



Virology

Survey of diagnostic testing for respiratory syncytial virus (RSV) in adults: Infectious disease physician practices and implications for burden estimates☆

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ABSTRACT

Respiratory syncytial virus (RSV) often causes respiratory illness in adults. Over 40 RSV vaccine and monoclonal antibody products are currently in preclinical development or clinical trials. Because RSV diagnostic practices may impact disease burden estimates, we investigated infectious disease physicians' RSV diagnostic practices among their adult patients.

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1. Introduction

Respiratory syncytial virus (RSV) is a common respiratory virus that causes cold-like symptoms in otherwise healthy adults. Older adults, persons with underlying chronic cardiopulmonary disease, and immunocompromised individuals are at higher risk for severe disease when infected with RSV (Falsey et al., 2005, 2014). In the United States, RSV accounts for approximately 177,000 hospitalizations and 14,000 deaths among adults 65 years and older (Falsey et al., 2005). Prophylaxis with palivizumab is available for use in high-risk pediatric patients to reduce severe acute lower respiratory tract infections (The Impact-RSV Study Group, 1998; Englund and Chu, 2017). However, there is currently no specific antiviral or vaccine for RSV for any age group, which may discourage use of RSV diagnostic testing since a result does not change clinical management (Centers for Disease Control and Prevention, 2016; Sundaram et al., 2014; Talbot et al., 2016; Walsh et al., 2007).

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There are several types of RSV diagnostic tests available, including nucleic acid amplification tests (NAAT) (including polymerase chain reaction [PCR]), rapid antigen detection tests (RADT), and fluorescent antibody assays. These tests vary in sensitivity, specificity, and their usefulness in different populations. NAATs provide greater sensitivity as compared to RADTs for RSV infected individuals, particularly for older adult populations (Ginocchio and McAdam, 2011; Talbot and Falsey, 2010). For example, one systematic review and meta-analysis estimated the pooled sensitivity of RADTs in children to be 81% [95% CI, 78–84%]; however, the pooled sensitivity in adults was estimated to be 29% [95% CI, 11–48%] (Chartrand et al., 2015).

RSV often circulates during the same time periods as other respiratory viruses, such as influenza and human metapneumovirus (HMPV). These viruses have similar clinical presentations to RSV infection and also cause a significant number of hospitalizations in older adults (Falsey et al., 2005; Talbot et al., 2016; Walsh et al., 2007; Widmer et al., 2012). While RSV test results are not routinely used to inform treatment options, they can be important for distinguishing between circulating respiratory viral infections. In addition, while a positive RSV test does not rule out a bacterial infection, it can help a clinician identify a viral etiology and thereby decrease the suspicion of bacterial infections. In turn, this may impact inappropriate use of antibiotics (Centers for Disease Control and Prevention, 2013; Talbot et al., 2016).

Table 1
Comparison of responders and non-responders.

	Responders N = 543 n (%)	Non-responders N = 728 n (%)
Region		
Northeast	134 (24.7)	143 (19.6)
South	153 (28.2)	208 (28.6)
Midwest	139 (25.6)	177 (24.3)
West	111 (20.4)	188 (25.8)
Puerto Rico	6 (1.1)	12 (1.7)
Years since infectious disease fellowship		
<5	90 (16.6)	140 (19.2)
5–14	175 (32.2)	277 (38.1)
15–24	103 (19.0)	149 (20.5)
≥25	175 (32.2)	162 (22.3)
Employment		
Hospital/clinic	182 (33.5)	216 (29.7)
Private/group practice	134 (24.7)	231 (31.7)
University/medical school	180 (33.2)	249 (34.2)
Veterans Affairs (VA) and military	42 (7.7)	31 (4.3)
State government	5 (0.9)	1 (0.1)
Primary hospital type		
Community	147 (27.1)	246 (33.8)
VA/Department of Defense (DOD)	43 (7.9)	38 (5.2)
Non-university teaching	138 (25.4)	170 (23.4)
City/county	27 (5.0)	31 (4.3)
University	188 (34.6)	243 (33.4)

Over 40 RSV vaccine and monoclonal antibody products are currently in development (PATH, 2017), and multiple antivirals are currently under investigation in clinical trials. It is important to understand current clinical RSV diagnostic practices among physicians, as these practices can impact RSV burden estimates, likely by underestimating when counting RSV laboratory-positive patients.

We conducted a survey among infectious disease physicians who currently diagnose and treat adult patients with acute respiratory illnesses (ARIs) in order to understand current RSV diagnostic testing practices and the implications for disease burden estimates.

2. Methods

The Infectious Diseases Society of America's (IDSA) Emerging Infections Network (EIN) is a sentinel network of over 1100 infectious disease physicians. At the time physicians join EIN, they provide basic practice and education information, which is maintained in a database (Pillai et al., 2014). EIN sent surveys to 1271 adult infectious disease specialists who are members of IDSA's EIN. The respondents had 27 days (November 1–27, 2016) to complete the survey, which included 10 questions regarding RSV knowledge, attitudes, beliefs, and diagnostic testing practices. Two reminders were sent to non-responders 8 days and 15 days after the survey was distributed (November 9, 2016 and November 16, 2016).

CDC conducted a frequency analysis on the practice and education characteristics of responders and non-responders and used chi-square

Table 2
RSV diagnostic testing practices by self-reported importance of diagnosing RSV in clinical practice*.

	Very/Somewhat n (%)	Not Very/Not At All n (%)	Total n (%)
In what settings have you ordered or recommended testing for RSV in adults?*	N = 322	N = 80	N = 402
Intensive care units	285 (88.5)	39 (48.8)	324 (80.6)
Inpatient, non-intensive-care units	248 (77.0)	17 (21.3)	265 (65.9)
Bone marrow transplant units	133 (41.3)	19 (23.8)	152 (37.8)
Outpatient	83 (25.8)	2 (2.5)	85 (21.1)
Long-term care settings	18 (5.6)	1 (1.3)	19 (4.7)
I have not ordered or recommended testing for RSV in adults in any settings	13 (4.0)	32 (40)	45 (11.2)
How has RSV infection been diagnosed in your adult patients?*	N = 320	N = 81	N = 401
Respiratory viral panel	243 (75.9)	44 (54.3)	287 (71.6)
RSV PCR test	104 (32.5)	18 (22.2)	122 (30.4)
RSV rapid antigen test	41 (12.8)	5 (6.2)	46 (11.5)
RSV diagnostic test not specifically ordered but received when influenza test is ordered	40 (12.5)	6 (7.4)	46 (11.5)
N/A, RSV not diagnosed	12 (3.8)	18 (22.2)	30 (7.5)
Not sure	6 (1.9)	6 (7.4)	12 (3.0)
Other	1 (0.3)	2 (2.5)	3 (0.7)
For hospitalized adults with ARI in the last year, how often do you order/recommend testing for RSV?	N = 293	N = 75	N = 368
Sometimes	130 (44.4)	22 (29.3)	152 (41.3)
Most of the time	57 (19.5)	1 (1.3)	58 (15.8)
Not applicable	37 (12.6)	7 (9.3)	44 (12.0)
Never	33 (11.3)	44 (58.7)	77 (20.9)
Always	32 (10.9)	0 (0.0)	32 (8.7)
Not sure	4 (1.4)	1 (1.3)	5 (1.4)
For which of the following hospitalized adults with ARI would you be more likely to order/recommend testing for RSV?*	N = 322	N = 81	N = 403
Solid organ or other transplant recipients	288 (89.4)	64 (79.0)	352 (87.3)
ICU patients	258 (80.1)	30 (37.0)	288 (71.5)
HIV/AIDS	161 (50.0)	16 (19.8)	177 (43.9)
Older adults (community-dwelling)	157 (48.8)	9 (11.1)	166 (41.2)
COPD exacerbation	156 (48.4)	9 (11.1)	165 (40.9)
Other immunosuppressed	150 (46.6)	20 (24.7)	170 (42.2)
Persons living in long-term care settings	137 (42.5)	10 (12.3)	147 (36.5)
Pregnant women	96 (29.8)	5 (6.2)	101 (25.1)
None of the above	4 (1.2)	9 (11.1)	13 (3.2)

* Not all respondents answered each question; therefore, the number of physicians who responded to an individual question was the denominator.

** Some questions allowed respondents to select more than one answer; thus, column percentages may not add to 100.

analysis to compare the two groups, where $P < 0.05$ was considered statistically significant. Physician information (practice and education characteristics) regarding responders and non-responders is available through EIN, of which the surveyed physicians are members. CDC analyzed the frequencies of all survey responses and categorized the results by whether the respondents felt being able to diagnose RSV in their adult patients was very or somewhat important, or not very or not at all important. This allowed for more robust analysis in making comparisons between the 2 groups. SAS 9.4 (Cary, NC) was used for this analysis.

3. Results

The survey received a response rate of 43.0% (543/1271). The response rates for each region of the country were similar. Respondents (physicians who completed the survey) were significantly more likely than non-respondents to have ≥ 25 years of infectious disease experience ($P < 0.0001$). Of the 543 respondents, 74.2% reported routinely caring for or consulting for adults with ARI. The remaining respondents who do not routinely care for adults with ARI ($n = 140$, 25.8%) did not complete the rest of the survey.

Eighty percent ($n = 322$) of physicians that cared for patients with ARI felt being able to diagnose RSV in adults was very or somewhat important, while 20% ($n = 81$) felt diagnosing RSV in adults was not very or not at all important. Among respondents who felt diagnosing RSV was not very or not at all important, 86.4% ($n = 70$) reported this was because no antiviral treatment or vaccine is currently available (Table 1).

Among the 322 respondents who felt being able to diagnose RSV in adults was very or somewhat important, they most commonly reported testing in intensive care units (ICU) (88.5%) and inpatient non-ICU settings (77.0%). Additionally, they were most likely to order or recommend testing in solid organ or other transplant patients (89.4%) and ICU patients (80.1%) (Table 2).

Respondents who felt being able to diagnose RSV in adults was not very or not at all important also most commonly ordered testing for RSV in adults in ICUs (48.8%, 39/80), though less frequently than those who felt diagnosing RSV was very or somewhat important. They were also most likely to order or recommend testing in solid organ or other transplant recipients (79.0%, 64/81). However, a substantial proportion (40.0%, 32/80) of those same physicians had not ordered or recommended testing for RSV in adults in any clinical setting (Table 2). In both groups, a little less than half of physicians ordered testing for community-dwelling older adult patients and patients with chronic obstructive pulmonary disorder (COPD) exacerbations (Table 2).

Of the 401 respondents who cared for adults with ARI, 71.6% reported that the most frequently used RSV diagnostic tests were molecular-based respiratory viral panels (RVP), followed by PCR (30.4%), RADT (11.5%), and diagnostic tests included with an influenza test (11.5%). Physicians who felt diagnosing RSV was very or somewhat important used RADTs slightly more frequently (12.8%) than all respondents. Of physicians who reported diagnosing RSV was not very or not at all important, 22.2% did not diagnose RSV in their patients (Table 2).

Sixty-three percent of physicians that cared for adults with ARI (252/401) were not aware that RSV candidate vaccines for older adults are in development. Among the 401 respondents, the most common motivators for RSV testing were antibiotic stewardship practices (69.0%) and recommendations by a professional medical association such as IDSA (56.0%). Some physicians ($n = 7$) also commented that more affordable testing would motivate them to increase RSV testing. If an RSV vaccine were to become available, respondents reported that the most helpful information would be RSV vaccination information, including safety, administration, and vaccine storage (77.0%) and burden of disease data (73.0%).

4. Discussion

While there are currently no vaccines or specific treatments available for RSV, multiple vaccine and antiviral products are in development and may become available in the next several years. Our survey reveals that knowledge of RSV vaccines in development is low. Of the respondents who answered that diagnosing RSV in adults was not very or not at all important, most replied that this was because no antiviral treatment or vaccine is available. If RSV is not tested for, then test-positive RSV detection data may likely underestimate the true burden of RSV disease. Therefore, understanding current clinical RSV testing practices among physicians is important for developing models to estimate disease burden.

Most of the respondents felt it was very or somewhat important to be able to diagnose RSV in adults. Physicians are more likely to test for RSV in some high risk groups (e.g. ICU, solid organ or other transplant patients). However, less than half of physicians ordered or recommended testing for community-dwelling older adult patients or patients with COPD exacerbations, which have previously been identified in scientific literature as high-risk groups with more hospitalizations and poorer outcomes (Falsey et al., 2005, 2014).

Of the respondents who answered that diagnosing RSV in adults was not very or not at all important, most replied that this was because no antiviral treatment or vaccine is available. Additionally, while RSV test results may not directly influence patient care they could help decrease the inappropriate use of antibiotics (Centers for Disease Control and Prevention, 2013; Talbot et al., 2016).

Of the available diagnostic tests for RSV, RADTs are less sensitive in adults (Talbot and Falsey, 2010). Our survey found that 12% of physicians used RADTs to diagnose RSV in adult patients, which is not the most sensitive assay for detection of RSV in this population. It is possible RADTs are used because they are the only option available, or more sensitive methods such as PCR are cost-prohibitive. Using PCR over RADT would detect more cases of RSV among adults, although PCR for RSV may not be widely available.

There were several limitations to this survey. First, EIN includes only physicians who are members of IDSA, and this might not be representative of the general infectious disease physician population or physicians overall. Second, those who did respond to the survey were significantly different compared to those that did not in terms of years of infectious disease experience. Third, the self-reported RSV diagnostic testing responses might be different from what is actually used in practice. Lastly, most cases of mild RSV are seen in primary care clinics, and these primary care providers may differ from infectious disease physicians in terms of their diagnostic practices.

5. Conclusions

RSV is a frequent cause of ARI among adults, and development of antivirals and vaccines are currently underway for this population. Some infectious disease physicians were not aware that an RSV vaccine for adults could become available in the near future and might not feel diagnosing RSV is currently important given that no approved therapeutics or modes of prevention are available. Furthermore, RADTs are not ideal in terms of sensitivity for detection of RSV among adults. These factors can impact disease burden estimates, most likely by underestimating the true number of infections caused by RSV. Continued evaluation of RSV testing practices, including expanding to other physician groups that treat adults (e.g., internal medicine, family medicine) will be crucial in order to develop models that will accurately estimate RSV burden.

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