

National Health and Nutrition Examination Survey

OMB No. 0920-0950

(Expires November 30, 2016)

**Nonsubstantive Change to conduct NHANES Comparison Study of
Waist Circumference Measurements and Liver Ultrasound
Elastography Pilot Study**

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This is a request for nonsubstantive changes to the National Health and Nutrition Examination Survey (NHANES) (OMB No. 0920-0950, exp. November 30, 2016), conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). The proposed changes would not alter the currently approved burden hours.

The projects planned include the following:

- a) **Liver Ultrasound Elastography Pilot Study**
Chronic liver disease (CLD) and cirrhosis are significant sources of morbidity and mortality. Combined they are the 12th leading cause of death in the U.S., accounting for 36,427 deaths in 2013 [1]. If feasible, NHANES would eventually propose to investigate the public health burden of components of CLD. This current request is to test the exam instrument/measures (liver elastography) in the NHANES environment.
- b) **Advance Transportation Allowance**
Currently, NHANES survey participants who have completed their home interviews and have an exam in the NHANES Mobile Examination Center (MEC) receive a transportation allowance as part of their overall remuneration. This remuneration (including the transportation allowance) is given after the MEC exam is complete. Allowing the transportation allowance to be offered in advance under certain circumstances without changing the amount is proposed. The target group for this project is low-income heads of household age 18 and over who have completed their household interview and made a MEC exam appointment which falls in the last 2 weeks of the MEC being on location in their community. The expected number of participants is approximately 100 per MEC location or roughly 1500 per year (given 15 MEC locations annually).
- c) **Electronic Digital Signature to Document Consent**
NHANES would like to implement a digital signature as part of the consent process. The content of the consent language would not change. Participants would still be provided a hard copy consent to read before signing electronically. And a hard copy of the consent with the participant's signature (obtained electronically) would be provided to the participant if requested.
- d) **Human Papillomavirus (HPV) Provider Record Check Pilot**
NHANES is the only national survey that tests for HPV in vaginal (since 2002), oral (since 2009), and penile (since 2013) specimens. Currently, NHANES asks participants to report HPV vaccination status but there is no subsequent provider record check. This proposal aims to evaluate the feasibility of obtaining provider verified HPV vaccination history among NHANES participants ages 14-29 years.

A. Justification

1. Circumstances Making the Collection of Information Necessary.

The NHANES contributes to the mission of CDC by collecting objective data that are used to promote health and to prevent and control disease and disability. CDC works with partners throughout the nation and the world to monitor public health, formulate and implement prevention strategies, develop health policies, promote healthy behaviors, and foster safe and healthful environments. In addition to the groups within the CDC, NCHS collaborates with over two dozen federal agencies to plan and fund the NHANES. The survey partners include numerous institutes of the National Institutes of Health, several programs within the U.S. Department of Agriculture, the Food and Drug Administration, and the U.S. Environmental Protection Agency. NHANES data are used to assess environmental exposures; evaluate nutrition program and policy impacts; and estimate prevalences of health risk factors, chronic conditions, and infectious diseases.

NHANES is a continuous survey, meaning survey data are collected every year. It includes a household interview, done in participants' homes and physical measures and additional interviews done at the NHANES MEC. There may also be follow-up interviews or components (such as a 2nd dietary interview) that take place after the MEC exam. A major advantage of continuous NHANES data collection is the ability to address emerging public health issues and provide objective data on more health conditions and issues. Because of the NHANES sample design, data are released in two year cycles. Some of the survey information gathered may change at the beginning of each two year cycle. In some cases, this means new content will be added. In other cases, this means that existing content may be modified.

New methodology must be tested before being implemented. There are many reasons for this. This allows us to find out how long the procedure being tested will take or how well received the procedure will be among our participants. The results of such testing also allow the NHANES program to make changes or adjustments to improve the methodology. It also provides hands on training opportunities for NHANES survey staff responsible for collecting the data. Testing is a vital step in making sure NHANES is effective and efficient in its use of resources. Such measures promote improved data quality once the data is collected in an actual survey. Since data collection is continuous, methodology studies must be conducted during ongoing NHANES data collection.

2. Purpose and Use of the Information Collection

The purposes and uses of each study are detailed below. Tests will include NHANES participants or remunerated volunteers (in circumstances when there aren't enough NHANES participants in the pilot's target group or when the pilot cannot be conducted in the NHANES setting, etc.). Participation is voluntary. Tests will be conducted as soon as clearance is received.

a) Liver Ultrasound Elastography Pilot Study

Chronic Liver Disease (CLD) is a significant source of morbidity and mortality as the 12th leading cause of death (all ages) in the U.S. accounting for 36,427 deaths in 2013 [1]. It is estimated that CLD represent the 5th leading cause of death for patients aged 45 to 54 years. The prevalence of cirrhosis is increasing due to the aging of persons with hepatitis C, coupled with an increase in obesity and associated fatty liver disease. These conditions are well-known to have health disparities in the U.S. population [2-6]. The incidence of viral hepatitis, and NAFLD disproportionately affect populations by sex, race, and socioeconomic status [2]. For example, the death rate varies among racial-ethnic groups with the age-adjusted liver disease mortality rate of 32.3 per 100,000 persons for Hispanics compared with the mortality rates of 21.6 per 100,000 persons for both non-Hispanic whites and non-Hispanic blacks [2]. CLD burden in the future may be greater than current population-based estimates due to the ongoing obesity epidemic, diabetes, and undiagnosed cryptogenic cirrhosis among individuals with risk factors for NAFLD compounded by significant racial/ethnic and socioeconomic disparities in the prevalence of cirrhosis [3-5]. In addition, NAFLD is an emerging morbidity with an increasing trend for end-stage liver disease, and recently nonalcoholic steatohepatitis has become the 2nd leading etiology of liver disease among adults awaiting liver transplantation in the U.S. followed by alcoholic liver disease [6].

The concept of collecting information to allow investigating the public health burden of NAFLD is an extension of earlier work using ultrasound information from the NHANES III gallbladder ultrasonography study conducted 20 years ago by the NCHS [7-9]. The ongoing obesity epidemic and its metabolic corollaries, such as hepatic steatosis and NAFLD, are a significant public health burdens as previously demonstrated by earlier population-based prevalence estimates from the Dallas Heart Study and NHANES III [10-11].

Before this can be done, it is necessary to test the liver elastography equipment in the NHANES environment. This non-substantive change is for the pilot study that will allow NHANES to examine how the equipment integrates into the existing MEC exam and how participants respond to this component. To complement this component, a hip measurement will be added back into the NHANES body measures (anthropometry) component. Hip measurement is used to determine the waist to hip ratio, which is considered to be an important indicator of central obesity, and therefore important to interpreting the liver findings. Waist measures are currently collected in NHANES. Hip measurements were last conducted in NHANES in 1988-1994. We will use the same protocol in the liver pilot, as in NHANES 1988-1994 to obtain hip measurements.

If this testing yields a response rate of at least 80% and the protocol proves satisfactory, the eventual goal would be to add this exam procedure, along with corresponding interview questions and lab measures, to the full NHANES. The addition of this component to NHANES would allow us to obtain estimates of the US prevalence of hepatic steatosis and liver stiffness (a marker of liver fibrosis). This will also make it possible to examine the relationship of factors related to these CLD in the U.S., namely obesity/metabolic status, excess alcohol consumption, and hepatitis B and C infections.

This current request is to test the exam instrument/measures only. A separate package will be submitted for testing other aspects of this project, such as questions and lab measures. Specifically, we will seek approval to conduct cognitive testing of alcohol consumption questions in the NCHS Questionnaire Design Laboratory. This will facilitate their use in the full NHANES, in the future.

Up to 575 NHANES participants ages 12 years and older who attend their scheduled NHANES visit to the MEC will be asked to have a liver ultrasound elastography while at the MEC. It will be measured using the same method as previously conducted in the NHANES anthropometry component. So the total amount of time needed per participant for this project is estimated at 15 minutes per person. If the proposed project is successful then the desired outcome would be to add this component to the full survey beginning in NHANES 2017-2018.

The objectives of this project can be summarized as follows:

1. Measure liver fatness (hepatic steatosis) and liver stiffness (an indicator of liver fibrosis) by gender and other demographic characteristics, such as race/ethnicity.
2. Test response rates and acceptability of the measurement device among NHANES participants
3. Evaluate the ability of this approach to operate similarly in all types of persons (e.g. teens, seniors, and obese persons)
4. Use existing survey information, such as medical conditions (e.g. diabetes) demographic information (e.g., age, sex, race/ethnicity) and risk factors (e.g. alcohol intake, obesity, nutritional status, etc.) to help interpret the new ultrasound findings
5. Assess technician proficiency in administering this component
6. Assess whether or not the quality of the data obtained is sufficient to report findings to participants
7. Determine if this component can be successfully added to NHANES 2017-2018

More details about the Liver Ultrasound Elastography Pilot Study are provided in Attachment A.

b) Advance Transportation Allowance

Currently, NHANES survey participants who have completed their home interviews and exam in the NHANES Mobile Examination Center (MEC) receive a transportation allowance as part of their overall remuneration. This takes place in the NHANES MEC, after the MEC exam has been completed.

Sometimes a person who has made a MEC appointment has to cancel and reschedule. In the first four weeks in a NHANES location, rescheduling can be easily accommodated. In the last two weeks in a MEC location, it is more difficult.

The goal of this request is to advance the transportation allowance ahead of the MEC exam in the last two weeks of a given MEC location in order to help low income participants keep their MEC exam appointments in the last two weeks of a MEC location.

For the transportation allowance to be offered in advance of the NHANES exam at the MEC, the following conditions must be met:

- 1) The survey participant must have demonstrated commitment to the NHANES survey by having already completed the home interview and having already scheduled their MEC appointment;
- 2) The survey participant must be head of a low-income household age 18 or older; and
- 3) The advance transportation allowance is only being offered to eligible participants with MEC appointments in the last two weeks in a given location for reasons described in the next paragraph.

In the first two to four weeks at a MEC location, there is still time to reschedule broken appointments. Also, during this window field interviewers are available to help drive participants they have interviewed to the MEC if transportation is a barrier. In the last two weeks at a MEC location it is generally not possible to reschedule broken appointments as there are fewer time slots. And field interviewers are no longer available to assist with transportation. This is because most interviewers will have already traveled to the next MEC location to begin interviews there. Those few interviewers remaining are completely dedicated to the process of refusal conversions and cannot take time away from this activity to provide transportation.

NHANES is aware that there is a risk associated with offering an advance transportation allowance because it creates the possibility of someone receiving the allowance, yet still not keeping their MEC appointment. Limiting the advance transportation allowance to just the two week period when broken appointments cannot be rescheduled and other transportation assistance is not available, reduces the window for this risk. It should be noted that if field interviewers have reason to believe that giving the transportation allowance in advance will not encourage attendance at the MEC exam, they are not required to offer it. Such reasons might include hesitancy in committing to an available exam appointment (while still scheduling it), anti-government attitudes, etc.

The implementation of an advance transportation allowance, as described above, is expected to help improve NHANES response rates in the target group by reducing the number of broken appointments in the last two weeks at a NHANES MEC location.

More details about the Advance Transportation Allowance implementation, including the existing NHANES the transportation allowance amount, are provided in Attachment B.

c) Electronic Digital Signature to Document Consent

NHANES would like to implement an electronic signature process (e-consent) for consents that allows a participant to sign via an electronic screen vs. a hard copy piece of paper. There are no changes to the consent protocol currently in place, except that the signature will be captured electronically. New Respondent Selection (RIQ) questions which ask for electronic documentation of consent replace RIQ questions which asked for hard copy documentation of consent. As such, there is no addition to burden for the consent process. A blank hard copy of the consent form(s) will also be left with each respondent. If the respondent requests a printed

signed copy of the form with all of the information captured electronically, this would be provided. The desired goal would be to implement e-consents at the start of the NHANES 2016 cycle among all participants who currently sign hard copy consents/assents.

More details about Electronic Digital Signature to Document Consent, including RIQ questions and screenshots of the electronic forms, are provided in Attachment C.

c) Human Papillomavirus (HPV) Provider Record Check Pilot

Human papillomavirus (HPV) is a sexually transmitted pathogen that causes anal, genital, and oropharyngeal diseases in males and females. Infection with high-risk HPV types, particularly HPV 16 & 18, causes virtually all cervical cancers. The same HPV types that cause cervical cancer also cause other cancers, including anal, oropharyngeal, penile, vaginal and vulvar cancer. On June 8, 2006, the Food and Drug Administration licensed the first HPV vaccine to prevent cervical cancer and other diseases. In the United States, there are currently three different HPV vaccines, each with different combinations of HPV types, licensed for females and males ages 9-26 years. Routine HPV vaccination is recommended by the Advisory Committee on Immunization Practices (ACIP) at age 11 or 12 years. ACIP also recommends vaccinating previously unvaccinated females aged 13-26 years and males aged 13 -21 years (or 13-26, depending on risk factors).

The National Immunization Survey (NIS)/ NIS-Teen, two CDC surveys, use the provider record check as the gold standard method for vaccine surveillance because of inaccuracies of vaccine histories based on parental recall. Based on the experiences of the NIS/ NIS-Teen, use of a provider record check to assess HPV vaccination status in NHANES will increase the accuracy of the HPV vaccination histories.

In conjunction with the vaginal, oral, and penile specimens collected in NHANES, provider-reported vaccination histories are expected to provide more accurate estimates of vaccine effectiveness. Unlike vaccine efficacy studies, which are often performed in the context of a randomized clinical trial, vaccine effectiveness studies are conducted in community settings and are used to evaluate how well licensed vaccines work in real world settings. National data on vaccine effectiveness may inform ACIP's vaccine recommendations, which impacts vaccine funding under the Vaccines for Children Program and Affordable Care Act, and cervical cancer screening recommendations. Moreover, accurate vaccination status will also be used to identify populations that may be inadequately protected and for whom targeted public health interventions may be needed.

Although there are long-standing CDC surveys using provider record checks to assess vaccination coverage, differences between these surveys and NHANES, including the differences in targeted age group and survey mode, suggests a pilot study prior to implementation in NHANES may prove informative. The NHANES provider record check will include an older age range (14-29 years) than NIS (19 to 35 months) and NIS-Teen (13-17 years). Consequently, there will likely be a different mix of provider-types in NHANES; for example, less pediatricians and more internists. NIS/NIS-Teen is conducted by a telephone interview while NHANES is conducted during an in-person interview. Moreover, due to the geographic mobility of some participants in this age group, contacting providers in more

geographic areas to verify old records may prove to be more resource-intensive. The extent to which response rates, at the participant level and provider level, will be impacted by the differences between NIS/NIS-Teen and NHANES is unknown.

This proposed pilot study is designed to assess the feasibility and test all procedures related to a vaccination provider record check within NHANES. This pilot study will be conducted to gain information that will be useful in planning to implement a vaccination provider record check as part of NHANES in 2017.

Objectives

The objectives of HPV Vaccination Provider Record Check Pilot Study proposed are:

- To assess the feasibility and test all procedures related to the provider record check
- To assess percent of participants who authorize disclosure of vaccination records
- To assess provider response rates
- To evaluate completeness of the returned data.

This proposed component is designed to perform provider record checks of HPV vaccination history on an estimated 275 NHANES interviewees ages 14-29 years in approximately 4 NHANES locations in 2016.

The data of primary interest from the providers are: 1) number of HPV vaccines given, 2) dates of administration of HPV vaccines, and 3) type of vaccine given (i.e. Cervarix, Gardasil, or Gardasil-9). Providers will also be queried on the receipt of meningococcal and Tdap (tetanus, diphtheria, and acellular pertussis) vaccinations because these vaccines may be given at a similar time as HPV and will be used to assess data quality and completeness. Capturing Tdap and meningococcal vaccine doses administered provides a measure of validation that the adolescent/young adult's vaccination providers have been identified. For example, persons with a negative history HPV vaccination but a positive history for Tdap and/or meningococcal vaccinations can be more confidently considered unvaccinated. Ultimately, if the HPV Vaccination Provider Record Check is incorporated into future NHANES surveys, accurate HPV vaccination histories in NHANES will be used in conjunction with the vaginal, penile, and oral HPV specimens obtained in the survey to produce vaccine effectiveness estimates and to identify populations that may be inadequately protected from HPV.

More details about the Human Papillomavirus (HPV) Provider Record Check Pilot , including proposed questions and forms, are provided in Attachment D1 (participants) and Attachment D2 (participants' providers).

9. Explanation of any payment or gift to respondents.

Participants in the Liver Ultrasound Elastography Pilot Study will not receive any additional remuneration for this study. They will just receive the existing approved remuneration that goes with participating in the regular NHANES MEC exam.

Participants will not receive any additional remuneration due to implementing an Advance Transportation Allowance. NHANES participants already receive remuneration, including a transportation allowance, after completing their MEC examination. This project is only

requesting a change in the timing of when this transportation allowance is given, to the target group described above, for this project. This project is not requesting any change to the amount of remuneration currently approved.

Participants will not receive any additional remuneration due to implementing Electronic Digital Signature to Document Consent. NHANES participants already provide signatures on hard copy consent forms. This project is only requesting a change to electronic signatures.

Participants in the HPV Provider Record Check Pilot will not receive any additional remuneration.

12. Estimates of Annualized Burden Hours and Cost

The Liver Ultrasound Elastography Pilot Study has been budgeted for 15 minutes. The maximum number of respondents would be 575 adults and the maximum burden 144 hours ($575 \text{ respondents} * 15 / 60 \text{ hour} = 144 \text{ hours (rounded up)}$).

There is no additional burden associated with implementing an Advance Transportation Allowance. Participants are already receiving a transportation allowance. Changing when they get the allowance from in the MEC after the exam to in the home after the household interview, should not add to participant burden. Therefore, there is no burden for this project in the table below.

The Electronic Digital Signature to Document Consent is budgeted for 2 minutes. The maximum number of respondents would be 5,000 and the maximum burden 167 hours ($5,000 \text{ respondents} * 2 / 60 \text{ hour} = 167 \text{ hours (rounded up)}$).

The Human Papillomavirus (HPV) Provider Record Check Pilot is budgeted for 10 minutes for participants and 15 minutes for providers. The maximum number of NHANES respondents would be 275 (ages 14-29 years) and the maximum burden 69 hours ($275 \text{ respondents} * 15 / 60 \text{ hour} = 69 \text{ hours (rounded up)}$). The maximum number of provider respondents would be 550 and the maximum burden 183 hours ($550 \text{ provider respondents} * 20 / 60 \text{ hour} = 183 \text{ hours (rounded up)}$).

The total burden for all projects combined is 396 hours. This time was already budgeted and approved in line 2 (Special Studies) of the original submission. No additional burden is sought.

TABLE 3 – ANNUALIZED BURDEN HOURS AND COSTS

Type of Respondent	Form	Number of Respondents	Number of Responses per respondent	Average Burden per Response (in hours)	Total Burden Hours
Liver Ultrasound Elastography Pilot Study Participants	Liver Ultrasound Elastography Pilot Study Form	575	1	15/60	144
Vaccination Provider Record Check Participants	The Human Papillomavirus (HPV) Provider Record Check Participants Form	275	1	15/60	69
Vaccination Provider Record Check Providers	The Human Papillomavirus (HPV) Provider Record Check Providers Form	550	1	20/60	183
Total					396

15. Explanation for Program Changes and Adjustments. There are no changes in this package from the previous-approved clearance. The burden hours were approved by OMB in the full clearance.

List of attachments:

- A1. Liver Ultrasound Pilot Description
- A2. Liver Ultrasound Elastography Pilot Study Form
- B. Advance TA
- C. EConsent
- D1. HPV PRC Pilot Description
- D2. HPV PRC Participants Form
- D3. HPV PRC Providers Form

References:

- 1) Deaths, percent of total deaths, and death rates for the 15 leading causes of death: United States and each State http://www.cdc.gov/nchs/data/dvs/LCWK9_2013.pdf CDC/NCHS, National Vital Statistics System, Mortality 2013

- 2) Ruhl CE, Unalp-Arida A. Racial-ethnic disparities in liver disease mortality in the United States. *J Hepatology* 2015; 62: S733-S734
- 3) Everhart JE. Chapter 21: Liver disease. Ruhl CE, Sayer B, Byrd-Holt DD, Brown DM. Chapter 25: Costs of digestive diseases. In: Everhart JE, editor. *The burden of digestive diseases in the United States*. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Washington, DC: US Government Printing Office, 2008; NIH Publication No. 09-6443 [pp. 111-114, 137-146].
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- 6) Wong RJ, Aguilar M, Cheung R, Perumpail RB, Harrison SA, Younossi ZM, Ahmed A. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. *Gastroenterol* 2015; 148: 547-555
- 7) NCHS. Third National Health and Nutrition Examination Survey. Gallbladder ultrasonography procedure manual. Available at: <http://www.cdc.gov/nchs/data/nhanes/nhanes3/cdrom/nchs/manuals/gallblad.pdf> Westat, Inc.: Rockville, MD, 1988
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- 10) Lazo M, Hernaez R, Eberhardt MS, et al. Prevalence of non-alcoholic fatty liver disease in the United States: The Third National Health and Nutrition Examination Survey, 1988-1994. *Am J Epidemiol* 2013; 178: 38-45

11) Victor RG, Haley RW, Willett DWL, et al. The Dallas Heart Study: A population-based probability sample for the multidisciplinary study of ethnic differences in cardiovascular health. *Am J Cardiol* 2004; 93: 1473-1480