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RSVP - Flu Like Illness and Respiratory Syndromes

COVID-19 Syndromic Reporting Tool Prototype

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ABSTRACT

Individuals infected with SARS-CoV-2, the virus that causes COVID-19, may be infectious between 1-3 days prior to symptom onset. People may delay seeking medical care after symptom development due to multiple determinants of health seeking behavior like availability of testing, accessibility of providers, and ability to pay. Therefore, understanding symptoms in the general public is important to better predict and inform resource management plans and engage in reopening. As the influenza season looms, the ability to differentiate between clinical presentation of COVID-19 and seasonal influenza will also be important to health providers and public health response efforts.

This project has developed an algorithm that when used with captured syndromic trends can help provide both differentiation to various influenza-like illnesses (ILI) as well as provide public health decision makers a better understanding regarding spatial and temporal trends. This effort has also developed a web-based tool to allow for the capturing of generalized syndromic trends and provide both spatial and temporal outputs on these trends.

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EXECUTIVE SUMMARY

The novel coronavirus, SARS-Cov-2, causes a disease (COVID-19) that has a unique presentation of clinical symptoms that enable it to be differentiated from seasonal respiratory viruses and seasonal allergies. Crowd-sourced symptom profiles with geospatial references can provide early warning to health departments and planners. A web-based symptom-based screening tool and underlying algorithm can be utilized for return-to-work screening to meet reopening recommendations or for active monitoring of contacts to identify new onset symptoms.

Case incidence and signs and symptoms were captured through literature review for COVID-19, seasonal influenza, other upper respiratory infections, and seasonal allergies. These values were converted into weights using traditional probability values of the disease occurring in the population P(A) combined with probability of the symptom of a given disease P(B | A) where B is the symptom. The final weight of the probability of both symptom and the disease is P(A and B). Secondary weights were incorporated based on subject matter expert opinion to further refine the sensitivity of the symptom constellation. Based on both synthetic data and case-study validation, the underly algorithm used in this web-based tool has demonstrated a high correlation between the modeled result and actual results.

Syndromic surveillance can serve as an early-warning indicator of potential case increases without delays associated with arranging a provider visit or tele-health appointment. Syndromic surveillance is an added tool that can help with prioritization of testing, contact tracing, and targeted non-pharmaceutical interventions.

Future efforts could include transition to partners with need for symptom monitoring of a population like health departments, large employers, and schools. Additional refinement of the algorithm and incorporation of new data on symptom presentations could improve the sensitivity and specificity of the syndromic screening tool.

ACRONYMS AND DEFINITIONS

Abbreviation	Definition
CDC	U.S. Centers for Disease Control and Prevention
COVID-19	Severe Acute Respiratory Syndrome Coronavirus 2, or novel corona virus disease
ESSENCE	Electronic Surveillance System for the Early Notification of Community-based Epidemics
ILI	influenza-like illness
ILINet	Outpatient Influenza-like Illness Surveillance Network
NM	New Mexico
NSSP	National Syndromic Surveillance Program
RSVP	Rapid Syndrome Validation Project
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
URIs	upper respiratory infections

1. INTRODUCTION

Syndromic surveillance is called for early outbreak detection, monitoring size, spread, and frequency of outbreaks, identifying disease trends, and providing information regarding the absence of an outbreak (K.J., 2004).

The Rapid Syndrome Validation Project (RSVP) offers an earlier avenue to detect syndromic cases in the general population that is absent in the National Syndromic Surveillance Program (NSSP) and the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) and other electronic health record-based syndromic surveillance or Centers for Disease Control and Prevention's (CDC's) Influenza-like Illness Surveillance Network's (ILINet) ambulatory care-clinic-based influenza surveillance. These syndromic surveillance systems can experience 1-3 day delays between the patient visit and availability of coded-surveillance data. In the case of ILINet, data may be subject to periodic or missed reporting by participating sites. These delays and inadequate sensitivity and poor positive predictive value can contribute to missing outbreaks. RSVP can be used anywhere and may be used by individuals who do not ultimately seek medical attention. RSVP results will be most valuable when correlated with laboratory-confirmation among those that ultimately seek care. Additional data points such as the number or geographic location of individuals that are referred for testing but choose to not seek care will also be informative to public health officials as they consider test and trace strategies.

RSVP has two primary objectives, the first is to provide the State of New Mexico (and possible other states) access to spatial and temporal information regarding the novel corona virus disease (COVID-19) and other influenza-like illness (ILI) syndromes to help support decision making regarding policies and testing. Currently confirmed positive test data are driving a majority of public health decision making. This indicator-based surveillance is limited to health seeking behaviors, access to care, and in the current COVID-19 pandemic, availability of testing. Event-based surveillance data, such as provided by RSVP, provides a mechanism to capture early-warning signals and is complimentary to laboratory-confirmed tests. The utility of syndromic data to help support decision making was demonstrated during the initial development and deployment of RSVP in the early 2000's[1]. The second objective of the project is to provide a framework to support return-to-work policies for companies, schools, and small businesses that are designed to reduce the continued spread of COVID-19 within the workplace or school. This framework can be used to support pre-work screening or to support on-site surveillance.

[1] RSVP was initially piloted in the United States and Singapore to help support detection of unusual outbreaks in the human population, and subsequently in the animal population. The project completed is pilot in 2002 and was licensed externally and elements of the original tool are still witnessed in many health screening systems.

2. MODELING AND ANALYSIS

The research hypothesis for this study is based on the original RSVP tool (Zelicoff A., 2001), but leverages specific COVID-19 symptom indicators. The answers to a collection of symptomatic, behavior, and geolocation questions can provide sufficient fidelity to differentiate between ILIs supporting spatial and temporal detection in disease occurrence that is more rapid than the existing analysis tools provide. This type of event-based or syndrome-based surveillance can help to capture early warning signals and complements the decisions made by laboratory based data such as number confirmed.

The analysis of the data is the unique element of RSVP. The original RSVP tool (Zelicoff A., 2001) included ILI and respiratory syndromes but did not include several of the questions specific to the CDC's symptom list for COVID-19. The RSVP question set was updated based on the April 2020 CDC COVID-19 symptoms. Below are the signs and symptoms included in this model. Each question is scored, weighted, and combined to define the potential for each of the included ILIs.

1. Typical Dry Cough (Harsh Cough)
2. Atypical Cough (Barking)
3. Wet Cough
4. Coughing Up Blood
5. Restrictive Breathing
6. Nasal Congestion
7. Runny/Sneezing
8. Sore Throat
9. Conductivities
10. Loss of Taste or Smell
11. Headache
12. Muscle Ache
13. Chills/Shaking
14. Fatigue
15. Diarrhea
16. Vomiting
17. Temperature > 38°C

These are coupled, in the tool, with behavior questions that include travel and possible exposures to COVID-19 or other ILIs. Geolocation data is pulled at the zip code level and date of entry is used to define the temporal aspects within the model. The analysis looked at each question as binary (yes or no), the web-based application to query the data used more defined questions allowing the user to select options which were used to define the binary answers.

For each question, literature was pulled to define case incidence and the expected portion of the population with the disease. These reports reflect the portion of those confirmed with the disease to have the various signs and symptoms. These were pulled for not only cases confirmed for COVID-19, but also for seasonal influenza, other upper respiratory infections (URIs), and spring allergies. These values were converted into weights using traditional probability values, where the probability of the disease occurring in the population P(A) was combine with the probability of the

symptom given the disease P(B | A) where B is the symptom. This reflects the final weight being the probability of both the symptom and the disease P(A and B).

For the current weights, the portion of the population expected to have COVID-19 was based on high population values for influenza (20%), as more data is available this value can be updated, and the weights recalculated. The portion of the population expected to have influenza annually was defined as between 5 and 20%, spring allergies 10 to 30%, and URIs 50%. These are based on U.S. data from the CDC.

The following table (Table 1) contains the values from published case reports regarding COVID-19 (Cascella, 2020) (CDC, 2020) (Guan, 2020) (WHO, 2020) (CDC, 2020), influenza (CDC, 2019) (CDC, 2019) (The Centre for Evidence-Based Medicine, 2020), URIs, and allergies (Chung, 2013).

Table 1 Case Instance Values

Symptom	% of those with COVID-19	% of people with influenza	% of people with spring allergies	% of people with URIs
Typical Dry Cough		60%	30%	50%
Atypical Cough	80%	10%		5%
Wet Cough	19%	5%	10%	40%
Coughing Blood	1%			
Restrictive Breathing	40%	5%	5%	5%
Nasal Congestion	4%	20%	63%	80%
Runny/Sneezing		20%	51%	80%
Sore Throat	14%	20%	20%	80%
Conductivities	1%		48%	
Loss of Taste or Smell	9%			
Headache		60%	5%	1%
Muscle Ache	35%	80%	5%	5%
Chills/Shaking	11%			
Fatigue	70%	80%	10%	5%
Diarrhea	4%	5%	0%	
Vomiting	5%	5%	0%	
Temperature > 38˚C	99%	88%	0%	1%

Six additional questions were included reflecting behavior patterns of the respondents. These included questions about recent travel and contact. The responses to these questions were also weighted and used in the overall analysis. These were weighted based on subject matter expert (SME) opinion considering CDC guidance.

Below (Table 2) are the current weights, it is expected that these may change as more data becomes available.

Table 2 Current (June 2020) RSVP Syndromic Weights

Question Number	Symptom	COVID-19	Influenza	Allergies	Other URI
1	Typical Dry Cough	0%	12%	9%	5%
2	Barking or Atypical Cough	16%	2%	0%	1%
3	Wet Cough	4%	1%	3%	4%
4	Coughing Blood	0%	0%	0%	0%
5	Restrictive Breathing	8%	1%	2%	1%
6	Nasal Congestion	1%	4%	19%	8%
7	Runny/Sneezing	0%	4%	15%	8%
8	Sore Throat	3%	4%	6%	8%
9	Conductivities	0%	0%	14%	0%
10	Loss of Taste or Smell	2%	0%	0%	0%
11	Headache	2%	12%	2%	0%
12	Muscle Ache	7%	16%	2%	1%
13	Chills/Shaking	3%	0%	0%	0%
14	Fatigue	14%	16%	3%	1%
15	Diarrhea	1%	1%	0%	0%
16	Vomiting	1%	1%	0%	0%
17	Temperature > 38°C	20%	18%	0%	0%
18	*Travel Country*	0%	0%	0%	0%
19	*Travel State*	0%	0%	0%	0%
20	*Travel City*	14%	16%	3%	1%
21	*Contact Illness*	1%	1%	0%	0%
22	*Contact COVID*	1%	1%	0%	0%
23	*Exposed COVID*	20%	18%	0%	0%

In the event, cough, restrictive breathing, loss of taste/smell, chills/shaking, and fever are all defined as true, there is an additional weight applied pushing the overall syndrome toward COVID since the combination of those symptoms is more indicative of COVID-19 than each symptom individually. This weight was defined by the SMEs to be a 20% increase. This calculation has been accomplished by a virtual 24th question that adds the 0.2 to the COVID syndrome if and only if the five questions are true but otherwise adds a 0. A zero is added to all other syndromes regardless of the responses.

Below is an example of a set of responses and the calculations:

Question Number	Symptom	Response	COVID-19	Influenza	Allergies	Other URI
1	Typical Dry Cough	N	0	0	0	0
2	Barking or Atypical Cough	*Y*	0.16	0.02	0	0.005
3	Wet Cough	N	0	0	0	0
4	Coughing Blood	N	0	0	0	0
5	Restrictive Breathing	N	0	0	0	0
6	Nasal Congestion	N	0	0	0	0
7	Runny/Sneezing	N	0	0	0	0
8	Sore Throat	N	0	0	0	0
9	Conductivities	N	0	0	0	0
10	Loss of Taste or Smell	Y	0.02	0	0	0
11	Headache	Y	0.02	0.12	0.015	0.001
12	Muscle Ache	N	0	0	0	0
13	Chills/Shaking	Y	0.03	0	0	0
14	Fatigue	Y	0.14	0.16	0.03	0.005
15	Diarrhea	N	0	0	0	0
16	Vomiting	N	0	0	0	0
17	Temperature > 38°C	Y	0.198	0.176	0	0.001
18	*Travel Country*	*N*	0	0	0	0
19	*Travel State*	*N*	0	0	0	0
20	*Travel City*	*N*	0	0	0	0
21	*Contact Illness*	Y	0.01	0.01	0	0
22	*Contact COVID*	*N*	0	0	0	0
23	*Exposed COVID*	*N*	0	0	0	0
24	*Five Syndromes Flagged?*	Y	0.2			
Syndrome Potential			**78%**	**49%**	**5%**	**1%**

These values have been peer reviewed and validated using case report data. The model has also been tested using synthetic data to allow for the temporal and spatial analysis and visualization to be finalized.

2.1. Temporal and Spatial Analysis

The temporal analysis is based on portions of the daily reports that reflect the ILI syndromes. Specifically, for each report the answers are weighed as defined above and combined to define a probability for each of the four syndromes (COVID-19, Influenza, Allergies, and Other URIs). If the resulting probabilities are virtually equal (that is there is less than a 5% variance) this data point is stored but not used in the temporal analysis. The temporal analysis sums all the reports for each day

and the count of reports where each of the four syndromes is the greatest and uses this to define the count per syndrome per day.

This temporal analysis can be visualized (Figure 1) within the RSVP web-based application or pulled into other statistical analysis tools for further view.

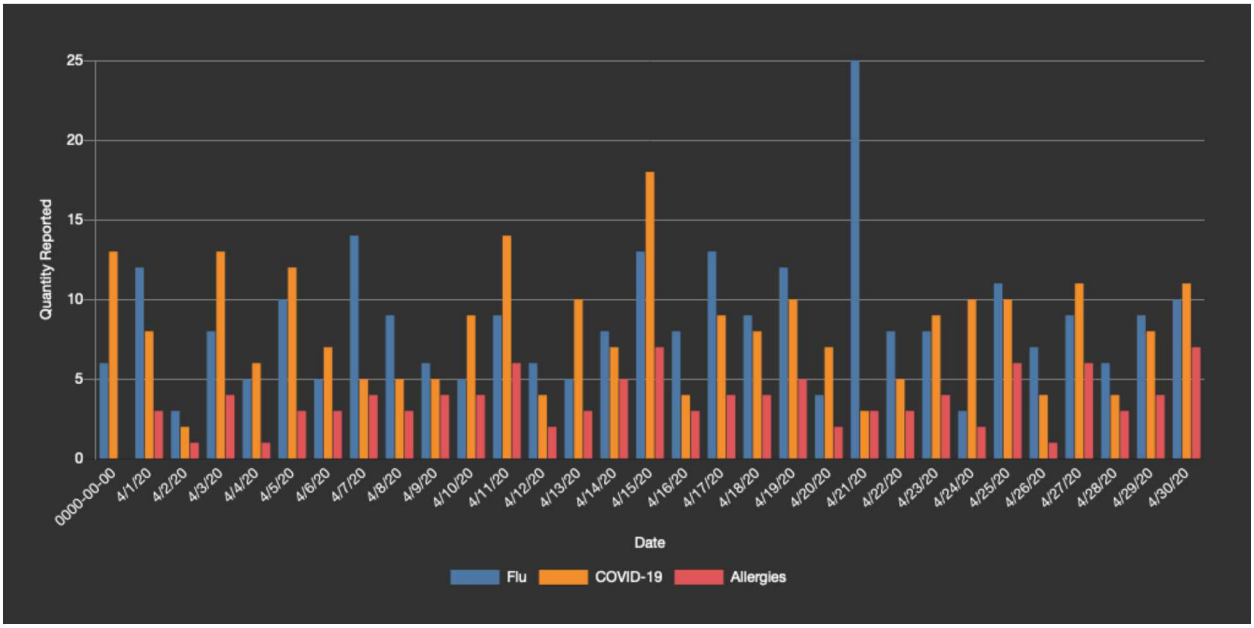


Figure 1 Example of Temporal Analysis Visualization

The spatial analysis uses a similar algorithm as the temporal analysis to define geographical relationships between instances of syndromes. The spatial tool, built using FASTMap,[2] pulls each report individually to include the zip code included in the report (reflecting the home or work zip code); the answers and are then weighed as defined above and combined to define a probability for each of the four syndromes (COVID-19, Influenza, Allergies, and Other URIs). The probabilities for each zip code are combined for each syndrome creating a density map of each syndrome.

The spatial data can be filtered to look at each syndrome, the predominant syndrome, and the count of reports for each zip code. This can also be expanded to look at county and state resolution. The spatial analysis tool also allows for looking at reports for any given date or cumulative across the defined time window.

[2] FASTMap is a software suite capable of providing detailed GIS-based and statistical data on important economic sectors as well as the location of critical infrastructure and economic assets at risk. Serves to answer questions directly or as pre-modeling input for more comprehensive future analysis. (Sandia National Laboratories, 2012)

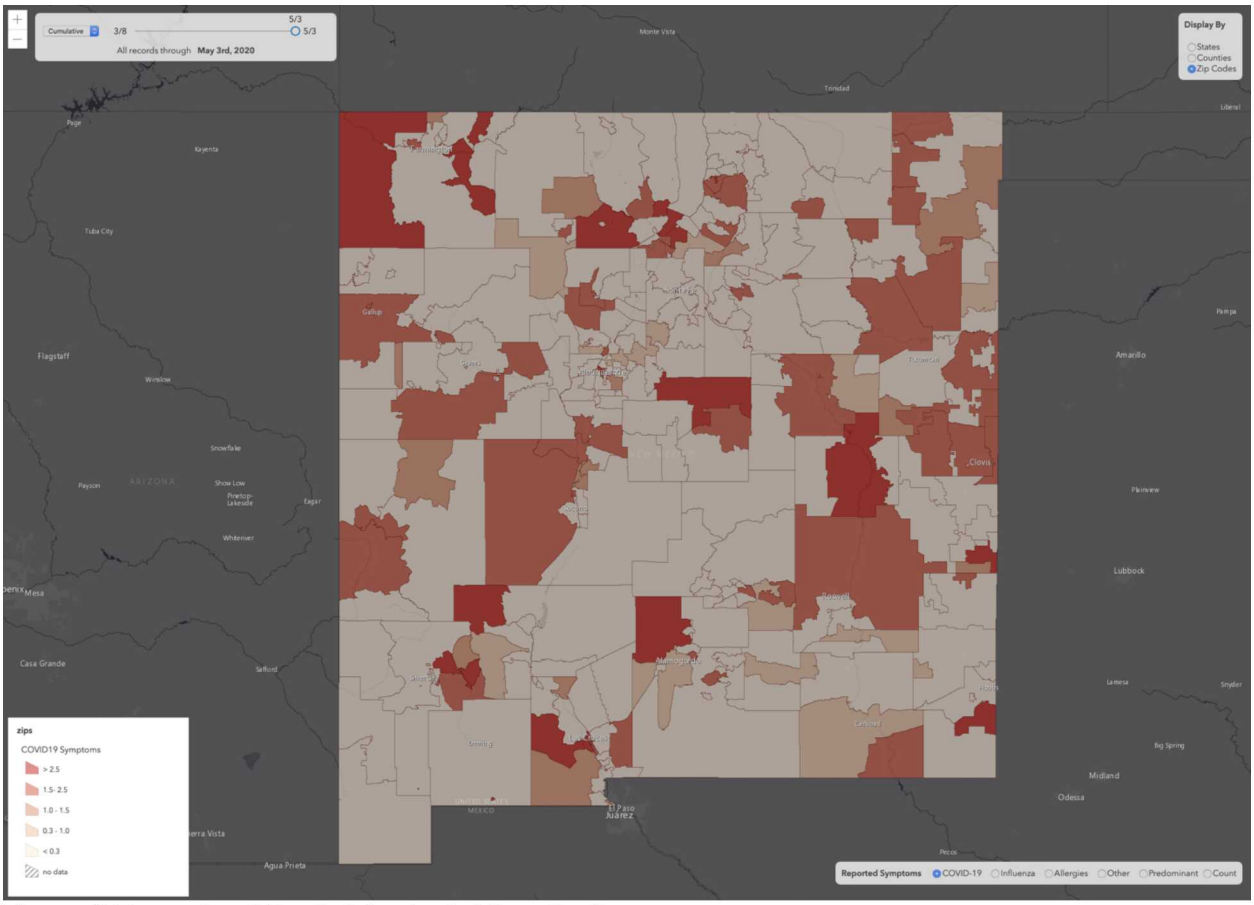


Figure 2 Example of Spatial Analysis Visualization

As with the temporal analysis, all the data used in the spatial tool can be exported for use in other analysis tools.

3. MODEL VALIDATION

Following the peer review and testing of the model using case reports, synthetic data was used to help test the spatial and temporal models and to further ensure the model was providing accurate representations of the possible underlying disease.

Eight case reports, which were not used in the model development, were used in the testing of the algorithm. These included six where COVID-19 was confirmed, one where influenza was confirmed, and one where no specific virus was identified. Of the six where COVID-19 was confirmed, only two were suspected cases before being confirmed by testing. The following table (Table 3) is an outline of the syndromes reported for each case and a table (Table 4) with the resulting values. From these results, the algorithm mirrors the actual testing results where COVID was confirmed. The algorithm struggled with the unknown virus which mirrored both influenza and COVID but was neither. For some case reports, the delta between COVID and influenza was minor where few COVID specific or influenza specific syndromes were witnessed. (Buonsenso, 2020) (Douedi, 2020) (Doron) (Doron, Case Study Pneumonia, 2014) (Sachdeva, 2020) (Chen, 2020)

Table 3 Case Reports

Question #	**Case Report 1: 52 year old man COVID +**	**Case Report 2: 46 year old woman COVID +**	**Case Report 3: 77 year old woman COVID +**	**Case Report 4: 77 year old woman COVID +**	**Case Report 5: 72 year old woman COVID +**	**Case Report 6: 77 year old woman COVID +**	**Case Report 7: 29 year old woman Influenza +**	**Case Report 8: 68 year old man (unknown virus)**
1							Y	Y
2	Y	Y		Y	Y			
3			Y					
4								
5		Y	Y			Y	Y	Y
6							Y	
7								
8								
9								
10	Y				Y	Y		
11	Y				Y	Y		
12								
13	Y				Y	Y		
14	Y						Y	
15								
16								
17	Y	Y		Y	Y	Y	Y	Y
18								
19								
20								
21	Y							
22		Y				Y		

23

Table 4 Case Report Results

	COVID	INFLUENZA	ALLERGIES	OTHER
CASE REPORT 1	78%	49%	5%	1%
CASE REPORT 2	45%	22%	2%	1%
CASE REPORT 3	12%	2%	5%	5%
CASE REPORT 4	36%	20%	0%	1%
CASE REPORT 5	63%	30%	2%	0%
CASE REPORT 6	36%	32%	3%	1%
CASE REPORT 7	43%	51%	32%	14%
CASE REPORT 8	28%	31%	11%	6%

For the synthetic data, 500 response sets were created using random numbers to define the Y/N answers. Each of these response sets were weighted based on the defined model and the results consider using standard static methods. Of interest was the delta between each of the four syndromes for each response set. From the diagram below (Figure 3), most of the response sets had a range of deltas close to 32% supporting the model's ability to distinguish between the four syndromes based on the entered data and weights. Of the data, where the 5 COVID-19 specific questions were all responded to with a 'yes' value the model also gave COVID the highest possible value an average of 97% of the time.

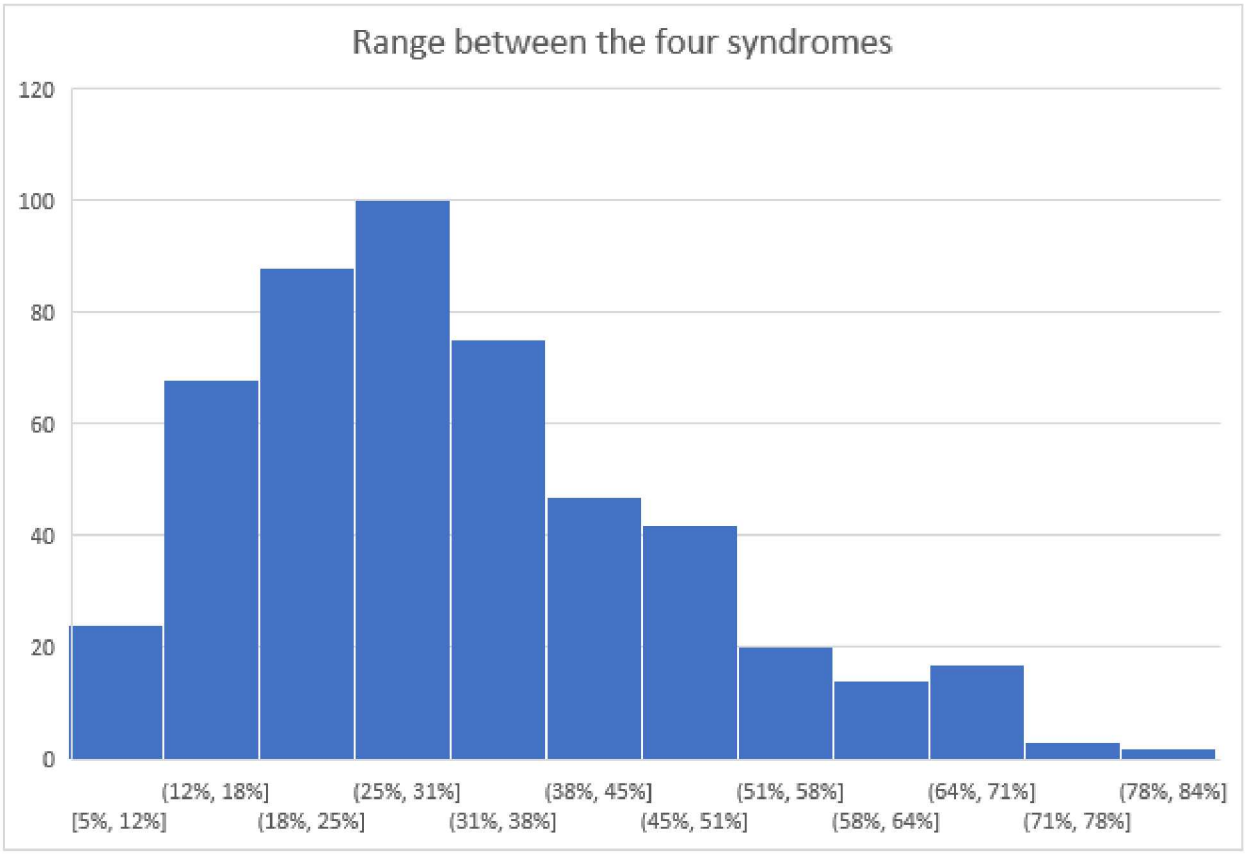


Figure 3 Range between syndrome scores

In looking at both the synthetic data and the case study data, there was only a 68% correlation between the results reflecting COVID and influenza and a -26% correlation between COVID and allergies. The SMEs reflected on these and felt this limited correlation was a good demonstration of the algorithm's ability to differentiate between syndromes given sufficient data.

4. WEB-BASED APPLICATION

As part of the RSVP pilot project, a web-based application was developed to allow collection of the data and presentation of the resulting analysis. The site is currently hosted outside Sandia by a public internet service provider (Southwest Cyberport) to facilitate transfer of the website to either a department of health or another external partner.

The underlying structure of the application is based on a SQL database with the interfaces using PHP to push and pull data from the database. The web pages are in html with supporting PHP and JavaScript to ensure data authentication. The analysis graphics are JSON files or built using FastMap.

The database runs on MySQL and includes seven tables. Six tables are used in the calculations or in the storage of the syndromic data, the seventh is currently not utilized but can be used to support multiple types of data entry (e.g. direct from individual or via a medical provider). Data is collected from 'users' and inserted into the proper data tables, and then pulled from those tables, combined with the model tables and displayed in the various visualizations. Interfaces to all database tables for direct access to the raw data have been developed but are not currently publicly accessible.

Table 5 MySQL tables

Table Name	Utility in RSVP	Additional data
tblCovid_Data	Contains all the 'user' data focusing on behaviors linked to COVID (travel, contact)	Tied to other tables via unique ID
tblHistory	Contains all the 'user' data focusing on preexisting health conditions that could impact the morbidity following a COVID infection	Tied to other tables via unique ID
tblPatient	Contains all the 'user' data focusing on location and age. Location is zip code defined.	Creates the unique ID used in other tables
tblSYNDROMIC_Data	Contains all the 'user' data regarding syndromic responses	Ties to other tables via unique ID
tblSYNDROMIC_Model	Contains the weights and underlying relationships between the data and the ILI considered as part of this model	
tblUSER_Types	Contains options for various types of 'users'. E.g. to allow medical professional to enter data that is mapped differently than that of the general public	Currently not used
ZIPCODES	Contains all the zip codes defined for the United States	Only those for New Mexico currently available for use in the model

The web-based interface has been designed with a simple to use interface that works on computer browsers, tablet browsers, and phone browsers. Not all platforms have been tested, but the basic interface should work on most standard browsers.

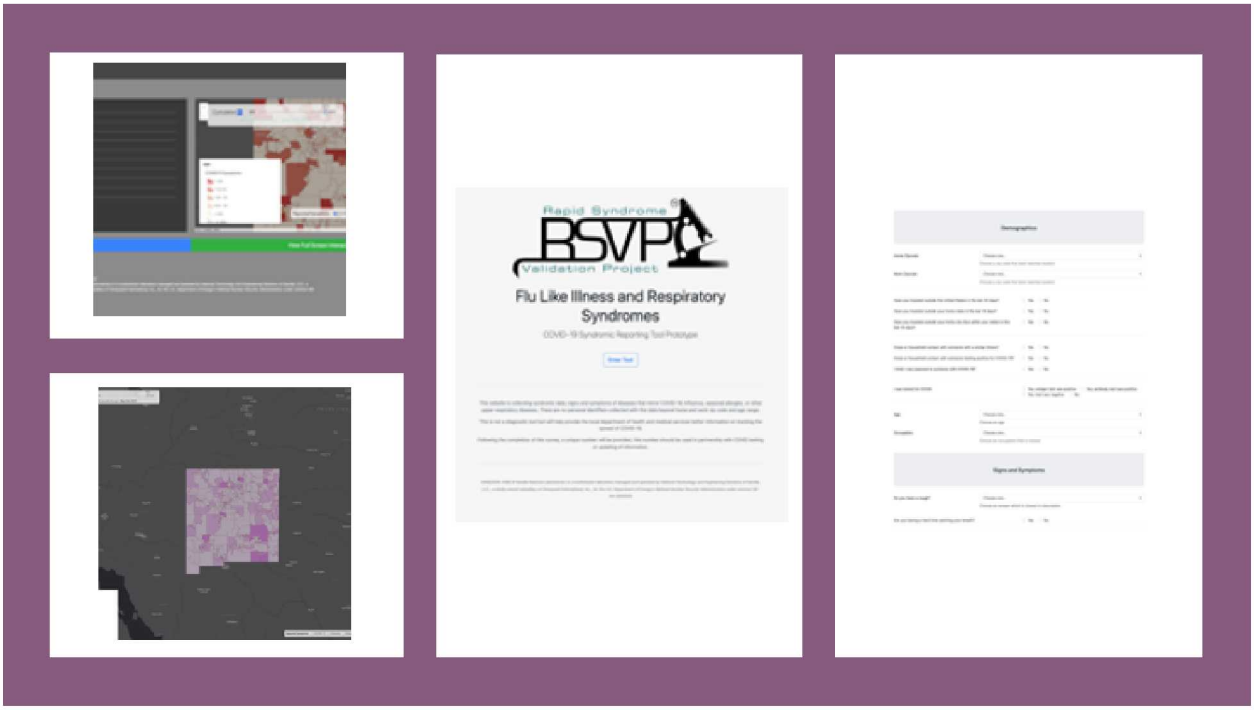


Figure 4 Screen Views of the Web-Application

5. RETURN-TO-WORK PRESCREENING

Conceptually, RSVP or an RSVP-like tool could be used to support prescreening of individuals prior to coming into work, school, or other community location. People with symptoms would be encouraged to remain at home either for just the day of the report or for a longer period depending on the responses. Daily, or prior to activity, screening would reduce risks of individuals transmitting an ILI while waiting for on-site screening such as on-site temperature checks and also reduce delays by individuals waiting for on-site screening.

Based on CDC guidance (May 2020), of the 20-plus questions within the RSVP model, only 12 directly link to an increased risk of COVID and can be used to support direct COVID screening for return-to-work or other activities. Of those 12, new or increased cough and fever are the most recognizable symptoms. To support return to work screening, a 'yes' to either of first two questions should result in a stay at home request or a 'yes' to multiple of the last ten (e.g. 'yes' to new loss of taste or smell and vomiting). The full list of 12 include:

1. New or increased cough?
2. Fever (temperature greater than 100.4˚F)?
3. Shortness of breath or difficulty breathing?
4. Chills and/or repeated shaking with chills?
5. Muscle pain?
6. Headache?
7. Sore throat?
8. New loss of taste or smell?
9. More exhausted than normal (fatigue)?
10. Vomiting?
11. Diarrhea?
12. Travel to a known COVID hotspot within last 14 days or travel on an airplane?

Other questions within the RSVP tool can support distinguishing if one of these 12 is more linked to COVID or another ILI; but for a simple prescreening tool, the more complex calculations may not be warranted.

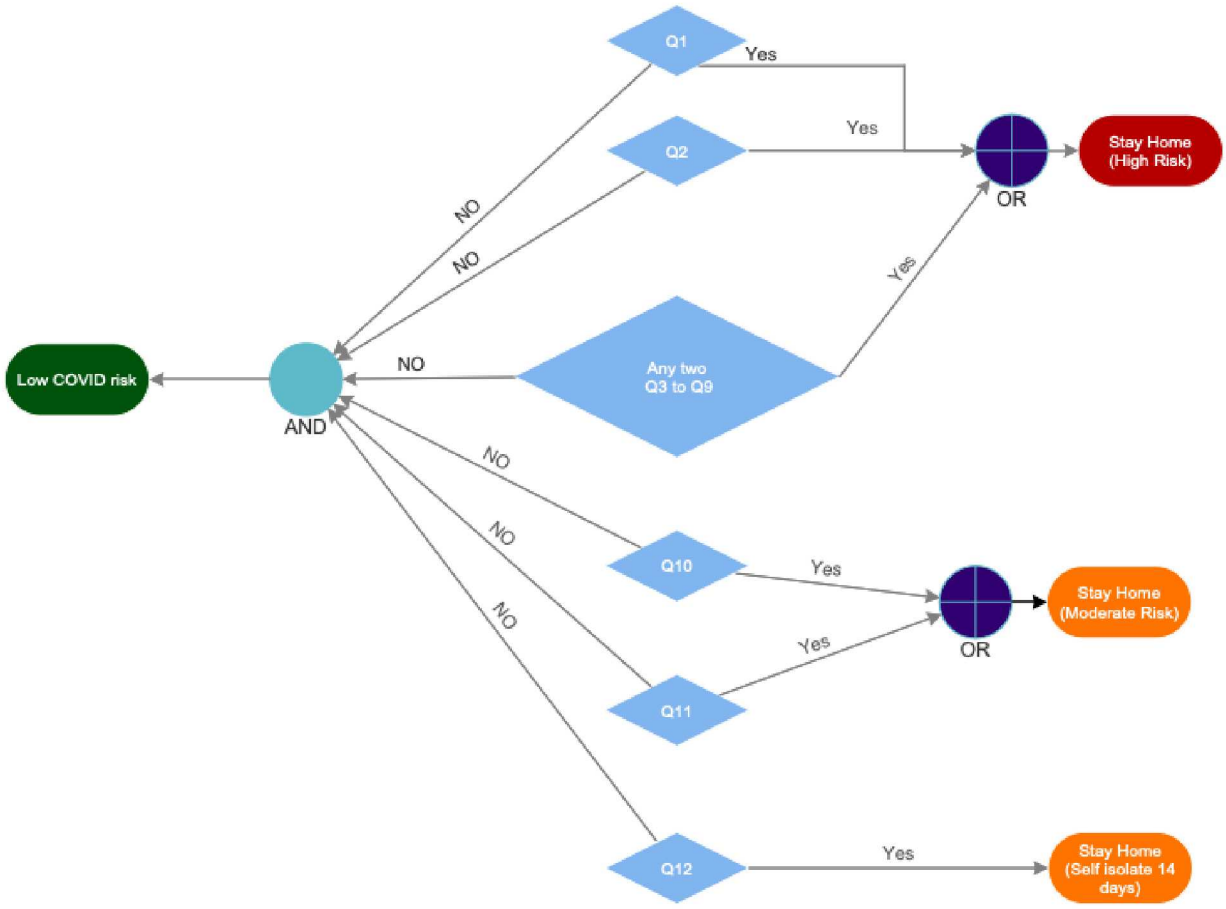


Figure 5 Logic diagram reflecting Pre-Screening Options for an RSVP like tool

6. CON-OPS FOR NMDOH

Sandia National Laboratories

RSVP

Rapid Syndrome Validation Project

FLU-LIKE ILLNESS AND RESPIRATORY SYNDROMES:
COVID-19 SYNDROMIC TOOL REPORTING TOOL PROTOTYPE

The Rapid Syndrome Validation Project (RSVP) was developed to provide the State of NM access to public reports of syndromic data and spatial and temporal analysis. The tool can be also be utilized to support decisionmaking relevant to COVID-19.

The model is in process of being finalized into an online tool that can be directly used by New Mexico Department of Health (NM DOH) without any additional development. To rapidly adopt the tool, NM DOH simply needs to establish a link to it from their COVID-19 informational site and provide the RSVP team a list of users requiring access to the raw data and analysis. Transitioning the tool and model to NM DOH can be formalized at a later date, and may be no more complicated than NM DOH assuming ownership of the current site.

What it Does

The tool currently collects syndromic data from the public, stores this generalized data in a database, and provides backend analysis to support decision making. The backend analysis includes spatial and temporal models which have been coded into the tool.

Additional NM DOH options:

Based on the CDC COVID screen guidance and their answers to the syndromic questions, users can receive additional recommendations to contact a doctor at the data entry phase.

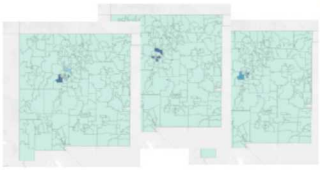
Daily summaries can be emailed to NM DOH–as opposed to being retrieved from the website

Syndrome Entry Interface

- Users input data via a web form (web-app)
- Data includes COVID-19 and other ILL syndromic data
- and meta data to include age ranges and home/work zip

Data Stored in Database

- User recieves unique identifer to be used if they are tested to help NM DOH link syndrome data to patient



Date	Number reports	COVID Max	FLU Max	Allergies Max	URI Max
2020-03-31	17	30.55%	15.7%	9.41%	15.96%
2020-04-01	21	44.49%	23.86%	18.64%	16.64%
2020-04-02	8	39.35%	19.09%	13.10%	12.67%

NM DOH Analysis

- Includes access to raw data and space and time analysis

General Analysis Reports

- General analysis includes generalized space and time graphics and links to NM DOH COVID-19 data

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