Hepatitis C Virus

Data reflected in this report are based solely on the collection of samples submitted to LabCorp for testing. Refer to the limitations section of this report for additional guidance in interpreting the data.

Enzyme Immunoassay and Recombinant Immunoblot

Hepatitis C virus continues to be a significant public health problem with an estimated 2.7 million with chronic HCV infection in the US. Chronic infection and the associated inflammatory response, which can persist for decades, may result in progressive liver injury, cirrhosis, and in some cases to hepatocellular carcinoma. Chronic HCV infection is the leading indication for liver transplantation and is the most common cause of liver disease-associated mortality in the US.[1] Screening is recommended for specific populations who may be at increased risk of infection as defined by the CDC.[2] CDC introduced a confirmatory algorithm for HCV EIA testing in 2003[3] using signal to cutoff ratios, which is currently in use at LabCorp. For the HCV EIA assay, samples with HCV EIA S/C ratios >11 are considered positive and there is no need for further confirmation by HCV Recombinant Immuno Blot Assay (RIBA). Global HCV EIA testing data analysis indicates a 6% confirmed positivity rate (S/C ratio > 11) with an additional 1% yielding repeat reactive EIA results with lower signal to cut-off (S/C) ratios between 1 and 11 among over 1.8 Million samples tested in 2009 (Figure 1).

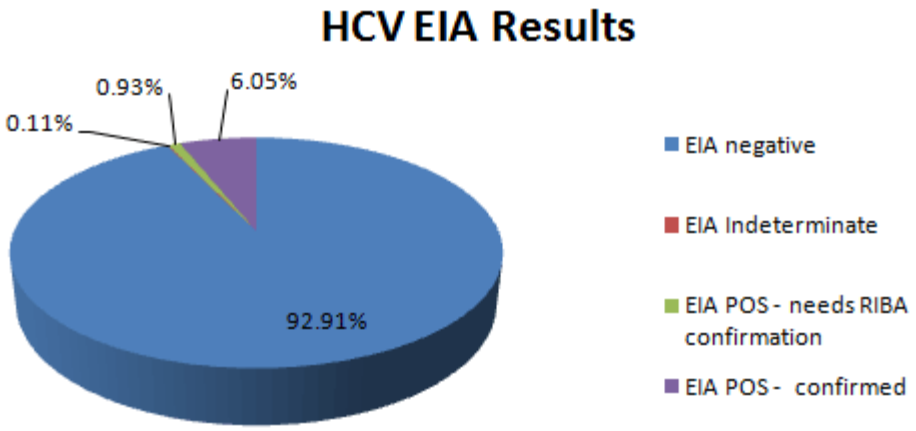


Figure 1. HCV EIA result distribution (includes differentiation of EIA repeat reactives based on EIA signal to cutoff ratios).

Samples with S/C between 1 and 11 are tested by RIBA to confirm the presence of HCV specific antibodies. The distribution of RIBA test results for various S/C ratios is presented in Figure 2

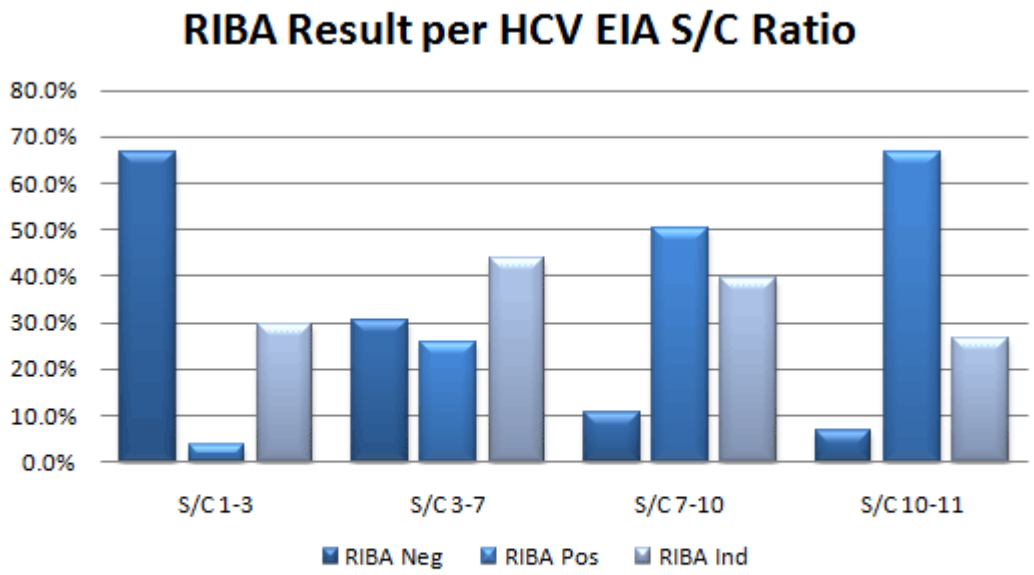


Figure 2. Distribution of Recombinant ImmunoBlot Assay (RIBA) results in various HCV EIA signal to cutoff ratio (S/C) groups.

showing a marked increased likelihood of a positive RIBA with increasing S/C ratio. A positive RIBA confirmed a reactive HCV EIA in 3.65% of samples with a S/C ratio of 1-3 vs. 66.67% of samples with a S/C ratio of 10-11 ($p < 0.0001$).

HCV EIA positivity rates increased with age and were higher in men than in women ($p < 0.0001$) (Figure 3

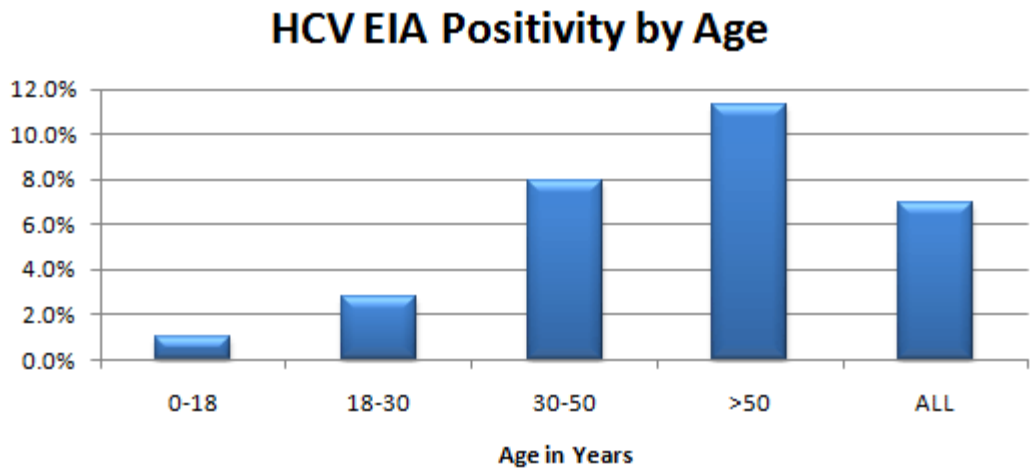


Figure 3. HCV EIA positive serology results (%) observed in various age groups.

and Figure 4).

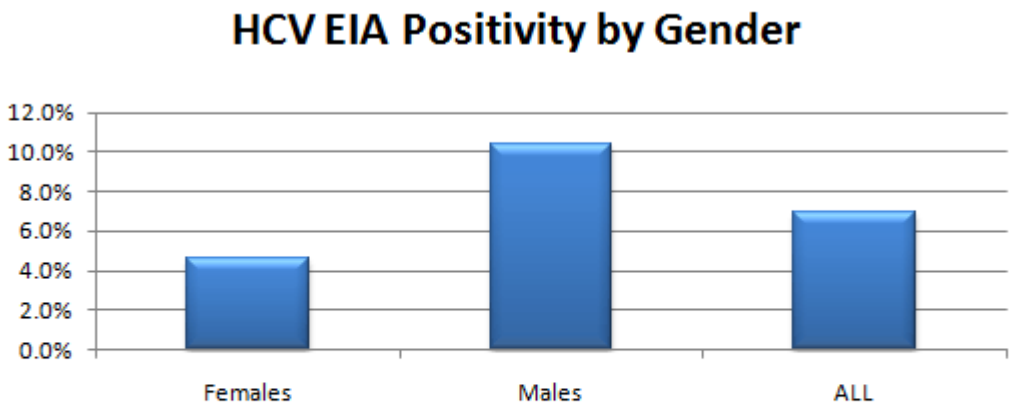


Figure 4. HCV EIA positive serology results (%) observed in various age groups.

HCV rates were higher in more racially mixed geographic areas (8.9% in areas with <50% Caucasians versus 6.1% in areas with >75% Caucasian P< 0.0001) and in lower median income areas (10.4% in areas where median income was < $30,000 as compared with 3.8% in areas where median income was greater than $50,000 (P<0.0001) (Figure 5

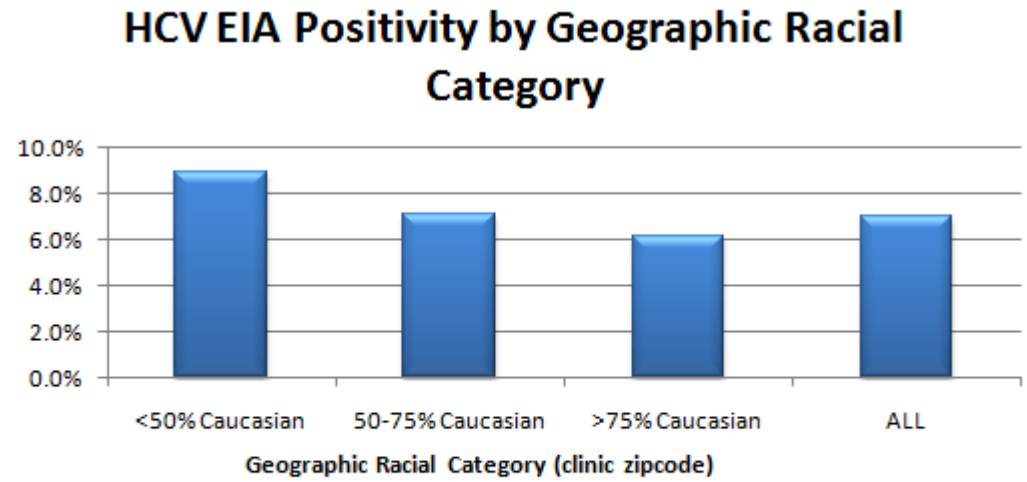


Figure 5. HCV EIA positive serology results (%) in various zipcode defined racial geographic categories.

and

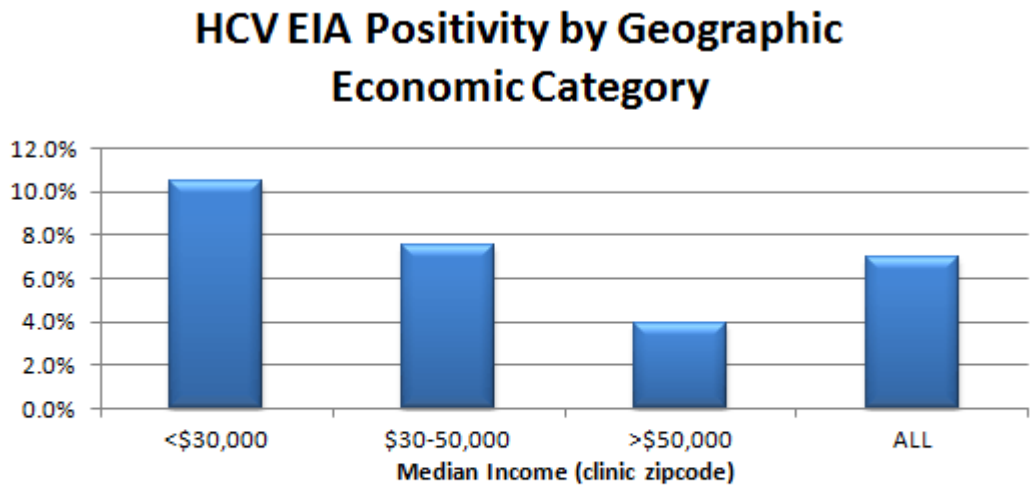


Figure 6. HCV EIA positive serology results (%) in various zipcode defined median income economic categories.

Figure 6). A recent study of HCV screening practices in an urban ambulatory care setting demonstrated a higher likelihood of being tested and a higher HCV infection rate.[4] Analysis of account specialty types with sufficient samples for analysis (>100 samples) are provided in Table 1.

Table 1.

HCV EIA positive serology results (%) in samples collected from various specialty clinics.

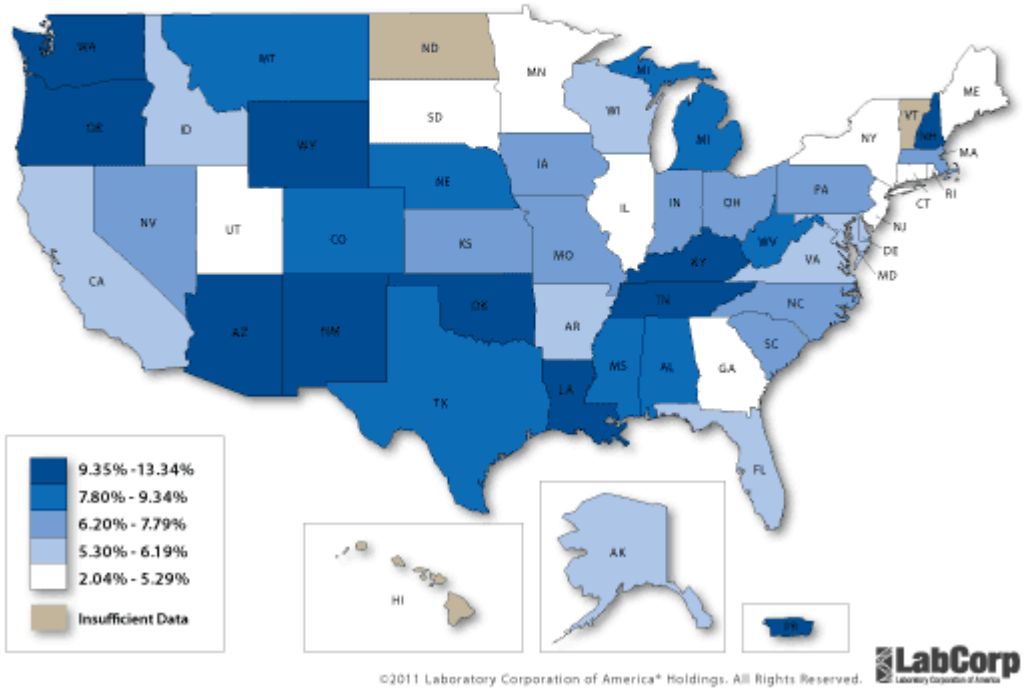
Specialty	HCV EIA Pos
Alcohol & Drug Abuse	21.7%
Cardiologist	6.7%
Clin Lab	8.3%
Dentistry & Oral Surgery	1.7%
Dermatology	2.4%
Ear Nose Throat	3.2%
Emergency Medicine	4.0%
Gastroenterology	11.5%
General medicine/internist/Fam Prac	6.6%
Hematologist	5.3%
Hemodialysis	37.7%
Home Health Care	18.4%
Hospital	10.1%
Infectious Disease	8.5%
Multispecialty clinic	8.8%
Nephrology	4.1%
Neurology	4.3%
Nursing Home/Geriatrics	8.6%
OB/GYN/IVF	1.0%
Occupational Med	3.2%
Oncology	7.0%
Pathology/Cadaveric	10.5%
Pediatrics	2.8%
Prisons	28.7%
Psychiatry	14.9%
Public Health	10.5%
Pulminologist	5.7%
Rheumatology/Allergy Immunology	2.5%
Surgery	6.7%
Urology	3.5%
ALL	7.0%

The highest positivity rates were seen in samples from alcohol and drug abuse clinics (21.7%), hemodialysis clinics (37.7%), and prisons (28.7%). Higher rates of HCV infection in these populations is consistent with other studies of increased HCV infection in IV drug abusing individuals[5] and in hemodialysis patients.[6] Account specialties with the lowest positivity rates were Obstetric/Gynecologists (1.0% HCV EIA positive) who may be using the assay as a screen during pregnancy. The HCV EIA state map provides positivity rates for states where sufficient test records (>100) were available for analysis

Figure 7

Hepatitis C Virus Antibody Positive (%)

United States map showing percentage of positive Hepatitis C virus antibody samples observed in 2009. Data classified using quintiles.



(Figure 7).

Quantitative RNA

HCV viral load analysis shows the distribution of HCV concentrations in our sample set

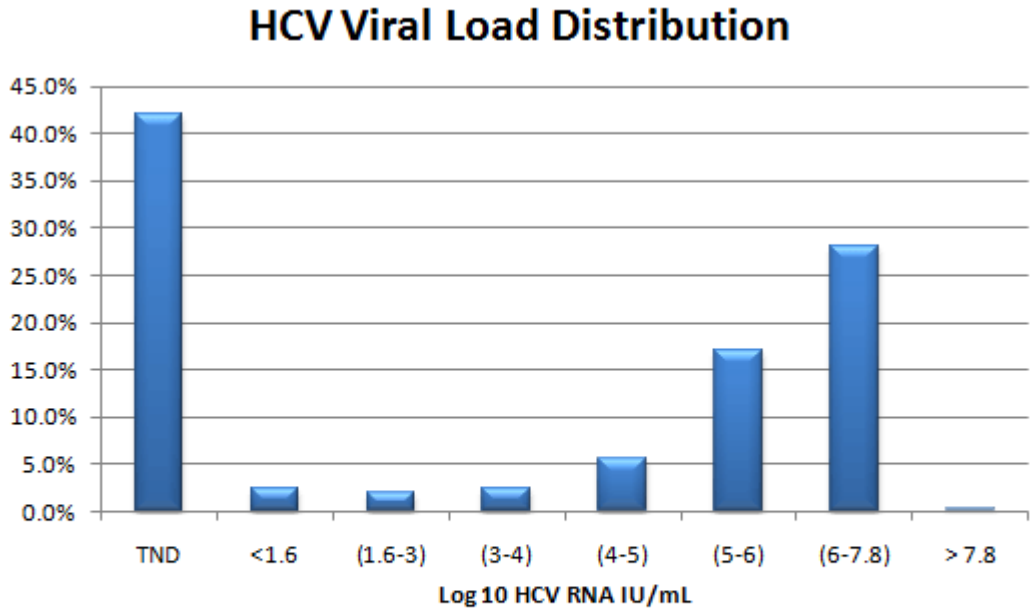


Figure 8. HCV viral load distribution in Log 10 IU/ml. (TND= Target not detected, <1.6 refers to detectable but below the limit of quantitation).

(Figure 8). Variation in HCV levels across various age groups HCV IU/ml is documented in Figure 9.

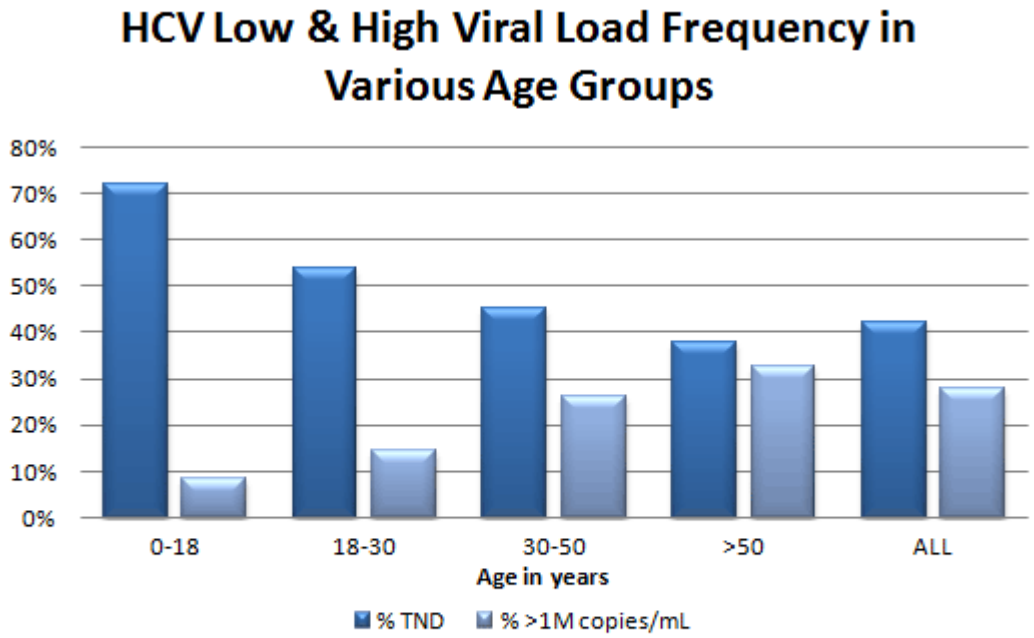


Figure 9. HCV undetectable viral loads (%) and HCV viral loads > 1 M IU/ml (%) in various age groups (TND= Target not detected).

Samples with concentrations exceeding 1 million IU/ml, which tend to be more refractory to treatment[1] were more likely to be seen in males (Figure 10)

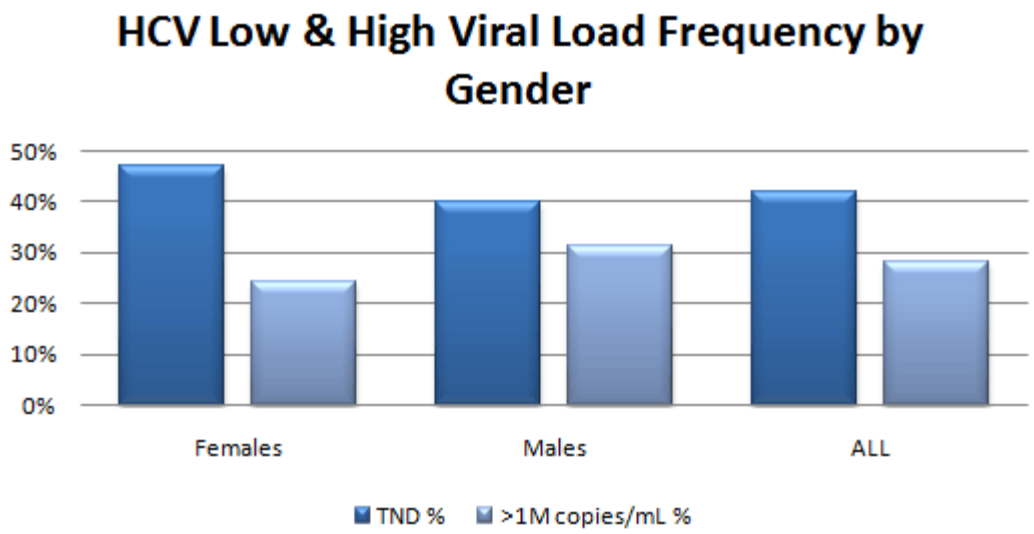


Figure 10. HCV undetectable viral loads (%) and HCV viral loads > 1 M IU/ml (%) differentiated by gender (TND= Target not detected).

and in those over 50 years of age (P< 0.0001)

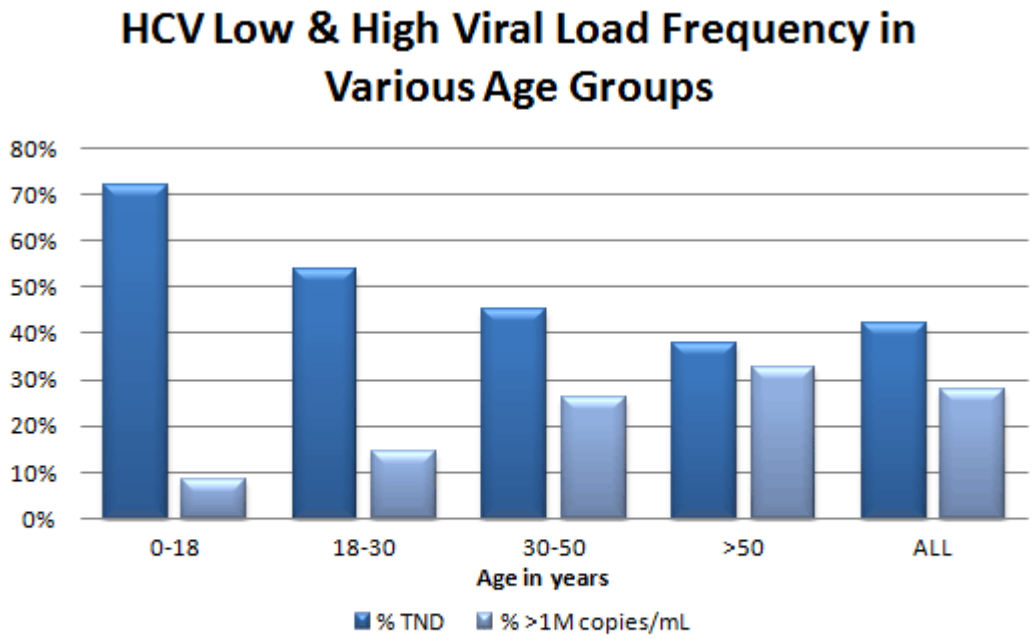


Figure 9. HCV undetectable viral loads (%) and HCV viral loads > 1 M IU/ml (%) in various age groups (TND= Target not detected).

(Figure 9). There was a lower rate of samples with viral loads below the detectable limit, in samples from geographic areas that were most racially diverse (<50% Caucasian) and in areas where median income was lowest (<$30,000) (Figure 11

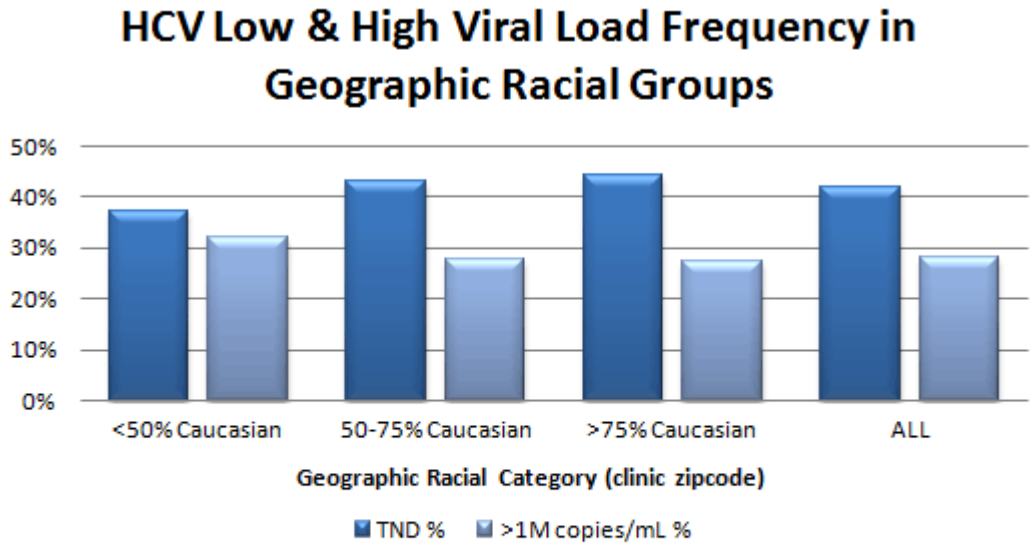


Figure 11. HCV undetectable viral loads (%) and HCV viral loads > 1 M IU/ml (%) in various zipcode defined geographic racial groups (TND= Target not detected).

and Figure 12).

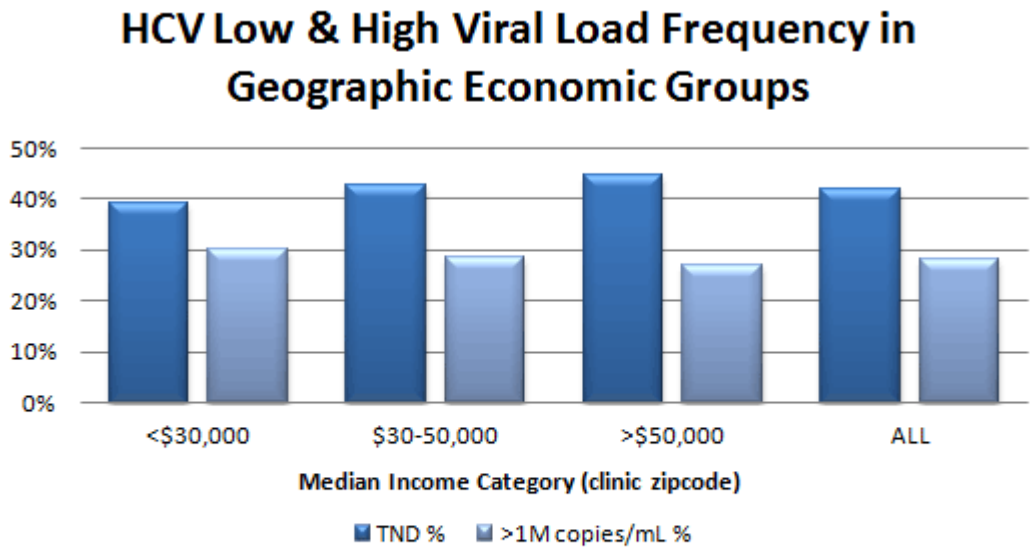


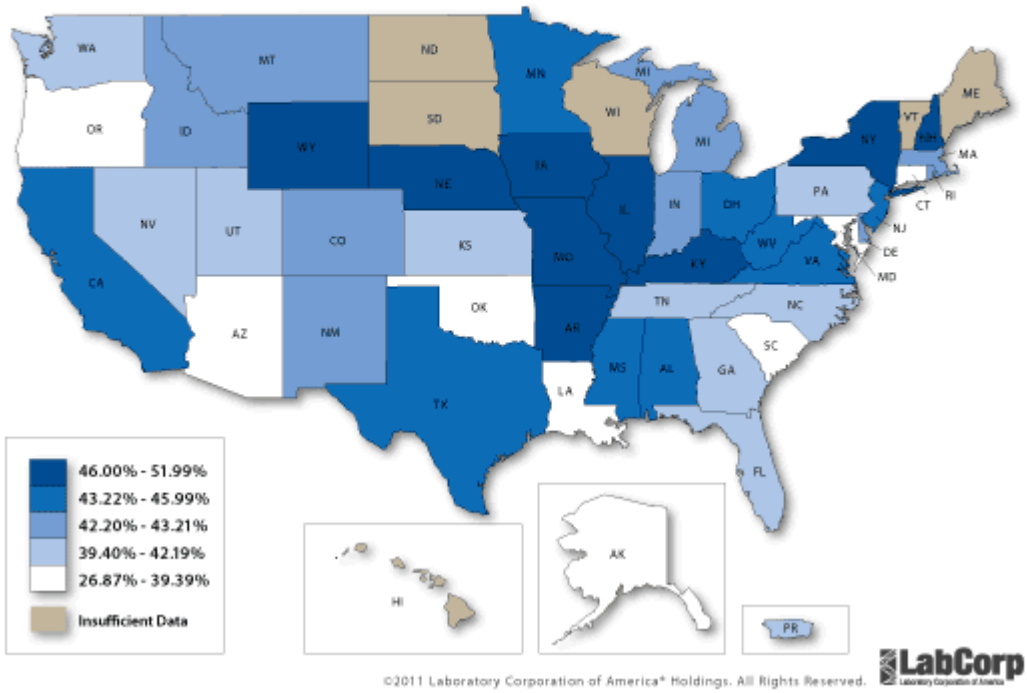
Figure 12. HCV undetectable viral loads (%) and HCV viral loads > 1 M IU/ml (%) in various zipcode defined median income economic groups (TND= Target not detected).

An undetectable viral load may be seen in patients who have resolved their infection spontaneously or in those who have had a successful treatment response. A number of factors including access to therapy[7] and recently identified genetic factors[8] impacting treatment response in various racial groups may contribute to lower rates of undetectable viral load in more racially diverse areas. An IL28B genotype has been found to be associated with early viral response and improved sustained treatment response of HCV genotype 1 infection to pegylated Interferon plus ribivirin therapy .[8,9] The favorable genotype is more common in individuals of European ancestry (37%) as compared to African Americans (14%) and Hispanics (29%), thus potentially explaining some of the observed differences in treatment response between racial groups.[9] The distribution of undetectable viral loads as a proportion of total viral load is shown in Figure 13

Figure 13

Hepatitis C Virus Undetectable Viral Load (%)

United States map showing percentage of Hepatitis C virus viral load samples, where RNA target was not detected, observed in 2009. Data classified using quintiles.



for the states with sufficient volume to analyze (>50 samples).

Genotyping

The HCV genotype distribution, shown in

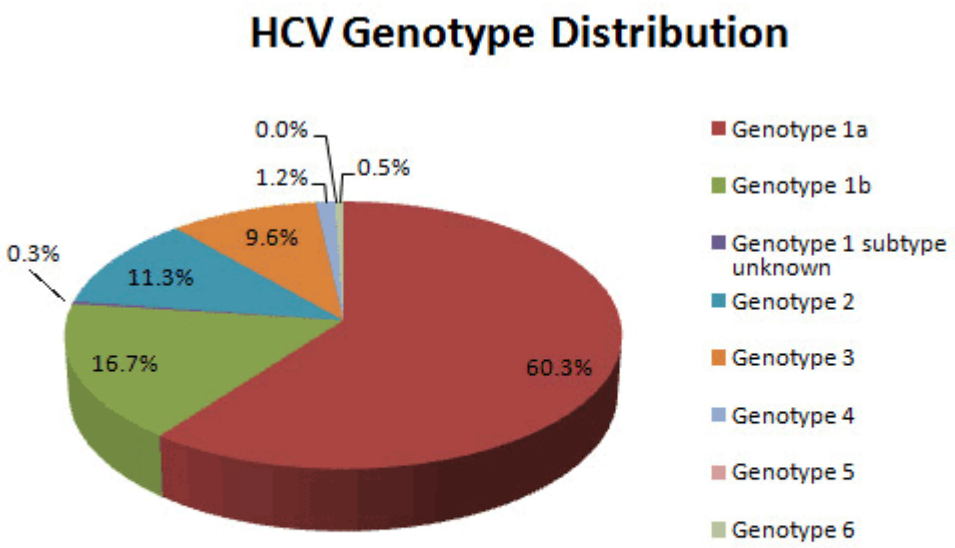


Figure 14. Distribution of HCV genotypes (1-6).

Figure 14, indicates that Genotype 1 is identified in about 77% of cases, which is consistent with previous publications of the distribution of HCV genotypes in the US.[10] The improvement in assay performance by inclusion of the core region, in addition to the 5' nontranslated region, has led to more accurate assessment of the distribution of subtypes 1a (60%) and 1b (17%) as compared with some of the earlier literature.[11,12] Genotype 1b was significantly more common in individuals >50 years of age ($P<0.0001$) whereas genotype 3 was more likely to be seen in the younger population (<30 years old) ($P<0.0001$)

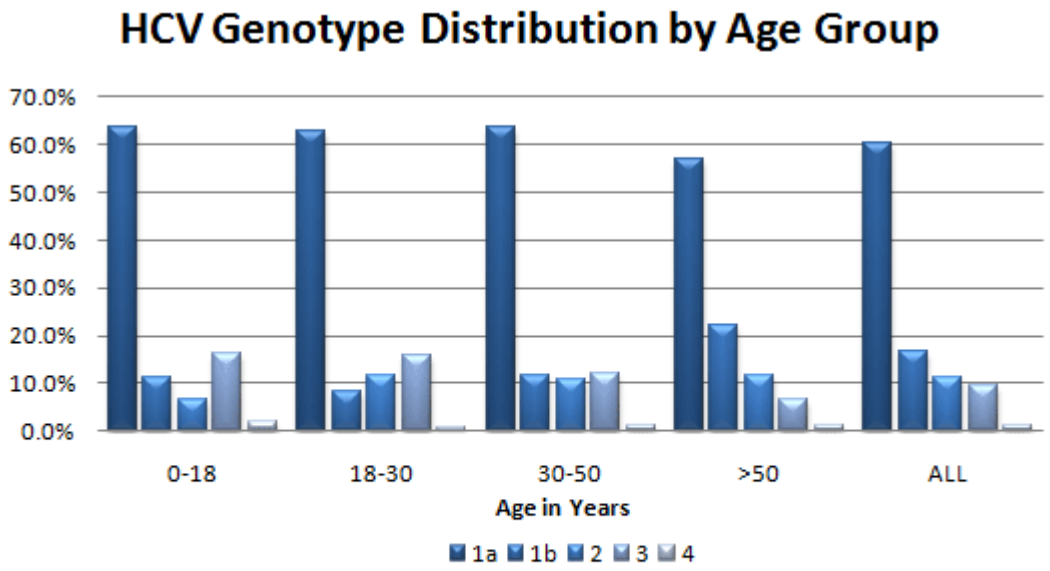


Figure 15. HCV genotype distribution of the more common HCV genotypes (1a,1b,2,3,and 4) in various age groups.

(Figure 15). Genotypes 5 and 6 were too infrequent to allow further analyses based on demographic features. Genotype distribution did not vary significantly by gender nor by median income geography but did show some differences based on geographic racial differences. Genotype 1 was more prevalent (83%) in samples coming from more racially mixed geographic areas (<50% Caucasian) than in other areas (P<0.0001)

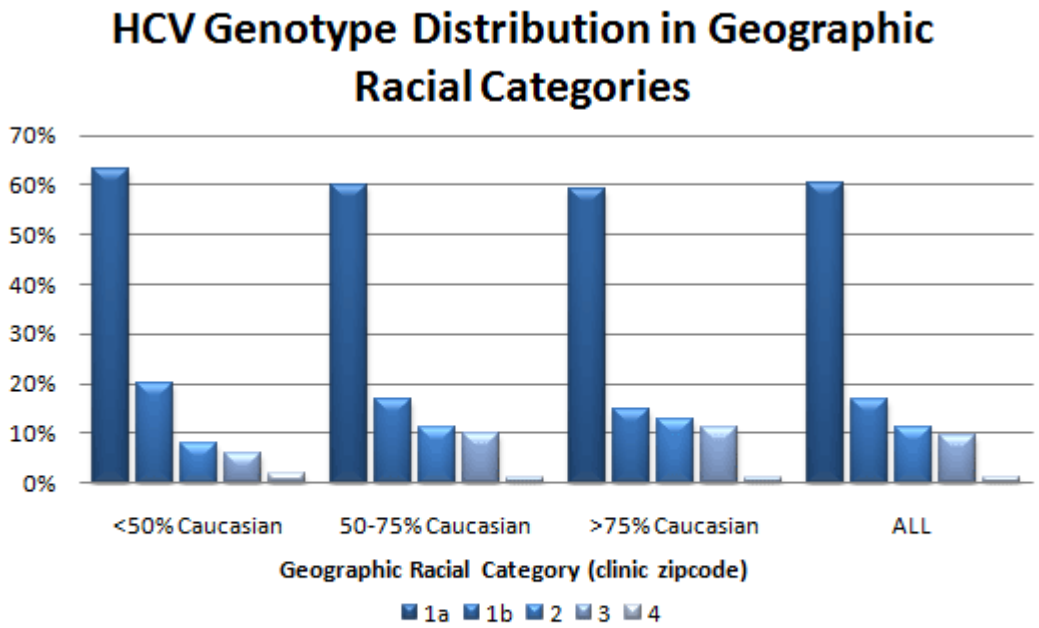


Figure 16. HCV genotype distribution of the more common HCV genotypes (1a,1b,2,3,and 4) in zipcode defined geographic racial groups.

(Figure 16). Genotype distribution of types 1a, 1b, 2, and 3, and 4 in individual states (>50 specimens) is included in Table 2.

Table 2

HCV genotype distribution of the more common HCV genotypes (1a,1b,2,3,and 4) observed in various states where sufficient samples were available for analysis.

State	1a	1b	2	3	4
AK	47%	14%	23%	12%	3.5%
AL	63%	16%	12%	7%	0.7%
AR	59%	16%	11%	12%	1.3%
AZ	57%	12%	14%	15%	1.3%
CA	54%	16%	14%	13%	1.2%
CO	58%	14%	13%	13%	1.6%
CT	53%	21%	12%	10%	3.4%
DC	66%	27%	4%	1%	1.6%
DE	75%	11%	8%	5%	1.3%
FL	56%	21%	13%	8%	1.1%
GA	60%	20%	12%	6%	0.9%
IA	52%	15%	25%	7%	1.3%
ID	45%	28%	17%	6%	4.3%
IL	62%	21%	9%	8%	0.4%
IN	53%	14%	17%	15%	0.3%
KS	54%	17%	13%	13%	1.1%
KY	65%	10%	14%	10%	0.8%
LA	66%	18%	9%	5%	0.9%
MA	58%	13%	12%	13%	3.4%
MD	67%	19%	8%	4%	0.9%
MI	64%	20%	9%	7%	1.1%
MN	56%	15%	9%	16%	2.1%
MO	63%	10%	13%	13%	0.6%
MS	60%	15%	14%	10%	0.4%
MT	53%	10%	22%	15%	0.0%
NC	65%	17%	8%	8%	1.0%
NE	57%	5%	18%	18%	0.0%
NH	68%	11%	13%	7%	1.3%
NJ	60%	18%	9%	9%	2.8%
NM	57%	13%	11%	18%	0.5%
NV	51%	20%	13%	13%	1.6%
NY	56%	20%	10%	12%	1.7%
OH	65%	14%	11%	8%	0.9%
OK	57%	11%	17%	14%	0.7%
OR	55%	12%	14%	16%	1.6%
PA	66%	15%	10%	7%	1.1%
PR	67%	8%	15%	10%	0.0%
RI	60%	9%	10%	14%	6.4%
SC	62%	19%	10%	8%	0.8%
TN	66%	12%	9%	10%	1.0%
TX	59%	15%	12%	10%	1.0%
UT	56%	11%	17%	15%	0.7%
VA	62%	18%	9%	8%	1.4%
WA	55%	13%	15%	15%	1.1%
WI	51%	22%	14%	14%	0.0%
WV	64%	9%	16%	11%	0.5%
WY	66%	12%	14%	8%	0.0%

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