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Sensitivity and specificity of surveillance case definitions in detection of influenza and respiratory syncytial virus among hospitalized patients, New Zealand, 2012–2016

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SUMMARY

Background: The WHO is exploring the value of adding RSV testing to existing influenza surveillance systems to inform RSV control programs. We evaluate the usefulness of four commonly used influenza surveillance case-definitions for influenza and RSV surveillance.

Methods: SHIVERS, a multi-institutional collaboration, conducted surveillance for influenza and RSV in four New Zealand hospitals. Nurses reviewed admission logs, enrolled patients with suspected acute respiratory infections (ARI), and obtained nasopharyngeal swabs for RT-PCR. We compared the performance characteristics for identifying laboratory-confirmed influenza and RSV severe acute respiratory infection (SARI), defined as persons admitted with measured or reported fever and cough within 10 days of illness, to three other case definitions: 1. reported fever and cough or shortness of breath, 2. cough and shortness of breath, or 3. cough.

Results: During April-September 2012–2016, SHIVERS identified 16,055 admissions with ARI; of 6374 cases consented and tested for influenza or RSV, 5437 (85%) had SARI and 937 (15%) did not. SARI had the highest specificity in detecting influenza (40.6%) and RSV (40.8%) but the lowest sensitivity (influenza 78.8%, RSV 60.3%) among patients of all ages. *Cough or shortness of breath* had the highest sensitivity (influenza 99.3%, RSV 99.9%) but the lowest specificity

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Declaration of Competing Interest

The authors on this paper have no conflicts of interest to declare.

(influenza 1.6%, RSV 1.9%). SARI sensitivity among children aged <3 months was 60.8% for influenza and 43.6% for RSV–both lower than in other age groups.

Conclusions: While SARI had the highest specificity, its sensitivity was limited, especially among children aged <3 months. *Cough or shortness of breath* was the most sensitive.

Keywords

Respiratory syncytial virus; Influenza; WHO; Clinical; Symptoms; Case definition; Shivers; New Zealand

Background

The World Health Organization (WHO) is exploring the value of adding respiratory syncytial virus (RSV) testing to existing influenza surveillance systems.[1, 2] RSV and influenza cause severe disease and mortality worldwide especially among those at the extremes of age.[3–5] Influenza vaccines are used to prevent influenza,[6] and several influenza antiviral medications are available for treatment.[7] Immunoprophylaxis through humanized monoclonal antibody (mAb) palivizumab is currently the only licensed preventative strategy for RSV. However, due to its requirement of monthly dosing and high costs, its use is limited to high-risk infants.[8] There are however several RSV vaccines, new mAbs, and treatments in clinical trials and preclinical development.[9] In anticipation of new technologies to prevent or treat RSV, there has been a call to strengthen global RSV surveillance[10]; however, the utility of using existing influenza surveillance systems to monitor RSV is not well understood.

The Global Influenza Surveillance and Response System (GISRS) network comprises 143 institutions in 115 WHO member states.[11] The objectives of GISRS are to monitor and characterize influenza viruses globally, identify candidate vaccine viruses for seasonal and pandemic vaccines, and serve as an alert system for the deployment of countermeasures to mitigate epidemics. Surveillance efforts can be costly and require use of case definitions that balance sensitivity and specificity to identify viruses and generate epidemiologic signals to guide response at minimal cost. WHO defines severe acute respiratory infection (SARI) as an illness with measured or reported fever AND a cough with onset within the last 10 days requiring hospitalization, and it recommends the use of this SARI case definition to identify influenza-like illness or illness due to influenza among hospitalized patients.[12, 13]

WHO is piloting the use of GISRS to monitor RSV.[2, 14] The primary objectives of the WHO Global RSV surveillance pilot are to test case definitions for RSV infection in different age groups, assess incremental costs of RSV testing, standardize laboratory procedures, identify RSV seasonality, determine age and risk groups for severe illness, and generate evidence for policy-making. Using a successful, long-established influenza surveillance platform to monitor RSV might cost-effectively accomplish some objectives without disrupting ongoing influenza surveillance. Limited data from phase 1 of the WHO pilot suggest that SARI case definitions are not optimal for RSV surveillance,[15] and few other published studies have investigated the performance of influenza surveillance case definitions for the detection of RSV illnesses.

The WHO pilot data and cohorts in South Africa, Kenya, and India suggest that the SARI case definition fever criterion might exclude 20%–50% of laboratory-confirmed hospitalized influenza and RSV illnesses among very young children,[15–18] and a substantive proportion of RSV illnesses among older adults.[19, 20] SARI and other commonly used influenza surveillance case definitions might therefore be of limited utility for some WHO Global RSV Surveillance objectives. We used data from the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS) study to evaluate the sensitivity and specificity of four variants of the WHO SARI case definition; as secondary objectives, we sought to identify those best suited to monitor influenza viruses sustainably among persons of all ages while fulfilling other RSV pilot objectives.

Methods

The shivers study

SHIVERS data offer an opportunity to evaluate case definitions for inpatient surveillance of laboratory-confirmed RSV and influenza. SHIVERS was a 5-year (2012–2016) multiagency and multidisciplinary study of influenza and other respiratory pathogens in Auckland, New Zealand.[21] SHIVERS conducted hospital-based surveillance for influenza and RSV during the April–September austral winter in four hospitals in the Auckland region, as described previously.[21] New Zealand has a government-subsidized healthcare system and integrated data systems that allowed SHIVERS to account for every acute respiratory overnight hospital admission in the study population.

SHIVERS enrollment and consent processes

During 2012–2016, SHIVERS sought to enroll all patients of any age who met the SARI case definition (measured or history of fever and cough within the previous 10 days), and a systematic sample of up to 50% of those with suspected acute respiratory infection (ARI) who did not meet the SARI case definition (non-SARI ARI). Study nurses working in each hospital reviewed patient logs daily to identify suspected ARI cases using admission diagnoses and clinical judgement.

For all identified ARI case patients (suspected SARI and suspected non-SARI), verbal consent was sought for participation in the study, a case report form was completed, and nasopharyngeal specimens collected for laboratory testing. Laboratory testing of swabs for RSV and influenza detection was conducted at ESR using the US Centers for Disease Control and Prevention's (CDC) RT-PCR protocol; additional influenza testing was conducted using AusDiagnostic PCR.[22] Recruitment of cases occurred during the last week of April through the end of September each year, coinciding with the annual influenza[23] and RSV epidemic periods in New Zealand.[24]

Case definitions used in this analysis

We evaluated variations of the SARI case definition proposed by WHO or used in the literature for influenza and RSV identification.[1, 11] The 2014 WHO definition of SARI cases was persons admitted to hospital with measured or reported fever AND a cough within 10 days of illness onset.[13] We tested three alternate case definitions (Table 1). The first was

Modified SARI case definition: persons admitted to hospital with measured or reported fever AND cough or shortness of breath (heretofore: fever-plus-cough-or-shortness of breath). The second was hospitalized illness with cough, which WHO calls *Extended SARI* in their pilot for Global Respiratory Syncytial Virus Surveillance (heretofore: *cough*).[1] The third was the *Modified ARI* case definition: persons admitted to hospital with cough OR shortness of breath (defined as increased work of breathing). All three required hospitalization within 10 days of illness onset. These last two case definitions exclude fever as a condition for case status. Case definitions were ascertained by study nurses, who used the case report form, observations, interview with the patient or a proxy and medical charts to determine which case definitions were met.

Statistical analysis

We analyzed overnight admissions with ARI that consented, were tested for influenza or RSV, had symptom onset within 10 days of hospital admission, and had no missing data for fever, cough or shortness of breath.

We stratified descriptive analyses by age (< or >= 5 years) and all other analyses by the following age categories: <3 months, 3–5 months, 6–11 months, 12–23 months, 24–59 months, and 5–17, 18–64, and ≥65 years, as presentation of influenza and RSV varies by age.[16] We compared the numbers of cases tested and positive for influenza and RSV by age, sex, ethnicity, underlying medical conditions, time from symptom onset to hospital admission, influenza type/subtype/lineage, and RSV subtype using chi-square tests with the surveyfreq procedure in SAS.

Analyses of the association between specific symptoms and PCR positivity, and of the performance characteristics of the case definitions were weighted to account for the higher proportion consented, tested, and with complete data among those with suspected SARI than those with suspected non-SARI (See Fig. 1 and appendix for calculations). We estimated the relative risk (RR) of PCR-confirmed influenza or RSV for patients with versus without specific symptoms, signs, or combinations of these used in case definitions. We calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each case definition for detection of PCR-confirmed influenza and RSV. We compared these performance characteristics for each case definition across all age groups using chi-square values calculated in the SAS surveyfreq procedure; the null hypothesis was that for each case definition (e.g., SARI), the value for each characteristic (e.g., sensitivity) was the same for each age group. Point estimates and confidence intervals for these analyses were estimated using a bootstrap method by 1) sampling from the original dataset with replacement to create 10,000 pseudo datasets of 16,055 records each, 2) calculating sampling weights and point estimates for case definition performance characteristics in each pseudo dataset, 3) generating distributions of the point estimates from 10,000 datasets, and 4) using the 2.5 and 97.5 percentiles of distribution of the point estimate as the 95% confidence interval. Data management and analyses were performed using SAS® 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethics approval

The New Zealand Ministry of Health Northern A Health and Disability Ethics Committee (HDEC) approved the SHIVERS study (Ethics ref: NTX/11/11/102). CDC's Internal Review Board granted reliance on the Northern A HDEC approval (CDC protocol 6270).

Results

Of 16,055 overnight admissions with ARI, 6374 consented, were tested for influenza or RSV, had symptom onset within 10 days of hospital admission, and had no missing data for fever, cough or shortness of breath. The analytic fractions included 5437 confirmed SARI and 937 confirmed non-SARI cases (6374 total) that were tested for influenza and 5206 confirmed SARI and 920 confirmed non-SARI cases that were tested for RSV (6126 total) (Fig. 1, Table 2). Proportions of RSV- and influenza-positive cases varied by age-group, ethnicity, case definition, underlying medical conditions, time from symptom onset to hospital admission, influenza type/subtype/lineage, and RSV subtype (Table 2).

The RR of laboratory-confirmed influenza and RSV varied by symptoms reported by the patient within several age groups (Table 3). In children aged under 3 months, fever was not associated with RSV (RR 0.9, 95%CI 0.7–1.1), although fever was associated with RSV for all other age groups under 5 years. For children aged under 3 months, cough, difficulty breathing runny nose, and wheezing were all associated with RSV (cough RR 13 0.5 95% CI 2.5–39.3; difficulty breathing RR 2.3 95% CI 1.4–4.0; runny nose RR 1.5 95%CI 1.0–2.3; wheezing RR 2.1 95%CI 1.5–3.0). These symptoms were not associated with RSV in other age groups. Conversely, fever was associated with influenza for children aged under 3 months (RR 4.2 95%CI 1.5–11.7), as well as all other age groups under 5 years, except for 3–5 months.

The majority (n = 5437 [85%]) of the 6374 persons tested for RSV and/or influenza met the WHO SARI case definition of measured or history of fever and cough. Larger proportions of tested patients met the three other case definitions under investigation; 86% (n = 5486) met the fever-plus-cough-or-shortness of breath case definition, 99% had cough (n = 6286), and 99% (n = 6338) met the *cough or shortness of breath* case definition.

For both RSV and influenza, case definitions that included fever were more specific, while case definitions that did not include fever were more sensitive. SARI was the most specific case definition for the detection of influenza- and RSV-positive cases, followed by *fever plus cough or shortness of breath* (SARI specificity = 40.6% and 40.8%, respectively, *fever plus cough or shortness of breath* specificity = 38.3% and 38.3%, respectively) (Table 4). The *cough or shortness of breath* case definition was the most sensitive for detection of influenza and RSV across all age groups. For both influenza and RSV, sensitivity of SARI was lowest and specificity was highest in the youngest and oldest age groups (influenza age <3 months: sensitivity [61%, 95% CI: 40–78] specificity [57%, 95% CI: 55–65]; influenza age > 65 years: sensitivity [63%, 95% CI: 51–77] specificity [52%, 95% CI: 45–57]; RSV age <3 months: sensitivity [60%, 95% CI: 68–76] specificity [41%, 95% CI: 38–43]; RSV age > 65 years: sensitivity [54%, 95% CI: 38–74] specificity [49%, 95% CI: 43–54].

Chi squared tests indicated that values for each performance characteristic (e.g., sensitivity) were not the same across all age groups for each case definition for influenza or for RSV ($p < 0.001$ for each performance characteristic).

Conclusion

We evaluated the performance characteristics of four influenza surveillance case definitions in identifying hospitalized patients with laboratory-confirmed Influenza or RSV illness. The *SARI* and *fever plus cough or shortness of breath* case definitions, both of which include fever, had the highest specificity to identify absence of influenza and RSV illnesses and the highest PPV. Surveillance systems designed to primarily identify viruses for vaccine strain selection might benefit from using these more specific case definitions because samples from these case-patients would be more likely to test positive and yield viruses for vaccine strain selection than those of patients meeting more sensitive case definitions.[1] Systems using such specific case definitions to identify patients for respiratory sampling may require fewer resources to identify a similar number of viruses than systems using more sensitive case definitions. Although less sensitive, specific case definitions still allow public health officials to pursue common surveillance objectives like timing influenza and RSV activity, establishing epidemic thresholds, and identifying risk groups disproportionately seeking care.

Although definitions including fever had the highest specificity, specificity was relatively low for these case definitions in all age groups for both influenza and RSV, including the youngest age group, which is the group of most concern. Utility of these definitions for surveillance for purposes other than virus identification might be improved by adding additional symptoms or testing all children in the highest risk age group for RSV. The public health community should continue to explore the fitness of these and other case-definitions in order to optimize surveillance systems.

The *cough* and *cough or shortness of breath* case definitions, neither of which include fever, had the highest sensitivity for both influenza and RSV. Sensitive case definitions are useful for detecting the majority of influenza or RSV cases. They are useful in cohort studies designed to quantify influenza and RSV burden and cost-effectiveness of prevention or treatment modalities.[25] Highly sensitive case definitions, however, require additional sampling to identify the same number of virus-positive cases compared to more specific case definitions. The relatively low specificity of case definitions like the *fever plus cough or shortness of breath* and *cough* might substantially increase testing cost of virologic surveillance systems, affecting their sustainability.

Our data also indicate lower sensitivity of all four case definitions for influenza and RSV for the youngest and oldest age groups, compared with other age groups. We recommend that persons using respiratory case definitions to estimate influenza and/or RSV burden adjust incidence calculations for the age-appropriate proportion of non-respiratory cases missed by respiratory illness case definitions. Such adjustments will avoid substantially underestimating the potentially preventable or treatable fraction of influenza and RSV infections and cost/benefit ratios of interventions.

Inclusion of measured or history of fever increases the specificity but decreases the sensitivity of case definitions for influenza illnesses.[13] Conversely, adding fever to a case definition lowers sensitivity to identify PCR-confirmed influenza and RSV disease. Platforms currently using respiratory illness case definitions that include measured fever (i.e. *SARI* or *fever plus cough or shortness of breath*) should anticipate missing a proportion of cases, especially among very young children, where RSV and influenza burden is typically highest.[4, 16, 19] A recent study in South Africa estimated the sensitivity for SARI for RSV to be 55%–81% and specificity 27%–54% for all ages, with lowest sensitivity for infants aged < 6 months.[18] Our findings of sensitivity (60%, 95% CI: 68–76) and specificity (41%, 95% CI: 38–43) are similar, as are our findings of SARI having the lowest sensitivity in the youngest age group. Analysis of data from the WHO RSV pilot study found that in infants <6 months, fever was associated with lower odds of testing positive for RSV (OR 0.7; 95% CI: 0.6–0.9)[15] ; similar findings were reported from studies in South Africa and Portugal.[18, 26] In our study in infants aged < 3 months, we found a similar but not statistically significant association between fever and RSV (RR 0.9, 95% CI: 0.7–1.1).

In our study, SARI sensitivity for RSV was only 44% among children aged <3 months, suggesting that in burden of disease estimates, case definitions including fever would result in under-ascertainment of RSV for young age groups. Case definitions with fever, however, have minimal impact on key WHO influenza surveillance objectives such as identifying novel viruses with pandemic potential and establishing epidemic thresholds, timing, and severity. As such, data with fewer false positives, i.e. from more specific case definitions, may be more useful for these surveillance objectives.[13]

Our data suggest clinical diagnosis, based solely on a single symptom or a surveillance case definition, are of limited utility for diagnosing influenza and/or RSV if not followed by laboratory confirmation even during epidemics when their positive predictive value is highest. For example, only one-quarter of persons admitted to the hospital with febrile respiratory illnesses during New Zealand's influenza epidemic period had PCR-confirmed influenza[27]; the other three quarters likely included persons with other etiologies for their respiratory illness and a few influenza false negatives. Conversely, assuming afebrile cases were not influenza illnesses would have misled clinicians into concluding that these cases would not have benefited from influenza antivirals.

Previously published analyses of New Zealand surveillance data from 2012 to 2016 confirm that influenza and RSV viruses cause substantial disease burden.[3, 24] During the New Zealand winter, approximately 2 out of 5 hospitalized children aged <5 years with ARI were RSV positive and more than half (55%) of RSV-positive hospital admissions occurred among infants aged <1 year. These findings are consistent with our data and global models suggesting that young infants aged <6 months have the highest burden of acute lower respiratory infections attributable to RSV.[3] An additional quarter of SHIVERS-enrolled hospitalized patients aged ≥5 years had a laboratory-confirmed influenza ARI. These hospitalizations were likely associated with substantive direct and indirect medical cost to affected families and New Zealand's single-payer healthcare system. Influenza and RSV disease burden estimates can also be used to evaluate the cost benefit of prevention and mitigation practices for other age groups, empiric antivirals for persons hospitalized with

respiratory illness during influenza season, and current or future monoclonal antibodies and vaccines for infants.

Our analyses have important limitations. SHIVERS identified 16,055 overnight admissions with suspected ARIs, of which half did not meet the SARI case definition. Fewer than one in eight non-SARI patients were enrolled and tested in our study. We weighted our analyses to compensate for this differential enrollment, but the weighting required assuming that records with full data were representative of those with missing data, and the validity of this assumption is unknown. Enrolling a greater proportion of non-SARI cases would have improved the accuracy of results. Enrolling only patients who were admitted overnight was done to reduce potential misclassification in hospitalization status, but it might bias the results towards more severe illnesses than if we had not included this condition. The probability of testing positive for influenza might be slightly lower in a set of more severe cases compared with those who seek only outpatient care. Although the four case definitions we studied captured the majority (>80%) of hospitalized patients with suspected ARI, they relied on only three signs and/or symptoms (i.e., fever, cough, and difficulty breathing). Case definitions based on other symptoms were not considered because the literature at the 2012 start of our study suggested these three symptoms were most likely to predict influenza ARI.[21] It is possible that including signs and symptoms like apnea[1, 15] might have identified additional RSV and influenza case patients among the very young, including SPO_2 might have improved case definition performance, and including respiratory rate would be useful to explore the subset of cases that might have lower tract disease. However, the tradeoff is creating a more complicated case definition that may be difficult to implement systematically on a global scale. Although the *cough or shortness of breath* case definition and *cough* are sensitive for identifying influenza, some very young or old individuals with influenza illness can present for care without respiratory symptoms.[28, 29] Multi-country cohort data suggest that one-third of hospitalized influenza-positive infants are discharged with non-respiratory diagnoses including like febrile seizures, sepsis-like-syndrome, or dehydration.[17] Similarly, adults with influenza might not present with fever or have respiratory complaints,[30] and present to hospitals too late to test positive for respiratory viruses through rt-PCR. Presentation of RSV disease can also vary with age; very young children tend to present with lower respiratory tract illness symptoms and wheezing, and fever is less common in this age group compared with older children and adults.[18, 31] Older children tend to present with upper respiratory tract illness symptoms. RSV tends to have less fever and fewer systemic symptoms than influenza thus, clinical case definitions may perform differently for influenza and RSV.[31]

Respiratory virus surveillance is useful in monitoring and anticipating influenza and RSV epidemics, assessing epidemic severity, and evaluating the value of programs to prevent and/or mitigate associated illnesses.[13] Respiratory case definitions typically used or piloted by global stakeholders perform significantly differently among different age groups.[12, 16, 19] Clinicians, public health officials, and research investigators might benefit from understanding their different sensitivity and specificity. Public health officials operating surveillance systems whose primary purpose is to identify viruses for vaccine strain selection might choose case definitions with a high PPV such as *SARI* that are more likely to include laboratory-confirmed influenza and RSV. Conversely, investigators primarily

interested in estimating influenza and/or RSV burden might choose sensitive respiratory (e.g., *cough* or *cough or shortness of breath* case definitions) or even non-respiratory illness case definitions that miss few illnesses, followed by serologic and/or molecular laboratory confirmation. Such a choice is particularly important in platforms designed primarily to assess cost-effectiveness of influenza and RSV prevention or treatment modalities.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available upon request from the corresponding author.

Appendix: Calculations of weights to account for higher consenting and testing of those with suspected SARI than those with suspected non-SARI. Note that weights did not differ by age group among those with suspected SARI, so one weight was used for all ages

	C1: All admissions	C2: Symptom onset 0–10 days	C3: Symptom onset >10 days	C4: Symptom onset unknown or missing	C5: Where symptom duration known, fraction 0–10 days	C6: Estimated number with symptoms 0–10 days*	C7: Non-missing data on age, symptoms, and symptom duration	C8: Consented and tested for flu	C9: Consented and tested for RSV	C10: Weight for analysis of flu**
Suspected SARI										
All ages	7660	5694	34	1925	0.99	7615	5651	5393	5162	1.41
Suspected non-SARI										
<1 year	1703	475	119	1109	0.80	1362	468	434	424	3.14
1–17 years	1458	288	114	1056	0.72	1045	287	252	248	4.14
18–64 years	2122	148	184	1790	0.45	946	147	144	143	6.57
>−65 years	3084	155	139	2790	0.53	1626	153	151	149	10.77

	C1: All admissions	C2: Symptom onset 0–10 days	C3: Symptom onset >10 days	C4: Symptom onset unknown or missing	C5: Where symptom duration known, fraction 0–10 days	C6: Estimated number with symptoms 0–10 days*	C7: Non-missing data on age, symptoms, and symptom duration	C8: Consented and tested for flu	C9: Consented and tested for RSV	C10: Weight for analysis of flu**
Missing	28	10	0	25			0	0	0	
Subtotal	8395	1076	556	6770			1055	981	964	
Total	16,055	6770	590	8695			6706	6374	6126	

*Assumes that the proportion with symptoms 0–10 days is the same in those with missing data as those with non-missing data

**Calculations

C5 = C2/(C2+C3)

C6 = C1*C5

C10 = C6/C8

C11 = C6/C9

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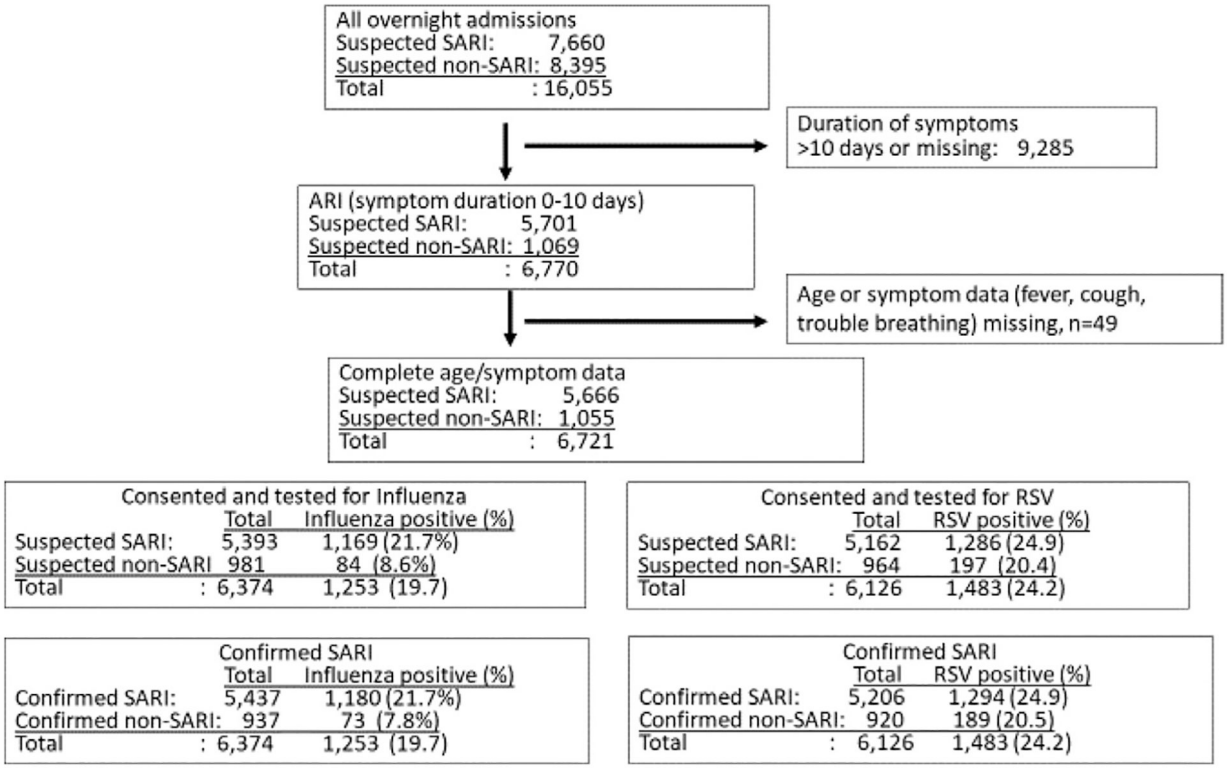

Fig. 1.

Overnight respiratory disease hospital admissions and SHIVERS enrollment in the Auckland region, April-September 2012–2016.

aSARI = severe acute respiratory illness

Table 1

Case definitions used or considered for influenza and respiratory syncytial virus surveillance.[9, 12].

Severe acute respiratory infection (SARI): Measured or history of fever and cough with illness onset within the last 10 days and requiring hospitalization.
Modified SARI: Measured or history of fever and cough or difficulty breathing with illness onset within the last 10 days and requiring hospitalization.
Extended SARI: Cough with illness onset within the last 10 days requiring hospitalization.
Modified ARI: Cough or difficulty breathing with illness onset within the last 10 days and requiring hospitalization.

Table 2

Distribution of respiratory syncytial virus (RSV) and influenza PCR-positive results by age group, patient characteristics and underlying medical conditions in hospitalized patients with acute respiratory illness, Auckland, New Zealand, 2012–2016.

	Age < 5 years (*n* = 2948)*						Age ≥5 years (*n* = 3430)					
	Influenza Positive/ Tested	%	*p*	RSV Positive/ Tested	%	*p*	Influenza Positive/ Tested	%	*p*	RSV Positive/ Tested	%	*p*
Overall	349/2947	11.8		1226/2873	42.7		904/3427	26.4		257/3253	7.9	
Age (years)												
<1	184/1801	10.2	<0.01	812/1757	46.2	<0.01	NA			NA		
1 to 4	165/1146	14.4		414/1116	37.1		NA			NA		
5 to 14	NA			NA			54/306	17.6	<0.01	32/296	10.8	<0.01
15 to 24	NA			NA			94/299	31.4		10/278	3.6	
25 to 44	NA			NA			197/618	31.9		28/564	5	
45 to 64	NA			NA			285/944	30.2		67/897	7.5	
≥ 64	NA			NA			274/1260	21.7		120/1218	9.9	
Sex												
Male	195/1696	11.5	0.5	696/1656	42	0.4	391/1543	25.3	0.2	111/1463	7.6	0.5
Female	154/1251	12.3		530/1216	43.6		513/1884	27.2		146/1787	8.2	
Ethnicity												
Asian	18/243	7.4	0.02	101/231	43.7	<0.01	98/324	30.2	0.5	20/298	6.7	0.3
Māori	99/911	10.9		365/893	40.9		159/666	23.9		36/638	5.6	
Pacific	196/1327	14.8		542/1302	41.6		317/1090	29.1		97/1041	9.3	
European and Other	36/466	7.7		218/446	48.9		330/1347	24.5		104/1273	8.2	
Underlying medical condition												
None	253/2128	11.9	0.9	950/2081	45.7	<0.01	222/605	36.7	<0.01	34/577	5.9	0.05
Asthma	13/143	9.1	0.3	33/134	24.6	<0.01	210/926	22.7	<0.01	71/873	8.1	0.8
Chronic lung disease other than asthma	15/69	21.7	0.01	22/64	34.4	0.2	48/249	19.3	<0.01	13/239	5.4	0.1
Cardiovascular/cerebrovascular disease	11/108	10.2	0.6	44/104	42.3	0.9	263/1155	22.8	<0.01	110/1107	9.9	<0.01
Immunodeficiency/Immunosuppression	4/12	33.3	0.02	3/12	25	0.2	49/238	20.6	0.04	19/226	8.4	0.8
Diabetes	0/2	0	0.6	0/2	0	0.2	160/645	24.8	0.3	57/617	9.2	0.2
1–7 days onset to admission	324/2837	11.4	<0.01	1184/2766	42.8	<0.01	872/3261	26.7	0.03	247/3090	8	<0.01
8–10 days onset to admission	25/110	22.7		42/107	39.3		32/166	19.3		10/163	6.1	

	Age < 5 years (*n* = 2948)*						Age ≥5 years (*n* = 3430)					
	Influenza Positive/ Tested	**%**	***p***	**RSV Positive/ Tested**	**%**	***p***	**Influenza Positive/ Tested**	**%**	***p***	**RSV Positive/ Tested**	**%**	***p***
Influenza type/subtype/lineage**												
Influenza A(H1N1)	99/445	22.2					235/1137	20.7				
Influenza a(h3N2)	144/490	29.4					428/1330	32.2				
Influenza A not subtyped	0/346	0					0/902	0				
Influenza B Victoria	30/376	8					14/916	1.5				
Influenza B Yamagata	26/372	7					112/1014	11				
Influenza B lineage not determined	47/12	12					106/1008	10.5				
RSV subtype***												
A				371/721	51.5	0.01				55/142	38.7	<0.01
B				307/730	42.1					52/153	34	

All estimates in this table are unweighted and represent characteristics of our sample that are not generalizable.

Māori are New Zealand's indigenous population.

* The question asked "How many days before coming to hospital did cough or fever start?" Observations in which the answer to this question was > 10 days were excluded.

** Influenza viruses missing type/subtype/lineage: *n* = 0 for age group <5 years and *n* = 7 for age group ≥5 years.

*** RSV-positive samples missing subtype: *n* = 521 for age group <5 years and *n* = 125 for age group ≥5 years.

Table 3

Association between symptoms of influenza or respiratory syncytial virus infection in hospitalized patients, Auckland, New Zealand, 2012–2016.

	Influenza				RSV			
	Number positive/number tested (% positive)				Number positive/number tested (% positive)			
Symptom	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**
All patients (*n* = 6374)					**All patients (*n* = 6126)**			
Fever (reported/recorded)	1194/5521 (22)	59/853 (7)	2.3	1.7–3.4	1299/5288 (25)	184/838 (22)	1.4	1.2–1.7
Cough	1239/6282 (20)	14/92 (15)	1.5	0.8–3.4	1478/6036 (24)	5/90 (6)	7.2	1.7–28.0
Difficulty breathing	1042/5609 (19)	211/765 (28)	0.7	0.5–0.8	1362/5396 (25)	121/730 (17)	1.5	1.1–1.9
Runny nose	918/3981 (23)	329/1597 (21)	0.9	0.8–1.2	1275/4556 (28)	202/1544 (13)	2.1	1.7–2.6
Wheezing	905/4829 (19)	333/1392 (24)	0.7	0.6–0.9	1200/4648 (26)	221/1331 (17)	1.5	1.2–1.8
Patients aged < 3 months (*n* = 600) *					**Patients aged < 3 months (*n* = 582)** *			
Fever (reported/recorded)	43/387 (11)	8/213 (4)	4.2	1.5–11.7	186/375 (50)	109/207 (53)	0.9	0.7–1.1
Cough	46/577 (8)	5/23 (22)	0.5	0.1–1.7	294/559 (53)	1/23 (4)	13.5	2.5–39.3
Difficulty breathing	38/511 (7)	13/89 (15)	0.6	0.3–1.4	274/495 (55)	21/87 (24)	2.3	1.4–4.0
Runny nose	41/519 (8)	10/79 (13)	0.8	0.3–1.9	263/506 (52)	30/74 (41)	1.5	1.0–2.3
Wheezing	26/433 (6)	25/153 (16)	0.4	0.2–0.8	242/418 (58)	42/150 (28)	2.1	1.5–3.0
Patients aged 3–5 months (*n* = 486) *					**Patients aged 3–5 months (*n* = 474)** *			
Fever (reported/recorded)	39/394 (10)	6/92 (7)	2.1	0.4–8.0	196/386 (51)	21/88 (24)	2.3	1.4–3.8
Cough	45/483 (9)	0/3 (0)	NA	NA	217/471 (46)	0/3 (0)	NA	NA
Difficulty breathing	39/443 (9)	6/43 (14)	0.8	0.2–2.9	203/432 (47)	14/42 (33)	1.6	0.8–3.2
Runny nose	41/425 (10)	4/60 (7)	3.3	0.7–14.3	190/417 (46)	26/56 (46)	1.1	0.7–1.7
Wheezing	39/407 (10)	5/60 (8)	1.9	0.4–8.0	191/397 (48)	17/58 (29)	1.6	0.9–2.9
Patients aged 6–11 months (*n* = 715) *					**Patients aged 6–11 months (*n* = 701)** *			
Fever (reported/recorded)	84/630 (13)	4/85 (5)	4.5	1.1–20.9	283/615 (46)	17/86 (20)	2.5	1.4–4.6
Cough	88/708 (12)	0/7 (0)	NA	NA	299/695 (43)	1/6 (17)	2.6	0.5–8.9
Difficulty breathing	79/667 (12)	9/48 (19)	0.8	0.3–2.0	285/655 (44)	15/46 (33)	1.5	0.8–2.9
Runny nose	82/662 (12)	5/51 (10)	1.8	0.5–6.5	278/649 (43)	21/50 (42)	1.2	0.7–2.0
Wheezing	77/618 (12)	9/70 (13)	1.1	0.4–2.8	258/608 (42)	27/66 (41)	1.2	0.8–1.8
Patients aged 12–23 months (*n* = 606) *					**Patients aged 12–23 months (*n* = 594)** *			
Fever (reported/recorded)	90/550 (16)	1/56 (2)	10.3	1.9–28.2	260/539 (48)	7/55 (13)	5.0	1.9–15.1

	Influenza				RSV			
	Number positive/number tested (% positive)				Number positive/number tested (% positive)			
Symptom	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**
Cough	89/595 (15)	2/11 (18)	1.1	0.2–3.9	265/584 (45)	2/10 (20)	3.0	0.7–10.8
Difficulty breathing	80/556 (14)	11/50 (22)	0.6	0.3–1.5	244/547 (45)	23/47 (49)	1.0	0.6–1.6
Runny nose	83/547 (15)	8/59 (14)	1.4	0.5–4.1	239/537 (45)	28/57 (49)	0.9	0.6–1.4
Wheezing	71/477 (15)	19/105 (18)	0.8	0.4–1.5	206/469 (44)	43/101 (43)	1.1	0.7–1.5
Vomiting	46/333 (14)	45/266 (17)	1.0	0.5–1.5	165/330 (50)	101/258 (39)	1.4	1.0–1.8
Diarrhea	35/201 (17)	56/401 (14)	1.4	0.8–2.3	96/197 (49)	171/393 (44)	1.2	0.9–1.5
Patients aged 24–59 months (*n* = 540) *					**Patients aged 24–59 months (*n* = 522)** *			
Fever (reported/recorded)	72/444 (16)	2/96 (2)	12.9	2.4–45.5	140/426 (33)	7/96 (7)	6.0	2.1–17.7
Cough	71/536 (13)	3/4 (75)	0.2	0.1–0.5	147/518 (28)	0/4 (0)	NA	NA
Difficulty breathing	51/478 (11)	23/62 (37)	0.3	0.1–0.5	133/463 (29)	14/59 (24)	1.3	0.6–2.6
Runny nose	66/456 (14)	8/84 (10)	0.3	0.1–0.5	120/441 (27)	27/81 (33)	0.8	0.5–1.3
Wheezing	47/390 (12)	26/140 (19)	1.8	0.6–5.3	101/377 (27)	42/135 (31)	0.8	0.5–1.2
Vomiting	37/294 (13)	36/243 (15)	0.5	0.3–1.0	88/285 (31)	59/234 (25)	1.2	0.8–1.9
Diarrhea	24/132 (18)	49/404 (12)	1.1	0.6–1.9	39/128 (30)	107/390 (27)	1.2	0.7–1.9
Patients aged 5–17 years (*n* = 369) *					**Patients aged 5–17 years (*n* = 353)** *			
Fever (reported/recorded)	72/294 (24)	2/75 (3)	14.4	2.7–49.6	31/280 (11)	5/73 (7)	2.4	0.6–8.9
Cough	73/364 (20)	1/5 (20)	0.8	0.2–2.8	36/348 (10)	0/5 (0)	NA	NA
Difficulty breathing	48/297 (16)	26/72 (36)	0.4	0.2–0.7	33/283 (12)	3/70 (4)	4.8	0.9–21.1
Runny nose	55/253 (22)	18/114 (16)	1.5	0.7–3.0	22/240 (9)	14/111 (13)	0.8	0.3–1.8
Wheezing	36/239 (15)	36/122 (30)	0.4	0.2–0.7	28/228 (12)	8/118 (7)	1.7	0.5–5.2
Vomiting	35/170 (21)	39/198 (20)	1.3	0.7–2.3	18/166 (11)	18/187 (10)	1.1	0.4–2.6
Diarrhea	13/71 (18)	61/297 (21)	1.3	0.5–2.4	6/66 (9)	30/287 (10)	1.2	0.2–3.0
Sore throat	41/182 (23)	28/162 (17)	1.4	0.7–2.5	21/170 (12)	12/159 (8)	2.0	0.7–5.2
Headache	44/179 (25)	22/157 (14)	2.2	1.1–4.2	12/173 (7)	20/148 (14)	0.7	0.2–1.7
Aching muscles	30/150 (20)	31/174 (18)	1.6	0.8–2.9	11/142 (8)	20/167 (12)	0.9	0.3–2.0
Abdominal pain	32/149 (21)	33/188 (18)	1.6	0.8–2.9	14/146 (10)	19/177 (11)	1.2	0.4–2.8
Nausea	38/153 (25)	31/195 (16)	0.5	0.3–0.9	13/16 (81)	21/187 (11)	1.3	0.5–3.2
Patients aged 18–64 years (*n* = 1798) *					**Patients aged 18–64 years (*n* = 1682)** *			
Fever (reported/recorded)	540/1692 (32)	16/106 (15)	2.2	1.2–4.3	95/1577 (6)	6/105 (6)	1.4	0.4–4.6

	Influenza				RSV			
	Number positive/number tested (% positive)				Number positive/number tested (% positive)			
Symptom	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**	**With Symptom**	**Without Symptom**	**Relative Risk**	**95% CI**
Cough	553/1772 (31)	3/26 (12)	4.0	0.9–16.7	101/1656 (6)	0/26 (0)	NA	NA
Difficulty breathing	476/1551 (31)	80/247 (32)	1.0	0.7–1.4	86/1452 (6)	15/230 (7)	1.3	0.6–2.7
Runny nose	387/391 (99)	167/628 (27)	1.4	1.1–1.7	75/1070 (7)	25/603 (4)	1.6	0.8–3.0
Wheezing	400/1308 (31)	150/460 (33)	0.9	0.7–1.1	74/1223 (6)	25/433 (6)	1.6	0.8–2.8
Vomiting	162/453 (36)	391/1336 (29)	1.4	1.1–1.7	21/412 (5)	79/1262 (6)	0.8	0.4–1.5
Diarrhea	102/280 (36)	444/1494 (30)	1.3	1.0–1.7	14/264 (5)	85/1399 (6)	0.8	0.3–1.6
Sore throat	373/1059 (35)	180/732 (25)	1.6	1.3–2.1	49/977 (5)	52/699 (7)	0.8	0.4–1.3
Headache	458/1385 (33)	93/402 (23)	1.6	1.2–2.2	70/1285 (5)	31/387 (8)	0.8	0.4–1.4
Aching muscles	434/1293 (34)	119/492 (24)	1.5	1.1–2.0	64/66 (97)	37/464 (8)	0.9	0.5–1.5
Abdominal pain	182/527 (35)	368/1255 (29)	1.3	1.0–1.6	32/480 (7)	69/1191 (6)	1.2	0.6–2.0
Nausea	238/243 (98)	314/1077 (29)	0.8	0.7–1.0	37/655 (6)	64/1011 (6)	1.3	0.7–2.2
Patients aged > 65 years (*n* = 1260) *					**Patients aged >65 years (*n* = 1218)** *			
Fever (reported/recorded)	254/1130 (22)	20/130 (15)	1.5	0.9–2.6	108/1090 (10)	12/128 (9)	1.2	0.6–2.7
Cough	274/1247 (22)	0/13 (0)	NA	NA	119/1205 (10)	1/13 (8)	1.4	0.3–4.4
Difficulty breathing	231/1106 (21)	43/154 (28)	0.7	0.4–1.1	104/1069 (10)	16/149 (11)	1.0	0.4–2.2
Runny nose	163/728 (22)	109/522 (21)	1.0	0.6–1.5	88/696 (13)	31/512 (6)	2.0	0.9–4.2
Wheezing	209/957 (22)	63/282 (22)	1.0	0.6–1.6	100/928 (11)	17/270 (6)	1.6	0.6–3.9
Vomiting	50/190 (26)	221/1062 (21)	2.1	1.2–3.2	13/183 (7)	107/1027 (10)	0.5	0.2–1.0
Diarrhea	31/161 (19)	239/1083 (22)	1.2	0.7–1.9	19/158 (12)	101/1045 (10)	0.9	0.5–1.6
Sore throat	125/529 (24)	147/719 (20)	1.2	0.8–1.8	67/504 (13)	52/703 (7)	1.9	0.9–3.6
Headache	160/667 (24)	110/576 (19)	1.3	0.8–2.0	72/644 (11)	45/558 (8)	1.7	0.8–3.3
Aching muscles	144/629 (23)	127/619 (21)	1.0	0.6–1.5	63/610 (10)	56/596 (9)	1.5	0.7–2.7
Abdominal pain	53/247 (21)	217/993 (22)	1.2	0.7–1.9	28/239 (12)	91/959 (9)	0.9	0.5–1.6
Nausea	78/357 (22)	193/891 (22)	0.8	0.5–1.2	41/349 (12)	77/858 (9)	0.8	0.4–1.4

* The n in each age category denotes number of consented patients who had cough or fever within 10 days of admission and were tested for influenza or RSV; values for n are unweighted, relative risk estimates were calculated using weights to account for differential sampling of SARI vs non-SARI patients (appendix).

Table 4

Performance of case definitions in the identification of influenza and respiratory syncytial virus among hospitalized patients, Auckland, New Zealand, 2012–2016. *.

Case definition**	Influenza Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Patients of all ages (*n* = 6374)				
Fever and cough (SARI)	78.8 (73–84)	40.6 (39–43.8)	21.7 (20.4–23.1)	90.1 (87.3–93.1)
Fever and cough or shortness of breath (Modified SARI)	80.7 (75–85.9)	38.3 (36.8–41.7)	21.5 (20.1–22.9)	90.5 (87.5–93.5)
Cough (Extended SARI)	97.4 (95.1–98.8)	4.2 (3.1–5.6)	17.6 (15.9–18.8)	88.5 (79.2–94.9)
Cough or shortness of breath (Modified ARI)	99.3 (98–99.9)	1.6 (1–2.4)	17.5 (15.8–18.7)	91.2 (77.1–98.6)
Patients aged < 3 months (*n* = 600)				
Fever and cough (SARI) ***	60.8 (39.4–77.7)	57.2 (54.9–65)	10.5 (6.9–14.8)	94.6 (90.4–97.7)
Fever and cough or shortness of breath (Modified SARI)	70.2 (48.2–86.2)	56.2 (53.7–64)	11.7 (7.8–16.5)	95.8 (91.7–98.5)
Cough (Extended SARI)	85.5 (66.6–97.4)	4.8 (2.6–8.2)	6.9 (4.5–9.5)	80 (56.3–96.6)
Cough or shortness of breath (Modified ARI)	95.1 (80.3–100)	3.5 (1.7–6.4)	7.5 (4.9–10.3)	89.7 (62–100)
Patients aged 3–5 months (*n* = 486)				
Fever and cough (SARI)	77.7 (54.2–93.8)	33.3 (29.3–42.6)	9.8 (6.5–13.8)	94.1 (86.7–98.7)
Fever and cough or shortness of breath (Modified SARI)	77.7 (54.2–93.8)	32.9 (28.9–42.1)	9.8 (6.4–13.8)	94 (86.6–98.7)
Cough (Extended SARI)	100 (100–100)	1 (0.2–3.3)	8.7 (5.7–12.2)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	0.7 (0.2–2.7)	8.7 (5.7–12.2)	100 (100–100)
Patients aged 6–11 months (*n* = 715)				
Fever and cough (SARI)	92.2 (78.3–99)	24.2 (21–32.2)	13.4 (10.2–16.9)	96 (89.4–99.6)
Fever and cough or shortness of breath (Modified SARI)	92.2 (78.3–99)	22.8 (19.6–30.6)	13.2 (10–16.7)	95.8 (88.7–99.5)
Cough (Extended SARI)	100 (100–100)	1.8 (0.5–4.4)	11.6 (8.6–14.5)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	0.5 (0.1–2)	11.4 (8.5–14.3)	100 (100–100)
Patients aged 12–23 months (*n* = 606)				
Fever and cough (SARI)	92.3 (77.5–100)	27.7 (22.4–35.9)	16.2 (12.5–20.4)	96 (87.9–100)
Fever and cough or shortness of breath (Modified SARI)	98.5 (87.6–100)	24.7 (19.4–32.6)	16.5 (12.7–20.8)	99.1 (92.4–100)
Cough (Extended SARI)	95.3 (82.5–100)	3.8 (1.3–7.7)	13 (9.8–16.4)	84 (47.1–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	0.5 (0.2–2.2)	13.3 (10–16.8)	100 (100–100)
Patients aged 24–59 months (*n* = 540)				

Fever and cough (SARI)	84.6 (66–96.8)	41 (35.9–49.5)	15.7 (11.6–20.3)	95.3 (88.7–99.2)
Fever and cough or shortness of breath (Modified SARI)	88 (70.1–98.5)	40.5 (35.5–49.1)	16.2 (12–21)	96.3 (89.9–99.6)
Cough (Extended SARI)	91.3 (74.9–100)	0.5 (0.2–2.2)	10.6 (7.6–13.8)	33.3 (6.7–100)
Cough or shortness of breath (Modified ARI)	94.6 (79.9–100)	NA	11 (7.8–14.3)	NA
Patients aged 5–17 years (*n* = 369)				
Fever and cough (SARI)	91 (73.4–100)	48.5 (41.6–58.1)	24.4 (18.3–30.7)	96.7 (89.6–100)
Fever and cough or shortness of breath (Modified SARI)	91 (73.4–100)	48.5 (41.6–58.1)	24.4 (18.3–30.7)	96.7 (89.6–100)
Cough (Extended SARI)	98.2 (85–100)	2.3 (0.3–6.4)	15.4 (11–19.8)	87.5 (28.6–100)
Cough or shortness of breath (Modified ARI)	98.2 (85–100)	1.7 (0.3–5.4)	15.3 (10.9–19.8)	83.3 (20–100)
Patients aged 18–64 years (*n* = 1798)				
Fever and cough (SARI)	85.6 (78.7–92.5)	32.5 (26.3–36.8)	32.2 (29.4–35)	85.8 (77.5–92.5)
Fever and cough or shortness of breath (Modified SARI)	87.9 (81.4–94.2)	29.6 (23.7–34)	31.8 (29–34.8)	86.8 (78.2–93.6)
Cough (Extended SARI)	98 (94–100)	6.5 (3.5–9.9)	28.2 (25.3–31.4)	89.6 (70.4–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	3.6 (1.5–6.3)	28 (25.2–31.3)	100 (100–100)
Patients aged ≥ 65 years (*n* = 1260)				
Fever and cough (SARI)	62.7 (50.5–77)	51.8 (44.9–57)	22.6 (19.7–25.8)	86.1 (78.1–92.5)
Fever and cough or shortness of breath (Modified SARI)	62.7 (50.5–77)	48 (40.8–53.5)	21.3 (18.4–24.5)	85.1 (76.6–91.9)
Cough (Extended SARI)	100 (100–100)	5.4 (2.3–9.6)	19.3 (15.6–23.7)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	0.5 (0.2–2)	18.5 (14.9–22.7)	100 (100–100)
	RSV			
	Sensitivity (95% CI)	**Specificity (95% CI)**	**PPV (95% CI)**	**NPV (95% CI)**
Patients of all ages (*n* = 6126)				
Fever and cough (SARI)	60.3 (67.7–76)	40.8 (38.1–43.4)	24.8 (23.4–26.3)	84.2 (81.1–87)
Fever and cough or shortness of breath (Modified SARI)	72.7 (68.5–76.9)	38.3 (35.6–40.9)	24.3 (22.8–25.8)	83.7 (80.6–86.8)
Cough (Extended SARI)	99 (97.5–99.9)	4.9 (43.4–6.3)	22.1 (20.6–23.6)	94.8 (87–100)
Cough or shortness of breath (Modified ARI)	99.9 (99.5–100)	1.9 (1.2–2.8)	21.7 (20.2–23.3)	98.3 (92.3–58.6)
Patients aged < 3 months (*n* = 582)				
Fever and cough (SARI)***	43.6 (36.5–51.3)	60.3 (53–67.2)	51.9 (45.3–58.6)	52.2 (44.1–60.3)
Fever and cough or shortness of breath (Modified SARI)	43.6 (36.5–51.3)	56.8 (49.2–64)	49.8 (43.2–56.5)	50.7 (42.3–58.9)
Cough (Extended SARI)	99.5 (97.7–100)	11.6 (6.4–17.5)	52.5 (46.9–58.1)	95.8 (81.8–100)
Cough or shortness of breath (Modified ARI)	99.5 (97.7–100)	7.6 (3.4–12.6)	51.4 (45.9–57)	93.7 (73.2–100)

Patients aged 3–5 months (*n* = 474)				
Fever and cough (SARI)	81.3 (72.4–89.4)	45.1 (36.6–53.3)	51.3 (45.1–57.6)	77.2 (66–87.1)
Fever and cough or shortness of breath (Modified SARI)	81.3 (72.4–89.4)	44.4 (35.9–52.6)	51 (44.8–57.3)	76.9 (65.5–86.9)
Cough (Extended SARI)	100 (100–100)	2 (0.3–5.1)	42 (36.2–47.9)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	1.5 (0.3–4.1)	41.9 (36–47.7)	100 (100–100)
Patients aged 6–11 months (*n* = 701)				
Fever and cough (SARI)	87.9 (81.1–93.7)	100 (26–39.8)	46.3 (41.4–51.3)	39.9 (69.5–89.9)
Fever and cough or shortness of breath (Modified SARI)	88.5 (82–94.3)	31.5 (24.6–38.4)	46 (41–51)	80.6 (69.5–90.4)
Cough (Extended SARI)	99.3 (97.2–100)	2.2 (0.4–5)	40.1 (35.4–44.8)	83.6 (35.7–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	1 (0.2–2.9)	39.9 (35.2–44.7)	100 (100–100)
Patients aged 12–23 months (*n* = 594)				
Fever and cough (SARI)	91 (83.6–97.1)	36.8 (28.3–45.3)	48.6 (43.3–53.9)	86.1 (74.5–95.4)
Fever and cough or shortness of breath (Modified SARI)	93 (86.3–98.2)	32.9 (24.4–41.3)	47.7 (42.4–53)	87.7 (75.7–96.8)
Cough (Extended SARI)	98 (93.7–100)	5.2 (1.5–10.3)	40.4 (35.1–45.7)	79.9 (42.9–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	1 (0.3–3.2)	39.8 (34.5–45)	100 (100–100)
Patients aged 24–59 months (*n* = 522)				
Fever and cough (SARI)	87.7 (76.4–96.8)	48.3 (40.7–55.5)	33.1 (27.4–38.9)	93 (85.8–98.3)
Fever and cough or shortness of breath (Modified SARI)	87.7 (76.4–96.8)	47.2 (39.6–54.5)	32.6 (27.1–38.5)	92.9 (85.5–98.2)
Cough (Extended SARI)	100 (100–100)	2.1 (0.2–5)	22.9 (18.4–27.8)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	1.2 (0.2–3.4)	22.8 (18.2–27.6)	100 (100–100)
Patients aged 5–17 years (*n* = 353)				
Fever and cough (SARI)	69.7 (44.4–93.5)	45.4 (37–53.4)	11.2 (6.8–16.2)	93.5 (85.6–98.9)
Fever and cough or shortness of breath (Modified SARI)	69.7 (44.4–93.5)	45.4 (37–53.4)	11.2 (6.8–16.2)	93.5 (85.6–98.9)
Cough (Extended SARI)	100 (100–100)	3.2 (0.5–7)	9.4 (5.7–14)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	2.6 (0.3–6.1)	9.4 (5.6–13.9)	100 (100–100)
Patients aged 18–64 years (*n* = 1682)				
Fever and cough (SARI)	78.8 (60.9–94.4)	27.7 (23.2–32.3)	6.2 (4.7–7.7)	95.4 (90.2–99)
Fever and cough or shortness of breath (Modified SARI)	78.8 (60.9–94.4)	24.9 (20.4–29.4)	6 (4.6–7.5)	94.9 (89.2–98.9)
Cough (Extended SARI)	100 (100–100)	5.8 (3.3–8.6)	6.1 (4.5–7.9)	100 (100–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	2.9 (1.2–5)	5.9 (4.3–7.7)	100 (100–100)
Patients aged > 65 years (*n* = 1218)				
Fever and cough (SARI)	53.9 (37.7–73.7)	48.7 (42.7–54.3)	9.9 (7.7–12.2)	90.6 (84–96.1)

Fever and cough or shortness of breath (Modified SARI)	57.4 (40.3–77.2)	45.6 (39.4–51.5)	9.9 (7.6–12.8)	90.8 (83.9–96.2)
Cough (Extended SARI)	96.4 (85.2–100)	4.6 (1.9–8.3)	9.7 (6.8–13.2)	92.3 (66.7–100)
Cough or shortness of breath (Modified ARI)	100 (100–100)	0.6 (0.2–1.9)	9.7 (6.8–13.2)	100 (100–100)

All results in this table are weighted

*Estimates were calculated using weights to account for differential sampling of SARI vs non-SARI patients (appendix).

**Including symptom onset within 10 days of hospitalization.

***p values for heterogeneity across all age groups for sensitivity, specificity, PPV and NPV for each case definitions were <0.001 for both influenza and RSV.