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Benjamin J. Silk

Completeness and Timeliness of
Infectious Disease Morbidity Reporting

By

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B.S., University of California, Davis, 1994
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An Abstract of
A dissertation submitted to the Faculty of the Graduate School of
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ABSTRACT

In the United States, health departments depend on reportable disease surveillance for prevention of numerous infectious diseases, but variations in the completeness and timeliness of these reporting systems had not been assessed systematically.

For the first two studies, state and large city/county health departments' laboratories and epidemiology programs were surveyed on their policies, practices, and capacities for West Nile fever (WNF) testing and reporting (Study 1) and meningococcal disease serogrouping (Study 2) for 2003 through 2005. Syndrome ascertainment ratios were calculated by dividing case counts of WNF by case counts of West Nile neuroinvasive disease. This indicator identified several factors associated with relatively complete WNF ascertainment, including minimal requirements for testing, conducting at least three surveillance-related activities, and dedication of at least 5.0 surveillance staff per million residents. In addition, the odds of WNF was 44% lower in Blacks and 31% lower in Hispanics compared with non-Hispanic Whites when multilevel modeling was used to predict fever versus neuroinvasive disease. In Study 2, more complete serogrouping (>80% of reported cases' isolates serogrouped) was frequently reported by states that monitored serogrouping completeness using defined targets, states that employed at least 50 analytic laboratorians, and states with at least one city/county laboratory. In multilevel analyses, presence of a serogroup result was marginally associated with serogroup monitoring and remained associated with laboratory staff size.

Study 3 documented reporting timeliness gains attributable to implementation of an internet-based reporting system in Georgia from July 2003 through December 2005.

Reporting-time quartiles were calculated for the interval between dates of specimen collection and first public health report. Giardiasis, hepatitis A virus infection, legionellosis, malaria, pertussis, and Rocky Mountain spotted fever reports submitted via the internet were timelier than reports submitted by phone, facsimile, or mail. In a Cox proportional hazards model, reports from smaller hospitals (< 200 acute care beds), laboratories that sent out all microbiologic cultures for workup, and infection control programs that described disease reporting as "non-routine" were less timely.

Collectively, the studies identified discrete components of the infectious disease reporting process where interventions can improve the quality, representativeness, and value of reportable disease surveillance data.

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It is my sincere hope that this work will someday benefit Abigail, Ashton, Brandon, Christian, Elizabeth, Harris, Jackson, and Sarah.

ABBREVIATIONS

AFP	Acute flaccid paralysis
APHL	Association of Public Health Laboratories
CDC	Centers for Disease Control and Prevention
CSF	Cerebrospinal fluid
CSTE	Council of State and Territorial Epidemiologists
EIP	Emerging Infections Program
ELR	Electronic laboratory reporting
FIPS	Federal Information Process Standards
FTE	Full-time equivalent
GDPH	Georgia Division of Public Health
ICP	Infection control professional
IOM	Institute of Medicine
IVEware	Imputation and Variance Estimation Software
LHD	Local health department
MAR	Missing at random
MCAR	Missing completely at random
MMWR	Morbidity and Mortality Weekly Report
NACCHO	National Association of City and County Health Officials
NCHS	National Center for Health Statistics
NEDSS	National Electronic Disease Surveillance System
NNDSS	National Notifiable Diseases Surveillance System
NPHPSP	National Public Health Performance Standards Program
SendSS	State Electronic Notifiable Disease Surveillance System
STI	Sexually-transmitted infection
WNF	West Nile fever
WNND	West Nile neuroinvasive disease
WNV	West Nile virus

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CHAPTER 1

INTRODUCTION

State and local health departments throughout the United States monitor the frequency and distribution of diseases and conditions of public health importance by designating them as reportable, thereby requiring physicians, laboratories, infection control professionals and others to report to them. With few exceptions (Kaufman, Reichard, and Walline 2004), reportable disease surveillance systems cover the entire United States. Most reportable events are communicable diseases, though other occurrences such as animal bites, birth defects, cancer diagnoses, elevated blood lead levels, poisonings, and illness clusters are also reportable (Council of State and Territorial Epidemiologists 2004). The set of reportable diseases and conditions varies according to state and regional public health priorities. Most of the nationally notifiable infectious diseases (Table 1-1) are designated as reportable by all states and, conversely, some states may require reporting for infectious diseases that are not nationally notifiable. For example, coccidioidomycosis is nationally notifiable, endemic in the Southwestern U.S., and reportable in Arizona and California but not in many other states beyond the Southwest.

All states have laws, statutes, or regulations that mandate disease reporting (Roush et al. 1999). In addition, most states have "generic authority to collect data on issues of public health importance, including disease outbreaks or unusual or unforeseen occurrences" (Council of State and Territorial Epidemiologists 2001). Few documented examples of enforcing liability for negligent public health reporting exist (Louisiana State

University Medical and Public Health Law Site 2002; Weiss, Strassburg, and Fannin 1988). Instead, public health agencies generally opt to promote reporting, considering reporting sources as partners in disease surveillance.

Reportable diseases surveillance systems operate through collaborations at multiple levels (Chorba et al. 1989; Roush et al. 1999). The systems link public heath agencies to healthcare providers, clinical laboratories, infection control professionals, and other hospital and clinic staff who report patients whose clinical presentations signify unexplained, severe problems or, more often, clinical and laboratory diagnoses meet case definitions for the diseases under surveillance (Centers for Disease Control and Prevention 1997). Public health officials use disease reports to initiate prevention and control measures locally (e.g., chemoprophylaxis of close contacts, outbreak investigations). States' organizational structures vary (Beitsch et al. 2006), but state health departments generally supervise or support local surveillance activities and consolidate disease reports from county or district public health agencies as well as from direct reporting sources (Beitsch et al. 2006). Ultimately, state epidemiologists are responsible for collection and use of reportable diseases data within their jurisdictions.

All states have voluntarily transmitted reportable diseases surveillance data to the U.S. Public Health Service since 1925 (Thacker and Berkelman 1988). The Centers for Disease Control and Prevention (CDC) currently oversees the National Notifiable Diseases Surveillance System (NNDSS) and disseminates NNDSS data via the *Morbidity and Mortality Weekly Report (MMWR)* and yearly summaries.

In recent years, most states have reported complete geographic coverage for public health services, either directly by local public health agencies (81%) or through the

state health department (16%). Beitsch and colleagues' 2001 survey also found that many states' district offices provide technical assistance to local health departments (LHDs) (2006). The degree to which data collection and communicable disease epidemiology functions were performed at the local and state levels differed regionally and according to organizational typologies. In states with centralized control, data collection (67%) and epidemiology (70%) generally were state-level functions. Overall, however, states frequently reported that all or some local public health agencies in their jurisdictions performed data collection (47%) and epidemiology (53%). Delivery of services for tuberculosis (TB), human immunodeficiency virus (HIV), and sexually transmitted infections (STI) often occurred at the local level. Localized services for these diseases were particularly common in Southeastern and Western states as well as states with public health districts. In 2001, most state health agencies (79%) cited responsibility for public health laboratories (Beitsch et al.. 2006).

A number of public health services are delivered by agencies inside and outside of the governmental public health system. Using a scaled approach for reporting service delivery in 1998 (Mays et al. 2004), large LHDs (serving more than 100,000 residents) often conducted investigations (mean score = 76%), but less often delivered laboratory services (mean score = 50%) or analyzed health determinants (mean score = 53%). Core public health activities like surveillance are typically advanced through partnerships. The Emerging Infections Programs (EIPs), for example, collects gold-standard surveillance data on invasive bacterial disease and foodborne illness in 12 defined geographies across the United States through collaborations between health departments, healthcare, and academic institutions (Pinner et al. 2003). Notably, Scutchfield and others found a

positive association between university-academic partnerships and public health system performance (2004).

Reportable disease surveillance systems provide essential information for initiating public health interventions and guiding policy. For example, morbidity reports may be used to assure appropriate provision of TB care (a patient-specific intervention) or for case ascertainment and subsequent control of an outbreak (an intervention that targets a community or a population) (Chorba et al. 1989). Consolidated morbidity reports (i.e., surveillance data) are used to guide the planning, implementation, and evaluation of policies and programs, such as vaccination recommendations. Other examples include tracking disease trends, identifying epidemiologic characteristics of disease, examining causes of morbidity and mortality, identifying etiologic hypotheses, prioritizing resources, projecting future trends, and generating and supporting research (Birkhead and Maylahn 2000; Centers for Disease Control and Prevention 2001).

Public health agencies improve their disease reporting systems through research and evaluation. To facilitate evaluation, CDC and other public health agencies have published guidelines for evaluating surveillance systems (Centers for Disease Control and Prevention 2001). These guidelines provide an outline of system attributes, which are criteria to assess a surveillance system's efficiency and utility. Common criteria for evaluating surveillance systems are acceptability, data quality, flexibility, predictive value positive, sensitivity, simplicity, and timeliness. Table 1-2 provides definitions for each criterion.

While certain surveillance attributes may be assessed qualitatively (e.g., acceptability, simplicity), this dissertation is oriented toward quantitative measurement of

reporting performance. Sensitivity, data quality, and timeliness are the focus and are contextualized within the conditional events framework described below. Three semantic considerations are necessary for the application of the framework to these attributes. Sensitivity, the likelihood that health-related events are identified by surveillance when they occur, is termed *completeness of case ascertainment* hereafter. This terminology avoids a potential misconception. Completeness of reporting, the proportion of diagnosed cases reported to a pubic health agency, is often used synonymously with surveillance sensitivity. By contrast, in this dissertation completeness of case ascertainment emphasizes whether or not diagnoses are established as well as reporting given a diagnosis. Second, *missing data* refers to the potential absence of each data element in a set of surveillance case reports (i.e., the surveillance data). Case reporting completeness is a form of data quality. Lastly, *timeliness of reporting* refers to the time from laboratory specimen collection to first public health notification.

Disease reporting from a conditional events framework

A "conditional events" perspective is introduced for the dissertation. The perspective is adopted to provide a contextual framework for the dissertation studies and the components of the reporting process addressed by each. The central premise of the conditional events perspective is that the process of testing, confirmation, and reporting of infectious disease morbidity can be considered as the culmination of a series of conditional events, whereby each subsequent event is contingent on previous events in the series (Figure 1-1). Any absent or delayed event early in the series implies that morbidity reports will also be absent, incomplete, or delayed.

There are four events in the series: 1) healthcare seeking; 2) receipt of a etiologic diagnosis that conforms with a case definition for a reportable disease (Centers for Disease Control and Prevention 1997); 3) receipt of a morbidity report by the public health agency; and 4) completion of all necessary data elements. The vertical axis in Figure 1-1 represents two concepts. The axis plots an individual's conditional probability of experiencing each of these four events. This probability is determined by measured and unmeasured covariates. The vertical axis also plots average probabilities for an ill cohort as the cohort progresses through events in the series. For these probabilities, individual counts of persons experiencing each event are summed and divided by all persons eligible for the event (i.e., all persons experiencing the previous event). The completeness of diagnosed case reporting, for example, is the quotient of the number of reported diagnoses over the number of diagnoses obtained. This quotient may be reported as a percentage (i.e., surveillance sensitivity) and is an estimate of the probability for event 3. In contrast, completeness of case ascertainment is the probability that events 2 and 3 both occur (i.e., diagnosis is confirmed and reported).

The event series is initiated with the onset of symptomatic disease following an infection. Depending on the natural history of the disease and its standard of care, some proportion of symptomatic case-patients will receive healthcare (event 1) with an etiologic diagnosis (event 2). If the infection causes fulminant disease, case-patients are more likely to seek healthcare. Meningococcal meningitis, for example, is characterized by conspicuous signs and symptoms (e.g., acute fever, intense headache, neck stiffness) that develop rapidly (Raghunathan, Bernhardt, and Rosenstein 2004). The varying clinical manifestations of meningococcal disease (e.g., bacteremia, respiratory infection,

and focal infection), however, can make clinical diagnosis challenging (Rosenstein et al. 2001). Meningococcal pneumonia may be underdiagnosed (Rosenstein et al. 1999), both because the presence of *N. meningitidis* in sputum samples does not distinguish disease from bacterial carriage and because clinicians may not consider meningococcal disease in their differential diagnosis of pneumonia. The sensitivity of blood and cerebrospinal fluid (CSF) cultures is also diminished when antibiotics are administered before samples are obtained (Wylie et al. 1997). In instances of prior antibiotic use, tests other than cultures may be necessary to establish a diagnosis.

In contrast to persons with meningococcal disease, 80% of persons with West Nile virus (WNV) infection experience asymptomatic or mild self-limited illness (Petersen and Marfin 2002). West Nile fever (WNF) occurs in approximately 20% of cases of WNV infection (Mostashari et al. 2001). WNF manifestations range from non-specific, flu-like symptoms (fever, headache, fatigue) to disease that is serious enough to warrant healthcare seeking and hospitalization (Chowers et al. 2001; Mostashari et al. 2001; Watson et al. 2004). Even with the potential severity of WNF (Watson et al. 2004), persons hospitalized with WNF may be discharged without clinical or laboratory assessment for WNV infection (Whitney et al. 2006).

While events 1 and 2 of the conditional events series occur in the healthcare domain, subsequent events are associated with the public health agency's disease reporting system. In spite of statutory reporting requirements, patients diagnosed with reportable diseases frequently are not reported to the public health agency (event 3). A U.S. review of disease reporting completeness demonstrated variability by disease (9-99%) (Doyle, Glynn, and Groseclose 2002). Reporting was generally more complete for

acquired immunodeficiency syndrome (AIDS), TB, and STIs than for other notifiable diseases. In fact, all states and large urban areas have categorically funded programs for TB, HIV/AIDS, and STI control that include well-developed surveillance programs. Most notifiable infectious diseases have not had such dedicated resources, so health department initiatives to ensure complete disease reporting may be less extensive (Silk and Berkelman 2005).

Completion of a morbidity report is the final event in the conditional series and may or may not occur simultaneously with event 3 (i.e., disease reports may be submitted complete or incomplete). Often, completed morbidity reports are an aggregation of data collected from multiple sources, such as clinicians, infection control practitioners, and medical records departments (e.g., demographic and clinical data), primary care providers (e.g., medical history, risk factors), patients and their next of kin (e.g., self-reports, exposures), and reference and public health laboratories (e.g., antimicrobial susceptibilities). Since completion of morbidity reports may require extensive investigation or collaboration with multiple entities, data may remain missing.

Many of the data elements necessary for completing morbidity reports vary by disease. Data may be required from supplemental public health laboratory testing (e.g., meningococcal disease serogrouping) (Association of Public Health Laboratories 2002). Professional linkage between public health agencies and laboratories is a key determinant of success in clinical specimen receipt, which is a prerequisite of testing in public health laboratories. Demographic data elements, such as race and ethnicity, are typically requested for all reports but may be incomplete (Gomez et al. 2003; Watson 1997).

These data are especially important for identifying subpopulations at increased risk for disease.

The measurement of reporting timeliness theoretically begins with the initial infection, even before apparent symptoms. The incubation period (i.e., time from infection to onset of symptoms) varies greatly by disease and host factors, ranging from hours to years. For a given disease, the incubation period also varies according to a distribution of incubation periods and may be shortened with a higher infectious dose (Giesecke 2002). However, awareness of an infection prior to symptom onset is unusual without suspicion of pathogen exposure. Therefore, it is practical to consider illness onset as a starting point for reporting timeliness (Figure 1-1), recognizing that once symptoms are apparent acquisition has already preceded subsequent reporting by at least the incubation period. In addition, selection of events to measure timeliness is likely to be a matter of whether or not information on the timing of these events is readily accessible.

Time is represented along the horizontal axis of Figure 1-1. The time from the preceding event to each subsequent event in the conditional events series is noted with a corresponding interval. These intervals are measured in days. For example, the number of days from illness onset to healthcare seeking (event 1) is interval 1. Similarly, time from healthcare seeking to diagnosis (event 2) is interval 2, which may or may not be zero based on whether a diagnosis is established immediately. Since events 1 and 2 occur in the healthcare domain, intervals 1 and 2 (time to seek healthcare and receive a diagnosis) also are influenced by the natural history of the disease, host factors, the standard of care for that disease, and patient interactions with the healthcare system.

Patients with meningitis and encephalitis, for example, are likely to seek immediate healthcare due to disease severity and associated signs and symptoms.

The time intervals between subsequent events in the series are dependent on the public health agency's disease reporting system. Many states explicitly specify time-specific reporting requirements in their disease reporting materials. In the state of Georgia, several infectious diseases are designated for immediate reporting (e.g., acute arboviral infections, meningitis, meningococcal disease, TB, and potential bioterrorism agents). All other infectious diseases require reporting within seven days. Figure 1-2 is a screen capture of the disease reporting poster for the State of Georgia's Department of Human Resources. Notably, the poster is split into columns for diseases that are to be reported immediately or within seven days. Interval 4, time to complete a morbidity report, may be zero if a report is initially submitted completely. Alternatively, the duration of the interval may be a week or more, such as when a clinical specimen is forwarded for advanced laboratory testing and the test results are subsequently used to complete the report.

In addition, advances in information technology systems are streamlining surveillance operations, thereby increasing completeness and timeliness of reporting and reducing workload for health department officials. Several reports have documented gains in completeness and timeliness with implementation of automated, electronic laboratory reporting (ELR) and with implementation systems that allow for internet-based disease reporting (Effler et al. 1999; Ward et al. 2005).

SendSS is an internet-based disease reporting system that was developed by the Georgia Division of Public Health (GDPH). In January of 2002, SendSS first became

widely available in Georgia. By January 2003, Georgia district and county health departments began routinely submitting disease reports through SendSS, which had incorporated a case management feature for public health follow-up at the local level. Additionally, healthcare providers, ICPs, and laboratories increasingly report cases directly to GDPH.

Based on the conditional events framework, three focus areas are delineated for the dissertation:

1. *Completeness of case ascertainment* is the likelihood that a disease will be diagnosed (event 2) and reported (event 3), given that healthcare is sought (event 1).
2. *Extent of missing data* is the proportion of case records with a data element absent in the surveillance dataset. Alternatively, this is the probability of case report completion (event 4), given that a case report is submitted (event 3).
3. *Timeliness of reporting* is the time from laboratory specimen collection to first public health notification (the sum of intervals 2-3).

Goals and research strategy

The goal of the dissertation is to formulate recommendations for strengthening the completeness and timeliness of the infectious disease morbidity reporting process in the United States. The conditional events framework described above illustrates how the completeness and timeliness of conditional events (i.e., healthcare seeking, etiologic diagnosis, disease reporting, and completion of morbidity reports) may be influenced by numerous demographic and clinical patient factors as well as administrative factors in the healthcare and public health domains. Based on this perspective, it is hypothesized that

public health agency factors, particularly among surveillance and laboratory programs, differentially influence the probability of progressing successfully through the conditional event series that culminates in complete ascertainment without missing data. Similarly, it is hypothesized that healthcare facility characteristics (i.e., sources for disease reports) also differentially influence the timeliness of progressing successfully through the conditional event series. In assessing specific programmatic factors, recommendations for strengthening completeness and timeliness can be directed appropriately and associated improvements in the quality, representativeness, and value of reportable diseases surveillance data can be anticipated.

Investigations of the roles of select factors that may explain variability in the three focus areas for assessment are operationalized through three complementary studies:

- Study 1 is a multilevel analysis of national WNF ascertainment;
- Study 2 is a multilevel analysis of national meningococcal disease serogrouping;
- Study 3 is a survival analysis of the timeliness of reporting to Georgia's State Electronic Notifiable Disease Surveillance System (SendSS)

The selection of completeness of WNF ascertainment and completeness of meningococcal disease serogroup reporting as models for researching the completeness of infectious disease morbidity reporting is an important part of the dissertation strategy.

In focusing on a single notifiable disease in each study, conditional event probabilities that would otherwise vary according to the natural history, standard of care, use and availability of valid diagnostics, or reporting likelihood of each disease are held

constant. Rationale for selection of these particular public health issues is discussed in Chapter 2.

The use of these two models (completeness of WNF ascertainment and meningococcal disease serogrouping) also recognizes the vital role of laboratory testing in infectious diseases surveillance. In fact, three core functions of state public health laboratories relate to the disease reporting system (Association of Public Health Laboratories 2002). They include disease prevention, control, and surveillance; integrated data management; and reference and specialized testing. A number of specific capabilities are also necessary components of the disease reporting process (Table 1-3). WNV ascertainment has required that public health laboratories "test epidemiologically significant specimens with potential public health implications" and "verify results of other laboratory tests." Meningococcal disease serogrouping "assist[s] in identification, understanding, and controlling disease outbreaks." In both cases, public health laboratories provide microbiologic expertise for epidemiology programs.

The capabilities of health departments' laboratory and epidemiology programs vary among states. This variability is likely to influence the completeness of WNF ascertainment and meningococcal disease serogrouping. By adopting a public health systems perspective for researching completeness of morbidity reporting, Studies 1 and 2 represent a comprehensive investigation of potential associations between surveillance completeness and varying programmatic approaches by states. A multilevel design for implementing the public health systems research perspective is described below.

Several novel applications of techniques for quantitatively assessing reporting performance are important strategic elements of the dissertation. Demonstrating the

utility of these applications is another goal of the dissertation. First, the WNF ascertainment and meningococcal disease serogrouping completeness studies both employ a multilevel design. Case records from national surveillance offer clinical and demographic data on case patients with WNV infection and meningococcal disease. Since data originate from public health agencies with varying structural and functional approaches to their epidemiology and laboratory programs, survey data capturing programmatic policies, practices, and capacities are used as a second level of information. Second, completeness of WNF ascertainment is assessed using the "WNV syndrome ascertainment ratio," a simple, measurable indicator that can be calculated from data that are readily available to public health agencies and their stakeholders. Third, Cox proportional hazards regression is used to assess factors associated with timeliness of diagnosis and reporting (Study 3). Despite the need for a standardized approach to evaluating surveillance timeliness (Jajosky and Groseclose 2004), little published work has addressed this need. Table 1-4 summarizes the studies, including their scope and the focus area addressed.

Objectives and hypotheses

Using WNV as a model, Study 1 assesses whether WNF ascertainment is less likely among Blacks and Hispanics and whether these differences are pronounced in states with inadequate (or less fully developed) infrastructure or program capacities. Hypotheses are tested by estimating the magnitude of associations between these categorical variables and a dichotomous WNV disease syndrome, fever or neuroinvasive disease. Using a multilevel design, correlations between the WNV disease syndrome and

varying surveillance and testing policies, procedures, and program capacities within state health departments are also accounted for and characterized.

Similarly, Study 2 assesses whether completeness of meningococcal disease serogrouping is reduced in states with inadequate infrastructure or program capacities. Using a multilevel design, correlations between serogroup data status (present or absent) and varying surveillance and testing capacities, policies, and program structures within state health departments are accounted for and characterized.

Study 3 documents improvements in reporting timeliness attributable to electronic, internet-based disease reporting by comparing the timeliness of reports submitted directly to SendSS by healthcare providers with the timeliness of reports received by mail, facsimile, or other communication mechanisms and subsequently submitted to SendSS either by county/district public health officials or by GDPH. The study also recognizes that reporting timeliness is a function of the interactions between healthcare providers and public health officials. Disease reports are linked to data on pertinent characteristics of Georgia hospitals, infection control programs, and clinical laboratories to determine if facility attributes associated with timeliness can be identified.

Table 1-1. Nationally notifiable infectious diseases, 2006

Acquired Immunodeficiency Syndrome (AIDS)
Anthrax
Arboviral neuroinvasive and non-neuroinvasive diseases
California serogroup virus disease
Eastern equine encephalitis virus
Powassan virus
St. Louis encephalitis virus
West Nile virus
Western equine encephalitis virus
Botulism
Botulism, foodborne
Botulism, infant
Botulism, other (wound and unspecified)
Brucellosis
Chancroid
Chlamydia trachomatis, genital infections
Cholera
Coccidioidomycosis
Cryptosporidiosis
Cyclosporiasis
Diphtheria

Table 1-1. Nationally notifiable infectious diseases, 2006 (continued)

Ehrlichiosis
Ehrlichiosis, human granulocytic
Ehrlichiosis, human monocytic
Ehrlichiosis, human, other or unspecified agent
Giardiasis
Gonorrhea
Haemophilus influenzae, invasive disease
Hansen disease (leprosy)
Hantavirus pulmonary syndrome
Hemolytic uremic syndrome, post-diarrheal
Hepatitis, viral, acute
Hepatitis A, acute
Hepatitis B, acute
Hepatitis B virus, perinatal infection
Hepatitis C, acute
Hepatitis, viral, chronic
Chronic Hepatitis B
Hepatitis C Virus Infection (past or present)
HIV infection
HIV infection, adult (≥ 13 years)
HIV infection, pediatric (<13 years)

Table 1-1. Nationally notifiable infectious diseases, 2006 (continued)

Influenza-associated pediatric mortality
Legionellosis
Listeriosis
Lyme disease
Malaria
Measles
Meningococcal disease
Mumps
Pertussis
Plague
Poliomyelitis, paralytic
Psittacosis
Q Fever
Rabies (animal or human)
Rocky Mountain spotted fever
Rubella
Rubella, congenital syndrome
Salmonellosis
Severe Acute Respiratory Syndrome-associated Coronavirus (SARS-CoV) disease
Shiga toxin-producing *Escherichia coli* (STEC)
Shigellosis
Smallpox

Table 1-1. Nationally notifiable infectious diseases, 2006 (continued)

Streptococcal disease, invasive, Group A
Streptococcal toxic-shock syndrome
Streptococcus pneumoniae, drug resistant, invasive disease
Streptococcus pneumoniae, invasive in children <5 years
Syphilis
Syphilis, primary and secondary
Syphilis, latent
Neurosyphilis
Syphilis, congenital
Syphilitic stillbirth
Tetanus
Toxic-shock syndrome (other than Streptococcal)
Trichinellosis (Trichinosis)
Tuberculosis
Tularemia
Typhoid fever
Vancomycin – intermediate or resistant *Staphylococcus aureus*
Varicella
Yellow fever

Source: Centers for Disease Control and Prevention. 2006. *Nationally Notifiable Diseases* [Web site]. Center for Disease Control and Prevention [cited February 17, 2006]. Available from http://www.cdc.gov/epo/dphsi/phs/infdis.htm.

Table 1-2. Common criteria for evaluating public health surveillance system performance and their definitions*

Acceptability is the degree to which participants and stakeholders support the system and its operations.
Data quality is the completeness, reliability, and validity of information.
Flexibility is the adaptability of the system to changing objectives and circumstances.
Predictive value positive is the likelihood that events identified are true events under surveillance.
Representativeness is the degree to which characteristics of persons experiencing identified events are distributed consistently with characteristics of all persons experiencing events in the population.
Sensitivity is the likelihood that health-related events under surveillance are identified when they occur.
Simplicity is the ease of use for persons participating in all steps of system operation.
Timeliness is the duration of time intervals between event occurrence, event reporting and report completion as well as information analysis, interpretation and dissemination.

Source: Silk, B., T. H. Hoke, and R. Berkelman. 2007. Public health surveillance. In *Public Health Administration: Principles for Population-Based Management*, edited by L. F. Novick, G. P. Mays, C. Morrow. Sudbury, Massachusetts: Jones and Bartlett Publishers.

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Figure 1-1. Disease reporting event probabilities/case counts and corresponding time intervals: a conditional events perspective.

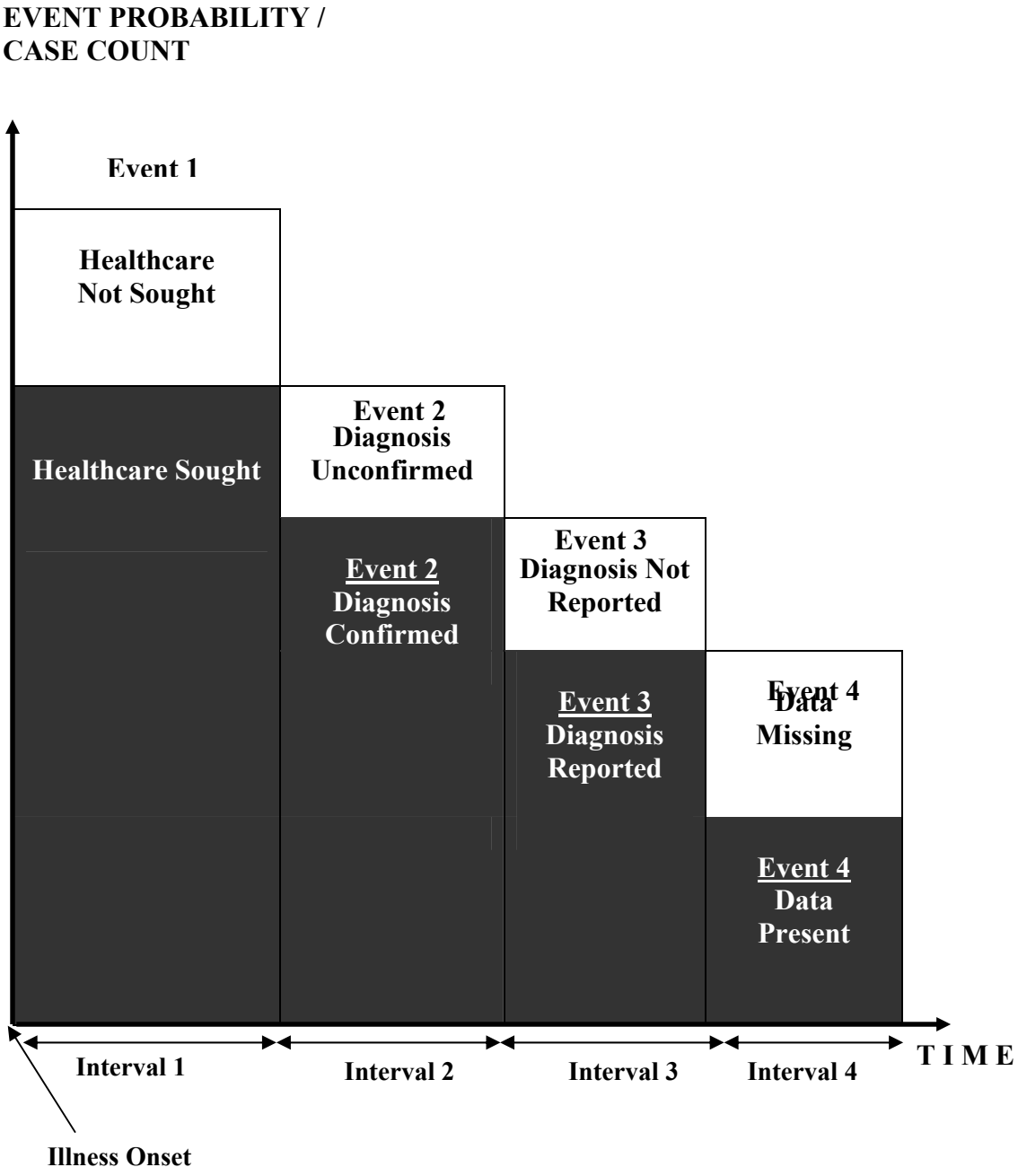
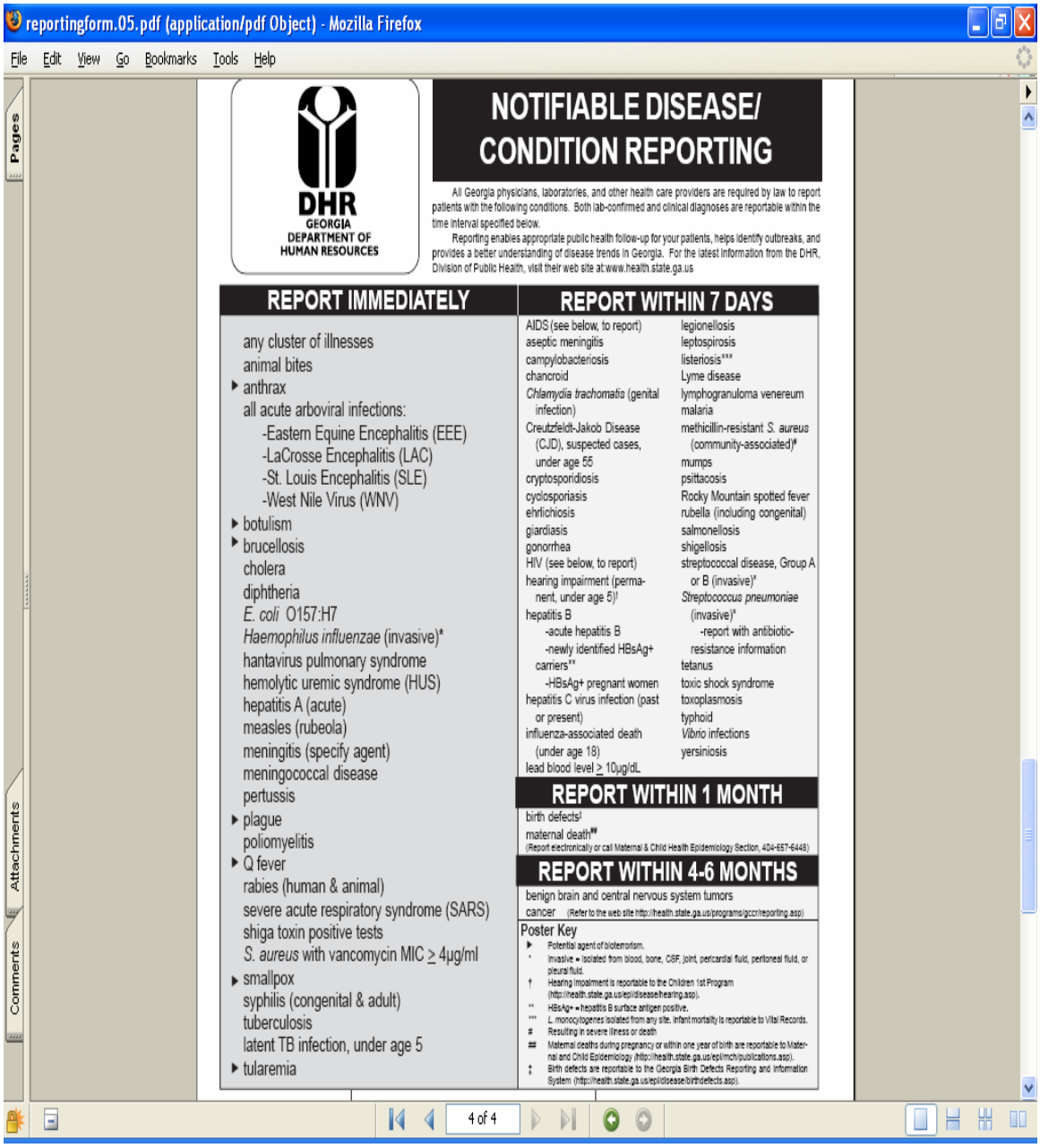


Figure 1-2. Screen capture of the disease reporting poster for the State of Georgia's Department of Human Resources



Source: Georgia Division of Public Health. 2006. Notifiable Disease/Condition Form [Web site]. Georgia Division of Public Health [cited June 8, 2006]. Available from http://health.state.ga.us/pdfs/epi/notifiable/reportingform.05.pdf.

Table 1-3. Select core functions and capabilities of state public health laboratories

1. Disease prevention, control, and surveillance

Provide accurate and precise analytical results in a timely manner for different diagnostic and analytical functions for assessment and surveillance of infectious, communicable, genetic, and chronic diseases, and environmental exposures.

Serve as a first line of defense in rapidly recognizing and preventing the spread of communicable diseases by:

- examining specimens for identifying disease outbreaks;
- isolating and identifying the causative agent;
- determining the source of infection;
- identifying carriers; and
- locating sources of infection in the environment.

Serve as a center of expertise for the detection and identification of biologic agents of significance in human disease; as such, ensure access to laboratory expertise and capabilities in the disciplines of:

- bacteriology;
- virology;
- parasitology;
- molecular microbiology;
- immunology and serology;
- mycobacteriology;
- mycology; and
- hematology and immunohemotology.

Provide specialized tests for low-incidence, high-risk diseases (e.g., tuberculosis, rabies, botulism, and plague); detect epidemiologic shifts; and detect newly emerging pathogens, including but not limited to:

- testing specimens from suspect cases of tuberculosis to identify *Mycobacterium tuberculosis* infections and determine effective antibiotic treatment;
- testing influenza specimens as directed by national and international surveillance efforts to identify viral strains and control influenza;
- testing animal specimens from suspected rabies carriers to detect the virus and ensure that prevention measures appropriately protect humans and domestic animals from exposure; and
- assisting public and private health-care providers in investigating and controlling communicable or environmental diseases.

Provide population surveillance, or screening, for conditions of interest to the public health community, including screening for inherited neonatal metabolic disorders, environmental toxins, immune status, risk factors, chronic blood diseases, blood lead, and antibiotic resistance.

Perform tests to meet specific program needs of public health agencies.

Table 1-3. Select core functions and capabilities of state public health laboratories (continued)

2. Integrated data management

Serve as the focal point for accumulating, blending, and disseminating scientific information in support of public health programs, including:

- capturing laboratory data essential for public health analysis and decision-making;
- ensuring the ability to maintain and communicate laboratory data by using standardized data formats;
- ensuring rapid dissemination of laboratory information to assist in identification, understanding, and controlling disease outbreaks;
- providing primary data necessary to provide information for and implement policy and planning; and
- providing a statewide disease reporting network, with centralized facilities for receipt, storage, retrieval, and analysis of data.

Participate as a key link in national database systems to collect, monitor, and analyze laboratory data, including as the primary data link with CDC for surveillance of diseases of national and global concern.

Serve the data needs of state epidemiologists, other laboratories, and practitioners in identifying trends and sentinel events that indicate emerging health problems.

3. Reference and specialized testing

Serve as the state's primary reference microbiology laboratory to:

- test for, and aid in the diagnosis of, unusual pathogens;
- confirm atypical laboratory test results;
- verify results of other laboratory tests;
- provide oversight for quality assurance;
- test epidemiologically significant specimens with potential public health implications;
- provide reference diagnostic testing to private sector laboratories that might not have the capability to fully identify disease agents of public health significance;
- test for diseases of public health consequence that are too rare or unusual for other laboratories to maintain capacity for testing, including human genetic markers of disease; and
- provide toxicology testing, including drug, alcohol, poison, and trace metal analyses.

Source: Association of Public Health Laboratories. 2002. Core functions and capabilities of state public health laboratories: A report of the Association of Public Health Laboratories. *Morb Mortal Wkly Rep Recomm Rep* 51 (RR-14):1-8.

Table 1-4. Summary of studies' scope, focus area, and novel applications of analytic techniques

Study	Scope	Focus Area	Novel Application of Techniques
1) West Nile fever ascertainment	National	Completeness of case ascertainment	Multilevel analysis of public health systems; WNV syndrome ascertainment ratio applied as a measurable indicator of WNF ascertainment
2) Meningococcal disease serogrouping	National	Extent of missing data	Multilevel analysis of public health systems
3) Timeliness of a state electronic notifiable disease surveillance system	Georgia	Timeliness of reporting	Cox proportional hazards regression for assessment of surveillance timeliness

CHAPTER 2

LITERATURE REVIEW

Public health infrastructure

There is agreement in what comprises and compromises the U.S. public health infrastructure (Baker et al.. 2005; Centers for Disease Control and Prevention 2001). At its foundation exist a multidisciplinary workforce, organizational structure, and information systems (Figure 2-1). A CDC report has characterized factors that are detrimental to this infrastructure (Centers for Disease Control and Prevention 2001). In the United States, complacency toward public health threats, a gap in necessary workforce skills, and suboptimal partnerships were emphasized. Baker and colleagues describe "fragmented and precarious public funding, an uneven and antiquated legal foundation, an inadequate workforce, inconsistent application of information technology, and organizational deficits" (2005). In other words, not only is the foundation of public health's infrastructure weak, but important financial and legal deficiencies also exist.

The national public health workforce includes administrators, environmental health specialists, epidemiologists, laboratorians, nurses, physicians, and other allied health professionals. Their roles also can be considered combinations of program area specialists and generalists who perform a variety of services (Gerzoff and Gebbie 2001). Despite growth in the U.S. population in the last two decades, the size of this workforce has remained relatively constant with 448,254 salaried persons employed at the local (34%), state (33%), and federal (19%) levels (Gebbie et al. 2003). This 2000 estimate

corresponds to one public health worker for every 635 members of the population, a 10% decrease over the 20-year period.

Data from numerous sources consistently reinforce concerns for workforce adequacy. The Council of State and Territorial Epidemiologists (2005) estimated that 2,580 epidemiologists were employed at the state and local levels in 2004. Overall, a 47% increase in staffing was deemed necessary for delivering certain essential public health services, including a 35% larger workforce for infectious disease program areas. The Association of Public Health Laboratories (APHL), which collects data on its member workforce, counts over 14,000 laboratory professionals (Gebbie et al. 2003), but leadership has become a key deficiency issue. Thirteen vacancies in state public health laboratory director (SPHLD) positions were noted during a 5-year period, equal numbers of vacancies were expected subsequently, and doubts that the existing candidate pool could replace current SPHLDs were common (Schoenfeld, Banfield-Capers, and Mays 2002).

In examining the public health workforces of six states with mixed forms of organizational control (CA, GA, MT, NM, NY, TX), the largest challenges to adequacy were financial, but difficulties in recruitment were common for a variety of professions within the field (Health Resources and Services Administration 2005). Data from New York, New Mexico, and Georgia indicated two primary sources of variability in the number of public health workers per capita. First, the per-capita workforce varied among states (61, 67, and 98 public health workers per 100,000 residents in NY, NM, and GA respectively). Second, workers per capita varied across state, urban local, and rural local sectors within states. Georgia had the greatest range across sectors: 10 workers per

100,000 at the state level; 41 per 100,000 at the urban-local level; and 216 per 100,000 at the rural level. The apparent trend of increased workforce coverage (from state to local and rural) is a function of changing population sizes (i.e., denominators) and types of functions performed.

A considerable amount of survey and formative research has characterized the organizational structure of the U.S. public health system. A 2001 survey of state health officers found that state health agencies often (56%) were free standing agencies, but almost equally often (44%) were located in health and human services "superagencies" (e.g., the Division of Public Health within the Georgia Department of Human Resources) (Beitsch et al. 2006). In the 2001 survey, use of health districts (an administrative level between state and local health departments) also was common (44%), particularly in southeastern states like Georgia (Figure 2-2) (Georgia Division of Public Health 2005).

The degree of centralization in structure and local oversight has varied among state health agencies over time. In reporting results of a 1974-1975 survey of local health officers, DeFriese and colleagues (1981) established a common organizational typology for state and local health departments' relationships. Centralized (33%), decentralized (33%), and shared (30%) organizational control were relatively common, while 6 states utilized mixed organizational structures (13%). Definitions for these categories and categorization of 46 states are presented in Table 2-1. A comprehensive *Profile of State and Territorial Public Health System* in 1991 (Centers for Disease Control and Prevention) listed 20% of states as centralized, 32% as decentralized, 14% shared, and 32% mixed typologies. In 2001, half of states (53%) shared responsibilities at the state and local levels; 24% of state health agencies guided LHDs completely, while 22% of

states were fully decentralized (Beitsch et al. 2006). Three features were significantly more common in states reporting supervision of local health operations: centralized control, district structure, and southern geography.

Using data from the National Association of City and County Health Officials (NACCHO) and the 1992 U.S. Census of Governments, Wall (1998) described interactions between state and local health departments by cross-tabulating percentages of local control over statewide health budgets and local contributions to the total share of LHD revenue in 13 states. Relative to the national average for both percentages, two or more states were positioned in each of four quadrants of control and revenue. High local control and revenue in Texas and Wisconsin indicated the most decentralization, while LHDs in Alabama and Florida had the lowest control, the lowest revenue, and therefore were the most centralized. Several states had high control and low revenue (CA, MI, MN, and NY), which may be considered ideal from a local perspective since dependence on tax support is low without compromising autonomy. In Massachusetts and New Jersey, more public health funds are generated locally, but local health boards have minimal staff, budgets, and spending authority.

Most states had local public health agencies organized as city/county combinations (51%) and county only (40%) health departments within their jurisdictions in 2001. City/county health departments were significantly more common in the Midwest and in states with non-centralized control; county-only configurations were more common in the West, South, and in centralized states (Beitsch et al. 2006).

Detailed cost data for public health services are not yet widely available (Institute of Medicine 2003). A national measurement system has not been established (Leviss

2001) and financing studies have often focused on public health agency budgets, rather than the public health system as a whole (Institute of Medicine 2003). Many studies of public health systems use simpler measures (e.g., per capita spending), conceding that each jurisdiction has a distinct approach to organizing and financing services. From a public health systems research standpoint, however, substituting financing for expenditures data may be problematic because expenditures are a potentially uncalibrated and relative measure of resources for service delivery. Noting that LHD per capita expenditures are variable (National Association of City and County Health Officials 2006) says little about the sufficiency or efficiency of spending across LHD jurisdictions.

Gostin and Hodge describe a diverse and complex array of state public health laws in the United States (Gostin and Hodge 2002). The scope of statutory definitions for public health ranges from relatively narrow views (e.g., disease prevention and control) to listings of public health service and broad summations of responsibilities and duties. Georgia code (GA Code Ann. § 31-2-1 2000) defines a broad set of 10 empowerments such as epidemiologic investigations and laboratory facilities for detection and control of disease, as well as research, investigation, and information dissemination. Since 1990, many states surveyed indicated that bills on public health infrastructure (71%) or comprehensive public health reform (46%) had been introduced, but fewer had passed in state legislatures (Gostin and Hodge 2002).

In comparing results from a 1989 survey of state health officials (Scott, Tierney, and Waters 1990) with their 1996 follow-up survey, Scutchfield and others found only a 3% increase in the number of states reporting modern disease control statutes (69%) (Scutchfield et al. 1997). Twenty-seven percent were developing this legal infrastructure

in 1996. In Wisconsin, Zahner and Vandermause (2003) noted that inadequate reporting of disease notification violations was the most common instance of noncompliance with state public health statutes and administrative rules among 93 LHDs.

To address deficiencies in the public health infrastructure, in 2001 CDC proposed an ambitious national effort (Centers for Disease Control and Prevention). Goals and recommendations for meeting them were set for the year 2010. For example, the goal set for effective health departments and laboratories is that each "will meet basic performance and accountability standards that recognize their population base, including census, geography, and risk factors, with specific needs identified through state public health improvement plans (Centers for Disease Control and Prevention 2001). A recommendation to meet that goal is to "ensure that each health department has access to rapid, high-quality testing and that standards for specimen collection, transport, testing, confirmation, and reporting are utilized." Notably, performance standards are emphasized as an integral part of building capacity through the CDC initiative.

Public health systems research

The Future of Public Health by the Institute of Medicine (IOM) (1988) is widely considered to have catalyzed contemporary efforts to understand and improve the local-state-federal public health system in the United States (Baker et al. 2005; Scutchfield et al. 1997; Turnock and Handler 1997). In the report, three core public health functions for governmental agencies were established: assessment, policy development, and assurance. By design, these functions correspond to stages for solving public health problems and a number of federal initiatives began in response to the report (Turnock and Handler 1997).

With representation from key national public health organizations, CDC led an effort to identify the specific activities necessary to fulfill the IOM's core functions (Dyal 1995). Similarly, essential public health services were identified following healthcare reform discussions during the Clinton administration (Baker et al. 1994). A primary result of these efforts was consensus in sets of 10 essential public health practices/services that could be monitored nationally in relation to the larger IOM functions (Table 2-3) (Derose et al. 2002).

In addition, the Healthy People 2000 objective to "increase to 90% the proportion of people who are served by a local health department that is effectively carrying out the core functions of public health" was established (U.S. Public Health Service 1990). To track progress in reaching this objective, CDC began funding research projects through schools of public health in 1991. These projects would design and establish a surveillance system for monitoring the effectiveness of the public health system and thereby "benchmark" the status of public health practice at the local level. Varying sets of indicator questions were developed to measure the extent to which the 10 public health practices/services were being effectively delivered, and by extension, the IOM functions were being achieved (Turnock, Handler, and Miller 1998).

Local public health performance measurement during the 1990s affirmed the IOM's characterization of a public health system in disarray; that is, much of the U.S. population was not receiving effective public health services (Richards et al. 1995; Turnock et al. 1994; Turnock, Handler, and Miller 1998). A 1993 stratified random sample of 208 LHDs estimated that 31% were functioning effectively, defined as any 7 of the 10 practices performed (Turnock et al. 1994). Using a different approach in 1993,

Richards and others coordinated with states' local health liaisons (AL, MD, NJ, WI) and district health offices (SC, MS) to survey 370 LHDs on effectiveness (Richards et al. 1995). Mean percent performance measures, which were based on 26 indicators, differed for the IOM's three core functions (assessment, policy development, and assurance). Assurance-related performance indicators were higher (68%) than corresponding policy development (53%) and assessment (43%) measures.

Research teams from the University of North Carolina and the University of Illinois-Chicago schools of public health subsequently collaborated in merging previous indicators (Handler et al. 1995; Miller et al. 1995) into the now widely adopted 20 *Core Function-Related Measures of Local Public Health Practice Performance* (Turnock and Handler 2001) (Table 2-4). Among them, three assessment measures are particularly relevant to the dissertation: 1) "For the jurisdiction served by your local public health agency, are timely investigations of adverse health events, including communicable disease outbreaks and environmental health hazards, conducted on an ongoing basis?" 2) "Are the necessary laboratory services available to the local public health agency to support investigations of adverse health events and meet routine diagnostic and surveillance needs?" 3) "For the jurisdiction served by your local public health agency, has an analysis been completed of the determinants and contributing factors of priority health needs, adequacy of existing health resources, and the population groups most impacted?"

In 1995, Turnock, Handler, and Miller applied their 20 indicators to a stratified sample of LHDs (1998). Effectiveness was found for only 22% of LHDs (when defined as performing four of six assessment-related activities, four of six policy development-

related activities, and six of eight assurance-related activities). Scores for specific indicators varied from 23% for conducting an analysis of age-specific participation in preventive and screening services to 94% for timely investigations of adverse health events conducted on an ongoing basis. Availability of necessary laboratory services to support investigations of adverse health events and meet routine diagnostic and surveillance needs was also high (89%).

In monitoring the effectiveness of public health service delivery, several factors associated with performance were also identified. In a 1993 stratified random sample, larger health departments serving populations greater than 50,000 self-reported higher compliance in assessment (63% vs. 50%) and policy development (50% vs. 44%), but not assurance-related practices (61% vs. 59%) (Turnock et al. 1994). Using six population size categories ranging from less than 25,000 to greater than 500,000, Richards and colleagues did not find a trend in increased mean percent performance of 26 indicators with LHDs serving increasing population sizes (1995). However, health departments serving more than 100,000 residents had better performance measures (66%) compared with those serving less than 100,000 residents (54%) ($p < 0.05$).

Type of organizational control also was identified as an important performance correlate (Richards et al. 1995). On average, shared typologies had the lowest performance of the 26 indicators (48%, 95% confidence interval [CI] = 44-51%). Decentralized organizations were intermediate (53%, 95% CI = 51-56%) and centralized organizations performed an average of 68% of the indicators (95% CI = 64-71%). A review of enteric disease surveillance activities in six states found key differences in three timeliness endpoints by organization type (Hedberg 2005). Decentralized states,

which interviewed cases through their LHDs, were able to conduct interviews 3 days faster (median = 4 days) than centralized states (median = 7 days). States with centralized reporting, on the other hand, completed pathogen molecular subtyping 9 days earlier (median = 4 days) than decentralized counterparts.

Handler and Turnock (1996) merged data from their 1993 survey (Turnock et al. 1994) with NACCHO's profiles of LHDs from 1992-1993 (National Association of City and County Health Officials 2006). The analysis was exceptional because it extended assessment of performance correlates beyond jurisdiction size and type. Using regression, four correlates remained independently associated with effectiveness: total number of staff, total annual expenditures, private health insurance as a significant budget source, and a female LHD director. Unlike previous studies, no relationship between LHD effectiveness and size or type of jurisdiction was identified.

Efforts to track performance and associated capacity to deliver public health services, at both the local and state levels, continued to advance after the turn of the century. Suen and Magruder (2004) conducted the first national and territorial survey of LHDs' capacities to meet the IOM core functions using the 20 core function-related indicators (Table 2-4). Mean scores increased consistently with population sizes, from 58% for jurisdictions with less than 25,000 to 74% for jurisdictions with over 500,000 residents. Scores also varied by type of jurisdiction (range: 55%-75%). With the exception of the smallest jurisdictions (< 25,000 residents), where assessment indicators were 5-12% lower than larger LHDs, an appreciable size trend was not present for timely investigations (range: 96-98%) or offering laboratory services (92-94%). Timely investigations and offering laboratory service were almost always reported for county,

city/county, district, and regional jurisdictions (94-98% and 90-98%, respectively). City/municipal jurisdictions less often performed timely investigations (90%) or offered laboratory services (88%).

Using the 20 core function-related indicators (Table 2-4), Mays and colleagues assessed availability and effectiveness of public health services in 71% of LHDs that serve jurisdictions larger than 100,000 residents (Mays et al. 2004). Several correlates of availability of public health services and perceived effectiveness of service delivery were identified (Mays et al. 2004). Five correlates were significantly related to service availability: larger population size ($p < 0.05$), lower percentage of the population below poverty level ($p < 0.01$), higher LHD spending per capita ($p<0.05$), presence of a local health board with policy authority ($p < 0.05$), and absence of centralized state-local administrative authority ($p < 0.05$). Perceived effectiveness was also significantly related to lower percent below poverty level ($p < 0.05$), higher LHD spending ($p < 0.10$), and a policymaking health board ($p < 0.01$) as well as a lower non-White percentage in the population ($p < 0.05$).

The National Public Health Performance Standards Program (NPHPSP) was released in 2002 as a national collaboration (Centers for Disease Control and Prevention 2006). Delivery of essential public health services, such as diagnosis and investigation of health problems (essential service 2), is measured through a set of indicators that are assessed through specific questions. Examples of specific questions include: "Do community health professionals submit timely reportable disease information to the state or local public health system?" and "Does the local public health system maintain ready access to laboratories capable of meeting routine diagnostic and surveillance needs?"

Completed NPHPSP assessments have provided new opportunities to identify correlates of public health system performance (Mays et al. 2006; Scutchfield et al. 2004). NPHPSP data from 2000-2001 were linked with NACCHO profiles of LHDs from 1996-1997 to assess potential relationships between 152 LHDs' capacities and system performances (Scutchfield et al. 2004). Multivariate analyses, where performance of the 10 services and total service performance were each modeled separately, explained between 24% and 45% of performance variability (R^2 range: 0.24-0.45). Significant predictors for diagnosis and investigation of health problems included: staff FTEs/100,000 population, expenditures per staff FTE, presence of a director with a Master's degree, and partnerships with university/academic centers. Total service performance was also related to three of the four predictors: expenditures per staff FTE, a director with a Master's degree, and partnerships with university/academic centers.

In another study (2006), Mays and colleagues merged NPHPSP assessments with county-level data from the 1996-1997 LHD profiles (National Association of City and County Health Officials 2006), demographic and health-related data for 2000 (Health Resources and Services Agency 2006), and Census data on federal spending for 2000 (U.S. Census Bureau 2005). Random-effects regression models were used to estimate the effects of health agencies' and communities' characteristics on performance of each of the 10 essential services (Table 2-3). Model terms captured performance variability across both states and public health systems within states.

Increased LHD spending per capita was strongly associated with performance of all 10 essential services ($p < 0.01$), while federal spending per capita was associated with 5 of 10 services ($p < 0.05$). The largest positive association with performance was in

communities of 20,000-100,000 residents. Smaller positive associations were found in communities with more than 500,000 residents while the largest communities had lower performance scores. Combined city-county governments were independently associated with increased performance of 4 services ($p < 0.05$), including diagnosis and investigation of health problems. Relative to shared administrative authorities, both centralized and decentralized relationships improved performance of some services and decreased performance of others (including diagnosis and investigation of health problems in both cases). Although physician density (per 100,000 residents) was not found to be significantly associated with most services, it was a significant predictor of diagnosis and investigation of health problems ($p < 0.05$). Community poverty rates were associated with performance of 5 services but not diagnosis and investigation. LHD staffing (per 100,000) was not an important predictor of performance.

Public health systems research at the state level has been relatively heterogeneous compared with the directed performance assessment efforts among LHDs. Researchers have assessed agencies' abilities to meet internal, state-specific standards (e.g., rules, regulations) (Mays, Halverson, and Miller 1998; Zahner and Vandermause 2003) and state health agencies' abilities to meet national performance standards (Ford, Duncan, and Ginter 2005; Scutchfield et al. 1997). In surveying 50 state health agencies, Mays, Halverson, and Miller (1998) found that overall most states' public health organizations (88%) were participating in performance assessment of local health agencies to some extent, although states with mixed organizational control over public health (Table 2-1) participated less often (76%) and decentralized states participated more often (93%). Increased percentages of the population below the federal poverty level and increased

percentages of the population receiving Medicaid were identified among assessment participants relative to non-participant states ($p < 0.01$).

Scutchfield and colleagues assessed changing compliance with the IOM core public health functions by comparing surveys from 1989 and 1996 of state health officials (1997). The existence of assessment activities was common (80%) in 1996 and had changed minimally since 1989 (-2%); assurance was less common (58%) but also changed minimally (+2%). Existing policy development activities were reported in half of the states (49%) and had decreased by 23%.

The focus on intermediate outcomes (Figure 2-3), such as delivery of public health services, is a key facet of the public health systems research described above (Derose et al. 2002). Few studies have attempted to link system performance measures with actual changes in health status (i.e., ultimate outcomes). Using data from the UnitedHealth Group's year rankings of states' health (UnitedHealth Group 2001), Ford and others assessed the impact of core public health functions in changing population health from 1990 to 2000 for 41 states (2005). Configurations of the IOM core functions were analyzed using qualitative comparative analyses and descriptive materials from state health agencies. An equation emerged in which all three functions (i.e., assessment, assurance, and policy development) as well as either resource availability or adaptability/proactivity were necessary correlates of improvements in population health.

Sources of bias in disease reporting

The requisite collaborations with the healthcare system that enable disease reporting also create the potential for bias. Romaguera and others describe two important

biases that may result from public health surveillance: case ascertainment and information bias (2000). *Case ascertainment bias* refers to differential testing, confirmation, and reporting of surveillance cases from different strata of the population. *Information bias* occurs when the public health agency receives reports of diagnosed cases, but data elements are either missing or incorrect differentially across population strata. The contextual framework in the introduction described how absent events in the conditional events series lead to incomplete morbidity reporting (Figure 1-1). Events in this series may be absent for specific reasons described below.

Barriers to etiologic diagnosis of infectious diseases are systematic (event 2, Figure 1-1). For example, the Infectious Disease Society of America guidelines for community-acquired pneumonia in immunocompetent adults (Mandell et al. 2003) indicate that testing for an etiologic agent is only considered the standard of care in hospitalized patients. Simple diagnostic tests, such as pretreatment blood cultures or Gram stains of expectorated sputum, are not recommended care for ambulatory patients. While empiric therapy may be appropriate from a clinical standpoint, without diagnosis diseases events such as pneumococcal pneumonia and legionellosis do not meet case definitions for inclusion in surveillance activities. Hospitalized patients with the most severe disease are more likely to be represented in diagnosed case reporting. Culturing enteric, bacterial pathogens from stool specimens illustrates how laboratory testing practices may be another barrier to etiologic diagnosis of infectious disease. A survey of 388 clinical laboratories (testing ~339,000 stool specimens in 1999) found that these laboratories routinely tested for *Salmonella, Shigella,* and *Campylobacter* species but less

than 60% of the laboratories tested for *E. coli* O157:H7 (57%), *Y. enterocolitica (50%),* or *Vibrio* species (50%) (Voetsch et al. 2004).

Barriers to reporting of diagnosed cases (event 3, Figure 1-1) are also numerous. Collaboration in the disease reporting system is voluntary. Reporting may be a relatively low priority for many healthcare providers who lack the time, incentives, or willingness to report or are unaware of the importance of reporting (Birkhead and Maylahn 2000). Physicians' surveys on disease reporting also have indicated a lack of awareness of the procedural aspects of reporting (Weiss, Strassburg, and Fannin 1988), the specific pathogens that are reportable (Konowitz, Petrossian, and Rose 1984), and the existence of case definitions for reportable diseases (Krause, Ropers, and Stark 2005). Confidentiality concerns have also been cited and physicians may not have information required for reporting readily available in patients' medical records (Jones et al. 1992).

Rothenberg and colleagues (1980) used gonorrhea reporting in metropolitan Denver to systematically assess putative reasons for physician underreporting through corresponding randomized interventions among five groups totaling 648 physicians and a control group of 946 physicians. Interventions (and putative reasons for underreporting) included the following: 1) a letter requesting participation in disease control efforts (saliency of reporting); 2) a letter acknowledging the conflict between physician loyalty to patients and professional duty to safeguard public health (patient interference in reporting); 3) a letter requesting numbers of patients with gonorrhea and reasons for not reporting (e.g., violation of doctor-patient confidentiality, burden of case follow-up); 4) a thank you note with a report on STIs (an incentive); and 5) an introductory letter and subsequent telephone call to arrange for periodic phone communication requesting

disease reports from physicians' staff (administrative obstacle). During the follow-up year (1976), only the removal of administrative obstacles led to significant increase in gonorrhea reporting ($p < 0.01$). Increases were greatest for physicians who had not previously reported and physicians who practiced medicine alone.

Because most case definitions for reportable diseases require laboratory confirmation (Silk and Berkelman 2005), state laboratory reporting requirements became a common way to circumvent physician underreporting (Sachs 1985). Yet after establishing mandatory laboratory reporting in Vermont in 1980, a survey of 192 physicians identified assumptions that the laboratory is reporting as the most common (66%) reason for noncompliance with disease reporting requirements (Schramm, Vogt, and Mamolen 1991). The 1986-1987 study also determined that laboratories had submitted 71% of 1,636 initial reports of confirmed cases for 11 diseases. The percentages of initial reports received from Vermont laboratories varied according to the disease reported. Most initial laboratory reports were enteric pathogens (*Salmonella*, *Campylobacter*, *Shigella*, and *Giardia* species). Approximately 25% of notifications for measles, *B. pertussis*, *H. influenzae* and *N. meningitidis* were from laboratories.

Physicians practicing in Georgia were frequently unaware of the immediacy of reporting requirements (23%) and that illness clusters also are reportable events (59%) (Silk et al. 2006). Again, the most common reason (55%) for not reporting was the belief that other entities report (e.g., clinical laboratories, infection control professionals). Georgia physicians frequently (64%) selected 'others report' as the sole basis for not reporting. A review on changing physician behavior, albeit in relation to quality of care,

suggests that guideline implementation and educational outreach may be effective (Bauchner, Simpson, and Chessare 2001).

Case finding in a stratified random sample of laboratories in Oklahoma found similar results as the Vermont study (Harkess et al. 1988). Of 69 *Shigella* cases reported during a six-month period in 1985, three had been reported by physicians. Laboratories in large hospitals (200 beds or more) were more likely to have reported *Shigella* than laboratories in smaller hospitals (reporting ratio [RR] = 2.5, 95% CI = 1.1-3.9) or reference laboratories (RR = 4.7, 95% CI = 1.2-55.9).

Smucker and Thomas (1995) found that completeness of reporting of gonorrhea (72%) was higher than reporting completeness for chlamydia (55%) among physicians in a rural North Carolina county with high rates of several STIs. The difference was attributed to the state's relatively newer chlamydia reporting requirements, which had been established in the previous five years.

A large number of publications have documented variability in completeness of infectious disease morbidity reporting (Doyle, Glynn, and Groseclose 2002). Many of these studies have identified specific populations and care settings in which AIDS cases are underreported. In South Carolina, state health department officials used hospital discharge billing records to identify 62 unreported AIDS cases from January 1, 1986 to June 30, 1987 (Conway et al. 1989). Reporting was more complete for Whites (72%) than for Blacks (53%).

A 1988 CDC-sponsored, multisite study of completeness of AIDS reporting also compared hospital discharge records with AIDS reporting systems (Rosenblum et al. 1992). Reporting completeness in hospitalized patients was 92% overall and above 90%

for adults, both genders, Blacks and Whites, several exposure categories (men reporting sexual contact with men, heterosexual contact, and persons reporting injecting-drug use), and among persons diagnosed before 1988. Site-specific analyses identified lower reporting rates in Maryland children under 12 years of age (61%, 95% CI = 24-80%), lower reporting in persons with no identified mode of HIV exposure in Los Angeles County (50%, 95% CI = 30-64%) and Georgia (77%, 95% CI = 53-86%), lower reporting in Maryland residents with blood/blood product HIV exposures (79%, 95% CI = 53-88%), and lower reporting among Blacks (89%, 95% CI = 68-90%) in Washington State relative to Whites (98%, 95% CI = 96-98%). In two sites with Medicaid data available as a secondary data source, outpatient reporting was lower (90%, 95% CI = 79-90%) than inpatient reporting (95%, 95% CI = 95-99%). Another study confirmed these latter findings. In San Francisco, alternative case finding among a weighted sample of 11 hospitals, 28 clinics, and 328 private physicians' offices found lower reporting completeness (75%) in offices that diagnosed AIDS ($p < 0.001$) (Schwarcz et al. 1999).

Reporting AIDS diagnoses from outpatient care settings has an effect on surveillance. A review of active surveillance data in Oregon and Washington found a significant increase ($p < 0.001$) in the proportion of outpatient AIDS diagnoses from 1987 (24%) to 1990 (51%) (Modesitt et al. 1993). Whites, residents of Multnomah and King Counties (the Portland and Seattle urban areas), persons with homosexual/bisexual contact, and persons diagnosed with AIDS-defining illnesses other than *Pneumocystis carinii* pneumonia were each significantly more likely to be diagnosed in outpatient care settings. Since reporting completeness was also lower in outpatient settings, the resulting

differential reporting completeness across population strata is an example of case ascertainment bias.

Findings from an enhanced AIDS surveillance effort contradict the studies described above. In a 1986 Oregon study, 29 unreported cases were identified by four case-finding techniques (Modesitt, Hulman, and Fleming 1990). The newly identified AIDS reports did not differ from previous reports in terms of case characteristics (age, race, county of residence, risk factors, vital status, or disease at diagnosis); physician characteristics (specialty, city of practice, or whether a previous AIDS report had been submitted); or hospital characteristics (whether a previous AIDS report had been submitted, number of beds, or location). The authors also acknowledged that their ability to detect significant differences may have been diminished by the small number of reports.

Studies of reporting completeness also have identified populations and care settings in which other infectious diseases are underreported. Investigation of an outbreak of drug-resistant *Shigella sonnei* in 1978 provided an opportunity to review the utility of the disease reporting system in the District of Columbia (Kimball, Thacker, and Levy 1980). Incomplete reporting led to a 6-month delay in recognition of the outbreak, delayed identification of drug resistance in the organism, and the potential for spurious conclusions about geographic clustering of cases.

Case reporting rates increased 52% in a 6-month period of active surveillance for acute viral hepatitis in Pierce County, Washington compared with the average rates reported during the previous 6-month period with passive surveillance (Alter et al. 1987). Most of the increased reporting came from private physicians for infections of hepatitis B

and hepatitis non-A, non-B. When newly identified exposure categories were examined, most individuals with hepatitis B infection were homosexual men and most hepatitis non-A, non-B infections were among persons who had undergone blood transfusions.

Reporting of pertussis is notoriously low because sensitive and specific laboratory methods are lacking, clinically atypical cases are common in infants, less severe, undetected disease occurs in adolescents and young adults with partial immunity from previous vaccination, and no laboratory testing may be performed for older children and adults (Sutter and Cochi 1992). In a national evaluation of completeness of pertussis reporting, the authors calculated that pertussis-related hospitalizations and mortality were at least three times higher than reported rates.

Many completeness of reporting studies are limited by their focus on ascertainment of diagnosed cases. Diagnosis in the conditional series is presumed to have occurred, despite the aforementioned barriers to etiologic diagnosis. Assessments of the extent of incomplete case ascertainment attributable to underdiagnosis and underreporting are lacking. In one study, the incidence of *E. coli* O157 was estimated to be 31% (Minnesota) to 240% (Georgia) higher than the reported incidence after estimating the proportions of physicians and laboratories for which stool culturing of *E. coli* O157 was inadequate (Bender et al. 2004).

Another study found differences in gonorrhea testing and reporting following a review of 936 medical records from three distinct District of Columbia emergency departments (EDs) during the 2-month study period (Kirsch, Shesser, and Barron 1998). In a community ED with a hospital policy requiring confirmatory testing of all suspected STIs and a part-time public health nurse to monitor testing and reporting, presumptive

treatment (without testing) was least common (9%). Sixty-two percent of patients were treated presumptively in a university-affiliated ED where testing was done in the hospital's laboratory for difficult diagnoses only. Cultures were not considered clinically useful and recontacting patients was deemed problematic at the facility. Presumptive treatment in a public ED that sent gonorrhea cultures to the public health laboratory was also common (33%). Differences in the proportions of presumptive treatment among the three EDs were significant ($p < 0.01$). Presumptive treatment was also more common in men (43%) compared with women (19%) and had a direct impact on gonorrhea reporting. The authors estimated that the 220 presumptively treated patients who were clinically diagnosed and should have been reported would have doubled the number of gonorrhea reports in the three EDs. Adding to the problem, the university hospital also had significantly lower reporting completeness (39%) than its community (94%) and public (100%) counterparts.

Race and ethnicity data

Among racial and ethnic minorities, a number of factors may create bias in surveillance data. Lindan and colleagues identified sources of AIDS mortality underreporting among minorities in the San Francisco Bay Area (1990). The frequency of deaths not attributed to AIDS in 1985 and 1986 was roughly equivalent for Whites, Blacks, and Hispanics (5-8%). Incorrect registration as still living was more common for Blacks (9%) and Hispanics (12%) than for Whites (5%) and incorrect race/ethnicity classification was significantly higher for Hispanics (20%). Using supplemental data from a patient registry to identify American Indian/Native American women who were

classified as White increased rates of chlamydia, gonorrhea, and syphilis by 32%, 57%, and 27%, respectively, in Oklahoma's STI surveillance data (Thoroughman et al. 2002).

Agreement between published and self-reported race/ethnicity is frequently lower for non-Whites (Boehmer et al. 2002). When self-reported race and ethnicity survey data were compared with Veterans Affairs data, Whites were incorrectly classified far less frequently (2%) than Blacks/African Americans (5%), Hispanics (14%), Asians (14%), and American Indians (71%). Allowing for multiple race classifications further increased misclassifications, particularly for Asians (38%) and American Indians (78%).

Blustein compared racial classifications in initial and subsequent admissions for myocardial infarction at another hospital (1994). Classifications were concordant for Whites (kappa = 0.72) and Blacks (kappa = 0.89) but a third category for all other races (including Asians and American Indians) was less concordant (kappa = 0.43). Self-reported race/ethnicity from survey data were largely concordant with HIV/AIDS surveillance data for White non-Hispanics, Black non-Hispanics, and Hispanics but not Asian/Pacific Islanders or American Indian/Native Americans (Lee et al. 2003).

Studies have also documented a lack of standardization in collection of race and ethnicity data in hospital settings where many cases were ascertained. Gomez and colleagues surveyed 60 hospital administrators in the San Francisco Bay Area on collection of race and ethnicity (2003). Most (85%) hospitals reported always collecting race data, while more than half (55%) never collected ethnicity. Race and ethnicity were obtained from a variety of sources, including from the patient or patient's family or friends, from birthplace or language, by noting physical appearance or surname, and from medical records. A study of race and ethnicity in 169 public health information systems

from six New England states found that 12% did not collect race/ethnicity, 34% collected race but did not have a separate field for ethnicity, and numerous other classification inconsistencies were noted across the data systems. Given the importance of race and ethnicity data in accurately assessing disparities in rates of reportable diseases, the extent to which these data are incomplete, inconsistent, and invalid is remarkable.

Incomplete race and ethnicity information in disease surveillance data pose a distinct missing data problem. The conventional approach to this problem has been to limit reporting of race- and ethnicity-specific incidence rates to case reports where these data are available (i.e., an 'available case only' analysis) (Buehler et al. 1989; Centers for Disease Control and Prevention 1992; Centers for Disease Control and Prevention 1999). This raises the question as to whether racial and ethnic frequency distributions are equivalent for cases with known race/ethnicity and cases with unknown race/ethnicity (Ross et al. 2004).

Several strategies for collecting or identifying race and ethnicity have been documented in the literature. A study in Massachusetts had limited success contacting patients' healthcare providers to request the race and ethnicity of patients seen for STIs (Chen et al. 2003). Morgan and others (2004) established the validity of combining surname matching with race in Medicare data to identify Hispanic and White elderly males in 16 U.S. counties and five states. Race and ethnicity data were relatively concordant for Whites (kappa = 0.87), Blacks (kappa = 0.95), and Hispanics (kappa = 0.86) when compared with self-reported data from surveys. County-specific race and ethnicity percentages obtained from the augmented data were also consistent with self-reported data from the U.S. Census. In New Mexico, surveillance officials have noted

that American Indians/Native American often have Hispanic surnames, which invalidates the approach (personal communication, Karen Edge, New Mexico Emerging Infections Program).

Studies evaluating Census-based race/ethnicity ascertainment from geocoding to the block level have reported mixed results. In Southern California (a demographically diverse region) mean percentages of the Blacks and Asians in census blocks were poor predictors of race recorded during hospitalize admission with Kaiser Permanente (Chen, Petitti, and Enger 2004). An evaluation in Detroit was more successful in distinguishing Blacks and Whites; there was 95% agreement with death certificates using 1980 Census data (Andjelkovich et al. 1990). A more recent study in North Carolina suggested that the technique works best for identifying Whites (85%) (Kwok and Yankaskas 2001).

Studies have also shown that race and ethnicity coding oversimplifies self-reported identities. In Chicago, researchers demonstrated that patients preferred to answer questions about race and ethnicity through open-ended questions. Allowing for responses in their own terms led to more accurate data, such as country of origin, and required 37 seconds on average for responding (Baker et al. 2006). A comparison in North Carolina of live birth records using National Center for Health Statistics (NCHS) coding with mothers' self-reported race showed a wider variety of category combinations than White, Black, or American Indian because Hispanic mothers typically list their race as Hispanic (i.e., other race), which is recoded as White for NCHS data (Buescher, Gizlice, and Jones-Vessey 2005).

Completeness of West Nile fever ascertainment

Documented evaluations of disease reporting often focus on surveillance sensitivity (Table 1-2), which is also described as completeness of reporting (Doyle, Glynn, and Groseclose 2002). Completeness of reporting generally refers to the proportion of diagnosed cases for which public health receives notification. This criterion is important because disease reports collectively form the surveillance data. Therefore, complete reporting increases the likelihood that endemic disease will be characterized accurately by using data that are representative of all case patients in a jurisdiction.

From the conditional events perspective, however, completeness of reporting measures the probability of event 3 given events 1 and 2. The use of diagnosed cases as a denominator for measuring completeness of reporting either implies that diagnosis is expected (e.g., AIDS) or may concede that addressing underdiagnosis, as a source of incomplete ascertainment, is beyond the scope of the evaluation. This concession may be appropriate if the intent of the evaluation is to identify and initiate measures to increase reporting of diagnosed cases. Populations and care settings in which AIDS (Fife, MacGregor, and McAnaney 1993; Lindan et al. 1990; Modesitt, Hulman, and Fleming 1990; Modesitt et al. 1993; Rosenblum et al. 1992; Schwarcz et al. 1999) and other diagnosed infectious diseases are underreported have been identified using this concession (Alter et al. 1987; Kimball, Thacker, and Levy 1980; Kirsch, Shesser, and Barron 1998; Markowitz et al. 1987; Sutter and Cochi 1992).

Many acute infectious diseases are treated empirically without etiologic diagnosis. Reportable disease examples include persons with pneumococcal pneumonia and

legionellosis discharged with diagnoses of community-acquired pneumonia and persons with salmonellosis discharged with diagnoses of gastroenteritis. In the absence of an etiologic diagnosis, these symptomatic disease events do not meet case definitions for inclusion in reportable disease surveillance counts (Centers for Disease Control and Prevention 1997). In other words, reporting cannot occur because specific diagnosis is absent. For this reason, sensitivity is defined more broadly as completeness of case ascertainment in Study 1. These terms highlight the importance of etiologic diagnosis, a prerequisite of reporting based on case definitions.

The clinical and epidemiologic characteristics of WNV disease provide a model for investigating the extent to which demographic, geographic, and programmatic characteristics contribute to variability in case ascertainment. The spectrum of symptomatic WNV infection includes a non-localized, self-limited febrile illness (WNF) and more severe neuroinvasive diseases (i.e., encephalitis, meningitis, or flaccid paralysis). These two clinical syndromes can be discretely categorized in a clinical setting and are distinguished using surveillance case definitions.

WNF and West Nile neuroinvasive disease (WNND) cases progress through the conditional events series differently. Given its severity, persons with WNND are likely to seek healthcare and be hospitalized (Patnaik, Harmon, and Vogt 2006). The conspicuous signs and symptoms that typically result from meningitis and encephalitis (e.g., high fever, headache, disorientation, paralysis) raise physicians' indices of suspicion such that etiologic diagnosis is often pursued. Many state health departments also promoted testing and diagnosis of WNND, particularly during epidemic periods. In 2004, for example, states frequently reported contacting infectious disease specialists

(82%), critical care specialists (57%), and neurologists (60%) to increase clinical suspicion and reporting of arboviral encephalitis (Council of State and Territorial Epidemiologists 2005). WNND reporting is believed to be "reasonably complete" in the United States (Council of State and Territorial Epidemiologists 2004).

Estimates of the proportion of persons with WNF seeking healthcare or requiring hospitalization vary. In New York City, 50% of cases visited a physician in a neighborhood-based, seroprevalence study (Mostashari et al. 2001). In Israel, 78% of patients with laboratory-confirmed WNF were hospitalized (Chowers et al. 2001). In Illinois and Denver, respectively, 31% and 14% of patients with WNF were hospitalized (Patnaik, Harmon, and Vogt 2006; Watson et al. 2004).

An enhanced WNV surveillance project suggested that WNF often may not have been diagnosed (i.e., conditional event 2) (Whitney et al. 2006). The project found four patients with positive WNV immunoglobulin (Ig) G and IgM among 268 persons (1.5%) hospitalized with fever at Grady Memorial Hospital (Atlanta, GA) from July to October of 2003. All four had a clinical illness compatible with WNV, but none were suspected of having WNV by the physicians who provided their care.

Public health laboratories' abilities to test for WNF have also varied. As the WNV epidemic initially spread, few laboratories outside the public health system had testing capacity. Demand for serologic testing overwhelmed many state public health laboratories before commercial testing was widely available. Health departments established varying recommendations or requirements for specimen submissions and case patients with neurologic or more serious disease were often prioritized for testing.

While WNF testing constraints may have been necessary given the availability of resources, they have been justified based on misconceptions that WNF is mild. A follow-up study that interviewed 98 patients who did seek care for WNF found that 79% missed school or work due to their illness and the median time to full recovery was 60 days (Watson et al. 2004). Difficulty concentrating, neck pain/stiffness, and persistent muscle fatigue/weakness were common symptoms. The enhanced surveillance project at Grady Memorial Hospital also demonstrated that patients not only received equivocal diagnoses, but, in one case, inappropriate treatment for a cerebral infarction was given (despite the absence of findings in a computerized tomography scan, a magnetic resonance image of her head, and a magnetic resonance angiography of her neck) (Whitney et al. 2006).

In short, WNND is a severe disease that is likely to be diagnosed and reported (conditional events 1-3). WNF can also cause serious disease, but etiology is less frequently determined (event 2) so under-ascertainment is more likely (events 2 and 3). To achieve more complete monitoring of WNV-related illness, CDC endorsed a 2004 Council of State and Territorial Epidemiologists (CSTE) position statement, calling for expansion of the national surveillance case definition of arboviral disease to include non-neuroinvasive illnesses (Council of State and Territorial Epidemiologists 2004).

A population-based estimate of the ratio of WNF counts to WNND counts is available for evaluating ascertainment completeness in the context of the expansion of WNV surveillance in the United States. A 1999 New York City seroprevalence study, which collected data on clinically and temporally compatible symptoms (e.g., fever), suggests that for every occurrence of WNND there may be 30 occurrences of WNF in a susceptible population (Mostashari et al. 2001). In contrast, most state-reported

syndrome ratios did not exceeded 10:1 in 2005 (Centers for Disease Control and Prevention 2005; Centers for Disease Control and Prevention 2004). Whether under-ascertainment of WNF occurs differentially in population strata has not been sufficiently reported in the literature. Unlike numerous evaluation projects that have focused on the completeness of reporting of diagnosed cases, Study 1 assesses not only incomplete disease reporting but also the role of underdiagnosis in surveillance ascertainment. These findings may be relevant for any reportable disease not routinely diagnosed by the healthcare system.

There are few examples of a model where two clinical forms of a notifiable disease exist, but one is ascertained more rigorously than the other and an estimate of the expected relative frequency of both clinical forms is available. Therefore, comparisons between WNF case ascertainment and acute flaccid paralysis (AFP) surveillance in the context of the World Health Organization's Global Polio Eradication Initiative are informative. Since only 1 in 200 poliovirus infections result in paralytic disease that is clinically apparent, using AFP as a broader surveillance case definition helps ensure that paralytic polio cases will be detected if they occur. This case definition is based on the fact that AFP is a main polio symptom but requires that non-polio cases of AFP (e.g., Guillain-Barré syndrome) be discerned by virologic testing of stool specimens. Though disputed (Harris, Durrheim, and Ogunbanjo 2003), a non-polio AFP case detection rate equal to or greater than 1 per 100,000 children under 16 years of age is generally accepted as a reference rate that indicates sensitive surveillance for AFP (and, by proxy, polio) (De Quadros 1994).

These two viral infections, poliovirus and WNV, have a clinically similar feature: severe disease with neurologic involvement occurring in a small, estimable proportion of cases. Through serosurveys conducted in the United States, it is estimated that less than 1 in 100 WNV infections result in neuroinvasive disease (Centers for Disease Control and Prevention 2001; Mostashari et al. 2001). In both diseases, neuroinvasive cases are described as "the tip of the iceberg," because many more undetected, and often subclinical, infections are present in a population where neuroinvasive cases are occurring. This clinical feature makes complete surveillance and detection of human transmission challenging for both viral infections, thereby motivating the use of surveillance indicators. Other surveillance indicators (e.g., testing of mosquito pools, equine mortality) may also provide additional evidence of WNV transmission. In contrast, humans are the only reservoir for poliovirus and therefore are the only source of transmission evidence. The contexts of the two surveillance indicators also differ. To date, efforts to ascertain WNF (or arboviral-related, febrile illnesses) have not been widely pursued in developing countries. However, AFP surveillance and polio elimination are currently global efforts.

Missing meningococcal disease serogroup data

Advanced laboratory testing of pathogens in public health laboratories is often a necessary component for case report completion. Testing entails coordination between public health laboratories and communicable disease control programs to ensure the following: antimicrobial resistance is monitored effectively in the population; the frequency distribution of pathogen strains, serogroups, or serotypes is characterized;

molecular epidemiology techniques are applied to identify clusters; unexplained illness is assigned etiology by specialized testing; and low incidence diseases of public health importance are identified. To obtain data from these advanced tests, clinical specimens or isolates must be forwarded to public health laboratories from healthcare providers and clinical laboratories. Therefore, testing is achieved through linkages between the healthcare and public health domains.

The clinical and epidemiologic features of meningococcal disease make it a model for investigating factors that may impede or favor case report completion by serogrouping in public health laboratories. Interventions for meningococcal disease have historically resided within the purview of health departments' communicable disease control programs. All state public health laboratories have the ability to distinguish common serogroups of *N. meningitidis* isolates (CDC, unpublished data). (*N. meningitidis* is a Gram-negative diplococcus with five serogroups that account for the vast majority of disease: A, B, C, Y, and W-135.) Fewer clinical laboratories have serogrouping capacity. In addition, endemic meningococcal disease is relatively rare (less than two cases per 100,000) (Raghunathan, Bernhardt, and Rosenstein 2004), such that testing demand is likely to be manageable in a public health laboratory setting. Linkages between clinicians, clinical microbiologists, and state health departments' epidemiology and laboratory programs are a prerequisite for meningococcal disease serogrouping and other advanced tests provided by public health laboratories (e.g., serotype-specific surveillance for *Salmonella*).

In introducing the conditional events framework, *N. meningitidis* infection was described as a fulminant disease process with signs and symptoms that are sufficiently

severe to motivate healthcare seeking and etiologic diagnosis. Like WNND, meningococcal meningitis is characterized by a pronounced clinical presentation (high fever, intense headache, neck stiffness, and confusion) that often develops within hours (Raghunathan, Bernhardt and Rosenstein 2004). Though complicated by patients with meningococcal pneumonia, diagnosis is generally facilitated by a characteristic petechial or purpuric rash. In most patients with meningococcal disease, *N. meningitidis is* detected in blood (77%) or CSF (35%) cultures that can be forwarded to public health laboratories for serogrouping (Rosenstein et al. 1999).

Given the severity of the disease and likely diagnosis and hospitalization, meningococcal disease case reporting is usually relatively complete. Ackman and colleagues estimated that 93% of meningococcal disease cases in New York State (excluding New York City) were reported to the public health department in 1991 (Ackman, Birkhead and Flynn 1996). Thus, persons with meningococcal disease are likely to receive healthcare (event 1), meningitis (a major form of the disease) is most likely to be diagnosed, and patients without meningeal infection are often diagnosed through blood cultures (event 2).

With the 2005 U.S. Food and Drug Administration licensure of the meningococcal conjugate vaccine that covers four of these five serogroups (A, C, Y, and W-135), serogrouping has renewed importance for surveillance and control of meningococcal disease. Serogroup-specific surveillance is now important for monitoring for vaccine failures and directing prevention and control with appropriate interventions. Recognizing the importance of serogroup-specific surveillance, in 2004 CSTE approved a position statement calling for universal serogrouping (Council of State and Territorial

Epidemiologists 2004). The position statement was directed to the CDC's National Notifiable Diseases Surveillance System (NNDSS), where serogrouping completeness has varied across states.

Internet-based disease reporting and timeliness

Electronic reporting procedures have multiple applications for public health surveillance in the United States (Silk, Hoke, and Berkelman 2008). Several reports have documented gains in completeness and timeliness with implementation of ELR. The first report came from Hawaii's state health department (Effler et al. 1999), which implemented a statewide ELR system by establishing electronic linkage with three major commercial laboratories. Relative to Hawaii's previous paper-based system, the number of *Giardia*, *Salmonella*, *Shigella*, invasive *S. pneumoniae*, and vancomycin-resistant *Enterococcus* reports more than doubled, 12 of 21 data fields were significantly more likely to be complete, and reports were received 3.8 days earlier. Internet-based case reporting, where disease reports can be submitted securely at a website, also shows promise for increasing completeness and timeliness of reporting. The Netherlands has fully replaced its paper-based system for data transmission from municipal public health services to national public health authorities (Ward et al. 2005). A 9-day improvement of median reporting time and an increase in completeness of case reporting were achieved.

As of April 2005, CDC estimated that 27 state health departments, New York City, and Los Angeles County had either implemented internet-based case reporting, an ELR system, or both (Centers for Disease Control and Prevention 2005). These systems are part of the National Electronic Disease Surveillance System (NEDSS), an initiative

initially funded by CDC in 2000. To address the disjointed and antiquated state of public health surveillance technology, NEDSS seeks to unite surveillance systems with current information technology standards (Centers for Disease Control and Prevention 2006). Data record formats are standardized with controlled message syntax and vocabulary (e.g., types and results of laboratory tests) that allow for connectivity across health information systems. Record transmission is secure and NEDSS architecture includes a base system and program-specific modules.

Hypothesized mechanisms

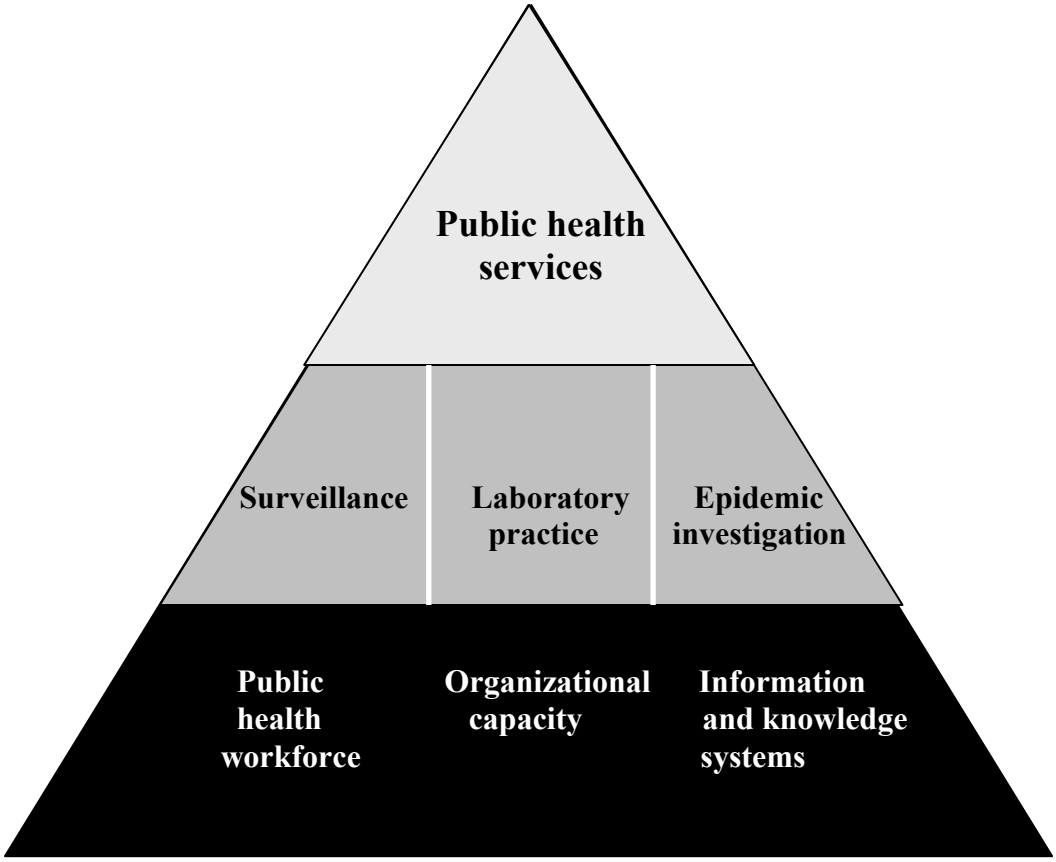
The work of Donabedian (1980) has been adapted to create a framework for measuring public health quality (Derose et al. 2002; Handler, Issel, and Turnock 2001; Scutchfield et al. 2004). In the framework, three dimensions are generally enumerated: structure, process, and outcomes (Figure 2-3). In understanding key components within each dimension, corresponding measures of quality can be formulated. Structure and process quality measures are then related to intermediate outcomes (or outputs), such as complete and timely reporting. These "short-term results of activities" are used to achieve ultimate outcomes – reduction of disease incidence in a community through directed prevention and control measures.

Paradoxically, since disease reporting systems are also used to monitor disease incidence, mediocre quality in surveillance activities may make it difficult to distinguish the relationships between intermediate and ultimate outcomes. Incomplete case ascertainment, for example, may lead to diminished incidence estimates and missed opportunities to interrupt transmission (increasing incidence).

Structures and processes are central considerations in the dissertation. For simplicity, consider two broad types of public health systems with respect to completeness and timeliness of morbidity reporting. The first type (type 1) includes jurisdictions in which completeness and timeliness of case reports are high. Structural aspects of the system, including the workforce, organization, and financing of the system, are more robust. This structural foundation, in turn, leads to surveillance and laboratory policies and procedures (i.e., processes) that may be more rigorous (Figures 2-1 and 2-4). In the second type of public health system (type 2), infrastructure and resources are inadequate to create programs that ensure high-quality, representative surveillance data. Indeed, state-level variability in health and public health financing and capacity has been documented by numerous organizations, including Trust for America's Health.

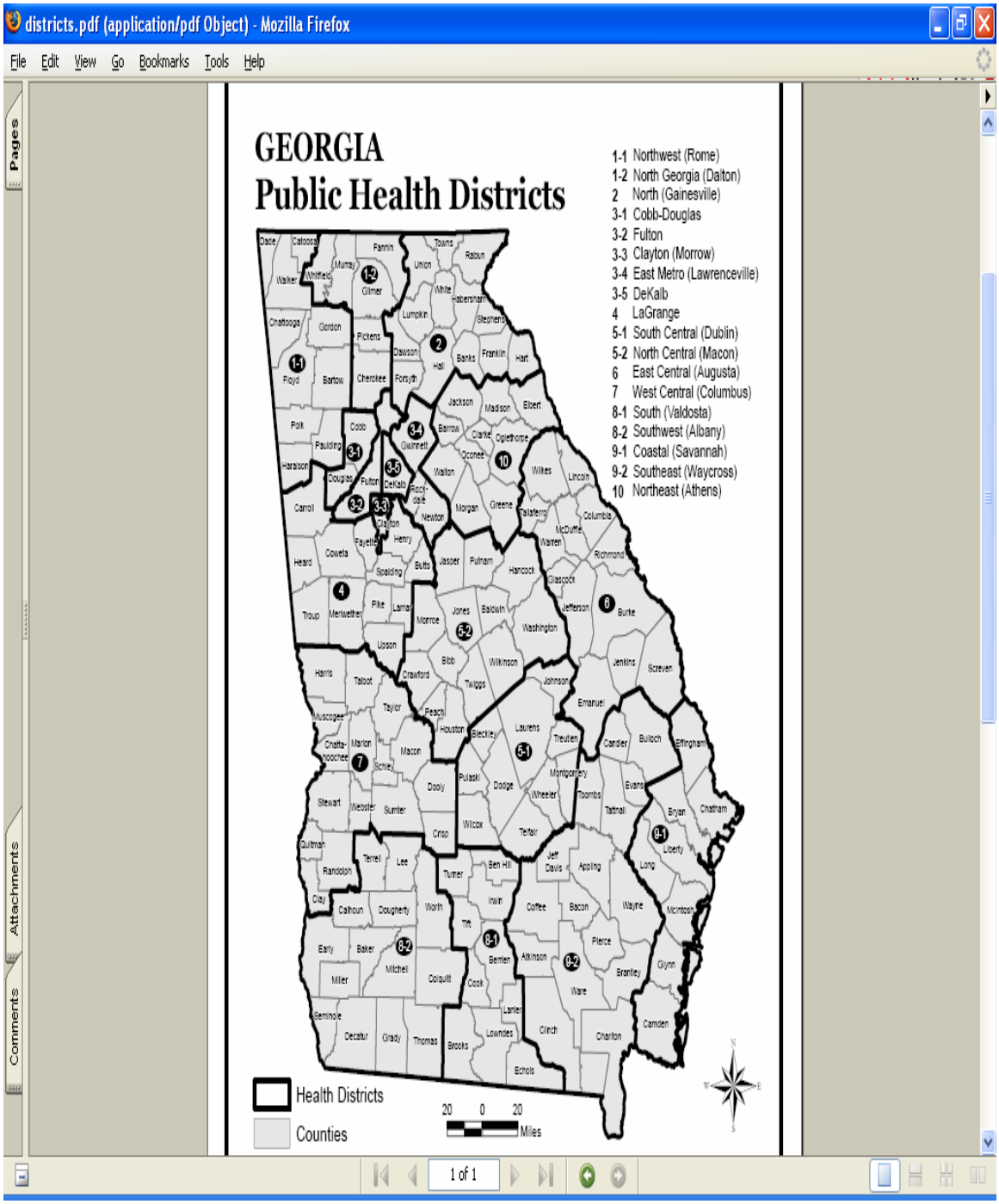
The hypothesized results are that completeness and timeliness of reporting vary in accordance with 'state type,' which is measured through indicators of infrastructure adequacy and through specific surveillance and laboratory program policies, practices, and capacities. The goal of the dissertation is to provide recommendations that can be implemented to improve the representativeness, quality, and value of data produced by notifiable diseases surveillance systems that link healthcare, public health, and laboratory systems nationally. By addressing interactions between these systems at multiple levels, sources of variability in completeness and timeliness can be identified and prioritized for intervention.

Figure 2-1. Public health infrastructure, capacities, and services



Source: Baker, E., M. Potter, D. Jones, S. Mercer, J. Cioffi, L. Green, P. Halverson, M. Lichtveld, and D. Fleming. 2005. The public health infrastructure and our nation's health. *Annu Rev Public Health* 26 303-18.

Figure 2-2. Screen capture of public health districts in Georgia



Source: Georgia Division of Public Health. 2006. *Georgia Public Health Districts* [Web site]. Georgia Division of Public Health [cited June 8, 2006]. Available from http://health.state.ga.us/pdfs/regional/districts.pdf.

Table 2-1. Classification of 45 state health departments by form of state-local administrative structures

Structure	Definition	States
Centralized organization	Local health units that function directly under the state's authority and are operated by a state department of public health or a state board of health, sometimes through regional administration and sometimes with the help of a local advisory board	AR, DE, FL, HI, KY, LA, MS, NM, OK, SD, VT
Decentralized organization	Local government (a city, township, county, or some combination) operates a health department either directly or with the intervening authority of a local board of health. Advice and consultation are offered by the state health department to the local board of health, the local health department, or both.	AZ, CA, IA, KS, MI, MN, MT, NE, NJ, OR
Shared organizational control	Local health departments are operated by local government either directly or through a local board of health. In certain circumstances these same health departments also fall under the authority of the state health department. For example, a state health department may retain appointive and line authority over local health officers who are also responsible to local boards or commissions. In some cases, local departments are required to submit program plans and budgets to the state health department in order to qualify for federal and/or state funds.	GA, IN, MD, NC, NH, OH, TN,
Mixed centralized and decentralized organizational control	Local health services in the same state may be provided either by the state health department, by local governmental units, or by local boards of health.	AL, CO, CT, ID, IL, MA, ME, NE, NY, PA, TX, UT, VA, WY

Source: DeFriese, G., J. Hetherington, E. Brooks, C. Miller, S. Jain, F. Kavaler, and J. Stein. 1981. The program implications of administrative relationships between local health departments and state and local government. *Am J Public Health* 71 (10):1109-15.

Table 2-2.Twenty five largest metropolitan health departments*

Location	Population size
Los Angeles County, CA	9,519,338
New York City, NY	8,008,278
Houston-Harris County, TX	3,400,578
Maricopa County, AZ	3,072,149
Chicago City, IL	2,896,000
Orange County, CA	2,846,289
San Diego County, CA	2,813,833
Miami-Dade County, FL	2,253,362
Dallas County, TX	2,218,899
Seattle-King County, WA	1,737,034
San Bernardino County, CA	1,709,434
Santa Clara County, CA	1,682,585
Broward County, FL	1,623,018
Riverside County, CA	1,545,387
Philadelphia City, PA	1,517,000
Alameda County, CA	1,443,741
Bexar County, TX	1,392,931
Clark County, NV	1,375,765
Nassau County, NY	1,334,544
Allegheny County, PA	1,281,666
Sacramento County, CA	1,223,499
Oakland County, MI	1,194,156
Palm Beach County, FL	1,131,184
Detroit City, MI	951,270
Contra Costa County, CA	948,816

* Based on the U.S. Census for 2000

Source: Plough, A. 2004. Understanding the financing and functions of metropolitan health departments: a key to improved public health response. *J Public Health Manag Pract* 10 (5):421-7.

Table 2-3. Ten public health practices/essential public health services

Public health practices	Essential public health services
Assessment	
Assess the health needs of the community	Monitor health status to identify and solve community health needs
Investigate the occurrence of adverse health effects and hazards	Diagnose and investigate health problems and health hazards in the community
Analyze the determinants of health needs	
Policy Development	
Advocate for public health, build constituencies, and identify resources in the community	Mobilize community partnerships and action to solve health problems
Set priorities among health needs	Develop policies and plans that support individual and community health efforts
Develop plans and policies to address priority health needs	
Assurance	
Manage and coordinate resources and develop the public health system's organizational structure	Assure a competent workforce—public health and health care
Implement programs by ensuring or providing services	Enforce laws and regulations that protect health and assure safety
Evaluate programs and provide quality assurance	Link people to needed personal health services and assure the provision of health care when otherwise unavailable
Inform and educate the public on health issues	Evaluate effectiveness, accessibility, and quality of personal and population-based health services
	Inform, educate, and empower people about health issues
	Research for new insights and innovative solutions to health problems

Source: Derose, S., M. Schuster, J. Fielding, and S. Asch. 2002. Public health quality measurement: concepts and challenges. *Annu Rev Public Health* 23 1-21.

Table 2-4. Core function-related measures of local public health practice performance

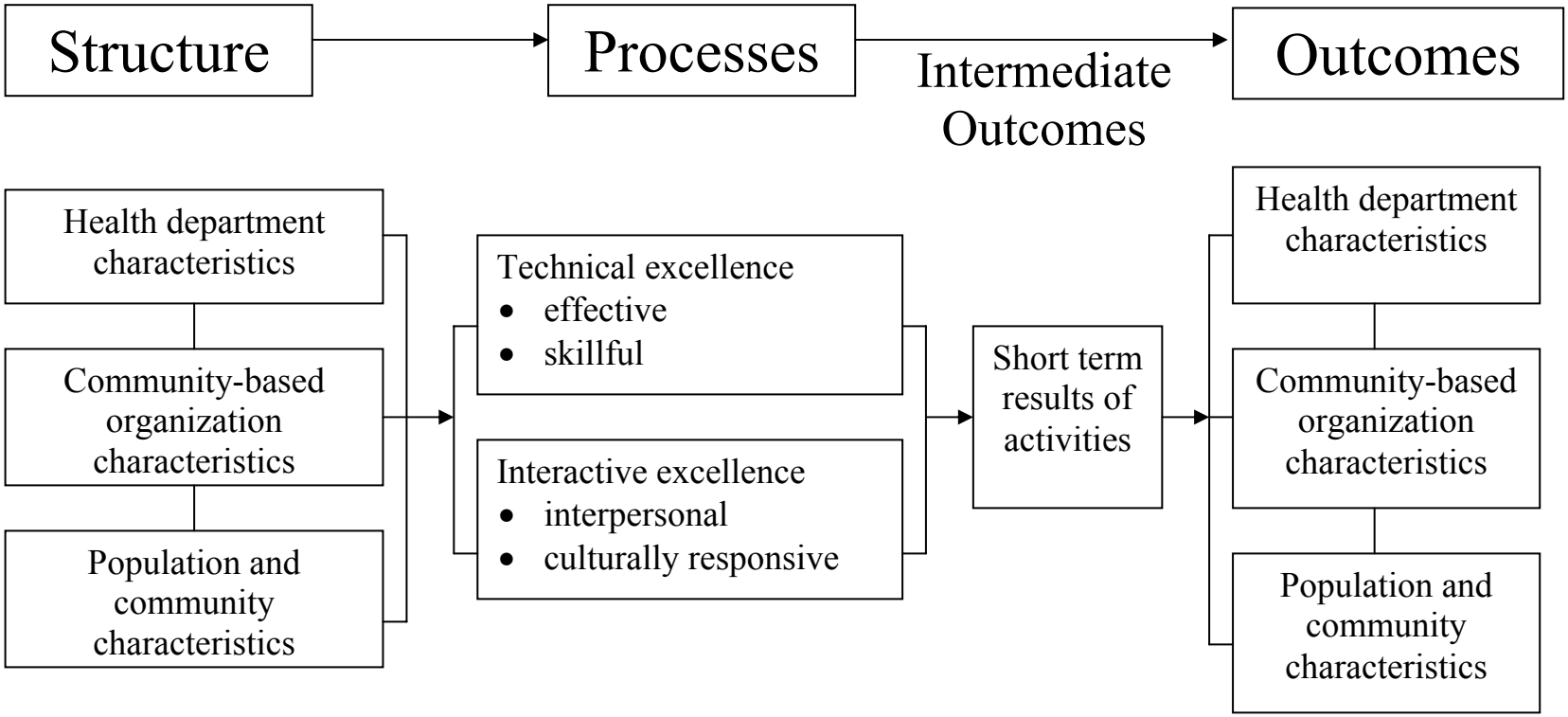
Assessment activities
1. In your jurisdiction, is there a community needs assessment process that systematically describes the prevailing health status in the community?
2. In the past 3 years in your jurisdiction, has the local public health agency surveyed the population for behavioral risk factors?
3. In your jurisdiction, are timely investigations of adverse health events conducted on an ongoing basis--including communicable disease outbreaks and environmental health hazards?
4. Are the necessary laboratory services available to the local public health agency to support investigations of adverse health events and meet routine diagnostic and surveillance needs?
5. In your jurisdiction, has an analysis been completed of the determinants of and contributing factors to priority health needs, the adequacy of existing health resources, and the population groups most affected?
6. In the past 3 years in your jurisdiction, has the local public health agency conducted an analysis of age-specific participation in preventive and screening services?
Policy development activities
7. In your jurisdiction, is there a network of support and communication relationships that includes health-related organizations, the media, and the general public?
8. In the past year in your jurisdiction, has there been a formal attempt by the local public health agency to inform elected officials about the potential public health impact of decisions under their consideration?
9. In your local public health agency, has there been a prioritization of the community health needs that have been identified from a community needs assessment?
10. In the past 3 years in your jurisdiction, has the local public health agency implemented community health initiatives consistent with established priorities?
11. In your jurisdiction, has a community health action plan been developed with community participation to address priority community health needs?
12. In the past 3 years in your jurisdiction, has the local public health agency developed plans to allocate resources in a manner consistent with community health action plans?

Table 2-4. Core function-related measures of local public health practice performance (continued)

Assurance activities
13. In your jurisdiction, have resources been deployed as necessary to address priority health needs identified in a community health needs assessment?
14. In the past 3 years in your jurisdiction, has the local public health agency conducted an organizational self-assessment?
15. In your jurisdiction, are age-specific priority health needs effectively addressed through the provision of or linkage to appropriate services?
16. In your jurisdiction, have there been regular evaluations of the effects of public health services on community health status?
17. In the past 3 years in your jurisdiction, has the local public health agency used professionally recognized process and outcome measures to monitor programs and to redirect resources as appropriate?
18. In your jurisdiction, is the public regularly provided with information about current health status, health care needs, positive health behaviors, and health care policy issues?
19. In the past year in your jurisdiction, has the local public health agency provided reports to the media on a regular basis?
20. In the past 3 years in your jurisdiction, has there been an instance in which the local public health agency has failed to implement a mandated program or service?

Source: Turnock, B., A. Handler, and C. Miller. 1998. Core function-related local public health practice effectiveness. *J Public Health Manag Pract* 4 (5):26-32.

Figure 2-3. Adaptation of Donabedian's framework for assessing quality in a public health system



Source: Derose, S., M. Schuster, J. Fielding, and S. Asch. 2002. Public health quality measurement: concepts and challenges. *Annu Rev Public Health* 23 1-21.

CHAPTER 3

METHODS

Surveillance data and public health jurisdictions

Data for both multilevel modeling studies (Studies 1 and 2) exist on two levels because cases (individuals) are nested within public health jurisdictions (groups) responsible for surveillance ascertainment and laboratory testing (Diez Roux and Aiello 2005). As a result, completeness of ascertainment and the extent of missing data (i.e., the dichotomous outcome variables) are often correlated within jurisdictions. Furthermore, since states' surveillance and associated laboratory programs operate semi-independently, between-state variability in completeness is important.

National case reports of WNV and meningococcal disease were used as the first levels of information. Finalized, WNV surveillance data for 2003-2005 were received on May 11, 2006 following a request to the Centers for Disease Control and Prevention (Fort Collins, Colorado). WNV case reports for three seasons, 2003 (64%), 2004 (16%), and 2005 (19%), are the units of analysis for the study of WNF ascertainment (n = 15,401). WNV cases have not been reported in all 50 states. However, there are 52 groups, which are defined as states or large city and county public health jurisdictions (Chicago, Houston, Los Angeles County, New York City, Philadelphia, and Washington DC) that received CDC funding for surveillance and prevention of WNV and other arboviruses.

Similarly, case counts of meningococcal disease for 2005 were finalized in May of 2007 (n = 4,115). Surveillance data originate from 53 autonomous disease reporting

entities (50 states plus New York City, Puerto Rico, and Washington D.C) in the NNDSS.

In general, measures of effect and aggregate analyses are weighted according to relative case frequencies across states because the scope of the studies is national. However, not all states had sufficient WNV cases among racial and ethnic minorities for stable statistical summaries. WNV cases among African Americans/Blacks, for example, occurred in 33 states but only 16 states had five or more cases. When stratified by surveillance year, the number states with cases occurring among people of minority race/ethnicity were further diminished. The multiple imputation process, in which records with missing race/ethnicity may be eligible to be assigned a minority categorization, increased minority case counts overall but to a lesser extent in states where African Americans/Blacks and Hispanics were a small portion of the population (see "Multiple imputation of race and ethnicity" below). Therefore, not all states were eligible for race- and ethnicity-specific analyses. Similarly, meningococcal disease is relatively rare. As such, public health jurisdictions that serve relatively small populations will typically also have relatively low meningococcal disease case counts.

Tables 3-1 and 3-2 describe the contents of the surveillance datasets, including basic demographic information, county and state of residence, and date of symptom onset. Limited clinical data are available in the datasets. Type of infection, specimen date and source, and vital status exist for the meningococcal disease data. Most notably, both surveillance datasets have fields corresponding to the outcomes of interest: disease syndrome (WNV) and pathogen serogroup (meningococcal disease).

Federal Information Processing Standards (FIPS) codes in each surveillance dataset can be used to ascertain cases' county and state of residence. These fields are meaningful because they link surveillance cases to the second level of information: public health jurisdictions. In addition, FIPS codes facilitate incorporation of county-level data from the U.S. Census, including the proportions of Black, Hispanic, and White in the population (see "Multiple imputation of race and ethnicity" below). Although the U.S. Census Bureau's America Community Survey now conducts ongoing data collection (in years between the decennial Census), the most recent county-specific social, economic, and housing data for many smaller counties are from the 2000 U.S. Census, Summary File 3.

State epidemiology and laboratory program surveys

Tables 3-3, 3-4, and 3-5 describe extant data on state public health departments, including epidemiology and laboratory program activities and capacity, which were available to the studies through data sharing agreements. Survey data from 2001 on structures and functions of state health agencies were collected by mailing questionnaires to state health officers (Table 3-3). The CSTE national assessment of epidemiologic capacity was completed by 50 states, the District of Columbia, and Puerto Rico in September of 2004 (Table 3-4). Survey data from the Association of Public Health Laboratories (APHL) were collected through various surveys of state laboratory directors and their personnel (i.e., APHL members) between 2002 and 2005 (Table 3-5).

Appendices 1-4 are the questionnaires for surveying state and large city/county public health laboratories and epidemiology programs on WNV and meningococcal disease serogrouping. Collectively, these survey items were intended to capture key policy- and program-related indicators of state health departments' surveillance and laboratory capacities, which are likely to correlate with surveillance completeness.

For these surveys, the geographic and jurisdictional unit of analysis is generally the state. Chicago, Houston, New York City, Philadelphia, Los Angeles County, Washington, D.C. and Puerto Rico are also included. Public health agencies in other large metropolitan areas (Table 2-2) complicate this approach because they are autonomous entities but may operate specific programs independently or in coordination with their state health departments. The largest metropolitan areas are concentrated in ten states, California (9), Florida (3), Texas (3), Michigan (2), New York (2), Pennsylvania (2), Arizona (1), Illinois (1), Nevada (1), and Washington (1).

In Los Angeles County and New York City, the two largest metropolitan areas, epidemiology and laboratory programs operate in ways that are substantially independent of their state health departments. New York City transmits disease reports, including meningococcal disease cases, directly to NNDSS at the CDC, while Los Angeles County reports via the California Department of Human Services (Centers for Disease Control and Prevention 2006). WNV serologic and *N. meningitidis* culture and serogroup tests are performed by public health laboratories within both jurisdictions (Los Angeles County Department of Public Health 2006; New York City Department of Health and Mental Hygiene 2006). In California and Texas, there are well developed epidemiology and laboratories programs in many LHDs, including Los Angeles, Orange, San Diego,

and Dallas Counties and the City of Houston. Conversely, Chicago's Department of Public Health uses the Illinois State Health Department's laboratory system but has its own communicable disease control program.

Thus, capturing data on epidemiology and laboratory program activities for large, semi-autonomous jurisdictions by only surveying states is a challenge. There are two ways in which this challenge was addressed. First, the 2001 survey of state health officers (Table 3-3) includes information on administrative relationships between state and local public health jurisdictions. The field "centralization" categorizes state health departments' span of organizational control as centralized, decentralized, mixed, or shared. Therefore, it may be that state-level survey data have less predictive value in decentralized states. Second, the surveys of state programs included requests for information on local/regional activities within the state. For example, the surveys captured whether other public health laboratories conduct initial tests for WNV infection or perform meningococcal disease serogrouping (including the names of the other public health laboratories that provide these services).

There are important analytic issues that arise from aggregation of several discrete datasets. The cumulative effects of missing data from survey or survey item non-response created a number of records in which one or more predictors are absent. Since the default specification for statistical analyses and, in particular, multivariate regression is often exclusion of these records, attention to diminishing datasets in tabulations and parsimonious statistical models are priorities for the analyses. In addition, there is the possibility for predictor misclassification originating from data that are collected and pertain to proximal but not identical time periods. The survey of state health agencies,

which achieved a 94% response rate, serves as a good example of both issues. Subsequent to the survey period in the summer of 2001, state public health structures or functions might have changed. These predictors would be inaccurately measured or categorized during the 2003-2005 study period. Moreover, for the three non-respondent states, these state-level data are absent for all surveillance cases in those states.

Multilevel modeling

The multilevel approach is equivalent to an analysis that adjusts for correlations within jurisdictions by using a single random effect for the intercept in a multilevel model that contains variables at both levels. A recommended approach for building multilevel models first examines level-1 predictors (Tables 3-1 and 3-2). At this stage, the analyses consider dichotomous outcomes (West Nile fever vs. neuroinvasive disease, presence vs. absence of serogroup data) using logit transformations. In these models, the effects of each level-1 predictor, or changes in the log odds of the binary events, can vary across states with the inclusion of random effects for the level-1 terms.

For Study 1, the models predict the odds of WNF ascertainment as the event of interest versus WNND ascertainment (1 – the probability of WNF) using the logit link function $\eta_{ij} = \ln (\Pr (WNF_{ij}) / \Pr (WNND_{ij}))$ and an assumed Bernoulli sampling distribution for the binary syndrome outcome. Models were specific to each year and the overall study period. A mixed-effects equation for the random intercepts model with case-level predictors is as follows:

$$\eta_{ij} = \gamma_{00} + \gamma_{10} * A\overline{ge}.. + \gamma_{20} * \text{Gender}_{ij} + \gamma_{30} * \text{Race}_{ij} + \gamma_{40} * \text{Ethnicity}_{ij} + u_{0j}$$

where γ_{00} is the background log odds of WNF ascertainment. Other γ parameters are fixed effects for age ($A\overline{ge}..$ to denote grand mean centering) and gender, race and ethnicity indicator variable covariates; u_{0j} is a random effect that represents additional, unmodeled variability (error) in states' log odds of WNF ascertainment.

This mixed-effects model can also be expressed in a multilevel format as the system of equations:

Level 1: $\eta_{ij} = \beta_{0j} + \beta_{1j}(A\overline{ge}..) + \beta_{2j}(\text{Gender}_{ij}) + \beta_{3j}(\text{Race}_{ij}) + \beta_{4j}(\text{Ethnicity}_{ij})$

Level 2: $\beta_{0j} = \gamma_{00} + u_{0j}$

$\beta_{gj} = \gamma_{g0}$, g = 1, 2, 3, 4

Subsequent models included potentially significant, state-level effects (generically as S_j) identified through univariate analyses of states' syndrome ascertainment ratios. Additional parameters are also a function of β_{0j}, such that the reduction in u_{0j} is estimated when accounting for states' WNV testing and surveillance policies/practices as well as U.S. Census region (West and Midwest versus Northeast and South) and population percentages of Blacks and Hispanics (both grand mean centered). To assess whether state-level effects on WNF ascertainment probabilities vary with Black race or Hispanic ethnicity, cross-level interactions were also initially specified:

$\eta_{ij} = \gamma_{00} + \gamma_{10}* A\overline{ge}.. + \gamma_{20}*\text{Gender}_{ij} + \gamma_{30}*\text{Race}_{ij} + \gamma_{40}*\text{Ethnicity}_{ij} + \gamma_{01}*S1_j + \ldots + \gamma_{06}*S6_j + \gamma_{31}*S1_j*\text{Race}_{ij} + \ldots + \gamma_{36}*S6_j*\text{Race}_{ij} + \gamma_{41}*S1_j*\text{Ethnicity}_{ij} + \ldots + \gamma_{46}*S6_j*\text{Ethnicity}_{ij} + u_{0j.}$

In modeling race and ethnicity β terms as functions of the S_j predictors, a multilevel system of equations can be written as:

Level 1: $\eta_{ij} = \beta_{0j} + \beta_{1j}(\overline{Age}_{..}) + \beta_{2j}(\text{Gender}_{ij}) + \beta_{3j}(\text{Race}_{ij}) + \beta_{4j}(\text{Ethnicity}_{ij})$

Level 2: $\beta_{0j} = \gamma_{00} + \gamma_{01}(S1) + \ldots + \gamma_{06}(S6) + u_{0j}$

$\beta_{1j} = \gamma_{10}$ $\beta_{3j} = \gamma_{30} + \gamma_{31}(S1) + \ldots + \gamma_{36}(S6)$

$\beta_{2j} = \gamma_{20}$ $\beta_{4j} = \gamma_{40} + \gamma_{41}(S1) + \ldots + \gamma_{46}(S6)$

For Study 2, the hierarchical, generalized linear models predict the odds of obtaining a serogrouping result using the logit link function $\eta_{ij} = \ln(\Pr(\text{serogrouped}_{ij}) / \Pr(\text{not serogrouped}_{ij}))$ and an assumed Bernoulli sampling distribution for the binary outcome. Models of specimen source (n = 973) and vital outcome (n = 1,321) were estimated separately because of missing data.

Mixed-effects equations for these random intercepts models with level-1 predictors are:

$\eta_{ij} = \gamma_{00} + \gamma_{10} * \text{Specimen1}_{ij} + \gamma_{20} * \text{Specimen2}_{ij} + \gamma_{30} * \text{Specimen3}_{ij} + u_{0j}$ and

$\eta_{ij} = \gamma_{00} + \gamma_{10} * \text{Outcome}_{ij} + u_{0j}$

where γ_{00} is the background log odds of a serogrouping result. Other γ parameters are fixed effects for the indicator variable covariates for either specimen source categories or vital outcome; u_{0j} is a random effect that represents additional, unmodeled variability (error) in states' log odds of serogrouping.

The model can also be expressed as the systems of equations:

Level 1: $\eta_{ij} = \beta_{0j} + \beta_{1j}(\text{Specimen1}_{ij}) + \beta_{2j}(\text{Specimen2}_{ij}) + \beta_{3j}(\text{Specimen3}_{ij})$

Level 2: $\beta_{0j} = \gamma_{00} + u_{0j}$

$\beta_{gj} = \gamma_{g0}$, g = 1, 2, 3 and

Level 1: $\eta_{ij} = \beta_{0j} + \beta_{1j}(\text{Outcome}_{ij})$

Level 2: $\beta_{0j} = \gamma_{00} + u_{0j}$

$\beta_{1j} = \gamma_{10}$

Subsequent models included significant level-1 effects (at an alpha level of 0.10) and potentially significant, level-2 (state-level) effects (generically as S_j) identified through univariate analyses of states' serogrouping completeness. In the models, additional S_j parameters are also a function of β_{0j}, such that the reduction in u_{0j} is estimated when accounting for state programs' policies, practices, and capacities. The mixed-effects model for specimen source, for example, is written as:

$\eta_{ij} = \gamma_{00} + \gamma_{10}*\text{Specimen1}_{ij} + \gamma_{20}*\text{Specimen2}_{ij} + \gamma_{30}*\text{Specimen3}_{ij} + \gamma_{01}*\text{S1}_j + \ldots$

$+ \gamma_{05}*\text{S5}_j + u_{0j}$.

As a multilevel system of equations, the model is:

Level 1: $\eta_{ij} = \beta_{0j} + \beta_{1j}(\text{Specimen1}_{ij}) + \beta_{2j}(\text{Specimen2}_{ij}) + \beta_{3j}(\text{Specimen3}_{ij})$

Level 2: $\beta_{0j} = \gamma_{00} + \gamma_{01}(\text{S1}) + \ldots + \gamma_{05}(\text{S5}) + u_{0j}$

$\beta_{gj} = \gamma_{g0}$, g = 1, 2, 3

In addition, a t-ratio statistic is used for testing effects' significance (Raudenbush and Bryk 2002). Backward elimination of interaction terms and main effects identified parsimonious models.

Syndrome ascertainment ratio

To illustrate the variability in testing, confirmation, and reporting of WNF among states, Study 1 uses a "syndrome ascertainment ratio." This ratio is the proportion of patients with febrile illness (WNF) over the proportion of patients with neuroinvasive disease (WNND), which simplifies to the ratio of WNF to WNND since the jurisdiction-specific denominator in both is the same (i.e., total number of cases). This is an indirect approach and assumes that variations among states in unmeasured host, agent, and environmental determinants that might affect disease severity given infection (and thus the syndrome ratio) are negligible relative to case- and surveillance-level correlates of WNF underreporting and underdiagnosis.

Chapter 2 described the evidence supporting the WNV syndrome ascertainment ratio as an ideal application of a ratio estimator (Hook and Regal 1995). In particular, the New York City seroprevalence study suggests that for every occurrence of WNND there may be 30 occurrences of WNF in a susceptible population (Mostashari et al. 2001). This expected frequency of WNF ascertainment relative to WNND can be considered an estimate boundary when the goal is to assure that transmission among humans is detected or "high-risk population groups or geographic areas [are identified] to target interventions and guide analytic studies" (Council of State and Territorial Epidemiologist 2006). In other words, states might expect as many as 30 WNF cases for every WNND case

diagnosed and reported in their jurisdiction. Yet even among the highest WNV syndrome ratios, few states approximated a 10:1 ratio of reported WNF to WNND in 2003, 2004, or 2005 (Figure 3-1). This is not surprising since the population-based, seroprevalence study in New York City tested for the presence of infection or mild illness that may not come to medical attention. However, among states reporting at least one case of each syndrome per year, improvements in the number of states reporting at least one WNF case for every WNND case occurred. In 2003, 10 of 39 (25.6%); in 2004, 14 of 33 (42.4%); and in 2005, 15 of 39 (38.5%) states' plotted ratios exceeded 1.0.

Additionally, within each state (i.e., imaginary vertical axes in Figure 3-1) the syndrome ratio for 2003 was usually lower than for ratios for 2004 or 2005. For most states with syndrome ratios equal or less than one, these indicators were essentially equivalent in 2004 and 2005. Year-specific indicators above 1.0, however, showed a greater relative amount of WNF ascertainment in 2004 compared with 2005.

The demographics of the susceptible population might alter the WNV syndrome ratio because the incidence of neuroinvasive disease is dependent on gender and age in particular (Hayes and Gubler 2006). In Figure 3-2, aggregated data for 2003 through 2005 are plotted and compare 36 states' crude WNV syndrome ratios with corresponding gender and age-group adjusted rate ratios along the same imaginary vertical axes. Syndrome ratios were adjusted using direct standardization and 2000 U.S. Census data for 6 categories of gender and age group (less than 40 years, 40-59 years, and 60 years and older). With few exceptions, adjustment for gender and age groups had a minimal effect on the syndrome ratios, though the need for adequate data within strata necessitated the use of three broad age groups.

Multiple imputation of race and ethnicity

Since race and ethnicity are hypothesized indicators of likelihood of testing and reporting of WNF in Study 1, but race and ethnicity data are missing in many reports, multiple imputation was used to provide statistical inference. To impute missing race and ethnicity, the models condition on all observed West Nile virus surveillance data and county-level Census data on population percentages of Blacks, Hispanics, and Whites. Using 0.01 as the minimum, initial marginal R-squared for race/ethnicity predictors' inclusion, plausible values of race (Black or White) and ethnicity (Hispanic or not) are generated using stepwise logistic regression. The logistic regression models assign a race (or ethnicity) value to each missing value and calculate model parameter estimates again using the full (imputed) data set. The multiple imputation process repeats to obtain a distribution of likely estimates of the model parameters.

Specifically, the approach sequentially overwrites previous draws from each posterior predictive distribution (prior distributions of regression parameters are assumed to be non-informative), and correlational structures accumulate among covariates with successive cycles of the specified 100 iterations and 10 imputations (Raghunathan, Solenberger, and Van Hoewyk 2007). In generating race values, for example, the equation is:

$$\text{logit}\,[\Pr(Y = 1)\,|X] = \beta_0 + \beta 1^{*}\,\text{Year}_1 + \beta 2^{*}\,\text{Year}_2 + \beta 3^{*}\text{Age group}_1 + \beta 4^{*}\,\text{Age group}_2 + \beta 5^{*}\text{Gender} + \beta 6^{*}\text{Syndrome} + \beta 7^{*}\text{Hispanic} + \beta 8^{*}\text{Percent Black} + \beta 9^{*}\,\text{Percent Hispanic} + \beta 10^{*}\,\text{Percent Black}$$

where X represents the most recently updated data. Predictors are a mixture of indicator variables (surveillance year, age group [0-39, 40-59, 60 or more years], gender, syndrome

[febrile illness or neuroinvasive disease], and ethnicity) and proportions (percent Black, Hispanic, and White). To generate ethnicity values, the equation above applies except that β7*Hispanic is replaced with β7*Race.

Actual imputation as Black (indicator variables coded as race = 1, ethnicity = 0), Hispanic (coded as race = 0, ethnicity = 1), or White (coded as race = 0, ethnicity = 0) is described using notation from Raghunathan and others (2001) in which **B** represents a matrix for the maximum likelihood estimates of the β coefficients from the regressions above, **V** is its asymptotic covariance matrix, and **T** is the Cholesky decomposition of **V**. The vector **z** contains the random normal deviates and row dimensions of **B**. **T** and **z** are multiplied and their product is added to **B** to produce each β_*. Predicted probabilities (P_*) for the race and ethnicity are based on these new coefficients (β_*) and Umiss, the recently updated data that remain missing: $P_* = [1 + \exp(-\text{Umiss} \cdot \beta_*)]^{-1}$. Predicted probabilities are compared with a vector (**u**) with row dimensions equal to Umiss and containing uniform random numbers (example shown below).

$$\mathbf{u} = \begin{pmatrix} 0.100973 \\ 0.809590 \\ 0.522916 \\ 0.902560 \end{pmatrix}$$

When each P_* exceeds its corresponding value in the u matrix, a value of 1 is imputed; when P_* is equal or less than its u value a 0 value is imputed.

Adjusted odds ratios are averaged from the imputed datasets, with variances for 95% confidence intervals incorporating both the variability within each dataset and the variability across the datasets (Little and Rubin 2002). Using Schafer's notation (1999), $\hat{Q} = \hat{Q}(\text{Yobs}, \text{Ymiss})$ are hierarchical model-based parameter estimates for race/ethnicity

effects, where Yobs and Ymiss denote race/ethnicity data that are partially complete and missing, respectively, and $\hat{Q}^{(l)} = \hat{Q}^{(l)}(\text{Yobs}, Y^{(l)}\text{miss})$ are the estimates, using imputed values for the missing data with $l = 1,\ldots, m$ iterations. The final imputation-based parameter estimates are a simple average: $\overline{Q} = m^{-1} \sum \hat{Q}^{(l)}$.

As noted above, two components are involved in order to calculate variances for the 95% confidence intervals. The within-imputation variance is averaged from variance estimates of each imputed dataset: $\overline{U} = m^{-1} \sum U^{(l)}$, with $\hat{U}^{(l)} = \hat{U}^{(l)}(\text{Yobs}, Y^{(l)}\text{miss})$ representing variance estimates as missing data are imputed $l = 1,\ldots, m$ times.

The between-imputation variance is calculated from the formula: $B = (m-1)^{-1} \sum (\hat{Q}^{(l)} - \overline{Q})^2$. Total variance combines within- and between-imputation variance: $T = (1 + m^{-1}) B + \overline{U}$.

A number of assumptions were required to justify the use of multiple imputation for Study 1. Persons in the surveillance dataset, and by extension the population, are assumed to belong to one of three mutually exclusive race/ethnicity categories: non-Hispanic African American/Black, Hispanic, and non-Hispanic White. The study assumes that useful predictors of race and ethnicity can be obtained from the surveillance records and/or from Census data that are ascertained from case records' residence information. The assumption that a residential county's composition correlates with one's own race and ethnicity within population strata was assessed using complete records. The assumption that race/ethnicity frequency distributions do not systematically

differ when those data are present versus missing cannot be tested, but county compositions were compared by missing data status.

In addition, data on race/ethnicity are assumed to be missing at random (MAR); that is, the extent of missing race/ethnicity data itself does not depend on the race or ethnicity. Following Little and Rubin's notation (2002), the data are MAR if: $Pr(M_i = 1 \mid y_{i1},\ldots,y_{ik}; \varphi) = Pr(M_i = 1 \mid y_{i1},\ldots,y_{ik-1}; \varphi)$, where $y_{i1},\ldots,y_{ik-1}$ represents remaining fully observed data, y_{ik} represents race or ethnicity, and M_i is an binary variable for the presence or absence of race/ethnicity data.

Modeling timeliness of reporting

Study 3 focuses on reporting timeliness for six diseases: acute hepatitis A, giardiasis, legionellosis, malaria, pertussis, and Rocky Mountain spotted fever. These six diseases were selected because they are not monitored as part of Georgia's Emerging Infections Program, a surveillance system with more resources, capacity, and complexity than a typical state-based reportable diseases surveillance program. For similar reasons, case reports of STIs and HIV/AIDs were not included in the study. The study period is the 18-month interval of disease reporting dates from July 1, 2003 to December 31, 2005. The interval is advantageous because the SendSS system was fully available in Georgia in 2003 and a SendSS field 'date of first public health notification' also had been established early in 2003. In addition, surveillance records for 2005 were finalized in May of 2006.

Reporting timeliness is calculated as the difference in the dates of first public health notification and laboratory specimen or isolate collection. Since laboratory testing

is a component of the case definitions for all six diseases, collection date data are near complete (range: 97-100%). The completeness of dates of first reports are 95% or greater for four diseases but lower for the two most frequent diseases: giardiasis (86%) and hepatitis A (78%). In contrast, information on dates of symptom onset or first medical care were generally unavailable.

Time to report was analyzed as a continuous outcome (number of days). The multivariate analysis includes survival analyses using Cox proportional hazards regression. A Cox proportional hazards modeling approach was used because these models are robust to departures from distributional assumptions of the dependent variable and often applied when an epidemiologic outcome involves time to an event.

The Cox proportional hazards models required assessment of the proportional hazards assumption. For each independent variable, proportional hazards assumptions were assessed using log-log survival curves and by examining variable interactions with the natural log of time to report ($p > 0.05$) (Kleinbaum 1996). Following backward elimination and significance testing, a parsimonious model was obtained.

Table 3-1. West Nile virus surveillance case reports, ArboNet Surveillance System, 2003-2005

Data field	Description
Season	2003, 2004, 2005 West Nile virus seasons
FIPS	State and county codes for case residency
Onset date	Date of illness onset
Age	Age of case-patient (in years or months)
Sex	Male or female
Race	Am. Indian/Alaska Native, Asian, Black, White, unknown
Ethnicity	Hispanic, non-Hispanic, unknown
Syndrome	Fever or neuroinvasive disease (other uncommon syndromes excluded)

Table 3-2. Meningococcal disease surveillance case reports, National Notifiable Diseases Surveillance System, 2003-2005

Data field	Description
State and county	FIPS codes
Event date	Earliest known date associated with disease incident
Event type	Describes event date as illness onset, specimen collection, or laboratory diagnosis
Age	Age of case-patient (in years or months)
Sex	Male or female
Race	Am. Indian/Alaska Native, Asian, Black, White, other, unknown
Ethnicity	Hispanic, non-Hispanic, unknown
Case status	Confirmed or probable case status
Outcome	Whether infection resulted in death
First culture	Date first positive culture obtained
Specimen	Specimen source (e.g., blood, CSF, joint)
Infection	Type of infection (e.g., bacteremia, pneumonia)
Serogroup	Serogroup of the organism (A, B, C, Y, W135, not groupable, other, or unknown)

Table 3-3. Extant survey data on state health departments, including epidemiology and laboratory programs and functions, 2001

Data field	Description
Structure	Freestanding/independent vs. part of superagency
Centralization	Centralized, decentralized, mixed, shared health governance
Liaison	Formal or informal liaison function between local and state
Districts	Administrative unit between state and local health department
District duties	Multiple variables (e.g., consult local health departments)
State board	State board or council of health exists
SHO appointed	Appointment of state health officer (SHO) by governor, health board, agency director, or other
SHO cabinet	Whether SHO is a cabinet-level appointment
SHO duties	Multiple variables (e.g., supervise local health departments)
Agency duties	Multiple variables (e.g., rural health, public health lab)
No. local	No. of local health departments in the state
Local board	Local boards or councils of health exists in the state
L-board duties	Local health board duties, multiple (e.g., policy)
L-board members	Local health board, multiple (e.g., private citizens)
Coverage	Whether entire state is served by a health department
Supervision	Local health department staff employed/supervised by state agency, local government, or combination
Function level	Location of functions (in all, most, or some locally vs. state level); includes reporting, epidemiology, and laboratory services
Local employees	No. of local health department employees (range)

Table 3-4. Extant survey data on state health departments' epidemiology program capacity, 2004

Data field	Description
Funding type	Whether federal, state, and other monies sources of funding for state epidemiology program
Funding source	% of funding for state epidemiology program
Program type	Epidemiologists organized together, by program, or combination
Program capacity	Extent epidemiology and surveillance capacity met for program areas, as none, minimal, partial, substantial, almost fully, fully met (e.g., infectious diseases)
Staffing number	No. epidemiologists in program areas (degree-specific)
Staffing need	Epidemiologists needed for programs (degree-specific)
Years employed	No. epidemiologists employed for 0-2, 3-5, 6-10, 11+ years
Number trained	No. employees trained in epidemiology in program areas (degree-specific)
Service capacity	Adequacy of epidemiologic capacity for 4 essential services, as none, minimal, partial, substantial, almost fully, fully met (e.g., diagnose/investigate health problems)

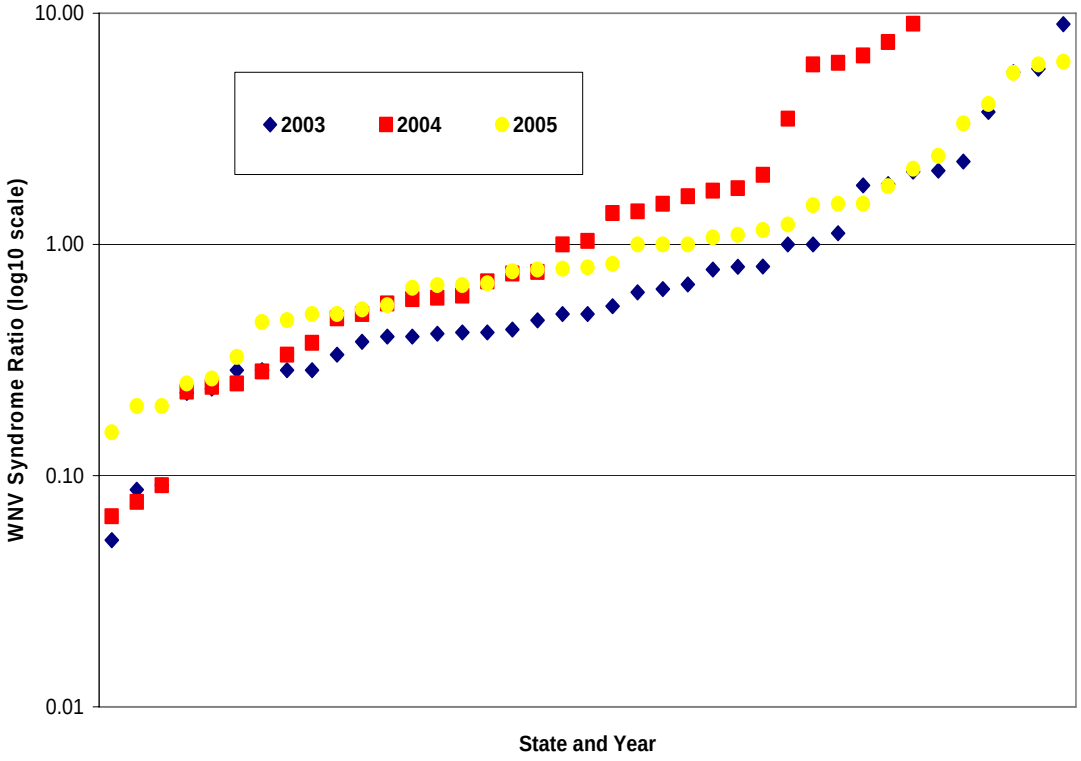
Table 3-5. Extant survey data on state health departments' laboratory program capacity, 2002-2005

Data field	Description (survey year)
Staff	No. technical lab staff (2005)
CDC programs	CDC surveillance program participation (2004)
Epi meetings	Whether staff meet regularly with epidemiology office (2004)
LIM reporting	Whether laboratory information system has electronic reporting capacity (2004)
Policy	Whether laboratory director regularly participates in developing policy for health related laboratories (2004)
Lab meetings	Whether laboratory staff meet with state's other public health laboratories regularly (2004)
Liaison1	Whether laboratory has someone whose sole responsibility is partnerships between public and private labs (2004)
Communicate	Whether laboratory sends newsletters to clinical/hospital laboratories (2004)
Other meetings	Whether laboratory meets with state's other program directors regularly (e.g., local health departments) (2004)
Manual	Whether laboratory has a guidance manual on testing services and specimen/isolate submission (2003)
Assess referrals	Whether laboratory has assessed microbiology patterns to determine which laboratories may not be referring specimens/isolates (2003)
Reporting audits	Whether state health department does systematic analysis to determine whether laboratories comply with disease reporting requirements (2003)
Report assurance	Whether state health department has someone who contacts private clinical laboratories to assure disease reporting (2003)

Table 3-5. Extant survey data on state health departments' laboratory program capacity, 2002-2005 (continued)

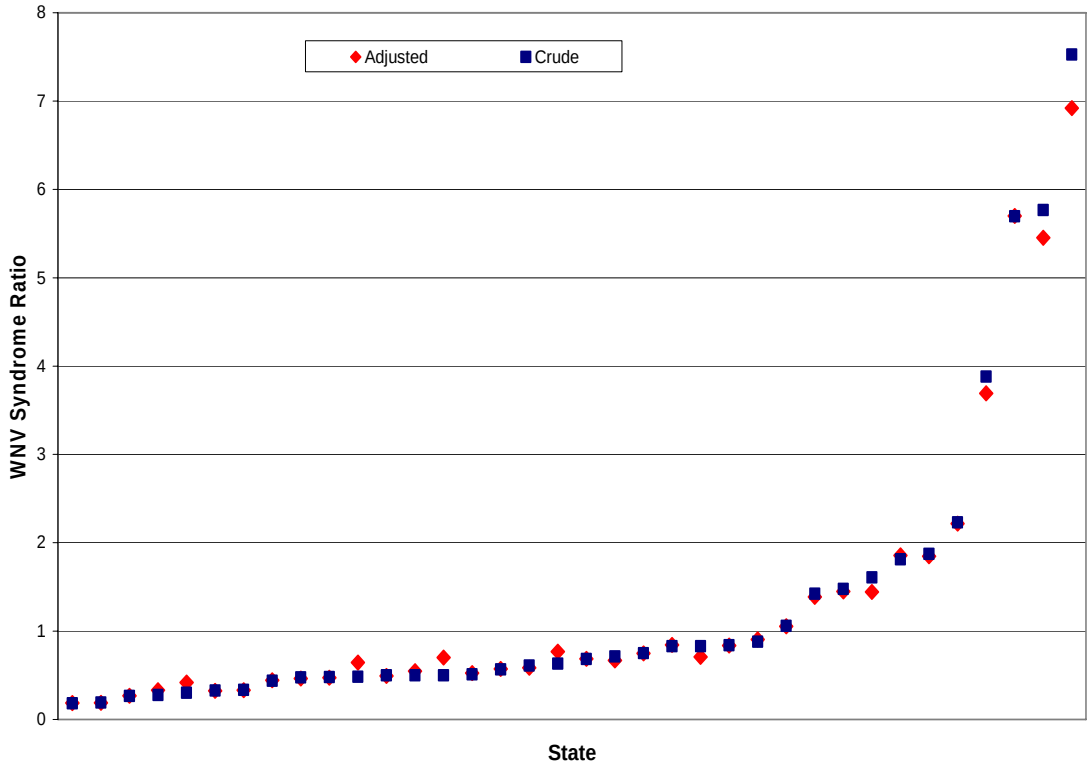
Data field	Description (survey year)
Rapid alerts	Whether laboratory has capacity to send rapid communications (2003)
Alerts topics	Whether laboratory has sent rapid communications in the past year (e.g., West Nile virus) (2003)
Courier	Whether laboratory system has intra-state courier system (2003)
Courier uses	System for all specimens, biologic specimens, etc. (2003)
Courier coverage	System has partial vs. full geographic coverage (2003)
Admin coverage	Whether laboratory has adequate administrative coverage (2003)
Clinical labs1	Whether laboratory has a database of all clinical laboratories in the state (2003)
Clinical labs2	Whether laboratory has a system to identify all clinical laboratories in the state (2003)
Public health labs	No. of public health laboratories in the state (2002)
Webpage	Whether laboratory has a webpage (2002)
Staff2	No. of FTEs that perform analytical testing (2002)
Liaison2	Whether laboratory has a liaison between public and private laboratories (2002)

Figure 3-1. State- and year-specific West Nile virus (WNV) syndrome ratios for 39 states, United States, 2003-2005*



* The WNV syndrome ratios plotted here are state- and year-specific case counts of WNF: WNND for states with one or more cases of West Nile fever and West Nile neuroinvasive disease each per year (39 states in 2003 and 2005, 33 in 2004). WNV syndrome ratios were sorted for visual comparison purposes.

Figure 3-2. Crude and gender- and age group-adjusted West Nile virus (WNV) syndrome ratios for 36 states, United States, 2003-2005*



* The WNV syndrome ratios plotted are state-specific and aggregated for 2003-2005. Crude WNV syndrome ratios are case counts of West Nile fever (WNF) over case counts of West Nile neuroinvasive disease (WNND) for cases where gender and age data were available. Adjusted syndrome ratios were calculated using direct standardization and 2000 U.S. Census data for 6 categories of gender and age group (less than 40 years, 40-59 years, and 60 years and older). States with a zero case count of WNF or WNND in no more than one gender/age group category were included. WNV syndrome ratios were sorted for visual comparison.

CHAPTER 4

DIFFERENTIAL WEST NILE FEVER ASCERTAINMENT

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Abstract

Given the burden and potential severity of West Nile fever (WNF), we described associations between WNF surveillance completeness and testing and reporting variations.

In 2006, we surveyed U.S. state and large city/county laboratory and epidemiology programs on WNF testing and reporting for 2003–2005 (82% and 79% responses, respectively). To evaluate associations between programs' capacities, practices, and surveillance completeness, we calculated yearly 'syndrome ascertainment ratios' using case counts of WNF and neuroinvasive disease (WNND) for jurisdictions with at least one case of each syndrome (2003: 40, 2004: 36, and 2005: 41). Separately, we assessed associations between race/ethnicity and syndrome by combining survey and surveillance data (n=14,584 cases) for multilevel models predicting WNF versus WNND, while accounting for capacities/practices.

Jurisdictions were more likely to ascertain one or more WNF cases per WNND case when one or no WNV testing criteria existed (e.g., hospitalization) compared to jurisdictions with more criteria (2003: OR=7.7, 95% CI=1.3, 46.4), when conducting >3 WNV surveillance activities (e.g., clinician trainings) (2004: OR=11.0, 95% CI=1.1, 106.4; 2005: OR=9.3, 95% CI=1.6, 54.8), and when at least 5.0 WNV surveillance staff per million residents were dedicated (2003-2005 combined: OR=6.4, 95% CI=1.0, 40.3). In multilevel analyses, the odds of WNF were lower in Blacks (OR=0.56, 95% CI=0.31, 0.97) and Hispanics (OR=0.69, 95% CI=0.48, 0.98) compared with Whites.

Jurisdictions with minimal testing criteria (2003), numerous surveillance activities (2004 and 2005), and greater surveillance staff rates (2003-2005) were more likely to ascertain WNF. WNF may have been disproportionately undercounted in Blacks and Hispanics.

Introduction

In the United States, West Nile virus (WNV) emerged in the New York City metropolitan area in 1999 (Nash et al. 2001). By the end of 2003, over 14,000 human WNV cases had been reported in 45 states (Centers for Disease Control and Prevention 2007). The epidemic's unprecedented size often exceeded public health laboratory testing and surveillance capacities for arboviral illness (Silk and Berkelman 2005).

The absence of licensed assays to detect WNV infection in clinical settings intensified the initial demand for serologic testing within public health laboratories, and patients with West Nile neuroinvasive disease (WNND) often were prioritized when testing volumes were high. When enzyme immunoassays (EIA) tests for WNV antibodies became commercially available in 2003, testing opportunities increased but the specificity of some tests was not optimal (Malan et al. 2004). Serologic cross-reactivity from previous flavirus infection (Martin DA et al. 2002), as well as the persistence of WNV-specific immunoglobulin M (IgM) in serum and cerebrospinal fluid (CSF) (Kapoor H et al. 2004; Prince et al. 2005; Roehrig et al. 2003), necessitated case confirmation with arboviral panels, plaque reduction neutralization tests (PRNT), and convalescent-phase sera testing. Incomplete disease reporting (Doyle, Glynn, and Groseclose 2002) and physicians' lack of awareness of reporting procedures (Konowitz, Petrossian, and Rose 1984; Krause, Ropers, and Stark 2005; Weiss, Strassburg, and Fannin 1988) also were challenging. Efforts to enhance surveillance (Silk and Berkelman 2005) and surveillance for WNV activity in nonhuman vertebrates and mosquitoes (Marfin et al. 2001) were required.

These challenges collectively resulted in substantial variability in states' West Nile fever (WNF) testing and reporting. With natural history studies accumulating, however, the potential duration (Watson et al. 2004), severity (Bode et al.. 2006; Patnaik, Harmon, and Vogt 2006), and neuropsychological sequelae (Carson et al. 2006; Haaland et al. 2006) of WNF was recognized. In 2004 the Centers for Disease Control and Prevention (CDC) endorsed a Council of State and Territorial Epidemiologists (CSTE) position statement to expand the national surveillance case definition to include non-neuroinvasive arboviral illnesses and monitor a wider spectrum of WNV disease (Council of State and Territorial Epidemiologists). In this paper, we identify public health program factors that were potentially associated with differential WNF testing, confirmation, and reporting (collectively called "ascertainment" hereafter) from 2003 through 2005. In addition, we estimate the extent of differential WNF ascertainment among Blacks and Hispanics relative to Whites by controlling for their associated public health agencies' laboratory testing and reporting procedures.

Methods

Final reports of 15,401 human WNV cases with illness onset dates from January 1, 2003 through December 31, 2005 were provided by CDC. Records with an unknown or 'other clinical' syndrome were excluded (2.6%). For the study, Blacks of unknown ethnicity (0.1%) were assumed to be non-Hispanic and Hispanics with unknown or other race (1.3%) were considered Hispanic but neither Black nor White. Whites of unknown ethnicity (15.0%) were not assumed to be non-Hispanic. Records of other race/ethnicity groups, which appeared infrequently in the data (< 2.0% each), were omitted because

data were insufficient for their specific analysis. Sixty-five percent of cases occurred in 2003, an additional 16% occurred in 2004 and the final 19% in 2005.

Ethnicity (15%) or race and ethnicity (26%) data were frequently missing. Rather than omit records with missing information, we used multiple imputation to provide parameter estimates and associated uncertainty levels (Little and Rubin 2002). Stepwise logistic regression models conditioned on all observed surveillance data (year, age group, gender, and syndrome) and county-level, U.S. Census data, which were added to the models to generate plausible values of race (Black or White) and ethnicity (Hispanic or not). To create these Census predictors of race and ethnicity, county-specific, population percentages of Blacks, Hispanics, and Whites were calculated within strata defined by gender and one of 23 age groups and matched to each case's gender and age group. U.S. Census data for 2000 (Summary File 1) were obtained using *DataFerret* 1.3.3 (Census Bureau/CDC) and linked to cases using Federal Information Processing Standards (FIPS) county codes. Ten imputed datasets were created using *IVEware* (Imputation and Variance Estimation Software, University of Michigan) (Raghunathan, Solenberger, and Van Hoewyk 2001).

We designed parallel, voluntary questionnaires to solicit data from state health departments' epidemiology and laboratory programs. Instructions designated January 1, 2003 through December 31, 2005 as the study period, and questionnaires referenced WNV-related disease surveillance and laboratory testing policies and procedures each year. In November or December of 2006, questionnaires were e-mailed to 103 arboviral surveillance coordinators or public health laboratory directors in state or large city/county (Houston, Los Angeles, New York City, Philadelphia, and Washington D.C.) health

departments where human WNV cases had been reported during the study period. (In reporting data from states or large city/county health departments, we subsequently refer to 'states' for simplicity.) Persons reporting front-line epidemiology (41%), management/supervisory (41%), or state epidemiologist (10%) functions completed 41 questionnaires (response rate = 79%). Laboratory directors (28%) or section supervisors/managers (66%) completed the 47 laboratory surveys (response rate = 84%).

Guidelines for WNV-specific, IgM-capture enzyme-linked immunosorbent assay (IgM ELISA) testing were obtained from survey participants and health department websites. Documents were parsed into six testing criteria: neuroinvasive disease, hospitalization, certain ages, calendar date ranges, epidemiology program approval, and health department contact prior to specimen submission. Indicator variables for each criterion (present or absent) were then combined to create an overall score of testing criteria stringency. Data from previous surveys conducted by the Association of Public Health Laboratories (APHL) (Inhorn et al. 2006), CSTE (Council of State and Territorial Epidemiologists 2004; Council of State and Territorial Epidemiologists 2005), and the Center on Medicine and Public Health at Florida State University were also analyzed (Beitsch et al. 2006; Beitsch et al. 2006). Surveys addressed public health laboratory capacities, services, and practices (2002-2004); epidemiology capacities (2004); WNV surveillance capacities (2004); and structures and functions of state public health agencies (2001), respectively. These survey data were analyzed in relation to aggregate surveillance data for the three-year study period.

To characterize WNF ascertainment completeness, a "WNV syndrome ascertainment ratio" was calculated for years and states with one or more reported cases

of WNF and WNND each. The ratio is obtained from counts of each syndrome (WNF / WNND), and serves as an indicator for assessing WNF ascertainment completeness. Ratio components are symptomatic infections, categorized clinically as either fever (without neuroinvasive disease) or neuroinvasive disease (e.g., encephalitis, meningitis, or flaccid paralysis). Symptom and serologic data from a New York City neighborhood-based study conducted in 1999 suggest as many as 30 WNF cases for every WNND case in a susceptible population (Mostashari et al. 2001).

In recent years, however, U.S. notifiable disease surveillance systems have ascertained approximately one or 2 WNF cases on average for each WNND case (Centers for Disease Control and Prevention 2007). Therefore, a 1.0 syndrome ascertainment ratio cutpoint was used to dichotomize the observed syndrome ascertainment ratios and assess state-level, programmatic factors associated with more complete (≥ 1.0) or less complete (< 1.0) relative WNF ascertainment. Since policies, procedures, and WNV activity vary over time, program correlates of ascertainment were assessed for each year. For aggregate analyses of 2003-2005, positive responses were coded from discordant yearly responses when 2003 alone (i.e., 65% of cases) or when 2004 and 2005 responses were affirmative. Two-tailed chi-squared and Fisher's exact tests are reported for contingency tables using an alpha level < 0.05 to define significance.

Multilevel models reflected the variability in WNF ascertainment created by autonomous states and their programs and the fact that case reports are nested in public health jurisdictions responsible for ascertainment. The models predict the odds of WNF ascertainment as the event of interest versus WNND ascertainment (1 – the probability of WNF) using the logit link function $\eta_{ij} = \ln (\Pr (WNF_{ij}) / \Pr (WNND_{ij}))$ and an assumed

Bernoulli sampling distribution for the binary syndrome outcome. Models were specific to each year or the overall study period. In each case, a random intercepts model with case-level predictors was initially fit (model 1), including fixed effects for age (grand mean centered) and the indicator variable covariates for gender, race, and ethnicity. Subsequent models included significant, state-level effects identified through univariate analyses of states' syndrome ascertainment ratios, U.S. Census region (West and Midwest versus Northeast and South), and population percentages of Blacks and Hispanics (both grand mean centered) (model 2). To assess whether state-level effects on WNF ascertainment probabilities vary with Black race or Hispanic ethnicity, cross-level interactions were specified by modeling race and ethnicity parameters as functions of the state-level predictors.

'Unit-specific' models were fit using restricted penalized quasi-likelihood (PQL) estimation in *HLM 6* (Scientific Software International, Lincolnwood, IL). A t-ratio statistic was used for testing effects' significance (Raudenbush SW and Bryk AS 2002), and for backward elimination of interaction terms. Adjusted odds ratios were averaged from the imputation datasets, with variances for 95% confidence intervals incorporating variability in each dataset plus variability across the imputed datasets (Little and Rubin 2002). Software for data storage and other analyses included *Microsoft Access 2003* (Microsoft Corp., Redmond, WA) and *SAS version 9.1 (*SAS Institute, Cary, NC). Institutional review board approval for the project was obtained from Emory University.

Results

Race and ethnicity

The final surveillance dataset included 14,584 records. States ascertained a median of 82.5 total cases during the three-year period (interquartile range [IQR]: 227). Forty-seven percent of ethnicity or race and ethnicity data were missing on average. Seventy-nine percent of states missing less than 33% of race/ethnicity data had total case counts in the lower 2 case-counts terciles. Six states with 67% or more of their race/ethnicity data missing were among 17 states with the highest case counts. The percentages of cases known to be Black or Hispanic increased steadily as counties' populations of Blacks and Hispanics increased within their gender and age-group Census strata (Appendix 4-A). The racial and ethnic composition of residential counties for Black, Hispanic, and White cases with missing ethnicity data, missing race and ethnicity data, and complete race/ethnicity data were generally comparable (Appendices 4-B, 4-C, and 4-D).

Census regions confounded the relationship between states' percentages of Blacks and the WNV syndrome ascertainment ratios. All eight states with 20% or more of the population comprised of Blacks were in the Southern region, and two-thirds of states with 10-20% Black residents were in Southern or Northeast regions. In addition, 81% of Southern states had syndrome ascertainment ratios below 1.0 in 2003. Hispanic population percentages were more evenly distributed among regions (states with ≥15% Hispanic residents were located in Southern [19%], Northeast [25%], Midwest [19%], and Western [38%] regions).

In Figure 4-1, states' race- and ethnicity-specific syndrome ascertainment ratios for the three-year study period are compared using incomplete, observed data and race/ethnicity data augmented through multiple imputation. For the observed and imputed data, syndrome ascertainment ratios were greater (i.e., WNF ascertainment was greater) for Whites relative to Blacks in 19 of 25 states (76%) with ≥ 1 case for each syndrome and racial category. Ratios were greater for Whites relative to Hispanics in 16 of 27 (59%) states with sufficient counts.

WNV testing and reporting

Thirty-five jurisdictions (63%) completed both surveys. When stratified by 2000 population size, CSF testing rates for WNV, surveillance rigor, year of peak case counts, WNND incidence, and WNV syndrome ascertainment ratio, the distributions of survey completion were relatively similar to the distributions of all states (Appendix 4-E). Ninety percent of decentralized agencies completed both surveys.

In 2003, WNV syndrome ascertainment ratios were ≥ 1.0 more often (38%) in states that encouraged healthcare providers to submit suspect WNF cases' specimens to a public health laboratory (or public and private laboratories) when compared with the 9 states (0% with ascertainment ratios ≥ 1.0) that either encouraged specimen referral solely to private laboratories or did not promote WNF testing (OR undefined) (Table 4-1). Of six individual WNV testing requirement components, only an association between the syndrome ascertainment ratio and a hospitalization requirement ($p = 0.05$) was marginally significant in 2003. However, syndrome ascertainment ratios below 1.0 were generally more common among states requiring the presence of neuroinvasive disease,

certain ages, calendar date ranges, and health department contact prior to specimen submission (data not shown). Syndrome ascertainment ratios ≥ 1.0 were more likely in states with 1 or none of these testing criteria (2003-2005: OR = 7.7, 95% CI = 1.3, 46.4, p = 0.04).

Syndrome ascertainment ratios were not associated with free testing or provision of free specimen shipping or shipping and containers (data not shown). No associations among states' syndrome ascertainment ratios and initial IgM ELISA or polymerase chain reaction (PCR) testing rates per 100,000 persons (2000 U.S. Census) were observed any year when rates were dichotomized at their medians (data not shown).

In 2003, states with WNV syndrome ascertainment ratios ≥1.0 were 6 times less likely to have commercial WNV testing available locally in their jurisdictions compared with states that indicated commercial testing was not yet being performed (OR = 0.2, 95% CI = 0.03, 0.9, p = 0.09) (Table 4-1). The estimated percentage of probable or confirmed cases reported through testing outside the public health laboratory system increased in 2005 to a median of 21% of cases (IQR = 71) from a median of 13-14% in the two previous years (2003: IQR = 40, 2004: IQR = 25). In 2005, states with at least one WNF case for each WNND case were almost seven times more likely to receive at least 50% of WNV case reports from outside testing (OR = 6.8, 95% CI = 1.3, 34.6, p = 0.04) when compared with states receiving a majority of reports from public health laboratories (Table 4-1).

By 2006, all but two epidemiology programs (95%) indicated that a WNV positive test result was laboratory reportable in their jurisdiction and 80% of jurisdictions required reporting of WNV positive tests from specimens collected within the state but

tested by out-of-state laboratories. Most programs (80%) have also designated WNF reportable in their jurisdictions. Syndrome ascertainment ratios were not significantly associated with establishment of WNV positive test results as laboratory reportable, requiring reporting of positive test results from out-of-state laboratories, or including WNF in states' lists of reportable diseases in any year (Table 4-2).

Among eight statewide activities to enhance WNV reporting, dissemination of advisories/recommendations (92%), surveillance manuals/protocols (74%), newsletters/other periodicals (62%), or conducting training/seminars on WNV reporting for clinicians (64%) were commonly reported. Less often, states established electronic laboratory reporting (41%), periodically telephoned reporting sources (31%), or conducted retrospective WNV case finding through laboratory (3%) or hospital records (0%) review. A syndrome ascertainment ratio ≥1.0 was associated with conducting training/seminars for the three-year period (OR = 10.0, 95% CI = 1.1, 89.8, p = 0.04) and in 2005 (OR = 15.8, 95% CI = 1.7, 148.1, p = 0.01). States ascertaining at least one WNF case for each WNND case were 11 times more likely to perform four or more surveillance activities (2003-2005: OR = 11.8, 95% CI = 1.3, 107.4, p = 0.03), with similar results in 2004 and 2005 (Table 4-2).

Laboratory and epidemiology capacity

For the three-year period, WNV syndrome ascertainment ratios ≥ 1.0 were no more likely (p = 0.4) in public health laboratories with 50 or more technical/analytic full-time equivalent (FTE) positions. No significant association between the syndrome ascertainment ratio and laboratory FTE rates above 3.0 per 100,000 residents was

observed (p = 0.7). States with three-year syndrome ascertainment ratios ≥ 1.0 were over 4 times more likely to have a designated a liaison to the states' private laboratories in 2002 (OR = 4.4, 95% CI = 1.1, 18.0, p = 0. 07).

When total FTE rates per one million residents were calculated, three-year syndrome ascertainment ratios ≥ 1.0 were six times more likely in health departments with WNV surveillance FTEs staffing rates of 5.0 or more (OR = 6.4, 95% CI = 1.0, 40.3, p = 0.1) and over four times more likely with infectious disease staff rates ≥ 5.0 (OR = 4.5, 95% CI = 1.1, 19.4, p = 0.08).

Multilevel WNF ascertainment

WNF was independently associated with each of the four case-level characteristics (age, gender, race, and ethnicity) and these associations were relatively unaffected either with the addition of select, state-level predictors or after stratifying by year (Table 4-3). The odds of WNF decreased by 2% for each year of age beyond the mean age (49 years) of all cases (2003-2005: OR = 0.98, 95% CI = 0.97, 1.0, p = 0.03). When compared with non-Hispanic Whites, the odds of WNF was lower among Blacks (2003-2005: 0.56, 95% CI = 0.31, 0.99, p = 0.05). In 2005, the likelihood of WNF ascertainment among Blacks was 60% lower in states where a majority (>50%) of case reports were received from WNV testing outside the public health laboratory system (OR = 0.40, 95% CI = 0.18, 0.90, p = 0.03), but did not differ relative to when states received a minority of reports from outside testing (OR = 0.86, 95% CI = 0.58, 1.29, p = 0.47). The likelihood of WNF ascertainment among Hispanics was 31% lower relative to non-Hispanic Whites (2003-2005: OR = 0.69, 95% CI = 0.48, 0.98, p = 0.04).

In multivariate analyses, the epidemiology and laboratory program characteristics that were potentially associated with WNF ascertainment varied by year (Table 4-3). The likelihood of WNF ascertainment was more than doubled in states where four or more activities focused on enhancing WNV surveillance were performed (2004: OR = 2.96, 95% CI = 1.76, 5.00, $p < 0.001$; 2005: OR = 2.62, 95% CI = 1.52, 4.51, $p < 0.01$). Models also accounted for Census regions, as the odds of WNF ascertainment were greater in the West and Midwest relative to Southern and Northeast regions (OR = 2.04, 95% CI = 1.08, 3.86, $p < 0.05$) in 2003.

Discussion

We used a WNV syndrome ascertainment ratio, the ratio of WNF and WNND case counts, to describe the completeness of WNF testing and reporting (ascertainment) in the United States from 2003 through 2005. Notably, ratio indicators for evaluating surveillance sensitivity had been previously introduced (Hook and Regal 1995) and applied to sexually transmitted diseases (Groseclose et al. 1999) and polio eradication (De Quadros 1994), but this is the first example of a WNV syndrome ascertainment ratio analysis. With recognition of the potential severities of WNV-related febrile illness and its sequelae (Bode et al. 2006; Carson et al. 2006; Haaland et al. 2006; Patnaik, Harmon, and Vogt 2006; Watson et al. 2004), there is a need for a measure of WNF surveillance sensitivity. Using this simple indicator, we demonstrated substantial variability in ascertainment of WNF each year relative to WNND ascertainment among states and large cities and counties.

Policies, practices, and capacities of health departments' epidemiology programs and public health laboratories were linked to the syndrome ascertainment ratios of their corresponding jurisdictions. These univariate analyses identified commercial testing unavailability (2003), one or no WNV testing requirement components (2003 and 2005), four or more surveillance activities (2004 and 2005), and receipt of a majority of case reports from testing outside the public health laboratory system (2005) as potentially related to increased WNF ascertainment. We also found variability associated with surveillance and infectious disease control staffing rates (2003-2005), variability between Census regions (2003), and that variability was dependent on population percentages of Blacks and Hispanics (2003). In detailing these sources of variation in WNF testing and reporting among health departments, we augmented a 2005 CSTE report on WNV surveillance capacity (Council of State and Territorial Epidemiologists).

In addition to differences among states, we also observed differences in WNF ascertainment according to the race and ethnicity of persons reported with WNV infection. WNF testing and reporting was usually lower in Blacks (76% of states) and Hispanics (59% of states) relative to Whites after missing data were accounted for using multiple imputation and county-level Census predictors to generate plausible data for race- and ethnicity-specific syndrome ascertainment ratios. These findings were reinforced by multilevel modeling. In multilevel analyses, the odds of WNF ascertainment were 44% lower in Blacks and 31% lower in Hispanics compared with non-Hispanic Whites, while accounting for both missing data uncertainty and state-level sources of variability in WNF testing and reporting.

There were limitations to both the univariate and the multilevel analyses. As a measure of WNF surveillance completeness, the syndrome ascertainment ratio assumes that persons with febrile illness are eligible for ascertainment because healthcare is sought. Estimates of the proportion of persons with WNF seeking healthcare or requiring hospitalization vary (Bode et al. 2006; Chowers et al. 2001; Mostashari et al. 2001; Patnaik, Harmon, and Vogt 2006; Watson et al. 2004). In addition, WNND testing, confirmation, and reporting are assumed to be complete. Persons with WNND are likely to be hospitalized (>90%) because of disease severity (Patnaik, Harmon, and Vogt 2006), but the proportion of people with WNND who are diagnosed as having WNV infection is unknown. Typically, a meningitis or encephalitis clinical presentation should raise physicians' indices of suspicion, particularly during WNV season and in the context of increasing publicity about WNV, making etiologic diagnosis of WNND more likely than WNF in most states. Also, many health departments promoted detection of WNND, particularly during epidemic periods (Council of State and Territorial Epidemiologists 2005). Although WNND reporting is believed to be "reasonably complete" in the United States (Council of State and Territorial Epidemiologists 2004), few (if any) studies of the completeness of WNND or WNV reporting have been published to date.

Simplicity was a goal in the multilevel modeling, but subjective decisions were made. At the case-level, we opted to center age using the grand mean. In general, centering is controversial and interpretation of corresponding results can become complicated (Enders and Tofighi 2007). In a supplemental analysis, however, centering race and ethnicity variables with group means had little effect on the magnitude or significance of their odds ratios. Also, the exclusion of significant numbers of states

when incomplete state-level data were added was a primary limitation. For this reason, we were unable to include all potentially significant program characteristics together in progressing to the multilevel models.

Estimates of the reduced likelihoods of WNF ascertainment among Blacks and Hispanics relative to Whites should be interpreted cautiously. A significant portion of the race data (25%) and the ethnicity data (40%) in particular were missing. Although suitable race/ethnicity predictors for imputation may not necessarily be reliable, uncertainty was appropriately represented by generating multiple, analogous datasets in which imputation results potentially vary. Multiple imputation assumes, however, that the extent to which race and ethnicity data are missing is statistically independent of one's own race or ethnicity after accounting for the remaining fully observed data (i.e., data are missing at random). In these analyses, this assumption was presupposed because the assumption is impossible to validate without supplemental data (Schafer 1999).

Studies have shown that the inclusion of auxiliary variables often improves the accuracy of multiple imputation-based parameter estimation (and is neutral at worst) (Collins, Schafer, and Kam 2001; Graham et al. 1997). The county-level, Census variables we used to generate plausible values rely on an assumption that a county's racial and ethnic composition likely correlates with one's own race and ethnicity within gender and age-group strata. Supplemental analyses (Appendices 4-A to 4-D) supported this assumption, but county population sizes vary nationally (Eisen and Eisen 2007). We did not have access to auxiliary variables for causes of missing data, which are likely to be diverse because surveillance data are aggregated from each state's disease reporting systems (Laws and Heckscher 2002). Furthermore, health information systems

frequently lack standards for race and ethnicity data, so misclassification bias may exist with the 'known' data (Boehmer et al. 2002; Gomez et al. 2003).

Several possibilities could explain the observed differences in WNF ascertainment by race and ethnicity. For example, the finding in 2005 that testing and reporting between Blacks and Whites is unequal only when most reports originated from outside the public health laboratory system suggests that differential use of commercial WNV diagnostic tests may play a role in the inequality we identified. Also, the combined effects of residency in regions where WNF ascertainment was less rigorous, together with higher percentages of Blacks in those populations, may create more missed opportunities for WNF ascertainment in Blacks.

Given the combinations of overall health disparities (Centers for Disease Control and Prevention 2005; Centers for Disease Control and Prevention 2004; Wong et al. 2005), specific disparities in infectious diseases rates (Centers for Disease Control and Prevention 2005), disparate access to health insurance and disparate healthcare experienced by Blacks and Hispanics (Agency for Healthcare Research and Quality 2005; Centers for Disease Control and Prevention 2004; Institute of Medicine 2002), our novel reporting of differential WNF ascertainment by race and ethnicity should be validated with studies that directly investigate the mechanisms behind these disparities. Collectively, reduced ascertainment, higher rates in Blacks and Hispanics, and low quality race/ethnicity data (Centers for Disease Control and Prevention 1992; Centers for Disease Control and Prevention 1999) could undermine surveillance objectives to monitor disease in populations at the most risk (Centers for Disease Control and Prevention 2001).

The ability to quantify sources of ascertainment variability and their relative importance at multiple levels is a significant tool for surveillance system evaluation. Previous evaluations have established that reporting completeness varies (Doyle, Glynn, and Groseclose 2002), but surveillance ascertainment variability had not been jointly measured at the individual and public health systems level. Also, few surveillance completeness evaluations have been extended to the series of conditional events that precede reporting of diagnosed cases (i.e., healthcare seeking, testing, and etiologic diagnosis) (Bender et al. 2004).

We identified active surveillance (performance of four or more surveillance activities) and staffing rates of 5.0 or more infectious disease control FTEs per million residents as potentially significant program characteristics associated with successful WNF ascertainment. While we did not have other data on program capacities or funding, these findings suggest that improvements in monitoring human disease can be achieved by agencies operating at optimal capacities. Unfortunately, concerns for the perceived impact of reduced federal funding for prevention and control of WNV and other emerging infectious diseases have already been raised (Council of State and Territorial Epidemiologists 2007), even while the Pandemic and All-Hazards Preparedness Act (Pandemic and All-Hazards Preparedness Act) calls for "establishing an effective and prepared public health workforce" with the capability to maintain "disease situational awareness domestically and abroad, including detection, identification, and investigation" (Hodge, Gostin, and Vernick 2007).

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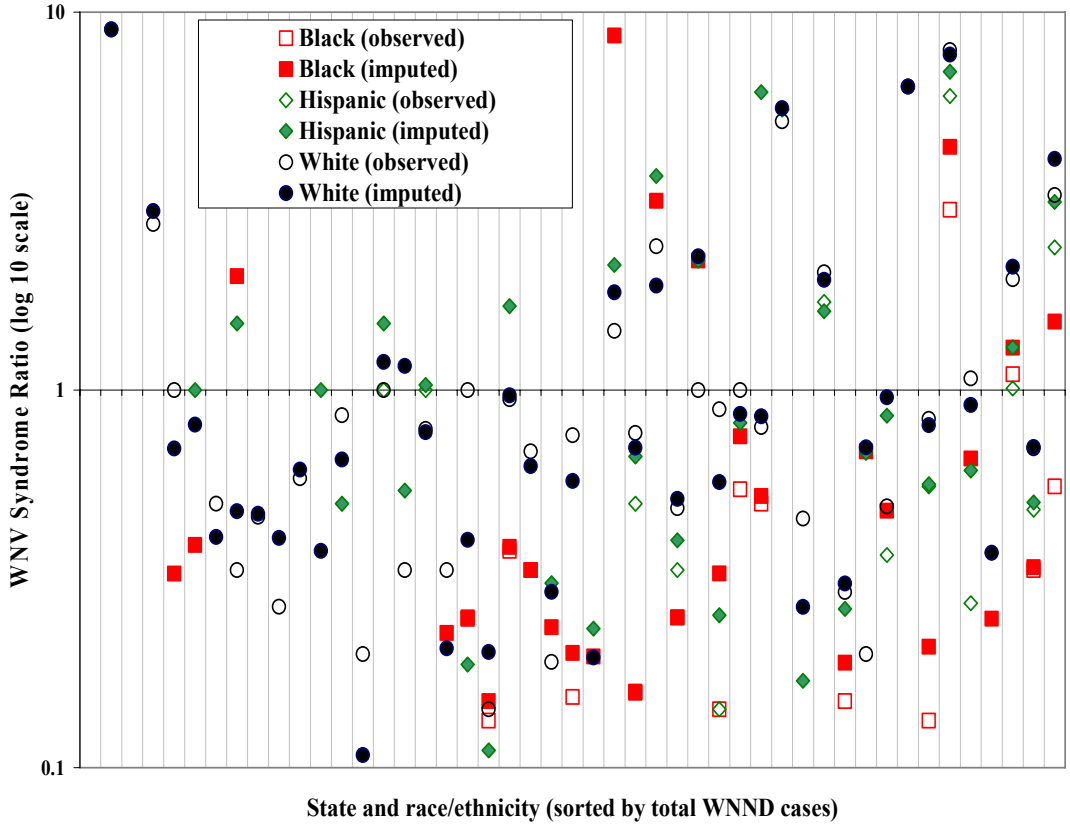
Figure 4-1. Race/ethnicity- and state-specific West Nile virus syndrome ascertainment ratios, 2003-2005*



* The syndrome ascertainment ratios (West Nile fever [WNF] / West Nile neuroinvasive disease [WNND]) plotted here are race- and ethnicity-specific of WNF and WNND case counts. States data (represented within vertical columns) are plotted when one or more cases of each syndrome in each race/ethnicity category exist. Observed (incomplete) data include 16 states for Blacks, 13 for Hispanics, and 42 for Whites (n=8,438). Ten imputations of race/ethnicity produced sufficient counts in 32 states for Blacks, 35 states for Hispanics, and 45 states for Whites (n= 145,556). The X axis is sorted by total WNND case counts for the three-year period, in ascending order from left to right. The Y axis is on a logarithmic scale, where the same absolute difference appears smaller as the distance from 1.0 increases in either direction.

Table 4-1. Laboratory testing and associated program correlates of West Nile fever ascertainment completeness, 2003-2005*

	2003		2004		2005	
	WNF/WNND**		WNF/WNND		WNF/WNND	
	≥ 1.0	< 1.0	≥ 1.0	< 1.0	≥ 1.0	< 1.0
TOTAL	12 (30%)	28 (70%)	17 (47%)	19 (53%)	18 (44%)	23 (56%)
Promote WNF tests[+]						
Public laboratory	9 (38%)	15 (63%)	8 (40%)	12 (60%)	12 (57%)	9 (43%)
None/private only	0	9 (100%)	4 (50%)	4 (50%)	3 (27%)	8 (73%)
Test requirements[++]						
1 or none	9 (56%)	7 (44%)	9 (69%)	4 (31%)	10 (71%)	4 (29%)
2 or more	2 (14%)	12 (86%)	6 (38%)	10 (63%)	6 (32%)	13 (68%)
Testing charges						
Free for all patients	8 (30%)	19 (70%)	10 (48%)	11 (52%)	11 (42%)	15 (58%)
Sometimes/not free	4 (57%)	3 (43%)	6 (75%)	2 (25%)	5 (63%)	3 (38%)
Commercial tests[+++]						
Available locally	5 (25%)	15 (75%)	15 (58%)	11 (42%)	15 (48%)	16 (52%)
Not available locally	6 (67%)	3 (33%)	1 (100%)	0	1 (100%)	0

Table continues

Table 4-1. Laboratory testing and associated program correlates of West Nile fever ascertainment completeness, 2003-2005 (continued)*

	2003		2004		2005	
	WNF/WNND**		WNF/WNND		WNF/WNND	
	≥ 1.0	< 1.0	≥ 1.0	< 1.0	≥ 1.0	< 1.0
TOTAL	12 (30%)	28 (70%)	17 (47%)	19 (53%)	18 (44%)	23 (56%)
Lab confirmation[#]						
Require	10 (37%)	17 (63%)	10 (48%)	11 (52%)	8 (36%)	14 (64%)
Not required	2 (40%)	3 (60%)	6 (75%)	2 (25%)	8 (67%)	4 (33%)
Outside testing[##]						
50% or more	2 (40%)	3 (60%)	2 (33%)	4 (67%)	9 (69%)	4 (31%)
Less than 50%	5 (22%)	18 (78%)	8 (44%)	10 (56%)	4 (25%)	12 (75%)

* Jurisdictions with ≥1 febrile and neuroinvasive case each year (2003: 40, 2004: 36, 2005: 41).

** The syndrome ascertainment ratio is West Nile fever (WNF)/West Nile neuroinvasive disease (WNND) case counts.

+ Promoted tests of suspect WNF cases in periods of West Nile virus (WNV) activity by encouraging specimen submission to public health lab or public and private labs vs. submission to private labs only or not promoted.

++ Five WNV testing criteria are hospitalization, neuroinvasive disease, certain ages, calendar date ranges, and health department contact prior to specimen submission.

+++ Commercial laboratory testing for WNV performed for at least some patients in the jurisdiction.

Require confirmation of positive results from commercial labs to count a case of WNV disease.

Year-specific % of confirmed/probable cases reported via tests outside the state's lab system.

Table 4-2. Epidemiologic surveillance and associated program correlates of West Nile fever ascertainment completeness, 2003-2005*

	2003		2004		2005	
	WNF/WNND**		WNF/WNND		WNF/WNND	
	≥ 1.0	< 1.0	≥ 1.0	< 1.0	≥ 1.0	< 1.0
TOTAL	12 (30%)	28 (70%)	17 (47%)	19 (53%)	18 (44%)	23 (56%)
Lab reportable[+]						
Yes	6 (29%)	15 (71%)	9 (47%)	10 (53%)	10 (38%)	16 (62%)
No	0	6 (100%)	1 (25%)	3 (75%)	1 (100%)	0
Out-of-state reports[+]						
Yes	9 (33%)	18 (67%)	10 (48%)	11 (52%)	13 (48%)	14 (52%)
No	0	6 (100%)	2 (29%)	5 (71%)	2 (40%)	3 (60%)
WNF reportable[+]						
Yes	3 (22%)	11 (79%)	6 (40%)	9 (60%)	7 (35%)	13 (65%)
No	2 (25%)	6 (75%)	3 (50%)	3 (50%)	3 (100%)	0

Table continues

Table 4-2. Epidemiologic surveillance and associated program correlates of West Nile fever ascertainment completeness, 2003-2005 (continued)*

	2003		2004		2005	
	WNF/WNND**		WNF/WNND		WNF/WNND	
	≥ 1.0	< 1.0	≥ 1.0	< 1.0	≥ 1.0	< 1.0
TOTAL	12 (30%)	28 (70%)	17 (47%)	19 (53%)	18 (44%)	23 (56%)
Peak year						
Current	9 (41%)	13 (59%)	1 (33%	2 (66%)	4 (100%)	0
Past	3 (18%)	14 (82%)	14 (47%)	16 (53%)	14 (38%)	23 (62%)
Enhance surveillance[++]						
4 or more activities	7 (41%)	10 (59%)	11 (58%)	8 (42%)	13 (65%)	7 (35%)
3 or fewer activities	2 (13%)	14 (88%)	1 (11%)	8 (89%)	2 (17%)	10 (83%)

* States with ≥1 febrile and neuroinvasive disease case each year (2003: 40, 2004: 36, 2005: 41).

** The syndrome ascertainment ratio is West Nile fever (WNF)/ West Nile neuroinvasive disease (WNND) case counts.

[+] Requirements for reporting of West Nile virus (WNV) positive lab results, WNV positive results from specimens collected in state but tested out-of-state, and WNF each designated reportable by May of year.

[++] See text for list of eight potential surveillance activities realized statewide in the study period.

Table 4-3. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) for West Nile fever ascertainment by case and program characteristics, 2003-2005

	2003	2004	2005	2003-2005
Number of cases (no. states)				
Model 1*	9282 (40)	2305 (36)	2635 (41)	14353 (48)
Model 2*	7763 (21)	1821 (27)	1110 (23)	9098 (22)
Intercept (u_{0j}) variance component (standard deviation)[+]				
Model 1	1.12 (1.06)	0.97 (0.98)	0.54 (0.73)	0.79 (0.89)
Model 2	0.16 (0.40)	0.53 (0.73)	0.38 (0.62)	0.28 (0.53)
	ORs (95% CI)			
Case-level characteristics[++]				
Age, years*				
Model 1	0.98 (0.97,0.98)	0.98 (0.98,0.99)	0.98 (0.98,0.99)	0.98 (0.98,0.98)
Model 2	0.98 (0.97,0.98)	0.98 (0.98,0.99)	0.98 (0.97,0.99)	0.98 (0.97,1.0)[a]
Female				
Model 1	1.30 (1.20,1.42)	1.36 (1.19,1.56)	1.06 (0.80,1.40)	1.25 (1.15,1.36)
Model 2	1.27 (1.16,1.38)	1.36 (1.19,1.57)	0.87 (0.61,1.23)	1.19 (1.0,1.41)
Black[+]				
Model 1	0.51 (0.34,0.76)	0.39 (0.22,0.70)	0.58 (0.42,0.81)	0.52 (0.42,0.65)
Model 2	0.47 (0.22,1.02)	0.39 (0.21,0.73)	0.86 (0.58,1.29)[b]	0.56 (0.31,0.99)
Hispanic[+]				
Model 1	0.74 (0.64,0.86)	0.68 (0.51,0.91)	0.57 (0.43,0.75)	0.67 (0.59,0.77)
Model 2	0.72 (0.61,0.86)	0.62 (0.45,0.86)	0.65 (0.28,1.50)	0.69 (0.48,0.98)

Table continues

Table 4-3. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) for West Nile fever ascertainment by case and program characteristics, 2003-2005

	ORs (95% CI)			
	2003	**2004**	**2005**	**2003-2005**
Program-level characteristics (model 2 only)[++]				
Available commercial tests	0.32 (0.21,0.51)	*not included*	*not included*	*not included*
One or no testing requirements	0.90 (0.48,1.68)	*not included*	1.0 (0.47,2.10)	1.33 (0.62,2.86)
Majority reports via outside testing	*not included*	*not included*	Black: 0.40 (0.18,0.89) White: 1.72 (0.85,3.46)	*not included*
Four or more surveillance activities	*not included*	2.96 (1.76,5.00)	2.62 (1.52,4.51)	1.35 (0.68,2.72)
5.0 or more infectious disease staff per million residents	*not included*	*not included*	*not included*	2.04 (0.86,4.81)
Census data (model 2 only)				
Western regions	2.04 (1.08,3.86)	1.98 (0.88,4.48)	1.65 (0.61,4.43)	1.63 (0.72,3.68)
Percent Black*	0.97 (0.94,1.0)	0.99 (0.96,1.02)	0.99 (0.96,1.02)	0.99 (0.95,1.03)
Percent Hispanic*	0.98 (0.97,0.99)	1.00 (0.98,1.03)	1.01 (0.97,1.04)	1.02 (0.98,1.06)

***** Model 1 has a random intercepts and case-level predictors only; model 2 adds state-level predictors and significant, cross-level interactions. Age, % Black, and % Hispanic centered.

+ Model estimates account missing race and ethnicity data via multiple imputation (see text).

++ See text for descriptions of program-level characteristics.

[a] Confidence intervals include 1.0 due to rounding.

[b] For Blacks in states with <50% reports via outside testing only (i.e., interaction modeled).

Appendix 4-A. Racial and ethnic frequency distributions of West Nile virus cases and their residential counties*

Percentage of corresponding race or ethnicity group in county	Percentage of all cases (no. of cases) in each race or ethnicity group known to be: Black n=463	Hispanic n =1101	White n = 6774
0-9%	1.2% (82)**	3.6% (185)**	100% (1)
10-19%	13.9% (104)	16.8% (212)	83.3% (5)
20-29%	36.1% (99)	26.9% (230)	55.6% (10)
30-39%	58.7% (81)	32.5% (157)	45.7% (16)
40-49%	69.8% (60)	46.2% (120)	42.6% (43)
50-59%	55.9% (19)	56.9% (62)	48.4% (192)
60-69%	80.0% (16)	65.9% (58)	60.9% (464)
70-79%	40.0% (2)	84.8% (50)	67.6% (876)
80-89%	0%	95.2% (20)	80.0% (1386)
90-100%	0%	100% (7)	97.6% (328)

* Among 8,338 (57%) West Nile virus (WNV) cases diagnosed and reported to the ArboNet surveillance system from 2003 through 2005 with race and ethnicity known. 2000 U.S. Census county-level data on racial and ethnic composition calculated within age group- and gender-matched strata corresponding to the cases' age, gender, and county of residence (181 counties not linked because case age or gender missing).

** The interpretation, for example, is that these 82 Black WNV cases are 1.2% of all WNV cases who reside in counties where 0-9% of the population is Black. Similarly, 185 Hispanic WNV cases are 3.6% of all cases in counties where 0-9% of the population is Hispanic.

Appendix 4-B. West Nile virus cases with missing or unknown race/ethnicity and the racial composition of residential counties*

Percent Black in County	Cases Missing Ethnicity Only % (No.)	Cases Missing Race & Ethnicity % (No.)	Cases with Known Race & Ethnicity % (No.)	Total
0-9%	81% (1787)**	87% (3267)**	84% (7033)	85% (12087)
10-19%	7% (148)	6% (239)	9% (748)	8% (1135)
20-29%	6% (143)	2% (93)	3% (274)	4% (510)
30-39%	4% (86)	2% (67)	2% (138)	2% (291)
40-49%	2% (37)	1% (49)	1% (86)	1% (172)
50-59%	<1% (10)	<1% (11)	<1% (34)	<1% (55)
60-69%	<1% (9)	1% (19)	<1% (20)	<1% (48)
70-79%	0%	<1% (1)	<1% (5)	<1% (6)
80-89%	0%	<1% (1)	0%	<1% (1)
90-100%	0%	0%	0%	0%
Total	15.5% (2220)	26.2% (3747)	58.3% (8338)	

***** 2000 U.S. Census county-level data on racial and ethnic composition calculated within age group- and gender-matched strata corresponding to the cases' age, gender, and county of residence (n=279 missing age and/or gender).

****** The interpretation, for example, is that 81% of cases with missing ethnicity data reside in counties where 0-9% of the population is Black. A similar percentage (87%) of cases with missing race and ethnicity data reside in counties where 0-9% of the population is Black.

Appendix 4-C. West Nile virus cases with missing or unknown race/ethnicity and the ethnic composition of residential counties*

Percent Hispanic in County	Cases Missing Ethnicity Only % (No.)	Cases Missing Race & Ethnicity % (No.)	Cases with Known Race & Ethnicity % (No.)	Total
0-9%	83% (1845)**	67% (2526)**	62% (5190)	67% (9561)
10-19%	10% (223)	16% (614)	15% (1265)	15% (2102)
20-29%	4% (86)	8% (309)	10% (856)	9% (1251)
30-39%	2% (38)	5% (188)	6% (483)	5% (709)
40-49%	1% (18)	2% (66)	3% (260)	2% (344)
50-59%	<1% (7)	1% (37)	1% (109)	1% (153)
60-69%	<1% (3)	<1% (5)	1% (88)	1% (96)
70-79%	0%	<1% (2)	1% (59)	<1% (61)
80-89%	0%	0%	<1% (21)	<1% (21)
90-100%	0%	0%	<1% (7)	<1% (7)
Total	15.5% (2220)	26.2% (3747)	58.3% (8338)	

***** 2000 U.S. Census county-level data on racial and ethnic composition calculated within age group- and gender-matched strata corresponding to the cases' age, gender, and county of residence (n=279 missing age and/or gender).

****** The interpretation, for example, is that 83% of cases with missing ethnicity data reside in counties where 0-9% of the population is Hispanic, while 67% of cases with missing race and ethnicity data reside in counties where 0-9% of the population is Hispanic.

Appendix 4-D. West Nile virus cases with missing or unknown race/ethnicity and the racial composition of residential counties*

Percent White in County	Cases Missing Ethnicity Only % (No.)	Cases Missing Race & Ethnicity % (No.)	Cases with Known Race & Ethnicity % (No.)	Total
0-9%	0%	0%	<1% (1)	<1% (1)
10-19%	<1% (1)	<1% (3)	<1% (6)	<1% (10)
20-29%	<1% (1)	<1% (12)	<1% (18)	<1% (31)
30-39%	1% (11)	1% (23)	<1% (35)	<1% (69)
40-49%	1% (24)	2% (60)	1% (101)	1% (185)
50-59%	4% (79)	5% (183)	5% (397)	5% (659)
60-69%	7% (164)	6% (240)	9% (762)	8% (1166)
70-79%	12% (259)	11% (408)	16% (1296)	14% (1963)
80-89%	16% (351)	24% (887)	21% (1733)	21% (2971)
90-100%	60% (1330)**	52% (1931)**	48% (3989)	51 % (7250)
Total	15.5% (2220)	26.2% (3747)	58.3% (8338)	

* 2000 U.S. Census county-level data on racial and ethnic composition calculated within age group- and gender-matched strata corresponding to the cases' age, gender, and county of residence (n=279 missing age and/or gender).

** The interpretation, for example, is that 60% of cases with missing ethnicity data reside in counties where 90-100% of the population is White. A similar percentage (52%) of cases with missing race and ethnicity data reside in counties where 90-100% of the population is White.

Appendix 4-E. Characteristics of health agencies and program survey completion

	Both	Epidemiology	Laboratory	Neither	Total*
TOTAL (n = 56)	35 (63%)	6 (11%)	12 (21%)	3 (5%)	
Agency structure[+]					
Centralized	6 (55%)	3 (27%)	1 (9%)	1 (9%)	11 (24%)
Decentralized	9 (90%)	0	1 (10%)	0	10 (22%)
Mixed or shared	16 (67%	2 (8%)	6 (25%)	0	24 (53%)
Population size (2000)					
Less than 2 million	11 (55%)	1 (5%)	5 (25%)	3 (15%)	20 (36%)
Two – less than 6 million	12 (60%)	5 (25%)	3 (15%)	0	20 (36%)
Six million or more	12 (75%)	0	4 (25%)	0	16 (29%)
CSF testing rate (2004)[++]					
Less than 2.0	11 (52%)	2 (10%)	6 (29%)	2 (10%)	21 (41%)
2.0 - 5.0	10 (77%)	0	3 (23%)	0	13 (25%)
Greater than 5.0	12 (71%)	3 (18%)	2 (12%)	0	17 (33%)
Surveillance (2004)[+++]					
Active and passive	17 (61%)	4 (14%)	6 (21%)	1 (4%)	28 (52%)
Passive alone	18 (69%)	2 (8%)	5 (19%)	1 (4%)	26 (48%)
Year of peak case count[#]					
2002	11 (61%)	3 (17%)	3 (17%)	1 (6%)	18 (38%)
2003	15 (65%)	3 (13%)	5 (22%)	0	23 (48%)
2004 or 2005	5 (71%)	0	1 (14%)	1 (14%)	7 (15%)

Table continues

Appendix 4-E. Characteristics of health agencies and program survey completion

	Both	Epidemiology	Laboratory	Neither	Total*
TOTAL (n = 56)	35 (63%)	6 (11%)	12 (21%)	3 (5%)	
WNND incidence[##]					
Less than 1.0	16 (76%)	1 (5%)	4 (19%)	0	21 (42%)
1.0 - 3.0	8 (50%)	4 (25%)	2 (13%)	2 (13%)	16 (13%)
Greater than 3.0	9 (69%)	1 (8%)	3 (23%)	0	13 (26%)
Syndrome ascertainment ratio[###]					
Less than 1.0	20 (59%)	6 (18%)	6 (18%)	2 (6%)	34 (71%)
1.0 or greater	11 (79%)	0	3 (21%)	0	14 (29%)

***** Row totals for characteristics and column percentages for each characteristic.

[+] Six non-states, 3 non-participants, and 2 non-respondents excluded. See references for data source.[27]

[++] Cerebrospinal fluid (CSF) testing rate is total number of CSF specimens tested in the state public health laboratory in 2004 per 100,000 persons (2000 U.S. Census). Four non-respondent states and one non-participant territory excluded. See references for data source.[26]

[+++] Self-reported, surveillance rigor for human WNV case ascertainment. Two non-respondents excluded. See references for data source.[26]

[#] Among 48 jurisdictions with ≥1 febrile and neuroinvasive disease case each for the January 1, 2003 to December 31, 2005 study period.

[##] Cumulative incidence per 100,000 persons of West Nile virus neuroinvasive disease (WNND) for the study period in 50 jurisdictions with WNND.

[###] Ratio of West Nile fever (WNF) to WNND counts for the study period in 48 jurisdictions with one or more cases of WNF and WNND.

CHAPTER 5

MENINGOCOCCAL DISEASE SEROGROUPING

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Abstract

Health departments monitor serogroup-specific trends in meningococcal disease by integrating case reporting, isolate submission, and laboratory testing. Resulting data inform vaccination recommendations during outbreaks and support assessments of the need for and impact of new vaccines. To characterize variations among states in the percentage of reported cases with available serogroup data, we examined program and patient factors for 2003–2005.

We received state surveys on meningococcal disease reporting and testing procedures for 49 epidemiology (response rate=92%) and 44 laboratory (response rate=83%) programs. Using data from 33 states where both programs returned complete surveys, we compared policies, practices, and capacities among states indicating less complete serogrouping (≤80% of isolates serogrouped [n=11]) with states indicating more complete serogrouping (>80% of isolates serogrouped [n=22]). For multilevel modeling, we linked states' data to confirmed case reports in a U.S. national surveillance database (n=4,115).

More complete serogrouping was frequently reported by states that specified isolate submission requirements in promotional materials (70%), legally mandated isolate submission (73%), provided free shipping (75%), monitored serogrouping using defined targets for completeness (81%), used 2 or more surveillance enhancement activities (85%), and used 4 or more activities to promote isolate submission (90%). Smaller proportions of states not utilizing these practices reported more complete serogrouping. In multilevel analyses, a serogroup result was marginally associated with serogroup monitored using defined targets (OR=2.8, 95% CI=0.9, 9.1), but unassociated with specimen type (blood, cerebrospinal fluid [CSF], blood and CSF, or other) and vital outcome (died versus survived).

Meningococcal disease serogrouping was more complete among states with systematic program efforts to promote and assure that isolates are submitted for serogroup testing.

Introduction

Characterization of structural differences in the polysaccharide capsule of *Neisseria meningitidis,* or serogrouping, is the first procedure performed for conventional strain designation of the pathogen (Tzeng and Stephens 2000). Meningococcal disease serogrouping has been performed for decades in the United States (Liu et al. 1971; Liu et al. 1971), and all state public health laboratories have the ability to distinguish the five predominant, pathogenic serogroups (A, B, C, Y, and W-135) isolated from sterile sites (U.S. Centers for Disease Control and Prevention [CDC], unpublished data 2004). State and local health departments routinely monitor serogroups by integrating case reporting with isolate submission and laboratory testing. Serogroup information becomes immediately important when health officials are deciding whether to implement a mass vaccination campaign for control of an outbreak (Centers for Disease Control and Prevention 1997).

In January 2005, the U.S. Food and Drug Administration licensed a meningococcal polysaccharide diphtheria toxoid conjugate vaccine (MCV4) based on clinical studies that demonstrated safety and short-term immunogenicity comparable to the previous U.S.-licensed meningococcal polysaccharide vaccine (Bilukha and Rosenstein 2005). MCV4 is a tetravalent vaccine, providing coverage against serogroups A, C, Y, and W-135 but not serogroup B disease. With increased use of MCV4, shifts in the serogroup frequency distribution are likely. Based on analogous experiences with *S. pneumoniae* and *H. influenzae* type b conjugate vaccines (Adams et al. 1993; Whitney et al. 2003), population-level reductions in the incidence of vaccine-preventable serogroups are also expected. The Council of State and Territorial Epidemiologists (CSTE) and

CDC recognized the renewed importance of serogrouping for monitoring vaccine-associated changes in the epidemiology of meningococcal disease by approving a 2004 position statement that called for universal serogrouping (Council of State and Territorial Epidemiologists 2004).

Considering these events, we selected meningococcal disease serogrouping as a model for an assessment of how state public health agencies successfully integrate disease surveillance with public health laboratory testing (Association of Public Health Laboratories 2002). We examined patient- and system-level factors associated with the presence of a serogroup testing result in the U.S. National Notifiable Diseases Surveillance System.

Methods

We designed parallel, internet-based surveys to solicit data from state health departments' epidemiology and laboratory programs regarding meningococcal disease surveillance and serogrouping-related policies and procedures present during the period from January 1, 2003 through December 31, 2005. In November of 2006, questionnaires were e-mailed to 100 state epidemiologists or public health laboratory directors and six counterparts in the District of Columbia, New York City, and Puerto Rico. (We refer to all of these jurisdictions as 'states' for simplicity.) Persons reporting front-line epidemiology (31%), management or supervisory (43%), or state epidemiologist (27%) functions completed 49 epidemiology questionnaires (response rate = 92%). Section supervisors or managers (68%) and laboratory directors (20%) most often completed the 44 laboratory questionnaires (response rate = 83%) (Figure 5-1). We also include

pertinent data from the Association of Public Health Laboratories (APHL) (Inhorn et al. 2006), CSTE (Council of State and Territorial Epidemiologists 2004), and the Center on Medicine and Public Health at Florida State University (Beitsch et al. 2006; Beitsch et al. 2006). These assessments included public health laboratory capacities, services, and practices (2002-2004); epidemiology capacity (2004); and structures and functions of state public health agencies (2001), respectively.

Finalized meningococcal disease case reports were extracted from the National Electronic Telecommunications System for Surveillance (NETSS) computer database at CDC in April 2007 (http://www.cdc.gov/EPO/dphsi/netss.htm). Probable and suspect cases (n = 203) were excluded because, by definition (Centers for Disease Control and Prevention 1997), these designations indicate that *N. meningitidis* was not isolated from a normally sterile site. Eighty-one cases with a non-groupable serogroup result or a serogroup result other than A, B, C, Y, or W-135 were also excluded because data were insufficient for analyses that distinguish these cases from other reasons for absent serogrouping results. Surveillance data were limited to 4,115 confirmed cases of meningococcal disease in 50 states, the District of Columbia, New York City, and Puerto Rico that were counted in published reports (http://www.cdc.gov/mmwr/) for 2003, 2004, and 2005 (Figure 5-2). Data included fields from a core record (e.g., age, sex) and a bacterial meningitis module (type of infection, specimen source, vital outcome, and serogrouping results). Supplemental data on type of infection (e.g., bacteremia), specimen source, outcome, and serogroup data were received from seven states with incomplete reporting to CDC (defined as ≤ 10% of cases' serogroup fields complete in one or more years). Another seven states that participate in the Emerging Infections

Program (EIP), a laboratory-based, active surveillance network sponsored by the CDC (Pinner et al. 2003), also provided data. Supplemental data were linked to the original records, such that 557 infection types, 690 clinical outcomes, 737 specimen types, and 749 serogroup fields were updated among the 4,115 case reports.

To characterize state-level, serogroup testing completeness during the overall three-year period, proportions serogrouped (i.e., cases successfully serogrouped / total cases reported) were calculated using the survey data. Proportions were dichotomized to compare epidemiology and laboratory programs' policies, practices, and capacities for states indicating ≤ 80% of isolates serogrouped with states where > 80% of isolates were serogrouped (i.e., termed less complete and more complete serogrouping hereafter). These cutpoints were relatively stringent but allowed for occasional lapses in serogroup testing. (Given that meningococcal disease is rare, this allowance was particularly important for the least populous states where testing lapses have a larger relative impact on proportions serogrouped because of small case counts.) One-tailed Fisher's exact tests are reported for contingency tables using an alpha level of 0.05 to define significance.

Unadjusted odds ratios (OR) and 95% confidence intervals (CI) are also reported. Survey data were considered valid for inclusion in the state-level, univariate analyses of serogroup testing completeness when year-specific, total case counts matched corresponding surveillance counts by 5 or fewer cases each year or differed by 15 or fewer cases for the three-year period (n = 33 states) (Figure 5-1).

Based on the univariate analyses, significant state-level characteristics were linked to surveillance data by state for hierarchical, generalized linear modeling of serogroup testing completeness during the three-year study period. To validate states'

reporting of case-specific serogroups, proportions serogrouped from the surveillance data were compared with proportions serogrouped from the surveys. Cases were included when states' serogrouping proportions were consistent (+/- 25%) each year (Figure 5-2). Cases were also included when the state's proportion serogrouped calculated from surveillance data was greater than 80%. Twenty states contributed data for only one (n = 8) or two (n = 12) years in the study period. All cases from states that provided supplemental data were also included, including five states that were divided according to whether cases occurred in a county and year when EIP surveillance was implemented. Thirty-nine states with 1,737 cases were initially included in the multilevel analyses.

Associations between the presence or absence of a serogroup testing result and age group (0-4, 5-14, 15-49, and 50 years and older), sex, specimen source (blood and cerebrospinal fluid [CSF], blood only, CSF only, or other source only, such as joint or peritoneal fluids), and vital outcome were tested using chi-squared tests with an alpha level of 0.05 to define significance. Since infection type and specimen source are correlated, and because infection type data were suspected to be less valid than specimen source data, the latter were used for the multilevel modeling. Models that included source (n = 973) and outcome (n = 1,321) were estimated separately because of missing data.

Multilevel models reflected the variability in serogrouping created by autonomous states and their epidemiology and laboratory programs (level 2) as well as the fact that case reports (level 1) are nested in public health jurisdictions. The models predict the odds of obtaining a serogrouping result using the logit link function, $\eta_{ij} = \ln (\Pr (\text{serogrouped}_{ij}) / \Pr (\text{not serogrouped}_{ij}))$, and an assumed Bernoulli sampling distribution

for the binary outcome. Random intercepts models with level-1 predictors only were initially fit (model 1), including indicator variables for either specimen source categories or vital outcome. Subsequent models included significant level-1 effects, at an alpha level of 0.10, and potentially significant, level-2 effects (generically as S_j) identified through univariate analyses of states' relative serogrouping completeness and programs' policies, practices, and capacities (model 2). Backward elimination was used to identify a final parsimonious model (model 3). A t-ratio statistic was used for testing effects' significance (Raudenbush and Bryk 2002). Adjusted odds ratios and 95% confidence intervals were also calculated.

Software for analysis included *SAS version 9.1 (*SAS Institute, Cary, NC) and *HLM 6* (Scientific Software International, Lincolnwood, IL). Institutional review board approval for the project was obtained from Emory University.

Results

Serogrouping and program policies/practices

Case counts from the survey and surveillance data matched for 33 states, which were included in state-level analyses of relative serogrouping completeness and program policies and practices (Figure 5-1). In these analyses, proportions serogrouped during the three-year study period varied from less than 25% (2 states), 33-55% (3 states), and 71-80% (6 states) to 81-90% (6 states) and 91% or greater (16 states) among the 33 states.

By January 2007, at least 33 survey respondents indicated that their states legally required clinical laboratories to submit isolates or specimens to the state public health laboratory and considered these requirements applicable to *N. meningitidis* isolates.

Isolate submission requirements were established prior to 2003 in 20 of 23 (87%) epidemiology programs that were aware of the date this requirement was established. Seventy-three percent of states with these requirements established reported more complete serogroup testing compared with 55% of states without these legal requirements, but this difference was not statistically significant ($p = 0.25$) (Table 5-1). Eight epidemiology programs used verbal or written notices of isolate submission failures among in-state laboratories. The frequencies of more complete serogrouping did not differ among states that used notices (67%) or did not use notices (72%) of isolate submission failures ($p = 0.59$).

Eighty-two percent of states in this study with established legal mandates for isolate submission also had promotional materials (e.g., posters) that listed the states' reportable diseases and specified this requirement. The proportions of states with more complete serogrouping did not significantly differ ($p = 0.39$) depending on whether these materials specified (70%) or did not specify (62%) submission requirements (Table 5-1). Epidemiology programs reported using five other types of statewide initiatives to enhance meningococcal disease surveillance: dissemination of written periodicals (e.g., newsletters) to healthcare providers (37%); surveillance manuals (35%); specific recommendations/advisories (29%); trainings/seminars on reporting for healthcare providers (27%); and automated or electronic laboratory reporting (22%). More complete serogrouping was frequently reported by states that used 2 or more initiatives (85%) compared with states that used fewer initiatives (55%), but this difference was not statistically significant ($p = 0.08$).

In the study, all but one state's (98%) epidemiology program required or recommended (but did not require) that clinical laboratories submit isolates to their public health laboratory. Six activities were used to promote the requirement or recommendation (disseminating surveillance manuals, written periodicals, and advisories; trainings/seminars; case finding inquires; and public health follow-up). While more complete serogrouping was usually (90%) reported by epidemiology programs with 4 or more requirement-promoting activities and less often (57%) reported by programs with fewer such activities (Table 5-1), this difference also did not reach statistical significance ($p = 0.07$). In contrast, the odds of more complete serogrouping was seven times smaller (OR = 0.14, 95% CI = 0.03, 0.71) in states where activities promoted isolate submission solely as a recommendation, compared with states with no activities promoting submission as a recommendation ($p = 0.02$).

While the majority reported serogrouping being performed at the state's central laboratory, 5 states noted that other public health laboratories in their states also performed serogroup testing. Many state public health laboratories paid for isolate shipping (64%), with half of these also providing containers (32%). More complete serogrouping was reported in 75% of these states (Table 5-1). While fewer (54%) states that did not provide shipping or shipping and containers had more complete serogrouping, this difference was not statistically significant ($p = 0.19$).

Almost all (96%) of the states that reported monitoring the completeness of *N. meningitidis* isolate serogroup testing indicated using one or more defined targets for completeness monitoring (data not shown). Definitions frequently included the number of isolates serogrouped either as a percentage of isolates received or a percentage of cases

reported and using 95% or 100% was a typical target. The odds of more complete serogrouping were five times higher in epidemiology programs with a defined target for monitoring completeness (OR = 5.10, 95% CI = 1.02, 25.54) compared with programs that either did not monitor serogrouping completeness or did not have a defined target for monitoring (p = 0.05).

Serogrouping and program capacities

Serogroup testing completeness was not statistically associated with infectious disease epidemiology staffing deficiencies (estimated need versus current staff) in 2004, which were assessed overall and within categories of full-time equivalent (FTEs) positions. When FTE rates per one million residents were calculated, a majority (69%) of states with infectious disease staff rates equal or greater than 5.0 per million residents also had more complete serogroup testing. Fifty-five percent of states with rates below 5.0 per million reported more complete serogrouping, but this difference was not statistically significant (p = 0.38). More complete serogrouping was seven times likelier (OR = 7.33, 95% CI = 1.11, 48.26) in public health laboratories with 50 or more technical/analytic FTEs (79%) compared with laboratories with fewer technical/analytic positions (33%) (p = 0.04). However, the frequencies of more complete serogrouping did not differ among states with laboratory FTE rates greater than or equal to 3.0 per 100,000 residents (63%) or staffing rates below 3.0 per 100,000 (60%) (p = 0.63).

In 2002, states' laboratory systems were divided between systems with one or more city or county public health laboratories (70%, range: 1 – 283 laboratories) and systems with a single, centralized laboratory (30%). The odds of more complete

serogroup testing were six times higher (OR = 6.25, 95% CI = 1.03, 38.08) in states with one or more city or county laboratories (79%) compared with states with a single, centralized laboratory (38%) ($p = 0.05$).

States' population size (median ≈ 4 million) confounded the relationships of laboratory staffing rates and centralization of laboratory systems with relative serogrouping completeness. The median population sizes of state laboratories with 50 or more FTEs and states with at least one city/county laboratory were 4.6 and 4.9 million, respectively, while the median populations of state laboratories with less than 50 FTEs and states without city/county laboratories were 1.3 and 1.2 million, respectively. In addition, the median population for states with less complete serogrouping was 1.8 million and the median population for states with more complete serogrouping was 4.8 million.

Few state public health laboratories (23%) assessed which laboratories may not be referring specimens or isolates to the state laboratory; about half (48%) systematically analyzed whether laboratories are complying with disease reporting requirements. More often (65%) states had a staff member contacting clinical laboratories to assure disease reporting. Serogrouping completeness was not associated statistically with any of these three practices. However, more complete serogrouping was common among states that assessed specimen/isolate referral patterns (78%) and analyzed whether laboratories comply with reporting requirements (71%) compared with states that did not perform either (59% each).

Multilevel serogrouping completeness

Proportions serogrouped were calculated from the survey data and from the surveillance data. The 39 states whose proportions matched were included in multilevel analyses of case-specific serogrouping completeness (Figure 5-2). The dataset for multilevel analyses included 1,268 cases for which isolate serogrouping results were obtained (73%) and 469 cases for which results were not obtained (27%) (n = 1,737 cases).

The proportions of cases with serogrouping results were similar for persons under 5 years of age (73%), 5-14 years of age (70%), 15-49 years of age (76%) and adults 50 years of age and older (70%) (p = 0.09). The frequency of serogrouping results did not differ between females (72%) and males (74%) (p = 0.33). Serogrouping frequencies differed by specimen source (p < 0.0001). When both blood and CSF specimens were tested, a serogrouping result was most likely (81%). Serogrouping frequencies were similar for blood (74%) and CSF (75%), while other sources (e.g., joint or peritoneal fluids) were uncommon and less often serogrouped (n = 36, 39%). Three-quarters (75%) of the 158 persons known to have died of invasive *N. meningitidis* infection had isolates serogrouped compared with 83% of patients who survived (p = 0.01).

Before inclusion of state-level characteristics (model 1, Table 5-2), there was a marginally significant 2.5-fold lower likelihood of a serogrouping result from other specimen sources relative to patients for whom blood and CSF specimens were obtained (adjusted odds ratio [aOR] = 0.39, 95% CI = 0.15, 1.05, p = 0.06). The likelihood of a serogroup result did not differ depending on whether patients survived or did not survive (aOR = 0.70, 95% CI = 0.43, 1.15, p = 0.16).

Substantially fewer data (n=564 cases in 19 states) were available when five potentially significant level-2 effects were added (model 2, Table 5-2). The odds of a serogroup testing result may have been increased in states that reported monitoring of serogrouping completeness with a defined target, relative to states that either did not monitor completeness or monitored without a defined target (aOR = 3.31, 95% CI = 0.78, 14.16). However, the association was not significant (p = 0.10). The final model (model 3, Table 5-2) identified two predictors of serogroup testing completeness at the state level. A potential association with monitoring of serogrouping completeness remained (aOR = 2.81, 95% CI = 0.87, 9.11, p = 0.08). In addition, the odds of a serogrouping result were over 4 times higher in state laboratories with greater than 50 technical/analytic FTEs (aOR = 4.56, 95% CI = 1.55, 13.41, p = 0.01).

When compared with model 2, a model that also accounted for population size (greater or less than the median state population size) did not appreciably change the state-level estimate of the effect of 50 technical or analytic FTEs (aOR = 3.00, 95% CI = 1.07, 8.47) on the likelihood of a serogrouping result (data not shown). The odds of serogrouping was over ten times higher (aOR = 13.23) in states with one or more city or county laboratories compared with states with a single, centralized laboratory (p = 0.01), but this estimate was imprecise (95% CI = 1.43, 122.24).

Discussion

Complete serogroup testing was associated with a variety of epidemiology and laboratory programs' policies, practices, and capacities from 2003 through 2005. More complete serogrouping was frequently reported by states that specified isolate submission

requirements in promotional materials (70%), legally mandated isolate submission (73%), provided free shipping (75%), monitored using defined targets for completeness (81%), used 2 or more surveillance enhancement activities (85%), and used 4 or more activities to promote isolate submission (90%). Smaller proportions of states without these practices reported more complete serogrouping. Generally, associations were consistent with hypothesized effects. In a number of instances, however, associations were not statistically significant, possibly reflecting the inherently limited number of states and thus the potential number of study observations.

Four significant associations with serogrouping completeness were identified. The odds of more complete serogrouping were reduced in programs that characterized activities to promote isolate submissions among clinical laboratories solely as recommendations (as opposed to requirements) and were increased among programs using a defined target for monitoring. The odds of more complete serogrouping were also higher among laboratory systems with one or more city/county laboratories and among state public health laboratories with 50 or more technical/analytic FTE positions. Two characteristics, using a defined target for monitoring completeness and state laboratories with 50 or more technical/analytic FTEs, remained potentially associated with obtaining a serogroup result in multilevel models. In analyzing case-level data, the odds of obtaining a serogroup result were reduced for non-blood or CSF specimen sources and for patients who did not survive, but these differences were not sustained in the models.

We used two types of analyses, in part because each had limitations. In the state-level analyses of program differences related to serogroup testing completeness, we used

an arbitrary cutoff (80%). When we compared our results to an alternative analysis that used 90% as a cutpoint, serogrouping above 90% remained more common in states that specified isolate submission requirements in promotional materials, legally mandated isolate submission, provided free shipping, monitored using defined targets for completeness, used 2 or more surveillance enhancement activities, and used 4 or more activities to promote isolate submission relative to states without these policies or practices to assure that isolates are submitted for serogrouping. However, none of the four potential associations (promoting isolate submission as recommendations, using a defined target for monitoring, laboratory staff counts, and laboratory systems with one or more city/county laboratories) were significant in the alternative analyses. Regardless of the cutoff, 100% completeness should be targeted in practice. Also, the proportion serogrouped was calculated for the overall, three-year period because most states had year-specific proportions that were consistently above or below this threshold. Since there were exceptions, interpretation of the state-level characteristics associated with serogrouping completeness applies to averaged proportions for the entire period. Similarly, there is potential misclassification with the surveys, which referenced a three-year period during which epidemiology and laboratory programs' policies, practices, and capacities may have changed. Sample size, inclusion criteria for the analyses, and incomplete survey and surveillance data were particularly problematic for the multilevel analyses. The resulting data subsets may not have been representative and findings were susceptible to subjective modeling decisions.

Apart from the use of diagnostic alternatives to bacterial culturing or unmet isolate submission requests, specimens or isolates may be inadvertently discarded, lost in

transit, nonviable, or may not be typeable at a state laboratory. Formal studies or evaluations might better describe these other reasons for incomplete serogroup testing as the laboratories we surveyed often did not have sufficient data on their relative frequencies.

Most importantly, we found that meningococcal disease serogrouping was relatively complete in many states. Programs may already be seeking to improve or sustain serogrouping completeness. For example, 90% of states we surveyed reported using serogrouping results for characterizing the epidemiology of meningococcal disease and 80% reported using results for consideration of prevention/control options. Future research could investigate the ultimate impact on disease incidence of integrating surveillance and prevention efforts with serogrouping results. We note that states with a reported, three-year incidence below the median (14.2 cases per million residents, using the 2000 Census) often had more complete serogrouping (82%). The frequency of more complete serogrouping in states with higher rates (46%) was significantly lower ($p = 0.04$). Furthermore, 63% states that used a defined target for monitoring serogrouping completeness had rates below the median, while rates were below the median in 30% of states that did not monitor completeness with a defined target ($p = 0.02$).

Given state public health agencies' roles as "the hub of the [public health] system in policy development, accountability, and resource allocation" (Bender, Landrum, and Bryan 2000), the data and recommendations from this work are worth consideration. Among our findings, establishing a defined target for monitoring the completeness of serogrouping, including reasons for absent serogrouping results, should be a particularly simple recommendation to operationalize. Changes to public health infrastructure in

pursuit of surveillance and laboratory data quality may be more difficult to achieve or substantiate, but would likely benefit a wider range of infectious disease prevention and control programs. Our finding that serogrouping completeness was related to the number of technical/analytic FTEs in state laboratories is consistent with numerous sources expressing concern for public health workforce adequacy (Council of State and Territorial Epidemiologists 2004; Gebbie et al. 2003; Schoenfeld, Banfield-Capers, and Mays 2002). At the same time, there are recognized challenges in workforce estimation (Gebbie et al. 2003). Ultimately, optimal staffing (Gerzoff, Brown, and Baker 1999) and organizational configurations can be determined only by agencies themselves, but these findings may motivate further consideration.

With a recognized need to conduct serogroup-specific surveillance for meningococcal disease (Council of State and Territorial Epidemiologists 2004), data already collected by many state epidemiology offices, and the recommendations for improving or sustaining serogrouping completeness suggested by this research, it should be possible to monitor meningococcal disease serogroups using national notifiable disease data.

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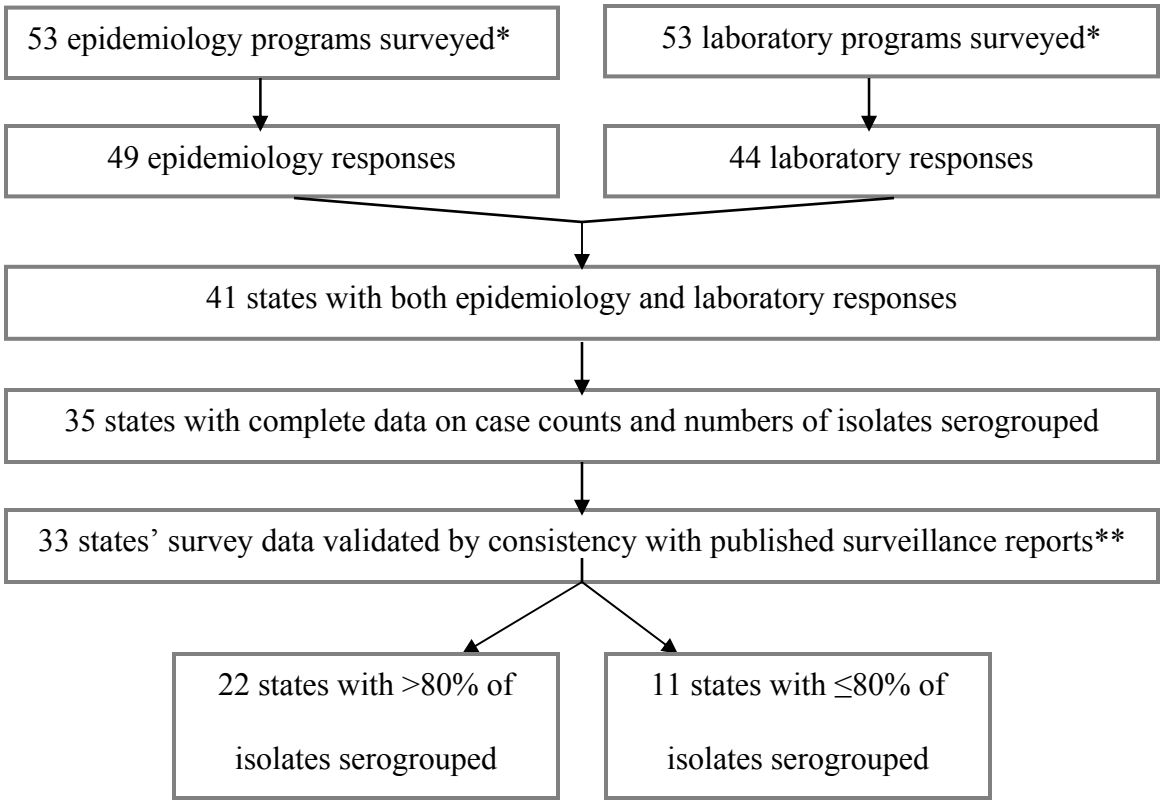
Figure 5-1. Inclusion criteria and survey data for univariate analyses of meningococcal disease serogrouping, 2003-2005



* State health departments and public health laboratories in 50 states and New York City, Puerto Rico, and Washington D.C. were surveyed.

** Case counts from surveys and CDC National Electronic Telecommunications Surveillance System surveillance data match within five cases each year or 15 cases for the three-year study period.

Figure 5-2. Inclusion criteria and surveillance data for multivariate analyses of meningococcal disease serogrouping, 2003-2005

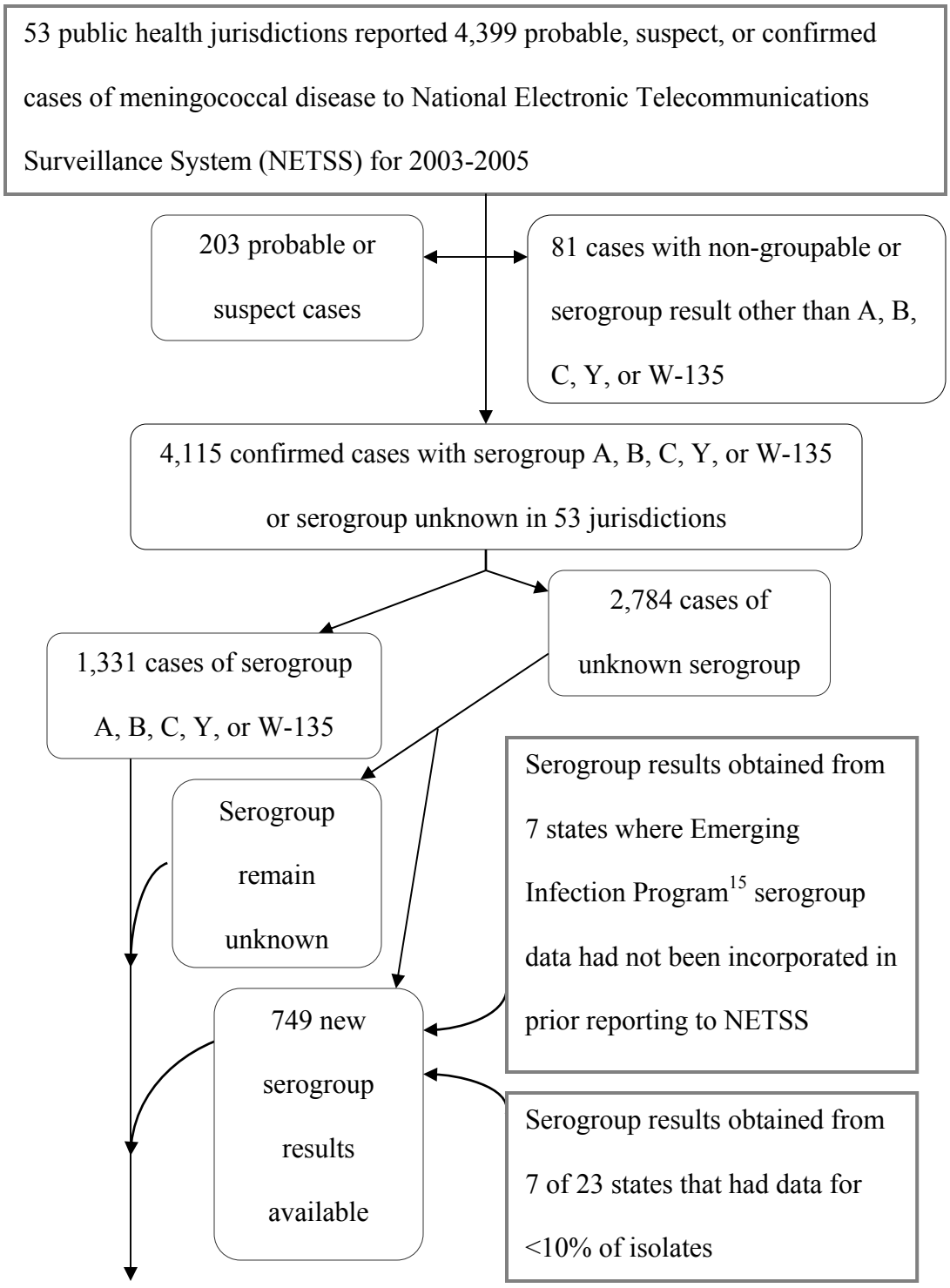
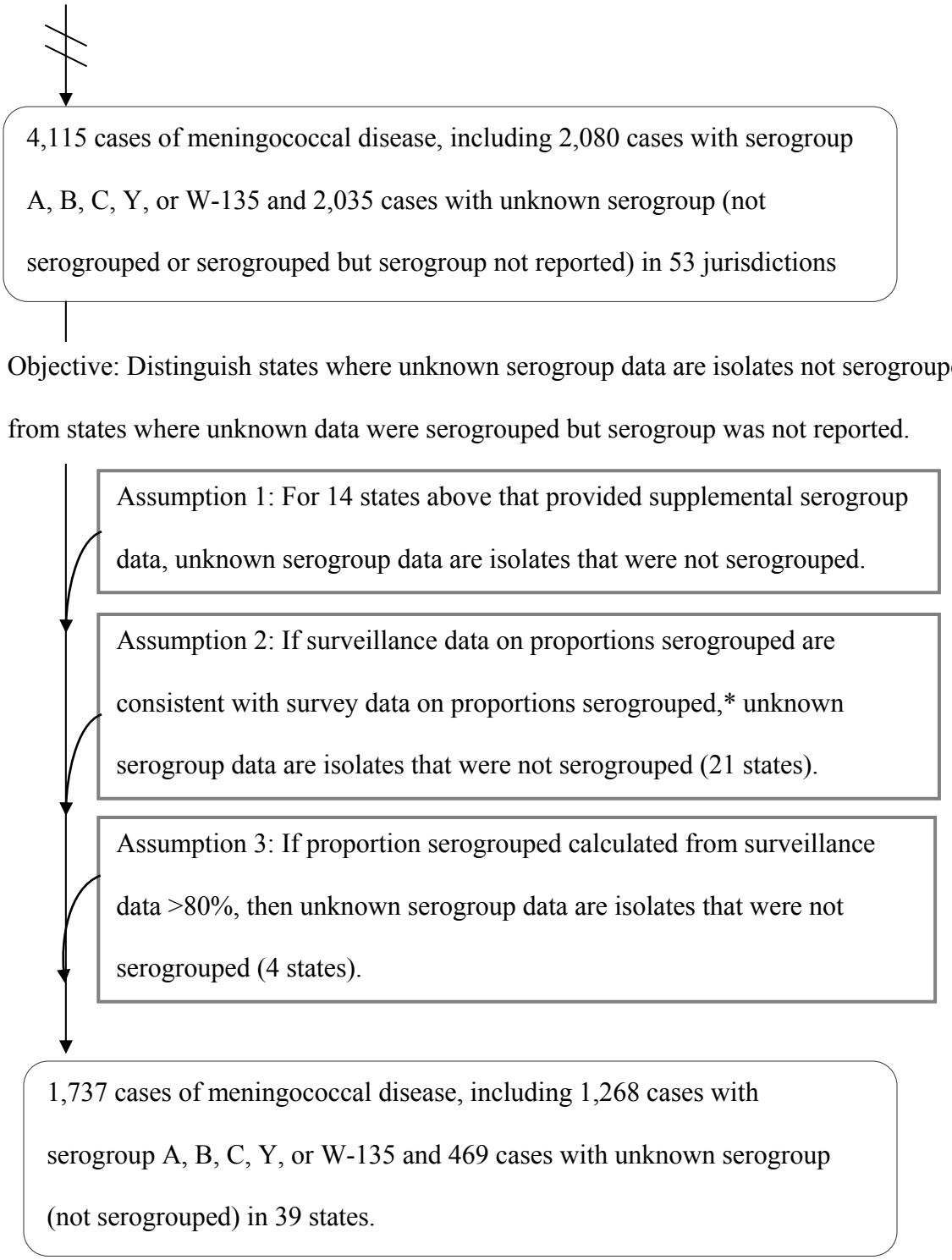


Figure continues on next page

Figure 5-2. Inclusion criteria and surveillance data for multivariate analyses of meningococcal disease serogrouping, 2003-2005 (continued)



* Proportions serogrouped (no. isolates serogrouped/no. cases) match +/- 25% per year.

Table 5-1. Meningococcal disease serogroup testing and policies and practices of state public health epidemiology and laboratory programs, 2003-2005*

	Serogroup testing completeness**		
	> 80 %	**≤ 80%**	**OR (95% CI)**
Program policy / practice [+]			
TOTAL	**22 (66.7%)**	**11 (33.3%)**	
Isolate submission requirement			22 (0.49, 10.09)
Legally established	16 (73%)	6 (27%)	
Not legally established[++]	6 (55%)	5 (45%)	
Isolate submission failures			0.77 (0.11, 5.61)
Notifications used	4 (67%)	2 (33%)	
Notifications not used [++]	13 (72%)	5 (28%)	
Reportable disease posters			1.46 (0.34, 6.35)
Specify submission requirements	14 (70%)	6 (30%)	
Don't submission requirements[++]	8 (62%)	5 (38%)	
Surveillance enhancement			50 (0.79, 25.77)
2 or more activities	11 (85%)	2 (15%)	
1 or no activities[++]	11 (55%)	9 (45%)	
Isolate submission as a requirement			92 (0.75, 64.02)
4 or more promoting activities	9 (90%)	1 (10%)	
3 or fewer promoting activities[++]	13 (57%)	10 (43%)	

Table continues

Table 5-1. Meningococcal disease serogroup testing and policies and practices of state public health epidemiology and laboratory programs, 2003-2005*

	Serogroup testing completeness**		
	> 80 %	**≤ 80%**	**OR (95% CI)**
Program policy / practice [+]			
TOTAL	**22 (66.7%)**	**11 (33.3%)**	
Isolate submission as recommended			0.14 (0.03, 0.71)
1 or more promoting activities	6 (43%)	8 (57%)	
No promoting activities[++]	16 (84%)	3 (16%)	
Isolate shipping and containers			2.57 (0.58,11.38)
Free shipping/shipping and containers	15 (75%)	5 (25%)	
Neither free[++]	7 (54%)	6 (46%)	
Completeness monitored			5.10 (1.02, 25.54)
Defined target for monitoring	17 (81%)	4 (19%)	
Undefined/no monitoring[++]	5 (45%)	6 (55%)	

***** Complete epidemiology and laboratory program surveys from 35 states were included when year-specific, survey case counts differed from surveillance case counts by 5 or fewer cases each year or differed by 15 or fewer cases for the three-year period (n = 33 states).

****** Three-year completeness estimates are the proportion of meningococcal disease case successfully serogrouped over total cases reported using survey data described in the text.

[+] See text and appendices for complete descriptions of program characteristics.

[++] Reference category for odds ratio (OR) and 95% confidence intervals (95% CI).

Table 5-2. Multilevel analyses of meningococcal disease serogrouping: Case and state public health epidemiology and laboratory program characteristics, 2003-2005

	aORs (95% CI)		
	Model 1*	**Model 2***	**Model 3***
Case-level characteristics			
Blood only	0.94 (0.51, 1.75)	0.86 (0.25, 3.00)	0.88 (0.26, 3.01)
CSF only	0.90 (0.42, 1.93)	1.14 (0.29, 4.57)	1.11 (0.29, 4.31)
Blood and CSF**			
Other source	0.39 (0.15, 1.05)[a]	0.45 (0.09, 2.31)	0.46 (0.09, 2.36)
Died	0.70 (0.43, 1.15)	---	---
Survived**			
Program-level policies/practices and capacities (models 2 and 3 only)[+]			
Isolate submission recommendation			
1 or more promoting activities		0.86 (0.23, 3.23)	---
No promoting activities**			
Completeness monitored			
Defined target for monitoring		3.31 (0.78, 14.16)[a]	2.81 (0.87, 9.11)[a]
Undefined monitoring/no monitoring**			
Laboratory system			
One or more city or county laboratories		2.32 (0.31, 17.23)	---
Single, centralized laboratory**			
Laboratory full-time equivalent (FTE) staff			
50 or more technical/analytic FTEs		3.02 (0.72, 12.65)	4.56 (1.55, 13.41)[b]
Less than 50 FTEs**			
Emerging Infections Program (EIP)			
Within EIP catchment area		2.00 (0.48, 8.31)	---
Outside EIP catchment area**			

Table continues

Table 5-2. Multilevel analyses of meningococcal disease serogrouping: Case and state public health epidemiology and laboratory program characteristics, 2003-2005

	Model 1*	Model 2*	Model 3*
Intercept (u_{0j}) variance component (standard deviation)			
Specimen models	1.55 (1.24)	1.30 (1.14)	1.13 (1.06)
Outcome models	1.68 (1.30)	---	---
Number of cases (no. states)			
Specimen models	973 (31)	564 (19)	572 (20)
Outcome models	1321 (37)	---	---

* Model 1 has a random intercepts and level-1 predictors only, model 2 adds 5 level-2 predictors, and model 3 is the most parsimonious model with level-1 and level-2 predictors (see text).

** Reference category for adjusted odds ratios (aOR) and 95% confidence intervals (CI).

+ See text for descriptions of program-level characteristics.

[a] $P < 0.10$

[b] $P < 0.01$

CHAPTER 6

TIMELINESS OF GEORGIA'S STATE ELECTRONIC NOTIFIABLE DISEASE SURVEILLANCE SYSTEM

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Abstract

We compared the timeliness of reports to Georgia's internet-based, notifiable disease surveillance system with the timeliness of reports received by other communication mechanisms. We also assessed whether timeliness was associated with select hospital, infection control program, and laboratory characteristics.

Reports of giardiasis, hepatitis A virus, legionellosis, malaria, pertussis, and Rocky Mountain spotted fever were included when specimens were collected between July 2003 and December 2005 (n=3,195). We compared reporting-time quartiles, evaluated timeliness sequentially in 6-month intervals, and assessed associations between facility characteristics and timeliness using stratified Cox proportional hazards models to calculate hazard ratios (HR) and 95% confidence intervals (95% CI).

Reports were timelier when healthcare providers reported using the internet (median=6.0 days, quartiles=3.0, 10.0) compared to reports received by state (median=13.0 days, quartiles=8.0, 19.0) or county/district (median=7.0 days, quartiles=3.0, 14.0) officials using other mechanisms. Overall timeliness did not improve as intervals elapsed. Reporting was timelier in hospitals with >200 beds (HR=1.73, 95% CI: 1.35, 2.23), timelier in infection control programs that routinely reported (HR=1.31, 95% CI: 1.05, 1.64), and less timely when laboratories sent out cultures for work-up (HR=0.59, 95% CI: 0.44, 0.81).

Internet-based reporting improved timeliness. Systematic efforts in healthcare settings could further improve reporting timeliness.

Introduction

In Georgia, all physicians, laboratories, and other healthcare providers are required by law to report to county, district, or state public health offices occurrences of selected diseases and conditions (Georgia Division of Public Health 2005). The Georgia Division of Public Health (GDPH) coordinates this process with district officials, and when necessary, supports local investigations and interventions. Georgia's shared state and local organizational responsibility for public health (Centers for Disease Control and Prevention 1991) encourages local surveillance activities, including immediacy in monitoring significant public health events occurring in the community. GDPH consolidates disease reports forwarded from county and district offices with reports received directly at the state level.

To improve the efficiency and timeliness of reporting procedures, which had previously been managed by facsimile, telephone, or mail communications, GDPH activated an internet-based disease reporting system in January of 2002. Functionality of the State Electronic Notifiable Disease Surveillance System (SendSS) has been continuously improved since activation and concomitant increases in use by local public health officials, health care providers (physicians and their staff, infection control professionals (ICPs), clinical laboratories), and other users have followed (Figure 6-1). This period of increasing SendSS use represented an opportunity to quantify gains in the timeliness of reportable diseases surveillance during a time in which similar systems were being implemented throughout the United States (Centers for Disease Control and Prevention 2005).

To document improvements in the timeliness of surveillance, we compared reports submitted directly to SendSS by healthcare providers, including ICPs and clinical laboratories, with disease reports received by mail, facsimile, or other communication mechanisms and subsequently submitted to SendSS either by county/district public health officials or by GDPH. In addition, we assessed the extent to which surveillance timeliness improved during intervals within the initial period of SendSS development and acceptance. Finally, we linked disease reports with data on pertinent characteristics of Georgia hospitals, infection control programs, and clinical laboratories to determine whether facility attributes associated with timeliness could be identified.

Methods

SendSS case reports

Laboratory-confirmed reports of giardiasis, acute hepatitis A virus (HAV), legionellosis, malaria, pertussis, and Rocky Mountain spotted fever (RMSF) were included in the analyses when the first date of specimen collection occurred during the 30-month study period from July 1, 2003 to December 31, 2005. These six diseases were selected because they are reportable diseases, are not part of categorically-funded programs that support surveillance programs (e.g., sexually transmitted diseases) and are not part of a specially funded program, the Georgia Emerging Infections Program (EIP) (Pinner et al. 2003).

Since data on specimen collection dates may have been missing, we initially extracted case report data from SendSS using date of record entry, a system-generated field with 100% completeness (Figure 6-2). Reports of disease events recorded in

SendSS between July 1, 2003 and September 1, 2006 were extracted (n = 5,076 records). (The September endpoint allowed for SendSS data entry delays.) Reports for 32 patients who did not reside in Georgia and for six records that did not have state residency data available were excluded.

SendSS includes an administrative status field to distinguish confirmed, unconfirmed, probable, and deleted reports. Using a unique identifier code, 14 unconfirmed HAV reports and 30 probable pertussis reports were excluded after verifying that duplicate, confirmed records did not exist for these patients. Eighty-eight percent of the 483 records with a deleted status also did not correspond to a confirmed case, and were excluded. Most exclusions were HAV (43%) and RMSF (26%) patients. Two hundred and twelve records were merged to reconcile duplicates and obtain available data from the remaining deleted records. Reports of the same disease in the same person within 30 days of specimen collection dates were merged into single records. A single confirmed case indicated the primary record for merging. When multiple duplicate records were confirmed, the earliest case report indicated the primary record. Duplicate records with 31 days or more between specimen collection dates represented less than 0.1% of all records and were considered discrete events in the analysis.

Timeliness measurement

Timeliness was defined as the number of days between the date of first specimen collection and the earliest date of public health notification at any level (i.e., county, district, or state). Date of symptom onset was used as a proxy for 26 records (19 giardiasis, 5 malaria, and 2 pertussis reports) where specimen collection date was

unavailable (<1%). First reporting date was initially missing for 593 records (16%). Data were retrieved from date-of-receipt stamps on available paper reports for 99 records sent to GDPH in 2004 or 2005. Remaining records with missing first report dates (n = 469), including 25 records with specimen collection dates in 2006, were excluded from analyses.

Forty-seven records with negative times (notification before specimen collection) were identified. Based on year of SendSS record entry and the sequence of months and days from specimen collection date to dates of first report and/or record entry, 10 records with likely errors in year of report were corrected. Similar logic was used to correct year of specimen collection in 1 record and month of specimen collection in 11 other records. The remaining 26 records were excluded because no likely data error pattern was discernible. None of the records were duplicate patients, precluding the possibility that either date belonged to a previous disease event in the same individual.

A SendSS text field captured 99% of the organizational affiliations of data entry personnel, and was used to distinguish reports submitted to SendSS by healthcare providers from reports received by other communication mechanisms and subsequently submitted to SendSS either by county/district public health officials or by officials at the GDPH epidemiology program office (Appendix 6-A). To assess changes in timeliness over time, specimen collection dates were used to divide the 30-month study period into five 6-month intervals: July – December 2003, January – June 2004, July – December 2004, January – June 2005, and July – December 2005.

Reporting source data

Descriptive data on Georgia healthcare facilities and clinical laboratories, such as numbers of hospital beds (a proxy for hospital size) as well as characteristics of infection control departments (e.g., whether disease reporting and health department communications were considered routine) and characteristics of clinical microbiology laboratories (e.g., numbers of blood and stool specimens processed) were obtained from two statewide assessments of bioterrorism and public health emergency preparedness. Following Health Resources and Services Administration (HRSA) sponsorship of a state program to characterize and improve healthcare system preparedness, all 164 Georgia hospitals that received a request partially or entirely completed the assessment in March of 2003. Similarly, Centers for Disease Control and Prevention (CDC) funding stimulated an assessment of laboratories' operational capacities and preparedness for infectious disease emergencies. We used a list of 150 acute care, critical access hospital facilities licensed through the Georgia Office of Regulatory Services to identify eligible clinical laboratories for the survey. The survey was also sent to a major commercial laboratory in Georgia. One hundred and forty laboratories (93%) completed the survey in March of 2005.

Data from the surveys were linked to the SendSS data by facility names. Eleven hospital facilities with similar names or name changes were clarified through written correspondences with district epidemiologists in the facilities' regions. A secondary SendSS user dataset, which included user affiliations, was also used to clarify reporting source facilities and data linkages. Most SendSS records had reporting source (90%) and laboratory facility (97%) text data available.

Statistical and analytic considerations

Timeliness was described by calculating the median (50%) and lower and upper quartiles (i.e., the lowest and highest 25% of the timeliness data). "Survival distributions" were based on product-limit estimates of the probability that a disease event was unreported at each observed time point following specimen collection date. Kaplan-Meier curves visually illustrated strata differences and log-rank tests of the equality of strata were performed using a 0.05 alpha level to define statistical significance. Strata were defined by case-report characteristics (disease, healthcare provider or health department SendSS submission, and study interval) as well as select hospital, infection control, and clinical laboratory characteristics. To eliminate the statistical influence of time outliers and scale Kaplan-Meier curves appropriately, maximum times for inclusion in analyses were designated when 95% of cases had been reported.

Proportional hazards assumptions were assessed separately for each independent variable using log-log survival curves and by examining variable interactions with the natural log of time to report ($p > 0.05$) (Kleinbaum 1996). Since reporting mechanism (SendSS submission by healthcare provider versus city/county or state health department officials' receipt of reports received by other communication mechanisms) did not meet the proportional hazards assumption, stratified Cox models were used. A likelihood ratio test of the 'no-interaction' assumption that coefficient estimates do not vary across the three reporting mechanisms' strata was not significant ($X^2 = 19.86$, 12 d.f., $p > 0.05$). Following backward elimination, a final model was obtained for testing the significance of the remaining hospital, infection control, and laboratory characteristics while

accounting for disease (giardiasis vs. HAV) and stratified reporting mechanisms. Insufficient case counts and incomplete survey data linkages precluded inclusion of other diseases, such that the final models were a subset of all SendSS case reports (n = 383, 12%). Parameter estimates were greater than their corresponding standard errors in the models.

Software for data management and analysis included *Microsoft Access 2000 (*Microsoft Corporation, Redmond, WA) and *SAS version 9.1 (*SAS Institute, Cary, NC). Institutional review board exemption for the project was obtained from Emory University.

Results

The majority of cases we analyzed were reports of giardiasis (58%) and HAV (25%); the dataset also included reports of legionellosis (3%), malaria (5%), pertussis (3%), and RMSF (6%) (n = 3,195) (Table 6-1). Average age varied by disease; persons with pertussis (14 years) and giardiasis (25 years) were younger, and persons with legionellosis were oldest on average (53 years). Females with malaria (31%), legionellosis (43%), and giardiasis (43%) were less commonly reported. Legionellosis (53%) and malaria (55%) were reported frequently in Blacks, while pertussis (46%) and RMSF (76%) were commonly reported in Whites. Seventy-two percent of reports were residents of one of 28 counties in the Atlanta Metropolitan area, but reports of RMSF (51%) were an exception. Based on a county-specific set of codes developed by the U.S. Department of Agriculture (http://www.ers.usda.gov/Data/UrbanInfluenceCodes), 91%

of reports were residents of areas considered to be relatively urban (i.e., urban influence codes 1-4).

Significant differences in timeliness existed among the 6 reportable diseases ($p < 0.0001$) (Figure 6-3, Appendix 6-C). HAV timeliness was shortest (median = 5.0 days; lower, upper quartiles = 3.0, 8.0), followed by pertussis (median = 7.0 days, quartiles = 3.0, 11.0) and malaria (median = 9.5 days, quartiles = 3.0, 17.0). In contrast, the median timeliness of legionellosis (13.0 days, quartiles = 7, 18), giardiasis (13.0 days, quartiles = 7, 19), and RMSF (15.0 days, quartiles = 11, 21) was close to 2 weeks.

Healthcare provider and health department SendSS submissions

Statistically significant differences were also found in comparing the timeliness of reports submitted to SendSS by healthcare providers with reports submitted by county/district health department officials or by officials at the state epidemiology office ($p < 0.0001$) (Appendix 6-D). The median timeliness of 343 SendSS reports submitted by healthcare providers (6.0 days, quartiles = 3.0, 10.0) and 1,103 reports submitted by county/district officials (7.0 days, quartiles = 3.0, 14.0) were comparable. At and above the upper quartile of times, however, additional delays of 4 days were associated with reports submitted by county/district officials. Reports submitted to SendSS by officials at the state office (n = 1,749) were substantially less timely (median = 13.0 days, quartiles = 8.0, 19.0).

The frequencies of healthcare provider and health department SendSS submissions differed significantly ($p < 0.0001$) by disease (Figure 6-3, Appendix 6-B). Fewer giardiasis (8%), HAV (12%), and RMSF (8%) reports were submitted by

healthcare providers compared with healthcare provider submissions of legionellosis (22%), malaria (27%), and pertussis (28%) over the 30-month study period. County and district public health officials more often submitted HAV (52%), legionellosis (43%), malaria (48%), and pertussis (58%) reports, while the state epidemiology office more often submitted giardiasis (68%) and RMSF (58%) reports.

Study intervals

Disease counts were distributed relatively evenly across the five 6-month time intervals (Appendix 6-B), with the exception of HAV. Half (51%) of HAV reports occurred from July through December of 2003 (when a large outbreak of HAV associated with raw or undercooked green onions served in restaurants occurred in the Southeast) (Amon et al. 2005). SendSS use was lower in this period (Figure 6-1) and less than 1% of HAV reports were submitted by healthcare providers (Appendix 6-B) in the second half of 2003. These data partially account for the lower proportion of direct HAV reporting during the entire study period described above.

Statistically significant differences in timeliness by interval were identified ($p < 0.001$), but these differences were less pronounced graphically (Appendix 6-E). There was no overall trend of improved timeliness with each subsequent interval. In addition, no clear changes in timeliness were observed for giardiasis, legionellosis, or pertussis as the percentages of SendSS reports submitted by healthcare providers increased over the 5 intervals (Figure 6-3). In contrast, the median timeliness of HAV, malaria and RMSF improved as the percentages of SENDSS reported submitted by health care providers increased. For HAV, reporting decreased from 6 days (July 2003-June 2004) to 5 days

(July 2004-June 2005) or 4 days (July-December 2005) as the percentage of SendSS reports from providers increased overall during the study period. Submissions of malaria reports by providers increased above 22% in July of 2004 and median timeliness improved from 10 days or more to 9 days or less subsequently. RMSF median timeliness improved from 18 days or more to 14 days or less when any amount (>0%) of provider submissions occurred.

Timeliness and reporting sources

Nine hundred and one records (28%) with reporting source data indicating a hospital facility were linked. Hospital linkages were more common among reports of legionellosis (41%), HAV (44%), malaria (44%), and pertussis (66%) compared with the percentages of linked reports of RMSF (11%) and giardiasis (20%) ($p < 0.0001$). In addition, reports submitted by healthcare providers were more often linked to hospitals (80%) than SendSS reports submitted by county/district officials (31%) or state office staff (16%).

Seventy-three percent of patients were tested in one of 5 commercial laboratories or the state public health laboratory. Almost all hospital labs participated in the Georgia survey but only one commercial laboratory participated. As a result, 746 records (23%) could be linked for hospital laboratories. Of the remaining records, half were tested at the one commercial lab who participated in the survey. Altogether, these 1,895 linked records were 59% of the final dataset. Differences in the percentages of successful laboratory linkages by disease were also significant ($p = 0.01$), but varied less than hospital linkages (giardiasis: 56%, RMSF: 58%, HAV: 64%, legionellosis: 64%, malaria:

67%, pertussis: 68%). Reports submitted by healthcare providers were also linked to laboratories more often (83%) than reports submitted by county/district or state officials (57%).

In linking hospital and clinical laboratory survey data from 98 healthcare facilities and one commercial laboratory to SendSS case reports, several facility characteristics were associated with timeliness. Median timeliness was 2 days more rapid (6.0 days, quartiles = 2.0, 10.0) in larger hospitals (i.e., 200 or more acute care beds) relative to hospitals with fewer beds ($p = 0.0001$) (Table 6-2). Below the upper quartile, timeliness did not differ substantially according to ICPs' educational background, but reports delayed 30 days or more were more common among ICPs with MD training (12%) compared with non-physician ICP colleagues (4%) ($p=0.001$). Infection control programs that described notifying county, district or state public health office of infectious disease occurrences as a routine process had 3-day gains in median timeliness (5.0 days, quartiles = 2.0, 12.0) compared with programs that did not describe disease notification as routine ($p = 0.0014$). ICPs that reported regular communication with a county/district health department had 7-day timeliness gains at the upper quartile (median = 7.0 days, quartiles = 3.0, 12.0) when compared with counterparts without regular communications ($p = 0.0001$). Daily tracking of microbiology culture results by ICPs was also associated with a one-day timeliness gain (median = 7.0 days, quartiles = 3.0, 13.0) relative to ICPs that did not track culture results ($p = 0.0002$).

Eighty-one percent of case reports originated from clinical laboratories that were always staffed (i.e., 24 hours/day, 7 days/week), and this characteristic was associated with a 7-day timeliness gain at the upper quartile (median = 7.0 days, quartiles = 3.0,

12.0) relative to laboratories that were not always staffed (p = 0.0001) (Table 6-3). Most notably, timeliness differed markedly in clinical laboratories that reported sending all microbial cultures to a reference laboratory for work-up (median = 14.5 days, quartiles = 7.0, 20.0) compared with laboratories that did not (median = 7.0 days, quartiles =3.0, 13.0) (p = 0.0001). Other characteristics, including fast internet connections (T1 or T3 versus DSL/cable) in hospitals (p = 0.79) (data not shown) and volumes of blood (p = 0.32) and stool (p = 0.55) specimens currently processed (Table 6-3), were not associated with sizable timeliness differences.

In multivariate analyses, three reporting source characteristics retained significant relationships with timeliness (Table 6-4). Hospitals with more than 200 beds were significantly more timely (hazard ratio [HR] = 1.73, 95% confidence interval (CI): 1.35, 2.23) compared with hospitals with less than 200 beds (p < 0.0001). Hospital laboratories that sent out all microbial cultures to a reference laboratory for work-up were significantly less timely (HR = 0.59, 95% CI: 0.44, 0.81) than laboratories that did not report this practice (p = 0.001). A smaller association between infection control programs routinely notifying public health officials of infectious disease occurrences and timelier reporting also retained significance (HR = 1.31, 95% CI: 1.05, 1.64) compared with programs where disease notifications were not considered routine (p = 0.02).

Discussion

Using six reportable diseases, we showed that the time from specimen collection to first public health notification at any level was significantly reduced when reports were submitted by physicians, ICPs, clinical laboratories, and other healthcare providers who

used the internet-based SendSS reporting system. Reports that were delivered to the state office by other communication mechanisms, such as telephone, facsimile or mail, and subsequently entered in SendSS were least timely. There was no significant trend found in increasing overall timeliness during the study period, however, presumably because the level of adoption of SendSS use by providers during the study period was relatively low and not sufficient to have a statistically demonstrable impact on overall reporting timeliness. A more recent or longer study period may be necessary to determine if overall timeliness has increased since our evaluation, coincident with continued increases in use of SendSS for disease reporting by providers.

Jajosky and Groseclose (2004) identified eight published studies of infectious disease surveillance systems in the United States with disease-specific, quantitative measures of timeliness. The authors concluded from their review that the literature was sparse, not comparable, and required a standardized approach to timeliness evaluation. Consistent with their first conclusions, only one of these eight studies included a disease in our evaluation (hepatitis A virus) (Birkhead et al. 1991), and this study was not comparable to our evaluation because a timeliness interval from illness onset to national reporting at CDC was assessed. Our study did encompass components of the proposed standardized approach, including explicit descriptions of the levels of the public health system under evaluation, the timeliness interval and its start and end dates, the activities within the interval that were measured, and the purposes of the evaluation. Whether our timeliness estimates meet the goals of the SendSS surveillance system is an important component in their standardized approach, but was beyond the scope of this evaluation. Instead, we focused on potential improvements to timeliness by identifying associated

factors in the domain of reporting sources. Jajosky and Groseclose also suggested this focus, and prior to this study, few (if any) published studies have investigated specific sources of variability in the timeliness of reportable diseases surveillance.

Specifically, we found that reporting was more timely in hospitals with >200 beds (i.e., larger healthcare facilities) and more timely among infection control programs that described reporting as routine. Healthcare facility size is likely a proxy for other determinants of timeliness that could be investigated further. A notable 1985 study of *Shigella* reporting in Oklahoma found a relationship between facility size and reporting completeness; laboratories in large hospitals (200 beds or more) were more likely to have reported than laboratories in smaller hospitals or reference laboratories (Harkess et al. 1988). Characterizing reporting as routine may simply indicate familiar or frequent reporting practices, or lack thereof. For example, physicians' surveys on disease reporting have frequently identified a lack of awareness of the procedural aspects of reporting (Weiss, Strassburg, and Fannin 1988), the specific pathogens that are reportable (Konowitz, Petrossian, and Rose 1984), and the existence of case definitions for reportable diseases (Krause, Ropers, and Stark 2005), which in turn, is believed to contribute to physician underreporting.

We also found that reports to the health department were significantly delayed when laboratories sent out microbiology cultures for work-up. Whether sending specimens to a commercial laboratory results in less complete or less timely reporting is controversial. The current consideration by the U.S. Centers for Medicare & Medicaid Services to undertake competitive bidding for microbiology laboratory services in the United States requires evaluation to assess whether there may be adverse implications for

infectious disease reporting, including the potential impact on timely detection of emerging infections or other public health threats.

A separate set of publications has documented gains in timeliness with implementation of automated, electronic laboratory reporting (ELR) and internet-based case reporting. For example, Hawaii's state health department implemented a statewide ELR system by establishing electronic linkage with three major commercial laboratories (Effler et al. 1999). Relative to the antecedent (paper-based) system, *Giardia*, *Salmonella*, *Shigella*, invasive *S. pneumoniae*, and vancomycin-resistant reports were received 3.8 days earlier. In the Netherlands, a 9-day improvement of median reporting timeliness was achieved via internet-based reporting, where this modality has fully replaced mailings of paper case report forms from the municipal public health services to national public health authorities (Ward et al. 2005). A 2004 assessment from Colorado is most comparable to our study in its focus on web-based reporting, its use of the same timeliness interval from specimen collection to public health reporting date, and its overlapping diseases (Vogt et al. 2006). The median, web-based reporting timeliness of giardiasis (4.0 days), HAV (3.0 days), legionellosis (5.0 days), and pertussis syndrome (3.0 days) were each more rapid than our findings for Georgia (where use of the SendSS system by healthcare providers was still increasing during the study period).

Importantly, the timeliness interval we measured includes both laboratory testing 'turnaround time' (time from specimen collection to receipt of a laboratory testing result) and disease reporting timeliness (time from laboratory testing results to first disease notification). Creation of a field to collect date of first positive lab result would facilitate ongoing, direct analyses of reporting timeliness. In addition, accurate data on date of

onset would have allowed for analyses of the interval from illness onset to specimen collection. Although onset date data were complete, often date of specimen collection was used when onset date was unavailable because onset date is a required field within SendSS. An unintended consequence of this requirement was inclusion of inaccurate, proxy data in lieu of recording onset date as unknown (or more rigorous pursuit of these data). Since it is possible that specimens will be collected the same day of illness onset, proxy and actual onset dates could not be distinguished.

Two date fields were required for our calculations of the timeliness interval. Although few records (n=26) had missing specimen collection dates, missing date of first public health notification required the exclusion of 469 (15%) records from timeliness analyses. Whether these missing records were a random subset of all records is unknown. Of note, records without first reporting dates were more common earlier in the study period (July–December 2003: 45%, January–June 2004: 20%, July–December 2004: 17%, January–June 2005: 9%, July–December 2005: 9%). This trend likely occurred because paper records with date-of-receipt stamps for retrieving first reporting dates were not available for 2003. Also, SendSS users may have increasingly complied with a policy decision implemented on March 31, 2003 to record systematically date of first report to public health.

The analyses of reporting source characteristics and timeliness may not have been representative of all SendSS reports, as several factors besides submission of SendSS reports by health department officials made linkages to the survey data particularly unavailable. Patients who either received care outside of hospital settings or received care in a hospital setting, but were subsequently reported by commercial laboratories or

the state public health laboratory often could not be linked. In addition, patients may have actually received care in affiliated or satellite settings where data reported by the primary facility may or may not be applicable. As a result, both illness severity and location of laboratory testing may relate to linkage probability. Indeed, fewer reports of giardiasis and RMSF were linked because both are more frequently tested by commercial labs, many of which were not surveyed.

Nevertheless, the reporting source characteristics that were associated with timeliness represent opportunities for refinements to the practices of surveillance programs, infection control departments, and clinical laboratories. For example, surveillance programs should work with ICPs to establish timely and routine reporting mechanisms, communicate regularly on infectious disease occurrences in the community, and encourage ongoing monitoring of microbiology results in ICPs' facilities. Similarly, surveillance programs' collaboration with clinical laboratories can also improve timeliness, particularly when laboratories are not always staffed and when most or all specimens are tested at reference laboratories. Surveillance programs also may need to direct additional attention to smaller healthcare facilities, if there is evidence of reduced resources or capacities for timely reporting. Increasing use of the internet for submission of disease reports should be a priority for both surveillance programs and reporting sources.

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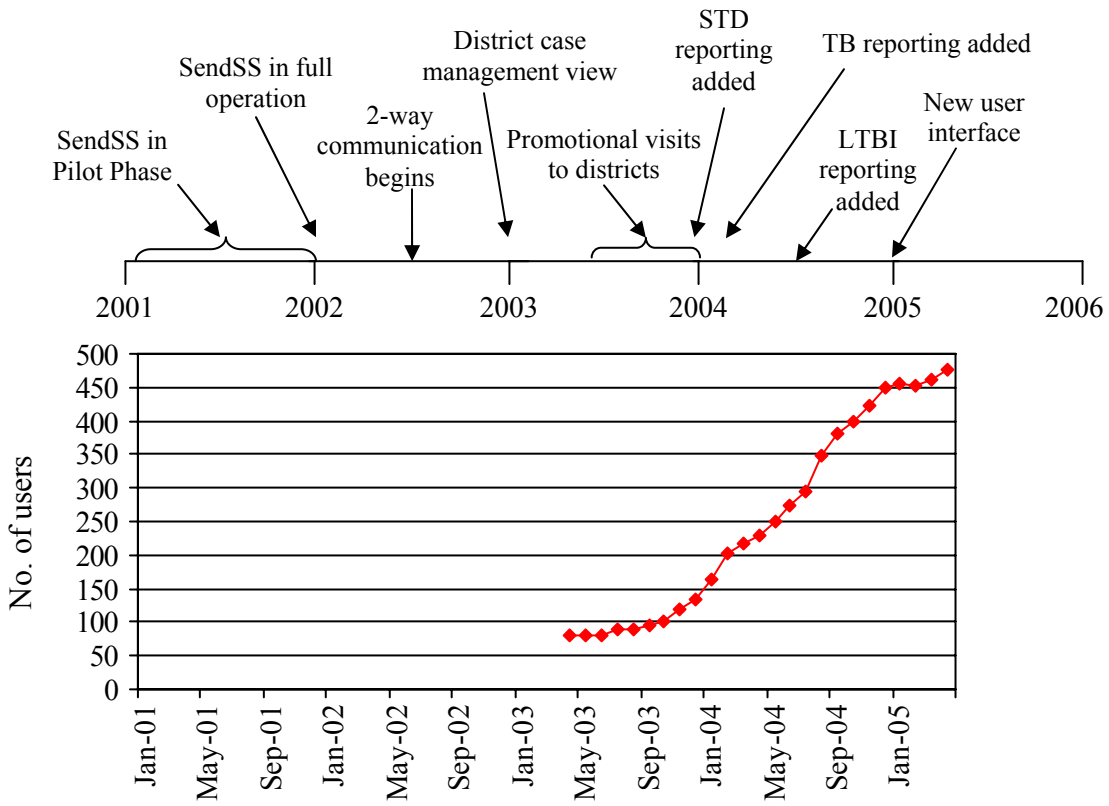
Figure 6-1. Georgia State Electronic Notifiable Disease Surveillance System (SendSS) development milestones and number of registered users*



* Data on number of SendSS users not plotted before May of 2003.

Abbreviations: 2-way communication: ability to report and view case reports; STDs: sexually transmitted diseases; TB: tuberculosis; LTBI: latent TB infection.

Figure 6-2. Inclusion criteria and Georgia State Electronic Notifiable Disease Surveillance System (SendSS) data, July 2003–Dec. 2005 (n=3,195)

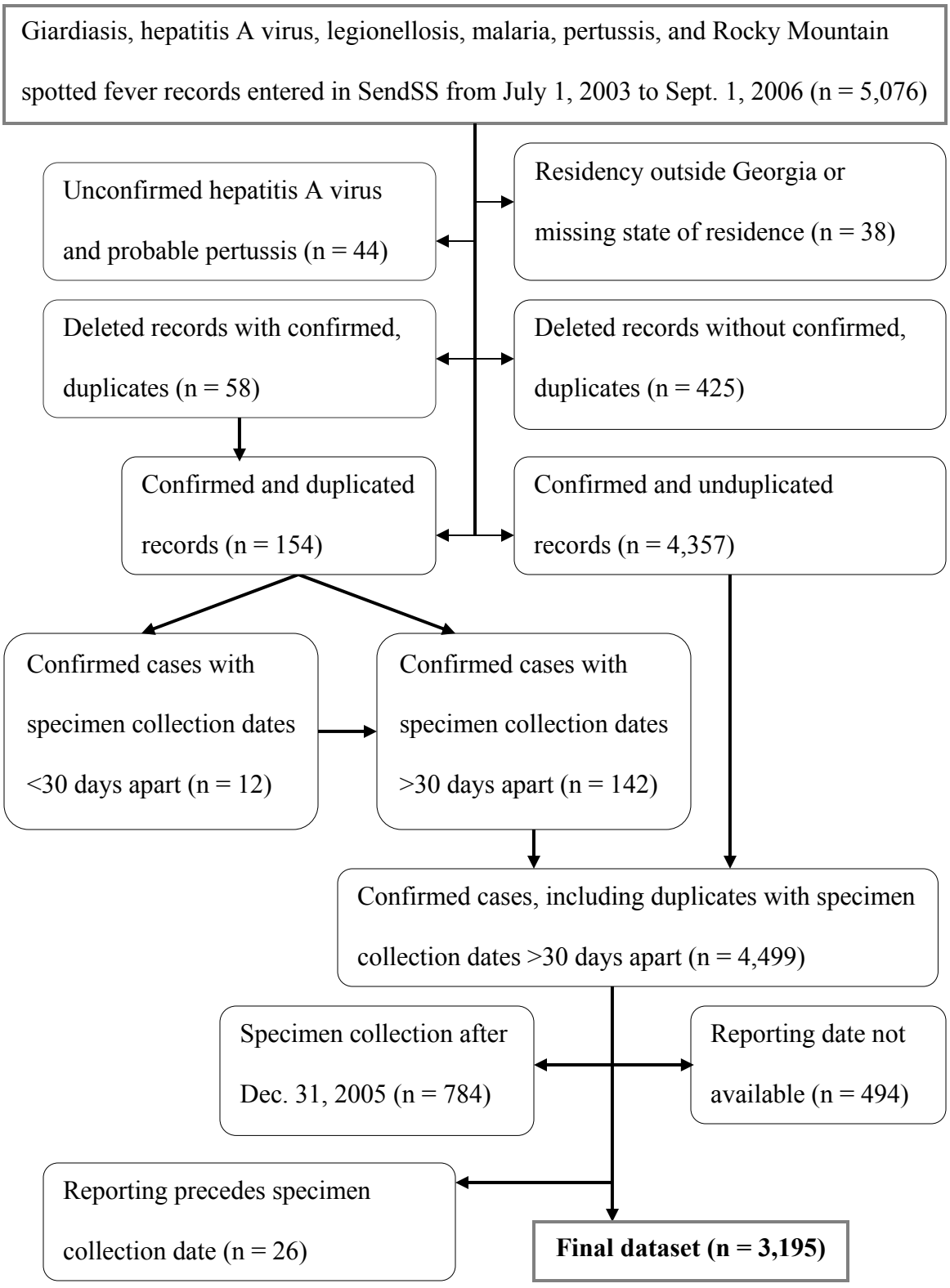


Table 6-1. Demographic and geographic characteristics of patients reported to Georgia State Electronic Notifiable Disease Surveillance System, July 2003–Dec. 2005 (n=3,195)

	Giardiasis (n=1,865)	HAV (n=785)	Legionellosis (n=94)	Malaria (n=158)	Pertussis (n=91)	RMSF (n=202)
Age (years)						
Mean (range)	25 (0-88)	38 (1-100)	53 (21-87)	34 (1-78)	14 (1-62)	43 (4-92)
% Female	43.0%	48.1%	42.6%	31.0%	53.3%	47.0%
Race/ethnicity						
Black	17.3%	12.9%	53.2%	55.1%	24.2%	6.5%
Hispanic	2.6%	7.6%	0%	5.1%	17.6%	3.0%
White	16.8%	49.8%	41.5%	17.1%	46.2%	76.1%
Other	3.3%	2.8%	0%	7.6%	2.2%	0.5%
Unknown	60.1%	26.9%	5.3%	15.2%	9.9%	13.9%
Metro Atlanta Counties						
% in MSA**	76.9%	64.8%	67.0%	79.8%	72.5%	50.5%
Urban Influence* **						
More urban	92.9%	88.5%	90.4%	94.9%	93.4%	83.7%
Less urban	7.1%	11.5%	9.6%	5.1%	6.6%	16.3%

* Other race includes American Indians/Alaska Natives (n=2), Asians (n=36), Hawaiians/Pacific Islanders (n=2), Multiracial persons (n=5), and persons of other races (n=53).

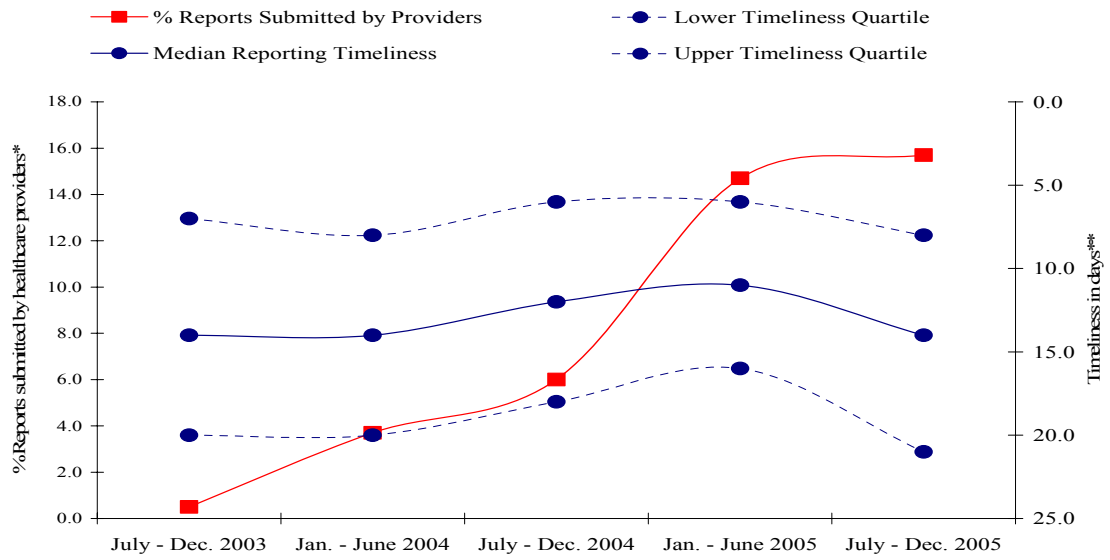
** Residency in Atlanta Metropolitan Statistical Area (28 counties, 2006); 42 records unknown.

*** USDA 2003 Urban Influence Codes: http://www.ers.usda.gov/Data/UrbanInfluenceCodes.

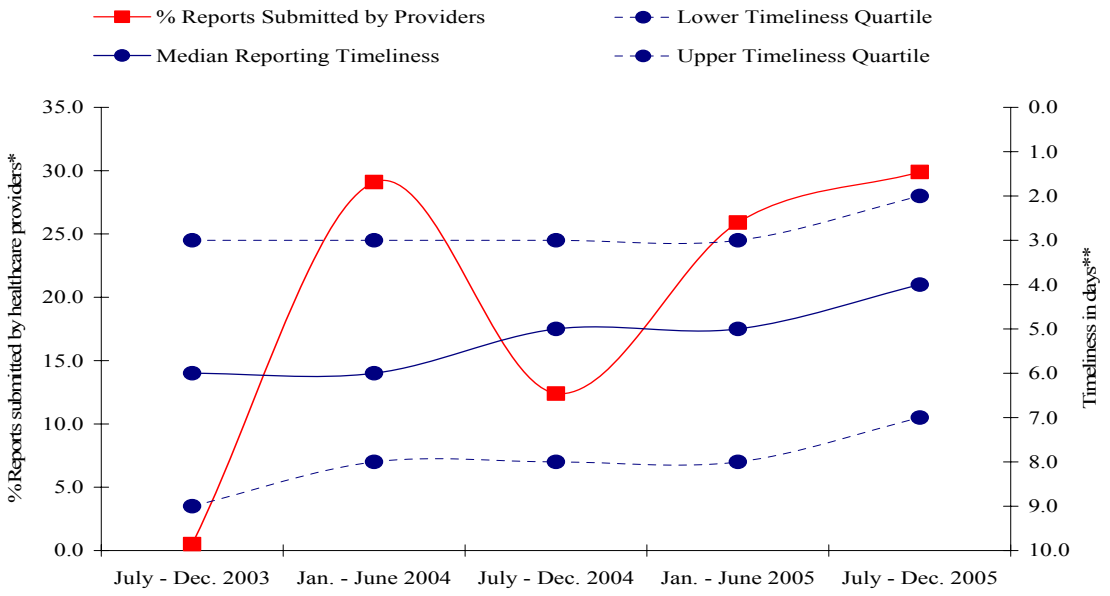
Abbreviations: Hepatitis A virus (HAV), Rocky Mountain spotted fever (RMSF)

Figure 6-3. Healthcare provider submissions to Georgia State Electronic Notifiable Diseases Surveillance System and reporting timeliness in days, July 2003–Dec. 2005

A. Giardiasis (n = 1,865)



B. Hepatitis A virus (n = 785)

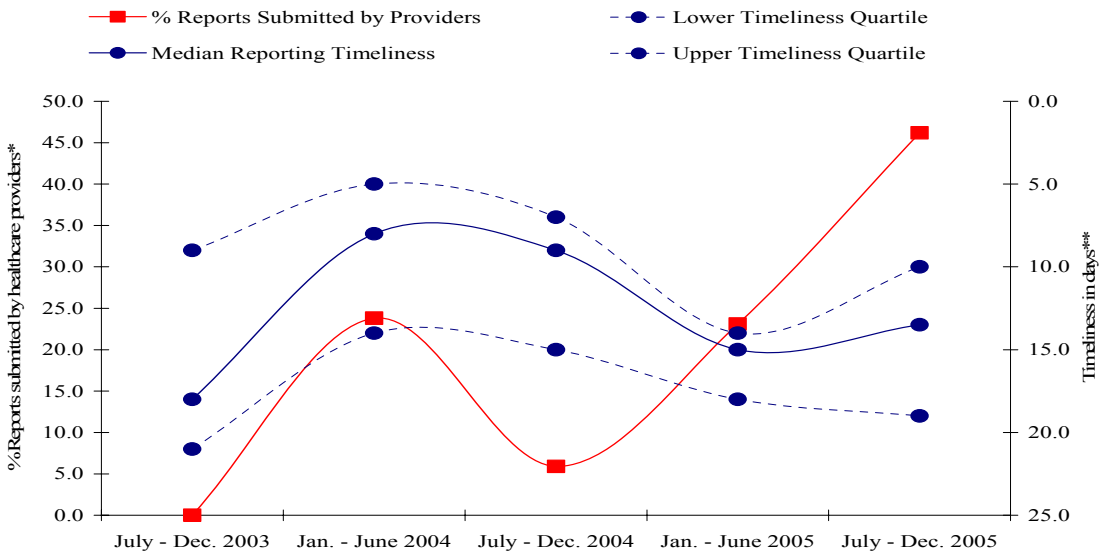


* Reports submitted to SendSS by healthcare providers as a percentage of all reports submitted.

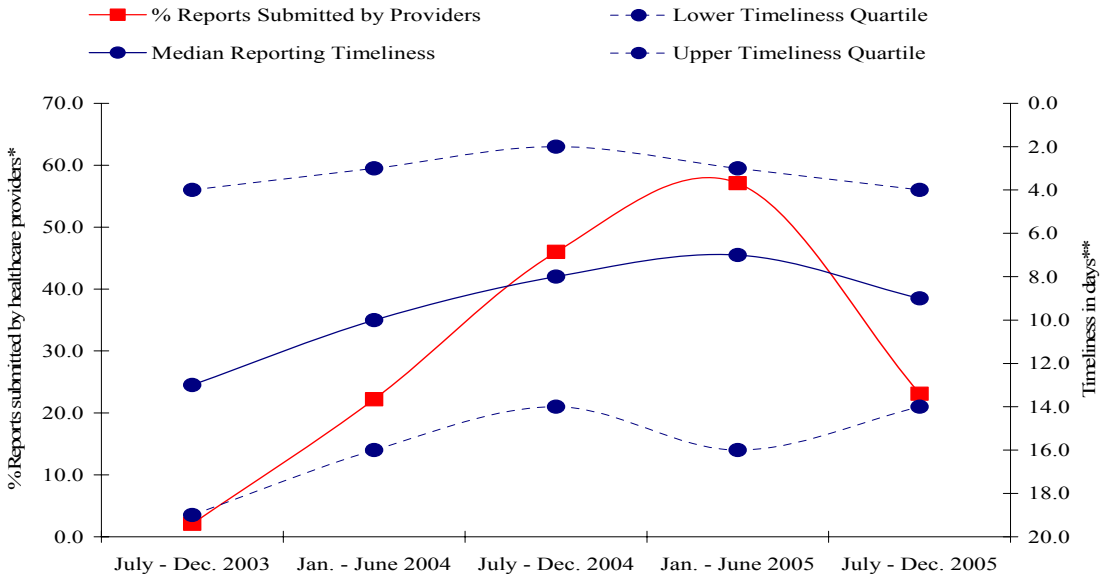
** Timeliness defined as the number of days between the date of first specimen collection and the earliest date of public health notification. Timeliness axis scaled in reverse order to plot potential timeliness improvements parallel with increasing SendSS submissions by providers.

Figure 6-3. Healthcare provider submissions to Georgia State Electronic Notifiable Diseases Surveillance System and reporting timeliness in days, July 2003–Dec. 2005

C. Legionellosis (n = 94)



D. Malaria (n = 158)

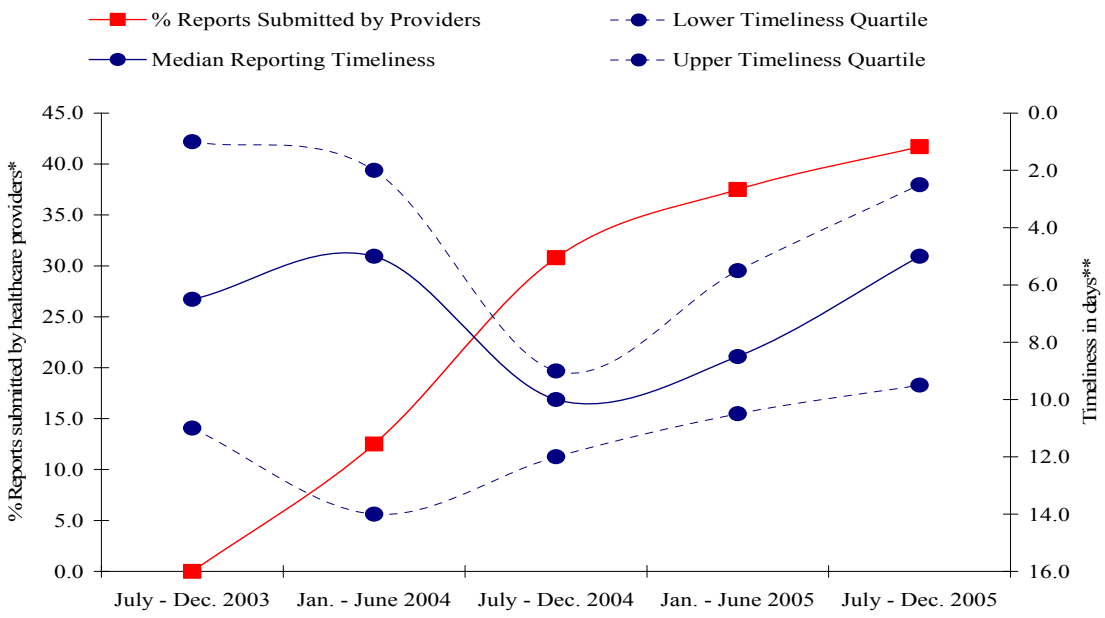


* Reports submitted to SendSS by healthcare providers as a percentage of all reports submitted

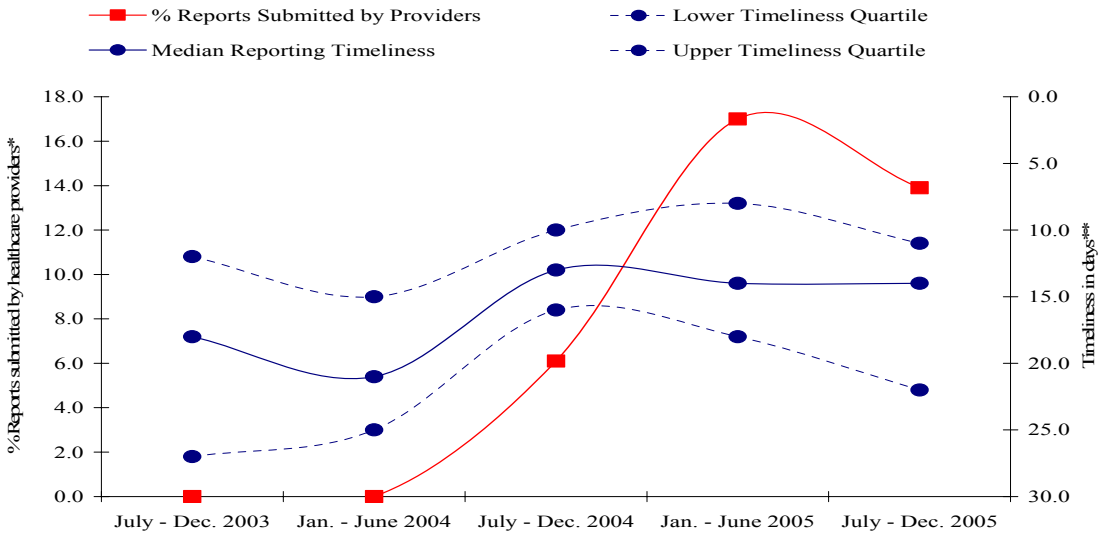
** Timeliness defined as the number of days between the date of first specimen collection and the earliest date of public health notification. Timeliness axis scaled in reverse order to plot potential timeliness improvements parallel with increasing SendSS submissions by providers.

Figure 6-3. Healthcare provider submissions to Georgia State Electronic Notifiable Diseases Surveillance System and reporting timeliness in days, July 2003–Dec. 2005

E. Pertussis (n = 91)



F. Rocky Mountain spotted fever (n = 202)



* Reports submitted to SendSS by healthcare providers as a percentage of all reports submitted.

** Timeliness defined as the number of days between the date of first specimen collection and the earliest date of public health notification. Timeliness axis scaled in reverse order to plot potential timeliness improvements parallel with increasing SendSS submissions by providers.

Table 6-2. Hospital/infection control characteristics and Georgia State Electronic Notifiable Disease Surveillance System timeliness, July 2003–Dec. 2005 (n = 901)*

	Timeliness in Days Median (Lower, Upper Quartiles)	P-value
No. acute care beds+		0.0001
Fewer than 50 (n = 82)	8.0 (5.0, 18.0)	
50-199 (n = 245)	8.0 (4.0, 14.0)	
200 or more (n = 335)	6.0 (2.0, 10.0)	
ICP education+		0.0011
MD (n = 339)	7.0 (4.0, 14.0)	
RN (n = 336)	7.0 (3.0, 13.0)	
Other (n = 164)	7.0 (3.0, 14.0)	
Routine reporting by ICPs		0.0014
Yes (n = 219)	5.0 (2.0, 12.0)	
No/Unknown (n = 682)	8.0 (4.0, 14.0)	
ICP communication with health dept.		0.0001
Regularly (n = 724)	7.0 (3.0, 12.0)	
Not regularly/Unknown (n = 177)	9.0 (5.0, 19.0)	
Track microbiology cultures daily		0.0002
Yes (n = 658)	7.0 (3.0, 13.0)	
No/Unknown (n = 243)	8.0 (4.0, 15.0)	

* Timeliness is specimen collection to reporting date (see text); comparisons via log-rank test.

+ Excludes unknown bed counts (n=239) and infection control professional (ICP) education (n=62).

Table 6-3. Clinical microbiology characteristics and Georgia State Electronic Notifiable Disease Surveillance System reporting timeliness, July 2003–Dec. 2005 (n=901)*

	Timeliness in Days Median (Lower, Upper Quartiles)	P-value
In-patient laboratory always staffed		0.0001
Yes (n = 727)	7.0 (3.0, 12.0)	
No (n = 174)	9.0 (5.0, 19.0)	
All cultures workup at reference lab[+]		0.0001
Yes (n = 1,136)	14.5 (7.0, 20.0)	
No (n = 737)	7.0 (3.0, 13.0)	
No. blood specimens processed[++]		0.32
Fewer than 20 daily (n = 86)	7.5 (4.0, 15.0)	
20-59 daily (n = 354)	7.0 (3.0, 11.0)	
60 or more daily (n = 119)	6.0 (3.0, 13.0)	
No. stool specimens processed[++]		0.55
Fewer than 10 daily (n = 417)	6.0 (3.0, 12.0)	
20 or more daily (n = 145)	7.0 (4.0, 11.0)	

***** Timeliness is specimen collection to reporting date (see text); comparisons via log-rank test.

+ Data from a separate survey of clinical laboratories in Georgia (n = 1,895).

++ Data on numbers of blood and stool specimens currently processed missing for 342 and 339 reports, respectively.

Table 6-4. Multivariate analysis of reporting source characteristics and timeliness of giardiasis and hepatitis A virus reporting, Georgia State Electronic Notifiable Disease Surveillance System July 2003–Dec. 2005 (n=383)*

	Hazard Ratio (95% Confidence Intervals)	P-value
No. acute care beds		< 0.0001
200 or more	1.73 (1.35, 2.23)	
Fewer than 200	Ref.	
All culture workup at reference lab		0.001
Yes	0.59 (0.44, 0.81)	
No	Ref.	
Routine reporting by ICPs		0.02
Yes	1.31 (1.05, 1.64)	
No/Unknown	Ref.	

* Cox proportional hazards models predict timeliness (number of days between the date of first specimen collection and the earliest date of public health notification), account for disease (giardiasis versus hepatitis A virus), and stratify by type of SendSS submission (healthcare provider versus county/district or state health department SendSS submission).

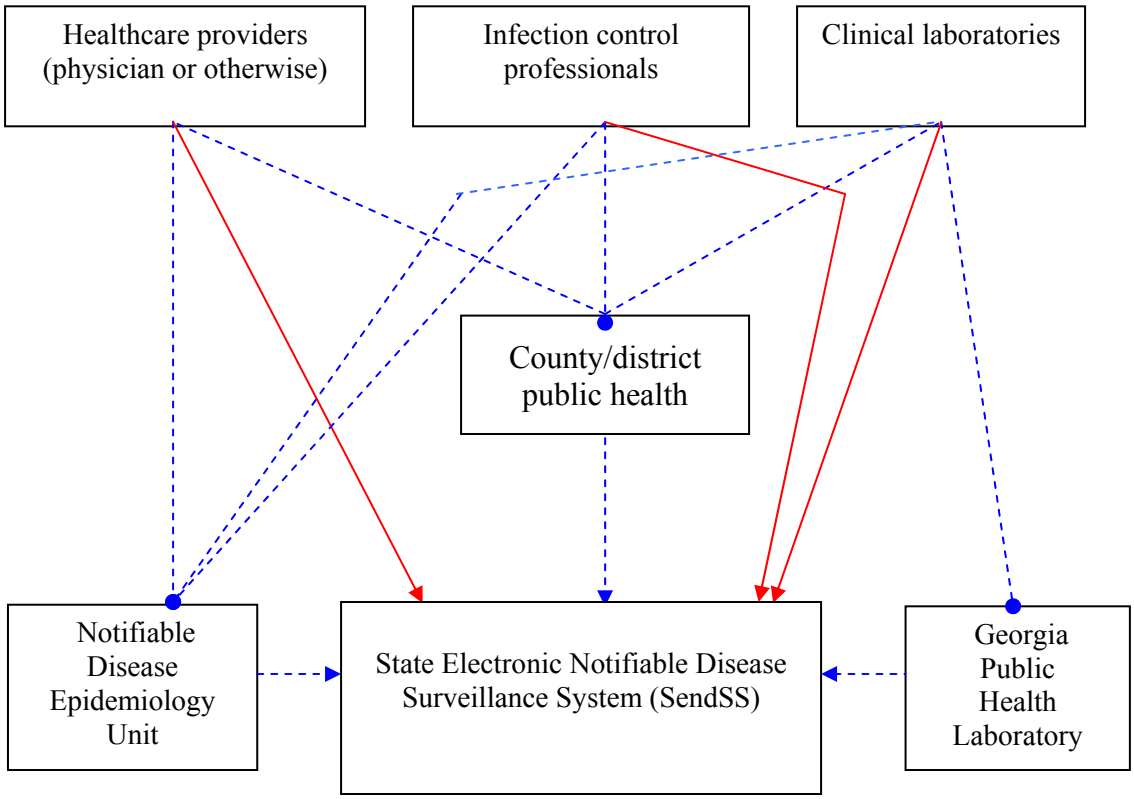
Abbreviation: Infection control professional (ICP).

Appendix 6-A. Schematic representation of data and information flow for disease reporting in Georgia

Legend (see text):

Health department submission of SendSS report

Healthcare provider submission of SendSS report



Appendix 6-B. Healthcare provider or health department submissions to Georgia State Electronic Notifiable Diseases Surveillance System and median timeliness in days (lower, upper quartiles), by interval and disease, July 2003–Dec. 2005*

	Giardiasis	HAV	Legionella	Malaria	Pertussis	RMSF
July – Dec. 2003						
Count (column %)	380 (20%)	404 (51%)	17 (18%)	47 (30%)	14 (15%)	41 (20%)
% Provider submissions	0.5%	0.5%	0.0%	2.1%	0.0%	0.0%
% County/district submissions	18.4%	69.6%	35.3%	70.2%	64.3%	41.5%
% State submissions	81.1%	30.0%	64.7%	27.7%	35.7%	58.5%
Median timeliness (quartiles)	14 (7, 20)	6 (3, 9)	18 (9, 21)	13 (4, 19)	6.5 (1, 11)	18 (12, 27)
Jan. – June 2004						
Count (column %)	351 (19%)	151 (19%)	21 (22%)	27 (17%)	16 (18%)	29 (14%)
% Provider submissions	3.7%	29.1%	23.8%	22.2%	12.5%	0.0%
% County/district submissions	26.2%	23.8%	47.6%	59.3%	75.0%	24.1%
% State submissions	70.1%	47.0%	28.6%	18.5%	12.5%	75.9%
Median timeliness (quartiles)	14 (8, 20)	6 (3, 8)	8 (5, 14)	10 (3, 16)	5 (2, 14)	21 (15, 25)

Table continues.

Appendix 6-B. Healthcare provider or health department submissions to Georgia State Electronic Notifiable Diseases Surveillance System and median timeliness in days (lower, upper quartiles), by interval and disease, July 2003–Dec. 2005*

	Giardiasis	HAV	Legionella	Malaria	Pertussis	RMSF
July – Dec. 2004						
Count (column %)	466 (25%)	105 (13%)	17 (18%)	37 (23%)	13 (14%)	49 (24%)
% Provider submissions	6.0%	12.4%	5.9%	46.0%	30.8%	6.1%
% County/district submissions	30.7%	38.1%	52.9%	18.9%	61.5%	26.5%
% State submissions	63.3%	49.5%	41.2%	35.1%	7.7%	67.4%
Median timeliness (quartiles)	12 (6, 18)	5 (3, 8)	9 (7, 15)	8 (2, 14)	10 (9, 12)	13 (10, 16)
Jan. – June 2005						
Count (column %)	293 (16%)	58 (7%)	13 (14%)	21 (13%)	24 (26%)	47 (23%)
% Provider submissions	14.7%	25.9%	23.1%	57.1%	37.5%	17.0%
% County/district submissions	21.8%	37.9%	53.9%	28.6%	54.2%	36.2%
% State submissions	63.5%	36.2%	23.1%	14.3%	8.3%	46.8%
Median timeliness (quartiles)	11 (6, 16)	5 (3, 8)	15 (14, 18)	7 (3, 16)	8.5 (5.5, 10.5)	14 (8, 18)

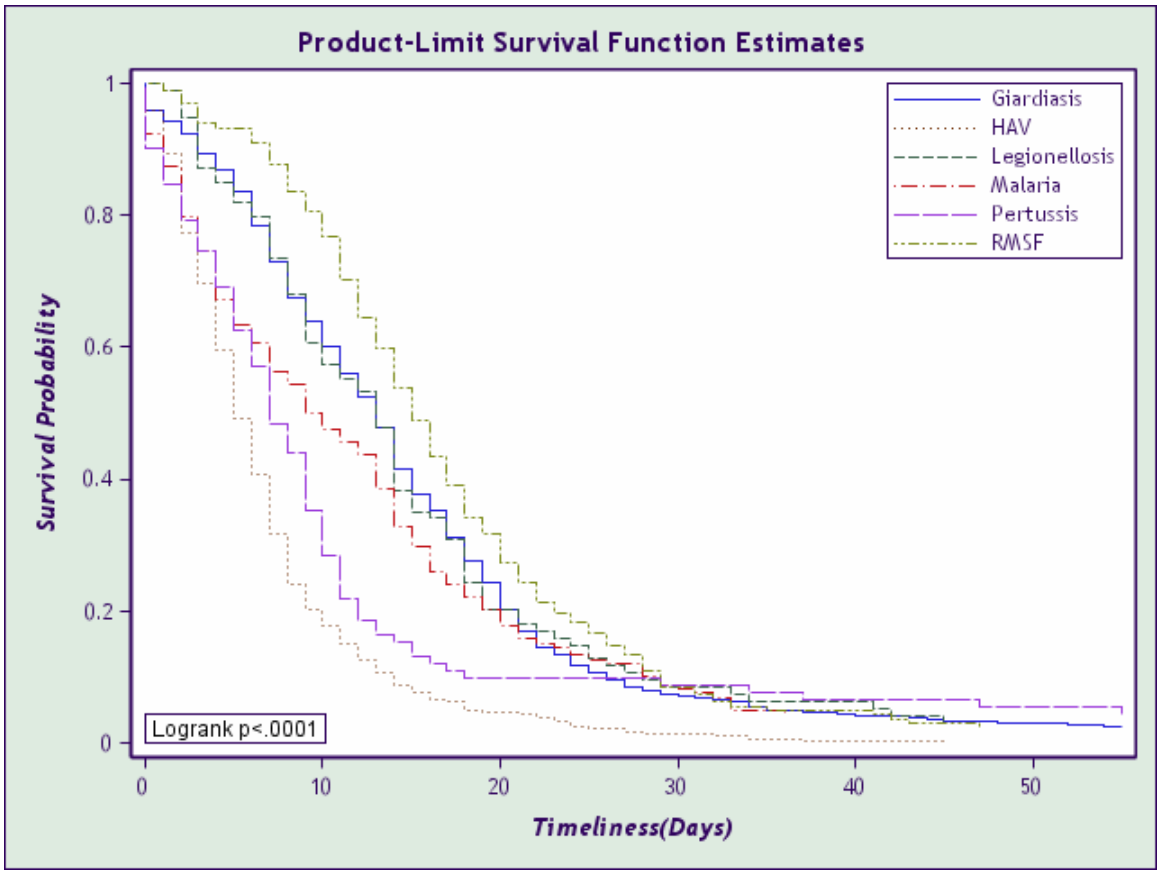
Table continues

Appendix 6-B. Healthcare provider or health department submissions to Georgia State Electronic Notifiable Diseases Surveillance System and median timeliness in days (lower, upper quartiles), by interval and disease, July 2003–Dec. 2005*

	Giardiasis	HAV	Legionella	Malaria	Pertussis	RMSF
July – Dec. 2005						
Count (column %)	375 (20%)	67 (9%)	26 (28%)	26 (16%)	24 (26%)	36 (18%)
% Provider submissions	15.7%	29.9%	46.2%	23.1%	41.7%	13.9%
% County/district submissions	22.7%	47.8%	30.8%	53.9%	45.8%	41.7%
% State submissions	61.6%	22.4%	23.1%	23.1%	12.5%	44.4%
Median timeliness (quartiles)	14 (8, 21)	4 (2, 7)	13.5 (10, 19)	9 (4, 14)	5 (2.5, 9.5)	14 (11, 22)
JULY 2003 – DEC. 2005						
% Provider submissions	7.8%	12.0%	22.3%	26.6%	27.5%	7.9%
% County/district submissions	24.3%	52.4%	42.6%	48.1%	58.2%	34.2%
% State submissions	67.9%	35.7%	35.1%	25.3%	14.3%	57.9%
Median timeliness (quartiles)	13 (7, 19)	5 (3, 8)	13 (7, 18)	9.5 (3, 17)	7 (3, 11)	15 (11, 21)

* Reporting timeliness is first specimen collection to first reporting date; intervals determined based on specimen collection date (see text). Percentages may not sum to 100 because of rounding. Abbreviations: Hepatitis A virus (HAV), Rocky Mountain spotted fever (RMSF).

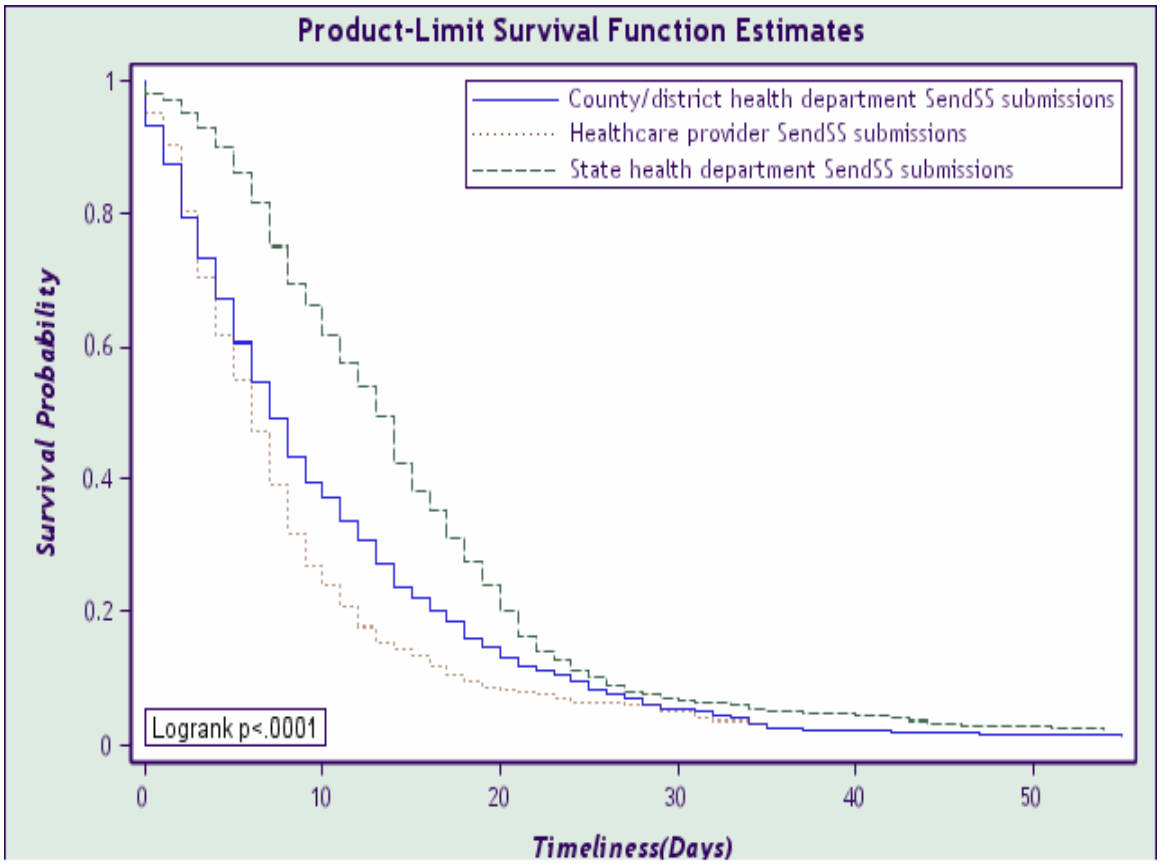
Appendix 6-C. Kaplan-Meier curves comparing timeliness of SendSS reports of giardiasis, HAV, legionellosis, pertussis, malaria, and RMSF*



* "Survival probability" estimates the probability that a disease event is unreported based on the percentage of reported cases at each time point.

Abbreviations: State Electronic Notifiable Disease Surveillance System (SendSS), Hepatitis A virus (HAV), Rocky Mountain spotted fever (RMSF).

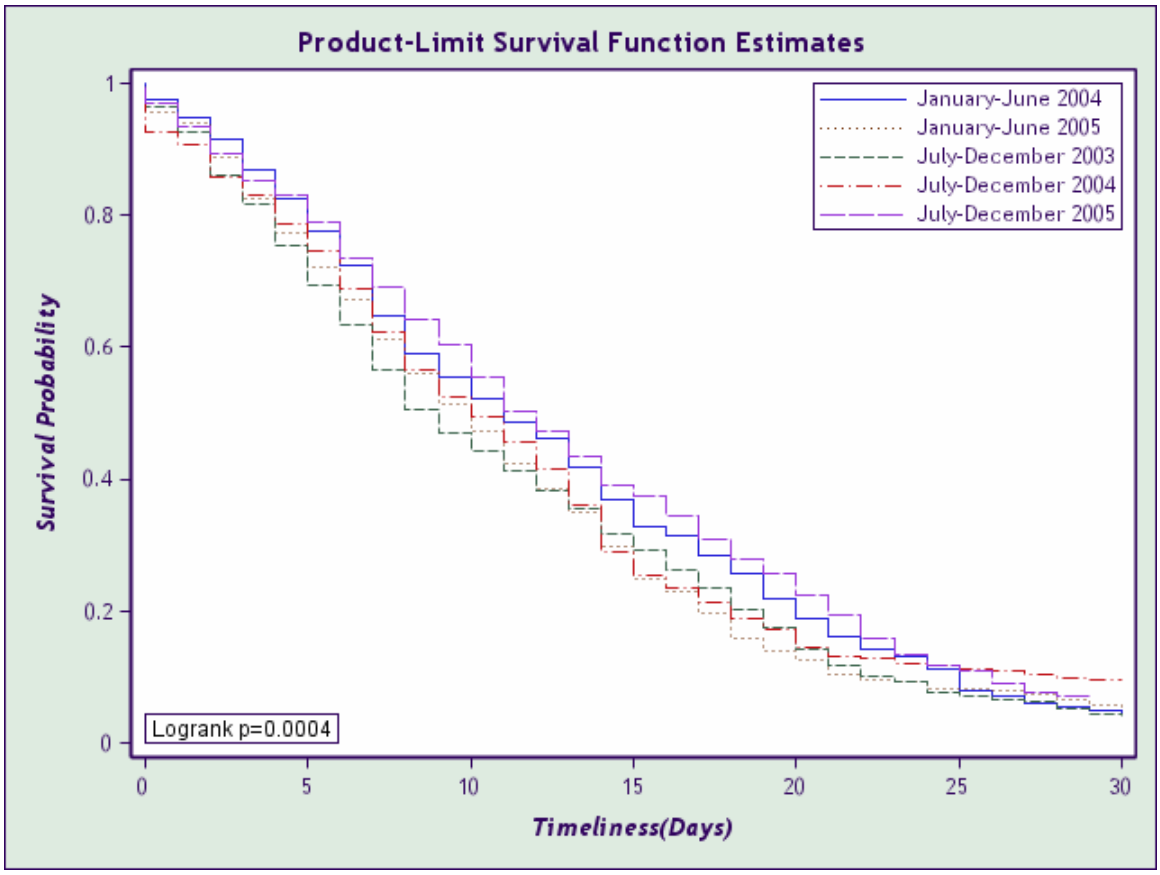
Appendix 6-D. Kaplan-Meier curves comparing timeliness for healthcare provider and health department SendSS submissions



* "Survival probability" estimates the probability that a disease event is unreported based on the percentage of reported cases at each time point.

Abbreviations: State Electronic Notifiable Disease Surveillance System (SendSS), Hepatitis A virus (HAV), Rocky Mountain spotted fever (RMSF).

Appendix 6-E. Kaplan-Meier curves comparing timeliness of SendSS reports submitted during five 6-month time intervals*



* "Survival probability" estimates the probability that a disease event is unreported based on the percentage of reported cases at each time point.

Abbreviations: State Electronic Notifiable Disease Surveillance System (SendSS), Hepatitis A virus (HAV), Rocky Mountain spotted fever (RMSF).

CHAPTER 7

CONCLUSIONS

Summary of findings

Nationally, it was hypothesized that public health agency factors, particularly among surveillance and laboratory programs, would differentially influence the probabilities of progressing through the conditional event series that culminates in complete case ascertainment without missing data. Varying WNV testing and surveillance policies and practices were identified among state and large city/county public health departments. In particular, commercial testing availability in 2003, one or no WNV testing requirement components in 2003 and 2005, four or more surveillance activities in 2004 and 2005, and receipt of a majority of case reports from testing outside the public health laboratory system in 2005 were potentially significant sources of WNF ascertainment variability. Variability was also associated with surveillance and infectious disease control staffing rates for 2003-2005, and there was variability between Census regions in 2003.

Similarly, relatively complete meningococcal disease serogrouping data were frequently reported by states that specified isolate submission requirements in promotional materials, legally mandated isolate submission, provided free shipping, monitored using defined targets for completeness, used 2 or more surveillance enhancement activities, and used 4 or more activities to promote isolate submission. Complete serogrouping was less likely in programs that characterized activities to promote isolate submissions among clinical laboratories solely as recommendations (as opposed to requirements) and was more likely among programs using a defined target for

monitoring. Also, complete serogrouping was likelier among laboratory systems with one or more city/county laboratories and among state public health laboratories with 50 or more technical/analytic FTE positions.

It was also hypothesized that healthcare facility characteristics in Georgia would differentially influence the timeliness of progress through the conditional event series. Reporting was more timely in hospitals with >200 beds (i.e., larger healthcare facilities) and more timely among infection control programs that described reporting as routine. Reports to the health department were significantly delayed when laboratories sent out microbiology cultures for work-up.

Demographic and limited clinical case report data were also incorporated into the studies because cases are nested within public health jurisdictions responsible for complete and timely surveillance ascertainment and laboratory testing. Case- and program-level data were analyzed together using multilevel (hierarchical) modeling. Remarkably, the odds of WNF ascertainment were 44% lower among Blacks and 31% lower among Hispanics relative to non-Hispanic Whites for the three-year study period. These findings accounted for missing race/ethnicity data using multiple imputation, with county-level Census predictors generating plausible data, and controlled for varying WNV testing and surveillance policies among states. This differential WNF ascertainment may undermine surveillance objectives to monitor disease in most-at-risk populations.

Type of specimens for microbiologic testing and vital outcome may have been related to meningococcal disease serogrouping. When both blood and CSF specimens were tested, a serogrouping result was most likely (81%), while non-blood or CSF

sources (e.g., joint or peritoneal fluids) were uncommon and less often serogrouped (39%). Three-quarters of the patients known to have died of meningococcal disease had isolates serogrouped compared with 83% of patients who survived. These clinical data were limited, however, and potential relationships between specimen type, vital outcome, and a serogroup result were not sustained.

In Georgia, the method of communicating a surveillance case report was an important determinant of reporting timeliness. The time from specimen collection to first public health notification was significantly reduced when reports were submitted by physicians, ICPs, clinical laboratories, and other healthcare providers who used the internet-based SendSS reporting system. Reports that were delivered to the state office by other communication mechanisms and subsequently entered in SendSS were least timely.

Summary of limitations

The findings summarized above were achieved in spite of several methodological limitations. Missing data from non-responses to surveys or particular survey items as well as incomplete surveillance records was a challenge for all three projects. Often, there were sizable reductions in the number of records where predictors of interest were collectively complete. While there was no evidence to suggest that data were systematically incomplete, the statistical analyses (and multivariate analyses in particular) were based on subsets of the data that may not have been representative of all public health jurisdictions or case reports. This challenge made parsimonious statistical models

priorities for the analyses. In merging these incomplete data, complicated data inclusion criteria were needed.

There was the possibility for recall bias originating from national surveys that were administered in 2006 but pertained to the period from 2003 through 2005. In addition, predictor misclassification was possible when survey questions referenced the three-year period but public health agencies' activities were dynamic during this time. To offset these challenges, questionnaires were appropriately year-specific. This allowed respondents to describe changing program policies and practices, and select "don't know" when information was partially unavailable. Analyses were also year-specific when this stratification was necessary. In Georgia, surveys of hospital facilities and clinical laboratories had been conducted immediately prior to the study period, which provided a reasonably accurate assessment of their characteristics. The survey periods also coincided with surveillance data reporting periods in Studies 1 and 2.

The national studies were partially based on state-level evaluations, where the unit of analysis was the health department. This facet created a limited number of observations simply because there are only 50 states and not all states had sufficient data for analyses. Also, cutoff decisions for the state-level, univariate analyses were subjective (e.g., 80% for relatively complete meningococcal disease serogroup testing).

State-level public health performance measurement efforts are appropriate as states are recognized for their role as "the hub of the [public health] system in policy development, accountability, and resource allocation" (Bender, Landrum, and Bryan 2000). However, distinct state-level challenges that are relevant to the dissertation have been identified. Bender, Landrum, and Bryan (2000) described fragmented public heath

functions, significant differences in administrative relationship types between state and local health agencies, non-governmental partnerships in delivery of public health services, and varying positions of state health officials in governments (with varying authority, political accountability, or encumbrance).

While we did not specifically examine metropolitan health departments, several were included in the analyses, particularly in examining WNF ascertainment completeness. Plough emphasized the unique service role and financial situation of these health departments, which are defined as health agencies that serve populations of 350,000 or more residents (2004) (Table 2-2). Though they are fewer in number, these agencies serve 55% of the U.S. population, often operate relatively independently from their state health departments, and serve large populations. Since they are centered in urban areas, where at-risk racial and ethnic minorities often live, they also play an important role in addressing health disparities.

Our findings were consistent with the workforce adequacy concerns highlighted in Chapter 2. However, there are recognized challenges in workforce estimation. To some extent, public health workforce deficits are offset by approximately 2.86 million volunteers in health and health-related organizations (e.g., the American Red Cross) as well as various partners surrounding the official public health agency that indirectly performs a number of public health services (Gerzoff and Gebbie 2001). Choice of measures (e.g., full-time equivalents [FTEs] vs. headcounts) and varying job titles are additional challenges. For example, 25% of titles could not be classified specifically in a 2000 assessment (Gebbie et al. 2003).

Chapter 2 also described the unavailability of cost data for public health services and the lack of a corresponding, national measurement system in the United States. For these reasons, and because we did not have access to public health finance data, we did not investigate potential associations between state public health programs' funding, resource allocation, or spending efficiency and completeness or timeliness of morbidity reporting. Notably, however, systematic efforts to understand public health financing have begun (Honore and Amy 2005). For example, several lessons were learned from the process of developing a methodology to measure the cost of local public health in Georgia (Hadley, Feldman, and Toomey 2004).

Summary of strengths

The dissertation specifically addressed incomplete, national West Nile fever ascertainment; missing, national data on meningococcal disease serogroups; and timeliness of disease reporting in Georgia. These timely projects reflected issues of current importance to public health. CDC has endorsed a 2004 CSTE position statement, calling for expansion of the national surveillance case definition of arboviral disease to include non-neuroinvasive illnesses and achieve more complete monitoring of WNV-related illness. In fact, persons with WNF often seek healthcare, but the disease is underdiagnosed and underreported. Whether under-ascertainment of WNF occurs differentially in population strata had not been reported in the literature. Likewise, with licensure of a meningococcal conjugate vaccine that covers four of five common *N. meningitidis* serogroups, serogroup-specific surveillance provides vital information for determining appropriate disease control interventions and for monitoring the distribution

of serogroups causing disease. Recognizing the importance of serogroup-specific surveillance, CDC also endorsed a 2004 CSTE position statement calling for universal serogrouping. In Georgia, increasing SendSS use during the study period was an opportunity to quantify gains in timeliness of reporting during a time when similar systems were being implemented throughout the United States.

The analytic methods used in the three studies were strengths. Multilevel modeling allowed for measurement of the relative importance of sources of variability in WNF ascertainment and meningococcal disease serogroup completeness; this multi-level approach is a significant advance for surveillance system evaluation. Similarly, the assessment of reporting timeliness using survival analyses to identify associated factors in the domain of reporting sources. In applying a WNV syndrome ascertainment ratio, the dissertation proposed a novel application of a ratio estimator for assessing surveillance sensitivity. To date, most evaluations of sensitivity use capture-recapture methods that are often based on untenable assumptions and less accessible statistical methodology.

The goal of the dissertation was to formulate recommendations for strengthening the completeness and timeliness of the national infectious disease morbidity reporting process. National recommendations can be formulated based on assessments of epidemiology and laboratory programs' policies, practices, and capacities at the state public health agency level. In Georgia, assessments were directed toward the partnerships with reporting sources that reside in the healthcare domain.

Collectively, the studies represent evaluations of a series of events and time intervals in the conditional events framework (Figure 1-1), which was adopted to identify

discrete components of the infectious disease morbidity reporting process where interventions can be directed appropriately and associated improvements in the quality, representativeness, and value of notifiable diseases surveillance data can be achieved.

CHAPTER 8

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Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005

Instructions: This survey focuses on testing for West Nile virus (WNV) during 2003, 2004, and 2005. If practices or policies existed during any part of these periods, please answer yes for that question. For simplicity, questions will reference "your laboratory" and "your state" in referring to the public health laboratory in your state, county, or city health department. Please note that underlined terms are defined in the glossary at the end of this document.

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1. Please name your state: _____

2. Please indicate your name and a preferred telephone number or email address:

_____

_____

3. Please indicate your employment function(s):

(Check one that best describes your functions.)

- ☐ Section laboratory manager / director (e.g., microbiology)
- ☐ Laboratory supervisor (e.g., virology)
- ☐ Journey-level professional (> 5 years bench experience)
- ☐ Intern / Trainee
- ☐ Other, please specify:_____

4. What were the total numbers of initial tests for WNV infection performed at your public health laboratory?

**If data are unavailable, indicate with "9999".*

	2003	2004	2005
Cerebrospinal fluid (CSF) specimens:	_____	_____	_____
Serum specimens:	_____	_____	_____
IF unavailable by specimen source, please indicate numbers of tests with either serum or CSF	_____	_____	_____

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

5. What were the total numbers of initial positive tests for WNV infection at your public health laboratory?

**If data are unavailable, indicate with "9999".*

	2003	2004	2005
CSF specimens:	_____	_____	_____
Serum specimens:	_____	_____	_____
IF unavailable by specimen source, please indicate numbers of tests with either serum or CSF	_____	_____	_____

6. During all or part of the study period, has your public health laboratory outsourced WNV-specific IgM-capture enzyme-linked immunosorbent assay (IgM capture ELISA) testing to another laboratory?

❑ Yes, commercial laboratory ❑ Yes, another public health laboratory ❑ No ❑ Don't know

7. Do other public health laboratories in your state also perform WNV-specific IgM capture ELISA testing?

❑ Yes ❑ No ❑ Don't know

7a. IF YES, please name the other public health laboratories in your state that also perform WNV- specific IgM capture ELISA testing:_____

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

8. Was laboratory testing for WNV performed by commercial laboratories for at least some patients in your jurisdiction?

	2003	2004	2005
Yes	❑	❑	❑
No	❑	❑	❑
Don't know	❑	❑	❑

9. Was WNV testing of human specimens free of charge at your public health laboratory?

	2003	2004	2005
Yes, all testing free	❑	❑	❑
Yes, free for certain patients	❑	❑	❑
No	❑	❑	❑
Don't know	❑	❑	❑

9a. IF testing was free for certain patients, please describe the criteria that had to be met to qualify for free testing: _____

10. Did your public health laboratory pay for shipping or provide containers for sending specimens for WNV testing at your public health laboratory?

	2003	2004	2005
Yes, pay for shipping AND containers	❑	❑	❑
Yes, pay for shipping only	❑	❑	❑
Yes, provide containers only	❑	❑	❑
No	❑	❑	❑
Don't know	❑	❑	❑

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

11. Is a WNV positive test designated laboratory-reportable in your jurisdiction?

❑ Yes ❑ No ❑ Don't know

11a. IF YES, what month and year was WNV designated laboratory-reportable in your state? _____

12. In order to count a human case as confirmed or probable, did your agency require confirmation of commercial-laboratory positive specimens by your public health laboratory or a diagnostic reference laboratory?

	2003	2004	2005
Yes	❑	❑	❑
No	❑	❑	❑
Don't know	❑	❑	❑

13. If your laboratory has used a plaque reduction neutralization test (PRNT) test, how has it been used? *(Check all that apply.)*

	2003	2004	2005
All positive ELISAs	❑	❑	❑
Early season and any unusual ELISAs throughout the season	❑	❑	❑
Only on equivocal ELISAs	❑	❑	❑
Other use for PRNT, specify: _____	❑	❑	❑
PRNT not performed in our laboratory	❑	❑	❑

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

14. IF PRNT is not performed in your public health laboratory, where is confirmatory testing performed? *(Check all that apply.)*

	2003	2004	2005
At CDC	❑	❑	❑
At another state's public health laboratory	❑	❑	❑
ELISA positives not confirmed by PRNT	❑	❑	❑

15. To what extent did staff at your laboratory participate in the development of previously publicized clinical requirements or recommendations for WNV-specific IgM capture ELISA testing at your public health laboratory?

	2003	2004	2005
WNV testing requirements/recommendations developed entirely by laboratory personnel	❑	❑	❑
WNV testing requirements/recommendations developed in collaboration with epidemiology program or other health department personnel	❑	❑	❑
WNV testing requirements/recommendations developed entirely by epidemiology program or other health department personnel	❑	❑	❑
Not applicable, WNV testing requirements/recommendations not publicized	❑	❑	❑

15a. If you indicated that your laboratory staff partly or entirely developed previously publicized clinical requirements or recommendations for IgM capture ELISA WNV testing, please describe the requirements or recommendations in the space provided. If past requirements or recommendations for testing are available electronically and easier to provide as such, please either indicate below the addresses (URLs) to the internet website(s) where requirements/recommendations are archived or send as attachments to bsilk@sph.emory.edu.

_____

_____

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

15b. Was WNV testing still performed by your public health laboratory on all specimens submitted regardless of whether they met criteria for testing?

❑ Yes ❑ No ❑ Not applicable, given requirements for testing ❑ Don't know

16. Please use the comment space below to communicate any additional information regarding West Nile virus testing in your state or comments related to your responses to this survey.

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

Glossary

Culture-confirmed: The 1997 CDC/CSTE case definition for culture-confirmed is isolation of *Neisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid).

Culture dates: Can refer to either the date when the specimen is initially cultured in a clinical laboratory or the date the specimen is initially collected for a clinical laboratory.

Initial (positive) tests: West Nile virus (WNV) initial testing includes WNV-specific IgM-capture enzyme-linked immunosorbent assays (IgM capture ELISA) and WNV-specific polymerase chain reaction (PCR), if applicable. The terms "initial tests" are distinguished from confirmatory testing, such as plaque reduction neutralization test (PRNT), but include testing of paired sera. For example, if an acute and convalescent serum were each submitted, and either one or both were positive, count this as one test for survey question 1 and one positive test for question 2. If acute sample only was submitted and was positive, also count as one test (question 1) and one positive (question 2). If sera and cerebrospinal fluid were both tested for an individual, each would count as a test and each would count as a positive, if positive.

Appendix 1. Questionnaire on state and large city/county public health laboratories' West Nile virus testing, 2003-2005 (continued)

Glossary

Laboratory-reportable: A disease reporting law, statute, or regulation that requires clinical laboratories to submit reports of diagnosed case patients to the health department.

Outsourced: Another public or private laboratory performing *N. meningitidis* serogrouping or WNV testing on behalf of your laboratory.

Pay for shipping: Includes directly or indirectly covering the costs of shipping through a courier or specimen pickup and transportation.

Percentage: Specify a number between 0 and 100 without decimals.

Routinely: At least one instance per year.

State: Refers to your public health jurisdiction, which may be a state, territory, or a large city or county.

Study period: The period from January 1, 2003 to December 31, 2005.

Universal: Equal or greater than 90%.

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005

Instructions: This survey focuses on human disease and surveillance for West Nile virus (WNV) during the period from January 1, 2003 to December 31, 2005. For simplicity, questions will reference "your program" and "your state" in referring to the infectious diseases surveillance and epidemiology program in your state, territory, county, or city health department. Please note that underlined terms are defined in a glossary at the end of this document.

1. Please name your state: _____

2. Please indicate your name and a preferred telephone number or email address:

_____

3. Please indicate your employment function(s):

(Check one that best describes your functions.)

- ☐ Administrative
- ☐ Assignee (e.g., CSTE Fellow, EIS Officer, etc.)
- ☐ Front-line epidemiologist
- ☐ Program manager or supervisor
- ☐ State epidemiologist (or jurisdiction equivalent)

4. In your state, please provide the number of cases of WNV disease with each case status for each period: *

	Total confirmed	Total probable
Onset dates of Jan. 1 – Dec. 31, 2003:	_____	_____
Onset dates of Jan. 1 – Dec. 31, 2004:	_____	_____
Onset dates of Jan. 1 – Dec. 31, 2005:	_____	_____

* For each period, please use the case definition used by your state, whether a modified case definition specific to your jurisdiction or the national CDC/CSTE case definitions (i.e., the 2001 CDC/CSTE definition that was revised in 2004). If your state reported any presumptively viremic blood donors, include in case counts only those that were subsequently verified as symptomatic cases of West Nile Fever, meningitis, encephalitis, or meningoencephalitis.

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005 (continued)

5. For each of the following years, what percentage of confirmed or probable human cases was reported through laboratory testing outside the public health laboratory or laboratories in your state?

2003: _____

2004: _____

2005: _____

6. Is a WNV positive test designated laboratory-reportable in your state?

☐ Yes ☐ No ☐ Don't know

IF YES, what month and year was WNV designated laboratory-reportable in your state? _____

7. Were out-of-state laboratories required to report positive WNV tests on human specimens collected within your state?

2003	☐ Yes	☐ No	☐ Don't know
2004	☐ Yes	☐ No	☐ Don't know
2005	☐ Yes	☐ No	☐ Don't know

8. Is West Nile fever (or non-neuroinvasive arboviral disease, including WNV) currently reportable in your state?

☐ Yes ☐ No ☐ Don't know

If yes, what month and year was West Nile fever added to your state notifiable diseases list? _____

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005 (continued)

9. Did your program, or local health departments in your state, take initiatives to enhance reporting of WNV disease from 2003 to 2005?

☐ Yes, statewide ☐ Yes, select region(s) or counties ☐ No ☐ Don't know

If yes, state wide OR select region(s) / counties, indicate which surveillance activities were performed: (*Please check all that apply.*)	State Wide	Select Region(s) or Counties
Automated or electronic laboratory reporting	☐	☐
Dissemination of advisories / recommendations for WNV reporting	☐	☐
Dissemination of surveillance manuals / protocols	☐	☐
Dissemination of periodicals (e.g., newsletters) to clinicians or hospital staff	☐	☐
Periodic telephone inquiries to reporting sources	☐	☐
Retrospective case finding through hospital records review	☐	☐
Retrospective case finding through laboratory records review	☐	☐
Trainings / seminars on WNV reporting for clinicians or hospital staff	☐	☐
Other, please specify: _____	☐	☐

10. From 2003 to 2005, did your program encourage testing of suspected West Nile fever cases during periods of WNV activity?

☐ Yes, statewide ☐ Yes, select region(s) or counties ☐ No ☐ Don't know

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005 (continued)

If yes, state wide OR select region(s) / counties, how was testing of suspect West Nile fever encouraged: (*Please check all that apply.*)

	2003	2004	2005
Healthcare providers encouraged to submit specimens to public health laboratory for WNV testing	☐	☐	☐
Healthcare providers encouraged to test for WNV through referral of specimens to private laboratories	☐	☐	☐
Other, please specify:_____	☐	☐	☐

11. To what extent did staff at your program participate in the development of previously publicized clinical requirements or recommendations for WNV-specific IgM capture ELISA testing at your public health laboratory?

	2003	2004	2005
WNV testing requirements/recommendations developed entirely by epidemiology personnel	☐	☐	☐
WNV testing requirements/recommendations developed in collaboration with public health laboratory	☐	☐	☐
WNV testing requirements/recommendations developed entirely by public health laboratory	☐	☐	☐
Not applicable, WNV testing requirements/recommendations not publicized	☐	☐	☐

12. Was WNV testing performed by your state public health laboratory on all specimens submitted regardless of whether patients met criteria for testing?

☐ Yes ☐ No ☐ Don't know ☐ Not applicable, given requirements for testing

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005 (continued)

13. If you indicated that you or your staff partly or entirely developed clinical requirements or recommendations for WNV testing, please describe the requirements or recommendations in the space provided. If past requirements or recommendations for testing are available electronically and easier to provide as such, please either indicate below the addresses (URLs) to the website(s) where requirements / recommendations are archived or send as email attachments to bsilk@sph.emory.edu.

2003

2004

2005

14. Please add any comments you would like:

Appendix 2. Questionnaire on state and large city/county epidemiology programs' West Nile virus surveillance, 2003-2005

(continued)

Glossary

Cases of WNV disease: Symptomatic illness associated with acute West Nile virus infection that conforms to the surveillance case definition used by your state for case counting in humans.

Laboratory-reportable: A disease reporting law, statute, or regulation that requires clinical laboratories to submit reports of diagnosed case patients to the health department.

Percentage: Specify a number between 0 and 100 without decimals.

Program: Refers to your infectious diseases surveillance, epidemiology and disease control program.

State: Refers to your public health jurisdiction, which may be a state, territory, or a large city or county.

Study period: The period from January 1, 2003 to December 31, 2005.

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005

Instructions: This part focuses on serogrouping of invasive meningococcal disease during a study period spanning January 1, 2003 to December 31, 2005. If practices or policies existed during any part of this period, please answer yes for that question. For simplicity, questions will reference "your laboratory" and "your state" in referring to the public health laboratory in your state, territory, county, or city health department. Please note that underlined terms are defined in the glossary at the end of this document.

1. Will the lab Director be completing Part 1 of the questionnaire?

❑ Yes ❑ No

If yes, please skip to question 4.

2. Please enter the contact information of the laboratory staff member that will be completing Part 1.

a. First name: _____

b. Last name: _____

c. Email address: _____

d. Phone Number: _____

3. Please select the employment function of the person completing Part 1.

❑ Section laboratory manager / director (e.g., microbiology)

❑ Laboratory supervisor (e.g., bacteriology)

❑ Journey-level professional (> 5 years bench experience)

❑ Entry-level professional (< 5 years bench experience)

❑ Intern / Trainee

❑ Other, please specify:_____

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

4. Please provide the number of culture-confirmed cases of invasive meningococcal disease for which **serogrouping was successfully performed by your public health laboratory** for each of the following periods: *

Culture dates of Jan. 1 – Dec. 31, 2003:	_____
Culture dates of Jan. 1 – Dec. 31, 2004:	_____
Culture dates of Jan. 1 – Dec. 31, 2005:	_____

* If data are unavailable, indicate "don't know" with 9999.

5. Please provide the number of culture-confirmed cases of invasive meningococcal disease **for which serogroup results were not obtained by your public health laboratory** for each of the following reasons: **

	Jan. 1 – Dec. 31, 2003	Jan. 1 – Dec. 31, 2004	Jan. 1 – Dec. 31, 2005
Isolates discarded / unavailable at the clinical lab:	_____	_____	_____
Isolates were physically lost during shipping / transit to public health lab:	_____	_____	_____
Isolates received were not viable or otherwise inadequate upon arrival at public health lab:	_____	_____	_____
Isolates received were viable but not typeable at public health lab:	_____	_____	_____

** If data unavailable in either the laboratory or epidemiology program, indicate "don't know" with 9999.

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

6. Has your public health laboratory monitored completeness of serogrouping of *N. meningitidis* isolates during all or part of the study period from January 1, 2003 to December 31, 2005?

❑ Yes ❑ No ❑ Don't know

6a. If yes, please specify the goal for serogrouping completeness as a percentage in the row corresponding to the definition for completeness used by your lab. For example, please enter a goal of ninety percent as **"90"**

		Percentage
❑	Yes, the number of isolates serogrouped / number of isolates received	_____
❑	Yes, the number of isolates serogrouped / number of cases reported	_____
❑	Yes, another definition, please specify: _____	_____

7. Is responsibility for the completeness of serogrouping of *N. meningitidis* isolates designated to a single individual in your public health laboratory?

❑ Yes ❑ No ❑ Don't know

8. Do your laboratory regulation(s) currently require clinical laboratories to submit to your public health laboratory *N. meningitidis* isolates from residents of your state?

❑ Yes ❑ No ❑ Don't know

8a. IF YES, in what month and year was this requirement added to the law / regulation: _____

8b. Has this regulation been enforced?

❑ Yes ❑ No ❑ Don't know

8c. IF YES, please indicate how the regulation is enforced. (*Check all that apply.)*

Notice of failure to submit isolates by in-state laboratories	❑
Notice of failure to submit isolates by out-of-state laboratories	❑
Certification or licensure suspension / revocation	❑
Other, please specify: _____	❑

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

9. During all or part of the study period, have any hospital laboratories or commercial laboratories used by hospitals in your state performed serogrouping of *N. meningitidis* isolates?

❑ Yes ❑ No ❑ Don't know

9a. IF YES, are results of serogrouping shared with your laboratory or epidemiology program in the form of case-specific data?

❑ Yes, always shared ❑ Yes, sometimes shared ❑ No, not shared ❑ Don't know

10. During all or part of the study period, has your public health laboratory outsourced *N. meningitidis* serogrouping to another laboratory?

❑ Yes, commercial laboratory ❑ Yes, another public health laboratory ❑ No ❑ Don't know

11. Do other public health laboratories in your state also perform *N. meningitidis* serogrouping?

❑ Yes ❑ No ❑ Don't know

11a. IF YES, please list the public health laboratories in your state that perform *N. meningitidis* serogrouping:_____

12. During all or part of the study period, did your public health laboratory pay for shipping or provide containers for sending *N. meningitidis* isolates to your public health laboratory?

❑ Yes, pay for shipping AND provide containers ❑ Yes, pay for shipping only ❑ Yes, provide containers only ❑ No ❑ Don't know

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

13. During all or part of the study period, which of the following measures has your public health laboratory taken to improve the completeness of serogrouping of *N. meningitidis* isolates: *(Please check all that apply and specify the method.)*

	In written communications (e.g., advisories, manuals, newsletters)	In oral communications (e.g., trainings, meetings)
Promote to clinical laboratories that isolates of *N. meningitidis* be submitted to your public health laboratory for serogrouping	❑	❑
Promote to clinical laboratories that specimens be submitted to your public health laboratory for PCR testing when cultures are negative but meningococcal disease is suspected or clinically diagnosed	❑	❑
Provided guidance on how to prepare clinical isolates of *N. meningitidis* for shipping to your public health laboratory	❑	❑
Provided specific guidance on where and to whom *N. meningitidis* isolates should be shipped	❑	❑

13a. Are you able to share samples of the informational materials noted above?

❑ Yes ❑ No

IF YES, please provide a website address and/or the name and contact information for requesting sample materials:

_____

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

14. If *N. meningitidis* isolate submission and serogrouping has not been universal (or near universal), what have been barriers to accomplishing this task? (*Check one response per row.*)

	Relevant	Not relevant
Lack of culturing by clinical labs:	❑	❑
Lack of isolate submission by clinical labs:	❑	❑
Competing public health laboratory staff priorities:	❑	❑
Lack of demonstrated need for public health:	❑	❑
Lack of funding for submission / serogrouping:	❑	❑
Other, please specify: _____	❑	❑

15. If your laboratory is trying to achieve universal (or near universal) *N. meningitidis* isolate submission, describe what has been key to accomplishing this task:

_____

16. During all or part of the study period, has your public health laboratory routinely received isolates of *N. meningitidis* for serogrouping directly from each of the following sources? *(Please check all that apply.)*

Clinical laboratories:	❑
Health care providers (physicians, etc.):	❑
Infection control professionals or hospital epidemiologists:	❑
State-level epidemiologists or disease control specialists:	❑
Regional/county/local-level epidemiologists or disease control specialists:	❑
Other, please specify: _____	❑

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

17. Please use the comment space below to communicate any additional information regarding serogrouping in your state or comments related to your responses to this survey.

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

Glossary

Culture-confirmed: The 1997 CDC/CSTE case definition for culture-confirmed is isolation of *Neisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid).

Culture dates: Can refer to either the date when the specimen is initially cultured in a clinical laboratory or the date the specimen is initially collected for a clinical laboratory.

Initial (positive) tests: West Nile virus (WNV) initial testing includes WNV-specific IgM-capture enzyme-linked immunosorbent assays (IgM capture ELISA) and WNV-specific polymerase chain reaction (PCR), if applicable. The terms "initial tests" are distinguished from confirmatory testing, such as plaque reduction neutralization test (PRNT), but include testing of paired sera. For example, if an acute and convalescent serum were each submitted, and either one or both were positive, count this as one test for survey question 1 and one positive test for question 2. If acute sample only was submitted and was positive, also count as one test (question 1) and one positive (question 2). If sera and cerebrospinal fluid were both tested for an individual, each would count as a test and each would count as a positive, if positive.

Laboratory-reportable: A disease reporting law, statute, or regulation that requires clinical laboratories to submit reports of diagnosed case patients to the health department.

Appendix 3. Questionnaire on state and large city/county public health laboratories' meningococcal disease serogrouping, 2003-2005 (continued)

Glossary

Outsourced: Another public or private laboratory performing *N. meningitidis* serogrouping or WNV testing on behalf of your laboratory.

Pay for shipping: Includes directly or indirectly covering the costs of shipping through a courier or specimen pickup and transportation.

Percentage: Specify a number between 0 and 100 without decimals.

Routinely: At least one instance per year.

State: Refers to your public health jurisdiction, which may be a state, territory, or a large city or county.

Study period: The period from January 1, 2003 to December 31, 2005.

Universal: Equal or greater than 90%.

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005

Instructions: The assessment focuses on serogrouping of invasive meningococcal disease isolates during a study period of January 1, 2003 to December 31, 2005. If practices or policies existed during any part of this period, please answer yes for that question. For simplicity, questions will reference "your state" and "your program" in referring to the communicable disease surveillance and epidemiology program in your state, territory, county, or city health department. The last page of this document is a glossary of terms used for the assessment.

1. Please indicate your name and a preferred telephone number or email address:

   Name: _____

   Title: _____

   Phone: _____

   Email: _____

2. Please indicate your employment function(s):

(Check one that best describes your functions)

- ❑ Administrative
- ❑ Assignee (e.g., CSTE Fellow, EIS Officer, etc.)
- ❑ Front-line epidemiologist
- ❑ Program manager or supervisor
- ❑ State epidemiologist (or jurisdiction equivalent)

3. In your state, please provide the number of cases of invasive meningococcal disease with each case status for the following periods: *

	Total lab-confirmed	Total Probable
Report dates of Jan. 1 – Dec. 31, 2003:	_____	_____
Report dates of Jan. 1 – Dec. 31, 2004:	_____	_____
Report dates of Jan. 1 – Dec. 31, 2005:	_____	_____

* Please use the 1997 CDC/CSTE case definition. *Confirmed* is clinically compatible case that is laboratory-confirmed (and would include culture-confirmed). *Probable* is a case with a positive antigen test in CSF or clinical purpura fulminans in the absence of a positive blood culture. If data are unavailable, please indicate "don't know" with 9999.

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

4. Has your program monitored completeness of serogrouping of *N. meningitidis* isolates during the study period of January 1, 2003 to December 31, 2005?

❑ Yes ❑ No ❑ Don't know

If yes, does a defined goal for monitoring completeness of serogrouping exist?
(*Check all definitions that apply and specify the goal as a percentage.)*

	Percentage
❑ Yes, the number of isolates serogrouped / number of isolates received	_____
❑ Yes, the number of isolates serogrouped / number of cases reported	_____
❑ Yes, ascertaining every possible case, getting all isolates possible, and serogrouping every possible isolate	_____
❑ Yes, another definition, specify: _____	_____

5. Is responsibility for the completeness of serogrouping of *N. meningitidis* isolates designated to a single individual in your program?

❑ Yes ❑ No ❑ Don't know

6. Does your state's notifiable disease reporting law(s) or regulation(s) currently require clinical laboratories to submit *N. meningitidis* isolates to your public health laboratory?

❑ Yes ❑ No ❑ Don't know

IF YES, in what month and year was this requirement added to the law / regulation:_____

Has this law / regulation been enforced?

❑ Yes ❑ No ❑ Don't know

IF YES, please indicate how. (*Check all that apply)*

- ❑ Verbal or written notice of failure to submit isolates by in-state labs
- ❑ Verbal or written notice of failure to submit isolates by out-of-state labs
- ❑ Certification or licensure suspension / revocation
- ❑ Other, please specify: _____

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

7. In your state, are there currently posters or other promotional materials with the list of notifiable diseases AND specification that clinical laboratories are required to submit isolates or samples of *N. meningitidis*?

❑ Yes ❑ No, materials exist but don't specify submission requirement ❑ No, posters/ promotional materials don't exist ❑ Don't know

IF YES, in what year was the requirement that clinical laboratories are required to submit isolates or samples of *N. meningitidis* first specified on these posters or other materials:

_____

8. Other than participating in the Emerging Infections Program (if applicable), has your program, or local health departments in your state, taken initiatives to enhance surveillance of invasive meningococcal disease during the study period?

❑ Yes, state wide ❑ Yes, select region(s) / counties ❑ No ❑ Don't know

If yes, state wide OR select region(s) / counties, indicate which surveillance activities were performed for case ascertainment: (*Please check all that apply.*)

	State Wide	Select Region(s) or Counties
Automated or electronic laboratory reporting	❑	❑
Case finding through hospital records review	❑	❑
Case finding through laboratory records review	❑	❑
Dissemination of advisories / recommendations specifically for meningococcal disease	❑	❑
Dissemination of surveillance manuals / protocols	❑	❑
Periodic telephone inquiries to reporting sources	❑	❑
Reporting promoted via written periodicals (e.g., newsletters) to clinicians or hospital staff	❑	❑
Trainings / seminars on reporting to clinicians or hospital staff	❑	❑
Other, please specify: _____	❑	❑

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

9. In your state, do you conduct public health follow-up (identification and chemoprophylaxis of close contacts) on every case of invasive meningococcal disease?

❑ Yes ❑ No

If no, why is follow-up not conducted on every case?

❑ Considered clinicians' responsibility ❑ Another reason: _____ ❑ Don't know

10. Has your program, or local health departments in your state, required or recommended each of the following during the study period?

That clinical laboratories submit isolates to your public health laboratory	❑ Yes	❑ No	❑ Don't know
That clinicians request bacterial cultures while caring for patients with invasive meningococcal disease	❑ Yes	❑ No	❑ Don't know

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

If yes to either, please indicate how required or recommended for each.

	Clinical laboratories submit isolates to your public health laboratory		Clinicians request bacterial cultures while caring for patients with invasive meningococcal disease	
	Required	Recommended	Required	Recommended
By disseminating surveillance manuals / protocols	❑	❑	❑	❑
During case finding inquiries to reporting sources	❑	❑	❑	❑
In advisories / recommendations for meningococcal disease	❑	❑	❑	❑
In trainings / seminars on reporting	❑	❑	❑	❑
Via written periodicals (e.g., newsletters)	❑	❑	❑	❑
While conducting public health follow-up of cases	❑	❑	❑	❑
Other, please specify: _____	❑	❑	❑	❑

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

11. Based on your experience, which of the following, if any, increased emphasis on *N. meningitidis* serogrouping among public health officials in your state? (*Check one response per row.*)

	Very important	Somewhat important	Not important
The FDA licensure of the meningococcal conjugate vaccine	❑	❑	❑
The 2004 CSTE / CDC approved position statement recommending universal serogrouping of *N. meningitidis* isolates	❑	❑	❑
The Advisory Committee on Immunization Practices (ACIP) / CDC recommendations for routine vaccination of adolescents	❑	❑	❑
An outbreak of meningococcal disease in your state	❑	❑	❑
Other, please specify: _____	❑	❑	❑

12. Based on your experience, if submission and/or serogrouping of *N. meningitidis* isolates has not been universal (< 90%) in your state, what have been barriers to accomplishing this task during the study period? (*Check one response per row.*)

	Relevant	Not relevant	Don't know
Clinical diagnosis of suspected meningococcal disease:	❑	❑	❑
Use of non-culture methods by clinical labs:	❑	❑	❑
Lack of isolate submission by clinical labs:	❑	❑	❑
Interactions with local health departments:	❑	❑	❑
Lack of demonstrated need:	❑	❑	❑
Lack of funding for submission / serogrouping:	❑	❑	❑
Data transfer issues among information / surveillance systems	❑	❑	❑
Other, please specify: _____	❑	❑	❑

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

13. If your program is trying to achieve is currently universal (or near universal) *N. meningitidis* isolate submission, describe what has been key to accomplishing this task:

_____

_____

14. How does your program use the results of each of the following? (*Check all that apply.*)

	N. meningitidis isolate serogrouping	Pulsed-field gel electrophoresis (PFGE) subtyping of *N. meningitidis*
To characterize the epidemiology of invasive meningococcal disease in your state	❑	❑
For determination of linkages between cases	❑	❑
For consideration of prevention / control options	❑	❑
Other, please specify: _____	❑	❑
Not used	❑	❑

15. Please add any comments you would like.

_____

_____

Appendix 4. Questionnaire on state and large city/county epidemiology programs' meningococcal disease surveillance, 2003-2005 (continued)

Glossary

State: Refers to your public health jurisdiction, which may be a state, territory, or a large city or county.

Report dates: Refers to the first date public health was notified of the case.

Study period: The period from January 1, 2003 to December 31, 2005.

Percentage: Specify a number between 0 and 100 without decimals.

Universal: Equal or greater than 90%.