

Case Investigation of Cervical Cancer Study

Supporting Statement – Section B

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1LIST OF ATTACHMENTS

Attachment 1 – Section 301 of the Public Health Service Act

Attachment 2 – 60-Day FRN

Attachment 3 – Letter to Physicians

Attachment 4a – CICC Survey, English

Attachment 4b – CICC Survey, Spanish

Attachment 5a – Patient Cover Letter, English

Attachment 5b – Patient Cover Letter, Spanish

Attachment 6a – Research Participant Information Sheet, English

Attachment 6b – Research Participant Information Sheet, Spanish

Attachment 7a – Medical Release & Healthcare Source Forms, English

Attachment 7b – Medical Release & Healthcare Source Forms, Spanish

Attachment 8a – Phone follow-up script, English

Attachment 8b – Phone follow-up script, Spanish

Attachment 9 – Chart abstraction form

Attachment 10 – Battelle IRB Approval Letter

Section B – Data Collection Procedures

B1. Respondent Universe and Sampling Methods

This study consists of all cervical cancer survivors 21 years and older diagnosed with invasive cervical cancer between January 1, 2014 and December 31, 2016 within three state cancer registries. The respondent universe includes respondents in one of three state cancer registries who are alive, have agreed to allow the cancer registry to contact them, and whose eligibility has been confirmed by the registry. We have entered into agreements with the state cancer registries in Louisiana, Michigan, and New Jersey. These registries were selected for (a) the racial and ethnic diversity in state population, (b) their geographic dispersion within the United States, (c) large number of cervical cancer survivors, and (d) a demonstrated capacity with similar research. Based on preliminary data provided by the state cancer registries, the universe is estimated to be 1,670 eligible cervical cancer survivors. As a result of the sampling frame employed in this collection, which collects data from cancer survivors in three state cancer registries, outcomes may not be representative of the entire population of women diagnosed with cervical cancer in the United States and are thus not intended to be generalized to broader populations. Any limitations posed by the sampling methodology and frame employed in this study with regard to the non-generalizability of the data to broader populations will be clearly described in any presentations, publications, or communications associated with this collection.

Table 1 illustrates our expected sample size by race for whites, blacks and Hispanics. The sample for recruitment will be comprised of the entire population of cervical cancer survivors diagnosed between January 1, 2014 and December 31, 2016. With an expected survey response rate of 50% across the entire sample and an 80% acceptance rate for medical chart verification among survey respondents, this design will yield around 668 women with completed surveys and chart reviews.

Table 1: Projected Sample Size by State and Race/Ethnicity (n=668)

State	Eligible Cervical Cancer Survivors (n) 2014–2016 ^a	Estimated No. of cancer survivors who complete (a) the survey and (b) medical release & healthcare source forms			
		White ^b	Black	Hispanic	Total ^c
Louisiana	530	118	85	10	213
Michigan	590	183	41	12	236
New Jersey	550	130	44	46	220
Total ^d	1,670	431	169	68	668 ^e

^a Estimated total number of eligible cervical cancer survivors ages 21 years and older at diagnosis as provided by the cancer registries. The survey will be administered starting in January 2017 starting with cases identified in 2014. Rapid case assessment will be used to identify cases diagnosed in 2016 and women will be contacted no earlier than 3 months after diagnosis.

^b Distribution by race/ethnicity was based on counts of invasive cervical cancer by state for 2012 as published in *United States Cancer Statistics* (<http://nccd.cdc.gov/uscs/cancersbystateandregion.aspx>, accessed on 02/16/2016).

^c Sum of the estimated number of cancer survivors who complete the survey and medical release and healthcare source forms separately by registry and combined.

^d The proportions reported are derived by summing all cases across the three cancer registries.

^e Total projected sample size is based on calculations from the estimated total number of eligible cancer survivors (1,670 cases * 50% survey response rate * 80% medical release and healthcare source response rate = 668 cases). Differences with the sum of the estimate total count by race-ethnicity by individual registry (n=669) are due to rounding during the estimation process.

B2. Procedures for the Collection of Information

The survey instrument for the proposed study includes sections on: (A) cervical cancer history, including whether the survivor was diagnosed as the result of a routine exam or was seeking medical care related to symptoms; use of cervical cancer screenings and follow-up for abnormal tests in the five years prior to diagnosis; and, barriers and facilitators to screening and any necessary follow-up; (B) health insurance; (C) other medical conditions; (D) respondent demographic characteristics; and (E) interest in cervical self-sampling technology, HPV vaccination of children and awareness of HPV prior to diagnosis. **(Attachments 4a and 4b).**

If the respondent completed the medical release and healthcare source forms **(Attachments 7a and 7b)**, a chart verification will collect information in the following sections from all providers

for the five years prior to and including the date of the cancer diagnosis: Pap and HPV testing, cervical diagnostic testing and patient history of symptoms associated with cervical disease.

2.1 Data Collection Procedures

Cancer registries will use information in their registry database to identify women who were diagnosed with cervical cancer in 2014-2016. Women will be excluded if they are under the age of 21, reported as deceased, or have been previously classified as “do not contact.” Each eligible woman will be assigned a randomly generated study ID. Before distributing the survey and other study materials, the cancer registry will contact her diagnosing physician to ensure that there are no contraindications or concerns regarding contacting her for the study. The cancer registry will send a cover letter and the opt-out forms to the physician (**Attachment 3**). The physician has up to two (2) weeks to contact the cancer registry. If the cancer registry does not hear from the physician, contacting the woman can proceed.

Once the physician contact phase is complete, the cancer registry will distribute study materials to the potential participant, including: the paper-based survey in English (**Attachment 4a**) and Spanish (**Attachment 4b**), a cover letter in English (**Attachment 5a**) and Spanish (**Attachment 5b**), a research participant information sheet in lieu of a written consent form in English (**Attachment 6a**) and Spanish (**Attachment 6b**), medical release and healthcare source forms in English (**Attachment 7a**) and Spanish (**Attachment 7b**), and a pre-paid self-addressed stamped envelope. Starting one week (or five business days) after the initial mailing, the cancer registry will conduct two to three follow-up phone calls at varying times of the day and different days of the week with at least one evening call made between the hours of 5-8pm (Eastern Time (EST) in New Jersey and Michigan and Central Time (CT) in Louisiana). Three weeks after initial mailing, a second packet will be sent. Starting one week after the second mailing (four weeks after initial mailing), the cancer registry will conduct two to three additional follow-up phone calls at varying times of the day and different days of the week with at least one evening call made between the hours of 5-8pm (EST in New Jersey and Michigan and CT in Louisiana). If a woman cannot be reached or has not responded after six weeks, a survey will be mailed to women one final time. At each phone contact, women will be offered to complete a phone interview if that is their preference. When the materials are received at the cancer registry a \$25

incentive will be mailed. Respondents will have a period of 90 days to complete the instrument. Survey forms will not contain any personal identifier information and will be marked only with the participant study ID.

The following steps will be completed for women who have consented to medical chart verification. The cancer registry will send the medical record release form along with a cover letter to the primary care physicians that were identified by the participants in the healthcare source form. The cover letter will inform them of the study and its objectives, and provide instructions for sending copies of medical records to each of the cancer registries. Traditional protocols have allowed for mailed paper copies via overnight carrier, encrypted email, or secure file transfer protocol (SFTP). If a physician is unable to send copies of medical records, the cancer registries will send trained abstractors with an encrypted laptop to the physician's office to either make the copies of the records or conduct on-site abstraction. Abstraction forms (**Attachment 9**) will not contain any patient identifiers but will be indexed with the participant's study ID.

2.2 Estimation Procedure

Survey Weights

If all eligible cervical cancer survivors at three cancer registries are unable to be recruited, survey weights for nonresponse will be generated by SAS PROC SURVEYSELECT. The sample survey data analysis procedures in SAS (SAS Institute 2012) will be used to generate sample estimates of means or proportions adjusted for non-response, and to conduct statistical tests of differences among these estimates.

Power Analysis

The three selected state cancer registries have estimated a total of 1,670 eligible cervical cancer survivors. From discussions with the 3 cancer registries and their prior experience with survey response and consent to chart review, we expect a survey response rate of 50% across the entire sample and an 80% acceptance rate for medical chart verification among survey respondents, this design will yield around 668 women with completed surveys and chart verification.

One of the central outcomes of interest is to estimate the proportion of women diagnosed with cervical cancer who did not have a cancer screening test during a five-year period prior to diagnosis. In previous work conducted by Leyden et al. 2005, the authors found that among 833 records of women with a cervical cancer diagnosis from several health systems, a proportion of 0.56 of these had no screening test within the three years prior to their diagnosis. Using a proportion of 0.56, a sample of 668 cases would yield a detectable difference of 0.054 with 80% power while controlling for Type I error at a rate of 5%.

B3. Methods to Maximize Response Rates and Deal with Nonresponse

In order to increase response, the cancer registries will conduct follow-up phone calls and additional mailings. Starting one week (or five business days) after the initial mailing, two to three follow-up phone calls will be conducted at varying times of the day and different days of the week with at least one evening call made between the hours of 5-8pm (Eastern Time [ET] for New Jersey and Michigan and Central Time [CT] for Louisiana). Three weeks after initial mailing, second packets will be sent. Starting one week after the second mailing (four weeks after initial mailing), two to three additional follow-up phone calls will be conducted at varying times of the day and different days of the week with at least one evening call made between the hours of 5-8pm (ET for New Jersey and Michigan and CT for Louisiana). If the woman cannot be reached or has not responded after six weeks, a final mailing to women will be sent. At each phone contact, women will be offered to complete a phone interview if that is their preference.

In addition, a \$25 monetary incentive is offered. A review of 49 experiments has shown that incentives significantly increase the odds of survey completion (Edwards et al., 2007). Finally, a toll-free number will be provided that can be used by survey participants to contact survey staff from 9am to 5pm ET (8am to 4pm CT) to address specific questions or obtain clarifications.

B4. Test of Procedures or Methods to be Undertaken

The questionnaire was pilot tested with nine English-speaking cervical cancer survivors living in the state of South Carolina and in the Atlanta and Seattle metropolitan areas. The pilot tests assessed clarity, quality and usability of the study materials (**Attachments 4a, 5a, 6a, 7a**) and

were used as a tool to estimate time burden associated with completing the survey and other study materials that are provided in the initial mailing. Feedback from pilot testing was incorporated into the final version of the study materials. The estimates of time burden presented in Part A of the Supporting Statement were generated from pilot testing results. The chart abstraction tool has been reviewed and evaluated by three gynecologic oncologists and the participating cancer registries.

Descriptive statistics and logistic regression will be applied to understand self-reported barriers and facilitators to screening and follow-up treatment, and medical record abstraction reports of screening and diagnostic testing.

B5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Vicki Benard, Ph.D., of the Division of Cancer Prevention and Control, is the Principal Investigator and Technical Monitor for the study, and has overall responsibility for overseeing the design, conduct, and analysis of the study. She will approve and receive all contract deliverables. Telephone: 770-488-1092.

The survey instrument, sampling and data collection procedures, and analysis plan were designed in collaboration with researchers at Battelle. Battelle will oversee the data collection which will be conducted at each of three cancer registries. With the provision of optional funds, Battelle will perform data analysis and participate in dissemination of findings, in consultation with the CDC investigators.

April Greek, Ph.D. [206-528-3167] has overall technical and financial responsibility for the study at Battelle and led the Battelle effort to design this protocol. Dr. Greek will direct the overall data collection and analysis effort.

Other personnel involved in design of the protocol and data collection instruments are:

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