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Hepatitis C Virus Infection Among Reproductive-Aged Women and Children in the United States, 2006 to 2014

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Background: In the United States, hepatitis C virus (HCV) infection has increased among young persons who inject drugs, but the extent of this epidemic among reproductive-aged women and their children is unknown.

Objective: To estimate numbers and describe characteristics of reproductive-aged women with HCV infection and of their offspring.

Design: Analysis of the National Notifiable Diseases Surveillance System (NNDSS) from 2006 to 2014 and the Quest Diagnostics Health Trends national database from 2011 to 2014.

Setting: United States.

Participants: 171 801 women (aged 15 to 44 years) and 1859 children (aged 2 and 13 years) with HCV infection reported to the NNDSS; 2.1 million reproductive-aged women and 56 684 children who had HCV testing by Quest Diagnostics.

Measurements: NNDSS HCV case reports and Quest laboratory data regarding unique reproductive-aged women and children who were tested for HCV infection.

Results: The number of reproductive-aged women with acute and past or present HCV infection in the NNDSS doubled, from 15 550 in 2006 to 31 039 in 2014. Of 581 255 pregnant women tested by Quest from 2011 to 2014, 4232 (0.73% [95% CI, 0.71% to 0.75%]) had HCV infection. Of children tested by Quest, 0.76% (CI, 0.69% to 0.83%) had HCV infection, but the percentage was 3.2-fold higher among children aged 2 to 3 years (1.62% [CI, 1.34% to 1.96%]) than those aged 12 to 13 years (0.50% [CI, 0.41% to 0.62%]). Applying the Quest HCV infection rate to annual live births from 2011 to 2014 resulted in an estimated average of 29 000 women (CI, 27 400 to 30 900 women) with HCV infection, who gave birth to 1700 infants (CI, 1200 to 2200 infants) with the infection each year.

Limitations: Only a fraction of HCV infections is detected and reported to the NNDSS. Quest data are potentially biased, because women who are asymptomatic, do not access health care, or have unreported risks may be less likely to be tested for HCV infection.

Conclusion: These data suggest a recent increase in HCV infection among reproductive-aged women and may inform deliberations regarding a role for routine HCV screening during pregnancy.

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Approximately 3.5 million U.S. residents are estimated to have hepatitis C virus (HCV) infection (1, 2). After years of declining incidence (3), the number of newly detected and reported HCV cases in the United States increased from 781 in 2009 to 2194 in 2014 (3), suggesting that after adjustment for underascertainment and underreporting (4), about 30 000 incident infections occurred in 2014 (3). This rise in incidence is thought to result from an overall national increase in injection drug use among young persons, albeit with a much greater concentration in some geographic areas (5–7). Among young persons who inject drugs, about half are women of reproductive age (5–7). Thus, concerns have arisen about the risk for vertical transmission to infants born to HCV RNA–positive mothers (8), especially because an increase in the HCV detection rate has been observed in recent years among reproductive-aged women (8), but in the absence of standard interventions to prevent HCV transmission to infants. Although birth to an HCV-infected mother is a known risk factor for HCV infection in the infant, perinatal transmission is infrequent. Only 5% to 6% of women transmit HCV to their infants, although rates are higher among women with HIV co-infection or very high HCV viral loads (>6 log) (9–12). The prevalence of HCV infection among pregnant women has been difficult to determine, because HCV screening is not performed routinely in this population but rather is risk based. As a result, many HCV infections may go undetected because of underrecognition of risk behaviors, as well as concerns about stigmatization or legal consequences if risk behaviors are disclosed. Even when HCV infection is detected, 1 study concluded that most at-risk children born to known HCV RNA–positive women are not screened subsequently (13) and therefore do not receive appropriate medical care.

To assess the extent of HCV infection in reproductive-aged and pregnant women, as well as in infants born to them, we analyzed 2 of the largest population data sets available in the United States.

See also:

Editorial comment 1

Web-Only
Supplement

METHODS

Data Sources

Data were analyzed from the National Notifiable Diseases Surveillance System (NNDSS) of the Centers for Disease Control and Prevention (CDC) and the Quest Diagnostics Health Trends database. The NNDSS is a nationwide collaboration that enables public health agencies at local, state, territorial, federal, and international levels to share notifiable disease-related health information. Because the great majority of HCV infection cases are asymptomatic and are detected sporadically over time, the NNDSS tracks those that meet a specific definition for reporting according to state and local statutes and requirements. No new enhancements in detection and reporting or substantial changes in HCV surveillance case definitions were made during the period from which these NNDSS data were drawn (**Appendix Tables 1** and **2**, available at Annals.org). The current analysis used NNDSS data to evaluate trends in (rather than the prevalence of) HCV infection in reproductive-aged women and children aged 2 to 13 years from 2006 to 2014. Follow-up investigations are performed by state and local health jurisdictions with the resources available to collect extended data elements, such as injection drug use behavior, by using standard case report forms. Forms for reporting viral hepatitis cases are available from the CDC Division of Viral Hepatitis–Statistics and Surveillance Web site (www.cdc.gov/hepatitis/statistics/) in the Surveillance Guidelines and Forms section.

Quest Diagnostics is a commercial laboratory system serving approximately one third of the U.S. adult population annually and approximately one half over a 3-year period. It receives specimens from an estimated one half of all physicians and hospitals in the United States (14). Quest Diagnostics data were obtained through a multiyear contractual agreement between the CDC and Quest Diagnostics Health Trends (15). Data on HCV infection (prevalence) in reproductive-aged women, pregnant women, and children aged 2 to 13 years were analyzed for 2011 through 2014.

Cases

Standard HCV surveillance case definitions are used by jurisdictions to classify cases of acute and past or present HCV infection in accordance with the Council of State and Territorial Epidemiologists in collaboration with the CDC. Laboratory data on HCV are not submitted to the NNDSS; therefore, parsing current HCV infection cases from the pool of past and present cases in that database was not possible. To ensure consistency over time, we verified that these HCV case definitions did not change substantively during the NNDSS study period (**Appendix Tables 1** and **2**). We considered that ascertainment and reporting of cases may be affected by changes in surveillance resources over time. However, reporting has remained a mainly unfunded mandate for the state health departments over the years, without the federal resources to increase numbers of reported cases nationally.

We included all reports in the NNDSS of HCV cases in females aged 15 to 44 years that met the criteria for either confirmed acute or past or present infection. For children, we assumed that maternal antibodies and, consequently, anti-HCV assay positivity could persist for 18 months after birth and that infection might resolve spontaneously in about half of infected infants up to 3 years after occurrence (12). Given that most infections that resolve do so before the age of 2 years, we limited our analysis to children aged 2 years (24 months) through 13 years, almost all of whom would be infected perinatally. The pediatric cases examined met the definition for either confirmed acute or past or present HCV infection.

To ensure consistency, we applied the age criteria of the NNDSS definitions to the Quest laboratory data: 15 to 44 years for reproductive-aged women and 2 to 13 years for children. Persons who tested positive for HCV antibody were identified as having a past or present HCV infection, whereas those who tested positive for HCV RNA or had a genotyped HCV infection were considered to have a current HCV infection. Persons who tested negative for HCV antibody or RNA were considered not currently infected.

Statistical Analyses

For HCV cases reported to the NNDSS from 2006 to 2014, the number and proportion of reproductive-aged women and children overall and of those with information on demographic characteristics (geographic location, age, sex, race/ethnicity) and injection drug use (women only) were calculated.

From Quest data, the following laboratory tests were included: HCV antibody, HCV RNA, and HCV genotype. Among persons without a current HCV infection, the number and proportion of women or children with each demographic characteristic (year of service, geographic region of the provider ordering the test, and age group) were examined, where the denominator for calculating the proportions for each characteristic was the number of women aged 15 to 44 years and the number of children aged 2 to 13 years who had any HCV testing performed by Quest in 2011 through 2014. We also examined pregnancy status, type of insurance, provider setting, and specialty of provider ordering the test. We calculated 95% CIs around each proportion to measure variability. Interquartile ranges (IQRs; first to third quartiles) for the median age of acute versus past or present HCV-infected women and children for the NNDSS and HCV-infected versus non–HCV-infected women and children for Quest were calculated to assess the range of the middle 50% of the age distribution.

To estimate the number of HCV-infected women who gave birth in the United States, we multiplied the Quest HCV infection prevalence in pregnant women by the average annual number of births that occurred in the United States from 2011 to 2014, which was obtained from National Vital Statistics Reports (16–19) (**Supplement**, available at Annals.org). The Quest HCV infection prevalence in pregnant women was calcu-

lated by dividing the annual number of pregnant women with HCV infection by the annual number of unique women who had 1 or more HCV tests performed by Quest. Clopper–Pearson 95% CIs were calculated for the HCV infection rate among these pregnant women. To estimate the number of infants with HCV infection, we multiplied the overall perinatal HCV infection rate of 5.8% (95% CI, 4.2% to 7.8%), determined recently by Benova and colleagues (9) on the basis of a thorough systematic review and meta-analysis of HCV perinatal transmission rates in 109 studies, by the calculated number of parturient women.

Because all data were obtained from secondary sources without patient-identifying information, the study did not require approval by an institutional review board. All analyses were performed by using SAS software, version 9.3 (SAS Institute).

Role of the Funding Source

This work was done by a CDC employee as a part of her routine work.

RESULTS

HCV in Reproductive-Aged Women

Of 425 322 women with confirmed HCV infection reported to the NNDSS from 2006 to 2014, 171 801 (40.4%) were of reproductive age (15 to 44 years) (Table 1). The reported number of acute cases in these women increased 3.4-fold, and the reported number of past or present cases doubled from 2006 to 2014 (Table 1); by 2012, the total number of cases reported in reproductive-aged women surpassed that of women aged 45 to 64 years (Figure). Non-Hispanic white women accounted for about half (2342 [57%]) of all acute infections; for the 2069 women with available risk information, 1310 (63%) acknowledged injection drug use (Table 1). Among reproductive-aged women with HCV infection, the median age was 28 years (IQR, 23 to 34 years) for those with acute infection and 31 years (IQR, 25 to 39 years) for those with past or present infection.

From 2011 to 2014, Quest performed approximately 10.6 million HCV diagnostic tests, 3.3 million (31.3%) of which were done in 2.1 million unique reproductive-aged women (that is, those with individual identifiers). Of these women, 51 117 (2.39% [CI, 2.37% to 2.41%]) had past or present HCV infection and 28 693 (1.34% [CI, 1.32% to 1.36%]) had current HCV infection (Table 2), as determined by the following: 28 646 (93.56% [CI, 93.27% to 93.84%]) had a positive HCV RNA result, 15 123 (52.71% [CI, 52.13% to 53.29%]) had an HCV genotype identified, and 13 276 (46.27% [CI, 45.69% to 46.85%]) had both a positive HCV RNA result and a genotype identified (data not shown). Of the women who had HCV genotyping, 70.81% (CI, 70.08% to 71.54%) had genotype 1, 10.41% (CI, 9.93% to 10.91%) genotype 2, 17.27% (CI, 16.67% to 17.88%) genotype 3, and 1.51% (CI, 1.32% to 1.71%) genotypes 4 through 6. The median age of reproductive-aged women was 32 years (IQR, 26 to 39 years) for those who had current HCV infection and 29 years (IQR, 24 to 36 years) for those who did not. With regard to regions where HCV testing was done in reproductive-aged women, the greatest concentrations of both HCV testing and current HCV infection were in the South, followed by the Northeast (Table 2). Women with HCV infection had their testing reimbursed by public insurance (Medicare or Medicaid) more frequently than other types of coverage. Providers from a wide range of specialties ordered HCV testing (Table 2). Of almost 600 000 women who were tested for HCV infection in their obstetrician's office, 0.37% (CI, 0.36% to 0.39%) had HCV RNA positivity (indicating current [active] HCV infection).

Of the 581 255 pregnant women aged 15 to 44 years tested by Quest from 2011 to 2014, 4232 (0.73% [CI, 0.71% to 0.75%]) had HCV infection (Table 2). The median age of reproductive-aged women with HCV infection was 27 years (IQR, 24 to 31 years) for those who were pregnant and 34 years (IQR, 27 to 40) for those who were not.

HCV in Children

Of the 1 149 646 confirmed cases of HCV infection reported to the NNDSS from 2006 to 2014, 1859 (0.2%) were in children aged 2 to 13 years (Table 1). Most of these cases were reported as past or present HCV infection (n = 1846) in children aged 2 to 5 years from the northeastern and southern regions. Cases were distributed approximately evenly by sex and year of report, with an average of 207 cases reported each year.

From 2011 to 2014, Quest performed 86 783 HCV tests in 57 136 children aged 2 to 13 years. Of these children, 882 (1.54% [CI, 1.44% to 1.65%]) had past or present HCV infection, 432 (0.76% [CI, 0.69% to 0.83%]) had current infection, and 56 252 (98.45% [CI, 98.35% to 98.55%]) were not currently infected (Table 2). For the remaining 452 children, current HCV infection status could not be established because of indeterminate or missing test results for HCV antibody, RNA, or genotype. Of the children with current HCV infection, 413 (95.60% [CI, 93.22% to 97.33%]) had a positive HCV RNA result, 145 (33.56% [CI, 29.12% to 38.23%]) had an HCV genotype reported, and 126 (29.17% [CI, 24.92% to 33.70%]) had both. Of the children who had HCV genotyping, 69.66% (CI, 61.48% to 77.01%) had genotype 1.

Among children, HCV testing was ordered most frequently for those living in the South, those aged 8 to 12 years, those with private insurance, and those seen in physician or pediatrician offices (Table 2). Among children with current HCV infection, the following characteristics were reported most frequently: age 2 to 3 years, coverage by private health insurance, HCV testing ordered by a physician's office, and HCV testing ordered by a pediatrician (Table 2). The median age was 7 years (IQR, 4 to 11 years) for children who had HCV infection and 9 years (IQR, 6 to 12 years) for those who did not.

The proportion of children with current HCV infection in the Quest database was 3.2-fold higher among those aged 2 to 3 years (1.62% [CI, 1.34% to 1.96%])

Table 1. Characteristics of Confirmed HCV Case Reports Among Women Aged 15–44 Years and Children Aged 2–13 Years Reported in the U.S. NNDSS, 2006–2014*

Characteristic	Women Aged 15–44 Years			Children Aged 2–13 Years (*n* = 1859)†‡§
	Acute HCV Cases (*n* = 4133 [2.4%])	Past/Present HCV Cases (*n* = 167 668 [97.6%])†	Total (*n* = 171 801)‡	
Year of report				
2006	249 (1.6)	15 301 (98.4)	15 550 (9.1)	188 (10.1)
2007	279 (1.7)	16 637 (98.4)	16 916 (9.9)	201 (10.8)
2008	284 (1.6)	17 586 (98.4)	17 870 (10.4)	265 (14.3)
2009	275 (1.9)	14 355 (98.1)	14 630 (8.5)	175 (9.4)
2010	294 (2.0)	14 442 (98.0)	14 736 (8.6)	181 (9.7)
2011	475 (2.8)	16 503 (97.2)	16 978 (9.9)	241 (13.0)
2012	659 (3.2)	19 955 (96.8)	20 614 (12.0)	200 (10.8)
2013	770 (3.3)	22 698 (96.8)	23 468 (13.7)	213 (11.5)
2014	848 (2.7)	30 191 (97.3)	31 039 (18.1)	195 (10.5)
Geographic location				
Midwest‖	845 (1.8)	46 476 (98.2)	47 321 (27.5)	406 (21.8)
Northeast¶	809 (1.6)	50 829 (98.4)	51 638 (30.1)	684 (36.8)
South**	1928 (3.8)	48 976 (96.2)	50 904 (29.6)	561 (30.2)
West††	551 (2.5)	21 387 (97.5)	21 938 (12.8)	208 (11.2)
Sex				
Male	–	–	–	908 (48.8)
Female	4133 (2.4)	167 668 (97.6)	171 801 (100.0)	913 (49.1)
Missing/unknown	–	–	–	38 (2.0)
Age group				
2–3 y	–	–	–	400 (21.5)
4–5 y	–	–	–	269 (14.5)
6–7 y	–	–	–	263 (14.2)
8–9 y	–	–	–	256 (13.8)
10–11 y	–	–	–	313 (16.8)
12–13 y	–	–	–	358 (19.3)
15–30 y	2513 (3.1)	78 253 (96.9)	80 766 (47.0)	–
31–44 y	1620 (1.8)	89 415 (98.2)	91 035 (53.0)	–
Median age (IQR), *y*	28 (23–34)	31 (25–39)	31 (25–39)	7 (4–11)
Race/ethnicity				
Non-Hispanic white	2362 (5.8)	38 134 (94.2)	40 496 (23.6)	256 (13.8)
Non-Hispanic black	73 (2.2)	3208 (97.8)	3281 (1.9)	33 (1.8)
Asian/Pacific Islander	16 (1.9)	831 (98.1)	847 (0.5)	41 (2.2)
American Indian/Alaskan native	104 (4.6)	2183 (95.5)	2287 (1.3)	14 (0.8)
Hispanic	219 (4.6)	4867 (95.7)	5086 (3.0)	109 (5.9)
Non-Hispanic other	58 (1.1)	5444 (99.0)	5502 (66.5)	63 (3.4)
Missing/unknown	1301 (1.1)	113 001 (98.9)	114 302 (66.5)	1343 (72.2)
Injection drug use				
Yes	1310 (14.0)	8041 (86.0)	9351 (5.4)	–
No	759 (16.5)	3850 (83.5)	4609 (2.7)	–
Missing/unknown	2064 (1.3)	155 777 (98.7)	157 841 (91.9)	–

HCV = hepatitis C virus; IQR = interquartile range; NNDSS = National Notifiable Diseases Surveillance System.
* Data obtained from the Centers for Disease Control and Prevention's NNDSS, 2006–2014. Values are numbers (percentages) unless otherwise indicated. Percentages may not sum to 100 due to rounding.
† Data from Texas are missing because the state did not collect this information between 2006 and 2014.
‡ Includes acute and past/present HCV cases. Percentages are column percentages.
§ 13 cases (<1%) were reported as acute.
‖ Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin.
¶ Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.
** Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Virginia, and West Virginia.
†† Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

than those aged 12 to 13 years (0.50% [CI, 0.41% to 0.62%]) (Table 2).

Estimated Number of HCV-Infected Women Who Gave Birth and of HCV-Infected Infants

Because 0.73% (CI, 0.69% to 0.78%) of pregnant women tested for HCV infection from 2011 to 2014 were found to have the infection and approximately 3.9 million live births occurred each year from 2011 to 2014 (19), it may be estimated that an average of 29 000 women (CI, 27 400 to 30 900 women) with HCV infection gave birth during that period. A recent systematic review and meta-analysis found a likely rate of

mother-to-infant transmission of 5.8 in 100 live births (CI, 4.2 to 7.8 in 100 live births) (20), suggesting that an estimated 1700 infants (CI, 1200 to 2200 infants) were born with HCV infection each year from 2011 to 2014.

Discussion

To our knowledge, this is the first national analysis to estimate numbers of HCV-infected pregnant women and their infants in the United States. The number of HCV cases in reproductive-aged women reported to the NNDSS essentially doubled from 2006 to 2014. The Quest Diagnostics data analysis further refines this picture by suggesting that about 0.73% of the 3.9 million women who give birth each year (19)–that is, about 29 000 women (CI, 27 400 to 30 900 women)–have HCV infection; by extension, an estimated 1700 infants (CI, 1200 to 2200 infants) are infected by this route each year. In contrast, only about 200 childhood cases per year are reported to the NNDSS, which may suggest a need for wider screening for HCV in pregnant women and their infants, as is recommended for HIV and hepatitis B virus. However, recommendations for screening in pregnant women and clearer testing guidelines for infants born to HCV-infected mothers do not exist at this time (21).

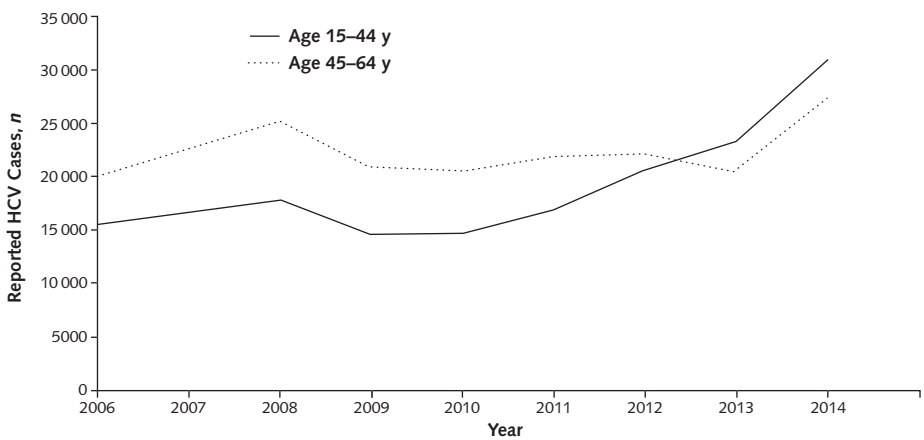
The HCV infection rate was 3.2-fold higher among children in the youngest than the oldest age group in the Quest data analysis: 1.62% (CI, 1.34% to 1.96%) in those aged 2 to 3 years and 0.50% (CI, 0.41% to 0.62%) in those aged 12 to 13 years. This difference may be the result of a decrease in testing over time in children who already are known to have chronic HCV infection or of spontaneous resolution of HCV infection, which occurs more often in infants and children (25% to 50% of those infected) than adults (12, 22). Treatment is considered on an individual basis but generally is recommended only in the rare instance of severe liver disease in children younger than 18 years; therefore, it likely has not contributed to the decline.

These data have several limitations. Data from both the NNDSS and Quest may be affected by ascertainment bias. For NNDSS data, increases in testing by providers or changes in case definition may have resulted in more cases being reported, thus showing a spurious increase in cases over time. However, federal funding for 7 to 10 "sentinel" surveillance sites has not changed during the past 20 years (3), and the case definitions have not changed substantially during that period either.

In the case of Quest data, the percentage of pregnant women with HCV infection may be inflated because providers are more likely to screen women they know or suspect are at risk, such as injection drug users, or who reside in areas with a high HCV incidence or prevalence. To explore this possibility further, we performed an ancillary analysis of the CDC National Health and Nutrition Examination Survey (NHANES) for 2003 through 2012. The NHANES interviews and tests about 5000 randomly selected U.S. residents each year to detect various diseases and conditions. Because the overall prevalence of HCV infection is only 1% (1), too few cases are identified in any year for yearly trends to be estimated, and HCV prevalence is analyzed by combining data from several years (3). Given these caveats, we found that of 7904 women aged 15 to 44 years tested in NHANES from 2003 to 2012, 33 (0.5% [CI, 0.3% to 0.7%]) had HCV RNA. This percentage aligns both with the 0.4% positivity in 598 819 women tested in obstetricians' offices and the 0.73% HCV infection rate in the 581 255 pregnant women in the Quest data from 2011 to 2014 (**Table 2**), a period overlapping the NHANES data we analyzed (from 2003 to 2012) by only 2 years–that is, before the HCV incidence increased in young women (3).

Although Quest provided laboratory services for approximately half of all U.S. physicians and hospitals during the period of study, we cannot verify that Quest did half of all HCV tests in the United States during that

Figure. Number of reported cases of HCV infection among women aged 15–44 years and 45–64 years in the United States, 2006–2014.



Data source: Centers for Disease Control and Prevention, National Notifiable Diseases Surveillance System. HCV = hepatitis C virus.

Table 2. Characteristics of Women Aged 15–44 Years and Children Aged 2–13 Years Currently Infected With HCV, Quest Diagnostics, 2011–2014*

Characteristic	Women Aged 15–44 Years		Children Aged 2–13 Years	
	Currently Infected With HCV/Tested, *n/N*	Percentage (95% CI)	Currently Infected With HCV/Tested, *n/N*	Percentage (95% CI)
Total	28 693/2 140 807	1.34 (1.32–1.36)	432/57 136	0.76 (0.69–0.83)
Year of testing				
2011	8545/589 158	1.45 (1.42–1.48)	157/16 196	0.97 (0.83–1.13)
2012	6512/533 624	1.22 (1.19–1.25)	111/14 585	0.76 (0.63–0.92)
2013	5929/487 672	1.22 (1.19–1.25)	77/13 206	0.58 (0.47–0.73)
2014	7707/530 353	1.45 (1.42–1.49)	87/13 149	0.66 (0.54–0.82)
Geographic region of provider ordering test				
Midwest†	2755/169 152	1.63 (1.57–1.69)	22/3182	0.69 (0.46–1.05)
Northeast‡	9585/703 408	1.36 (1.34–1.39)	111/15 828	0.70 (0.58–0.84)
South§	10 420/834 391	1.25 (1.23–1.27)	194/24 118	0.80 (0.70–0.93)
West‖	5898/431 374	1.37 (1.33–1.40)	104/13 965	0.74 (0.61–0.90)
Age group				
2–3 y	–	–	104/6415	1.62 (1.34–1.96)
4–5 y	–	–	68/6315	1.08 (0.85–1.37)
6–7 y	–	–	65/7475	0.87 (0.68–1.11)
8–9 y	–	–	38/9214	0.41 (0.30–0.57)
10–11 y	–	–	74/11 243	0.66 (0.52–0.83)
12–13 y	–	–	83/16 474	0.50 (0.41–0.62)
15–30 y	12 341/1 168 654	1.06 (1.04–1.07)	–	–
31–44 y	16 352/972 153	1.68 (1.66–1.71)	–	–
Median age (IQR), *y*	32 (26–39)	–	7 (4–11)	–
Sex				
Male	–	–	199/29 387	0.68 (0.59–0.78)
Female	28 693/2 140 807	1.34 (1.32–1.36)	229/27 645	0.83 (0.73–0.94)
Pregnancy status				
Yes	4232/581 255	0.73 (0.71–0.75)	–	–
No	24 461/1 559 552	1.57 (1.55–1.59)	–	–
Type of insurance				
Client bill	914/51 341	1.78 (1.67–1.90)	9/737	1.22 (0.64–2.35)
Patient	418/29 886	1.40 (1.27–1.54)	10/689	1.45 (0.78–2.70)
Medicare	1211/20 545	5.89 (5.57–6.24)	3/35	8.57 (2.76–26.58)
Medicaid	5502/247 303	2.22 (2.17–2.28)	94/13 048	0.72 (0.59–0.88)
Private	15 899/1 716 210	0.93 (0.91–0.94)	244/39 870	0.61 (0.54–0.69)
Provider setting				
Hospital	7159/93 501	7.66 (7.48–7.84)	135/3908	3.45 (2.92–4.09)
Physician office	21 078/2 036 070	1.04 (1.02–1.05)	293/53 062	0.55 (0.49–0.62)
Specialty of ordering provider				
Gastroenterology	3943/26 842	14.69 (14.24–15.16)	91/1628	5.59 (4.55–6.86)
Primary care	7029/434 261	1.62 (1.58–1.66)	28/8583	0.33 (0.23–0.47)
Infectious disease	469/7138	6.57 (6.00–7.19)	17/227	7.49 (4.66–12.05)
Obstetrics	2217/598 819	0.37 (0.36–0.39)	–	–
Physician assistant	1329/69 775	1.90 (1.80–2.01)	–	–
Pediatrics	260/26 003	1.00 (0.89–1.13)	105/20 986	0.50 (0.41–0.61)
Registered nurse	1943/126 143	1.54 (1.47–1.61)	–	–
All other specialties¶	1275/182 384	0.70 (0.66–0.74)	28/9910	0.28 (0.20–0.41)

HCV = hepatitis C virus; IQR = interquartile range.
* Current HCV infection was defined as having a positive result on HCV RNA qualitative or quantitative testing and/or having a genotyped HCV infection. No current HCV infection was defined as having a negative result on HCV antibody or RNA qualitative or quantitative testing.
† Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin.
‡ Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.
§ Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Virginia, and West Virginia.
‖ Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.
¶ Includes obstetrics, physician assistant, and registered nurse for children aged 2–13 y.

time. However, Quest laboratories performed HCV testing in more than 2 million reproductive-aged women, as reported here, and are located throughout the country. The reasons and motivations for testing also cannot be determined from these data, but the testing locations (Table 2) indicate that women were tested by providers from various specialties and children mainly by primary care and pediatric clinicians. Although HIV–HCV co-infection was not determined in this analysis, about 5% to 8% of persons with HCV infection are estimated to have HIV co-infection (23, 24).

In conclusion, these data suggest that the number of U.S. reproductive-aged women with HCV infection has increased substantially in recent years. Although no HCV treatments have been approved by the U.S. Food and Drug Administration for use in pregnant women, clinical trials of promising drugs are under way. Pregnancy may be the only time a young woman is seen by a clinician, so some clinicians already are screening pregnant women known or suspected to be at risk for HCV infection according to current guidelines (21). The data from this study may inform ongoing discussions of HCV screening for all pregnant women to protect their health and that of their offspring.

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

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Reproducible Research Statement: *Study protocol:* National viral hepatitis surveillance as performed by the CDC. *Statistical code:* Available from Ms. Ly (e-mail, KathleenLy@cdc.gov). *Data set:* Viral hepatitis surveillance data in the NNDSS are not classified as public use. Interested readers who wish to obtain viral hepatitis case data must contact individual state health departments to obtain the data. Summarized viral hepatitis case count data by state and year may be found within CDC annual viral hepatitis surveillance reports at www.cdc.gov/hepatitis/statistics/index.htm. Quest Diagnostics Health Trends data are proprietary data and therefore must be obtained directly through Quest Diagnostics.

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Appendix Table 1. Comparison of the 2004, 2007, 2011, and 2012 CDC/Council of State and Territorial Epidemiologists Surveillance Case Definitions: Acute HCV*

2004	2007	2011	2012
Clinical description—an acute illness with:			
a) Discrete onset of symptoms	No change from previous version	No change from previous version	A documented negative HCV antibody laboratory test result followed within 6 mo by a positive test result does not require an acute clinical presentation to meet the surveillance case definition
And either	And either	And either	And either
b) Jaundice	No change from previous version	Jaundice/dark urine	Jaundice
Or		Or	Or
Abnormal serum ALT levels	Defined as >400 IU/L	No change from previous version	No change from previous version
Laboratory criteria			
Serum ALT levels >7 times the upper limit of normal	Serum ALT levels >400 IU/L are not listed in the laboratory criteria because they are already listed as 1 of the clinical criteria	Serum ALT levels >400 IU/L are not listed in the laboratory criteria because they are already listed as 1 of the clinical criteria	Serum ALT levels >400 IU/L are not listed in the laboratory criteria because they are already listed as 1 of the clinical criteria
And			
IgM anti-HAV negative (if done)	Removed the wording "if done"	No change from previous version	No change from previous version
And	And	And	And
IgM anti-HBc negative (if done)	Removed the wording "if done"	No change from previous version	No change from previous version
Or			
HBsAg negative	This criterion was removed	No change from previous version	No change from previous version
And	And	And	And
Anti-HCV positive (repeat reactive) and RIBA confirmed	HCV RIBA positive	No change from previous version	No change from previous version
Or	Or	Or	Or
HCV RNA positive	No change from previous version	Added "including genotype"	Added "including qualitative, quantitative, or genotype testing"
Or	Or	Or	Or
Anti-HCV screening test positive with signal-to-cutoff ratio predictive of true positive as determined for the particular assay (e.g., ≥3.8 for the enzyme immunoassays)	Anti-HCV screening test positive with signal-to-cutoff ratio predictive of true positive as determined for the particular assay **as defined by CDC (for the signal-to-cutoff ratios: www.cdc.gov/hepatitis/HCV/LabTesting.htm)**	No change from previous version	No change from previous version
Case classification: confirmed			
Meets clinical case definition and is laboratory confirmed	Meets clinical case definition, is laboratory confirmed, **and is not known to have chronic HCV**	No change from previous version	No change from previous version

ALT = alanine aminotransferase; anti-HBc = antibody to hepatitis B core antigen; CDC = Centers for Disease Control and Prevention; HAV = hepatitis A virus; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; RIBA = recombinant immunoblot assay.
* Data from www.cdc.gov/nndss/conditions/hepatitis-c-acute. Definitions are used by state and local health jurisdictions for reporting cases to the National Notifiable Diseases Surveillance System. Boldface indicates additional wording that was added to the newer version of the CDC/Council of State and Territorial Epidemiologists case definition when compared with the previous case definition version.

Appendix Table 2. Comparison of the 2005, 2010, 2011, and 2012 CDC/Council of State and Territorial Epidemiologists Surveillance Case Definitions: Past/Present and Chronic HCV*

2005	2010	2011	2012
Condition			
HCV, past or present	HCV, chronic	HCV, past or present	HCV, past or present
Clinical description			
Symptoms are not required	No change from previous version	No change from previous version	No change from previous version
Laboratory criteria			
Anti-HCV positive (repeat reactive) and RIBA or HCV RNA confirmed	Anti-HCV positive (repeatedly reactive) by EIA **verified by ≥1 additional more specific assay**	No change from previous version	This criterion was removed
	or	or	or
	HCV RIBA positive	No change from previous version	No change from previous version
or	or	or	or
HCV RNA positive	No change from previous version	Added "including genotype"	Added "including qualitative, quantitative, or genotype testing"
or	or	or	or
Report of HCV genotype	No change from previous version	Combined with above laboratory criteria	Combined with above laboratory criteria
or	or	or	or
Anti-HCV screening test positive with signal-to-cutoff ratio predictive of true positive as determined for the particular assay as determined and posted by CDC	No change from previous version	No change from previous version	No change from previous version
Case classification			
Probable			
A case that is anti-HCV positive (repeat reactive) by EIA and has ALT values above the upper limit of normal, but the anti-HCV EIA result has not been verified by an additional more specific assay or the signal-to-cutoff ratio is unknown.	No change from previous version	No change from previous version	No change from previous version
Confirmed			
A case that is laboratory confirmed and that does not meet the case definition for acute HCV	No change from previous version	No change from previous version	No change from previous version. In persons aged <18 mo, only having a positive HCV RNA (including qualitative, quantitative, or genotype testing) would meet the case classification criteria.

ALT = alanine aminotransferase; CDC = Centers for Disease Control and Prevention; EIA = enzyme immunoassay; HCV = hepatitis C virus; RIBA = recombinant immunoblot assay.
* Data from www.cdc.gov/nndss/conditions/hepatitis-c-chronic. Definitions are used by state and local health jurisdictions for reporting cases to the National Notifiable Diseases Surveillance System. Boldface indicates additional wording that was added to the newer version of the CDC/Council of State and Territorial Epidemiologists case definition when compared with the previous case definition version.