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Correlation of Syndromic Surveillance of Gastrointestinal Illnesses with Laboratory-confirmed Notifiable Enteric Disease, by Time and Place, State of Georgia, 2015 – 2016

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An abstract of
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Abstract

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by Kelsey Patel

Background: The Georgia Department of Public Health (DPH) has used syndromic surveillance (SS) since 2004 as part of the public health protection activities for the G8 Summit in Sea Island, GA to identify events that may threaten the health of residents. A common problem in creating interoperable, analogous SS is the lack of standardization of syndrome definitions. This is as an area for further research to strengthen syndromic data collection and studies.
Objective: Describe the temporal relationship between GI-related syndromic and notifiable disease counts.
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Results: For the GI event, there is a statistically significant association between GI syndrome counts and enteric notifiable counts in the spring months only (spearman coefficient = 0.23, p=0.0045). Additionally, there is a statistically significant association between vomit syndrome counts and enteric notifiable counts in the spring months (spearman coefficient = 0.24, p=0.0036). For the diarrhea event, there are statistically significant associations with enteric notifiable counts during the spring months (spearman coefficient = 0.16, p=0.046) and winter months (spearman coefficient = -0.16, p=0.05). For both the bloody diarrhea (spearman coefficient = -0.27, p=0.0007) and bloody vomit (spearman coefficient = -0.17, p=0.033) syndromes, there are only statistically significant associations with enteric notifiable counts during the winter months.
Conclusions/Implications: To better understand the baseline counts of syndromic data by event, future studies should increase number of years used in the study. Summing counts over 3-4 years instead of two years could help establish a more accurate baseline from which to observe aberrations of counts from the baseline. Moving forward, DPH could conduct analyses like those done in this paper for all syndromes to assess the competency of Georgia's SS program.

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Chapter I: Literature Review

This paper aims to understand how syndromic and notifiable disease data for gastrointestinal illnesses (GI) in six counties in Georgia correlated spatially and temporally. I reviewed literature to determine the current status and practices for syndromic surveillance (SS) in the United States and globally. To analyze and review SS, we must understand how syndromes are defined and categorized. Then, examples of SS in the United States and accompanying research can be outlined and practices assessed.

Classifying GI Syndromes and Establishing Case Definitions

According to Brown, et al. emergency department (ED) databases that contain chief complaint (CC) or International Classification of Diseases, 9th revision, (ICD-9) codes are better equipped to aid in public health surveillance (PHS). ICD-9 codes are grouped into syndromes (e.g., "respiratory", "gastrointestinal," "fever", "influenza-like illness"). Assignment of syndromes is based on ICD-9 or CC codes and Brown, et al. suggests a combination of the two should be used to categorize ED visits into syndromes. However, CCs are often assigned in real-time while ICD-9 codes may be assigned later, during the billing process making the creation of ICD-9 codes a tenuous process (4).

Continuing to explore case definitions for SS, researchers in Quebec, Canada sought to determine if syndromic definitions were accurate in community settings, operating on the hypothesis that community clinics could offer timelier outbreak detection than emergency departments. From 2005-2007, the sensitivity, specificity, and positive predictive value (PPV) of physician claims were assessed in 3,600 community-based primary care physicians. As with most SS, ICD-9 codes were used to define syndromes. Cadieux, et al. found using diagnostic

codes to determine syndrome case definitions yielded low sensitivity, moderate to high PPV, and near-perfect specificity and NPV (6).

Additionally, Cadieux, et al expanded their study looking at the PPV of the same case definitions studied previously to determine physician, patient, encounter, and billing characteristics. The study team used the patient's medical chart as the gold standard to compare syndromes from physician-facilitated chart review to the gold standard. Researchers found that there was more likely to be agreement between the physician claim and the medical chart if the physician billed the same patient for the same syndrome multiple times. They recommend that patient, physician, and billing characteristics can be used to reduce false-positive alerts in SS by adjusting for these biases in diagnosis reporting (7).

A limitation for SS is that syndrome definitions are not standardized at state and national levels. This makes it difficult to assess performance and study trends across states and nationally. In response, Chapman, et al. sought to develop standard syndrome definitions for 10 SS in the United States. These included Aegis (Harvard), BioPortal (University of Arizona), BioSense (CDC), Boston Public Health Department, ESSENCE (Department of Defense), NC DETECT (University of North Carolina) and the NC Division of Public Health), New York City (NYC DOHMH), New York State, Seattle-King County and RODS (University of Pittsburg). Representatives reached a consensus on syndrome definitions for the four most common syndromes: respiratory, gastrointestinal (GI), constitutional, and influenza-like illness (ILI) (8).

The consensus included developing baseline syndrome definitions that encompassed each systems current definitions and discussion of those baseline definitions to include only essentials. For GI, the team identified 25 symptoms. From these, six symptoms were included in the

sensitive syndrome and three in the specific syndrome. The three in both were diarrhea, vomiting, and GI. Abdominal pain, nausea, and dehydration were included in the sensitive definition. The researchers noted the consensus syndromes had yet to be implemented (8).

SS Programs in the United States

There are several SS programs operating at the local, state and national level. Some are outline below and provide insight into gaps before being implemented. They demonstrate the types of data required to run a well-functioning SS.

BioSense

The BioSense Platform – established in 2004 – is part of CDC's National Syndromic Surveillance Program (NSSP) to detect, quantify, and localize possible bioterrorism attacks and other outbreaks of concern. BioSense collects and analyzes data from several sources including ambulatory diagnoses from Departments of Defense and Veterans Affairs and laboratory-test orders from Laboratory Corporation of America (3). CDC used the technology-driven BioSense 2.0 as the SS platform between 2008-2014. In late 2016, BioSense 2.0 was discontinued in favor of an integrated, standardized platform known as ESSENCE (20).

ESSENCE

The Electronic Surveillance System for the Early Notification of Community-Based Epidemics originally operated in the National Capital Region (NCR) and has helped healthcare personnel detect and monitor key health indicators since 2004 (16). ESSENCE is comprised of two versions: one serving military personnel and one serving civilians in the NCR region. ESSENCE was developed through collaborations of Johns Hopkins University Applied Physics Laboratory

(JHU/APL) and the Division of Preventative Medicine at the Walter Reed Army Institute of Research (18). ESSENCE now operates in most of the United States, including Georgia—the Georgia Department of Public Health (DPH) feeds data into ESSENCE.

RODS

The Real-time Outbreak and Disease Surveillance (RODS) Open Source Project of the University of Pittsburg uses ED chief complaints and sales of over-the-counter medications – data collected for other purposes – to identify outbreaks, especially those due to bioterrorism. RODS software was developed in 1999 to speed up the use of computer-based SS and has been used in several states since then. RODS software was used in the 2002 Winter Olympics in Salt Lake City, Utah (13).

EARS

Early Aberration Reporting System (EARS) – developed by CDC – uses three cumulative sum (CUSUM) detection methods for SS: C1, C2, and C3 (14). EARS consists of several components including quality-control (QC) charts, Shewhart chart (P-chart), moving average (MA), and variations of CUSUM. Many SS utilize the components of EARS, especially for temporal aberration detection (22). For over a decade, the CUSUM statistical methods of EARS has been used globally, due to the simplicity of the system design and ease of use (24).

BioSTORM

Biological Spatio-Temporal Outbreak Reasoning Model (BioSTORM) was developed in 2003 due to increasing demand for integrative PHS to rapidly analyze data from several sources.

BioSTORM uses common informatics processes to integrate data sources into standard data streams, map those streams, and respond to those maps to address potential outbreaks **(**21).

SS Research in the United States

SS is thought beneficial to identify bioterrorism events and for seasonal outbreaks like influenza; however, SS can also be useful during mass gatherings. During Super Bowl XLIX, the Maricopa County Department of Public Health (MCDPH) in Arizona, implemented several enhanced PHS, including SS for emergency room (ER) visits, urgent care facilities, hotels, and real-time onsite SS. Before the Super Bowl, Maricopa County participated in SS for ER visits as part of the Centers for Disease Control and Prevention's (CDC) National Syndromic Surveillance Program BioSense 2.0. Maricopa County added SS in hotels and urgent care facilities located within five miles of the stadium and associated Super Bowl events. Real-time SS at the football field recorded minor injuries and some cases of GI and neurological disease. SS from emergency room visits detected an increase in reports of measles, but this was associated with the Disneyland exposure in 2015 (2).

As stated, SS was first implemented in the United States after the 9/11 terrorist and anthrax attacks in 2001. Due to these heightened threats, the New York City Department of Health implemented a SS using ED visits to ensure that health officials were aware of syndrome clusters that could signify an outbreak within 24 hours after an attack. With help from CDC, 15 New York City hospitals categorized patient visits into syndromes—syndromes associated with bioterrorism agents were especially monitored. These syndromes included, but not limited to, diarrhea/gastroenteritis, botulism-like syndrome, upper/lower respiratory infection. The analyses

employed in this study are relevant to this paper and research question because researchers analyzed syndromic data trends temporally (9).

The researchers assumed that ED visits are binomially distributed and compared the probability of having a syndrome on a particular day to the probability of having a syndrome during baseline. After a week (a baseline established), researchers used cumulative sum (CUSUM) methods. This method compared proportion of syndrome to total visits on the previous three days compared to the mean proportion (baseline) plus one standard deviation. The article correctly identifies that "detection of a large outbreak would be limited by syndromes identified, syndrome coding, data resources, and the sensitivity of the system." Like used in New York Hospitals after the 9/11 terrorist attacks, The Georgia Department of Public Health (DPH) also uses CUSUM methods as well to identify flags in syndromic data, which lets epidemiologists know whether further investigation into a flagged syndrome is necessary (9).

New York's robust SS programs made it an interesting target for study. In 2014, Hsieh, et al. developed a retrospective study designed to determine a link between drinking water turbidity and GI illness in New York City using data from 2002 – 2009. The researchers used chief compliant syndromic data from EDs during that time period using the diarrhea syndrome. Researchers found that turbidity was associated with an increase in diarrhea chief complaints during the Spring, peaking at a 6-7-day lag. These methods should be used in future SS studies (17).

Global SS Research

SS programs have been implemented all over the world since after the anthrax attacks in the United States in 2001. Several studies on SS have been conducted to assess their viability and

usefulness. One study in Sweden compared local outbreak signals for three different SS data sources: telephone triage of acute gastroenteritis; web queries about symptoms of GI illness; and over-the-counter (OTC) pharmacy sales of antidiarrheal medication.

The study took those data sources and compared them against nine waterborne and foodborne outbreaks in Sweden between 2007 – 2011. It developed a national system for outbreak PHS by evaluating the efficiency of data sources for Early Event Detection (EED) and Situational Awareness (SA). It acknowledged that the majority of studies targeted seasonal epidemics that were easier to track like influenza and norovirus, leaving a lack of research on local outbreak PHS. "The study concluded that syndromic surveillance of point-source outbreaks for acute gastroenteritis can serve both SA and EED." The article further argues that in order to create a robust national SS, local outbreak data must be shared across borders (1).

A study from Canada assessed whether there was an association between sales of OTC GI-related medication and reportable infections. The Canadian National Enteric Surveillance Program is a laboratory-based PHS that obtains aggregate counts of GI-related notifiable diseases from each province.

This is relevant to our study because we are exploring temporal relationships between SS and notifiable disease data. In the case of the Canadian study, syndromic data were in the form of OTC product sales. Researchers looked for GI cases due to the same bacteria that this study includes—*Salmonella, Campylobacter, Escherichia coli, and Shigella*. The paper supports the hypotheses outlined in this study that one expects to see increases in GI-related illnesses (from bacterial and parasitic organisms) during the summer and early fall (11).

SS is equipped for mass gatherings due to the near real-time nature of the data and the ability to identify clusters of cases that could indicate an outbreak.

In 2012, the UK Health Protection Agency (HPA) developed the Emergency Department Sentinel Syndromic Surveillance (EDSSS) to help monitor disease outbreaks during the London Olympic and Paralympic Games. Researchers studied the ability of the EDSSS to monitor indicators of disease using patient visit data from six emergency departments. During the heightened visits, syndromic indicators like respiratory and GI were identified. SS has been used in both Olympic and Winter Olympic games—importantly, SS identified an outbreak of gastroenteritis due to *Salmonella* spp. (12).

There are several studies evaluating SS (sensitivity, specificity, and case definitions). Another example of global studies is from the University of Lyon hospital in France. The purpose was to evaluate the ability of SS algorithms for early detection of communicable diseases. The sensitivity and specificity of the algorithms for syndromes including respiratory, cutaneous, and GI was evaluated. For GI syndromes, the sensitivity of the detection algorithms was 79% and the specificity was 82%. The sensitivity and specificity for GI syndromes were both lower than the corresponding sensitivity and specificity for respiratory and cutaneous syndromes. The researchers determined that the specificity for the GI syndromes was low due to the high number of false positives compared to the number of infected patients. Gerbier-Colomban, et al. acknowledged that the algorithms for the GI groups are not operating at the sensitivity that is reasonable for SS, indicating that more work needs to be done to explore the ability of GI syndromes to properly detect outbreaks (15).

Summary of Current Problem and Study Relevance

Several studies mentioned the lack of standardization of syndrome definitions across SS as a necessary area for further research to strengthen syndromic data collection and studies. For this work, it is important to discuss the case definitions used by the Georgia Department of Public Health (DPH) for the GI-related syndromes so that study findings can be reproduced and compared across SS. Articles also suggested that there is not enough research to determine if SS is accurately gathering data in near real-time at an acceptable sensitivity, specificity, and positive predictive value (PPV). While the scope of this paper is not to determine the sensitivity, specificity, and PPV of GI syndromes in Georgia's SS, we hope to illuminate the temporal relationship between GI-related syndromic and notifiable disease data.

After reviewing the literature, there are several methods to analyze syndromic data (e.g., Poisson regression, negative binomial regression, scan statistics, distributed lag models). However, they rely on robust data with key demographic variables. This work utilizes some of these methods to describe the temporal trends of GI syndromic and notifiable data in six counties in Georgia.

Chapter II: Manuscript

Title, Author(s), Abstract

Correlation of Syndromic Surveillance of Gastrointestinal Illnesses with Laboratory-confirmed Notifiable Enteric Disease, by Time and Place, State of Georgia, 2015 – 2016

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Background: The Georgia Department of Public Health (DPH) has used syndromic surveillance (SS) since 2004 as part of the public health protection activities for the G8 Summit in Sea Island, GA to identify events that may threaten the health of residents in Georgia. A common problem in creating interoperable, analogous SS is the lack of standardization of syndrome definitions. This is as an area for further research to strengthen syndromic data collection and studies.

Objective: Describe the temporal relationship between GI-related syndromic and notifiable disease counts.

Methods: This analysis examined data from GI-related (shigellosis, salmonellosis, campylobacteriosis, and *E. coli*) SS and notifiable diseases from 2015 – 2016 in six counties in Georgia. The notifiable disease data were classified as enteric. Data analyses consisted of two methods: Spearman correlations to assess the relationship between syndromic and enteric (notifiable) disease counts by season and creation of figures showing syndromic and enteric counts varied by event, county, and time.

Results: For the GI event, there is a statistically significant association between GI syndrome counts and enteric notifiable counts in the spring months only (spearman coefficient = 0.23,

p=0.0045). Additionally, there is a statistically significant association between vomit syndrome counts and enteric notifiable counts in the spring months (spearman coefficient = 0.24, p=0.0036). For the diarrhea event, there are statistically significant associations with enteric notifiable counts during the spring months (spearman coefficient = 0.16, p=0.046) and winter months (spearman coefficient = -0.16, p=0.05). For both the bloody diarrhea (spearman coefficient = -0.27, p=0.0007) and bloody vomit (spearman coefficient = -0.17, p=0.033) syndromes, there are only statistically significant associations with enteric notifiable counts during the winter months.

Conclusions/Implications: To better understand the baseline counts of syndromic data by event, future studies should increase number of years used in the study. Summing counts over 3-4 years instead of two years could help establish a more accurate baseline from which to observe aberrations of counts from the baseline. Moving forward, DPH could conduct analyses like those done in this paper for all syndromes to assess the competency of Georgia's SS program.

Introduction

The purpose of syndromic surveillance (SS) is to rapidly detect clusters of symptoms, categorize them into syndromes and point to an outbreak. In SS, data are collected and analyzed in near real-time to identify public health threats. SS has evolved over time using various data sources such as emergency department (ED) visits, 911 calls, over-the-counter drug sales, pharmacy sales, and school or work absenteeism. SS is often considered controversial with some public health professionals questioning the usefulness and accuracy of SS to predict outbreaks. Champions argue that SS can supplement the traditional, laboratory-confirmed diagnoses, type of surveillance with quicker identification of outbreaks and potential to detect cases that were not sent for laboratory confirmation (19).

The Georgia Department of Public Health (DPH) has used SS since 2004 as part of the public health protection activities for the G8 Summit in Sea Island, GA to identify events that may threaten the health of residents in Georgia. In Georgia's coastal region, DPH used emergency department (ED) visits, 911 calls, and over-the-counter pharmacy sales.

In 2004, several public health districts in Georgia established their own syndromic surveillance systems, often utilizing systems like ESSENCE—unfortunately, those systems only allowed data to be available to the specific public health district. In September 2004, DPH created a centralized system called the Georgia Syndromic Surveillance Program. This program was created so that each Public Health District can view the pre-analyzed data from data providers (5).

A common problem in creating interoperable, analogous SS is the lack of standardization of syndrome definitions. This is as an area for further research to strengthen syndromic data collection and studies. For the study, it is important to discuss the case definitions used by DPH for the GI-related syndromes so findings can be reproduced and compared across SS. Several published articles have suggested that there is not enough research to determine if SS is accurately gathering data in near real-time at an acceptable sensitivity, specificity, and positive predictive value (PPV). While the scope of this paper is not to determine the sensitivity, specificity, and PPV of GI syndromes in Georgia's SS, we describe the temporal relationship between GI-related syndromic and notifiable disease.

Methods

This analysis examined data from GI-related (shigellosis, salmonellosis, campylobacteriosis, and E. *coli*) SS and notifiable diseases from 2015 – 2016 in six counties in Georgia: Chatham; Cobb; DeKalb; Fulton; Gwinnett; and Richmond (Table 1) were chosen as having at least two facilities participating in Georgia's SS (Table 2).

Table 1. Estimated Population in Six Counties, State of Georgia, 2016

County	Population*
Fulton	1,023,336
Gwinnett	907,135
Cobb	748,150
DeKalb	740,321
Chatham	289,082
Richmond	201,647

**U.S. Census Bureau, updated July 1, 2016 (23)*

Table 2. Facilities Reporting Syndromic Data from Six Counties, State of Georgia, 2016

County	Average Number of Facilities
Fulton	10.77
Gwinnett	2.54
Cobb	6.50
DeKalb	2.99
Chatham	2.99
Richmond	3.76

The five syndromes examined were GI, vomit, diarrhea, bloody vomit, and bloody diarrhea and the notifiable disease data were classified as enteric. The use of "enteric" is synonymous with notifiable disease data (Table 3).

Table 3. Case Definitions of Syndromes, State of Georgia, 2016

Syndrome	Case Definition
Diarrhea	Any text resembling diarrhea; enteric; F/D (fever and diarrhea); loose or watery BM; loose or watery bowel; loose or watery stool; N/D (nausea and diarrhea); or V/D (vomit and diarrhea).
BloodyDiarrhea	Any text resembling hematochezia; OR any text resembling (blood, black, bleed, tarry, or dark) AND the Diarrhea syndrome.
GI	Any text resembling the BloodyDiarrhea, Diarrhea, BloodyVomit, OR NauseaVomit syndromes.
BloodyVomit	Any text resembling blood or coffee ground PLUS the Nausea-Vomit syndrome; or hematemesis.
Vomit	Any text resembling D/V (diarrhea and vomiting); emesis; food poisoning; N/V (nausea and vomiting); nausea; puke; throw up; V/D (vomit and diarrhea); or vomit

To aid in analyses, we created variables to determine months correspond to each MMWR week and that categorized months into seasons (Table 4).

Table 4. Morbidity and Mortality Weekly Report Time Allocations, by Season and Month

Season	Months	MMWR Week
Spring	March, April, May	9-21
Summer	June, July, August	22-34
Fall	September, October, November	35-47
Winter	January, February, December	1-8, 48-52

Daily Flow of SS

Daily visits of patients to 120 emergency departments (ED) and urgent care facilities are sent electronically to the Georgia Department of Public Health's State Electronic Notifiable Diseases

Surveillance System (SendSS) on the following day, including weekends, with no personal identifiers. The information sent includes:

- Name of the facility
- Date/time of visit
- Chief complaint
- Discharge diagnoses (ICD9 or ICD 10 code)
- Age
- Race
- Gender
- Triage notes
- Discharge disposition
- Zip code of residence of patient
- Patient ID#

The syndromic notifications comprise two tiers of information: charts (flag-based and purely syndromic) and text-based (queries of key words in the chief complaint and discharge diagnosis fields). The charts or flag-based notifications rely on the chief complaint fields to classify ED visit in one or more of the 33 syndromes. These are then grouped into syndromes and statistical algorithms are applied to identify unusual temporal and geographic patterns indicating situations of public health concern. SendSS uses technical and administrative measures to ensure the security of the data and protect the confidentiality of the information. The analyses here utilized text-based notifications.

The 33 syndromes used in Georgia are:

Bt-EID (Bioterrorism / Emerging Infectious Disease)
FeverGI
ILI
FeverFlu
FeverRespiratory
Respiratory
RSV (Respiratory Syncytial Virus)
FeverFluRespiratoryAdmission
FeverFluRespiratoryDeath
Sepsis
VeryIll
FeverChest
BloodyRespiratory
BloodyVomit
Botulism
RashFever
Hemorrhagic
PoxRashFever
BloodyDiarrhea
GI
Diarrhea
NauseaVomit

Asthma	Poison	Mumps
DrugAlcohol	Throat	ND (Notifiable Disease)
Heat	Hepatitis	Rash
Injury	Meningitis	

Each syndrome count is charted on a daily and weekly basis at the following levels: statewide, public health district (18 units), and healthcare facilities (120 units). Flags are generated by the C1-C2-C3 algorithm created by the CDC (19). There are three different CUSUM methods that are calculated in different ways using different numerators and denominators. If these CUSUM results are greater than 3 standard deviations (SD) above the average, unique flags (C1, C2, or C3) are generated.

- **C1** – Identifies 1-day aberration in counts. Flags are generated due to a sharp rise from 1 day to the next. If a flag is noted on a particular day, the next day is less likely to produce a flag since the elevated count from the previous day will be immediately incorporated into the new baseline period. This flag has the lowest sensitivity and the highest specificity.
- **C2** – Identifies aberrant initial, rapid rise in counts and peak in counts. It is more likely to flag high consecutive values since those values would not be incorporated immediately into the baseline period after the initial flag. This flag has the higher sensitivity and comparable specificity with the C1 flag.
- **C3** – Identifies gradual rise in counts over short time. This flag has the highest sensitivity and the lowest specificity.

The resulting flags from these calculations are then loaded back into SendSS and made available in the syndromic surveillance interface. The data and flags are seen by DPH, District Public Health, and the data provider on a daily basis in SendSS.

The text-based syndromic notifications rely on querying the Chief Complaint and Discharge Diagnosis fields for keywords that may fall into one or more of these categories:

- Bioterrorism or emerging infectious disease
- Notifiable disease
- Cluster with common chief complaints / preliminary diagnosis
- Travel-related disease
- Food poisoning
- Institutional setting (daycare, school, college, nursing home)
- Social event (convention, festival, sport event)
- Natural event (hurricane, flood, tornado, wildfire)

The SS coordinator reviews both the purely syndromic and text-based events and in conjunction with the Georgia Public Health Preparedness Director, decides if follow-up is warranted. If so, an email with the notification is sent to the Public Health District Epidemiologists. Public Health District Epidemiologists follow up on the notification and prioritize the response depending on other local data they might have and weighing priorities.

Literature Review

A PubMed search using keywords "syndromic surveillance" AND "Gastrointestinal" yielded 96 results. Of these, those with just an abstract were excluded as well as those that were not about GI. We used 32 articles.

Notifiable Disease Reporting

We classified data for GI-related notifiable disease events of bacterial origin into a single category ("Enteric") and used this as a proxy for laboratory-confirmed diagnosis. The category encompassed all notifiable disease data for *E.coli* O157 species, salmonellosis, campylobacteriosis, and shigellosis. All physicians, laboratories and healthcare providers are required by law to report certain patient conditions to the DPH. Illnesses are required to be reported at a specific timeframe: immediately, within seven days, within one month, and within

six months. *E. coli* O157 required immediate reporting; the other three infections required reporting within seven days (c.f., appendix for a poster of reportable diseases in Georgia) (10).

Analyses

Data analyses consisted of two methods: Spearman correlations to assess the relationship between syndromic and enteric (notifiable) disease counts by season and creation of figures showing syndromic and enteric counts varied by event, county, and time. Spearman correlation was chosen as the appropriate statistical analysis measure because it is the nonparametric version of the Pearson correlation and measures the strength and direction of association between two ranked variables. Spearman correlation is used over the Pearson in this instance due to the monotonic (non-linear) relationship between the syndromic and notifiable disease counts. The Spearman correlation coefficient ranges from +1 to -1, with +1 indicating a perfect positive association, 0 indicating no association, and -1 indicating a perfect negative relationship. Spearman correlation was run using SAS edition 9.4.

Results

For each syndrome (GI, vomit, diarrhea bloody diarrhea, bloody vomit) 624 lines of data were collected over two years (2015 – 2016) (Table 1); each line of data presents the MMWR week. For the notifiable disease data, "enteric" 611 lines of data were collected for the same time period; each line of data presents the MMWR week.

The mean number of weekly counts of the GI event was 383.62, with a standard deviation of 293.08 and a max/min of 0/1455. For the vomit event, the mean number of weekly counts was 343.03, with a standard deviation of 263.28 and a max/min of 0/1280. For the diarrhea event, the mean number of weekly counts was 93.67, with a standard deviation of 72.04 and a min/max of 0/470. The mean number of weakly counts for the bloody diarrhea event was 2.63, with a standard deviation of 2.87 and a min/max of 0/24. For the bloody vomit event, the mean number of weakly counts was 11.75, with a standard deviation of 10.29 and a min/max of 0/56. Finally, the enteric (notifiable) event had a mean number of weekly counts of 7.68, with a standard deviation of 4.68 and a min/max of 1/27.

Tables 2-6 depict Spearman correlation results assessing the relationship between each syndrome event and notifiable disease event. For the GI event, there is a statistically significant association between GI syndrome counts and enteric notifiable counts in the spring months only (spearman coefficient = 0.23, p=0.0045). Additionally, there is a statistically significant association between vomit syndrome counts and enteric notifiable counts in the spring months only (spearman coefficient = 0.24, p=0.0036). For the diarrhea event, there are statistically significant associations with enteric notifiable counts during the spring months (spearman coefficient = 0.16, p=0.046) and winter months (spearman coefficient = -0.16, p=0.05). Interestingly, for both the bloody diarrhea (spearman coefficient = -0.27, p=0.0007) and bloody vomit (spearman

coefficient = -0.17, p=0.033) syndromes, there are only statistically significant associations with enteric notifiable counts during the winter months.

In Figure 1, "GI" and "enteric" counts are summed over 2015 and 2016, by MMWR week. Figure 2 compares vomit syndrome counts and enteric counts summed over two years (2015-2016) by MMWR week. Figure 3 compares diarrhea syndrome counts and enteric counts summed over two years (2015-2016) by MMWR week. Figure 4 compares bloody diarrhea syndrome counts and enteric counts summed over two years (2015-2016) by MMWR week. Figures 1-4 contain a secondary vertical axis due to differences in the ranges of syndromic and enteric counts. Figure 5 compares bloody vomit syndrome counts and enteric counts summed over two years (2015-2016) by MMWR week. Figure 5 contains one vertical axis due to the relatively similar range of syndromic and enteric counts.

Figures 6-10 depict syndromic counts by event in each of the six counties. Figure 6 shows GI syndrome counts over the two years in all six counties. There is a separate line of data to represent each county. In the figure, it is clear that Fulton county contributed the most counts of GI syndrome followed closely by Richmond, Gwinnett, and Cobb counties—who all had similar counts. For the GI syndrome, both Chatham and DeKalb counties had the lowest counts of GI syndrome. Figure 7 graphs vomit syndrome counts over the two years for all six counties and follows the same count trend as the GI syndrome. Figure 8 depicts diarrhea syndrome counts over two years for all six counties and it is clear that Fulton county had the most counts of diarrhea over the two years, followed closely by Richmond county. Gwinnett and Cobb counties, respectively, had fewer counts than Richmond county. Finally, Chatham and DeKalb counties have similar, lower counts of Diarrhea syndrome. Figure 9 graphs bloody diarrhea syndrome counts over the two years for all six counties. This graph displays different trends than the graphs

for the GI, vomit, and diarrhea syndromes. Richmond county had the most counts of bloody diarrhea with a spike of counts around MMWR week 7 in February. Fulton county has the second most counts of bloody diarrhea over 2015-2016. Chatham, Cobb, DeKalb, and Gwinnett counties have similar, low counts of bloody diarrhea over the time period. Figure 10 depicts bloody vomit syndrome counts from 2015-2016, with Fulton county having the most counts, followed by Richmond county—also displaying a sharp spike in counts around MMWR week 7. The number of counts is than followed by Cobb county, with the fewest counts from Chatham, Gwinnett, and DeKalb counties, respectively.

Discussion

There are significantly fewer counts of "bloody vomit" and "bloody diarrhea" in all six counties than other syndromes. These counts are expected because it is more likely for patients to suffer from cases of non-bloody diarrhea and vomit than similar symptoms with blood. Presence of blood in the vomit or diarrhea is a sign of a more nefarious illness and is more likely to be further investigated by healthcare workers.

We also expect there to be a larger amount of syndromic event counts due to the sensitive nature of SS. SS is designed to capture as many cases as possible to try and predict an outbreak, and therefore sacrifices specificity. Opposite to syndromic counts, we expected—and observed—fewer counts of enteric events (corresponding to notifiable conditions). This was due to the higher specificity of laboratory-confirmed diagnoses.

We hypothesize that the reason why Fulton county consistently had the largest (or second largest) number of counts for all syndromes is that Fulton county has the largest population and therefore should have a larger number of patients reporting symptoms at EDs. This is supported by the fact that Fulton county had, on average, the most facilities reporting SS. Interestingly, Richmond county consistently had at least the second most counts of data for each syndrome. Richmond county is the least populated of the six counties in this study. There could be a number of reasons why Richmond county had a large amount of counts—people who reside in neighboring counties may visit EDs in Richmond county or Richmond county could truly have more incidences of disease compared to counties with larger populations. These hypotheses should be evaluated in future studies. It is also possible that the other counties had 0 counts of illness for several weeks while Richmond county maintained a consistent number of weekly disease counts.

In Figure 1, the lines of the graph cross at a few points, but it is difficult to assess the relationship between the counts because the scale for the syndromic (GI) counts is significantly larger than the scale for the notifiable (enteric) counts. This is also true for Figures 2-3 that graph vomit and diarrhea counts versus enteric counts respectively. Both the bloody vomit and bloody diarrhea syndromes had fewer counts than the other syndromes, making it a rarer symptom recorded during patient visits to emergency departments in the counties in our study population. These syndromes versus enteric counts, (Figures 4-5), have scales more similar to the enteric count scales making it easier to assess the relationship between syndromic and enteric counts. Spearman correlations coefficients and corresponding p-values yielded interesting results. For the GI syndrome, there is a statistically significant correlation between GI syndrome counts and enteric notifiable counts during the spring months. This is expected due to a traditionally higher number of cases of enteric illnesses during the warmer months. Also as expected, there is a statistically significant correlation between vomit syndrome counts and enteric notifiable counts during spring. Interestingly, for the diarrhea syndrome, there is a statistically significant correlation between diarrhea syndrome counts and enteric notifiable counts for both the spring and winter months. This indicates that there is a closer association between syndromic and notifiable counts during the colder months from about December to May for the diarrhea syndrome. The spearman coefficient for the winter months is negative, indicating a statistically significant negative relationship between diarrhea syndrome counts and notifiable enteric counts. Both the bloody vomit and bloody diarrhea syndrome counts only indicated statistically significant associations with enteric notifiable counts during the winter months, again with a strong negative relationship. Further studies should be conducted to explore the relationship

between the ‘bloody’ syndromes and notifiable disease counts. It is likely that there is a seasonal illness that causes bloody vomit and diarrhea.

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Tables

Table 1. Description of Disease Events, State of Georgia, 2015 – 2016

Event	#	Mean	Std. Dev	Median	Min	Max
GI	624	383.62	293.08	346	0	1455
Vomit	624	343.03	263.28	318	0	1280
Diarrhea	624	93.67	72.04	88.5	0	470
Bloody Vomit	624	11.75	10.29	10	0	56
Bloody Diarrhea	624	2.63	2.87	2	0	24
Enteric*	611	7.68	4.68	7	1	27

**Event for notifiable diseases*

Table 2. Spearman Correlation for GI Syndrome and Enteric Notifiable Disease Counts, by Season, State of Georgia, 2015 – 2016

Season	#	Mean	Std. Dev	Spearman Coefficient	p-value*
Spring					
GI Syndrome Counts	156	385.20	283.44	0.23	**0.0045**
Enteric Notifiable Counts	150	6.47	3.97	--	--
Summer					
GI Syndrome Counts	156	355.02	266.09	0.15	0.063
Enteric Notifiable Counts	156	9.75	4.90	--	--
Fall					
GI Syndrome Counts	156	375.63	299.61	0.093	0.25
Enteric Notifiable Counts	155	8.43	5.06	--	--
Winter					
GI Syndrome Counts	156	418.63	319.69	-0.048	0.56
Enteric Notifiable Counts	150	5.94	3.58	--	--

**Spearman Correlation test for non-linear continuous variables*
***Bold** represents statistically significant at an alpha level of 0.05*

Table 3. Spearman Correlation for Vomit Syndrome and Enteric Notifiable Disease Counts, by Season, State of Georgia, 2015-2016

Season	#	Mean	Std. Dev	Spearman Coefficient	p-value*
Spring					
Vomit Syndrome Counts	156	345.15	256.60	0.24	**0.0036**
Enteric Notifiable Counts	150	6.47	3.97	--	--
Summer					
Vomit Syndrome Counts	156	313.42	238.84	0.15	0.061
Enteric Notifiable Counts	156	9.75	4.90	--	--
Fall					
Vomit Syndrome Counts	156	334.35	267.62	0.086	0.29
Enteric Notifiable Counts	155	8.43	5.06	--	--
Winter					
Vomit Syndrome Counts	156	379.21	289.73	-0.056	0.50
Enteric Notifiable Counts	150	5.94	3.58	--	--

**Spearman Correlation test for non-linear continuous variables*
***Bold** represents statistical significance at an alpha level of 0.05*

Table 4. Spearman Correlation for Diarrhea Syndrome and Enteric Notifiable Disease Counts, by Season, State of Georgia, 2015 – 2016

Season	#	Mean	Std. Dev	Spearman Coefficient	p-value*
Spring					
Diarrhea Syndrome Counts	156	95.58	68.18	0.16	**0.046**
Enteric Notifiable Counts	150	6.47	3.97	--	--
Summer					
Diarrhea Syndrome Counts	156	82.21	54.71	0.14	0.088
Enteric Notifiable Counts	156	9.75	4.90	--	--
Fall					
Diarrhea Syndrome Counts	156	88.34	67.24	0.063	0.43
Enteric Notifiable Counts	155	8.43	5.06	--	--
Winter					
Diarrhea Syndrome Counts	156	108.52	91.15	-0.16	**0.05**
Enteric Notifiable Counts	150	5.94	3.58	--	--

**Spearman Correlation test for non-linear continuous variables*
***Bold** represents statistical significance at an alpha level of 0.05*

Table 5. Spearman Correlation for Bloody Diarrhea Syndrome and Enteric Notifiable Disease Counts, by Season, State of Georgia, 2015 – 2016

Season	#	Mean	Std. Dev	Spearman Coefficient	p-value*
Spring					
B. Diarrhea Syndrome Counts	156	2.46	2.94	-0.029	0.73
Enteric Notifiable Counts	150	6.47	3.97	--	--
Summer					
B. Diarrhea Syndrome Counts	156	2.62	2.62	-0.014	0.87
Enteric Notifiable Counts	156	9.75	4.90	--	--
Fall					
B. Diarrhea Syndrome Counts	156	2.93	2.71	-0.047	0.56
Enteric Notifiable Counts	155	8.43	5.06	--	--
Winter					
B. Diarrhea Syndrome Counts	156	2.53	3.18	-0.27	**0.0007**
Enteric Notifiable Counts	150	5.94	3.58	--	--

**Spearman Correlation test for non-linear continuous variables*
***Bold** represents statistical significance at an alpha level of 0.05*

Table 6. Spearman Correlation for Bloody Vomit Syndrome and Enteric Notifiable Disease Counts, by Season, State of Georgia, 2015-2016

Season	#	Mean	Std. Dev	Spearman Coefficient	p-value*
Spring					
B. Vomit Syndrome Counts	156	10.83	9.28	0.095	0.25
Enteric Notifiable Counts	150	6.47	3.97	--	--
Summer					
B. Vomit Syndrome Counts	156	10.62	9.24	-0.011	0.89
Enteric Notifiable Counts	156	9.75	4.90	--	--
Fall					
B. Vomit Syndrome Counts	156	12.56	11.39	-0.017	0.83
Enteric Notifiable Counts	155	8.43	5.06	--	--
Winter					
B. Vomit Syndrome Counts	156	13	10.94	-0.17	**0.033**
Enteric Notifiable Counts	155	5.94	3.58	--	--

**Spearman Correlation test for non-linear continuous variables*
***Bold** represents statistical significance at an alpha level of 0.05*

Figures

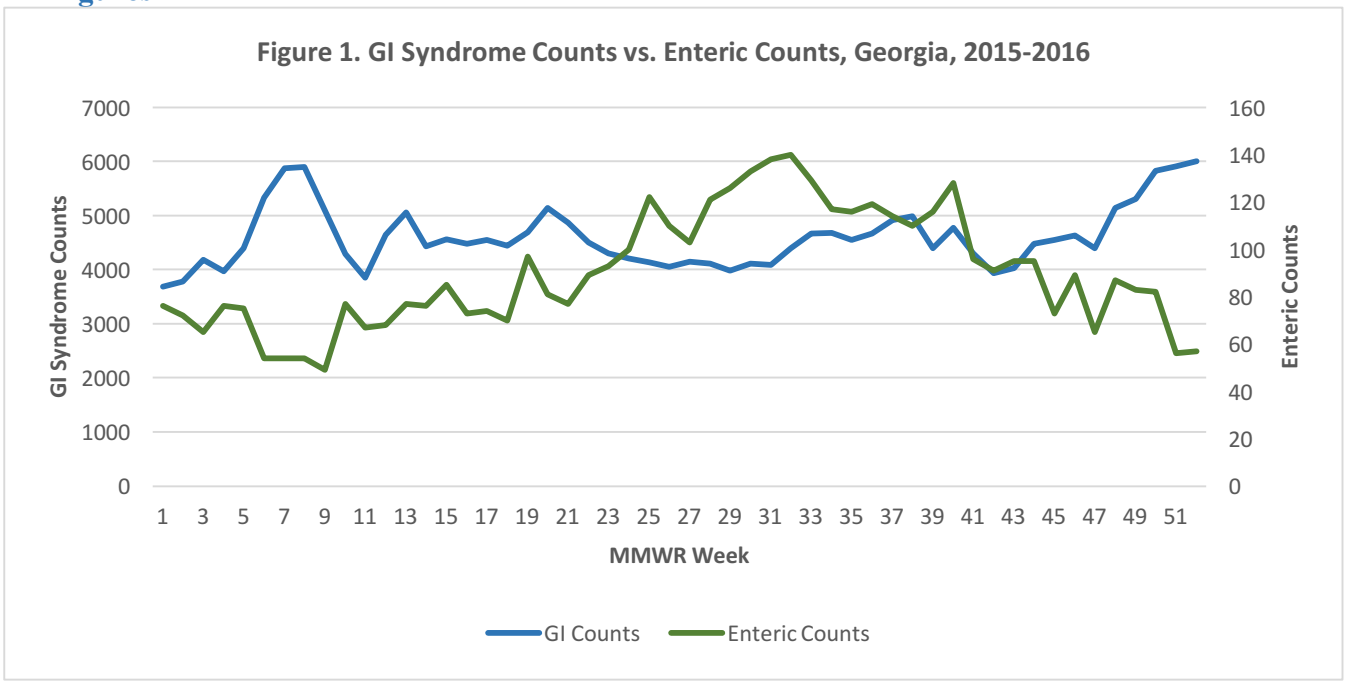


Figure 1. GI Syndrome Counts vs. Enteric Counts, Georgia, 2015-2016
GI Syndrome Counts
Enteric Counts
MMWR Week
GI Counts
Enteric Counts

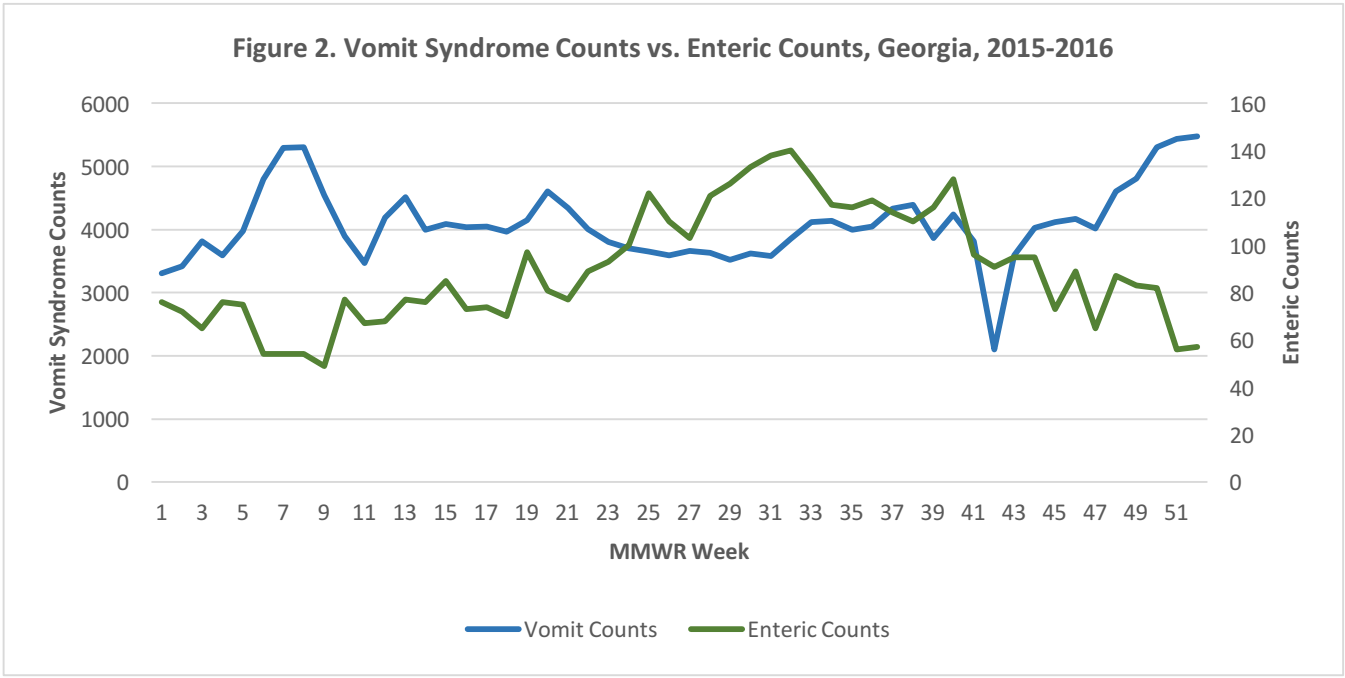


Figure 2. Vomit Syndrome Counts vs. Enteric Counts, Georgia, 2015-2016
Vomit Syndrome Counts
Enteric Counts
MMWR Week
Vomit Counts
Enteric Counts

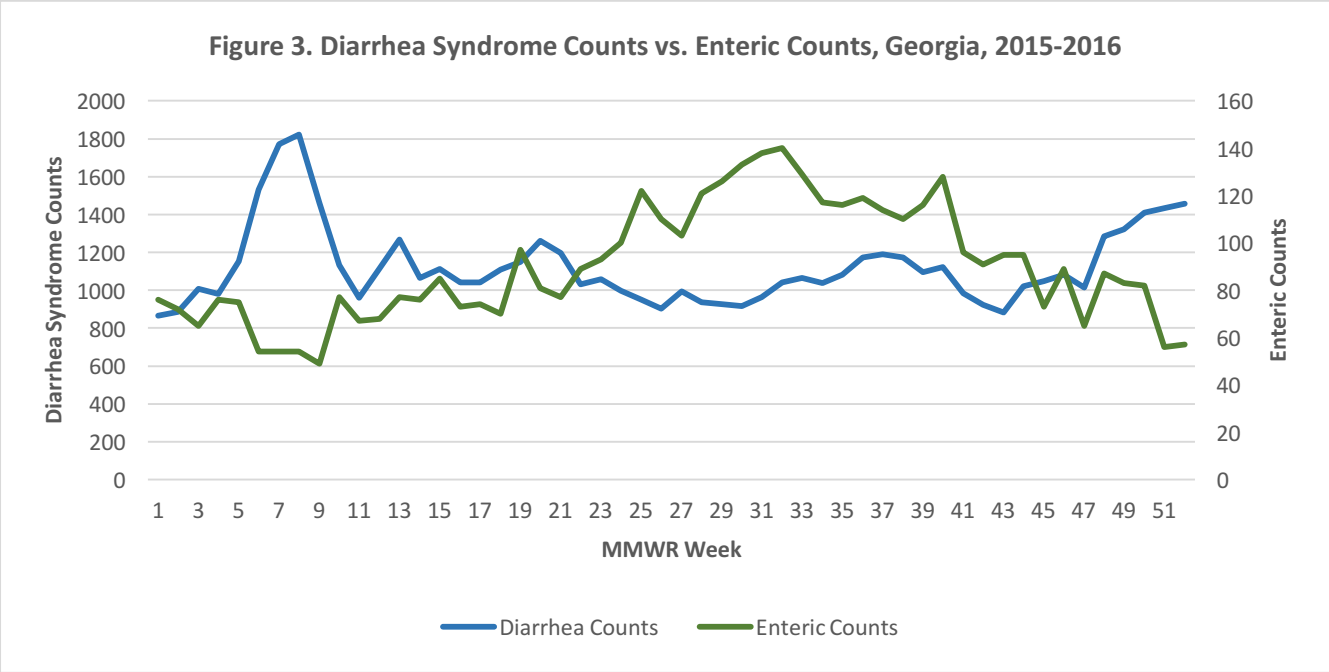


Figure 3. Diarrhea Syndrome Counts vs. Enteric Counts, Georgia, 2015-2016
Diarrhea Syndrome Counts
Enteric Counts
MMWR Week
Diarrhea Counts
Enteric Counts

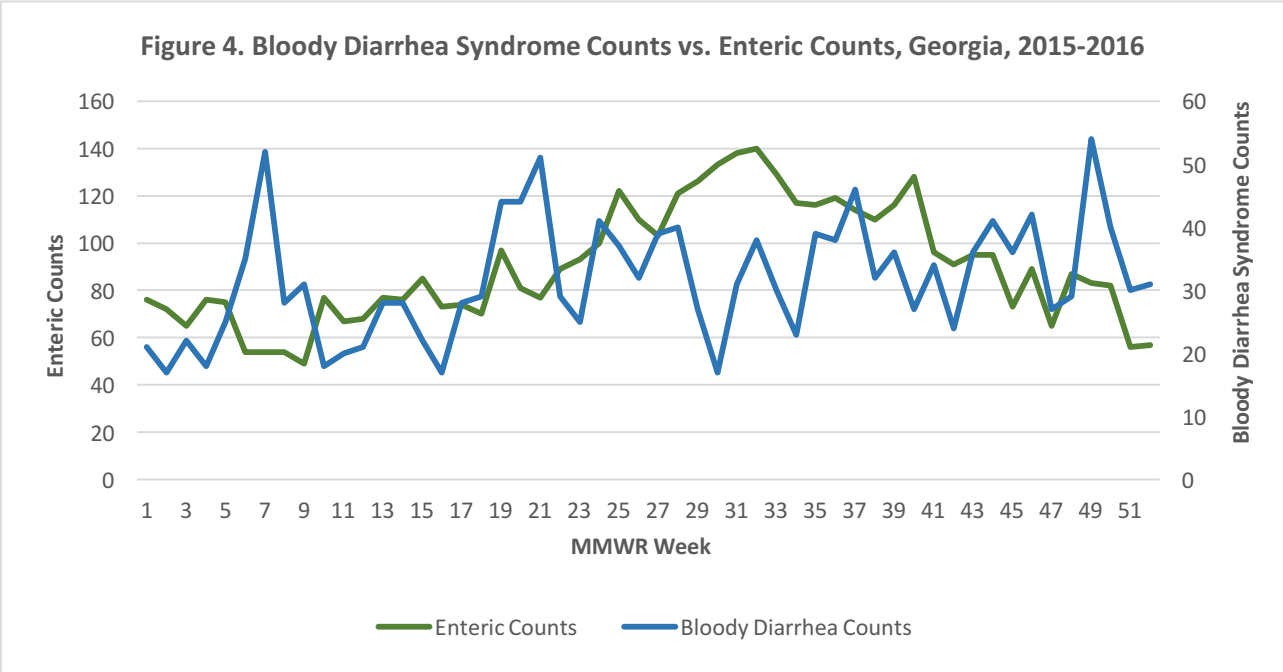


Figure 4. Bloody Diarrhea Syndrome Counts vs. Enteric Counts, Georgia, 2015-2016
Enteric Counts
Bloody Diarrhea Syndrome Counts
MMWR Week
Enteric Counts
Bloody Diarrhea Counts

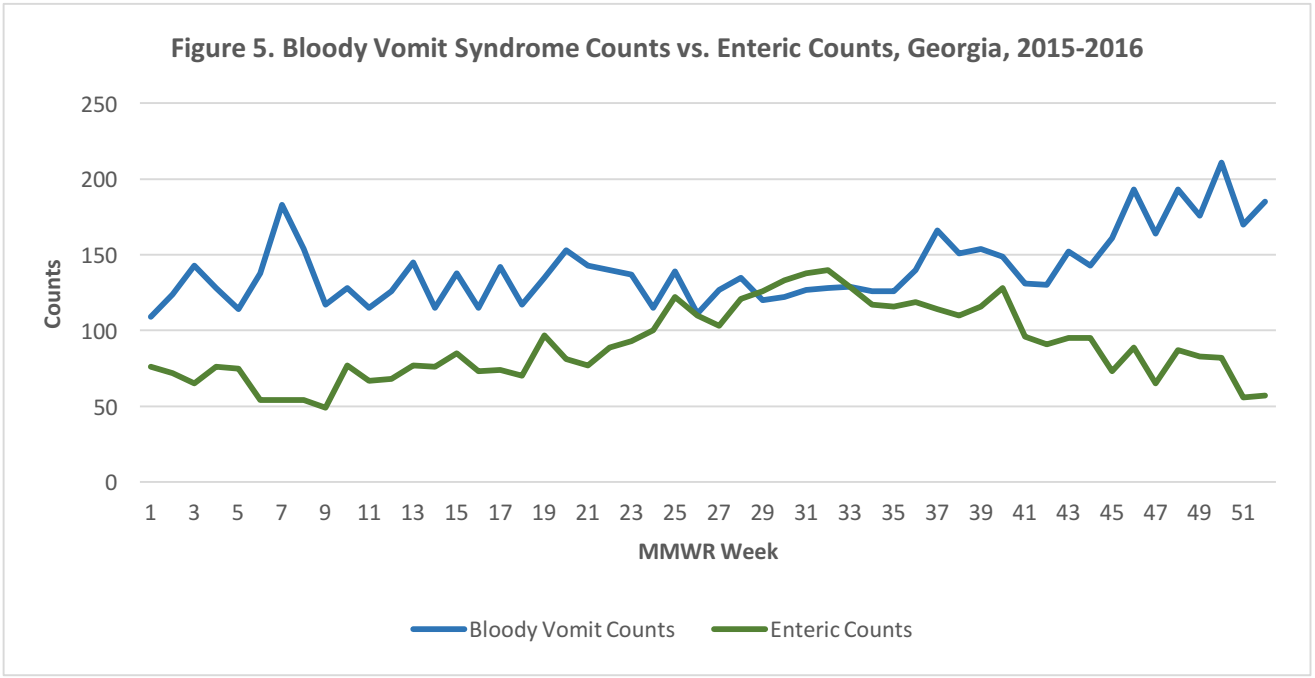


Figure 5. Bloody Vomit Syndrome Counts vs. Enteric Counts, Georgia, 2015-2016
250
200
150
100
50
0
Counts
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51
MMWR Week
Bloody Vomit Counts
Enteric Counts

Figure 6. Gastrointestinal Syndrome Counts by County, State of Georgia, 2015 – 2016

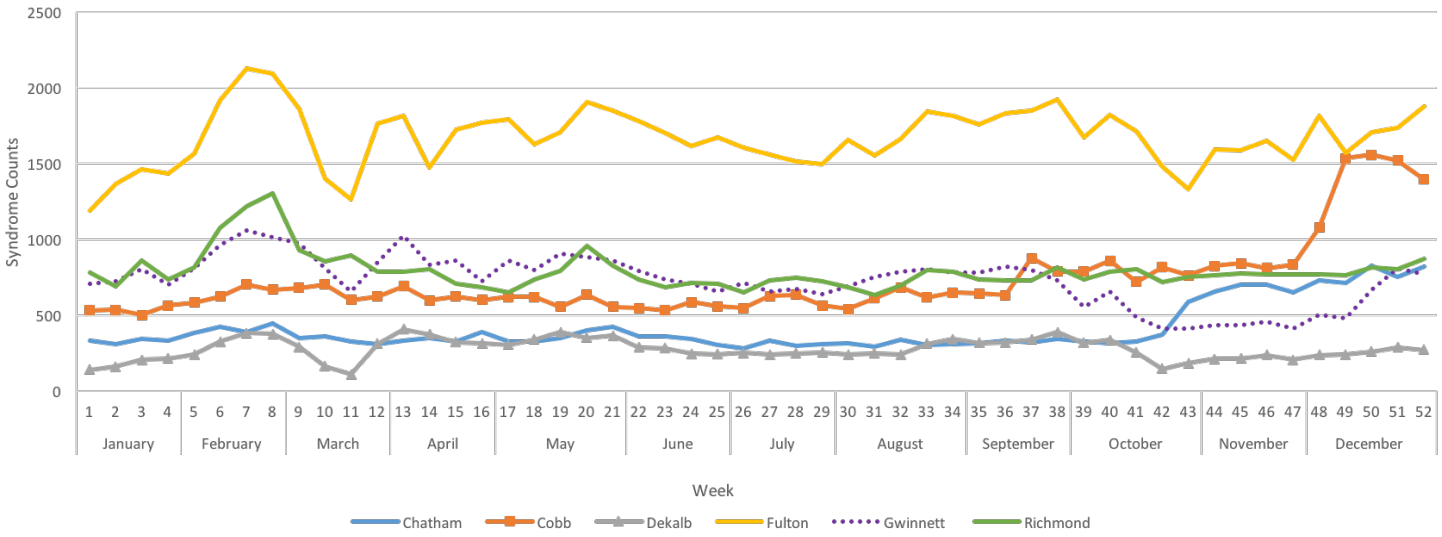


Figure 7. Vomit Syndrome Counts by County, State of Georgia, 2015 – 2016

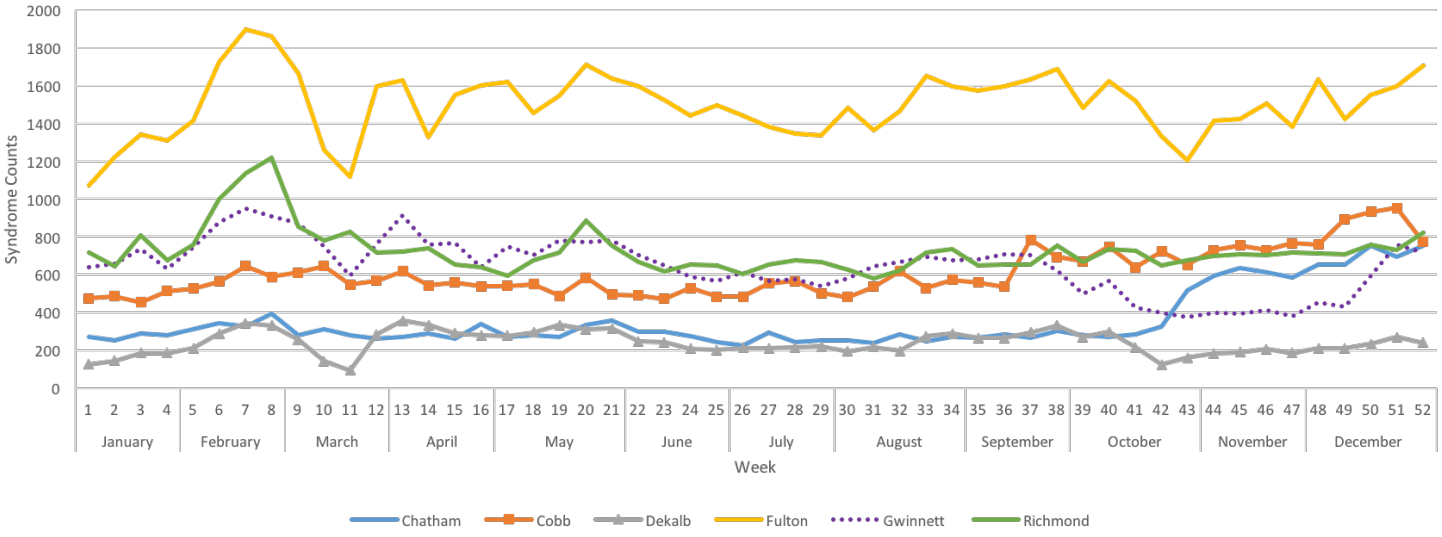


Figure 8. Diarrhea Syndrome Counts by County, State of Georgia, 2015 – 2016

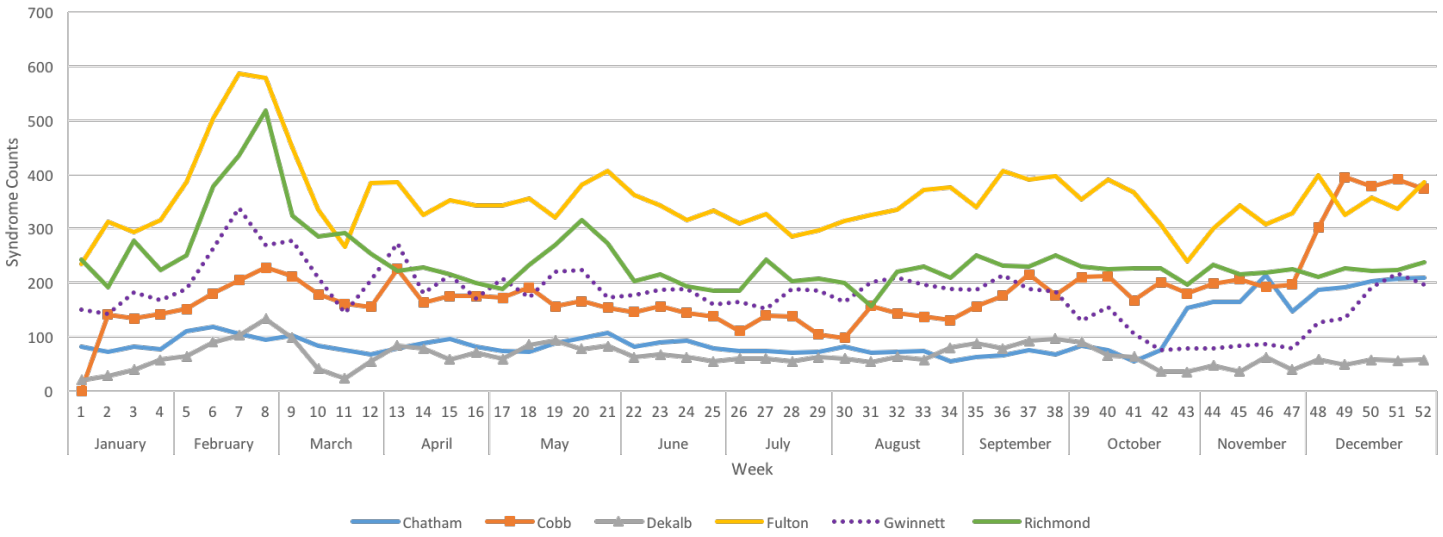


Figure 9. Bloody Diarrhea Syndrome Counts by County, State of Georgia, 2015 – 2016

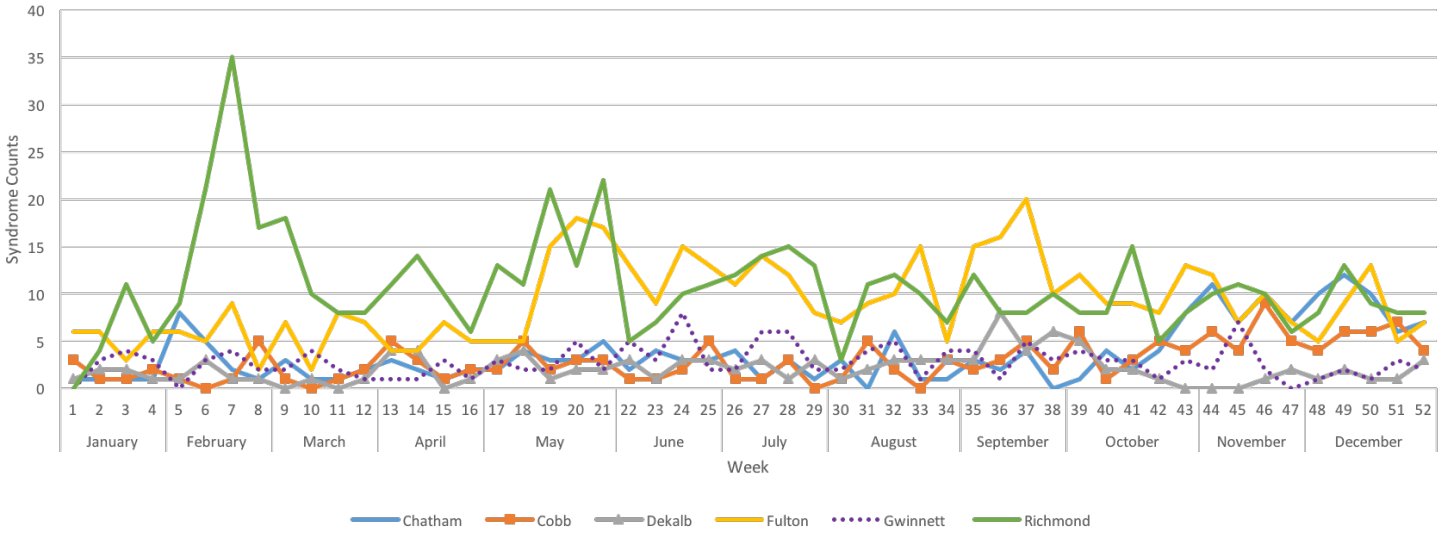
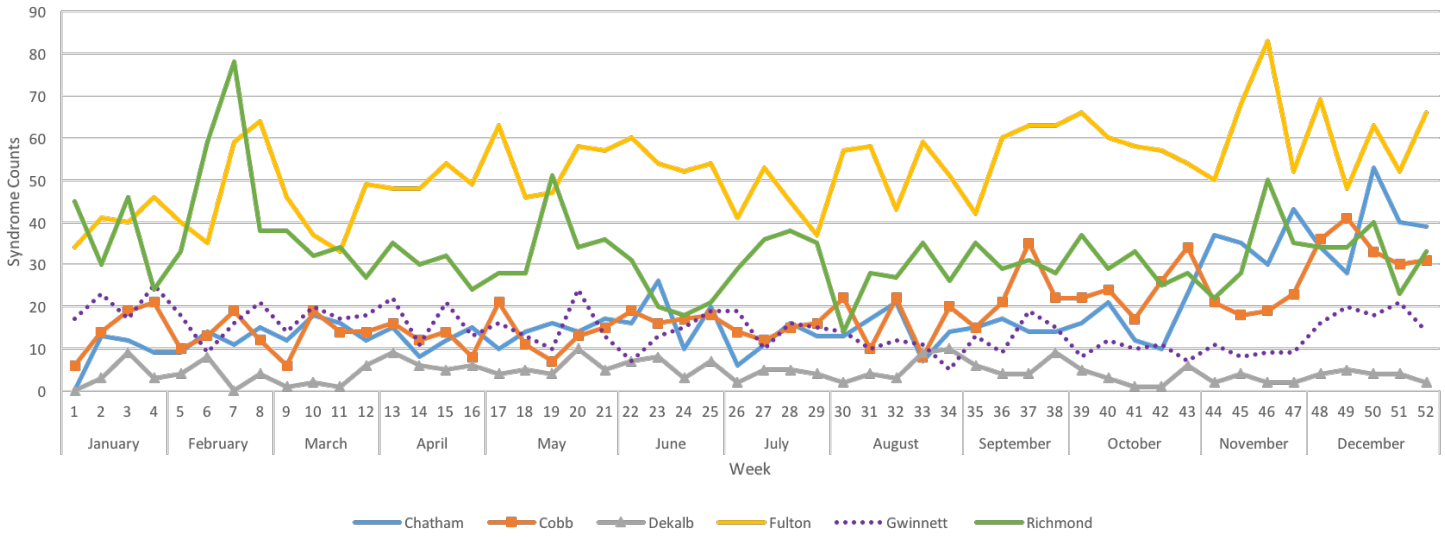


Figure 10. Bloody Vomit Syndrome Counts by County, State of Georgia, 2015 – 2016



Chapter III: Summary, Public Health Implications, Possible Future Directions

The results of these analysis showed there are interesting correlations between syndromic and notifiable disease counts for several enteric symptoms in six counties in Georgia, varying by season. Future studies should aim to identify the lag time between syndromic data flags and notifiable disease reports. This is a difficult task without linking a patient's symptom record with the laboratory-confirmed diagnosis. It would also be interesting and meaningful to explore potential causal relationships between syndromic and notifiable disease counts using this link. Further studies should be conducted to determine why bloody vomit and bloody diarrhea were only statistically significant during the winter months.

The study was limited due to the nature of the data—a more robust analysis could be conducted with demographic and descriptive variables (e.g., age, sex, history of enteric illness). It could then be possible to stratify the analysis by these demographic and descriptive variables to assess effect modification or confounding affecting the association between syndromic counts and notifiable disease counts. It would be interesting to geocode the healthcare facilities participating in SS to assess if location of the healthcare facilities is a factor in determining if people have adequate access to those healthcare facilities. For example, it is possible that patients may reside in one county, but go to a neighboring county's healthcare facility to receive care due to distance to facility or reputation of facility to give better care.

To better understand the baseline counts of syndromic data by event, future studies should increase number of years used in the study. For example, summing counts over 3-4 years instead of two years could help establish a more accurate baseline from which to observe aberrations of counts from the baseline.

Moving forward, DPH could conduct the analyses above for all syndromes to assess the competency of Georgia's SS program. DPH could find that SS is better at accurately identifying cases of certain diseases, like ILI.

Appendices

Georgia Department of Public Health

NOTIFIABLE DISEASE / CONDITION REPORTING

All Georgia physicians, laboratories, and other health care providers are required by law to report patients with the following conditions. Both lab-confirmed and clinical diagnoses are reportable within the time interval specified below.

Reporting enables appropriate public health follow-up for your patients, helps identify outbreaks, and provides a better understanding of disease trends in Georgia. For the latest information from the DPH, Department of Public Health, visit their web site at: dph.georgia.gov/

REPORT IMMEDIATELY

To Report Immediately
Call: District Health Office or
1-866-PUB-HLTH (1-866-782-4584)

- any cluster of illnesses
- animal bites
- ▶ anthrax
- all acute arboviral infections:
  - -Eastern Equine Encephalitis (EEE)
  - -LaCrosse Encephalitis (LAC)
  - -St. Louis Encephalitis (SLE)
  - -West Nile Virus (WNV)
- ▶ botulism
- ▶ brucellosis
- cholera
- diphtheria
- *E. coli O157*
- *Haemophilus influenzae (invasive)**
- hantavirus pulmonary syndrome
- hemolytic uremic syndrome (HUS)
- hepatitis A (acute)
- measles (rubeola)
- meningitis (specify agent)
- meningococcal disease
- novel influenza A virus infections
- pertussis
- ▶ plague
- poliomyelitis
- ▶ Q fever
- rabies (human & animal)
- severe acute respiratory syndrome (SARS)
- shiga toxin positive tests
- *S. aureus with vancomycin MIC ≥ 4µg/ml*
- ▶ smallpox
- syphilis (congenital & adult)
- tuberculosis
- latent TB infection in children<5 years old
- ▶ tularemia
- ▶ viral hemorrhagic fevers

▶ Potential agent of bioterrorism.

* Invasive = isolated from blood, bone, CSF, joint, pericardial, peritoneal, or pleural fluid.

REPORT WITHIN 7 DAYS

To Report Within 7 Days
Report cases electronically through the State Electronic Notifiable Disease Surveillance System at http://sendss.state.ga.us (SEE REPORTING FOOTNOTES BELOW.)

- AIDS#
- aseptic meningitis
- blood lead level (all)
- campylobacteriosis
- chancroid
- *Chlamydia trachomatis* (genital infection)
- Creutzfeldt-Jakob Disease (CJD), suspected cases, under age 55
- cryptosporidiosis
- cyclosporiasis
- ehrlichiosis
- giardiasis
- gonorrhea
- HIV infection and Perinatal HIV exposure*
- hearing impairment† (permanent, under age 5)
- hepatitis B
  - -acute hepatitis B
  - -newly identified HBsAg+ carriers**
  - -HBsAg+ pregnant women
- hepatitis C virus infection (past or present)
- influenza-associated death (all ages)
- legionellosis
- leptospirosis
- listeriosis***
- leprosy or Hansen's disease (*Mycobacterium leprae*)
- Lyme disease
- lymphogranuloma venereum
- malaria
- maternal deaths## (during pregnancy or within 1 year of end of pregnancy)##
- mumps
- Neonatal Abstinence Syndrome
- psittacosis
- Rocky Mountain spotted fever
- rubella (including congenital)
- salmonellosis
- shigellosis
- streptococcal disease, Group A or B (invasive)*
- *Streptococcus pneumoniae* (invasive)*
  - -report with antibiotic-resistance information
- tetanus
- toxic shock syndrome
- toxoplasmosis
- typhoid
- Varicella (Chickenpox)
- *Vibrio* infections
- yersiniosis

* Invasive = isolated from blood, bone, CSF, joint, pericardial, peritoneal, or pleural fluid.
** HBsAg+ = hepatitis B surface antigen positive.
*** *L. monocytogenes* isolated from blood, bone, CSF, joint, pericardial, peritoneal, or pleural fluid, or other normally sterile site; or from placenta or products of conception in conjunction with fetal death or illness. Infant mortality is reportable to Vital Records.

REPORTING HIV/AIDS:

Report forms and reporting information for HIV/AIDS available by telephone (1-800-827-9769) OR at http://dph.georgia.gov/georgias-hivaids-epidemiology-surveillance-section. For mailing HIV/AIDS reports, please use double envelopes marked "confidential", addressed to Georgia Department of Public Health Epidemiology Section, P.O. Box 2107, Atlanta, GA 30301

Report forms and reporting information for maternal deaths are available at http://dph.georgia.gov/documents/forms-surveys-and-documents

† Report forms and reporting information for **hearing impairment** available at http://dph.georgia.gov/documents/forms-surveys-and-documents

REPORT WITHIN 1 MONTH

birth defects (under age 6)

Report forms and reporting information for **birth defects** available at http://dph.georgia.gov/documents/forms-surveys-and-documents

Healthcare-associated Infections (HAIs)
For facilities required to report HAI data to CMS via NHSN. Report in accordance with the NHSN protocol. Reporting requirements and information available at http:/dph.georgia.gov/notifiable-hai-reporting.

REPORT WITHIN 6 MONTHS

benign brain and central nervous system tumors
cancer

Report forms and reporting information for **tumors and cancer** found at http://dph.georgia.gov/georgia-comprehensive-cancer-registry.

(Rev 2-1-16)