Community- Associated *Clostridium difficile* Risk Factor Study Protocol

Protocol Version # 2

Version Date: 11/25/2013

New Submission

Prepared by Susan Hocevar

Table of Contents: **Page Number**

1. **Protocol Summary** **3**
2. **Background and Justification** **3**
3. **Objectives** **4**
4. **Study Personnel** **5**
5. **Study Design** **7**
6. **Protection of Human Research Subjects** **17**
7. **Progress Evaluation** **22**
8. **Timeline** **22**
9. **References** **23**
10. **Appendices** **25**

11.

I. Protocol Summary

This study poses no more than minimal risk to the study participants as there will be no interventions or modifications to the care study subjects receive. Emerging Infections Program (EIP) surveillance personnel will identify community-associated *Clostridium difficile* (CA-CDI) cases through existing population-based surveillance for CDI. Cases will be included, based on age, in the adult (≥ 18 years) or child (1- 5 years) study groups. Controls will be matched to cases on the basis of age group and gender; a questionnaire will be administered to each participant. Outcomes of this study will include estimates of the magnitude of association between disease status and selected exposures.

II. Background and Justification

The Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases, Division of Healthcare Quality Promotion (DHQP), in collaboration with state public health authorities, plans to assess risk factors for community-associated *Clostridium difficile* infection through the CDC's Emerging Infections Program (EIP).

Clostridium difficile is an anaerobic, spore-forming, gram positive bacillus that produces two pathogenic toxins: A and B. *C. difficile* infection (CDI) ranges in severity from mild diarrhea to fulminant colitis and death.[1] Transmission of *C. difficile* occurs primarily in healthcare facilities as environmental contamination by *C. difficile* spores combined with patient exposure to antimicrobial drugs creates an opportunity for infection. Traditional risk factors for CDI include antibiotic use, advanced age, and prior hospitalization.[2] CDI increasingly has been reported among young, healthy individuals residing in the

community without traditional CDI risk factors.[3-6] Community-associated CDI is estimated to represent 32% of all CDI based on population-based figures from the Emerging Infections Program,[5,7,8] with an incidence of 30-40 per 100,000 population in the United States.[5] Previous reports have shown approximately 40% of patients acquiring community-associated CDI were not exposed to antibiotics,[3-6] suggesting that additional factors may contribute to infections. Although the U.S. Food and Drug Administration issued a communication on February 8, 2012 advising physicians to consider the diagnosis of CDI among patients taking proton pump inhibitors, the data on the association of CDI with proton pump inhibitors are still controversial and studies to quantify this association are needed. In addition to understanding factors that predispose patients to CDI, further evaluation of potential *C. difficile* exposure sources in the community is necessary to guide prevention efforts. Although several sources of *C. difficile* in the community such as food, water, outpatient healthcare environment, and daycare centers have been raised as potential risks, the magnitude of association of these risks with disease development has not been evaluated to date.[5,6,9,10].

This case-control study will enable investigators to evaluate these associations and focus future investigations and prevention strategies on those factors identified as significantly associated with disease development.

III. Objectives

This multi-center, population based case-control study of persons with CA-CDI matched with controls will address the following objectives:

1. Quantify the magnitude of the association between exposure sources and development of disease for community-associated *Clostridium difficile* infection for the following potential exposure sources :
    - Outpatient healthcare exposures (e.g. dental/doctor's visits)
    - Infants in the home, children in diapers, and children in daycare centers
    - Household member(s) with CDI

2. Identify exposures other than antibiotics that can perturb the intestinal microbiome thereby increasing risk for CA-CDI including:
    - Proton pump inhibitors, H2 Blockers, antidepressants
    - Chemotherapy
    - Steroids
    - Food Preferences

IV. Study Personnel

The EIP is a collaborative project of the CDC and ten states. Investigators in the proposed study include personnel from the Division of Healthcare Quality Promotion (DHQP, NCEZID), the Division of Foodborne, Waterborne and Environmental Diseases (DFWED, NCEZID), and EIP-funded university-affiliated and state health department personnel. CDC investigators will be responsible for study design, oversight, analysis and interpretation of data. Investigators from EIP sites (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) will contribute to the study design and will be responsible for enrollment of study subjects, data collection, data entry and analysis, and interpretation of coded data.

EIP CDI site coordinators:

California: Lisa Winston, MD; Joelle Nadle, MD

Colorado: Wendy Bamberg, MD; Helen Johnston, MPH

Connecticut: James Meek, MPH; Carol Lyons, MS, MPH; Danyel Olson MPH

Georgia: Monica Farley MD; Wendy Baughman, MSPH; Andrew Revis, MPH; Olivia Almendares, MSPH; Zirka Thompson, MPH

Maryland: Lucy Wilson, MD, Sc.M;MPH; Rebecca Perlmutter, MPH;

Minnesota: Stacy Holzbauer, DVM, MPH

New Mexico: Erin Phipps, DVM, MPH;

New York: Ghinwa Dumyati, MD;

Oregon: Zintars Beldavs, MS

Tennessee: John Dunn, DVM, PhD; Brenda Rue, RN, BSN

CDC personnel:

DHQP

CDI Risk-Factor Study Lead: Susan Hocevar, MD

CDI Surveillance Lead: Fernanda Lessa, MD, MPH

CDI Surveillance Coordinator: Jessica Cohen, MPH

Microbiologist: Brandi Limbago, PhD

DFWED:

Senior Epidemiologist: Hannah Gould, PhD, MS

V. Study Design

A. Case Definitions

Case Definition: A case of CA-CDI will be defined as a positive *C. difficile* specimen either by toxin or molecular assay collected as an outpatient or within 3 days after hospital admission in a surveillance area resident aged 1 to ≤ 5 years or ≥18 years who did not have a prior positive *C. difficile* assay and a documented overnight stay in a healthcare facility in the twelve weeks prior to specimen collection.

B. General Inclusion and Exclusion Criteria for Cases and Controls

B.1. Case Enrollment

Eligible Case:

All residents aged 1 year to 5 years and ≥ 18 years in the surveillance areas with a positive *C. difficile* stool by either toxin or molecular assay and without documentation of a prior positive *C. difficile* assay will be eligible for investigation. This will include children and pregnant women (refer to vulnerable subjects section on page 17).

Inclusion Criteria for Cases:

1. An eligible CDI case**,** and

2. Stool specimen collected as an outpatient or within 3 days after admission, and
3. No report of overnight stay in a healthcare-facility during telephone interview

Each person can be enrolled as a case only once during the study period. A person enrolled as a case cannot serve as a control. In order to limit patient's difficulty in recalling exposures, patients will be interviewed as soon as possible after the illness is identified.

Exclusion Criteria for Cases:

1. Patient did not have a sample from which a positive *C. difficile* toxin assay or a positive *C. difficile* molecular assay was obtained, or
2. Ever reports a *C.difficile* diagnosis prior to the current specimen collection date, or
3. Had an overnight stay in a healthcare facility in the 12 weeks prior to specimen collection documented in the medical record or reported during interview, or
4. Is not in the age group of 1 year to 5 years and ≥ 18 years at the time of stool collection, or
5. Is not reachable after 8 unsolicited telephone attempts on at least 6 different dates using a valid telephone number. At least one attempt on a weekend and between 5-8 pm on a weekday should be made, or
6. Cannot be interviewed within 90 days after positive *C. difficile* stool collection date, or
7. Does not have a telephone number available, or
8. Does not speak either English or Spanish, or
9. Cannot be matched to an eligible control after 40 attempts, or
10. Does not report diarrheal illness (at least 3 watery / loose stools in a 24 hour period) associated with the submission of the clinical specimen from which *C. difficile* was detected, or

11. Is deceased or incapacitated (i.e. a proxy will not answer for the case subject), or
12. Was not a resident of the EIP catchment area at the time of specimen collection, or
13. Does not provide informed consent to participating in the study, or
14. Is an inmate in a prison or other correctional facility.

B.2. Control Enrollment

Eligible Control

One control will be identified for each case included in the study. Eligible controls will be matched to cases by age group and gender and will be randomly selected from commercially available lists of residential telephone numbers or from birth registries (i.e. for subjects between 12 and 24 months of age) A person cannot serve as a control more than once in the study.

Inclusion criteria:

1. An eligible control, and
2. Resident of the EIP catchment area at the time of matched case's positive *C. difficile* stool collection, and
3. Age is within the same age- and gender-strata as the matched case-patient. The age strata are as follows:

CHILDREN AGE GROUP	**ADULT AGE GROUP**
12-23months	18–29 years
24-47months	30-39 years
48-60 months	40-49 years

	50-59 years
	60-69 years
	>70 years

Exclusion criteria:

1. Resides outside the EIP catchment area at the time of matched case's *C. difficile* specimen collection, or
2. Is not in the age group of 1 year to 5 years and ≥ 18 years at the time of matched case's stool collection, or
3. Is not reachable after 8 unsolicited telephone attempts on at least 6 different dates using a valid telephone number. At least one attempt on a weekend and between 5-8 pm on a weekday should be made,
4. Reports a history of *C. difficile* diagnosis, or
5. History of diarrhea (at least 3 watery / loose stools in a 24 hour period) during the 12 weeks prior to the matched case patients Illness Onset date/ Specimen Date, or
6. Reports an overnight stay in a healthcare facility in the 12-weeks prior to the specimen collection date / or onset of illness date of the matched case subject, or
7. Cannot be interviewed within 90 days after matched case's positive *C. difficile* stool collection date, or
8. Is deceased or incapacitated (i.e. a proxy will not answer for the control subject), or
9. Does not speak English or Spanish, or
10. Is an inmate in a prison or other correctional facility, or
11. Does not provide informed consent to participating in the study.

C. Selection of Controls

We will attempt to enroll one control for each enrolled case. Controls will be matched to cases on gender and age group as described on section V.B.2. Once a case-patient has been interviewed, controls should be enrolled as soon as possible. Controls may be enrolled up to 90 days after the specimen collection date of the matched case, but every effort will be made to enroll them as soon as the matched case interview has been completed.

Controls in all except those aged 1year to 2 years will be selected from commercially available lists of residential telephone numbers, by EIP catchment, area that include age and gender information on household members, allowing for the rapid identification of households at which an age and gender-matched control might be available for a given case. Birth registries will be used to select controls in the youngest age group (1-2 years of age).

We will use a commercial online database that uses various data sources to determine the age / gender of persons living in households with landline telephone numbers listed in the White Pages. To optimize efficiency in recruiting controls, lists of telephone numbers for a given EIP catchment area and age-gender group will be uploaded by CDC to a secure FTP site for transmission to the sites. The size of each list will vary for each site due to the wide variation in CA CDI case numbers by EIP site and by age group. The transmission will be done at the beginning of the study and as requested during the course of the study. The lists sent to sites will contain phone numbers of possible controls in that age/ gender group as well as mailing address for the head of the household. Phone numbers and address are never entered into study databases. All lists of phone numbers and addresses will be deleted before study completion when no longer needed. To enroll controls, the site will randomly sort the potential age-gender control list once

obtained from CDC. Surveillance staff will call potential controls starting from the top and moving down the list. Every phone call attempt will be logged directly in the spreadsheet. If a control is recruited, the telephone number will be marked as completed and successful. If after 40 attempts to enroll a control for a given case are made unsuccessfully, sites will exclude the case. The second time controls of a specific age/ gender group combination need to be recruited staff will start with the next phone number on the sub-list where they had last left off. When the end of a sublist is reached study coordinators will cycle back to the top of the sublist and begin calling phone numbers on the sublist a second time. Up to 8 unsolicited telephone attempts may be made to given telephone number during the course of the study. More than 8 total calls can be made if someone in the household asks to be called back. After completing 8 unsuccessful unsolicited calls, or after learning that a person of the relevant age and gender stratum does not live in the household, or after someone in the household asks to not be called back or hangs up, that telephone number will be marked as completed and unsuccessful, and no additional attempts to contact the household will be made. Calls to enroll controls will be made during weekdays (10am-5pm), weeknights (5:01pm-8pm), and weekends (Saturday 10am-8pm, Sunday noon-8pm).

Because commercial companies are unable to provide reliable age information for very young children, birth registries will be used as the preferred method of selecting controls for case-patients in the 1-2 year (i.e., 12 through 24 months old) age group. Controls may be identified from birth registries within the EIP catchment area. EIP sites will sort these lists by date of birth and will attempt to enroll those with the closest birth dates before and after the matched case-patient's birth date. Efforts will be made to enroll these potential controls, including 8 unsolicited phone calls on at least 6 different dates using a valid telephone number. At least one attempt on a weekend and between 5-8 pm on a weekday should be made.

D. Sample Size Estimates

The sample size estimates in the following tables pertain to identifying risk-factors for CA-CDI. There is limited data on risk factors for CA-CDI and this study will provide the first estimates of odds ratios for certain suspected exposures. A sample size calculation for a 1:1 matched case-control study was done using SAS software, version 9.2 (SAS Institute Inc., Cary, NC). For the adult study group, a conservative sample size calculation was performed using a power of 0.80, an alpha of 0.05, and an estimated prevalence of exposure to infants in diapers in adult control-patients of 10.2%.to detect a matched odds ratio of 2.0 for cases compared to controls. The exposure to infants in diapers was used as risk factor because prior studies have suggested that infants may serve as a source for CDI. The estimated prevalence of exposure to infants in diapers was based on census household data for children less than 4 years of age present in homes (10.2%). Based on these numbers a total sample size of 426 would be required (Table 1). For the pediatric study group, a conservative sample size calculation was performed using a power of 0.80, an alpha of 0.05, and a prevalence of gastric or jejunostomy (G-J) tubes in pediatric cases of 19% to detect a matched odds ratio of 2 for cases compared to controls. G-J tube usage was chosen as the variable of interest in children because previous studies on hospital-associated CDI have demonstrated an association with this method of feeding; the estimated prevalence in cases was noted in these studies.[11] Based on these numbers a total sample size of 468 would be required (Table 1). EIP site CA-CDI case numbers are displayed in Table 2.

Table 1: Sample Size Calculations for Adult and Pediatric Study Groups

Study Group	Odds Ratio	Cases	Controls	Total
Adult	2	213	213	426

Pediatric	2	234	234	468

Table 2: 2011 EIP site Adult and Pediatric CA CDI Cases over twelve months

Month of year	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**Total**
CA-CDI cases ≥ 18 years	236	235	262	267	255	261	281	268	326	283	279	300	3253
Pediatric CA-CDI cases 1-5 years	28	21	19	35	19	16	13	29	24	27	23	25	279

E. Enrollment methods

Cases: An EIP staff member or local health department staff in each site will interview case-patients by telephone. Eligible case-patients will be identified through routine EIP active CDI surveillance. Each site will attempt to enroll every eligible patient within the designated age ranges that meet the study inclusion criteria outlined above until the study sample size is met. EIP or local health department staff will contact eligible patients by phone and those who meet inclusion criteria based on the screening form (Refer to Appendix A1 (Adult) and A2 (Child)) will be offered participation in the study. Some sites may choose to perform a preliminary screening of eligible cases using medical records before the patient is contacted for a telephone interview since review of medical records is part of the routine EIP CDI surveillance and approved under CDC protocol #5558. Although protocol #5558 is considered research at CDC, and

it was reviewed and approved by CDC IRB, many of the participating EIP states consider this activity to be non-research, as *C. difficile* is a reportable condition in many EIP sites. Screening will be repeated during the telephone interview. The study subject will be read the verbal consent form (refer to Appendix B) and will be invited to participate in the study if inclusion criteria are met. Verbal consent will be obtained and recorded by the interviewer on the consent form. For children, verbal permission from a parent or guardian will be obtained. The parent or guardian will be the respondent. Case-patients may be enrolled up to 90 days after specimen collection date, but every effort will be made to enroll them as soon as possible after their infection is identified.

Controls: Controls will be recruited from the study population in participating sites as outlined above in the control selection section. EIP or local health department staff will contact eligible controls by phone and those who meet inclusion criteria based on the screening form (Refer to Appendix A1, A2) will be offered participation in the study. Verbal consent (refer to Appendix B) will be obtained and documented on the consent form for every participant that meets inclusion criteria. For children, verbal permission from a parent or guardian will be obtained and the parent will be the respondent.

F. Questionnaires

Two questionnaires were developed; one for adults and one for children. Both questionnaires cover demographic characteristics, clinical history, food preferences, environmental exposures, medications, and healthcare visits (Refer to Appendix C1 (Adult) and C2 (Child)). The difference between children and adult questionnaires are related to underlying conditions and age-specific exposures (e.g. daycare centers). None of the questionnaires include name, address or contact information, or sensitive questions such as sexual activity or use of illegal substances. The exposure period of interest for study subjects will be the

12 weeks before illness onset for all exposures aside from food which will be a diet preference. Questionnaires will be translated into Spanish. Interviews will be conducted in English or Spanish, depending on the preference of the person being interviewed. Interviews will take approximately 30 minutes.

G. Data management

Standardized forms will be used to collect information. Completed forms will be kept in a locked file cabinet at the local EIP sites and destroyed at the end of the study. Data will be entered by EIP sites into a password protected database on a secure limited access server. Data will be transferred to CDC through a secure FTP site by the 5th day of every month. No patient identifiers such as name, address, phone number or medical record number will be transferred to CDC. The database will be developed by CDC and deployed to the EIP sites that in turn will be responsible to maintain the database. The addition of EIP site-specific variables will be permitted and these fields, along with case identifiers, will not be submitted to CDC.

H. Data analysis

Data analysis will be performed to identify modifiable risk factors for CA-CDI and quantify the magnitude of the association of these factors. Statistical analysis will be performed at CDC, with input of co-investigators, using SAS software, version 9.2 (SAS Institute Inc., Cary, NC). Matched odds ratios (mOR) and *P* values will be calculated for univariate and multivariate analysis using conditional logistic regression. Variables from univariate analysis with a *P* value <0.20 will be included as candidates for the risk model. Multivariate analysis using stepwise conditional logistic regression will be performed to

identify independent risk factors. A two-sided *P* value of < 0.05 will be considered statistically significant.

VI. Protection of Human Research Subjects

The proposed activity meets the definition for human subjects' research. The prepared protocol will be submitted to CDC under expedited review, and, after CDC review, will be submitted at each EIP site local IRB.

A. Study population

Eligible cases will be identified by existing surveillance for *C. difficile* infection at EIP sites. Eligible cases that meet the study inclusion criteria outlined on section V.B. 1 will be invited to participate in the study. The number of study subjects to be enrolled at each site will vary depending on the size of the population under surveillance and the number of CDI eligible cases identified monthly.. All patients between the ages of 1-5 years and 18 years of age or greater with a positive *C. difficile* specimen either by toxin or molecular assay and no previous documentation of a positive *C. difficile* assay will be eligible for the study. Controls will be matched to case-patients by gender and age group and will be identified through either commercially online database that uses various data sources to determine the age / gender of persons living in households with landline telephone numbers listed in the White Pages or birth registries as described on section V.C. of this protocol.

B. Vulnerable subjects

The study will include study subjects from vulnerable populations. Pregnant women are at risk for developing CDI and pregnancy status will be ascertained through interview. Infants less than one year of age will be excluded because distinction between *C. difficile* disease and colonization in this age group has

not been well established and they are not included in the ongoing surveillance system. Children aged 1 year to 5 years will be included. CA-CDI is the most common type of CDI in this age group, and, given that adult risk factors and exposures are likely very different from those of young children, the inclusion of adults only would prohibit the assessment of pediatric risk factors for CA-CDI. Children in the older age groups (>5 years) make up proportionally fewer CA-CDI cases reported to EIP sites indicating that the disease may not be as common in this age group; hence, children ages 1-5 years will be the focus of the pediatric study. This research involves minimal risk, and the purpose is to identify risk factors and magnitude of risk for developing CA-CDI. Exclusion of pregnant women and children might introduce bias, and the risk factors for these groups are of interest to prevention efforts. We are excluding prisoners because the study required telephone interview and the study objectives can be met without evaluating this vulnerable population.

C. Confidentiality

All individual survey responses and clinical data are confidential. Any published information will be aggregated across the 10 participating sites. All cases will be assigned a unique study identification code. These identification codes will not contain patient identifiers. The link between patient identifiers and the study identification codes will be maintained at each participating EIP site. CDC will only receive coded data and will not be able to link any data back to the study participant. Coded data will be entered into a secure password protected database at the EIP sites. Completed questionnaires and data collection forms will be maintained in secure locations at each EIP site according to local IRB regulations. A limited number of local project personnel will have access to completed forms containing public health information. Personal identifiers, including patient names, address, phone numbers, will be removed from any forms sent to CDC. Within 6 months of the study's completion or according to local IRB regulations,

all copies of the questionnaires containing personal identifiers should be destroyed, eliminating the possibility to link coded data back to study participant.

D. Request for Verbal Consent

EIP sites will obtain information via a phone interview on eligible study subjects. We request written informed consent be replaced with verbal consent. If a case or control participant is deceased, or unable to provide responses during the health interview, a proxy interview with a surrogate (eg. next-of-kin) will *not* occur and the study subject will be ineligible. For all study subjects aged 1-5 years parents or guardians will serve as the proxy. Spanish-speaking case and control patients will be contacted for interview using Spanish-speaking personnel and translated materials. Other non-English speaking subjects will not be interviewed for the study.

Verbal consent (Refer to appendix B) will be obtained from all eligible study subjects or from their parent / legal guardian for child study subjects. Because this study requires that study subjects be interviewed in a timely manner, all study subjects will be interviewed over the telephone. This research presents no more than minimal risk of harm to patients. Only questionnaire data are involved. No procedure for which written consent is normally required outside of the research context is involved. This waiver of written documentation of informed consent will not adversely affect the rights and welfare of study subjects.

The consent will be read to study subjects who agree to the health interview. Some sites may require a consent form with HIPAA language, which has been provided on Appendix B. If required by the local

site, a copy of the consent form with the study participant's response noted and signed by the interviewer, will be kept with each completed questionnaire. Study subjects who agree to the interview will have a copy of the consent form sent to them by United States Postal Service mail immediately after the interview. For the sites that require it, study subjects will also have a copy of the HIPAA/Privacy Notice mailed to their household.

Depending on the local IRBs, it may be required that potential cases and controls (from both vital records department records and phone lists) be sent introduction letters (refer to appendix D) by mail allowing them to call the health department to opt out of being called. Introduction letters will likely delay enrollment of controls in the study, potentially increasing the chances of recall bias. Introduction letters will not be mailed to eligible study participants unless it is required by local EIP sites. In addition, the letter will only have the name of the household member for control participants and not exactly the name of the potential enrollee; hence, reliable responses from the intended participant cannot be guaranteed.

Eight different attempts will be made to reach the potential enrollee on at least 6 different dates. To minimize the chance that attempts will be perceived as a nuisance, project personnel should not call more than twice within a single day nor leave a recorded message at each attempt. When leaving a message, the person will be asked to call back and designate a convenient time for a callback.

When a potential enrollee is successfully contacted via telephone, project personnel will obtain verbal consent for participation. A phone script will be used to aid site personnel when speaking with case- or control-patients (Refer to Appendix A1, pages: 25-26 and 28-29.and A2 pages: 32-33 and 35-36).

Upon completion of the interview, participants will be sent a $20 gift card as a token of appreciation. The address of the study subject will be confirmed at the end of the interview by EIP staff. CDC will purchase these gift cards and send them to the EIP sites to distribute to the cases and controls who were interviewed. Address information of study participants will not be shared with CDC. This gift card amount is commensurate with time and effort provided by participant and is consistent with what has been provided in other CDC studies involving the same level of time and effort. The amount proposed is not of such a magnitude to interfere with voluntary participation. A Thank You letter with the gift card will be sent to participants (Appendix E).

E. Risks to Study Subjects

The only reasonably foreseeable risk to study subjects is the potential for disclosure of PHI to those other than authorized study personnel. To minimize the risk, all information and identifiers will be kept confidential. Names and personal identifiers will reside at each EIP office and will not be shared with CDC.

There is no penalty for not participating. There is minimal risk to the patient or his or her caretaker, and the only cost is time spent (approximately 30 minutes) being interviewed. Study subjects may refuse to answer any of the questions or stop at any time. This study involves telephone interviews only, and we do not foresee any adverse events other than those related to confidentiality.

There is minimal risk involved and adverse events are not anticipated. Should a breach of confidentiality occur such that CDC receives personal identifiers, the site would be contacted about this breach in confidentiality and other sites would be reminded not to send personal identifying information.

F. Benefits to Study Subjects

Although no benefit will be directly conferred to study subjects, data attained from this activity will allow estimation of the association of proposed risk factors for CA-CDI. This information may lead to public health measures that can help prevent CA- CDI in the future. There is no penalty for declining to participate in the study. Study subjects may refuse to answer any of the questions or stop at any time.

VII: Progress Evaluation

There will be monthly conference calls between CDC and sites to review results and to discuss study progress. These conference calls will provide opportunities to discuss data sensitivity, completeness, and to identify ongoing difficulties. In addition, a the CDI Pathogen Group composed of members from the EIP sites, the Infectious Disease Society of America, and CDC will oversee the progress of this study. As sites get closer to reach the study targeted sample size, there will be weekly conference calls to report and evaluate progress.

VIII. Timeline

August–September 2013: Submit protocol to CDC human subjects review.

October–February 2013: Obtain IRB approvals from local participating institutions.

May 2013–June 2014: OMB approval.

March–April 2014: Training of study personnel on data collection.

July 2014–December 2015: Enroll cases and controls, abstract data, perform phone interview and submit data to CDC. (Roll-out will vary by site, estimated 12 months of study/site).

January 2015–May 2015: Analyze data and report findings.

References

1. Kuijper EJ, Coignard B, Tull P, et al. Emergence of Clostridium difficile-associated disease in North America and Europe. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 2006;12 Suppl 6:2-18.

2. Bartlett JG. Historical Perspectives on Studies of Clostridium difficile and C. difficile Infection. Clinical Infectious Diseases 2008;46:S4-S11.

3. Centers for Disease C, Prevention. Severe Clostridium difficile-associated disease in populations previously at low risk--four states, 2005. MMWR Morbidity and mortality weekly report 2005;54:1201-5.

4. Centers for Disease C, Prevention. Surveillance for community-associated Clostridium difficile--Connecticut, 2006. MMWR Morbidity and mortality weekly report 2008;57:340-3.

5. Kutty PK, Woods CW, Sena AC, et al. Risk factors for and estimated incidence of community-associated Clostridium difficile infection, North Carolina, USA. Emerging infectious diseases 2010;16:197-204.

6. Kuntz JL, Chrischilles EA, Pendergast JF, Herwaldt LA, Polgreen PM. Incidence of and risk factors for community-associated Clostridium difficile infection: a nested case-control study. BMC infectious diseases 2011;11:194.

7. Karlstrom O, Fryklund B, Tullus K, Burman LG. A prospective nationwide study of Clostridium difficile-associated diarrhea in Sweden. The Swedish C. difficile Study Group. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 1998;26:141-5.

8. Centers for Disease C, Prevention. Vital signs: preventing Clostridium difficile infections. MMWR Morbidity and mortality weekly report 2012;61:157-62.

9. Stevens V, van Wijngaarden E. Proton pump inhibitor use may be associated with an increased risk of Clostridium difficile infection. Evidence-based medicine 2012.

10. Chitnis AS, Holzbauer SM, Belflower RM, et al. Epidemiology of Community-Associated Clostridium difficile Infection, 2009 Through 2011. JAMA internal medicine 2013:1-9.

11. Sandora TJ, Fung M, Flaherty K, et al. Epidemiology and risk factors for Clostridium difficile infection in children. The Pediatric infectious disease journal 2011;30:580-4

APPENDICES

Appendix A: Adult and Pediatric Case and Control Screening Forms

Public reporting burden of this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Information Collection Review Office, 1600 Clifton Road NE, MS D-74, Atlanta, Georgia 30333; ATTN: PRA (0920-0892).

Appendix A1: Adult Case and Control Screening Forms

CASE SUBJECT

INITIAL CALL INTRODUCTION

1. [To the person who answers the phone, IF ADULT, otherwise ask to speak to an adult]: "Hello, my name is _____. I am calling from the [*State health dept.*]. May I please speak to [*Potential enrollee*]?"

___Yes: person who answered is potential enrollee; [go to case patient call script]

___Yes: coming to the phone; [go to case patient call script]

___No: person is unavailable – *record call back time on phone log if given*

___ No: person is deceased: **-STOP- CASE INELGIBLE SAY**:

"I would like to offer my condolences and apologize for any inconvenience that this call may have caused to you. Thank you for your time

___No: person is incapacitated; **-STOP- CASE INELGIBLE SAY:**

"Thank you for your time. Have a nice day"

___Does not speak English; [record language in comment section of phone log.]

- IF SPANISH SPEAKING: "We will try to call back with someone who speaks Spanish, thank you."
- IF OTHER LANGUAGE: "Thank you for your time. Have a nice day" [If case speaks a language other than English or Spanish, he/she is not eligible. Record on tracking log as "No English or Spanish." =stop=]

CASE PARTICIPANTS Call Script:

"I am calling on behalf of the Centers for Disease Control and Prevention (CDC) and the [*State Health Dept.*] because you may be eligible to participate in a public health study. This study is being performed by CDC and your State Health Department. We are calling you because you had an infection with a germ called *Clostridium*

difficile; sometimes it is also called *C. diff*. The <state health department> routinely tracks how often people in your area get sick from *C.difficile* infections and is notified whenever a person develops this infection. Participation is voluntary and involves completing a 30 minute interview over the phone. It will include questions about your illness, healthcare visits, medical history, and recent medications. Please know that your answers will be kept secure and you may choose not to answer any question. If you agree to participate we will send you a $20 gift card as a token of appreciation. May I tell you more about the study?"

___Yes; [go to CASE SCREENING
___No; [go to Q3]

3. "Your participation in this study is very important. We are trying to better understand why people develop *Clostridium difficile* infection. May I schedule a time to talk that would be better for you?"

___Yes; [Record day/time on Phone Log].

- "Thank you very much for your time, I will call you back later."[=STOP=and call the person back at the requested day/time.]

___No;

- "Sorry to have disturbed you. Good-bye." [=STOP=and record in the interview tracking log as "Refused to participate."]

*********BEFORE YOU PROCEED, HAVE A CALENDAR IN FRONT OF YOU********

CASE SUBJECT SCREENING QUESTIONS

I will ask you questions about your illness, healthcare contacts, household contacts, other exposures and medical history. It may be difficult to remember, but I would like your best guess for each question. Because I will be asking about specific dates around the time your illness began, it may be helpful for you to have a calendar or datebook in front of you. I can hold while you get these things. The dates we are interested in are between [12 weeks *before* positive specimen collection Date_____/_____/_____] to [positive specimen collection date _____/_____/_____]. When Participant returns say "I would like to begin with a few questions to be sure you are eligible to participate in the study"

1. Have you ever been diagnosed with *C. difficile* ***before*** the collection of your stool specimen on [specimen collection date_____/_____/_____]?
   Yes.....1
   (If Yes –STOP Interview and say: "We are only interviewing people who have not had a previous C. difficile diagnosis. Thank you for your time")

   No.....2
   Don't know/Not sure.....7

Refused.....9

2. Did you stay overnight in a hospital, long term care facility, or nursing home in the 12 weeks ***before*** [specimen collection date_____/_____/_____]?

Yes.....1

(*If Yes –STOP Interview and say "We are only interviewing people who did not stay in a hospital during that time." Thank you for your time.*

No.....2 (**Go to Q.3)**

Don't know/Not sure.....7
Refused.....9

(If Don't know/ Refuse- STOP Interview and say: "We are only interviewing people who did not stay in a hospital during that time". Thank you for your time")

3. Did you have diarrhea at the time your stool specimen was collected on [specimen collection date_____/_____/_____]? We define diarrhea as 3 or more loose stools in a 24 hour period.

Yes.....1 ***(Go to Q. 3A)***

No.....2
Don't know/Not sure.....7
Refused.....9

(IF No, Don't know, Refuse- STOP Interview and say "We are only interviewing people who had diarrhea with their C. difficile diagnosis. Thank you for your time.)

3.A. ***If yes,*** Do [you] remember when your diarrhea began?

Yes.....1 ***(If Yes –fill in date diarrhea began and use as reference date)***
No.....2 ***(fill in date of specimen collection and use as reference date.)***
Don't know/Not sure.....7 ***(fill in date of specimen collection and use as reference date.)***
Refused.....9 ***(fill in date of specimen collection and use as reference date.)***

€ REFERENCE DATE: _____/_____/_____
(mm/dd/yyyy)

2 week before _____/_____/_____
4 weeks before _____/_____/_____
12 weeks before _____/_____/_____

<u>CASE CONSENT SCRIPT</u>: GO TO CASE CONSENT AND SAY "Now that I know you are eligible to participate, I would like to share some additional details about the study and obtain your

verbal permission for participation. Feel free to stop me and ask questions at any time."
[AFTER CONSENT COMPLETE CONTINUE WITH INTERVIEW SECTION 1]

CONTROL SUBJECTS
INITIAL CALL INTRODUCTION

1. [To the person who answers the phone, IF ADULT, otherwise ask to speak to an adult]: "Hello, my name is _____. I am calling from the [*State health dept.*]. I am calling about a public health study on an infection called *Clostridium difficile.* For this study we are looking for people who are [insert sex / age group:_____ _____]. Is there anyone in your household in this group who I can speak with?"

___Yes: person who answered is a potential enrollee; [go to control patient call script]

___Yes: coming to the phone; [go to control patient call script]

___No: person is unavailable – *record call back time on phone log if given*

___No: person is deceased: **-STOP- CONTROL INELGIBLE SAY**:

"I would like to offer my condolences and apologize for any inconvenience that this call may have caused to you. Thank you for your time."

___No: person is incapacitated; **-STOP- CONTROL INELGIBLE SAY**:

"Thank you for your time"

___Does not speak English; [record language in comment section of phone log.]

- IF SPANISH SPEAKING: "We will try to call back with someone who speaks Spanish, thank you."
- IF OTHER LANGUAGE: "Thank you for your time. Have a nice day" [If control speaks a language other than English or Spanish, he/she is not eligible. Record on tracking log as "No English or Spanish." =stop=]

Control Participants Call Script

"I am calling on behalf of the Centers for Disease Control and Prevention (CDC) and the [*State Health Dept*.] because you may be eligible to participate in a public health study. This study looks at how people living in the community get an illness caused by a germ called *Clostridium difficile* (also called *C. diff*). As part of our study, we need to talk to people **who did not** become ill with *C.diff*, but live in the same area as someone who did and who is around the same age as the ill person. Participation is voluntary and involves completing a 30 minute interview over the phone. It will include questions about your healthcare visits, medical history, and recent medications. Please know that your answers will be kept secure and you may choose not to answer any question. If you agree to participate we will send you a $20 gift card as a token of appreciation. May I tell you more about the study?"

___Yes; [go to CONTROL SCREENING]
___No; [go to Q 2].

2. “Your participation in this study is very important. We are trying to better understand why people develop *Clostridium difficile* infection. May I schedule a time to talk that would be better for you?”

___Yes; [Record day/time on Phone Log].

- “Thank you very much for your time.”[=STOP= and call back at requested day and time.]

___No;

- “Sorry to have disturbed you. Good-bye.” [=STOP= and record on interview tracking log as “Refused to participate.”]

*********BEFORE YOU PROCEED, HAVE A CALENDAR IN FRONT OF YOU********

Control Subject Screening Questions

I will ask you questions about your healthcare contacts, household contacts, other exposures and medical history. It may be difficult to remember, but I would like your best guess for each question. Because I will be asking about specific dates, it may be helpful for you to have a calendar or datebook in front of you. The dates we are interested in are between [12 weeks *before Matched CASE participant's* Reference Date_____/_____/_____] to [matched *case participant's* Reference Date_____/_____/_____]. I can hold while you get these things. Do you need a minute to go get any of these items?

When Participant returns say “I would like to begin with a few questions to be sure you are eligible to participate in the study”

1. Were you between the ages of [matched case patient age group_____] on [REFERENCE Date _____/_____/_____]?

Yes.....1 (**Go to Q.2)**

No.....2
Don't know/Not sure.....7
Refused.....9
(If No, Don't know / Refuse STOP Interview and say:" We are only interviewing patients in that age group. Thank you for your time".)

2. Did you live in [EIP catchment area counties] on [REFERENCE Date _____/_____/_____]?

Yes.....1 (**Go to Q.3)**

No.....2
Don't know/Not sure.....7
Refused.....9
(If No, Don't know / Refuse STOP Interview and say:" We are only interviewing patients who lived in

that area. Thank you for your time".)

3. Did you stay overnight in a hospital, long term care facility, or nursing home in the 12 weeks ***before*** [REFERENCE Date _____/_____/_____]?

Yes.....1
(*If Yes –STOP Interview and say: "We are only interviewing people who did not stay in a hospital during that time." Thank you for your time.)*

No.....2 (**Go to Q.4)**

Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not stay in a hospital during that time. Thank you for your time")

4. Had you ever been diagnosed with *C. difficile* before [REFERENCE date_____/_____/_____]?
Yes.....1
(*If Yes –STOP Interview and say: "We are only interviewing people who have not had a previous C. difficle diagnosis. Thank you for your time.)*

No.....2 (**Go to Q.5)**

Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not have C. difficile in the past. Thank you for your time")

5. Did you have diarrhea between [12 weeks before REFERENCE date ____/_____/_____] and [REFERENCE date_____/_____/_____]? We define diarrhea as 3 or more loose stools in a 24 hour period.
Yes.....1
(IF YES- STOP Interview and say "We are only interviewing people who did not have diarrhea. Thank you for your time.)

No.....2 ***(GO TO CONTROL CONSENT SCRIPT BELOW)***

Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not have diarrhea. Thank you for your time")

<u>CONTROL CONSENT SCRIPT</u>: GO TO CONTROL CONSENT AND SAY "Now that I know you are eligible to participate, I would like to share some additional details about the study and obtain your verbal permission for participation. Feel free to stop me and ask questions at any time." <u>[AFTER CONSENT COMPLETE CONTINUE WITH INTERVIEW SECTION 1]</u>

APPENDIX A2: Pediatric Case and Control Screening Forms

CASE SUBJECT

INITIAL CALL INTRODUCTION

1. [To the person who answers the phone, IF ADULT, otherwise ask to speak to an adult]: "Hello, my name is _____. I am calling from the [*State health dept.*]. May I please speak to [*parent/ guardian of potential enrollee*]?"

___Yes: person who answered is parent or guardian of enrollee; [go to case patient call script]

___Yes: coming to the phone; [go to case patient call script]

___No: person is unavailable – *record call back time on phone log if given*

___Does not speak English; [record language in comment section of phone log.]

- IF SPANISH SPEAKING: "We will try to call back with someone who speaks Spanish, thank you."
- IF OTHER LANGUAGE: "Thank you for your time. Have a nice day" [If case speaks a language other than English or Spanish, he/she is not eligible. Record on tracking log as "No English or Spanish." =stop=]

CASE PARTICIPANTS Call Script:

2. "I am calling on behalf of the Centers for Disease Control and Prevention (CDC) and the [*State Health Dept.*] because your child may be eligible to participate in a public health study. This study is being performed by CDC and your State Health Department. We are calling you because your child had an infection with a germ called *Clostridium difficile;* sometimes it is also called *C. diff*. The <state health department> routinely tracks how often people in your area get sick from *C.difficile* infections and is notified whenever a person develops this infection. Participation is voluntary and involves completing a 30 minute interview over the phone. It will include questions about your child's illness, healthcare visits, medical history, and recent medications. Please know that your answers will be kept secure and you may choose not to answer any question. If you agree to participate we will send you a $20 gift card as a token of appreciation. May I tell you more about the study?"

___Yes; [go to Case Subject Screening]

___No; [go to Q3]

3. "Your participation in this study is very important. We are trying to better understand why people develop *Clostridium difficile* infection. May I schedule a time to talk that would be better for you?"

___Yes; [Record day/time on Phone Log].

- "Thank you very much for your time, I will call you back later."[=STOP=and call the person back at the requested day/time.]

___No;

- "Sorry to have disturbed you. Good-bye." [=STOP=and record in the interview tracking log as "Refused to participate."]

*********BEFORE YOU PROCEED INTERVIEW, HAVE A CALENDAR IN FRONT OF YOU********

CASE SUBJECT SCREENING QUESTIONS

I will ask you questions about your child's illness, healthcare contacts, household contacts, other exposures, and medical history. It may be difficult to remember, but I would like your best guess for each question. Because I will be asking about specific dates around the time your child's illness began, it may be helpful for you to have a calendar or datebook in front of you. I can hold while you get these things. The dates we are interested in are between [12 weeks *before* positive specimen collection Date_____/_____/_____] to [positive specimen collection date _____/_____/_____]. Do you need a minute to go get any of these items?

When Participant returns say "I would like to begin with a few questions to be sure you are eligible to participate in the study"

1. Today, what is your child's health status? I will read some choices:

Well……..1
Ill or sick……..2
Deceased……..5
" If deceased say : "I would like to offer my condolences and apologize for any inconvenience that this call may have caused to you and we do not need to continue with the interview. Thank you for your time."

Don't know/Not sure.....7
Refused.....9
If Don't know / refused say "We are only interviewing parents if the child's health status is known. Thank you for your time"

2. Has your child been diagnosed with *C. difficile* ***before*** the collection of your child's stool specimen on [specimen collection date_____/_____/_____]?

Yes.....1
(If Yes –STOP Interview and say "We are only interviewing people who have not had a previous C. difficle diagnosis. Thank you for your time.)
No.....2
Don't know/Not sure.....7
Refused.....9

3. Did your child stay overnight in a hospital, long term care facility, or nursing home in the 12 weeks ***before*** [Reference Date _____/_____/_____]?

Yes.....1

(*If Yes –STOP Interview and say "We are only interviewing people who did not stay in a hospital during that time." Thank you for your time.)*

No.....2
Don't know/Not sure.....7
Refused.....9

4. Did your child have diarrhea at the time your child's stool specimen was collected on [specimen collection date_____/_____/_____]? We define diarrhea as 3 or more loose stools in a 24 hour period.

Yes.....1 ***(Go to Q. 5)***
No.....2
Don't know/Not sure.....7
Refused.....9

(IF NO, DON'T KNOW, REFUSE- STOP Interview and say "We are only interviewing people who had diarrhea with their C. difficile diagnosis. Thank you for your time.)

5.A.Do [you] remember when your child's diarrhea began?

Yes.....1 ***(If Yes –fill in date diarrhea began and use as reference date)***
No.....2 ***(fill in date of specimen collection and use as reference date.)***
Don't know/Not sure.....7 ***(fill in date of specimen collection and use as reference date.)***
Refused.....9 ***(fill in date of specimen collection and use as reference date.)***

€ REFERENCE DATE: _____/_____/_____
(mm/dd/yyyy)

2 week before _____/_____/_____
4 weeks before _____/_____/_____
12 weeks before _____/_____/_____

GO TO CASE CONSENT AND SAY "Now that I know you are eligible to participate, I would like to share some additional details about the study and obtain your verbal permission for participation. Feel free to stop me and ask questions at any time." [AFTER CONSENT COMPLETE CONTINUE WITH INTERVIEW]

CONTROL SUBJECTS

INITIAL CALL INTRODUCTION

1. [To the person who answers the phone, IF ADULT, otherwise ask to speak to an adult:] "Hello, my name is _____. I am calling from the [*State health dept.*]. I am calling about a public health study on an infection called *Clostridium difficile.* For this study we are looking for children who are [insert sex / age group]. Is there a parent or guardian of a child in this group who I can speak with?"

___Yes: person who answered is parent or guardian of enrollee; [go to control patient call script]

___Yes: coming to the phone; [go to control patient call script]

___No: person is unavailable – *record call back time on phone log if given*

___Does not speak English; [record language in comment section of phone log.]

- IF SPANISH SPEAKING: "We will try to call back with someone who speaks Spanish, thank you."
- IF OTHER LANGUAGE: "Thank you for your time. Have a nice day" [If control speaks a language other than English or Spanish, he/she is not eligible. Record on tracking log as "No English or Spanish." =stop=]

CONTROL PARTICIPANTS Call Script:

2. "I am calling on behalf of the Centers for Disease Control and Prevention (CDC) and the [*State Health Dept.*] because your child may be eligible to participate in a public health study. This study looks at how people living in the community get an illness caused by a germ called *Clostridium difficile* (also called *C. diff*). As part of our study, we need to talk to the parents of children who **did not** become ill with *C.diff*, but live in the same area as someone who did and who is around the same age as the ill person. The study is voluntary and involves completing a 30 minute interview over the phone. It will include questions about your child's healthcare visits, medical history, and recent medications. Please know that your answers will be kept secure and you may choose not to answer any question. If you agree to participate we will send you a $20 gift card as a token of appreciation. May I tell you more about the study?"

___Yes; [go to CONTROL SCREENING QUESTIONS]

___No; [go to Q 3].

3. "Your participation in this study is very important. We are trying to better understand why people develop *Clostridium difficile* infection. May I schedule a time to talk that would be better for you?"

___Yes; [Record day/time on Phone Log].

- "Thank you very much for your time."[=STOP= and call back at requested day and time.]

___No;

- "Sorry to have disturbed you. Good-bye." [=STOP= and record on interview tracking log as "Refused to participate."]

*********BEFORE YOU PROCEED, HAVE A CALENDAR IN FRONT OF YOU********

Control Subject Screening Questions

I will ask you questions about your child's healthcare contacts, household contacts, other exposures, and medical history. It may be difficult to remember, but I would like your best guess for each question. Because I will be asking about specific dates, it may be helpful for you to have a calendar or datebook in front of you. The dates we are interested in are between [12 weeks *before Matched CASE participant's* Reference Date_____/_____/_____] to [matched *case participant's* Reference Date_____/_____/_____]. I can hold while you get these things. Do you need a minute to go get any of these items?

When Participant returns say "I would like to begin with a few questions to be sure you are eligible to participate in the study"

1. Today, what is your child's health status? I will read some choices:

Well……..1
Ill or sick……..2
Deceased……..5
" If deceased say : "I would like to offer my condolences and apologize for any inconvenience that this call may have caused to you and we do not need to continue with the interview. Thank you for your time."
Don't know/Not sure.....7
Refused.....9
If Don't know / refused say "We are only interviewing parents if the child's health status is known. Thank you for your time"

1. Was your child between the ages of [matched case patient age group_____] on [REFERENCE Date _____/_____/_____]?

Yes.....1 (**Go to Q.2)**

No.....2
Don't know/Not sure.....7
Refused.....9
(If No, Don't know / Refuse STOP Interview and say:" We are only interviewing patients in that age group. Thank you for your time".)

2. Did your child live in [EIP catchment area counties] on [REFERENCE Date _____/_____/_____]?

Yes.....1 (**Go to Q.3)**

No.....2
Don't know/Not sure.....7
Refused.....9

(If No, Don't know / Refuse STOP Interview and say:" We are only interviewing patients who lived in that area. Thank you for your time".)

3. Did your child stay overnight in a hospital, long term care facility, or nursing home in the 12 weeks ***before*** [Reference Date _____/_____/_____]?

Yes.....1
(If Yes –STOP Interview and say "We are only interviewing people who did not stay in a hospital during that time." Thank you for your time.)
No.....2 (**Go to Q.4)**
Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not stay in a hospital during that time. Thank you for your time")

4. Has your child ever been diagnosed with *C. difficile* in the past?
Yes.....1
(If Yes –STOP Interview and say "We are only interviewing people who have not had a previous C. difficle diagnosis. Thank you for your time.)
No.....2 (**Go to Q. 5)**
Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not have C. difficile in the past. Thank you for your time")

5. Did your child have diarrhea within the 12-weeks before [REFERENCE date_____/_____/_____]? We define diarrhea as 3 or more loose stools in a 24 hour period.
Yes.....1
(IF YES- STOP Interview and say "We are only interviewing people who did not have diarrhea. Thank you for your time.)
No.....2 ***(GO TO CONSENT SCRIPT BELOW)***
Don't know/Not sure.....7
Refused.....9
(If Don't know / Refuse STOP Interview and say "We are only interviewing people who did not have diarrhea. Thank you for your time")

<u>CONTROL CONSENT SCRIPT</u>: GO TO CONTROL CONSENT AND SAY "Now that I know you are eligible to participate, I would like to share some additional details about the study and obtain your verbal permission for participation. Feel free to stop me and ask questions at any time."
<u>[AFTER CONSENT COMPLETE CONTINUE WITH INTERVIEW</u>

APPENDIX B: VERBAL CONSENT FOR PARTICIPATION WITH AND WITHOUT HIPPA LANGUAGE

VERBAL CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT (Non-HIPPA language)

Study Title: Community- Associated *Clostridium difficile* Risk Factor Study
Principal Investigator: _____
Funding Source: (State Department of Public Health); Centers for Disease Control and Prevention

Invitation to Participate and Description of Project

We are asking you to take part in an assessment to look at how people get infections with *Clostridium difficile*, a germ that can make people sick with diarrhea and might put them in the hospital. This study is being conducted by staff at <state health department>in conjunction with the Centers for Disease Control and Prevention (CDC). These infections are very important. We are doing this study to try to learn more about where they come from and how to prevent them.

We are contacting you to ask [you to participate / you to participate on your child's behalf] because [you/your child] or someone who lives in your area had this infection.

Procedures

The <state health department> routinely tracks how often people in your area get sick from *C.difficile* infections and is notified whenever a person develops this infection. Your medical doctor is required to report cases of *C. difficile* to the state health department. If you agree to take part in this study we will ask you to complete a survey over the phone. To understand where these infections come from and how they can be prevented we need to talk to people who got sick **and** to people who **did not** get sick. We will ask both groups about [your/your child's] healthcare, household, medications, and about the types of food [you/ your child] eat(s).

The interview will take about 30 minutes. You can refuse to answer any of the questions. You are free to not participate, if you don't want to.

Risks and Inconveniences

There are no risks to you for being in this research study, other than the possibility that some questions may be uncomfortable or difficult to answer. There are no direct benefits to you for joining this study. There is no penalty for not being in this study. You do not have to answer any questions you are uncomfortable with. You may stop at any time. After your participation in the study, we will send you a $20 gift card to show our appreciation for your time and effort.

Security of Information

All we learn about [you/ your child] and your family will be kept private as much as the law allows. We will only use information grouped with information from many other participants, without using names or other personal information. Any information collected that could identify your child will be destroyed when the evaluation is done.

Voluntariness and Withdrawal

You are free to choose not to take part in this study. Refusing to take part will not affect any medical care or benefits [you/your child] receive. If you decide later that you want to stop, you should write to (state Principal Investigator _____) at the following address:_____.If you choose to withdraw from the study, the data collected in this interview will be destroyed and removed from any database associated with this project. You can also refuse to answer any questions or stop the interview at any time.

Questions

If you have questions about this study or you feel you may have been harmed by this study, you may call the <EIP site> at <contact number>.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, <name of EIP CDI investigator and contact number>. If you have any questions about your rights as a research subject, you may contact the < name and contact number to the Chair of the local IRB or Research Ethics, etc>.

If you feel you have been harmed in any way by taking part of this study, or if you have questions about your rights, you may also contact CDC's Human Research Protection Office at 1-800-584-8814; leave a message with your name, phone number, and refer to CDC protocol #XXXX and someone will call you back.

Authorization

Now that I have told you about the study, do you have any questions for me about the study? (Answer all questions before proceeding to next question)

Do you agree to participate (on behalf of your child)? (Verbal consent given)
Yes _____**IF YES**-> say "Thank you. Now I will ask you some questions. You may refuse to answer any question that makes you uncomfortable"
No _____ **IF NO**-> say "Thank you for you time. If you change your mind please call me at: (_) _-_____.

_____
Name of Subject

_____
Name of Parent/Guardian

*Interviewer signature*_____*Date*_____

I will be happy to mail a copy of this consent form as well as information about *C. diff* infection if you would like. (Record mailing information separately)

MATCHED CASE PATIENT ID: _____

VERBAL CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
HIPPA LANGUAGE VERSION

Study Title: Community- Associated *Clostridium difficile* Risk Factor Study
Principal Investigator: _____
Funding Source: (State Department of Public Health); Centers for Disease Control and Prevention

Invitation to Participate and Description of Project

We are asking you to take part in an assessment to look at how people get infections with *Clostridium difficile*, a germ that can make people sick with diarrhea and might put them in the hospital. This study is being conducted by staff at <state health department>in conjunction with the Centers for Disease Control and Prevention (CDC). These infections are very important. We are doing this study to try to learn more about where they come from and how to prevent them.

We are contacting you to ask [you to participate / you to participate on your child's behalf] because [you/your child] or someone who lives in your area had this infection.

Procedures

The <state health department> routinely tracks how often people in your area get sick from *C.difficile* infections and is notified whenever a person develops this infection. Your medical doctor is required to report cases of *C. difficile* to the state health department If you agree to take part in this study we will ask you to complete a survey over the phone. To understand where these infections come from and how they can be prevented we need to talk to people who got sick **and** to people who **did not** get sick. We will ask both groups about [your/your child's] healthcare, household, medications, and about the types of food [you/ your child] eat(s).

The interview will take about 30 minutes. You can refuse to answer any of the questions. You are free to not participate, if you don't want to.

Risks and Inconveniences

There are no risks to you for being in this research study, other than the possibility that some questions may be uncomfortable or difficult to answer. There are no direct benefits to you for joining this study. There is no penalty for not being in this study. You do not have to answer any questions you are uncomfortable with. You may stop at any time. After your participation in the study, we will send you a $20 gift card to show our appreciation for your time and effort.

Security of Information

All we learn about [you/ your child] and your family will be kept private as much as the law allows. We will only use information grouped with information from many other participants, without using names or other personal information. Any information collected that could identify your child will be destroyed when the evaluation is done.

HIPAA Authorization

While we will make every effort to keep what we learn about you private, this cannot be guaranteed. Results of the research may be presented at meetings or in publications, but your name will not be used. The Federal Health Insurance Portability and Accountability Act (HIPAA) requires us to get your permission to use health information collected as part of research. This permission is called an Authorization. We will use information we collect about [you/your child] including information from the survey such as exposures and demographics [and information about your/ your child's illness]. If you decide to take part, the Authorization for this study will not expire unless you cancel (revoke) it. The information collected will be kept until the study is completed and all

data is analyzed and presented/published. You can always cancel by writing to the (study investigator). If you cancel your Authorization, you will also be removed from the study. By giving consent, you give us permission to use and/or share your health information.

Voluntariness and Withdrawal

You are free to choose not to take part in this study. Refusing to take part will not affect any medical care or benefits [you/your child] receive. If you decide later that you want to stop, you should write to (state Principal Investigator _____) at the following address:_____.If you choose to withdraw from the study, the data collected in this interview will be destroyed and removed from any database associated with this project. You can also refuse to answer any questions or stop the interview at any time.

Questions

If you have questions about this study or you feel you may have been harmed by this study, you may call the <EIP site> at <contact number>.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, <name of EIP CDI investigator and contact number>. If you have any questions about your rights as a research subject, you may contact the < name and contact number to the Chair of the local IRB or Research Ethics, etc>.

If you feel you have been harmed in any way by taking part of this study, or if you have questions about your rights, you may also contact CDC's Human Research Protection Office at 1-800-584-8814; leave a message with your name, phone number, and refer to CDC protocol #XXXX and someone will call you back.

Authorization

Now that I have told you about the study, do you have any questions for me about the study? (Answer all questions before proceeding to next question)

Do you agree to participate (on behalf of your child)? (Verbal consent given)
Yes _____**IF YES**-> say "Thank you. Now I will ask you some questions. You may refuse to answer any question that makes you uncomfortable"
No _____ **IF NO**-> say "Thank you for you time. If you change your mind please call me at: (_) _-_____.

_____
Name of Subject

_____
Name of Parent/Guardian

*Interviewer signature*_____*Date*_____

I will be happy to mail a copy of this consent form as well as information about *C. diff* infection if you would like. (Record mailing information separately)

MATCHED CASE PATIENT ID: _____

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

APPENDIX C: ADULT AND PEDIATRIC QUESTONAIRRES

Public reporting burden of this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to CDC/ATSDR Information Collection Review Office, 1600 Clifton Road NE, MS D-74, Atlanta, Georgia 30333; ATTN: PRA (0920-0892).

APPENDIX C1: COMMUNITY ASSOCIATED *CLOSTRIDIUM DIFFICILE* ADULT CASE AND CONTROL INTERVIEW

SECTION 1: IDENTIFIERS- CASES AND CONTROLS

1. € CASE € CONTROL
2. Study ID: _____

3. Reference date: _____/_____/_____
(mm/dd/yyyy)

2 week before _____/_____/_____
4 weeks before _____/_____/_____
12 weeks before _____/_____/_____

4. Age (years) €€€

5. Sex € Male € Female

SECTION 2: ILLNESS QUESTIONS- *******CASES ONLY ****CONTROLS SKIP TO SECTION 3, Q. 10********

Now I will ask you questions about your illness.

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

6. How many days did your diarrhea last? €€€

Don't know/Not sure……7

Refused.....9

6A. On the worst day of your diarrhea, what was the approximate number of stools you had in a 24-hour period?

≥3-<5 stools.....1
5-10 stools.....2
>10 stools.....3
Don't know/Not sure.....7
Refused.....9

7. Did you have any of the following symptoms associated with your *C. difficile* illness?

[READ LIST]	Yes	No	DK/NS	Refused
Bloody stools	1	2	7	9
Fever	1	2	7	9
Nausea	1	2	7	9
Vomiting	1	2	7	9
Abdominal pain	1	2	7	9
Other	1	2		

Specify:_____

8. Were you hospitalized overnight for your *C. difficile* illness?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

8A. **If yes**, where:_____(*name of hospital will not be transmitted to CDC)*

9. At the time of your *C. difficile* diagnosis, were you told by a doctor or healthcare provider that you had any other stomach [enteric, gastrointestinal] infection?

Yes.....1
No.....2 ***(Go to Q.10)***
Don't know/Not sure.....7 ***(Go to Q.10)***
Refused.....9 ***(Go to Q.10)***

9A. ***If yes,*** what was the name of the infection?

[Read list if necessary] Yes No DK/NS Refused

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Campylobacter	1	2	7	9
E. coli	1	2	7	9
Listeria	1	2	7	9
Salmonella	1	2	7	9
Shigella	1	2	7	9
Vibrio	1	2	7	9
Yersinia	1	2	7	9
Cryptosporidium	1	2	7	9
Giardia	1	2	7	9
Rotavirus	1	2	7	9
Norovirus	1	2	7	9
Other	1	2		

Specify:_____
____

SECTION 3: HEALTHCARE CONTACTS- CASES AND CONTROLS

Now I will ask you questions about your healthcare contacts between [12 weeks *before* Reference Date_____/_____/_____] to [Reference Date_____/_____/_____].

10. Did you receive care in any doctor's office, dental office, hospital, or any other medical facility in the 12 weeks *before* [REFERENCE DATE_____/_____/_____]?

Yes.....1
No.....2 ***(Go to Q.11)***
Don't know/Not sure.....7 ***(Go to Q.11)***
Refused.....9 ***(Go to Q.11)***

10A. I will now ask you about the types of places you visited for your healthcare and when you made your visit**.** Did you visit any of the following places?

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

[READ LIST]	**YES=1**	**NO=2**	**DN/ NS=7**	**Refuse=9**	**If yes, How many weeks prior to** (Reference Date_____/_____/_____) **did you visit this place?**		
					2 weeks	4 weeks	12 weeks
Ambulatory / Outpatient procedure center							
Ambulatory / Outpatient Surgery center							
Dental office							
Doctor's office							
ED							
Hemodialysis							
Hospital							
Outpatient lab							
Physical Therapy Center							
Urgent Care							
Other							

IF NO TO ALL OPTIONS IN Q.10A then SKIP to Q.11

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

10B. during those visits in the 12 weeks before (Reference Date_____/_____/_____) did you have any of the following procedures performed?

*****If Subject answered YES to dental visits only in 10A then only ask about last two items (oral surgery and dental cleaning)********

[READ LIST]	**YES=1**	**NO=2**	**DN/NS=7**	**Refuse=9**	**If yes, How many weeks prior to** (Reference Date_____/_____/_____) **did this procedure happen?**		
					2 weeks	4 weeks	12 weeks
Upper Endoscopy (Did the doctors pass a tube through your mouth or nose into your stomach?)							
Colonoscopy or Sigmoidoscopy (Did the doctors pass a tube into your rectum to look into your colon/bowel?)							
X-ray that required GI Prep (Did you have an X-ray performed where you had to swallow something first?)							
Chemotherapy							
Surgery in an operating room as an outpatient →**If yes, Specify type:**							
Other Medical							

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Procedure:							
Oral Surgery							
Dental Cleaning							

11. Did you visit a person in or accompany anyone to a doctor's office, dental office, hospital, nursing home, or any other medical facility in the 12 weeks before [Reference Date_____/_____/_____]?

Yes.....1
No.....2 ***(Go to Q.12)***
Don't know/Not sure.....7 ***(Go to Q.12)***
Refused.....9 ***(Go to Q.12)***

11A. What type of facility did you visit or accompany someone to in the 12 weeks before [Reference Date____/_____/_____]?

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

[READ LIST]	**YES=1**	**NO=2**	**DN/NS=7**	**Refuse=9**	**If yes, How many weeks prior to** (Reference Date_____/_____/_____) **did you visit this place?**		
					2 weeks	4 weeks	12 weeks
Ambulatory / Outpatient procedure center							
Ambulatory / Outpatient Surgery center							
Dental office							
Doctor's office							
ED							
Hemodialysis							
Hospital							
Long term care/ skilled nursing facility							
Outpatient lab							
Physical Therapy Center							
Urgent Care							
Other							

SECTION 4:

HOUSEHOLD CONTACTS

The next few questions are about you and persons who lived with you during the 12 weeks before [Reference Date_____/_____/_____].

12. How many people lived in your household including yourself during that time? € ***If answer is one (subject lives alone) skip to Q.19***

12A. How many household members, not including yourself were in each of these age groups? **[List number of people in each group]**

Ages € <1 € 1 to 3 € 4 to 10 € 11 to 17 € 18 to 34 € 35 to 59 € 60+

13. Did any household member excluding yourself wear diapers? (Including adults in diapers)
Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

14. Did you have household members excluding yourself that attended a group childcare setting, daycare, or adult daycare? We consider daycare to be any place inside or outside your home where a household member spends at least 4 hours per week under an adult's care with at least two adults or children who did not live with you

Yes.....1
No.....2 (**Skip to Q 15)**
Don't know/Not sure.....7 (**Skip to Q 15)**
Refused.....9 (**Skip to Q 15)**

14A. ***If yes,*** which household members attended daycare and what type of daycare setting was it? **[*Read description of setting types if necessary*]**

AGE Group	**Type of Daycare Setting**					
	Home	**Center**	**Nanny**	**Other (specify)**	**Don't know**	**Refused**
< 1	1	2	3		7	9
1 to 3	1	2	3		7	9
4 to 10	1	2	3		7	9
11 to 17	1	2	3		7	9
18 to 34	1	2	3		7	9
35 to 59	1	2	3		7	9
60 +	1	2	3		7	9

Home – care is provided in someone's home typically by one person
Center- care is provided typically in a commercial building with many providers and rooms
Nanny / care provider share- two or more families have a single nanny / care provider to take care of their household member either full-time or part-time

15. In the 12 weeks before [Reference Date_____/_____/_____)], did any household member stay overnight in a hospital?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

16. In the 12 weeks before [Reference Date_____/_____/_____)], did any household member stay overnight in a nursing home?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

17. In the 12 weeks before [Reference Date_____/_____/_____)], did anyone else in your household have diarrhea?

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Yes.....1
No.....2 ***(Go to Q.18)***
Don't know/Not sure.....7 ***(Go to Q.18)***
Refused.....9 ***(Go to Q.18)***

17A. ***If yes,*** did you assist this person with toileting (including diaper changes)?
Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

17B. Was this person diagnosed with *C. difficile?*
Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

18. Did any of your household members work or volunteer, in any capacity, at a hospital, other medical facility, or in any facility where patient care is provided in the 12 weeks before [Reference Date_____/_____/_____)]?
Yes.....1
No.....2 ***(Go to Q.19)***
Don't know/Not sure.....7 ***(Go to Q.19)***
Refused.....9 ***(Go to Q.19)***

18A. ***If yes,*** what type of healthcare setting?

(READ LIST)	Yes	No	DK/NS	Refused
Hospital	1	2	7	9
Emergency department	1	2	7	9
Doctor's office	1	2	7	9
Dentist	1	2	7	9
Long term care (skilled nursing facility)	1	2	7	9
Hemodialysis facility	1	2	7	9
Other facility	1	2		

Specify:_____

__

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

18B. Did their job involve direct physical contact with the patients? For example, touching the patient to help her get out of a chair

Yes.....1
No.....2 ***(Go to Q.19)***
Don't know/Not sure.....7 ***(Go to Q.19)***
Refused.....9 ***(Go to Q.19)***

18B1. ***If yes,*** what was their main job?

_____

_____

18B2. Job Code€€-€€€€ ***(Fill in job code after interview is finished)***

19. Did you work or volunteer, in any capacity, at a hospital, other medical facility, or in any facility where patient care is provided in the 12 weeks before [Reference Date_____/_____/_____)]?

Yes.....1
No.....2 ***(Go to Q.20)***
Don't know/Not sure.....7 ***(Go to Q.20)***
Refused.....9 ***(Go to Q.20)***

19A. ***If yes,*** what type of healthcare setting?

(READ LIST)	Yes	No	DK/NS	Refused
Hospital	1	2	7	9
Emergency department	1	2	7	9
Doctor's office	1	2	7	9
Dentist	1	2	7	9
Long term care (skilled nursing facility)	1	2	7	9
Hemodialysis facility	1	2	7	9
Other facility	1	2		

Specify:_____

__

19B. Did your job involve direct physical contact with the patients? For example, touching the patient to help her get out of a chair

Yes.....1
No.....2 ***(Go to Q.20)***
Don't know/Not sure.....7 ***(Go to Q.20)***
Refused.....9 ***(Go to Q.20)***

19B1. ***If yes,*** what was your main job?

_____

_____

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

19B2. Job Code €€-€€€€ ***(Fill in job code after interview is finished)***

20**.** Did you attend an adult daycare in the 12 weeks before [Reference Date_____/_____/_____)]? We consider daycare to be any place inside or outside your home where a household member spends at least 4 hours per week under an adult's care with at least two adults who do not live with you

Yes.....1
No.....2 (**Skip to Q.21)**
Don't know/Not sure.....7 (**Skip to Q.21)**
Refused.....9 (**Skip to Q.21)**

20A. ***If yes,*** what type of care setting? **[Read list if necessary]**
Home – care is provided in someone's home typically by one person 1
Center- care is provided typically in a commercial building with many providers and rooms 2
Nanny / care provider share- two or more families have a single nanny / care provider to take care of their household member either full-time or part-time 3
Other 4
Specify: _____
Don't know/Not sure 7
Refused 9

SECTION 5: DIET EXPOSURES

I'd like to change direction now and ask you about the foods you generally eat in a given week and the kind of water you drink.

21. Did you receive food / formula through a feeding tube called a G-tube or J-tube in the 12 weeks before [Reference Date_____/_____/_____)]?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

22. In a typical week how frequently do you consume the following foods?

[READ LIST]	Often	Sometimes	Rarely	Never	DK/NS	Refused
	>5/week	**2-5 /week**	**<2/ week**	**Never**		
Eggs	1	2	4	5	7	9
Dairy (milk, yogurt)	1	2	4	5	7	9
Fresh raw Vegetables	1	2	4	5	7	9
Plant based protein (tofu, tempeh, seitan)	1	2	4	5	7	9
Red Meat (beef, lamb, pork, other game meat)	1	2	4	5	7	9
Poultry (chicken, turkey)	1	2	4	5	7	9
Seafood (fish, shellfish)	1	2	4	5	7	9

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

23. Which one of the following is the source of tap water in your home (select only one):
☐ water utility ☐ private well ☐ spring ☐ unknown ☐ other

Name of the water utility, if known _____

If other, specify type and location _____

23A. At home, what type of unboiled water do you most often use for drinking (chose only one)?
_____ Tap water not treated in the home
_____ Tap water treated in the home (for example, filtered, UV light, distilled, or whole house point-of-entry device)
_____Commercially bottled water
_____Other _____

SECTION 6: MEDICAL HISTORY

The next sets of questions are about medications you may have been taking in the 12 weeks before [Reference Date____/____/_____]. Medicine bottles or records may help you remember about specific medications. Would you like to gather this information before we go on?

24. Did you take any antibiotics by mouth or in your vein in the 12 weeks before [Reference Date____/____/_____]?
Yes.....1
No.....2 ***(Go to Q.28)***
Don't know/Not sure.....7 ***(Go to Q.28)***
Refused.....9 ***(Go to Q.28)***

24A. Why did you take these antibiotic(s)?
Note: Subjects may indicate more than one reason (For example, if more than one course of antibiotics was taken for different illnesses or if one antibiotic was taken for and ear infection and a pneumonia)

[DO NOT READ LIST]	Yes	No
Acne	1	2
Bronchitis/ pneumonia	1	2
Dental cleaning	1	2
Ear, sinus, upper respiratory infection	1	2
Eye infection	1	2
Oral surgery	1	2

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Skin or soft tissue infection (abscess or cellulitis)	1	2
Surgery	1	2
Urinary tract infection	1	2
Urinary tract prophylaxis	1	2
Refused	9	9
DK/NS	7	7
Other	1	2
Specify:_____		

24B. Which antibiotic(s) did you take in the 12 weeks before [Reference Date_____/_____/_____]? **[DO NOT READ LIST]**

[DO NOT READ LIST]		***If yes,*** *How many weeks prior to (Reference Date_____/_____/_____) did you take this antibiotic?*		
	YES	**2-weeks**	**4-weeks**	**12-weeks**
Amoxicillin	1			
Amoxicillin/Clavulanate	1			
Ampicillin	1			
Augmentin	1			
Azithromycin	1			
Bactrim	1			
Biaxin	1			
Ceclor	1			
Cefaclor	1			
Cefadroxil	1			
Cefdinir	1			
Ceftin	1			
Cefixime	1			
Cefuorixime	1			
Cefzil	1			
		If yes, *How many weeks prior to (Reference Date_____/_____/_____) did you take this antibiotic?*		
[DO NOT READ LIST]		**2-weeks**	**4-weeks**	**12-weeks**
Cephradine	1			
Ciprofloxacin or Cipro	1			
Clarithromyc	1			
Cleocin	1			
Clindamycin	1			
Dapsone	1			
Doxycycline	1			
Duricef	1			
Erythromycin	1			

Erythromycin/sulfa	1			
Flagyl	1			
Floxin	1			
Keflex	1			
Keftab	1			
Levofloxacin	1			
Levoquin	1			
Monurol	1			
Metronidazole	1			
Norfloxacin or Norflox	1			
Ofloxacin or Oflox	1			
Omnicef	1			
Penicillin or Pen VK	1			
Pediazole	1			
Septra	1			
Suprax	1			
Tetracycline	1			
Trimox	1			
Trimethoprim/Sulfa	1			
Vancomycin	1			
Zithromax or Z-Pak	1			
Clindamycin	1			
Other antibiotic 1	1			
Specify: _____	1			
Other antibiotic 2	1			
Specify: _____	1			
Don't know/Not sure	7			
Refused	9			

25. Did you use any antibiotic eye drops in the 12 weeks before [Reference Date_____/_____/_____]?

Yes.....1
No.....2 ***(Go to Q.26)***
Don't know/Not sure.....7 ***(Go to Q.26)***
Refused.....9 ***(Go to Q.26)***

25 A. ***If yes,*** what was the name of the drop (**read list if necessary**)?

Polytrim (Polymyxin sulfate / TMP)…….1
Ciloxan (Ciprofloxacin)……..2
Ocuflox (Ofloxacin)……3
Vigamox, Moxeza (Moxifloxacin) ……..4
Other……9
Specify : .....

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

26. In the 12 weeks before [Reference Date_____/_____/_____], did you regularly take any acid-reducing medications to treat excessive stomach acid, heartburn, or gastroesophageal reflux disease (GERD)? We define regular use as use of the product at least 3 days per week. Such medications might include Tums, Prevacid, Maalox, Mylanta, Tagamet, Zantac, Prilosec, or Nexium.

Yes.....1
No.....2 ***(Go to Q.27)***
Don't know/Not sure.....7 ***(Go to Q.27)***
Refused.....9 ***(Go to Q.27)***

26A. ***If Yes*****,** please specify which medicine you regularly took in the 12 weeks before [Reference Date_____/_____/_____]

[DO NOT READ LIST]	**YES= 1**	**NO=2**	**If yes, How many weeks prior to** (Reference Date_____/_____/_____) **did you take this medication?**		
			2 weeks	4 weeks	12 weeks
Aciphex/rabeprazole	1	2			
Alka-Seltzer	1	2			
Maalox	1	2			
Mylanta	1	2			
Nexium/esomeprazole	1	2			
Pepcid/famotidine	1	2			
Prevacid/lansoprazole	1	2			
Prilosec/omeprazole	1	2			
Protonix/pantoprazole	1	2			
Rolaids	1	2			
Tums	1	2			
Tagamet/cimetidine	1	2			
Zantac/ranitidine	1	2			
Other:	1	2			
Don't Know/not sure	7	7			
Refuse	9	9			

If yes*,* in the 2 weeks before

I am now going to ask about medications that are given for many reasons including things like chronic pain, depression, anxiety, to stop smoking, and to help sleep. We are asking about these medications to determine if they could put people at risk for *C. diff*. Examples of these medications include: Prozac, Celexa, Remeron, Paxil, and Trazadone.

27. In the 12 weeks before [Reference Date_____/_____/_____], did you regularly take any such medications? We define regular use as use of the product at least 3 days per week.

Yes.....1
No.....2 ***(Go to Q.28)***
Don't know/Not sure.....7 ***(Go to Q.28)***
Refused.....9 ***(Go to Q.28)***

27A. ***If Yes,*** *please specify which medicine you regularly took in the 12 weeks before [Reference Date_____/_____/_____]*

€ CASE € CONTROL

Patient ID:_____ State ID:_____

REFERENCE Date_____

[DO NOT READ LIST] *(mm/dd/yyyy)*			**If yes, How many weeks prior to** (Reference Date_____/_____/_____) **did you take this medication?**		
	YES	**NO**	2 weeks	4 weeks	12 weeks
Amitriptyline	1	2			
Anafranil (Clomipramine)	1	2			
Asendin (Amoxapine)	1	2			
Celexa, Cipramil (Citalopram)	1	2			
Cymbalta (Duloxetine)	1	2			
Effexor (Venlafaxine)	1	2			
Eldepryl, Emsam, Zelapar (Selegiline)	1	2			
Escitalopram	1	2			
Limbitrol (Chlordiazepoxide/Amitriptyline)	1	2			
Ludiomil,(Maprotiline)	1	2			
Luvox (Fluvoxamine)	1	2			
Marplan, (Isocarboxazid)	1	2			
Nardil, Nardelzine (Phenelzine sulfate)	1	2			
Norpramin (Desipramine)	1	2			
Nortriptyline	1	2			
Parnate,(Tranylcypromine)	1	2			
Paxil (Paroxetine)	1	2			
Pristiq (Desvenlafaxine)	1	2			
Prozac, Sarafem, Fontex (Fluoxetine)	1	2			
Remeron, Avanza, Zispin (Mirtazapine)	1	2			
Savella, (Milnacipran)	1	2			
Serzone, (Nefazodone)	1	2			
Silenor, Prudoxin, Zonalon (Doxepin)	1	2			
Surmontil (Trimipramine)	1	2			
Symbyax (Olanzapine/fluoxetine)	1	2			
Tofranil, (Imipramine)	1	2			
Trazadone	1	2			
Triptafen (amitriptyline/perphenazine)	1	2			
Viibryd (Vilazodone)	1	2			
Vivactil, (Protriptyline)	1	2			
Wellbutrin, Zyban (Bupropion)	1	2			
Zoloft, Lustral (Sertraline)	1	2			
Other: Specify:__	1	2			
Don't know/Not Sure	7	7			
Refuse	9	9			

If yes, in the

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

2 weeks before

Now I am going to ask you about medical conditions you may have had.

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

28. **Prior to** [Reference Date_____/_____/_____], were you ever told by a medical provider that you had any of the following medical conditions?

[READ LIST – including information in parentheses]

READ LIST	Yes	No	DK/NS	Refused
Diabetes				
Heart attack				
Congestive heart failure				
Stroke				
High blood pressure				
Peripheral vascular disease (intermittent claudication, gangrene, peripheral arterial bypass)				
Chronic renal (kidney) failure				
→**If yes,** are you on dialysis or awaiting dialysis?				
Chronic lung disease (COPD, emphysema)				
Asthma				
Cystic fibrosis				
Chronic Hepatitis B infection				
Chronic Hepatitis C infection				
Organ transplant				
Bone marrow transplant				
Leukemia or lymphoma				
Sickle cell disease (not sickle cell trait)				
Solid tumor cancer (e.g. bone, liver, brain)				
Short gut disease (bowel/ intestinal insufficiency				
Inflammatory bowel disease (Crohn's disease, Ulcerative colitis)				
Lupus				
Rheumatoid arthritis				
Depression				
Other illness:				

29. There is some evidence that how much you weight may effect infection with *C. difficile*. What is your height and Weight?
Height:_____Ft_____in or _____cm
Weight:_____lbs or _____ Kg
Don't Know/ Not Sure….7
Refused ……..9

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

SECTION 8: DEMOGRAPHICS

Now I would like to ask you a few final questions.

30. Do you consider yourself to be? **[Read responses 1 & 2]**
( ) 1 Hispanic or Latino
( ) 2 Not Hispanic or Latino
( ) 7 Don't Know/Not Sure (DO NOT READ)
( ) 9 Refused (DO NOT READ)
( ) 10. Other racial category (DO NOT READ)

31.I am going to read a list of racial categories. Which one or more of the following do you consider yourself to be…? **[Read responses 1-5 and allow respondent to select one or more]**
( ) 1 White/Caucasian
( ) 2 Black or African-American
( ) 3 American Indian or Alaska Native
( ) 4 Native Hawaiian or Other Pacific Islander
( ) 5 Asian
( ) 7 Don't Know/Not Sure (DO NOT READ)
( ) 9 Refused (DO NOT READ)
( ) 10. Other racial category (DO NOT READ)

32. What is your occupation? _____

33. What was your main type of health care coverage during (12 weeks before Reference Date_____/_____/_____) ***I'm going to read all the choices***.

Private insurance, such as an HMO, PPO or a managed care plan 1
Public insurance, such as Medicaid, Medicare or state assistance program 2
A combination of private and public insurance 3
No health insurance 4
DO NOT READ: Other [specify] _____ 8
Don't know or not sure 7
Refused 9

Because education and income can affect access to healthcare, I'd like to ask you about a couple of questions on these subjects.

34 What is the highest grade or year of school you completed?
___1 Never attended school or kindergarten only
___2 Elementary or middle school; 1st-8th grade
___3 Some high school; 9th-11th grade

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

___4 High school graduate; 12th grade or GED
___5 College or technical school for 1-3 years
___6 College for 4 years, with or without a degree
___9 Refused

35 In your home, what is the annual gross household income from all sources, including social security and pensions? ***READ EACH RESPONSE IN ORDER UNTIL RESPONDENT AGREES***.

___0 Dependent college student
___1 Less than $15,000 ___5 Less than $70,000
___2 Less than $25,000 ___6 $70,000 or more
___3 Less than $35,000 ___7 Don't know or not sure
___4 Less than $50,000 ___9 Refused

That was my last interview question. Thank you very much for your time and participation!

36. Comments:
_____

_____

_____

_____

_____

37. Interview Completed? € Yes € No

38. Date of interview: ____/____/_____
(mm/dd/yyyy)

39. Interviewer initials: _____

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Health Interview Appendix—Job Codes

OFFICE OF MANAGEMENT AND BUDGET - 1998 Standard Occupational Classification

29-0000 Healthcare Practitioners and Technical Occupations
- 29-1000 Health Diagnosing and Treating Practitioners
  - 29-1010 Chiropractors
  - 29-1020 Dentists
    - 29-1021 Dentists, General
    - 29-1022 Oral and Maxillofacial Surgeons
    - 29-1023 Orthodontists
    - 29-1024 Prosthodontists
    - 29-1029 Dentists, All Other Specialists
  - 29-1030 Dietitians and Nutritionists
  - 29-1040 Optometrists
  - 29-1050 Pharmacists
  - 29-1060 Physicians and Surgeons
    - 29-1061 Anesthesiologists
    - 29-1062 Family and General Practitioners
    - 29-1063 Internists, General
    - 29-1064 Obstetricians and Gynecologists
    - 29-1065 Pediatricians, General
    - 29-1066 Psychiatrists
    - 29-1067 Surgeons
    - 29-1069 Physicians and Surgeons, All Other
  - 29-1070 Physician Assistants
  - 29-1080 Podiatrists
  - 29-1110 Registered Nurses
  - 29-1120 Therapists
    - 29-1121 Audiologists
    - 29-1122 Occupational Therapists
    - 29-1123 Physical Therapists
    - 29-1124 Radiation Therapists
    - 29-1125 Recreational Therapists
    - 29-1126 Respiratory Therapists
    - 29-1127 Speech-Language Pathologists
    - 29-1129 Therapists, All Other
  - 29-1130 Veterinarians
  - 29-1190 Miscellaneous Health Diagnosing and Treating Practitioners
    - 29-1199 Health Diagnosing and Treating Practitioners, All Other
- 29-2000 Health Technologists and Technicians
  - 29-2010 Clinical Laboratory Technologists and Technicians
    - 29-2011 Medical and Clinical Laboratory Technologists
    - 29-2012 Medical and Clinical Laboratory Technicians
  - 29-2020 Dental Hygienists
  - 29-2030 Diagnostic Related Technologists and Technicians
    - 29-2031 Cardiovascular Technologists and Technicians
    - 29-2032 Diagnostic Medical Sonographers
    - 29-2033 Nuclear Medicine Technologists
    - 29-2034 Radiologic Technologists and Technicians
  - 29-2040 Emergency Medical Technicians and Paramedics
  - 29-2050 Health Diagnosing and Treating Practitioner Support Technicians
    - 29-2051 Dietetic Technicians
    - 29-2052 Pharmacy Technicians

- 29-2053 Psychiatric Technicians
- 29-2054 Respiratory Therapy Technicians
- 29-2055 Surgical Technologists
- 29-2056 Veterinary Technologists and Technicians
- 29-2060 Licensed Practical and Licensed Vocational Nurses
- 29-2070 Medical Records and Health Information Technicians
- 29-2080 Opticians, Dispensing
- 29-2090 Miscellaneous Health Technologists and Technicians
- 29-2091 Orthotists and Prosthetists
- 29-2099 Health Technologists and Technicians, All Other

29-9000 Other Healthcare Practitioners and Technical Occupations

- 29-9010 Occupational Health and Safety Specialists and Technicians
- 29-9011 Occupational Health and Safety Specialists
- 29-9012 Occupational Health and Safety Technicians
- 29-9090 Miscellaneous Health Practitioners and Technical Workers
- 29-9091 Athletic Trainers
- 29-9099 Healthcare Practitioners and Technical Workers, All Other

31-0000 Healthcare Support Occupations

- 31-1000 Nursing, Psychiatric, and Home Health Aides
- 31-1010 Nursing, Psychiatric, and Home Health Aides
- 31-1011 Home Health Aides
- 31-1012 Nursing Aides, Orderlies, and Attendants
- 31-1013 Psychiatric Aides

31-2000 Occupational and Physical Therapist Assistants and Aides

- 31-2010 Occupational Therapist Assistants and Aides
- 31-2011 Occupational Therapist Assistants
- 31-2012 Occupational Therapist Aides
- 31-2020 Physical Therapist Assistants and Aides
- 31-2021 Physical Therapist Assistants
- 31-2022 Physical Therapist Aides

31-9000 Other Healthcare Support Occupations

- 31-9010 Massage Therapists
- 31-9090 Miscellaneous Healthcare Support Occupations
- 31-9091 Dental Assistants
- 31-9092 Medical Assistants
- 31-9093 Medical Equipment Preparers
- 31-9094 Medical Transcriptionists
- 31-9095 Pharmacy Aides
- 31-9096 Veterinary Assistants and Laboratory Animal Caretakers
- 31-9099 Healthcare Support Workers, All Other

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

APPENDIX C2: COMMUNITY ASSOCIATED *CLOSTRIDIUM DIFFICILE PEDIATRIC CASE AND CONTROL INTERVIEW*

SECTION 1: IDENTIFIERS*CASES AND CONTROLS*********

1. € CASE € CONTROL

2. Study ID: _____

3. Reference date: _____/_____/_____
(mm/dd/yyyy)

2 week before _____/_____/_____
4 weeks before _____/_____/_____
12 weeks before _____/_____/_____

4. Age: _____Years _____Months

5. Sex € Male € Female

SECTION 2: ILLNESS QUESTIONS- *******CASES ONLY ****CONTROLS SKIP TO SECTION 3, Q. 10**********

Now I will ask you questions about your child's illness.

6. How many days did your child's diarrhea last? €€€

Don't know/Not sure.....7
Refused.....9

6A.On the worst day of your child's diarrhea, what was the approximate number of stools your child had in a 24-hour period?

≥3-<5 stools.....1
5-10 stools.....2
>10 stools.....3
Don't know/Not sure.....7
Refused.....9

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

7. Did your child have any of the following symptoms associated with [his/ her] *C. difficile* illness?

[READ LIST]	Yes	No	DK/NS	Refused
Bloody stools	1	2	7	9
Fever	1	2	7	9
Nausea	1	2	7	9
Vomiting	1	2	7	9
Abdominal pain	1	2	7	9
Other	1	2		

Specify:_____

8. Was your child hospitalized overnight for [his/ her] *C. difficile* illness?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

*8A. **If yes,** where: _____(name of hospital will not be transmitted to CDC)*

9. At the time of your child's *C. difficile* diagnosis, was your child told by a doctor or healthcare provider that [she/ he] had any other stomach [enteric, gastrointestinal] infection?

Yes.....1
No.....2 ***(Go to Q.10)***
Don't know/Not sure.....7 ***(Go to Q.10)***
Refused.....9 ***(Go to Q.10)***

9A. ***If yes,*** what was the name of the infection?

[Read list if necessary]	Yes	No	DK/NS	Refused
Campylobacter	1	2	7	9
E. coli	1	2	7	9
Listeria	1	2	7	9
Salmonella	1	2	7	9
Shigella	1	2	7	9
Vibrio	1	2	7	9
Yersinia	1	2	7	9
Cryptosporidium	1	2	7	9
Giardia	1	2	7	9
Rotavirus	1	2	7	9
Norovirus	1	2	7	9
Other	1	2		

Specify:_____

____

SECTION 3: HEALTHCARE CONTACTS- CASES AND CONTROLS

Now I will ask you questions about your child's healthcare contacts between [12 weeks *before* Reference Date_____/_____/_____] to [Reference Date_____/_____/_____].

10. Did your child receive care in any doctor's office, dental office, hospital, or any other medical facility in the 12 weeks *before* [REFERENCE DATE ____/_____/_____]?

Yes.....1

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

No.....2 ***(Go to Q.11)***
Don't know/Not sure.....7 ***(Go to Q.11)***
Refused.....9 ***(Go to Q.11)***

10A. I will now ask you about the types of places your child visited for [his / her] healthcare in that time period and when [he / she] made the visit**.** Did your child visit any of the following places?

[READ LIST]	**YES=1**	**NO=2**	**DN/ NS=7**	**Refuse=9**	**How many weeks prior to** (Reference Date_____/_____/_____) **did your child visit this place?**		
					2 weeks	4 weeks	12 weeks
Ambulatory / Outpatient procedure center							
Ambulatory / Outpatient Surgery center							
Dental office							
Doctor's office							
ED							
Hemodialysis							
Hospital							
Outpatient lab							
Physical Therapy Center							
Urgent care							
Other							

IF NO TO ALL OPTIONS IN Q.10A then SKIP to Q.11

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

10B. during those visits in the 12 weeks before (Reference Date_____/_____/_____) did your child have any of the following procedures performed?

*******If Subject answered YES to dental visits only in 10A then only ask about last two items (oral surgery and dental cleaning)**********

[READ LIST]	**YES=1**	**NO=2**	**DN/NS=7**	**Refuse=9**	**How many weeks prior to** (Reference Date_____/_____/_____) **did this procedure happen?**		
					2 weeks	4 weeks	12 weeks
Upper Endoscopy (Did the doctors pass a tube through your mouth or nose into your stomach?)							
Colonoscopy or Sigmoidoscopy (Did the doctors pass a tube into your rectum to look into your colon/bowel?)							
X-ray that required GI Prep (Did you have an X-ray performed where you had to swallow something first?)							
Chemotherapy							
Surgery in an operating room →**If yes, Specify type:**							
Other Medical Procedure:							
Oral Surgery							

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Dental Cleaning							

11. Did your child visit a person in or accompany anyone to a doctor's office, dental office, hospital, nursing home, or any other medical facility in the 12 weeks before [Reference Date_____/_____/_____]?

Yes.....1
No.....2 ***(Go to Q.12)***
Don't know/Not sure.....7 ***(Go to Q.12)***
Refused.....9 ***(Go to Q.12)***

11A. What type of facility did your child visit or accompany someone to in the 12 weeks before [REFERENCE DATE ____/_____/_____]?

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

SECTION 4:

[READ LIST]	**YES=1**	**NO=2**	**DN/NS=7**	**Refuse=9**	**How many weeks prior to** (Reference Date_____/_____/_____) **did your child visit this place?**		
					2 weeks	4 weeks	12 weeks
Ambulatory / Outpatient procedure center							
Ambulatory / Outpatient surgery center							
Dental office							
Doctor's office							
ED							
Hemodialysis							
Hospital							
Long term care/ skilled nursing facility							
Outpatient lab							
Physical Therapy Center							
Urgent care							
Other							

HOUSEHOLD CONTACTS

The next few questions are about your child and persons who lived with your child during the 12 weeks before [Reference Date_____/_____/_____].

12. Excluding your child, how many people lived in your child's household during that time? €

12A. How many household members, not including your child, were in each of these age groups? **[List number of people in each group]**

Ages € <1 € 1 to 3 € 4 to 10 € 11 to 18 € 19 to 34 € 35 to 59 € 60+

13. Did any household member excluding your child wear diapers? (Including adults in diapers)

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

14. Did any household members excluding your child attend a group childcare setting, daycare, or adult daycare? We consider daycare to be any place inside or outside your home where a household member spends at least 4 hours per week under an adult's care with at least two other people who do not live with your child.

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Yes.....1
No.....2 (**Go to Q.15)**
Don't know/Not sure.....7 (**Go to Q.15)**
Refused.....9 (**Go to Q.15)**

14A. ***If yes,*** which household members attended daycare and what type of daycare setting was it? **[*Read description of setting types if necessary*]**

AGE Group	**Type of Daycare Setting**					
	Home	**Center**	**Nanny**	**Other (specify)**	**Don't know**	**Refused**
< 1	1	2	3		7	9
1 to 3	1	2	3		7	9
4 to 10	1	2	3		7	9
11 to 17	1	2	3		7	9
18 to 34	1	2	3		7	9
35 to 59	1	2	3		7	9
60 +	1	2	3		7	9

Home – care is provided in someone's home typically by one person
Center- care is provided typically in a commercial building with many providers and rooms
Nanny / care provider share- two or more families have a single nanny / care provider to take care of their household member either full-time or part-time

15. In the 12 weeks before [Reference Date_____/_____/_____)], did any household member stay overnight in a hospital?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

16. In the 12 weeks before [Reference Date_____/_____/_____)], did any household member stay overnight in a nursing home?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

17. In the 12 weeks before [Reference Date_____/_____/_____)], did anyone else in your child's household have diarrhea?

Yes.....1
No.....2 ***(Go to Q.19)***
Don't know/Not sure.....7 ***(Go to Q.19)***

Refused.....9 ***(Go to Q.19)***

18A. ***If yes,*** did your child assist this person with toileting (including diaper changes)?
Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

18B. Was this person diagnosed with *C. difficile?*
Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

19. Did any of your child's household members work at or volunteer, in any capacity, at a hospital, other medical facility, or in any facility where patient care is provided in the 12 weeks before [Reference Date_____/_____/_____)]?
Yes.....1
No.....2 ***(Go to Q.20)***
Don't know/Not sure.....7 ***(Go to Q.20)***
Refused.....9 ***(Go to Q.20)***

19A. ***If yes,*** what type of healthcare setting?

(READ LIST)	Yes	No	DK/NS	Refused
Hospital	1	2	7	9
Emergency department	1	2	7	9
Doctor's office	1	2	7	9
Dentist	1	2	7	9
Long term care (skilled nursing facility)	1	2	7	9
Hemodialysis facility	1	2	7	9
Other facility	1	2		

Specify:_____

—

19B. Did their job involve direct physical contact with patients? For example touching the patient to help her get out of a chair
Yes.....1
No.....2 ***(Go to Q.20)***
Don't know/Not sure.....7 ***(Go to Q.20)***
Refused.....9 ***(Go to Q.20)***

19C. ***If yes,*** what was their main job?

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

_____

_____

Job Code€€-€€€€ ***(Fill in job code after interview is finished)***

20**.** Did your child attend a group childcare or daycare in the 12 weeks before [Reference Date_____/_____/_____)] ? We consider daycare to be any place inside or outside your home where your child spends at least 4 hours per week under an adult's care with at least two children who do not live with you

Yes.....1
No.....2 (**Go to Q.16)**
Don't know/Not sure.....7 (**Go to Q.16)**
Refused.....9 (**Go to Q.16)**

20A. ***If yes,*** what type of childcare setting? **[Read list if necessary]**

Home – care is provided in someone's home typically by one person 1
Center- care is provided typically in a commercial building with many providers and rooms 2
Nanny / care provider share- two or more families have a single nanny / care provider to take care of their household member either full-time or part-time 3
Other 4
Specify: _____
Don't know/Not sure 7
Refused 9

SECTION 5: DIET EXPOSURES

I'd like to change direction now and ask you about the foods your child generally eats in a given week and the kind of water your child drinks.

21. Did your child receive food / formula through a feeding tube called a G-tube or J-tube in the 12 weeks before [Reference Date_____/_____/_____)]?

Yes.....1
No.....2
Don't know/Not sure.....7
Refused.....9

22. In a typical week how frequently does your child consume the following foods?

[READ LIST]	Often	Sometimes	Rarely	Never	DK/NS	Refused
	>5/week	**2-5 /week**	**<2/ week**	**Never**		
Eggs	1	2	4	5	7	9
Dairy (milk, yogurt)	1	2	4	5	7	9
Fresh-cut raw Vegetables	1	2	4	5	7	9
Plant based protein (tofu, tempeh, seitan)	1	2	4	5	7	9
Red Meat (beef, lamb, other game meat)	1	2	4	5	7	9

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Poultry (chicken, turkey)	1	2	4	5	7	9
Seafood (fish, shellfish)	1	2	4	5	7	9

23. Which <u>one</u> of the following is the source of tap water in your child's home (select only one):
☐ water utility ☐ private well ☐ spring ☐ unknown ☐ other

Name of the water utility, if known _____

If other, specify type and location _____

23A. At home, what type of unboiled water does your child most often use for drinking (chose only one)?
_____ Tap water not treated in the home
_____ Tap water treated in the home (for example, filtered, UV light, distilled, or whole house point-of-entry device)
_____Commercially bottled water
_____Other _____

24. During the first 6-months of your child's life, would you say: (*read choices*)

Almost 100% of feedings were breast milk with no or very little formula…….1

Most feedings (about 75%) were breast milk and the rest were formula…….2

About half (or 50%) of feedings were breast milk and half were formula…..3

Most feedings (about 75%) were formula and the rest were breast milk…….4

Almost 100% of feedings were formula with no or very little breast milk……..5

Don't know/Not sure.....7
Refused.....9

SECTION 6: MEDICAL HISTORY

The next set of questions are about medications your child may have been taking in the 12 weeks before [Reference Date____/____/_____]. Medicine bottles or records may help you remember about specific medications. Would you like to gather this information before we go on?

25. Did your child take any antibiotics by mouth or in [his / her] vein in the 12 weeks before [Reference Date_____/_____/_____]?

Yes.....1
No.....2 ***(Go to Q.27)***
Don't know/Not sure.....7 ***(Go to Q.27)***
Refused.....9 ***(Go to Q.27)***

26. Why did your child take these antibiotics?

Note: Subjects may indicate more than one reason (For example, if more than one course of antibiotics was taken for different illnesses or if one antibiotic was taken for and ear infection and a pneumonia)

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

[DO NOT READ LIST]	Yes	No
Bronchitis/ pneumonia	1	2
Dental cleaning	1	2
Ear, sinus, upper respiratory infection	1	2
Eye infection		
Oral surgery		
Skin or soft tissue infection (abscess or cellulitis)	1	2
Surgery	1	2
Urinary tract infection	1	2
Urinary tract infection prophylaxis		
DK/NS	7	7
Refused	9	9
Other	1	
Specify:_____		

26A. Which antibiotic(s) did your child take in the 12 weeks before [Reference Date_____/_____/_____]?
[DO NOT READ LIST]

		If yes, *How many weeks prior to (Reference*

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

		Date_____/_____/_____) did your child take this antibiotic		
[DO NOT READ LIST]		**2-weeks**	**4-weeks**	**12-weeks**
	Yes	Yes	Yes	Yes
Amoxicillin	1			
Amoxicillin/Clavulanate	1			
Ampicillin	1			
Augmentin	1			
Azithromycin	1			
Bactrim	1			
Biaxin	1			
Ceclor	1			
Cefaclor	1			
Cefadroxil	1			
Cefdinir	1			
Ceftin	1			
Cefixime	1			
Cefuorixime	1			
Cefzil	1			
Cephradine	1			
Ciprofloxacin or Cipro	1			
Clarithromyc	1			
Cleocin	1			
Clindamycin	1			
Dapsone	1			
Doxycycline	1			
Duricef	1			
Erythromycin	1			
Erythromycin/sulfa	1			
Flagyl	1			
Floxin	1			
Keflex	1			
Keftab	1			
Levofloxacin	1			
Levoquin	1			
Monurol	1			
Metronidazole	1			
Norfloxacin or Norflox	1			
Ofloxacin or Oflox	1			
Omnicef	1			
Penicillin or Pen VK	1			
Pediazole	1			
Septra	1			
Suprax	1			
Q. 26A CONTINUED		***If yes,*** *How many weeks prior to (Reference Date_____/_____/_____) did your child take this antibiotic*		
[DO NOT READ LIST]		**2-weeks**	**4-weeks**	**12-weeks**

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

Trimox	1			
Trimethoprim/Sulfa	1			
Vancomycin	1			
Zithromax or Z-Pak	1			
Clindamycin	1			
Other antibiotic 1	1			
Specify: _____	1			
Other antibiotic 2	1			
Specify: _____	1			
Don't know/Not sure	7			
Refused	9			

27. Did your child use any antibiotic eye drops in the 12 weeks before [Reference Date_____/_____/_____]?
Yes.....1
No.....2 ***(Go to Q.28)***
Don't know/Not sure.....7 ***(Go to Q.28)***
Refused.....9 ***(Go to Q.28)***

27 A. ***If yes,*** what was the name of the drop (**read list if necessary**)?

Polytrim (Polymyxin sulfate / TMP)…….1
Ciloxan (Ciprofloxacin)……..2
Ocuflox (Ofloxacin)…….3
Vigamox, Moxeza (Moxifloxacin) ……..4
Other……9
Specify : .....

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

28. In the 12 weeks before [Reference Date_____/_____/_____], did your child regularly take any acid-reducing medications to treat excessive stomach acid, heartburn, or gastroesophageal reflux disease (GERD)? We define regular use as use of the product at least 3 days per week. Such medications might include Prevacid, Tums, Maalox, Mylanta, Tagamet, Zantac, Prilosec, or Nexium.

Yes.....1
No.....2 ***(Go to Q.29)***
Don't know/Not sure.....7 ***(Go to Q.29)***
Refused.....9 ***(Go to Q.29)***

28A. ***If Yes*****,** please specify which medicine your child regularly took in those 12 weeks.

[DO NOT READ LIST]	**YES= 1**	**NO=2**	**How many weeks prior to** (Reference Date_____/_____/_____) **did your child take this medication?**		
			2 weeks	4 weeks	12 weeks
Aciphex/rabeprazole	1	2			
Alka-Seltzer	1	2			
Maalox	1	2			
Mylanta	1	2			
Nexium/esomeprazole	1	2			
Pepcid/famotidine	1	2			
Prevacid/lansoprazole	1	2			
Prilosec/omeprazole	1	2			
Protonix/pantoprazole	1	2			
Rolaids	1	2			
Tums	1	2			
Tagamet/cimetidine	1	2			
Zantac/ranitidine	1	2			
Other:	1	2			
Don't Know/not sure	7	7			
Refuse	9	9			

If yes, in the 2 weeks before

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

I am now going to ask about medications that are given for many reasons including things like chronic pain, depression, anxiety, and to help sleep. We are asking about these medications to determine if they could put people at risk for *C. diff*. Examples of these medications include: Prozac, Celexa, Remeron, Paxil, and Trazadone.

29. In the 12 weeks before [Reference Date_____/_____/_____], did your child regularly take any such medications? We define regular use as use of the product at least 3 days per week.

€ CASE € CONTROL

Patient ID:_____ State ID:_____

REFERENCE Date: ____/____/_____ ***[DO NOT READ LIST]***
(mm/dd/yyyy)

			How many weeks prior to (Reference Date_____/_____/_____) **did your child take this medication?**		
	YES	**NO**	2 weeks	4 weeks	12 weeks
Amitriptyline	1	2			
Anafranil (Clomipramine)	1	2			
Asendin (Amoxapine)	1	2			
Celexa, Cipramil (Citalopram)	1	2			
Cymbalta (Duloxetine)	1	2			
Effexor (Venlafaxine)	1	2			
Eldepryl, Emsam, Zelapar (Selegiline)	1	2			
Escitalopram	1	2			
Limbitrol (Chlordiazepoxide/Amitriptyline)	1	2			
Ludiomil,(Maprotiline)	1	2			
Luvox (Fluvoxamine)	1	2			
Marplan, (Isocarboxazid)	1	2			
Nardil, Nardelzine (Phenelzine sulfate)	1	2			
Norpramin (Desipramine)	1	2			
Nortriptyline	1	2			
Parnate,(Tranylcypromine)	1	2			
Paxil (Paroxetine)	1	2			
Pristiq (Desvenlafaxine)	1	2			
Prozac, Sarafem, Fontex (Fluoxetine)	1	2			
Remeron, Avanza, Zispin (Mirtazapine)	1	2			
Savella, (Milnacipran)	1	2			
Serzone, (Nefazodone)	1	2			
Silenor, Prudoxin, Zonalon (Doxepin)	1	2			
Surmontil (Trimipramine)	1	2			
Symbyax (Olanzapine/fluoxetine)	1	2			
Tofranil, (Imipramine)	1	2			
Trazadone	1	2			
Triptafen (amitriptyline/perphenazine)	1	2			
Viibryd (Vilazodone)	1	2			
Vivactil, (Protriptyline)	1	2			
Wellbutrin, Zyban (Bupropion)	1	2			
Zoloft, Lustral (Sertraline)	1	2			
Other:					
Don't know/Not Sure	7	7			
Refuse	9	9			

If yes, in the

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

2 weeks before

Now I am going to ask you about medical conditions your child may have had.

30. **Prior to** [Reference Date_____/_____/_____], were you ever told by a medical provider that your child had any of the following medical conditions? **[READ LIST – including information in parentheses]**

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

READ LIST	**Yes**	**No**	**DK/NS**	**Refused**
Congenital heart disease Specify:				
Diabetes				
Chronic renal (kidney) failure				
If yes, is your child on dialysis or awaiting dialysis?				
Chronic lung disease (BPD)				
Asthma				
Cystic fibrosis				
Organ transplant				
Bone marrow transplant				
Leukemia or lymphoma				
Sickle cell disease (not sickle cell trait)				
Cancer (e.g. bone, liver, brain)				
Short gut disease (bowel/ intestinal insufficiency)				
Depression				
Born by C-section?				
Stay in the NICU at birth?				
If yes, was your child premature? How many weeks premature?_____				
If yes, how many weeks in the NICU?				
Other illnesses:				

31. There is some evidence that how much you weigh may effect infection with *C. difficile*. What are your child's most recent height or length and weight?

Don't know/ Not Sure….7 [***Prompt by saying: Sometimes children's doctors give parents records or charts with their child's weight and height. If you have these I can wait while you get them***]
Refused ……..9
Height/ length:_____Ft_____in (or _____cm)
Weight:_____lbs (or _____Kg)

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

SECTION 8: DEMOGRAPHICS

Now I would like to ask you a few final questions.

32. Do you consider your child to be? **[Read responses 1 & 2]**
( ) 1 Hispanic or Latino
( ) 2 Not Hispanic or Latino
( ) 7 Don't Know/Not Sure (DO NOT READ)
( ) 9 Refused (DO NOT READ)
( ) 10. Other racial category (DO NOT READ)

33.I am going to read a list of racial categories. Which one or more of the following do you consider your child to be…? **[Read responses 1-5 and allow respondent to select one or more]**
( ) 1 White/Caucasian
( ) 2 Black or African-American
( ) 3 American Indian or Alaska Native
( ) 4 Native Hawaiian or Other Pacific Islander
( ) 5 Asian
( ) 7 Don't Know/Not Sure (DO NOT READ)
( ) 9 Refused (DO NOT READ)
( ) 10. Other racial category (DO NOT READ)

34. What was your child's main type of health care coverage during (12 weeks before Reference Date_____/_____/_____ and Reference Date_____/_____/_____)? **I'm going to read all the choices**.

Private insurance, such as an HMO, PPO or a managed care plan 1
Public insurance, such as Medicaid, Medicare or state assistance program 2
A combination of private and public insurance 3
No health insurance 4
DO NOT READ: Other [specify] _____ 8
Don't know or not sure 7
Refused 9

I have just a few more questions about the parent or guardian who cares for [child's name] most often. Because education and income can affect access to healthcare, I'd like to ask you about a couple of questions on these subjects.

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

35. What is the highest grade or year of school that any of the household members completed? **Please answer this question based on the highest level of education in your household**

___1 Never attended school or kindergarten only
___2 Elementary or middle school; 1st-8th grade
___3 Some high school; 9th-11th grade
___4 High school graduate; 12th grade or GED
___5 College or technical school for 1-3 years
___6 College for 4 years, with or without a degree
___9 Refused

Because income can affect access to healthcare, I'd like to ask you about annual income.

36. In your child's home, what is the household income from all sources? **READ EACH RESPONSE IN ORDER UNTIL RESPONDENT AGREES.**

___1 Less than $15,000 ___5 Less than $70,000
___2 Less than $25,000 ___6 $70,000 or more
___3 Less than $35,000 ___7 Don't know or not sure
___4 Less than $50,000 ___9 Refused

That was my last interview question. Thank you very much for your time and participation!

37. Comments:
_____

_____

_____

_____

_____

38. Interview Completed? € Yes € No

39. Date of interview: ____/____/_____
(mm/dd/yyyy)

40. Interviewer initials: _____

Health Interview Appendix—Job Codes

OFFICE OF MANAGEMENT AND BUDGET - 1998 Standard Occupational Classification

€ CASE € CONTROL
Patient ID:_____ State ID:_____
REFERENCE Date _____/_____/_____
(mm/dd/yyyy)

29-0000 Healthcare Practitioners and Technical Occupations
- 29-1000 Health Diagnosing and Treating Practitioners
  - 29-1010 Chiropractors
  - 29-1020 Dentists
    - 29-1021 Dentists, General
    - 29-1022 Oral and Maxillofacial Surgeons
    - 29-1023 Orthodontists
    - 29-1024 Prosthodontists
    - 29-1029 Dentists, All Other Specialists
  - 29-1030 Dietitians and Nutritionists
  - 29-1040 Optometrists
  - 29-1050 Pharmacists
  - 29-1060 Physicians and Surgeons
    - 29-1061 Anesthesiologists
    - 29-1062 Family and General Practitioners
    - 29-1063 Internists, General
    - 29-1064 Obstetricians and Gynecologists
    - 29-1065 Pediatricians, General
    - 29-1066 Psychiatrists
    - 29-1067 Surgeons
    - 29-1069 Physicians and Surgeons, All Other
  - 29-1070 Physician Assistants
  - 29-1080 Podiatrists
  - 29-1110 Registered Nurses
  - 29-1120 Therapists
    - 29-1121 Audiologists
    - 29-1122 Occupational Therapists
    - 29-1123 Physical Therapists
    - 29-1124 Radiation Therapists
    - 29-1125 Recreational Therapists
    - 29-1126 Respiratory Therapists
    - 29-1127 Speech-Language Pathologists
    - 29-1129 Therapists, All Other
  - 29-1130 Veterinarians
  - 29-1190 Miscellaneous Health Diagnosing and Treating Practitioners
    - 29-1199 Health Diagnosing and Treating Practitioners, All Other
- 29-2000 Health Technologists and Technicians
  - 29-2010 Clinical Laboratory Technologists and Technicians
    - 29-2011 Medical and Clinical Laboratory Technologists
    - 29-2012 Medical and Clinical Laboratory Technicians
  - 29-2020 Dental Hygienists
  - 29-2030 Diagnostic Related Technologists and Technicians
    - 29-2031 Cardiovascular Technologists and Technicians
    - 29-2032 Diagnostic Medical Sonographers
    - 29-2033 Nuclear Medicine Technologists
    - 29-2034 Radiologic Technologists and Technicians
  - 29-2040 Emergency Medical Technicians and Paramedics
  - 29-2050 Health Diagnosing and Treating Practitioner Support Technicians
    - 29-2051 Dietetic Technicians
    - 29-2052 Pharmacy Technicians
    - 29-2053 Psychiatric Technicians
    - 29-2054 Respiratory Therapy Technicians
    - 29-2055 Surgical Technologists

29-2056 Veterinary Technologists and Technicians
29-2060 Licensed Practical and Licensed Vocational Nurses
29-2070 Medical Records and Health Information Technicians
29-2080 Opticians, Dispensing
29-2090 Miscellaneous Health Technologists and Technicians
29-2091 Orthotists and Prosthetists
29-2099 Health Technologists and Technicians, All Other
29-9000 Other Healthcare Practitioners and Technical Occupations
29-9010 Occupational Health and Safety Specialists and Technicians
29-9011 Occupational Health and Safety Specialists
29-9012 Occupational Health and Safety Technicians
29-9090 Miscellaneous Health Practitioners and Technical Workers
29-9091 Athletic Trainers
29-9099 Healthcare Practitioners and Technical Workers, All Other
31-0000 Healthcare Support Occupations
31-1000 Nursing, Psychiatric, and Home Health Aides
31-1010 Nursing, Psychiatric, and Home Health Aides
31-1011 Home Health Aides
31-1012 Nursing Aides, Orderlies, and Attendants
31-1013 Psychiatric Aides
31-2000 Occupational and Physical Therapist Assistants and Aides
31-2010 Occupational Therapist Assistants and Aides
31-2011 Occupational Therapist Assistants
31-2012 Occupational Therapist Aides
31-2020 Physical Therapist Assistants and Aides
31-2021 Physical Therapist Assistants
31-2022 Physical Therapist Aides
31-9000 Other Healthcare Support Occupations
31-9010 Massage Therapists
31-9090 Miscellaneous Healthcare Support Occupations
31-9091 Dental Assistants
31-9092 Medical Assistants
31-9093 Medical Equipment Preparers
31-9094 Medical Transcriptionists
31-9095 Pharmacy Aides
31-9096 Veterinary Assistants and Laboratory Animal Caretakers
31-9099 Healthcare Support Workers, All Other

APPENDIX D: Introduction letter For Participants

INTRODUCTION LETTER FOR PARTICIPANTS

Note: Letter will be on health department or Emerging Infections Program letterhead only for sites that require introduction letter

MONTH, DAY, YEAR

JANE DOE
100 MAIN STREET
ANYTOWN, USA 11111

Dear *MS. DOE*:

The *[HEALTH DEPT/EIP NAME]* and the Centers for Disease Control and Prevention are working together to assess factors that may put persons under risk of developing *Clostridium difficile* or *C. diff* infection outside of the hospital. *C. diff* is a germ that can cause severe diarrhea and it can be very hard to treat. People in hospitals are at most risk of getting this germ, but *C. diff* can also occur in people who have not been hospitalized. We don't know why people in the community who have not been hospitalized get this infection, but to help us understand possible reasons we need to interview people who were sick with *C. diff* as well as people who were *not* sick with *C. diff.* The goal of this study is to learn more about *C. diff* in people living in the community so that steps can be taken to prevent this infection. We are contacting you because either you or someone in you household has developed *C. diff* infection **or** you or someone in your home lives in the same area and is around the same age as someone who developed this infection.

Someone from *[HEALTH DEPT/EIP NAME]* may call you and ask if you would like to participate. If you agree, the person from the health department will ask you a series of questions about your health and healthcare exposures (or about your child's health and healthcare exposures). The interview will take about 30 minutes. After your participation, a $20 gift card will be sent to you to show our appreciation for your time and effort.

Being in this study is voluntary. Most likely there will be no direct value to you for taking part in this study. However, the results of this study will help doctors plan ways to prevent infections with this germ. There are no risks or costs to you for participating. If you choose not to be in the study, your health care will not be affected in any way. We hope you will participate. If you do not want to take part or hear more about this study, please send back the enclosed postcard.
Thank you for your help.

Sincerely,

[STUDY COORDINATOR'S NAME]
[TITLE]

Enclosure: postcard

Appendix D: Post Card

REFUSAL POSTCARD

POSTCARD

Front:
[STUDY COORDINATOR NAME]
[ADDRESS]

Back:
Participant number _____ *[HEALTH DEPT/EIP NAME] use only*

____ Please do not contact me. I do not want to participate in the study.

Appendix E: Thank You Letter

THANK YOU LETTER TO EVALUATION PARTICIPANTS

Note: Letter will be on health department of Emerging Infections Program letterhead
Reading level: Grade 7.8 using Flesch-Kincaid Scale

Month, day, year

Jane Doe
100 Main Street
Anytown, USA 11111

Dear Ms. Doe:

Thank you very much for participating in this study to learn more about *Clostridium difficile* in people in the community. Your help will assist us in learning more about this disease.

To thank you for your time participating in this important evaluation, we are sending you a $20 certificate as a token of our appreciation. Also enclosed is a copy of the consent form for your records.

Your participation is much appreciated.

Please call me at [phone number] if you have any questions.

Sincerely,

EIP Representative
Contact information

Enclosure: Gift Certificate, Consent Form