



WHO RSV surveillance, performance of case definitions

Jocelyn Moyes

Center for Respiratory Diseases and Meningitis,
National Institute for Communicable Diseases,
Johannesburg, South Africa

Background

- Case definitions used in RSV surveillance based on influenza case definitions
- A significant proportion of RSV- associated LRTI patients, particularly very young and the elderly, may not present with fever
- Unpublished data (Rha et al) describe that case definition excluding fever are more sensitive in predicting RSV infection

Methodology: Case definitions

- Hospitalised patients
 - WHO SARI case definition
 - Onset of symptoms with 10 days
 - Cough
 - Fever ($\geq 38^{\circ}\text{C}$) or history of fever
 - Expanded SARI case definition
 - Onset of symptoms with 10 days
 - Cough
 - Additional case definition in those < 6 months of age
 - Apnoea
 - Neonatal sepsis
- Outpatients (ARI)
 - ARI
 - Onset within 10 days
 - Measure fever ($\geq 38^{\circ}\text{C}$)
 - Cough and one of following (coryza, sore throat, shortness of breath)
 - Influenza like illness
 - Onset with 10 days
 - Cough and fever
 - Influenza like illness no fever
 - Onset with 10days
 - Cough

Methodology: Patients included in this analysis

- Duration of symptoms 0-10 days included
- Excluded cases with no RSV result
- Recoded cases definitions by symptoms
- Age groups defined as per sample selection
 - 0-<6m:
 - 6m to <5years:
 - 5 years to 64 years:
 - 65years=)

Results: Numbers included by case definition

- Hospitalised patients=5333
 - SARI: 4117
 - SARI no fever: 4725
 - Apnoea (<6 months): 160
 - Sepsis (<6 months) : 259
- Outpatients=1251
 - ILI : 996
 - ILI no fever: 1165
 - ARI:523

Table 1: Clinical characteristics of patients by RSV detection , WHO RSV surveillance 2017, hospitalized patients

	RSV positive n/N (%)	RSV negative n/N (%)	OR (95% CI)
Age			
< 6 m	386/1175 (33)	1014/4158 (24)	3.1 (2.5-4.0)
6 m to 4 y	309/1175 (26)	1102/4158 (27)	2.3 (1.8-2.9)
5 to 64 y	106/1175 (9)	868/4158 (21)	Ref
≥ 65	374/1175 (32)	1174/4158 (28)	2.6 (2.1-3.3)
Cough	1120/1145 (98)	3605/4077 (88)	5.9 (3.9-8.8)
Wheeze	325/761 (43)	937/3192 (29)	1.8 (1.5-2.1)
Fever measured	925/1114 (83)	3268/4074 (80)	1.2 (1.0-1.4)
History of fever	461/934 (49)	1879/3233 (58)	0.7 (0.6-0.8)
Chest retractions	363/612 (59)	862/2129 (54)	2.1 (1.8-2.6)
Shortness of breath	672/1003 (67)	1973/3953 (50)	2.1 (1.8-2.6)

Table 2: Clinical characteristics of patients by RSV detection , WHO RSV surveillance 2017, outpatients

	RSV positive n/N (%)	RSV negative n/N (%)	OR (95% CI)
Age			
< 6 m	2/88(2)	20/1163(2)	3.2 (0.7-15.0)
6 m to <5 y	37/88 (42)	269/1163 (23)	4.5 (2.5-8.1)
5 to 64 y	17/88 (19)	552/1163 (47)	Ref
≥ 65 y	32/88 (36)	332/1163 (28)	3.2 (1.8-6.0)
Cough	87/88 (99)	1078/1163 (93)	6.3 (0.8-46.4)
Wheeze	0/88 (0)	18/1028 (2)	-----
Coryza	3 /4 (75)	15/175 (9)	32.0 (3.0-327)
Sore throat	58/85 (68)	464/1152 (40)	0.7 (0.4-1.1)
Fever measured	83/88 (94)	984/1157 (85)	2.9 (1.2-7.3)
History of fever	57/88 (57)	809/1158 (70)	0.8 (0.5-1.3)
Chest retractions	1 /3 (33)	9/46 (20)	2.1 (0.2-25.3)
Shortness of breath	11/88 (13)	112/1158 (10)	1.3 (0.7-2.6)

Table 3: clinical predictors frequency and associations in RSV patients by age group, hospitalised patients

	<6 months		6 months to < 5 years		5 to 64 years		65 + years	
	RSV+ n/N (%)	OR (95% CI)	RSV+ n/N	OR (95% CI)	RSV+ n/N	OR (95% CI)	RSV+ n/N	OR (95% CI)
Cough	382/386 (99)	24 (8.8-64.8)	302/307 (98)	2.6 (1.0-6.7)	106/106 (100)		330/346 (95)	3.0 (1.8-5.1)
Wheeze	161/357 (45)	1.5 (1.2-1.9)	90/188 (48)	1.5 (1.1-2.0)	5/24 (21)	1.5 (0.6-4.2)	69/192 (36)	1.8 (1.3-2.5)
Short of breath	11/386 (30)	2.3 (1.8-2.9)	211/291 (73)	1.9 (1.5-2.7)	82/101 (81)	5.4 (3.2-9.0)	122/225 (54)	1.0 (0.8-1.4)
Chest retractions	206/356 (58)	2.2 (1.7-2.8)	89/154 (60)	1.7 (1.2-2.4)				
Fever measured	376/386 (97)	2.0 (1.0-4.0)	278/300 (93)	2.9 (1.8-4.6)	86/101 (85)	1.3 (0.7-2.2)	185/327 (57)	1.3 (0.7-2.2)
Fever history	179/353 (51)	1.0 (0.8-1.3)	137/281 (49)	0.6 (0.5-0.8)	18/101 (18)	0.2 (0.1-0.3)	127/199 (64)	1.0 (0.8-1.4)

Table 4: Clinical predictors frequency and associations in RSV + patients, by age group, outpatient patients

	<6 months		6 months to < 5 years		5 to 64 years		65 + years	
	RSV+ n/N(%)	OR (95% CI)	RSV+ n/N	OR (95% CI)	RSV+ n/N	OR (95% CI)	RSV+ n/N	OR (95% CI)
Cough	2/2 (100)		37/37 (100)		31/32 (97)	2.5 (0.3-19.2)	31/32 (97)	2.5 (0.3-19.2)
Wheeze	0/2 (0)		0/37 (0)		0/31		0/32	
Coryza	1 / 2 (50)	3.0 (0.2-57.4)	1/1 (100)		1/1		1/1	
Sore throat			9/37 (24)	0.8 (0.4-1.8)	3/30 (10)	0.6 (0.2-2.2)	6/32 (19)	2.2 (0.9-5.8)
Chest retractions	1 / 2 (50)	1.8 (0.1-34.4)	0/1 (0)					
Short of breath	1 / 2 (50)	0.6 (0.03-10.0)	3/37 (9)	0.6 (0.03-10.0)	6/32 (19)	2.2 (0.9-5.8)	6/32 (19)	2.2 (0.9-5.8)
Fever measured	2/2 (100)		36/37 (97)	8.2 (1.1-61.4)	29/32 (91)	2.2 (0.6-7.4)	29/32 (91)	2.2 (0.6-7.4)
Fever history	2/2 (100)		24/37 (65)	0.8 (0.4-1.7)	23/32 (72)	0.9 (0.4-2.0)	23/32 (72)	0.9 (0.4-2.0)

Table 5: Sensitivity and specificity of case definition in predicting RSV infection, by age group, hospitalised patients

Hospitalised patients			
Age group	Case definition	Sensitivity % (95% CI)	Specificity % (95% CI)
< 6 months	SARI	98 (96-99)	22 (19-24)
RSV detection 386/1400 (28%)	SARI no fever	99 (97-100)	20 (18-23)
	Apnoea	7 (5-10)	91 (88-92)
	Sepsis	7 (5-10)	81 (78-83)
6 months to 5 years	SARI	92 (78-92)	15 (13-19)
RSV detection 309/1411 (22)	SARI no fever	98 (95-100)	5 (6-4)
5 years to 64 years	SARI	86 (78-92)	21 (19-24)
RSV detection 106/974 (11)	SARI no fever	100 (97-100)	11 (9-13)
65 years +	SARI	56 (50-61)	37 (34-40)
RSV detection 374/1548 (24)	SARI no fever	88 (85-91)	17 (15-20)

Table6: Sensitivity and specificity of case definition in predicting RSV infection, by age group, outpatients

Hospitalised patients			
Age group	Case definition	Sensitivity % (95% CI)	Specificity % (95% CI)
< 6 months	ILI	100 (16-100)	85(62-75)
2/22 (9)	ILI no fever	100 (15-100)	10 (1-37)
	ARI	100 (15-100)	25 (7-49)
6 months to 5 years	ILI	97 (86-99)	25 (20-31)
37/306 (12)	Ili no fever	100 (91-100)	7 (5-11)
	ARI	35 (20-52)	69 (63-75)
5 years to 64 years	ILI	94 (71-100)	15 (81-100)
17/569 (3)	ILI no fever	100 (81-100)	7 (5-9)
	ARI	76 (50-93)	42 (37-46)
65 years +	ILI	88 (71-97)	26 (21-31)
32/352 (9)	ILI no fever	97 (84-100)	8 (5-12)
	ARI	25 (12-43)	80 (75-84)

Conclusion

- Age group RSV detection rates are consistent with published data
- Classic symptoms predict RSV (cough, wheeze, shortness of breath and chest indrawing)
- History of fever appears to be poor predictor of RSV infection
- Outpatient data numbers are small as associations are not as strong
- Sensitivities are generally higher in the case definitions with no fever
- Numbers are very small in apnoea and sepsis but case definitions are strongly specific.

Conclusions

- Application of case definitions is a concern
- Collection of symptoms defining case definition important
- New analysis with age group < 3 months and 3-6 months, 1-2 years
- Consider analysing duration of symptoms 7 days or less
- Data
 - Monthly data checks with queries to sites
 - 6 monthly analysis to confirm application of case definitions

Data cleaning findings

- No symptom duration available (missing date of onset or date of sample collection)(1215/8731 (14%))
- No RSV results (76/8731 (0.1%))
- Hospitalization poorly classified (ILI in hospital SARI as not hospitalized)
- Cough missing (261/6941 (4%))
- Fever/not missing (242/6941 (4%))
- SARI with no fever (measured or history)=646/1115 (58%)
- SARI with no cough=127/1731 (7%)
- SARI no fever with no cough=109/1123 (10%)
- ILI no fever 237/281 have fever (84%)
- ILI with no cough (66/1171 (0.1%))
- Recode hospitalization and then dropped if missing (357/6941)

Summary of case definition

- SARI (cough and fever) 4117/5333 (77%)
- SARI (cough only) 4173/5333 (89%)
- Apnea (<6 months) 112/1273 (9%)
- Sepsis (<6 months) 188/1195 (16%)
- ILI :
- ILI no fever
- ARI