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The Cost-Effectiveness of Birth-Cohort Screening for Hepatitis C Antibody in U.S. Primary Care Settings

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Abstract

Background—In the United States, hepatitis C virus (HCV) infection is most prevalent among adults born from 1945 through 1965, and approximately 50% to 75% of infected adults are unaware of their infection.

Objective—To estimate the cost-effectiveness of birth-cohort screening.

Design—Cost-effectiveness simulation.

Data Sources—National Health and Nutrition Examination Survey, U.S. Census, Medicare reimbursement schedule, and published sources.

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Target Population—Adults born from 1945 through 1965 with 1 or more visits to a primary care provider annually.

Time Horizon—Lifetime.

Perspective—Societal, health care.

Intervention—One-time antibody test of 1945–1965 birth cohort.

Outcome Measures—Numbers of cases that were identified and treated and that achieved a sustained viral response; liver disease and death from HCV; medical and productivity costs; quality-adjusted life-years (QALYs); incremental cost-effectiveness ratio (ICER).

Results of Base-Case Analysis—Compared with the status quo, birth-cohort screening identified 808 580 additional cases of chronic HCV infection at a screening cost of $2874 per case identified. Assuming that birth-cohort screening was followed by pegylated interferon and ribavirin (PEG-IFN + R) for treated patients, screening increased QALYs by 348 800 and costs by $5.5 billion, for an ICER of $15 700 per QALY gained. Assuming that birth-cohort screening was followed by direct-acting antiviral plus PEG-IFN + R treatment for treated patients, screening increased QALYs by 532 200 and costs by $19.0 billion, for an ICER of $35 700 per QALY saved.

Results of Sensitivity Analysis—The ICER of birth-cohort screening was most sensitive to sustained viral response of antiviral therapy, the cost of therapy, the discount rate, and the QALY losses assigned to disease states.

Limitation—Empirical data on screening and direct-acting antiviral treatment in real-world clinical settings are scarce.

Conclusion—Birth-cohort screening for HCV in primary care settings was cost-effective.

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Approximately 4.1 million Americans are antibody-positive for hepatitis C virus (HCV), and approximately 75% of them are chronically infected; most of the latter were infected 20 to 40 years ago, before the discovery of HCV (1). In 2005, hepatitis C resulted in 7000 to 13 000 deaths (2–7). Because HCV progresses slowly, the risk for serious complications is increasing among infected Americans as time passes (8). Without changes in current case identification and treatment, deaths from HCV are forecasted to increase to 35 000 annually by 2030 (5).

In clinical trials, antiviral therapy with pegylated interferon and ribavirin (PEG-IFN + R) has resulted in a sustained viral response (SVR) (that is, cure) of HCV infection in 46% of patients infected with genotype 1 (which infects 70% and 90% of chronically infected white and African American persons in the United States, respectively) and as many as 81% of those infected with genotypes 2 or 3 (9, 10). Treatment with PEG-IFN + R is cost-effective at these rates of efficacy (11).

The Centers for Disease Control and Prevention currently recommends antibody screening of persons with past behaviors, exposures, or health indicators associated with HCV infection, such as a history of injection-drug use, hemodialysis, or elevated alanine

aminotransferase levels (12). Despite these recommendations, only 25% to 50% of patients with chronic hepatitis C are aware of their infection (12–16). Low case identification may result from difficulty in implementing risk-based screening given the limited time of primary care visits and the awkwardness of discussing behavioral risks.

Expanding screening recommendations to cover the birth cohort born from 1945 through 1965 (among whom HCV prevalence is highest) offers a potential complement to current risk-based screening recommendations. However, although birth-cohort screening would increase health care costs by increasing the number of persons screened, the extent to which it would translate into health benefits is unknown. Currently, many diagnosed patients forgo treatment because of contraindications, inability to pay, lack of specialist access, or personal choice (17–20). Further, the effectiveness of antiviral therapy in community settings is lower than in clinical trials (17, 21–23).

In this article, we used a previously validated simulation model to estimate the cost-effectiveness of birth-cohort screening for HCV in the United States (5). Our results can be used to inform ongoing discussions about the suitability of a birth-cohort screening strategy as policy recommendation.

Methods

Decision Analytic Model

We programmed (Microsoft Visual Studio 2008, Redmond, Washington) a Markov chain Monte Carlo simulation model of the prevalence of hepatitis C antibody stratified by age, sex, race/ethnicity, and history of injection-drug use and of the natural history of chronic hepatitis C. A more thorough description of the disease components is provided elsewhere (5). Briefly, we modeled chronic HCV infection based on Meta-Analysis of Histologic Data in Viral Hepatitis (METAVIR) scale units (24). We stratified annual disease progression by age at infection, sex, and alcohol consumption history and determined disease progression at model initiation by using historical HCV incidence data and published observations of annual progression in METAVIR units (Supplement 1, available at www.annals.org) (2, 25). Patients who progressed to a METAVIR score of 4 were classified as having cirrhosis and experienced subsequent annual probability of 0.039 for progressing to decompensated cirrhosis (DCC) and a probability of 0.025 for developing hepatocellular carcinoma (HCC) (3, 26). Patients with DCC or HCC experienced an annual probability of transplantation or death (27–29). Data reported in Supplement 1 were obtained from multiple sources (30–48).

Model Cohorts

We modeled the U.S. population that was born from 1945 through 1965 and had at least 1 primary care visit in 2006. Using data from the National Health and Nutrition Examination Survey (NHANES, for 2001 through 2006), we divided this population into 40 mutually exclusive groups stratified by age, race/ethnicity, history of injection-drug use, and prescription drug coverage (49). We further stratified these cohorts into those with and those without antibody to HCV and divided those with antibodies into those with chronic (75%) and those with cleared (25%) infections (8, 49). We estimated that 28% of chronically

infected patients were already aware of their infection and would not benefit from additional screening (13–16).

Background Mortality

We used census life-tables to calculate the annual probability of mortality from nonhepatic causes (50). We multiplied this background mortality probability by 1.42 for people aged 40 years or older who reported ever injecting drugs. The relative risk for death was equal to a weighted average of the relative risk for death of inactive users (assumed to be 1.00) and that of active users; it was weighted by the proportion of people who admitted ever injecting drugs in the NHANES who did and did not report use within the past 12 months (49, 51).

Screening and Treatment Scenarios

We simulated 4 scenarios: 1) no screening or treatment; 2) risk-based screening, in which 18.5% (1% per year over the next 20 years) of persons unaware of their chronic infection were screened and offered PEG-IFN + R treatment if identified; 3) birth-cohort screening in which all people born from 1945 through 1965 and unaware of their HCV antibody status were offered 1-time HCV antibody screening during their 2006 primary care visit, then were offered PEG-IFN + R treatment if identified; and 4) an identical birth-cohort screening scenario in which patients with genotype 1 disease who initiated treatment received direct-acting antiviral (DAA) treatment in addition to standard therapy and patients with genotypes 2 and 3 received PEG-IFN + R. Screening occurred once to identify prevalent cases. We did not consider repeated screenings because birth-cohort screening is not a useful strategy to prevent HCV incidence.

Screening, Contraindication, and Antiviral Initiation

We assumed that 91% of those offered screening would accept it, 90% of those who tested positive would receive those results, and all patients with prescription drug insurance coverage (87.6%) and no patients without prescription coverage would be considered for treatment (30, 49). We estimated that 23.1% of patients considered for treatment were contraindicated for modifiable reasons (such as substance abuse or major depression), 11.5% were contraindicated for nonmodifiable reasons (such as uncontrolled diabetes or autoimmune disorders), and 8.5% declined treatment (20, 31). After adjustment for these barriers, 40.8% of positive patients offered testing accepted, were identified, and initiated treatment.

Effectiveness of Antiviral Therapy

We set SVR rates for standard therapy to the average of that reported in 4 studies of antiviral therapy administered in primary care settings, yielding an SVR rate of 0.33 for genotypes 1/4 and 0.69 for genotypes 2/3 (17, 22, 43, 52). We set the SVR rate for DAA plus standard therapy to 0.54, a value equal to the ratio of the average SVR rate of standard therapy (0.33) divided by the SVR of standard therapy observed in clinical trials (0.46) multiplied by the SVR rate observed for 12-week DAA plus PEG-IFN + R treatment in clinical trial data (0.75) (32).

Other Treatment

Diagnosed patients with insurance who did not undergo antiviral therapy or achieve an SVR received clinical management described in The Cleveland Clinic Monograph on hepatitis C management (39) or the American Association for the Study of Liver Diseases guidelines (40). Patients who achieved an SVR also received care in subsequent years. Clinical management other than antiviral therapy increased costs but did not result in any modeled benefit.

Medical Costs

We estimated screening costs from data provided by a federally qualified health center that conducted routine hepatitis B screening of at-risk patients, replacing the reimbursement costs for hepatitis B antigen testing with the costs of a hepatitis C antibody testing (38). We estimated the costs of standard antiviral therapy as the sum of the average monthly cost of PEG-IFN + R observed in the Kaiser Permanente Health System of Georgia in 2009 multiplied by the estimated months of therapeutic adherence observed in the control group of a published therapy-discontinuation study (43, 53). To these costs, we added the estimated monthly outpatient and laboratory expenses of treatment as outlined in The Cleveland Clinic Monograph on hepatitis C management (39). We estimated the costs of adding DAA to standard treatment based on costs and response-based treatment algorithms obtained through personal communication (technical report available at www.norc.org/PDFs/Cost-effectiveness%20of%20BC%20Screening%20Technical%20Report_v7.pdf). We estimated the costs of clinical services used to treat patients in each disease stage by converting the procedures associated with each disease stage outlined in medical guidelines into their corresponding procedure codes. We assigned reimbursement costs to codes based on the Medicare fee schedule (39–42).

Productivity Losses

We estimated hours of productivity losses associated with the antiviral therapy by multiplying the number of hours per week lost during therapy estimated by 1 source by the discontinuation of therapy distribution (in weeks) observed in a second study (54, 55). We multiplied weeks of productivity losses by the median weekly wages obtained from the U.S. Bureau of Labor Statistics, adjusted by age and sex (56). We also estimated productivity losses from end-stage liver disease.

Utility Losses

Persons without hepatitis C experienced a background QALY that decreased as patients aged to account for the prevalence of other health conditions (57). For people with HCV, we collected utility losses from 5 empirical studies for 7 hepatitis C disease states: SVR, METAVIR 0 to 1, METAVIR 2 to 3, compensated cirrhosis, DCC, HCC, and post–liver transplantation cirrhosis (58–62). We standardized results for each study by dividing the observed QALY value for each HCV state by the QALY value for the no-HCV state. We multiplied the mean of the standardized values for each HCV state by the background QALY of the patient with disease. For patients receiving antiviral therapy, we again

multiplied the patient's QALY value by 0.88 for patients with genotype 1 and by 0.97 for patients with genotype 2 (26).

Simulation, Outcomes, and Sensitivity Analysis

We estimated medical outcomes, costs, and QALYs associated with each scenario, accounting for uncertainty in each of the model's key parameters. We simulated each scenario 1000 times, holding prevalence constant and using 1 of 1000 sets of parameters, wherein each parameter was selected randomly from its distribution. We report the mean of the simulated values for the overall population outcomes and the mean and the empirical 95% credible interval for per-person costs and QALYs. We used these values to calculate the incremental cost-effectiveness ratios (ICERs) and their credible intervals of the birth-cohort screening scenario compared with the baseline risk-based scenario. The ICER was calculated as the incremental difference in medical cost between 2 scenarios divided by the incremental difference in QALYs.

We tested the sensitivity of the ICER of birth-cohort screening with standard treatment compared with risk-based (status quo) screening to univariate differences in QALY losses; the discount rate; the probability of an SVR for genotypes 1, 2, and 3; the proportion of virus that is genotype 1; the cost of screening; and the costs of standard treatment. We tested the sensitivity of the ICER of birth-cohort screening with DAA plus standard treatment compared with standard treatment alone to univariate differences in the costs and effectiveness of treatment.

We calculated cost-effectiveness acceptability curves for willingness-to-pay (WTP) values per QALY gained ranging from $0 to $100 000 by calculating the probability that each scenario had the greatest net benefit (and thus was the most cost-effective) at each WTP value.

Role of the Funding Source

This research was funded by the Centers for Disease Control and Prevention's Division of Viral Hepatitis, which employed 4 authors (Drs. Smith, Patel, Ward, and Weinbaum) who participated in conceptualization, review, and revisions.

Results

We estimated that 66.9 million Americans born from 1945 through 1965 visited a primary care provider at least once in 2006. Of these, 2.4 million were antibody-positive for HCV, 1.9 million were chronically infected, and 1.2 million were chronically infected and unaware of their status (Supplement 2, available at www.annals.org). With no screening, we estimated that 618 000 birth-cohort members would develop DCC or HCC and die of hepatitis. Under risk-based screening, 14.8 million persons received antibody screening, 135 000 were treated, and 53 000 achieved an SVR. Under risk-based screening, 592 000 birth-cohort members developed DCC or HCC and died of hepatitis C.

Under birth-cohort screening with standard treatment, 60.4 million persons received antibody testing, 1 070 840 new cases were identified, 552 000 patients were treated, 229

000 patients achieved an SVR, and the number of deaths from HCV was reduced to 509 000 (a decrease of 82 000 deaths compared with risk-based screening). Birth-cohort screening increased QALYs by 348 800, medical costs by $5.5 billion, and productivity losses by $6.9 billion.

Birth-cohort screening with DAA plus standard treatment increased screening, cases identified, and persons treated by the same amount as did birth-cohort screening with standard treatment, but (compared with risk-based screening) increased the number of patients achieving an SVR by 311 000 and reduced the number of deaths from HCV to 470 000 (a reduction of 121 000 deaths compared with risk-based screening). Compared with risk-based screening, birth-cohort screening increased QALYs by 532 000, medical costs by $19.0 billion, and productivity losses due to therapy by $6.7 billion. Productivity losses were not used to calculate ICER values.

The ICER of birth-cohort screening with standard treatment was $15 700 per QALY saved compared with risk-based treatment (Supplement 3, available at www.annals.org). The ICER of birth-cohort screening with DAA plus standard treatment was $35 700 per QALY saved compared with risk-based screening and $73 700 per QALY saved compared with birth-cohort screening with standard treatment. When we considered only the incremental costs of screening, we estimated a cost of $2874 per new case of HCV identified.

The ICER of birth-cohort screening with standard treatment compared with risk-based screening was most sensitive to the inclusion of QALY losses from disease states before liver disease, the discount rate, and the probability of an SVR given genotype 1 disease. For this comparison, we estimated an ICER of $31 200 per QALY saved when we assumed no QALY losses from pre–liver disease states, $28 400 per QALY saved when we assumed a discount rate of 5%, and $20 100 per QALY saved when we assumed a 0.23 probability of an SVR for those with genotype 1 disease who initiated treatment (Figure 1).

When we assumed birth-cohort screening in both scenarios, the ICER of additional DAA treatment compared with standard treatment alone was $39 600 per QALY saved when we assumed an SVR probability of 0.70; the ICER was $337 000 per QALY saved when we assumed an SVR probability of 0.38 (data not shown). The ICER of additional DAA treatment compared with standard treatment alone was $19 600 when we assumed the costs were half our baseline value and was $114 200 when we assumed the costs were 50% higher.

We estimated that no screening was the most cost-effective up to a WTP of $16 000 per QALY gained, birth-cohort screening with standard treatment was the most cost-effective between a WTP of $16 000 and $75 000 per QALY, and birth-cohort screening with DAA and standard treatment was the most cost-effective at WTP values above that (Figure 2). When we dropped birth-cohort screening with standard treatment from our analysis and considered only the other 3 scenarios, no screening was the most cost-effective scenario up to a WTP of $16 000 per QALY, risk-based screening was most cost-effective between $16 000 and $36 000 per QALY, and birth-cohort screening with DAA plus standard treatment was most cost-effective at WTP values of $36 000 per QALY saved and higher.

Discussion

Without new case identification strategies, the adverse consequences of chronic HCV infection are forecasted to result in an increasing public health burden over the next 2 decades. Deaths from HCV are forecasted to double to more than 18 000 per year by 2020 and to more than triple to 35 000 per year by 2030 (5). In this article, we investigated a new case identification strategy of screening those born from 1945 through 1965 (the birth cohort with the highest HCV prevalence) and estimated its cost-effectiveness by using conservative assumptions about the uptake and effectiveness of treatment. We found that compared with the current strategy of risk-based screening, birth-cohort screening followed by standard treatment reduced deaths by 82 300 at a cost of $15 700 per QALY gained (95% credible interval, $11 500 to $30 100). Incorporating new DAA treatments would prevent approximately 121 000 deaths compared with risk-based screening at a cost of $35 700 per QALY saved (95% credible interval, $28 200 to $47 200).

No universally accepted standard exists to determine what level of cost-effectiveness is appropriate to justify the implementation of a new strategy. However, by using the standards outlined by the National Committee on Prevention Priorities, birth-cohort screening with standard treatment alone when compared with risk-based screening ranks equivalently to colorectal cancer screening, hypertension screening, influenza vaccination of adults aged 50 years or older, pneumococcal vaccination of adults aged 65 years or older, and vision screening of adults aged 65 years or older (63). Birth-cohort screening with DAA plus standard treatment (when compared with risk-based screening) ranks below those interventions but equivalently to cervical cancer or cholesterol screening (63).

If fully implemented, birth-cohort screening in primary care would identify 808 580 new cases (85.9% of all undiagnosed cases in the birth cohort, compared with 21.0% under risk-based screening) at a screening cost of $2874 per new infection identified. This cost is similar to other estimated costs per new diagnosis of hepatitis B or C (30, 38). Birth-cohort screening is more costly than screening based on injection-drug use or elevated alanine aminotransferase levels, but those strategies probably miss many infected patients. The Centers for Disease Control and Prevention estimates that screening predicated on elevated alanine aminotransferase levels would identify less than half of the patients identified via birth-cohort screening (64). Furthermore, testing based on alanine aminotransferase elevations is already recommended in the Centers for Disease Control and Prevention’s 1998 recommendations, but many persons with chronic HCV infection remain undiagnosed (12).

Our study has some limitations. First, to be conservative, we assumed that patients without insurance were not offered treatment, although many are currently offered treatment through compassionate use programs and clinical trial participation. Further, when the Affordable Care Act is fully implemented, insurance coverage will be extended to 95% of U.S. residents. Excluding uninsured persons from treatment limits our analysis by underestimating the aggregate benefits of the policy but has little effect on the cost-effectiveness. Of note, if birth-cohort screening received an A- or a B-level recommendation from the U.S. Preventive Services Task Force, payment for screening would be mandated by the Affordable Care Act for all insurers (65).

Second, our estimates of the costs and effectiveness of DAA plus standard treatment were necessarily speculative because clinical implementation data have yet to be reported. In our baseline analysis, in which we assumed a conservative probability of SVR (54%), our DAA plus standard treatment results were favorable when compared directly with risk-based screening and acceptable when compared with birth-cohort screening with standard care. Future research should replicate this analysis by using the real-world effectiveness and implementation costs of the DAAs telaprevir and boceprevir.

Third, fibrosis progression among undiagnosed persons is unknown. Our model capped the possible duration of disease before the start of the model at 20 years, an assumption that may underestimate disease progression in our population. The effect of this assumption is to make our screening intervention seem slightly less cost-effective than if we allowed for a longer possible duration at model initiation.

Fourth, as a simplification, we assumed that all screening (background and intervention) occurred in the first modeled year. This results in a slightly less favorable ICER than would a more realistic structure because it frontloads the costs of testing and treatment to the present time.

Fifth, our model does not incorporate elevated mortality risks from non-HCV causes among people with HCV but without past injection-drug use. Recent research indicates that excess mortality among these individuals for both hepatic and nonhepatic causes may be substantial, and this limitation probably led to a more favorable ICER (66).

Sixth, the NHANES data used for prevalence included only noninstitutionalized and nonhomeless populations. Institutionalized and homeless persons have a higher prevalence of HCV than NHANES respondents (67, 68), but they also have different competing risks for death and adherence to antiviral therapy. The effect of this limitation on cost-effectiveness is unknown, so these analyses do not apply to institutional or homeless settings. Finally, we excluded the benefits of lifestyle counseling to slow disease progression, as well any benefits from averting secondary transmission; this approach led to a less favorable ICER.

We predicted that, compared with the status quo, birth-cohort screening would identify an additional 808 580 cases of HCV infection and prevent 82 000 HCV-related deaths, at a cost of $2874 per new case identified and $15 700 per QALY saved assuming standard treatment and $35 700 per QALY saved assuming DAA with standard therapy. Birth-cohort screening seems to be a reasonable strategy to identify asymptomatic cases of HCV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med. 2006; 144:705–14. [PubMed: 16702586]
2. Thomas DL, Seeff LB. Natural history of hepatitis *C*. Clin Liver Dis. 2005; 9:383–98. [PubMed: 16023972]
3. Davis GL, Albright JE, Cook SF, Rosenberg DM. Projecting future complications of chronic hepatitis C in the United States. Liver Transpl. 2003; 9:331–8. [PubMed: 12682882]
4. Deuffic-Burban S, Poynard T, Sulkowski MS, Wong JB. Estimating the future health burden of chronic hepatitis C and human immunodeficiency virus infections in the United States. J Viral Hepat. 2007; 14:107–15. [PubMed: 17244250]
5. Rein DB, Wittenborn JS, Weinbaum CM, Sabin M, Smith BD, Lesesne SB. Forecasting the morbidity and mortality associated with prevalent cases of pre-cirrhotic chronic hepatitis C in the United States. Dig Liver Dis. 2011; 43:66–72. [PubMed: 20739252]
6. Wise M, Bialek S, Finelli L, Bell BP, Sorvillo F. Changing trends in hepatitis C-related mortality in the United States, 1995–2004. Hepatology. 2008; 47:1128–35. [PubMed: 18318441]
7. Wong JB, Davis GL, Pauker SG. Cost effectiveness of ribavirin/interferon alfa-2b after interferon relapse in chronic hepatitis C. Am J Med. 2000; 108:366–73. [PubMed: 10759092]
8. 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; 31:777–82. [PubMed: 10706572]
9. Shepherd J, Brodin H, Cave C, Waugh N, Price A, Gabbay J. Pegylated interferon alpha-2a and -2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review and economic evaluation. Health Technol Assess. 2004; 8:iii–iv. 1–125.
10. Nainan OV, Alter MJ, Kruszon-Moran D, Gao FX, Xia G, McQuillan G, et al. Hepatitis C virus genotypes and viral concentrations in participants of a general population survey in the United States. Gastroenterology. 2006; 131:478–84. [PubMed: 16890602]
11. Shepherd J, Brodin HF, Cave CB, Waugh NR, Price A, Gabbay J. Clinical- and cost-effectiveness of pegylated interferon alfa in the treatment of chronic hepatitis C: a systematic review and economic evaluation. Int J Technol Assess Health Care. 2005; 21:47–54. [PubMed: 15736514]
12. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. Centers for Disease Control and Prevention. MMWR Recomm Rep. 1998; 47:1–39.
13. Kwiatkowski CF, Fortuin Corsi K, Booth RE. The association between knowledge of hepatitis C virus status and risk behaviors in injection drug users. Addiction. 2002; 97:1289–94. [PubMed: 12359033]
14. Culver DH, Alter MJ, Mullan RJ, Margolis HS. Evaluation of the effectiveness of targeted lookback for HCV infection in the United States-interim results. Transfusion. 2000; 40:1176–81. [PubMed: 11061852]
15. Hagan H, Campbell J, Thiede H, Strathdee S, Ouellet L, Kapadia F, et al. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. Public Health Rep. 2006; 121:710–9. [PubMed: 17278406]
16. Wasley A, Finelli L, Bell B, Alter M. The knowledge and behaviors of HCV-infected persons identified in a seroprevalence survey, USA, 2001–2002. J Clin Virol. 2006; 36(Suppl 2):S198–9.
17. Antonucci G, Longo MA, Angeletti C, Vairo F, Oliva A, Comandini UV, et al. The effect of age on response to therapy with peginterferon alpha plus ribavirin in a cohort of patients with chronic HCV hepatitis including subjects older than 65 yr. Am J Gastroenterol. 2007; 102:1383–91. [PubMed: 17403072]
18. Fried MW. Side effects of therapy of hepatitis C and their management. Hepatology. 2002; 36:S237–44. [PubMed: 12407599]

19. Heathcote EJ, Shiffman ML, Cooksley WG, Dusheiko GM, Lee SS, Balart L, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. N Engl J Med. 2000; 343:1673–80. [PubMed: 11106716]
20. Falck-Ytter Y, Kale H, Mullen KD, Sarbah SA, Sorescu L, McCullough AJ. Surprisingly small effect of antiviral treatment in patients with hepatitis C. Ann Intern Med. 2002; 136:288–92. [PubMed: 11848726]
21. Backus LI, Boothroyd DB, Phillips BR, Mole LA. Predictors of response of US veterans to treatment for the hepatitis C virus. Hepatology. 2007; 46:37–47. [PubMed: 17567830]
22. Dudley T, O'Donnell K, Haydon G, Mutimer D. Disappointing results of combination therapy for HCV? [Letter]. Gut. 2006; 55:1362–3. [PubMed: 16905704]
23. Desmond CP, Roberts SK, Dudley F, Mitchell J, Day C, Nguyen S, et al. Sustained virological response rates and durability of the response to interferon-based therapies in hepatitis C patients treated in the clinical setting. J Viral Hepat. 2006; 13:311–5. [PubMed: 16637861]
24. Bedossa P, Poynard T. An algorithm for the grading of activity in chronic hepatitis C. The METAVIR Cooperative Study Group. Hepatology. 1996; 24:289–93. [PubMed: 8690394]
25. Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. Lancet. 1997; 349:825–32. [PubMed: 9121257]
26. Wright M, Grieve R, Roberts J, Main J, Thomas HC, UK Mild Hepatitis C Trial Investigators. Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation. Health Technol Assess. 2006; 10:1–113. iii.
27. Wong JB, McQuillan GM, McHutchison JG, Poynard T. Estimating future hepatitis C morbidity, mortality, and costs in the United States. Am J Public Health. 2000; 90:1562–9. [PubMed: 11029989]
28. Salomon JA, Weinstein MC, Hammitt JK, Goldie SJ. Empirically calibrated model of hepatitis C virus infection in the United States. Am J Epidemiol. 2002; 156:761–73. [PubMed: 12370165]
29. Planas R, Ballesté B, Alvarez MA, Rivera M, Montoliu S, Galeras JA, et al. Natural history of decompensated hepatitis C virus-related cirrhosis. A study of 200 patients. J Hepatol. 2004; 40:823–30. [PubMed: 15094231]
30. Honeycutt AA, Harris JL, Khavjou O, Buffington J, Jones TS, Rein DB. The costs and impacts of testing for hepatitis C virus antibody in public STD clinics. Public Health Rep. 2007; 122(Suppl 2):55–62.
31. Zeuzem S, Feinman SV, Rasenack J, Heathcote EJ, Lai MY, Gane E, et al. Peginterferon alfa-2a in patients with chronic hepatitis C. N Engl J Med. 2000; 343:1666–72. [PubMed: 11106715]
32. Jacobson IM, McHutchison JG, Dusheiko G, Di Bisceglie AM, Reddy KR, Bzowej NH, et al. ADVANCE Study Team. Telaprevir for previously untreated chronic hepatitis C virus infection. N Engl J Med. 2011; 364:2405–16. [PubMed: 21696307]
33. Bennett WG, Inoue Y, Beck JR, Wong JB, Pauker SG, Davis GL. Estimates of the cost-effectiveness of a single course of interferon-alpha 2b in patients with histologically mild chronic hepatitis C. Ann Intern Med. 1997; 127:855–65. [PubMed: 9382363]
34. Solomon L, Flynn C, Muck K, Vertefeuille J. Prevalence of HIV, syphilis, hepatitis B, and hepatitis C among entrants to Maryland correctional facilities. J Urban Health. 2004; 81:25–37. [PubMed: 15047781]
35. Ortner, NJ., Cosway, RG. US organ and tissue transplant cost estimates and discussion. Vol. 2005. Seattle, WA: Milliman Consultants and Actuaries; 2005.
36. Jain A, Reyes J, Kashyap R, Dodson SF, Demetris AJ, Ruppert K, et al. Long-term survival after liver transplantation in 4,000 consecutive patients at a single center. Ann Surg. 2000; 232:490–500. [PubMed: 10998647]
37. Vlahov D, Wang C, Ompad D, Fuller CM, Caceres W, Ouellet L, et al. Collaborative Injection Drug User Study. Mortality risk among recent-onset injection drug users in five U.S. cities. Subst Use Misuse. 2008; 43:413–28. [PubMed: 18365941]
38. Rein DB, Lesesne SB, Smith BD, Weinbaum CM. Models of community-based hepatitis B surface antigen screening programs in the U.S. and their estimated outcomes and costs. Public Health Rep. 2011; 126:560–7. [PubMed: 21800750]

39. Carey, WD., Fried, MW., Jeffers, L., Kugelmas, M., Layden, TJ., Treisman, G., et al. Hepatitis C management. In: The Cleveland Clinic. , editor. The Cleveland Clinic Monograph Series. Cleveland: The Cleveland Clinic Foundation; 2007. Accessed at https://www.clevelandclinicmeded.com/online/monograph/HEPc/introduction.htm on 30 October 2011
40. Strader DB, Wright T, Thomas DL, Seeff LB, American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C. Hepatology. 2004; 39:1147–71. [PubMed: 15057920]
41. Gray, L., Parkinson, J., editors. The Essential RBRVS. Salt Lake City: St. Anthoney's Publishing; 2003.
42. American Medical Association. CPT 2006: Current Procedural Terminology (Standard Edition). Florence, KY: Thomson Delmar Learning; 2007.
43. Roblin, D. Kaiser Permanente of Georgia Health System Reports. Atlanta: Kaiser Permanente; 2010.
44. Davis KL, Mitra D, Medjedovic J, Beam C, Rustgi V. Direct economic burden of chronic hepatitis C virus in a United States managed care population. J Clin Gastroenterol. 2011; 45:e17–24. [PubMed: 20628308]
45. Englesbe MJ, Dimick J, Mathur A, Ads Y, Welling TH, Pelletier SJ, et al. Who pays for biliary complications following liver transplant? A business case for quality improvement. Am J Transplant. 2006; 6:2978–82. [PubMed: 17294525]
46. Haubolt, RH. US organ and tissue transplant cost estimates. Vol. 2007. Milwaukee, WI: Milliman; 2007. Accessed at http://publications.milliman.com/research/health-rr/pdfs/2007-US-Organ-Transplant-RR11-01-07.pdf on 30 October 2011
47. Showstack J, Katz PP, Lake JR, Brown RS Jr, Dudley RA, Belle S, et al. Resource utilization in liver transplantation: effects of patient characteristics and clinical practice. NIDDK Liver Transplantation Database Group. JAMA. 1999; 281:1381–6. [PubMed: 10217053]
48. Salomon JA, Weinstein MC, Hammitt JK, Goldie SJ. Cost-effectiveness of treatment for chronic hepatitis C infection in an evolving patient population. JAMA. 2003; 290:228–37. [PubMed: 12851278]
49. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey Data 2001–2006. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2007. National Center for Health Statistics.
50. Arias E. United States life tables, 2003. Natl Vital Stat Rep. 2006; 54:1–40.
51. Vlahov D, Wang CL, Galai N, Bareta J, Mehta SH, Strathdee SA, et al. Mortality risk among new onset injection drug users. Addiction. 2004; 99:946–54. [PubMed: 15265091]
52. Thomson BJ, Kwong G, Ratib S, Sweeting M, Ryder SD, De Angelis D, et al. Trent HCV Study Group. Response rates to combination therapy for chronic HCV infection in a clinical setting and derivation of probability tables for individual patient management. J Viral Hepat. 2008; 15:271–8. [PubMed: 18086181]
53. Mauss S, Rockstroh JK. HCV/HIV-coinfection—is there a state of the art after APRICOT and RIBAVIC? J Antimicrob Chemother. 2005; 56:615–8. [PubMed: 16115826]
54. Mauss S, Berger F, Goelz J, Jacob B, Schmutz G. A prospective controlled study of interferon-based therapy of chronic hepatitis C in patients on methadone maintenance. Hepatology. 2004; 40:120–4. [PubMed: 15239094]
55. Perrillo R, Rothstein KD, Rubin R, Alam I, Imperial J, Harb G, et al. Comparison of quality of life, work productivity and medical resource utilization of peginterferon alpha 2a vs the combination of interferon alpha 2b plus ribavirin as initial treatment in patients with chronic hepatitis C. J Viral Hepat. 2004; 11:157–65. [PubMed: 14996351]
56. Bureau of Labor Statistics. Median weekly earnings of full-time wage and salary workers by selected characteristics. Washington, DC: U.S. Bureau of Labor Statistics; 2010. Household Data Annual Averages: 37. Accessed at ftp://ftp.bls-.gov/pub/special.requests/lf/aat37.txt on 30 October 2011
57. Gold MR, Franks P, McCoy KI, Fryback DG. Toward consistency in cost-utility analyses: using national measures to create condition-specific values. Med Care. 1998; 36:778–92. [PubMed: 9630120]

58. Chong CA, Gulamhussein A, Heathcote EJ, Lilly L, Sherman M, Naglie G, et al. Health-state utilities and quality of life in hepatitis C patients. Am J Gastroenterol. 2003; 98:630–8. [PubMed: 12650799]
59. Siebert U, Wasem J, Rossol S, Sroczynski G, Aidelsburger P, Ravens-Sieberer U, et al. Antiviral treatment initiation costs in chronic hepatitis C [Letter]. Gut. 2005; 54:172–3. [PubMed: 15591531]
60. Sherman KE, Sherman SN, Chenier T, Tsevat J. Health values of patients with chronic hepatitis C infection. Arch Intern Med. 2004; 164:2377–82. [PubMed: 15557419]
61. Thein HH, Krahn M, Kaldor JM, Dore GJ. Estimation of utilities for chronic hepatitis C from SF-36 scores. Am J Gastroenterol. 2005; 100:643–51. [PubMed: 15743364]
62. Grieve R, Roberts J, Wright M, Sweeting M, DeAngelis D, Rosenberg W, et al. Cost effectiveness of interferon alpha or peginterferon alpha with ribavirin for histologically mild chronic hepatitis C. Gut. 2006; 55:1332–8. [PubMed: 15994216]
63. Maciosek MV, Coffield AB, Edwards NM, Flottemesch TJ, Goodman MJ, Solberg LI. Priorities among effective clinical preventive services: results of a systematic review and analysis. Am J Prev Med. 2006; 31:52–61. [PubMed: 16777543]
64. Centers for Disease Control and Prevention. Evaluation of elevated ALT as an anti-HCV screening criterion in comparison with birth cohort (1945–1965) criterion. Atlanta: Centers for Disease Control and Prevention; 2011.
65. Cassidy, C. Health policy brief: health reform's changes in Medicare. Health Affairs. May 20. 2010 Accessed at www.healthaffairs.org/healthpolicybriefs/brief.php?brief_id=17 on 29 October 2011
66. Innes HA, Hutchinson SJ, Allen S, Bhattacharyya D, Bramley P, Delahooke TES, et al. Excess liver-related morbidity of chronic hepatitis C patients, who achieve a sustained viral response, and are discharged from care. Hepatology. 2011; 54:1547–58. [PubMed: 22045672]
67. Beech BM, Myers L, Beech DJ, Kernick NS. Human immunodeficiency syndrome and hepatitis B and C infections among homeless adolescents. Semin Pediatr Infect Dis. 2003; 14:12–9. [PubMed: 12748917]
68. Allen SA, Spaulding AC, Osei AM, Taylor LE, Cabral AM, Rich JD. Treatment of chronic hepatitis C in a state correctional facility. Ann Intern Med. 2003; 138:187–90. [PubMed: 12558357]

Context

Most people in the United States infected with hepatitis C virus (HCV) were born from 1945 through 1965 and are undiagnosed. Because complications of hepatitis C increase with time, its burden is now rapidly increasing.

Contribution

In simulated models, an approach of 1-time screening for hepatitis C in this birth cohort followed by treatment was cost-effective.

Caution

Data on the real-world effectiveness of newer drugs for hepatitis C are extremely limited.

Implication

A change from solely risk-based screening for hepatitis C to 1-time screening of all persons born from 1945 through 1965 should be considered.

—The Editors

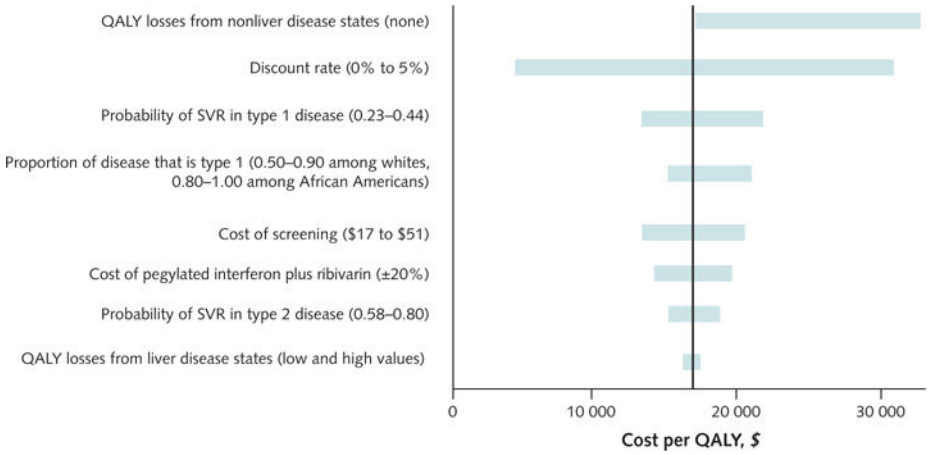

Figure 1. Univariate sensitivity of the incremental cost-effectiveness ratio of birth-cohort screening with standard treatment compared with risk-based screening assuming pegylated interferon with ribavirin treatment

QALY = quality-adjusted life-year; SVR = sustained viral response.

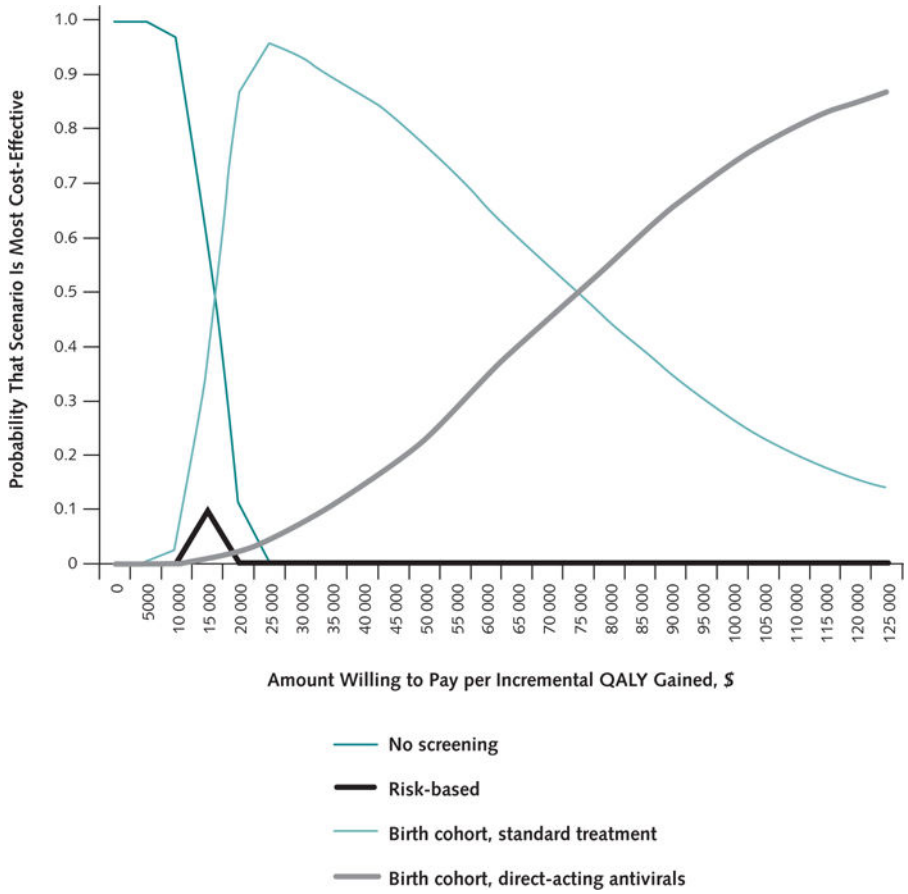

Figure 2. Cost-effectiveness acceptability curve: probability that each screening scenario is the most cost-effective by willingness to pay per incremental QALY gained

Birth cohort, standard treatment = 1-time screening of all individuals born from 1945 through 1965 with pegylated interferon with ribavirin (i.e., standard) treatment for those who enter treatment; birth cohort, direct-acting antivirals = 1-time screening of all individuals; no screening = no screening or treatment; risk-based = status quo equivalent of screening based on identified risk factors followed by pegylated interferon with ribavirin treatment for those who enter treatment. QALY = quality-adjusted life-year.