), and women infected with HCV (n=83). Extreme points are the 1st and 99th percentiles.

Figure 2.

- a. Receiver operating characteristic (ROC) curve for men. Points 1 to 5 represent potential alanine aminotransferase (ALT) activity upper limits of normal (ULN) with associated sensitivities and specificities shown in Table 2.
- b. Receiver operating characteristic (ROC) curve for women. Points 1 to 5 represent potential alanine aminotransferase (ALT) activity upper limits of normal (ULN) with associated sensitivities and specificities shown in Table 2.

Table 1

Characteristics of the total population and comparison of participants at low risk for liver disease and positive for hepatitis C virus (HCV) RNA.

Characteristic	Total population (N=18,518)	Low risk for liver disease (N=3,747)	HCV RNA positive (N=259)	p-value*
Age (years; mean (SD))	46.5 (16.8)	42.0 (16.9)	46.7 (10.4)	<0.001
Female (%)	51.9	57.1	31.2	<0.001
Race-ethnicity (%)				<0.001
Non-Hispanic white	71.4	74.6	65.0	
Non-Hispanic black	10.4	7.9	23.4	
Mexican American	7.7	6.4	5.1	
Other	10.5	11.1	6.4	
BMI (kg/m ² ; mean (SD))	28.3 (6.5)	22.1 (2.0)	26.5 (5.3)	<0.001
Waist circumference (cm; mean (SD))	96.8 (15.9)	80.6 (7.6)	95.5 (14.4)	<0.001
Doctor-diagnosed diabetes (%)	7.4	0	7.1	0.003
Hemoglobin A _{1c} ≥ 6.0% (%)	11.9	0	11.6	<0.001
Alcohol consumption (drinks/day; %)				<0.001
0	29.5	25.2	29.4	
>0–<1	54.9	66.4	34.2	
1–2	9.7	8.5	11.9	
>2	5.9	0	24.5	

SD, standard deviation.

* From t-test for continuous variables or Chi squared test for categorical variables comparing participants at low risk for liver disease and positive for HCV RNA.

Table 2

Comparison of potential alanine aminotransferase (ALT) activity upper limits of normal (ULN) for men and women with associated sensitivities, specificities and percentage of the U.S. population with ALT elevation.

		Sensitivity	Specificity	ALT (IU/L)	% elevated in U.S. population	
					By sex	Total
95% sensitivity (Point 1)	Men	95%	70%	24	53.9	51.2
	Women	95%	63%	18	48.7	
90% sensitivity (Point 2)	Men	90%	81%	28	39.3	35.7
	Women	90%	78%	21	32.3	
Greatest accuracy (Point 3)	Men	88%	83%	29	36.4	32.2
	Women	89%	82%	22	28.3	
90% specificity (Point 4)	Men	80%	90%	34	24.5	20.7
	Women	75%	90%	26	17.2	
95% specificity (Point 5)	Men	64%	95%	44	12.5	10.7
	Women	59%	95%	32	8.9	

Table 3

Percentage (weighted) with an elevated alanine aminotransferase (ALT) activity* by race-ethnicity, age and BMI† among the total U.S. population and persons at low risk for liver injury.

	Men			Women		
	N	% elevated	p-value	N	% elevated	p-value
All (N=18,518)						
Race-ethnicity			<0.001			<0.001
Non-Hispanic white	4,456	34.7		4,610	28.3	
Non-Hispanic black	1,714	29.5		1,889	22.4	
Mexican American	1,871	48.9		2,100	35.0	
Age (years)			<0.001			<0.001
20–39	2,906	40.4		3,639	23.7	
40–59	2,839	41.3		2,890	33.3	
60+	3,139	19.5		3,105	27.5	
BMI (kg/m ²)			<0.001			<0.001
<25	2,504	19.6		3,041	20.1	
25–<30	3,564	37.4		2,856	28.5	
30–<35	1,711	48.9		1,881	36.0	
≥35	883	55.8		1,648	38.3	
Low risk subgroup (N=3,747)						
Race-ethnicity			0.028			0.77
Non-Hispanic white	894	15.6		1,184	18.7	
Non-Hispanic black	351	18.0		241	17.1	
Mexican American	329	22.7		349	16.8	
Age (years)			0.10			<0.001
20–39	846	18.2		973	14.2	
40–59	400	18.6		551	20.8	
60+	503	13.8		474	24.6	

* Defined as >29 IU/L for men and >22 IU/L for women.

† Analyzed in the total U.S. population only.

Table 4

Characteristics of participants with elevated ALT* from the total population

Characteristic (%)	Men (N=2,964)	Women (N=2,711)
Age (years)		
20–39	43.8	31.3
40–59	45.0	44.9
60+	11.2	23.8
Race-ethnicity		
Non-Hispanic white	68.6	71.1
Non-Hispanic black	7.8	8.9
Mexican American	11.4	8.7
Other	12.2	11.4
Liver disease risk factors		
Hepatitis C RNA positive	4.5	2.4
Hepatitis C antibody positive	5.3	3.0
Hepatitis B surface antigen positive	0.61	0.21
Excessive alcohol intake [†]	12.8	7.1
Overweight (BMI $\geq$ 25 kg/m ²)	84.2	73.2
Obese (BMI $\geq$ 30 kg/m ²)	41.9	44.8
Waist circumference elevated [‡]	52.5	70.8
Doctor-diagnosed diabetes	6.7	9.0
Hemoglobin A _{1C} $\geq$ 6.0%	13.8	15.7
Abnormal glucose status [§]	14.6	17.3
1+ liver disease risk factors (based on overweight)	89.6	82.8
1+ liver disease risk factors (based on obesity)	68.4	77.4

* >29 IU/L for men and >22 IU/L for women.

[†] >2 drinks per day for men or >1 drink per day for women.[‡] >102 cm for men or >88 cm for women.[§] Doctor-diagnosed diabetes or hemoglobin A_{1C} $\geq$ 6.0%.