CDC'S CERVICAL CANCER STUDY (CX3) AN INTERVENTION PILOT STUDY OF HPV IN ILLINOIS NBCCEDP

SUPPORTING STATEMENT

PART B: COLLECTIONS OF INFORMATION
EMPLOYING STATISTICAL METHODS

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B.1. Respondent Universe and Sampling Methods

The Cx3 study is being conducted in 15 clinics (with several providers in each clinic) associated with six Federally Qualified Health Centers (FQHC) and FQHC look-alikes in the state of Illinois. FQHC's were selected because the client base was most similar to NBCCEDP clients and because the sliding fee scale available to patients would provide the greatest likelihood that study sample patients would remain in the clinic over three years of follow-up regardless of continued eligibility in NBCCEDP (low income and uninsured). Each clinic was assigned to one of two study arms: intervention (N=7) or control (N=8). The intervention and control arms were matched on clinic attributes such as geographical location (urban, rural, suburban), racial/ethnic characteristics of the patient population, hospital versus non-hospital status, provider specialty mix, and patient volume.

The universe for the 36-month follow-up provider survey includes the providers who were surveyed at baseline and who are still providing Pap testing at the 15 participating clinics. A total of 98 providers completed baseline surveys. Assuming that 20% of the providers will no longer be practicing at the participating clinics, the universe of providers for the 36-month provider survey would be 78. Assuming a 90% response rate (the rate observed in the baseline survey), we anticipate that approximately 70 providers will complete the 36-month provider survey. The universe for the in-person provider interviews includes all providers who are currently performing Pap testing at participating clinics (regardless of whether or not they participated in the study previsously). This is estimated to be approximately 90 providers. Of these we expect that approximately 75 will agree to participate in the in-person qualitative interviews.

The universe for the 18-month follow-up patient survey is the 984 patients that completed the patient baseline survey. Based on experience to date in Phase I, we expect approximately 787 completed patient follow-up surveys (calculated using a non-response rate of 14%, and 6% of patients being lost to follow up). Administration of the 18-month follow-up patient began in March 2011 is expected to continue into Phase II of the study. We estimate that 150 of the patients will be surveyed in Phase II of the study (after June 30, 2012).

The primary objective of the study is to determine whether or not the educational intervention will lead to an increase in the willingness of providers to extend the cervical cancer screening interval to three years for women who are HPV negative and Pap normal. A total of 2,002 of the 2,246 patients (89.1%) recruited into the study were HPV negative and Pap normal. Based on information received from patient medical records, we will examine the extent to which providers in the intervention and control arms are willing to extend the screening interval to three years. We conducted a power analysis to determine the adequacy of the patient sample to detect a 0.1 difference in the average prevalence of support for an extended screening interval between the intervention and comparison arms (i.e., an average prevalence of 0.2 in the control group and an average prevalence of 0.3 in the intervention group). We ran a simulation in which we generated 30 normal random variables with a mean of 0.3 and a standard deviation of 0.075 for 30 providers in the intervention arm and 30 normal random variables with a mean of 0.2 and a standard deviation of 0.075 for 30 providers in the control arm. For each provider in each study arm we generated 25 uniform random variables for 25 patients. We then applied the provider's

probability of recommending an extended interval to generate a success/failure data for each of the patients (we compared the patient's probability to its provider's probability). We ran this simulation 1,000 times. We then ran a logistic regression (using PROC GENMOD) with the simulated data and determined if the coefficient associated with the variable arm (study group) was statistically significant (two-tailed, alpha = 0.05). In doing this logistic regression, we took account of the correlation of the responses within providers by using provider as a "cluster" variable. Based on this analysis, a sample of 750 patients in each arm of the study with complete data over the three year study period will yield a power of .9 or greater to detect a 0.1 difference between the intervention and comparison arms in the willingness of providers to extend the Pap test screening interval to 3 years among women who are HPV negative and Pap normal.

B.2. Procedures for the Collection of Information

There are three data collection activities that are planned to begin or continue in Phase II of the study. These include:

- A provider follow-up survey will be conducted 36 months following study initiation to assess knowledge, attitudes, beliefs, and screening practices;
- An 18-month patient follow-up survey—which was begun in Phase I—will continue to assess knowledge, attitudes, beliefs, and screening behavior; and
- In-person qualitative interviews with providers at participating clinics will be conducted to identify facilitators and barriers to acceptance and appropriate use of the HPV test and longer screening interval.

Additional data for the study will be obtained from patient medical and billing records. These data will be used to assess clinic use, screening intervals, and follow-up to a positive diagnosis.

Provider Follow-up Survey. Prior to study initiation, all providers that perform Pap testing at the 15 participating clinics were surveyed prior to as well as 12 months following study implementation. In Phase II of the study, these providers will be asked to complete a final follow-up survey 36 months following study implementation. Battelle will be responsible for administering the follow-up provider survey. Providers will be sent a survey packet by Express Mail. The survey packet will include a cover letter, a hardcopy survey, a stamped and addressed envelope, and a $50 incentive to complete the survey. The survey cover letter will be personally addressed to each provider. The letter will be printed on CDC letterhead and signed by the CDC study leader. The letter will give the respondents a toll-free telephone number to call if they have questions regarding the study. The survey cover letter and the first page of the survey questionnaire constitute the informed consent. They describe how the survey data will be used, by whom, and describe the steps to protect the privacy of the data. They also clearly indicate that participation in the survey is voluntary.

Attachment C contains:

1. cover letter for follow-up surveys (Attachment C1a), and
2. follow-up provider survey (Attachment C1).

Follow-up Patient Surveys. A sample of 984 patients completed a baseline survey during their initial clinic visit. Beginning in March 2011 we began administering an 18-month follow-up survey to those patients who completed a baseline survey. In order to administer the follow-up surveys, patient contact information was obtained at the time of study enrollment. In addition to recording the address and telephone numbers of the patient, patients were asked to provide the name and telephone number of a friend or family member who will always know where to contact her, in case she has moved and we are having trouble contacting her. Using the contact information provided on the patient enrollment form, Battelle is administering the follow-up patient survey. Two weeks prior to mailing the survey, an initial postcard is mailed to tell patients to expect a survey in the mail. The postcards are sent "Return Services Requested," so that the Post Office will let us know if the postcard is undeliverable. For those postcards that are undeliverable, we call the contact numbers provided on the enrollment form in an effort to obtain a current address. The patient is then mailed a survey packet that includes a cover letter, a hardcopy survey, a stamped and addressed envelope, and a $5 incentive. A thank you/reminder postcard is sent two weeks after the survey is mailed. In addition, non-respondents receive a follow-up phone call four weeks after the mailing date. Surveys are returned directly to Battelle for data entry.

Attachment D contains the following:

1. patient consent form (Attachment D1a),
2. initial postcard (Attachment D1b),
3. cover letter for patient follow-up surveys (Attachment D1c),
4. reminder postcard (Attachment D1d),
5. script for reminder phone call (Attachment D1e), and
6. follow-up patient survey (Attachment D1).

In-person Qualitative Interviews with Providers. In-person qualitative interviews with providers are being proposed in Phase II of the study to identify the facilitators and barriers to acceptance and appropriate use of the HPV test and the willingness of providers to increase the cervical cancer screening interval to three years following a negative HPV test and a normal Pap test. A visit to each of the 15 participating clinics will be scheduled and providers will be asked to participate in an interview or a focus group discussion with other providers (depending upon the preferences of the providers). The interviews will be conducted with approximately five providers at each of the 15 participating clinics) at the conclusion of the study (three years after study implementation). The interviews will be scheduled at a time that is least disruptive to providing patient care. Prior to each interview or focus group discussion, the provider will be given a consent form that explains the purpose of the interview for their records. Interviewer notes will not contain the names of the providers.

Attachment C contains the following:

1. consent form for the qualitative interviews with providers (Attachment C2a), and
2. interview guide for in-person provider interviews (Attachment C2).

Data from Patient Medical and Billing Records. At the time of study enrollment, patients were asked to give consent for study personnel to access their medical and billing records. These data will provide the information necessary to answer the primary study question, namely does HPV co-testing with provider and patient education lead to extended screening intervals for women with negative results. Information will be obtained for a period of 3 years following study enrollment. The information that will be obtained includes (1) type of provider seen during each office visit, (2) date of the visit, (3) whether or not a Pap test was performed, and (4) whether or not the visit was for a wellness checkup. The chart review will also support the secondary study question of what type of follow-up is received by HPV positive women (i.e., abnormal Pap and/or positive HPV). This activity is conducted by study personnel (the data collection contractor) and does not impose burden on respondents. More detail about the information that will be collected during the chart review is provided in Attachment E.

B.3. Methods to Maximize Response Rates and Deal with Nonresponse

Every effort is being made to maximize the response rates to the provider and patient surveys. Multiple methods studies, reviews and meta-analyses have been conducted to determine which factors lead to an increase in response rates to mail surveys. Preliminary notification, multiple follow-ups with respondents, monetary and non-monetary incentives, use of Express Mail or first class stamped envelopes and appropriate salutations have positive effects on response rates while sponsorship or endorsement, use of personalization techniques in mailings, and length of questionnaires, have shown inconsistent effects on response rates. The approaches that we will use to maximize the response rates to the provider and patient surveys are described below.

*Provider Surveys***.** Health care providers who spend most of their time on direct patient care are a particularly difficult group to survey. Many medical practices have administrative personnel assigned to sort through mail and telephone messages and only pass on to physicians those most in need of his/her direct attention. Consequently, surveys of practicing physicians generally result in lower response rates than surveys of other groups of respondents, including other professionals. Nevertheless, reviews of survey methods clearly point to a number of procedures that improve response rates among physicians.

In a previous study, Battelle worked with the American Cancer Society and CDC to conduct focus groups with primary care physicians to obtain their input about strategies for maximizing response to physician surveys. There was clear consensus among these physicians that: (1) the survey should be sent by Express Mail because it gets the physician's attention and is unlikely to be screened by office staff; (2) a substantial monetary incentive should be provided; (3) the monetary incentive should be sent with the survey; (4) the reputation of CDC among physicians is good, and therefore the cover letter for CDC studies should clearly indicate that the study is being conducted by CDC.

To insure that the provider surveys will be delivered to the clinic providers, the survey packets for the follow-up provider surveys will be sent by Express Mail. The survey cover letter, which will stress the importance of the study, will be personally addressed to each provider. The letter will be printed on CDC letterhead and signed by the CDC study leader. The cover letter will give the respondents a toll-free telephone number to call if they have questions regarding the study. In addition to the provider survey and cover letter, the survey packet will contain a $50

incentive to complete the survey. Battelle has used these methods in several previous surveys of health care providers and they have been successful in achieving response rates in excess of 80%. The response rate achieved in the baseline provider survey for this study was 90% and, to date, the response rate to the provider follow-up survey is 76%.

*Patient Surveys***.** Patients who were selected for participation in the baseline and follow-up surveys, she were asked to complete the baseline survey in the clinic prior to seeing the health care provider. The follow-up surveys are being mailed to the patient's home address. In an effort to minimize loss to follow-up, patient contact information was obtained at the time of study enrollment. In addition to recording the address and telephone numbers of the patient, we also asked the patient to provide the name and telephone number of a friend or family member who will always know where to contact her, in case she has moved and we are having trouble contacting her. Prior to mailing the follow-up survey we mail an initial postcard telling the patient to expect to receive a survey in the mail. The postcards are sent "Return Services Requested," so that the Post Office will let us know if the postcard is undeliverable. For those postcards that are undeliverable, we call the contact numbers provided on the enrollment form in an effort to obtain a current address.

The surveys will be sent by First Class mail to the patient's home. The cover letter for the patient follow-up survey, which stresses the importance of the study, will be personally addressed to the patient. The letter will be printed on CDC letterhead and signed by the CDC study leader. The letter will give the respondents a toll-free telephone number to call if they have questions regarding the study. In addition to the patient survey and cover letter, the survey packet will contain a $5 incentive to complete the survey. Finally, a reminder postcard and a reminder telephone call will be used to encourage non-respondents to complete and return the survey.

B.4. Tests of Procedures or Methods to be Undertaken

The provider and patient baseline surveys were pilot tested to obtain an estimate of respondent burden, as well as to obtain comments and advice about the format, appropriateness and relevance of survey questions. The baseline provider survey was pilot tested with nine providers in the Atlanta area. The types of providers included in the pilot testing included obstetrician/ gynecologists, family practitioners, and nurse practitioners. Providers reported that, on average, the survey took 30-35 minutes to complete. The baseline patient survey was pilot tested with nine patients at a clinic in the Atlanta area. Patients were able to complete the survey in 15-20 minutes. Neither patients nor providers reported major problems in completing the survey. Minor modifications to the survey questions and response categories were made based on the feed-back received during the pilot tests.

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Vicki Benard, PhD., 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 also 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 Centers for Public Health Research and Evaluation. Battelle is conducting data collection and will perform data analysis, in consultation with the CDC investigators. Phase I activities are being performed under contract No. 200-2002-00573, Task Order No. 6 with the Centers for Disease Control and Prevention. Phase II data collection and analysis will be performed under Contract No. 200-2008-27956, Task Order 17 with the Centers for Disease Control and Prevention.

Diane L. Manninen, Ph.D. [206-528-3140] has overall technical and financial responsibility for the study at Battelle and led the Battelle effort to design this protocol. She will direct the overall data collection and analysis effort. She will also be responsible for writing the project reports.

Other CDC and Battelle personnel involved in designing the study protocol, development of the data collection instruments, data collection, and analysis include:

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