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THE BIRTH-COHORT EVALUATION TO ADVANCE SCREENING AND TESTING FOR HEPATITIS C (BEST-C)

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SUMMARY OF REQUEST

The CDC Foundation is seeking support of $1,000,000 dollars over two years ($500,000 annually) to support the *Birth-cohort Evaluation to Advance Screening and Testing for Hepatitis C (BEST-C)* project. This two-year study will evaluate a birth-cohort-based approach of routine one-time screening for hepatitis C virus (HCV) of all persons born between 1945 and 1964 in order to increase the proportion of people who are aware of their HCV status. This study will provide essential guidance for CDC as it works to update recommendations for the prevention and control of HCV in the U.S.

A detailed budget for the entire project is included for your review. The CDC Foundation is requesting support from multiple funders to expand the study's reach to all four regions of the U.S. and to ensure this project's screening goals are met. Other potential industry partners include Merck, Johnson and Johnson, Novartis, Gilead, Genentech/Roche and GlaxoSmithKline. Vertex Pharmaceuticals has already pledged their support and provided seed funding to begin site recruitment.

BACKGROUND AND NEED

In 1998 CDC published *Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease* (MMWR 1998;47:RR-9), recommending anti-HCV testing for populations "most likely to be infected with HCV," and since that time CDC has recommended HCV screening for persons with a history of injection drug use, blood product exposure and other risks for HCV infection. Continuing evidence supporting the value of these recommendations comes from Armstrong and colleagues (Ann Int Med 2006;144(10):705-14) who found that among participants of the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2002, 48% of anti-HCV positive persons reported a history of injection drug use.

However, Armstrong et al., also reported that 65-69% of anti-HCV-positive NHANES participants were born between 1945 and 1964. Risk-based strategies for HCV testing require assessments to determine which patients should be tested. Behavioral risks such as injection drug use are often viewed as socially undesirable activities resulting in underreporting of stigmatized behaviors and screening criteria with low sensitivity (Gunn et al., 2003; MMWR 2006;55(RR-14):4-5). CDC's 2006 revised HIV screening recommendations for medical settings

highlighted that behavioral risk assessment alone can lead to incorrect and late identification based on patient self-reported risk and is a barrier to HIV testing (MMWR 2006;55(RR14);1-17). Indeed, studies of NHANES participants found that a small proportion of those persons who knew of their HCV infection before survey enrollment had been tested as the result of risk ascertainment. Of the 199 anti-HCV-positive persons in the 2001-2002 NHANES study, 101 were followed up to find that only 49 (49%) previously knew their HCV status through routine physical exam (n=21), blood donation (n=6), evaluation of symptoms (diagnostic screening) (n=5), or because they had an identified risk factor (n=3). Among anti-HCV-positive persons, only half (24/50) of the HCV-infected people who visited a health care provider in the last 12 months knew they were anti-HCV-positive, suggesting that current recommendations as they are being implemented fail to identify at least half of infected persons.

PROJECT PROPOSAL

An estimated 50-70% of the 3.2 million persons with chronic HCV infection do not know their status (Hagan, 2006; Kwiatkowski, 2002; Volk, 2009). CDC's *Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease* recommend a risk-based anti-HCV screening strategy focusing on populations "most likely to be infected with HCV." However, weaknesses of risk-based screening strategies include physicians' resistance to asking potentially stigmatizing questions of their patients and patients' reluctance to disclose risk behaviors.

To increase the proportion of persons who are aware of their HCV status, CDC proposes evaluating a birth-cohort-based approach of routine one-time screening of all persons born from 1945 through 1964. The NHANES conducted during 1999-2002 found that persons born between 1945 and 1964 had an anti-HCV prevalence 4.6 higher than persons born prior to 1945 or since 1964 (3.37% versus 0.73%), with an overall prevalence of 1.6% in the general U.S. population (Armstrong, 2006).

The study will compare the effectiveness of the birth cohort HCV screening strategy with the current risk-based HCV screening approach to detect previously unidentified anti-HCV-positive persons who receive health care through their insurance in primary care systems. These systems usually consist of multiple service delivery sites across a local region. The primary care systems may include managed care organizations and community health clinics that serve insured populations. These systems will serve a diverse population in terms of race/ethnicity, age and socio-economic status.

Grantees will first collect and analyze baseline data for the study including anti-HCV screening practices and prevalence and stratify those data by demographics, socio-economic status and

reason to test (risks, including ALTs and injection drug use). Grantee sites will then develop a plan for the implementation of the birth-cohort-based testing. Those primary care systems with feasible implementation plans will then implement the birth-cohort testing and collect data for comparison to the baseline from a clinic-based sample of insured patients who visit the medical system within a given time period. Additional data will be collected to assess linkage to care for those testing positive, feasibility and acceptance of the new strategy by medical staff, cost effectiveness and patient impact.

This evaluation and comparison of testing approaches will first examine current provider anti-HCV testing practices followed by the implementation of routine (opt-out) HCV testing of patients born from 1945 to 1964. The yield of the birth-cohort screening approach will be compared with that of current risk-based testing practices to determine the net effect of this change in screening strategy. Other elements to be considered in the analysis will include the demographics and risk attributes of those tested and not tested, characteristics that predict anti-HCV-positive patients being assessed and referred into care and treatment, the experience of those who received a positive antibody test that was not confirmed by nucleic acid testing (i.e., not infected), provider impressions of risk-based vs. birth-year-based testing programs, and the characteristics of providers, clinic sites, and primary care systems. It is expected that at least four different clinic systems will be included to test the birth-year-based testing approach in different settings and patient populations. These primary care systems will select sites/clinics that are a part of the system to implement the birth-cohort screening, and the demographics of the patient populations seen with these clinics should be as representative of the U.S. population as possible.

OUTCOMES

The evaluation will compare the number and percentage of newly identified anti-HCV-positive persons identified by current risk-based testing approaches and a birth-year-based testing approach, and evaluate the difference in cost effectiveness between these testing approaches. The accuracy with which self-reported risk characteristics accurately predict anti-HCV positivity in patients within the 1945-1964 birth cohort will also be evaluated.

Other selected outcomes of interest:

- An estimate of the proportion of anti-HCV-positive patients identified using birth-year-based testing, as compared with the proportion identified using current risk-based screening practices alone, and a combination of the two approaches.
- Costs of HCV screening and comparison of the cost per newly identified anti-HCV positive person that received their results using the birth-year-based and risk-based testing strategies.
- Comparison of the cost per anti-HCV-positive person that received their results using the birth-year based and risk-based testing strategies.
- The number of missed opportunities to identify persons who are anti-HCV-positive using risk-based testing alone.
- The proportion of eligible patients accepting anti-HCV testing.
- The proportion of persons with ongoing risk behaviors.
- The proportion of HCV-infected persons receiving appropriate laboratory and other diagnostic follow-up testing.
- The proportion of HCV-infected persons with evidence of liver disease or co-factors (HIV, ETOH abuse) for development of chronic liver disease and hepatocellular carcinoma.
- The proportion of newly diagnosed patients with the intention and financial capacity to initiate antiviral therapy
- The proportion of patients that initiate antiviral therapy and levels of their treatment success.

BUDGET AND REQUEST

The CDC Foundation is seeking support of $1,000,000 over two years ($500,000 annually). To increase generalizability of findings, one primary care system from each of four regions (West, Midwest, South, Northeast) will be funded for this study. The total study budget is $3,781,911. At least three to four partners will be required to support the study at this level to ensure that all four primary care systems are funded. The cost for each site breaks down to $751,988, approximately $380,000 annually.

CDC Foundation
BEST-C Study Budget (1-25-2010)

	Year 1	Year 2	Total
Personnel			
CDCF Program officer (.05 of $50,000)	$2,500	$2,600	$5,100
CDCF Administrative assistant (.10 of $35,000)	$3,500	$3,640	$7,140
CDC Site Contractor: Statistician (GS-13 equivalent) (1 FTE)	$86,520	$89,981	$176,501
Senior Economist for Cost Effectiveness Assessment	$60,000	$60,000	$120,000
Study costs for four sites ($751,988 per site over two years)			
Site principal investigator (.50 FTE of $168,000 per site)*4	$336,000	$349,440	$685,440
Site co-investigator (.25 FTE of $168,000 per site)*4	$168,000	$174,720	$342,720
Case Manager - Linkage to Care (.25 FTE of $40,000 per site)*4	$40,000	$41,600	$81,600
Project coordinator (1 FTE at 60,000 per site)*4	$240,000	$249,600	$489,600
Data manager (.50 FTE of $60,000 per site)*4	$120,000	$124,800	$244,800
Benefits 23% (for all personnel at 4 sites)	$207,920	$216,237	$424,157
Antibody tests (5,000*$10 annually, per site)*4	$200,000	$200,000	$400,000
Contractor Supplies & Equipment (per site)*4	$24,000	$24,000	$48,000
Promotional Materials (per site)*4	$24,000	$15,224	$39,224
Local site travel and to Annual Meeting (per site)*4	$14,800	$14,800	$29,600
Site overhead (8% each per site)*4	$93,344	$95,535	$188,879
Study travel for CDC and CDCF	$15,000	$15,000	$30,000
Annual Meeting Costs			
Meals (2 group breakfast, 2 lunches, 1 dinner)	$4,200	$4,620	$8,820
Rent, A/V and Materials	$5,000	$5,500	$10,500
Subtotal	$1,644,784	$1,687,296	$3,332,080
CDC Foundation Admin. Fee (13.5%)	$222,046	$227,785	$449,831
TOTAL	**$1,866,830**	**$1,915,081**	**$3,781,911**

PARTNER RECOGNITION

The CDC Foundation is pleased to work with our partners to acknowledge gifts and, when appropriate, to publicize program activities and outcomes. The CDC Foundation communicates with a large network of individuals and organizations concerned about public health issues through a newsletter, our website (www.cdcfoundation.org), and e-mail updates and alerts. The CDC Foundation also works with the news media to publicize newsworthy announcements and success stories.

CDC FOUNDATION

Established by Congress, the CDC Foundation began operations in 1995 as an independent, nonprofit enterprise committed to forging effective partnerships between CDC and individuals, foundations and corporations to fight threats to health and safety. These partnerships help CDC do more, faster, offering CDC flexibility and resources to enhance CDC's impact in the United States and around the world. The CDC Foundation provides a doorway for the private sector to work with CDC to create new programs and address public health priorities.

The CDC Foundation will provide administrative oversight for the project, working closely with CDC and partner organizations to coordinate the program as well as provide administrative and budget activities including:

- Preparing contracts and agreements with all partner organizations to ensure a strong foundation for the operation of the program
- Hiring/contracting for personnel as needed
- Convening meetings between program partners as necessary to ensure successful operations
- Administering and tracking budgets
- Processing program invoices and arranging payment to personnel and contractors
- Assuring compliance with accepted accounting and business practices

The Foundation will ensure that the program is implemented according to program goals and according to the established timetable and budget. It will provide financial and narrative reports in accordance with requirements. The CDC Foundation is a 501(c)(3) organization and its Federal Identification Number is 58-2106707.