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05/03/2021

Date

An Assessment of Symptom and Risk Screening to Determine COVID-19 Testing Eligibility in
the State of Georgia, March 2020- April 2020

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Symptom and Risk Screening to Determine COVID-19 Testing Eligibility in the State of
Georgia, March 2020- April 2020

By

Katherine Topf

B.S., James Madison University, 2019

Thesis Committee Chair: Robert Bednarczyk, PhD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

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By Katherine Topf

Importance: The emergence of SARS-CoV-2 led to rapid, but limited rollout of diagnostic testing causing the CDC and states to make dynamic decisions on testing eligibility to match available test kits. Historically, symptom based screening and traveler screening have been proven ineffective for determining disease risk, but little is known about how symptom presentation impacted decisions to approve test requests and ultimate test disposition¹⁻⁴. This study will assess the use of the COVID-19 testing request form at the Georgia Department of Public Health (GDPH) during the first month of the pandemic.

Objective: Assess the symptom and risk screening tool developed by GDPH, based on CDC testing eligibility requirements, to determine testing request approval for Georgia Public Health Labs GPHL and provide recommendations for future outbreaks and pandemics.

Design: This cross-sectional study was conducted utilizing data obtained from COVID-19 testing requests received between March 5, 2020 and April 11, 2020 to reflect the first iteration of the testing request form used during the COVID-19 pandemic in the state of Georgia.

Setting: Study data was collected at healthcare facilities across Georgia.

Participants: The sample included all individuals who had COVID-19 testing requests submitted during the study time period.

Main Outcomes and Measures: The main outcomes of interest are test request approval or denial, and results of the approved tests. Both outcomes of interest were assessed relative to presenting symptom profiles.

Results: In total, there were 4828 test requests approved or denied in this time period. Among all submitted requests, 3712 (80.6%) indicated the patient exhibited coughing. Of approved test requests, 678 (14.0%) tested positive for COVID-19; key symptoms presentation differences between positive and negative tests were rhinorrhea and sore throat. Using factor analysis, we identified a subset of symptoms more likely to be associated with approved test requests and positive tests. Factors were reduced to assess parsimony and further narrow the symptom profiles most common with each outcome level.

Conclusion and Relevance: Real time data analysis should be conducted during the early phases of a pandemic. It provides valuable insight that can be used to create evidence-based recommendations to best allocate limited supplies in a pandemic setting.

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Chapter 1: Introduction

Introduction and Rationale

Beginning in December 2019, there were cases of an unknown pneumonia like illness in Wuhan, China hospitals^{5,6}. As clusters formed and transmission continued, research helped identify this previously unknown illness as being caused by a novel coronavirus, SARS-CoV-2, with the disease later known as COVID-19⁵. The first known case in the United States was reported on January 20, 2020 in Washington state⁷. In the state of Georgia, the first positive COVID-19 case was confirmed via reverse transcription polymerase chain reaction (RT-PCR or PCR) testing on March 2, 2020⁸. Following the index COVID-19 case in the state of Georgia, Governor Brian Kemp implemented a ban on large gatherings March 23, 2020, a shelter in place order on April 2, 2020, and implemented an extension of the stay at home order on May 1, 2020⁹.

During the early months of the COVID-19 pandemic, widespread testing was not made readily available and limited resources caused constraints on eligibility criteria for testing. In the state of Georgia, COVID-19 RT-PCR testing was mainly conducted at the Georgia Public Health Labs (GPHL). Limited quantities of COVID-19 test kits were provided to GPHL and during this time commercial labs were not capable of conducting the test. Due to the limitations in testing kit availability and ability to run the RT-PCRs, a testing request procedure and protocol had to be created to best manage the limited supplies GPHL was allocated. In efforts to manage testing request influx, an online testing request form was created within the Georgia State Electronic Notifiable Disease Surveillance System (SendSS). Testing request forms can be completed by medical professionals or those in healthcare settings. The form is divided into the following sections: clinician information, general information, clinical information, possible risk factors,

and lab specimen information. There are no required fields to complete this form so it can be fully completed or have minimal information. Testing approval guidance was created by the state epidemiologists at Georgia Department of Public Health (DPH). To best reflect the everchanging nature of COVID-19, a triage guidance flowchart was created based on the most up to date guidance provided by both the CDC and DPH. The flowchart was then used by both state epidemiologists and epidemiology assistants to determine if an individual was able to be approved for COVID-19 testing through GPL. Main themes within the flowchart included hospitalization status, other diagnostic tests, healthcare worker status, etc.

Upon identification of the SARS-CoV-2, the need for a diagnostic test was imminent. Early case definitions and symptom profiles showed similar characteristics to other, more common, respiratory diseases making it difficult to differentiate a COVID-19 case from those other diseases. Historical models of respiratory diseases show downfalls in symptom-based screening for seasonal diseases and early data showed the same for COVID-19. The state of Georgia utilized a symptom-based screening mechanism for testing approval, which could have impacted the overall number of cases identified in the early stages of the pandemic.

Problem Statement

The COVID-19 pandemic has provided valuable insight into the early stages of pandemics to better identify processes and procedures that can be utilized for managing disease testing request forms when resources are limited by increasing overall knowledge of providers about the purpose and importance of data quality.

Purpose Statement

The purpose of this thesis is to assess the symptom and risk-based screening testing request approval form used by GPHL and DPH during March 2020-April 2020 to provide recommendations for managing limited resources in a pandemic setting.

Research Question

How can COVID-19 testing request data between March 2020-April 2020 be used to improve testing request form data collection and testing allocation in future pandemics?

Significance Statement

The importance of pandemic preparedness has become increasingly more relevant since the onset of the COVID-19 pandemic. During pandemic situations, testing for the specific disease often need to be developed or have limited quantities early on. This thesis assesses early testing request data from March 2020- April 2020 which was an everchanging and dynamic time for the public health world. Addressing strengths and weaknesses of this time can be used to better inform health department practices during future outbreaks.

Definition of Terms

Symptom profile: the physical manifestation of SARS-CoV-2 that is wither self-reported by the patient to medical providers or identified by a medical provider

Chapter 2: Literature Review

Symptom Profile

In this paper, symptom profile will be defined as the physical manifestation of SARS-CoV-2 that is either self-reported by the patient to medical providers or identified by a medical provider. Cases can fall on a spectrum ranging from asymptomatic to severe pneumonia or death⁵. Some of the most common symptoms of COVID-19 infection include fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of smell or taste, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea^{7,10-13}. COVID-19 has a difficult symptom profile to navigate. Some of the main initial symptoms include fever, cough, headache, and muscle pain or fatigue^{14,15}. While many of the symptoms can be observed without diagnostic testing or lab work, a CT scan or chest x-ray may be ordered to observe the impact of symptoms for those with more severe cases¹⁶. For example, ground-glass opacities can be viewed in the lungs¹⁶. With the uncertainty surrounding the disease during the early stages of the pandemic, symptoms were some of the primary characteristics used to identify if testing is warranted.

Surveillance

Public health surveillance can be defined as “the ongoing, systematic collection, analysis, and interpretation of health-related data essential to planning, implementation, and evaluation of public health practice”¹⁷. There are many different forms of surveillance and the selected type is dependent on the need for the surveillance system. Some examples include active surveillance, passive surveillance, syndromic surveillance, laboratory based surveillance, and more¹⁸. Active surveillance can be defined as a form of surveillance that requires actively searching for cases of disease by contacting healthcare providers, laboratories, schools, etc.¹⁹. Actively searching for

cases can be beneficial but two main considerations when choosing this method include overall cost and the human resources that are required to achieve this form of surveillance. Passive surveillance involves healthcare providers or laboratories reporting cases of diseases to states or local officials¹⁹. This style of surveillance allows a wide range of locations to be assessed on an ongoing basis but leaves room for incomplete information or underreporting. Syndromic surveillance can be used to assess information that is already being collected, such as symptoms, that could signal a potential outbreak or increased levels of cases of a specific disease²⁰. It is thought that syndromic surveillance can be used to predict clustering of cases in an outbreak situation or potentially identify a new outbreak or pandemic²¹⁻²⁴. Laboratory-based surveillance collections information based on the bacteria that were collected from specimens of people who were sick²⁵. Some surveillance types can be beneficial in certain situations, but all are beneficial to assesses the disease presence in areas. For COVID-19, each of these have been used and shown to be beneficial but there are improvements that need to be made in both.

Disease Screening

Traveler screening and symptom-based screening were two of the main methods used to determine if an individual should be tested for COVID-19. Historically, international air travel has increased the overall spread of pathogens including the 2003 SARS, 2009 H1N1, imported cases of H7N9, 2013 MERS-CoV, and Ebola^{1-4,26}. One major challenge faced with consideration to traveler screening and COVID-19 included the possibility of cases to be missed if individuals are asymptomatic or in the incubation period^{14,26,27}. This makes it exceedingly more difficult to use both travel based or symptom based measures and early mathematical modeling of COVID-19 showed that less than half of infected travelers will be detected²⁶. One early method of detection for traveler screening included the use of thermal temperature screenings since fever

was one of the earliest detectable symptoms^{14,28,29}. A specific example of this includes a group of 126 German nationals traveling from the Hubei Province, China to Frankfurt, Germany on February 1, 2020. Upon arrival in Germany, individuals underwent a symptom based screening evaluation where 115 patients passed the screening and were tested using an RT-PCR³⁰. Despite passing the symptom based screening, two patients, or 1.8%, tested positive indicating a flaw in the symptom based screening system³⁰. Another study assessed performance models of two respiratory viruses, Influenza Type A and Respiratory Syncytial Virus, with consideration to common symptoms including coughing, wheezing, and rhinorrhea, to predict the likelihood of an individual having COVID-19³¹. These findings indicate a potential problems or limitations in symptom-based screening strategies when determining testing eligibility for COVID-19.

Gaps in Literature

COVID-19 has truly been an unprecedented time with many unknowns. From March 2020 - April 2021 when this data set was created, COVID-19 was still new to not only the world but just beginning to spread across the United States. There was so much literature and information provided it was nearly impossible to sort through it all and stay as up to date as possible. With all of the literature that was being released, guidance was constantly changed to stay up to date and new recommendations were being made. This study is one of the few, or even first, of its kind to assess this type of data set to identify differences in testing outcomes to provide future recommendations so there was limited literature available directly related to this topic.

Chapter 3: Manuscript

Contribution of Student

Katherine Topf cleaned the data set, wrote the manuscript, conducted the analysis, and created the tables and figured. She intends on submitting this manuscript to the Journal of the American Medical Association. Submission is contingent on approval from the Georgia Department of Public Health.

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Abstract

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Methods

Study Design and Sample

This cross-sectional study was conducted utilizing data obtained from COVID-19 testing requests received between March 5, 2020 and April 11, 2020 to reflect the first iteration of the testing request form used during the COVID-19 pandemic in the state of Georgia. All completed test request forms through SendSS during the specified time frame were used in this analysis (N=4828). The test request form included submitter information, patient information, symptoms, hospitalization information, travel history, potential exposure history, and other diagnostic tests that were run. Test request forms were reviewed by Georgia Department of Public Health (GPHL) epidemiologists and GPHL epidemiology assistants. Each test request form was reviewed with consideration to a triage guidance flowchart to determine if the request should be approved or denied for testing. With limited testing capabilities, the triage guidance flowchart was updated to correspond with the most recent CDC COVID-19 updates which often occurred

multiple times per week. Major themes in the flowchart included hospitalization status, healthcare worker status, severity of illness, etc. The triage flowchart was an internally created document by DPH epidemiologists and was not used outside of this setting.

Data and Outcome

The dataset used for this analysis was exported from SendSS. All PUI testing requests (N=4828) were either approved or not approved for testing. To further classify beyond approved or not approved, PUIs were manually searched in the master search function of SendSS, which allows access to all COVID-19 related records for a case, including electric lab records. They were given the following outcome classifications: (1) not approved for testing coded as not approved, (2) approved for testing and testing negative coded as approved negative, (3) approved for testing and tested positive coded as approved positive, and (4) other to indicate all cases that did not fall into prior categories. Some examples of the other classification include the specimen was not received for testing, it was a duplicate testing request, or the specimen came back with an inconclusive RT-PCR result. Information was deidentified by removing PUI number, name, and date of birth after being classified in the four outcome levels. Dates were excluded from analysis due to lack of relevance to outcome of interest. Other variables not assessed included free text fields, type of specimen collected, and other diagnostic testing information. Death was removed as a variable due to the sensitive nature of that topic and lack of information confirming if COVID-19 was primary cause of death. In addition, data that included less than five observations were removed due to DPH data use protocol.

Statistical Analyses

Univariate Analysis

Basic descriptive were run to identify the frequency and percent of each question on the GPHL testing request form without differentiation between if the test was approved or not approved. The total number of missing values was included for each row. The approved category was further broken down into approved and tested positive and approved tested negative to represent the outcome of the COVID-19 test. Basic descriptive statistics of counts and percents were also run on this classification. Using these classifications of outcome, a chi-square test was then conducted on to determine the potential association between each question on the GPHL testing request form and the corresponding outcome for each request.

Exploratory Factor Analysis

Testing request form items were grouped into five main categories including: (1) symptoms, (2) hospitalization, (3) chronic or preexisting conditions, (4) travel and exposure history, and (5) diagnostic testing. The main category utilized for the exploratory factor analysis was the symptom category to serve as a proof-of-concept analysis to narrow in on symptom-based testing protocols. The twelve symptoms included in this analysis were fever (> 100.4), subjective fever (felt feverish), muscle aches (myalgia), runny nose (rhinorrhea), sore throat cough (new onset or worsening), shortness of breath (dyspnea), nausea or vomiting, headache, abdominal pain, and diarrhea (≥ 3 loose stool). An individual factor analysis was run using the symptom categories for the not approved, approved negative, and approved positive outcome variables. The number of symptoms retained were dependent on the results at each level of the factor.

Correlation Analysis

A correlation analysis was conducted on designated symptoms retained from the factor analysis. A correlation was conducted on each factor grouping within all three outcome levels. The standardized Cronbach Alpha was noted for each factor. The correlation was rerun with the least correlated variable to assess the impact of removing one variable on the overall standardized Cronbach Alpha.

Ethical Review

Institutional Review Board (IRB) approval was not required for completion of this thesis through Emory or DPH. IRB will be contacted prior to publication submission to obtain the necessary approvals.

Results

Univariate Analysis

Demographic data was not assessed in these analyses. Table 1 indicates the frequencies of each answer for all testing requests and total number of missing responses for each question on the testing request form. Frequencies of each outcome level based on testing request question can be viewed in Table 2. The four observed levels of outcomes for testing requests processed included approved positive, approved negative, not approved, and other. In total, there were 2563 (53%) of testing requests approved, 1271 (26.3%) were not approved, and 994 (20.6%) that could be classified as other (Table 3). Corresponding chi-square and p-values relating to outcome are show in Table 4.

Table 1. Frequencies of each question on GPHL Testing Request Form [n(%)]				
	Yes	No	Unknown	Total Missing
Symptoms Present	4407 (93.8%)	239 (5.1%)	53 (1.13%)	129
Fever	2278 (49.9%)	1940 (42.5%)	351 (7.7%)	259
Subjective Fever	2739 (62.1%)	1352 (30.6%)	321 (7.3%)	416
Myalgia	2047 (46.5%)	1879 (42.7%)	479 (10.9%)	423
Rhinorrhea	1385 (32.0%)	2445 (56.5%)	499 (11.5%)	499
Sore Throat	1443 (33.37%)	2382 (55.1%)	499 (11.5%)	504
Cough	3712 (80.6%)	733 (15.9%)	159 (3.5%)	224
Shortness of Breath	3047 (67.1%)	1345 (26.6%)	148 (3.3%)	288
Nausea or Vomiting	849 (19.6%)	3067 (70.8%)	418 (9.6%)	494
Headache	1251 (29.0%)	2539 (58.9%)	523 (12.1%)	515
Abdominal Pain	482 (11.2%)	3286 (76.6%)	522 (12.17%)	538
Diarrhea	626 (14.6%)	3141 (73.3%)	518 (12.1%)	543
Pneumonia	1594 (37.2%)	2295 (53.6%)	397 (9.3%)	542
ARD	495 (12.08%)	3238 (79.0%)	364 (8.9%)	731
Abnormal Chest X-Ray	1814 (42.6%)	2036 (47.8%)	407 (9.6%)	571
Another Diagnosis	586 (14.8%)	2815 (71.1%)	561 (14.2%)	866
Hospitalized	2413 (54.0%)	2059 (46.0%)	-----	356
ICU	617 (17.5%)	2919 (82.6%)	-----	1292
Mechanical Ventilation	326 (9.4%)	3126 (90.6%)	-----	1376
Chronic Lung Disease	1239 (28.8%)	2839 (65.9%)	226 (5.3%)	524
Diabetes Mellitus	1107 (25.6%)	3032 (70.2%)	181 (4.2%)	508
Cardiovascular Disease	1423 (33.0%)	2694 (62.5%)	195 (4.5%)	516
Chronic Renal Disease	542 (12.8%)	3453 (81.6%)	236 (5.6%)	597
Chronic Liver Disease	118 (2.8%)	3796 (90.8%)	266 (6.4%)	648
Immunocompromised	621 (14.7%)	3303 (78.1%)	308 (7.3%)	596
Neurologic Condition	330 (7.9%)	3574 (85.7%)	265 (6.4%)	659
Currently Pregnant	38 (0.9%)	3904 (94.5%)	188 (4.6%)	698
Current Smoker	600 (14.4%)	3135 (75.1%)	440 (10.5%)	653
Former Smoker	678 (17.5%)	2623 (67.83%)	566 (14.5%)	961
US Healthcare Worker	668 (15.8%)	3382 (80.0%)	177 (4.2%)	601
Travel to Mainland China	10 (0.2%)	4200 (96.2%)	157 (3.6%)	461
Travel to Outside of US	163 (3.7%)	3991 (91.6%)	201 (4.6%)	473
Household Contact	131 (2.8%)	3643 (83.7%)	588 (13.5%)	476
Community Contact	476 (10.9%)	2785 (63.6%)	1121 (25.6%)	446
Cluster Exposure	340 (7.8%)	2953 (68.0%)	1047 (24.1%)	488
Healthcare Worker in China	172 (4.0%)	3866 (89.0%)	306 (7.0%)	484
Animal Exposure	68 (1.6%)	3602 (83.8%)	630 (14.6%)	528
Healthcare Contact	273 (6.9%)	2551 (64.8%)	1110 (28.2%)	894

Table 2. Frequencies of outcomes reported on GPLH Testing Request Form.

	Approved Positive			Approved Negative			Not Approved			Other		
	Yes	No	Unk	Yes	No	Unk	Yes	No	Unk	Yes	No	Unk
Symptoms	633 96.4%	20 3.0%	4 0.6%	1716 93.4%	99 5.4%	22 1.2%	1150 92.8%	73 5.9%	16 1.3%	908 94.0%	47 4.9%	11 1.1%
Fever	449 70.9%	141 22.3%	43 6.8%	791 43.8%	870 48.2%	144 8.0%	555 46.4%	546 45.6%	96 8.0%	483 51.7%	383 41.0%	68 7.3%
Subjective Fever	417 70.2%	137 23.1%	40 6.7%	989 56.8%	582 33.5%	169 9.7%	746 64.1%	365 31.4%	53 4.6%	587 64.2%	268 29.3%	59 6.5%
Myalgia	329 54.6%	207 34.3%	67 11.1%	662 38.4%	833 48.4%	228 13.2%	606 51.8%	485 41.5%	79 6.8%	450 49.5%	354 38.9%	105 11.6%
Rhinorrhea	141 24.5%	357 62.0%	78 13.5%	395 23.2%	1058 62.2%	248 14.6%	548 47.0%	541 46.4%	77 6.6%	301 34.0%	489 55.2%	96 10.8%
Sore Throat	138 3.2%	360 62.6%	77 13.4%	427 25.2%	1014 59.8%	254 15.0%	550 47.3%	544 46.7%	70 6.0%	328 36.9%	464 52.1%	98 11.0%
Cough	540 84.8%	80 12.6%	17 2.7%	1413 78.3%	307 17.0%	84 4.7%	1006 82.9%	186 15.3%	22 1.8%	753 79.4%	160 16.9%	36 3.8%
Shortness of Breath	457 74.0%	144 23.3%	17 2.8%	1328 73.8%	409 22.7%	62 3.5%	604 51.1%	537 45.5%	40 3.4%	658 69.9%	255 27.1%	29 3.1%
Nausea or Vomiting	115 19.7%	398 68.3%	70 12.0%	338 19.9%	1165 68.3%	197 12.0%	199 17.2%	897 77.5%	62 5.4%	197 22.1%	607 68.0%	89 10.0%
Headache	140 24.3%	357 62.0%	79 13.7%	359 21.2%	1068 63.1%	266 15.7%	465 40.2%	614 53.1%	78 40.2%	287 32.4%	500 56.4%	100 11.3%
Abdominal Pain	69 12.0%	418 72.8%	87 15.2%	186 11.0%	1263 74.7%	241 14.3%	123 10.7%	944 82.4%	79 6.9%	104 11.8%	661 75.1%	115 13.1%
Diarrhea	106 18.3%	402 69.3%	72 12.4%	196 11.8%	1212 72.7%	260 15.6%	173 15.0%	904 78.4%	76 6.6%	151 17.1%	623 70.5%	110 12.4%
Pneumonia	365 61.6%	185 31.2%	43 7.3%	794 48.2%	719 43.7%	133 8.1%	90 7.8%	899 78.2%	160 13.9%	345 38.4%	492 54.8%	61 6.8%
ARD	90 16.5%	411 75.3%	45 8.2%	280 17.8%	1164 74.1%	128 8.1%	23 2.0%	976 85.7%	140 12.3%	102 12.1%	687 81.8%	51 6.1%
Abnormal Chest X-Ray	383 65.6%	168 28.8%	33 5.7%	940 57.3%	584 35.6%	117 7.1%	111 9.7%	833 72.7%	202 17.6%	380 42.9%	451 50.9%	55 6.2%
Another Diagnosis	67 12.9%	386 74.2%	67 12.9%	256 16.7%	1053 68.8%	221 14.4%	143 12.9%	788 71.0%	179 16.1%	120 15.0%	588 73.3%	94 11.7%
Hospitalized	455 73.3%	166 26.7%	_____	1321 76.1%	414 23.9%	_____	134 11.3%	1052 88.7%	_____	503 54.1%	427 45.9%	_____
ICU	102 19.6%	418 80.4%	_____	339 22.7%	1156 77.3%	_____	21 2.6%	770 97.4%	_____	155 21.2%	575 78.8%	_____
Mechanical Ventilation	48 9.5%	457 90.5%	_____	187 12.8%	1278 87.2%	_____	10 1.3%	767 98.7%	_____	81 11.5%	624 88.5%	_____
Chronic Lung Disease	128 22.2%	417 72.2%	33 5.7%	625 37.2%	943 56.2%	111 6.6%	227 19.5%	901 77.3%	38 3.3%	259 29.4%	578 65.6%	44 5.0%
Diabetes Mellitus	227 39.1%	336 57.8%	18 3.1%	508 30.3%	1076 64.2%	92 5.5%	163 13.9%	981 83.6%	30 2.6%	209 23.5%	639 71.9%	41 4.6%
Cardiovascular Disease	234 40.0%	325 55.6%	26 4.4%	727 43.3%	866 51.6%	86 5.1%	195 16.7%	935 80.0%	39 3.3%	267 30.4%	568 64.6%	44 5.0%
Chronic Renal Disease	101 17.7%	437 76.7%	32 5.6%	284 17.4%	1247 76.2%	106 6.5%	54 4.7%	1057 91.7%	42 3.6%	103 11.8%	712 81.8%	56 6.4%
Chronic Liver Disease	7 1.3%	517 92.7%	34 6.1%	67 4.1%	1421 87.7%	133 8.2%	19 1.7%	1088 94.6%	43 3.7%	25 2.9%	770 90.5%	56 6.6%
Immunocomp- romised	83 14.6%	439 77.3%	46 8.1%	308 18.8%	1191 72.6%	141 8.6%	99 8.6%	1000 87.0%	51 4.4%	131 15.0%	673 77.0%	70 8.0%

Neurological Condition	50 9.0%	466 84.1%	38 6.9%	167 10.3%	1323 81.8%	127 7.9%	41 3.6%	1059 92.7%	43 3.8%	72 8.4%	726 84.9%	57 6.7%
Pregnant	1 0.2%	525 94.3%	31 5.6%	13 0.8%	1490 93.8%	85 5.6%	11 1.0%	1085 95.8%	37 3.3%	13 1.5%	804 94.4%	35 4.1%
Current Smoker	33 5.9%	448 80.1%	78 14.0%	281 17.4%	1126 69.8%	207 12.8%	157 13.7%	919 80.1%	72 6.3%	129 15.1%	642 75.2%	83 9.7%
Former Smoker	81 15.5%	359 68.6%	83 15.9%	313 21.5%	883 60.5%	263 18.0%	145 13.4%	839 77.8%	95 8.8%	139 17.3%	542 67.3%	125 15.5%
US Healthcare Worker	85 14.5%	481 81.8%	22 3.7%	280 16.9%	1301 78.5%	76 4.6%	78 7.1%	984 89.1%	42 3.8%	225 25.6%	616 70.2%	37 4.2%
Travel to Mainland China	2 0.3%	568 95.6%	24 4.0%	1 0.1%	1610 95.2%	80 4.7%	7 0.6%	1165 98.2%	14 1.2%	0 0.0%	857 95.6%	39 4.4%
Travel Outside US	9 1.5%	547 92.7%	34 5.8%	35 2.1%	1559 92.3%	95 5.6%	102 8.6%	1055 89.3%	25 2.1%	17 1.9%	830 92.8%	47 5.3%
Household Contact	32 5.4%	462 77.9%	99 16.7%	25 1.5%	1402 83.1%	261 15.5%	35 3.0%	1049 88.7%	99 8.4%	29 3.3%	730 82.2%	129 14.5%
Community Contact	91 15.2%	324 54.1%	184 30.7%	128 7.5%	1119 65.9%	450 26.5%	127 10.7%	818 69.0%	241 20.3%	130 14.4%	524 58.2%	246 27.3%
Cluster Exposure	59 10.0%	370 62.8%	160 27.2%	94 5.6%	1128 67.1%	460 24.4%	67 5.7%	899 76.1%	216 18.3%	120 13.5%	556 62.7%	211 23.8%
Healthcare worker in China	28 4.8%	514 87.6%	45 7.7%	73 4.3%	1480 87.6%	133 7.9%	20 1.7%	1103 93.2%	60 5.1%	51 5.7%	769 86.6%	68 7.7%
Animal Exposure	8 1.4%	473 81.8%	97 16.8%	18 1.1%	1387 83.3%	261 15.7%	26 2.2%	1031 87.5%	122 10.4%	16 1.8%	711 81.1%	150 17.1%
Healthcare Contact	41 7.5%	322 59.2%	181 33.3%	121 7.9%	927 60.2%	491 31.9%	32 3.1%	786 76.2%	213 20.7%	79 9.6%	516 62.9%	225 27.4%

Outcome	Frequency
Approved Positive	678 (14.0%)
Approved Negative	1885 (39.0%)
Not Approved	1271 (26.3%)
Other	994 (20.6%)

Table 4. Chi-Square Analysis				
	Chi-Square	P-Value	DF	Sample Size
Symptoms Present?	9.95	0.13	6	4699
Fever	152.39	<0.0001	6	4569
Subjective Fever	58.91	<0.0001	6	4412
Myalgia	95.18	<0.0001	6	4405
Rhinorrhea	209.06	<0.0001	6	4329
Sore Throat	198.65	<0.0001	6	4324
Cough	28.66	<0.0001	6	4604
Shortness of Breath	202.45	<0.0001	6	4540
Nausea	48.55	<0.0001	6	4334
Headache	154.19	<0.0001	6	4313
Abdominal Pain	45.08	<0.0001	6	4290
Diarrhea	70.76	<0.0001	6	4285
Pneumonia	669.59	<0.0001	6	4286
ARD	183.63	<0.0001	6	4097
Abdominal Chest X-Ray	800.25	<0.0001	6	4257
Another Diagnosis	17.40	0.0079	6	3962
Hospitalized	1305.6	<0.0001	3	4472
ICU	157.49	<0.0001	3	3536
Mechanical Ventilation	82.79	<0.0001	3	3452
Chronic Lung Disease	151.15	<0.0001	6	4304
Diabetes	187.80	<0.0001	6	4320
CVD	258.66	<0.0001	6	4312
Renal Disease	130.33	<0.0001	6	4231
Chronic Liver Disease	45.37	<0.0001	6	4180
Immunocompromised	83.65	<0.0001	6	4232
Neurological Condition	67.75	<0.0001	6	4169
Pregnant	15.18	0.02	6	4130
Current Smoker	85.30	<0.0001	6	4175
Former Smoker	89.14	<0.0001	6	3867
US Healthcare Worker	133.00	<0.0001	6	4227
Travel to Mainland China	39.03	<0.0001	6	4367
Travel Outside US	127.10	<0.0001	6	4355
Household Contact	64.96	<0.0001	6	4352
Community Contact	78.3	<0.0001	6	4382
Cluster Exposure	102.02	<0.0001	6	4340
Healthcare Worker in China	36.49	<0.0001	6	4344
Animal Exposure	30.46	<0.0001	6	4300
Healthcare Contact	94.82	<0.0001	6	3934

Factor Analysis and Correlation Analysis

An individual factor analysis was conducted with the symptoms reported for the outcomes including not approved for testing, approved positive, and approved negative (Table 5). Other was omitted for the purpose of this analysis. Symptoms with an asterisk indicate those that will be retained for the factor analysis. No limit was set on how many factors would be retained. Strict criteria were not set to determine retention. A total of six primary correlation

analyses were run to determine the standardized Cronbach Alpha of the symptoms retained within each factor. Within factor 1 of each outcome level, nausea, headache, abdominal pain, and diarrhea were retained. Factor 2 showed variability within symptoms that were retained, but cough was present in each outcome level.

	Not Approved			Approved Positive			Approved Negative		
Initial Correlations	Factor 1	Nausea Headache Abdominal Pain Diarrhea	$\alpha= 0.85$	Factor 1	Rhinorrhea Sore Throat Nausea Headache Abdominal Pain Diarrhea	$\alpha=0.91$	Factor 1	Nausea Headache Abdominal Pain Diarrhea	$\alpha=0.90$
	Factor 2	Fever Subjective Fever Myalgia Rhinorrhea Sore Throat Cough	$\alpha=0.76$	Factor 2	Cough Shortness of Breath	$\alpha=0.67$	Factor 2	Fever Subjective Fever Cough Shortness of Breath	$\alpha=0.65$
Reduced Factors for Parsimony	Factor 1	Nausea Abdominal Pain Diarrhea	$\alpha= 0.85$	Factor 1	Sore Throat Nausea Headache Abdominal Pain Diarrhea	$\alpha=0.90$	Factor 1	Nausea Headache Abdominal Pain	$\alpha=0.89$
	Factor 2	Subjective Fever Myalgia Rhinorrhea Sore Throat Cough	$\alpha= 0.76$	Factor 2	Cough Shortness of Breath	$\alpha=0.67$	Factor 2	Subjective Fever Cough Shortness of Breath	$\alpha=0.63$

Discussion

The analyses conducted focus primarily on symptoms to represent the symptom based testing strategies that were used early within the pandemic^{26,27}. When assessing systemic symptoms of potential COVID-19 cases, fever and subjective fever were the most common is consistent with previous literature¹⁵. The most common respiratory symptom among testing request forms was cough which is also consistent with previous¹⁵. When assessing symptoms related to the ear, nose, and throat, sore throat and rhinorrhea were the most common symptoms and sore throat was found to be one of the second most common symptom among COVID-19 within this category¹⁵. When assessing gastrointestinal symptoms among testing requests, nausea and vomiting were the most common which is different than the typical most common gastrointestinal symptom of diarrhea¹⁵.

The factor analyses provide insight on how symptoms varied among the levels of outcome indicating the potential issues with symptom-based testing strategies. There were two primary groupings of symptoms among those who were not approved for testing. The first factor indicated similarities in symptoms including nausea, abdominal pain, and diarrhea. The second factor indicated similarities with subjective fever, myalgia, rhinorrhea, sore throat, and cough. Among those that were approved for testing and tested positive, the first factor indicated a grouping of rhinorrhea, sore throat, nausea, headache, abdominal pain, and diarrhea and the second factor included cough and shortness of breath. Among those who were approved for testing and tested negative, factor one indicated a grouping of nausea, headache, and abdominal pain and factor two indicated a grouping of subjective fever and cough. When looking at each of these outcomes, it is difficult to rule out potential COVID-19 cases based on symptoms alone. All three levels of outcome include symptoms that could be deemed as positive case based on

case definition alone^{7,10-13,15}. Those in the approved positive category had a more widespread grouping of symptoms including systemic, respiratory, ear, nose, and throat, gastrointestinal, and central nervous system symptoms. Those who were approved, and tested negative had a less diverse range of symptoms that were experienced. With a novel disease, symptoms can be some of the primary factors used in determining a case definition. The findings of this analysis support the need for further criteria to determine testing eligibility.

As seen in past outbreaks, such as H1N1 and SARS-CoV-1, traveler screening and symptom based screening are often turned to as the go to method for identifying potential cases or determining testing criteria^{1,2,4,14,26,28,29}. While symptom-based testing might be the easiest in the early phases of an outbreak or pandemic of a novel disease, efforts must be made to specify the case definition and expand it outside of symptoms alone. For COVID-19, fever, cough, headache, and myalgia are some of the primary symptoms and are not specific enough to identify a case of COVID-19 in comparison to other respiratory illnesses such as seasonal Influenza^{14,15}. Both the factor analyses and correlation analyses were not able to differentiate the difference from positive and negative COVID-19 cases. Further information, such as travel history, exposure history, or preexisting conditions may be beneficial in creating a more accurate screening tool to determine if testing is needed. While this information was collected, there was too much missing data to conduct an analysis on it (Table 1). Specific information about other risk factors needs to be collected in addition to symptoms to adequately determine if a patient should be considered for testing in a pandemic or outbreak situation.

Testing request data provides a unique opportunity to provide near real time information and feedback that can help shape the next steps of making decisions at the health department level. In Georgia, as previously mentioned, testing capacity was extremely limited during this

phase of the pandemic. In addition, this was a dynamic time where more information about COVID-19 was discovered on an almost daily basis requiring guidance and recommendations to be updates multiple times per week. Assessing the information coming in via testing request forms can be used to identify potential trends in testing request forms based on submission location, symptom profile, pre-existing conditions or comorbidities, and more. When resources are limited, recommendations need to be provided to best utilize the resources. This data serves as an untapped evidence-based that can be used to help inform decisions relating to testing criteria and allocation in conjunction with guidance being published by CDC.

Limitations

One main limitation in this data set was the overall quality of data. Due to the format of the testing request form, there were no required fields so medical professionals could be as specific or vague as possible when reporting information. This led to numerous patterns related to missing or unknown data. Another limitation was the other category classified in the outcome variable. There were 994, or 20.6%, of testing requests that fell into this category. Primary reasons for this classification included duplicate requests, practice test request forms being processed, inconclusive lab results, or samples never being sent to GPHL labs. Factors influencing these reasons can include but are not limited to miscommunication on the purpose of the test request form, lack of communication between providers in a facility, and incorrect specimen collection strategies and storage. Another limitation would be the fast-paced guidance changes as new information surrounding the COVID-19 pandemic emerged. New information led to at least daily updates that may not have been recognized by all people on the response working to approve testing requests. Additionally, linkage of test results to records within SendSS were dependent on laboratory reporting and matching on name and date of birth (DOB).

It is possible that some persons missing test results may have been tested at other laboratories and not reported or not matched within the system. All laboratory linkage and search functions are based on an exact match, so spelling errors or DOB errors would result in a non-match and difficulty finding the result manually within a system with over 4 million laboratory results.

Conclusion

In a pandemic situation, continual data monitoring and analysis of early testing request data can be utilized to utilize the most up to date data to inform updated guidance and support recommendations. Assessing common trends within testing request forms can be used to identify not only symptoms consistent with illness but risk factors among those who may have been exposed. Risk factors are necessary to determine what the high-risk groups are to help ensure testing kits are allocated to those most at risk. In addition, there is a need for increased provider education on completion of testing request forms. Early COVID-19 data indicated not only missing data but also a large number of tests that were approved for testing and not tested (as shown by the other category). Trainings should be conducted by local and/or state health departments to provide information on the importance of data quality in testing request forms to inform evidence-based decisions. To encourage provider participation and buy in, these courses can be offered for Continuing Medical Education (CME) credit. In addition, this material can be applied to other diseases, such as seasonal Influenza. The COVID-19 testing request data collected between March 2020 – April 2020 provides a unique insight on data quality and use within Georgia and should be used to inform future pandemic preparedness plans.

Chapter 4: Implications/Recommendations

Despite the cliché, the COVID-19 pandemic is an unprecedented time. We are able to look back at other outbreaks, such as H1N1 and SARS-CoV-1, to assess what went well and what needs improvement for pandemic preparedness. In a pandemic situation, continual data monitoring and analysis of early testing request data can be utilized to utilize the most up to date data to inform updated guidance and support recommendations. The results of this study indicate differences in symptom profiles between those who were approved versus not approved and then within the approved category compare positive versus negative results. The factor analysis further assessed the relationships between these groupings. Limitations within this study are one main area that can be used to inform future recommendations for pandemic preparedness and address the need for continual data monitoring and healthcare provider education.

Overall data quality was limitation within this study that was attempted to be addressed. There were many meetings and discussions on the overall data quality of what was being received, but limited funding and personal restricted what could be done in real time. One push made by the DPH Commissioner, Dr. Kathleen Toomey, and the American Medical Association was sending out “Dear Doctor” letters pleading for providers to provide better data. While this may have not been the most successful effort, it draws attention to the need for this education on data quality, especially in pandemic settings, in an every day setting before a pandemic occurs.

Provider education needs to go beyond telling providers to complete more aspects of the testing request forms. Education needs to occur before a pandemic happens. With such in depth and lengthy forms for completing testing requests, it is critical that providers are educated on the purpose. The purpose in the case of COVID-19 was to collect as much information on potential cases as possible so triaging patients and allocating testing supplies was done in the best way

possible. There are many limitations that exist, but a pandemic setting with a new diagnostic test makes them even more prevalent. Telling providers to do a better job at completing these forms will not make a difference but educating them on the why public health is making the request may resonate more with them. There is also the potential to make these educational sessions part of a Continued Medical Education (CME) course which providers are required to take each year.

Another recommendation in preparing for future pandemics, is a shifted focus on data to assess the granular level data that may have tell a story missed when assessing population level data or assessing bigger picture items such as total case counts. A success story from this is related to identification of hospital outbreaks or potential hospital outbreaks based on the influx of testing request forms that were coming in. When this was identified, the health department districts were able to connect with the facility indicating an increased need for testing to have a better idea of what is going on in that setting. This also brings attention to the need for and importance of improved sentinel site surveillance systems. With the limited resources DPH had, identifying potential clusters or addressing concerns at an early level is a great way to make the most out of limited resources.

All in all, the main limitation for this study and the early COVID-19 pandemic was lack of funding and resources. Many of the limitations presented could have been avoided with not only more funding, but earlier funding for pandemic preparedness and response. In March 2020 there were no COVID-19 epidemiologists. All epidemiologists had to be pulled from other areas within DPH to help with surge capacity during this time. With limited resources, epidemiologists and biostatisticians had to transition into COVID-19 roles and out of their daily roles and responsibility since funding was not available to hire more staff. One big win was the acknowledgement of increased staffing needs and the ability to pull volunteers from local MPH

programs to help with surge capacity. One of the first groups of students who became involved in the response, were the Student Outbreak and Response Team at the Rollins School of Public Health. Student volunteers were able to be pulled in from this organization to initially help with testing request approvals. This can be viewed as a win early within the response, but more still could have been done. With increased funding towards pandemic preparedness and response, health departments can be more adequately prepared to respond with hiring new staff to manage surge capacities. In addition, this funding could go towards provider education on pandemic preparedness and response. Assessing the triumphs and pitfalls early in the COVID-19 pandemic provide valuable insight that can be used to create evidence-based recommendations to best allocate limited supplies in a pandemic setting and prepare for future pandemics.

References

1. Brockmann D, Helbing D. The Hidden Geometry of Complex, Network-Driven Contagion Phenomena. *Science*. 2013;342(6164):1337-1342. doi:10.1126/science.1245200
2. William T, Thevarajah B, Lee SF, et al. Avian Influenza (H7N9) Virus Infection in Chinese Tourist in Malaysia, 2014 - Volume 21, Number 1—January 2015 - Emerging Infectious Diseases journal - CDC. doi:10.3201/eid2101.141092
3. Cauchemez S. Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility. 2014;14:7.
4. McCarthy M. Liberian man being treated for Ebola in Texas dies. :1.
5. The SARS-CoV-2 outbreak: What we know - ScienceDirect. Accessed April 18, 2021. <https://www.sciencedirect.com/science/article/pii/S1201971220301235>
6. Tang X, Wu C, Li X, et al. On the origin and continuing evolution of SARS-CoV-2. *Natl Sci Rev*. 2020;7(6):1012-1023. doi:10.1093/nsr/nwaa036
7. Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med*. 2020;382(10):929-936. doi:10.1056/NEJMoa2001191
8. Gov. Kemp, Officials Confirm Two Cases of COVID-19 in Georgia. Georgia Department of Public Health. Accessed May 2, 2021. <https://dph.georgia.gov/press-releases/2020-03-02/gov-kemp-officials-confirm-two-cases-covid-19-georgia>
9. COVID-19 Status Report. Georgia Department of Public Health. Accessed April 18, 2021. <https://dph.georgia.gov/covid-19-daily-status-report>

10. Menni C, Sudre CH, Steves CJ, Ourselin S, Spector TD. Quantifying additional COVID-19 symptoms will save lives. *The Lancet*. 2020;395(10241):e107-e108. doi:10.1016/S0140-6736(20)31281-2
11. CDC. Coronavirus Disease 2019 (COVID-19) – Symptoms. Centers for Disease Control and Prevention. Published February 22, 2021. Accessed April 18, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>
12. Coronavirus. Accessed April 18, 2021. <https://www.who.int/westernpacific/health-topics/coronavirus>
13. What is COVID-19? Georgia Department of Public Health. Accessed April 18, 2021. <https://dph.georgia.gov/what-covid-19>
14. Kang S, Peng W, Zhu Y, et al. Recent progress in understanding 2019 novel coronavirus (SARS-CoV-2) associated with human respiratory disease: detection, mechanisms and treatment. *Int J Antimicrob Agents*. 2020;55(5):105950. doi:10.1016/j.ijantimicag.2020.105950
15. Grant MC, Geoghegan L, Arbyn M, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. Hirst JA, ed. *PLOS ONE*. 2020;15(6):e0234765. doi:10.1371/journal.pone.0234765
16. Zheng J. SARS-CoV-2: an Emerging Coronavirus that Causes a Global Threat. *Int J Biol Sci*. 2020;16(10):1678-1685. doi:10.7150/ijbs.45053

17. Introduction to Public Health Surveillance|Public Health 101 Series|CDC. Published July 15, 2020. Accessed May 2, 2021.
<https://www.cdc.gov/training/publichealth101/surveillance.html>
18. Nsubuga P, White ME, Thacker SB, et al. *Public Health Surveillance: A Tool for Targeting and Monitoring Interventions*. The International Bank for Reconstruction and Development / The World Bank; 2006. Accessed May 2, 2021.
<https://www.ncbi.nlm.nih.gov/books/NBK11770/>
19. Types of Surveillance. Accessed May 2, 2021.
<http://www.masslocalinstitute.info/diseasesurveillance/diseasesurveillance4.html>
20. Hughes HE, Edeghere O, O'Brien SJ, Vivancos R, Elliot AJ. Emergency department syndromic surveillance systems: a systematic review. *BMC Public Health*. 2020;20(1):1891. doi:10.1186/s12889-020-09949-y
21. Desjardins MR. Syndromic surveillance of COVID-19 using crowdsourced data. *Lancet Reg Health - West Pac*. 2020;4:100024. doi:10.1016/j.lanwpc.2020.100024
22. Maharaj AS, Parker J, Hopkins JP, et al. The effect of seasonal respiratory virus transmission on syndromic surveillance for COVID-19 in Ontario, Canada. *Lancet Infect Dis*. 2021;21(5):593-594. doi:10.1016/S1473-3099(21)00151-1
23. Chan AT, Brownstein JS. Putting the Public Back in Public Health — Surveying Symptoms of Covid-19. *N Engl J Med*. Published online June 5, 2020. doi:10.1056/NEJMp2016259

24. Nomura S, Yoneoka D, Shi S, et al. An assessment of self-reported COVID-19 related symptoms of 227,898 users of a social networking service in Japan: Has the regional risk changed after the declaration of the state of emergency? *Lancet Reg Health - West Pac.* 2020;1:100011. doi:10.1016/j.lanwpc.2020.100011
25. About National Surveillance | National Surveillance | CDC. Published September 13, 2018. Accessed May 2, 2021. <https://www.cdc.gov/nationalsurveillance/about.html>
26. Gostic K, Gomez AC, Mummah RO, Kucharski AJ, Lloyd-Smith JO. Estimated effectiveness of symptom and risk screening to prevent the spread of COVID-19. Franco E, Ferguson NM, McCaw JM, eds. *eLife.* 2020;9:e55570. doi:10.7554/eLife.55570
27. Gostic KM, Kucharski AJ, Lloyd-Smith JO. Effectiveness of traveller screening for emerging pathogens is shaped by epidemiology and natural history of infection. *eLife.* 2015;4:e05564. doi:10.7554/eLife.05564
28. Wuhan China Virus: What Airports Are Doing to Stop 2019-NCov Spread. Accessed April 23, 2021. <https://www.businessinsider.com/wuhan-china-virus-airports-actions-screening-stop-spread-travel-2020-1>
29. Stein RA. The 2019 coronavirus: Learning curves, lessons, and the weakest link. *Int J Clin Pract.* 2020;74(4):e13488. doi:<https://doi.org/10.1111/ijcp.13488>
30. Hoehl S, Rabenau H, Berger A, et al. Evidence of SARS-CoV-2 Infection in Returning Travelers from Wuhan, China. *N Engl J Med.* 2020;382(13):1278-1280. doi:10.1056/NEJMc2001899

31. Callahan A, Steinberg E, Fries JA, et al. Estimating the efficacy of symptom-based screening for COVID-19. *Npj Digit Med*. 2020;3(1):95. doi:10.1038/s41746-020-0300-0