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Primary care physicians' perspectives on respiratory syncytial virus (RSV) disease in adults and a potential RSV vaccine for adults

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ABSTRACT

Background: Deaths attributable to respiratory syncytial virus (RSV) among adults are estimated to exceed 11,000 annually, and annual adult hospitalizations for influenza and RSV may be comparable. RSV vaccines for older adults are in development. We assessed the following among primary care physicians (PCPs) who treat adults: (1) perception of RSV disease burden; (2) current RSV testing practices; and (3) anticipated barriers to adoption of an RSV vaccine.

Methods: We administered an Internet and mail survey from February to March 2017 to national networks of 930 PCPs.

Results: The response rate was 67% (620/930). Forty-nine percent of respondents (n = 303) were excluded from analysis as they reported never or rarely caring for an adult patient with possible RSV in the past year. Among respondents who reported taking care of RSV patients (n = 317), 73% and 57% responded that in patients ≥ 50 years, influenza is generally more severe than RSV and that they rarely consider RSV as a potential pathogen, respectively. Most (61%) agreed that they do not test for RSV because there is no treatment. The most commonly reported anticipated barriers to a RSV vaccine were potential out-of-pocket expenses for patients if the vaccine is not covered by insurance (93%) and lack of reimbursement for vaccination (74%).

Conclusions: Physicians reported little experience with RSV disease in adults. They are generally not testing for it and the majority believe that influenza disease is more severe. Physicians will require more information about RSV disease burden in adults and the potential need for a vaccine in their adult patients.

1. Introduction

Respiratory syncytial virus (RSV) is the most commonly identified cause of lower respiratory tract infection in young children [1]; however, the causative role of RSV in adult respiratory infections is less well known. RSV poses a number of diagnostic challenges in adults: there is no distinctive syndrome; adults shed lower concentrations of antigen for shorter periods of time than infants, making the virus difficult to detect; and the respiratory infection caused by RSV may exacerbate underlying chronic medical conditions like chronic obstructive pulmonary disease and congestive heart failure and RSV may not be recognized as a contributing factor [2].

A modeling study that evaluated age-specific estimates of U.S. deaths attributable to RSV found that 92% of the annual 11,321 RSV-associated deaths occurred among persons 50 and older [3]. A prospective study conducted over three consecutive winters in a single U.S. county found hospitalization rates for adults with RSV to be comparable to influenza at 15 and 12 per 10,000, respectively [4]. Other modeling and prospective studies have shown that

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RSV is an important pathogen, especially for older adults and those with cardiopulmonary or immunocompromising conditions [4–8].

Treatment of RSV in adults is primarily supportive. As a result of the identified disease burden and lack of specific treatment, RSV vaccines are being investigated to decrease disease severity. Currently, over 40 RSV vaccines and monoclonal antibody products are in development and target all age groups; several RSV vaccines for older adults are in early clinical trials [9].

As physician recommendations are important in patient decisions to receive vaccines [10–13] and physician survey responses have been shown to be generally accurate predictors of eventual reported vaccination practices [14], we sought to assess using survey methodology the following among general internists (GIM) and family physicians (FP): (1) perception of the burden of RSV disease, (2) practices regarding testing for RSV disease, and (3) anticipated barriers to a potential RSV vaccine. Investments in understanding physicians' knowledge, attitudes and beliefs regarding RSV and a potential RSV vaccine at this early juncture are an important aspect of new vaccine development and eventual implementation efforts.

2. Methods

2.1. Study setting

From February to March 2017, we administered a survey to a national network of physicians who had agreed to participate in surveys about vaccine policy issues and who spent at least half their time practicing primary care. The institutional review board at the University of Colorado Denver approved this study as exempt research.

2.2. Study population

The Vaccine Policy Collaborative Initiative [15], a survey mechanism to assess physician attitudes about vaccine issues, in collaboration with the Centers for Disease Control and Prevention (CDC), conducted the survey. We developed a network of primary care physicians by recruiting GIMs and FPs from the memberships of the American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP). In order for physicians to be eligible for the network, they need to spend at least fifty percent of their time doing primary care. We performed quota sampling [16] to ensure that networks of physicians were similar to the ACP and AAFP memberships with respect to region, urban versus rural location, and practice setting. We previously demonstrated that survey responses from network physicians were similar to those of physicians randomly sampled from American Medical Association physician databases with respect to reported demographic characteristics, practice attributes, and attitudes about vaccination issues [16].

2.3. Survey design

We developed the survey collaboratively with CDC. We used 4-point Likert scales for assessing how often a physician considers RSV in patients 50 years or older with a serious respiratory illness ("Rarely/Never" to "Almost always/Always"), and anticipated barriers to a possible RSV vaccine ("Major barrier" to "Not a barrier"). For assessing how often in the past year physicians had taken care of adult patients they suspected to have RSV in various settings (outpatient, inpatient and long-term care facility), response options included a 4-point Likert scale from "Rarely/Never" to "Very Often," but also included an option to report not seeing patients in a particular setting. When we asked about attitudes towards RSV-related disease, including the importance of the RSV pathogen in various patient groups, response options included 4-point Likert scales from "Very important" to "Not at all important" and "Strongly agree" to "Strongly disagree" as well as a "Don't Know" category. We also asked physicians how often in the past 12 months they had ordered viral diagnostic testing for RSV, and what specific type of testing was ordered (viral culture, serology or a rapid test). If they reported ordering a rapid test for RSV, we asked what type of rapid testing they ordered ("polymerase chain reaction (PCR)," "direct fluorescent antibody (DFA)," "other," or "don't know"). Some respondents said they had never or had rarely in the past 12 months taken care of patients in outpatient, inpatient, or long-term care facility settings who they suspected to have RSV. These physicians did not answer more in-depth questions that assessed practices when considering a patient for RSV infection because those questions would not pertain to them. A national advisory panel of GIMs (n = 4) and FPs (n = 9) pre-tested the survey, which was modified based on their feedback. We pilot-tested the survey among 23 GIMs and 14 FPs nationally and further modified the survey instrument based on their feedback.

2.4. Survey administration

Depending on physician preference, the survey was administered through the Internet [17] or U.S. mail. We sent the Internet group an initial e-mail with up to 8 e-mail reminders, and we sent the mail group an initial mailing and up to 2 additional mail reminders. Non-respondents in the Internet group were also sent up to 2 mail surveys in case of problems with e-mail correspondence. Due to an initial low response rate and feedback from non-respondents that they had had little experience with RSV, we re-ordered the survey questions and allowed respondents to skip out of most of the questions if they reported rare or no experience with RSV in the outpatient, inpatient or long-term care facility settings. We patterned the mail protocol on Dillman's Tailored Design Method [18].

2.5. Statistical analysis

We pooled Internet and mail surveys for analyses because other studies have found that physician attitudes are similar when obtained by either method [18–20]. We compared responses from those respondents who took the original version of the survey to those who received the re-ordered survey using chi-square analyses. We compared respondents with non-respondents on all available characteristics using t-tests for continuous variables and Pearson's chi-squared tests for categorical variables; characteristics of non-respondents were obtained from the recruitment survey for the sentinel networks. All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, North Carolina).

3. Results

3.1. Survey response and characteristics of respondents

The response rate was 67% (620/930). Responses did not differ if respondents took the original or the reordered survey. Respondents and non-respondents did not differ significantly by census location (urban, suburban, or rural) or number of providers in the practice. Respondents were less likely to be from the South and more likely to be from the West ($p = 0.04$), were more likely to be in a private practice setting ($p = 0.0005$), were less likely to be male ($p = 0.004$) and were younger ($p = 0.001$) than non-respondents. Characteristics of respondents and non-respondents, and further characteristics of respondents' practices

Table 1
Demographic and Practice Characteristics of Respondents in a Study of Physicians' Perspective on RSV in Adults, United States, 2017.

Characteristic	Non-Responder (n = 310)	Responder (n = 620)	P Value
Provider Specialty			
FP	41%	54%	0.0001
GIM	59%	46%	
Provider Gender			
Male	66%	56%	0.004
Female	34%	44%	
Setting			
Private practice	82%	72%	0.005
Hospital or clinic	15%	22%	
HMO	3%	6%	
Census Location			
Urban	49%	44%	
Suburban	49%	51%	0.12
Rural	3%	5%	
Region			
Midwest	25%	26%	0.04
Northeast	18%	21%	
South	38%	30%	
West	18%	24%	
Decision-making			
Independent	61%	55%	0.07
Larger system level	39%	45%	
Mean (sd)/Median provider age in years			
	56 (8.3)/57	54 (8.5)/54	0.001
Mean (sd)/Median number of providers in practice			
	13 (34.9)/5	28 (292)/6	0.007*
See Patients in the Outpatient Setting	N/A	99%	

* Wilcoxon test.

and patient populations, are shown in Table 1. Ninety-nine percent of respondents reported seeing patients in the outpatient setting.

3.2. Physician perception of burden of RSV disease

Forty-nine percent (303/620) of respondents reported that they had not taken care of an adult patient, at least occasionally, who they thought had RSV disease in the last 12 months in an outpatient, inpatient, or long-term care facility setting. These individuals were excluded from further analysis. The final study cohort was 317 primary care physicians.

Fig. 1 shows the perceived importance of RSV as a pathogen in various groups of patients among those physicians who reported seeing RSV-infected patients. Higher proportions of physicians reported RSV was a very important pathogen in adults 65 years or older with cardiopulmonary disease and adults of any age with an immunocompromising condition than the other patient populations. In general, physicians reported RSV was a more important pathogen for patients of all ages with, as opposed to those without, cardiopulmonary disease. Seven to 14% of physicians reported not knowing about the importance of RSV as a pathogen in these various patient groups.

Eighty-six percent of respondents agreed they needed more information about the burden of RSV disease among adult patients (data not shown).

3.3. Physician attitudes and Behaviors regarding RSV and influenza disease

The majority of physicians strongly or somewhat agreed with the statement that influenza is generally more severe than RSV among patients 50 years or older (Fig. 2). Fifty-seven percent agreed that they rarely consider RSV as a potential pathogen in patients 50 years or older with a respiratory disease. The majority of physicians agreed that they do not test for RSV because there is no available treatment. Half of physicians (50%) disagreed that RSV and influenza cause about the same amount of hospitalizations among patients 50 years or older.

3.4. Physician reported diagnostic testing for RSV disease

Less than half of physicians agreed they knew the best test to diagnose RSV in their adult patients (data not shown). Few physicians reported having ordered viral diagnostic testing in the outpatient setting to specifically detect RSV. Of the 59 total physicians

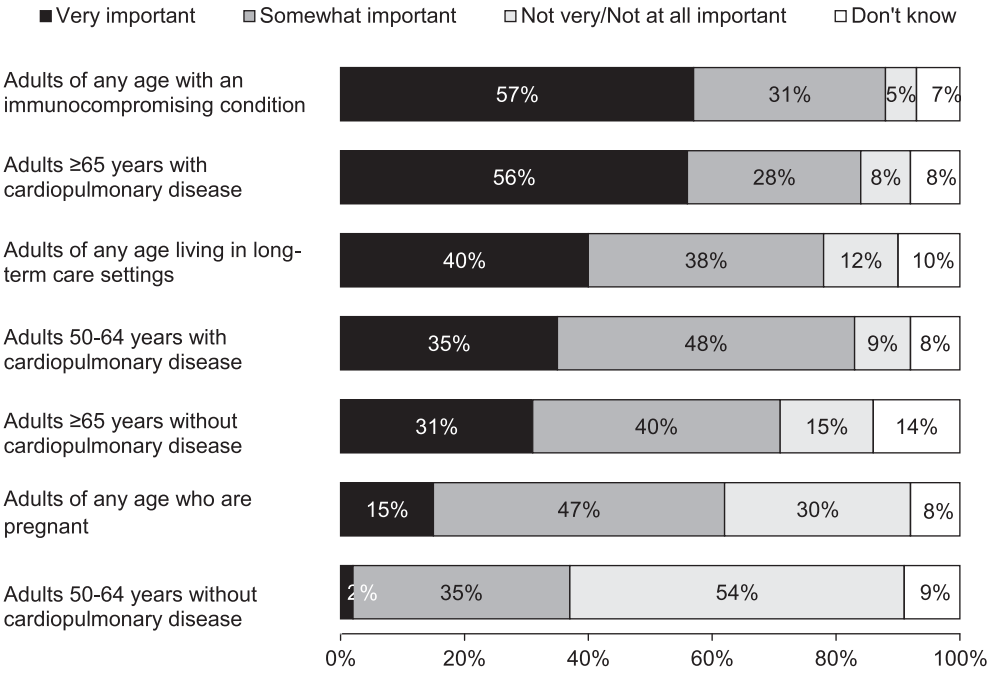

Fig. 1. Physician Perception of Importance of RSV as a pathogen in the following groups of patients, United States, 2017 (n = 317).

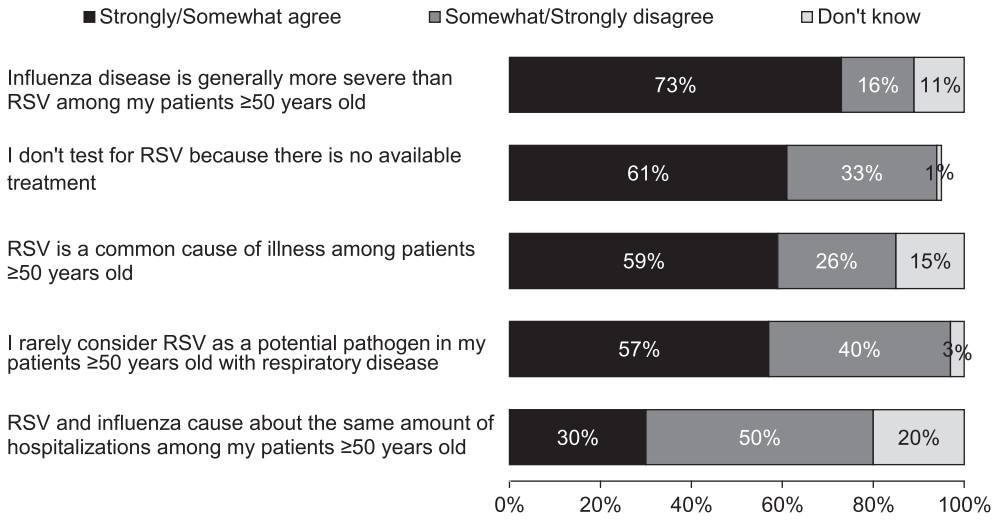

Fig. 2. Physician Attitudes and Behaviors Regarding RSV and Influenza Disease in their Adult Patients, United States, 2017 (n = 317).

who had done so, most (n = 49) reported only performing rapid testing; 33 reported performing PCR, 1 ordered a DFA, and 15 reported they did not know what type of rapid test they had ordered.

3.5. Physician reported anticipated barriers to a RSV vaccine

The two most commonly reported anticipated barriers to a RSV vaccine were financial: potential out of pocket expenses for patients if the vaccine is not covered by insurance, and lack of adequate reimbursement for vaccination (Fig. 3).

4. Discussion

Understanding physician knowledge, attitudes and beliefs regarding a potential vaccine preventable disease is important to future implementation strategies for that vaccine. To our knowledge, this is the first study to assess primary care physicians' perception of RSV disease in adults. The fact that half of physicians in this study reported having had no or little experience with taking care of an adult patient with RSV in the past year strongly suggests low awareness of the true burden of RSV disease in adults. The vast majority of physicians who reported some experience caring for

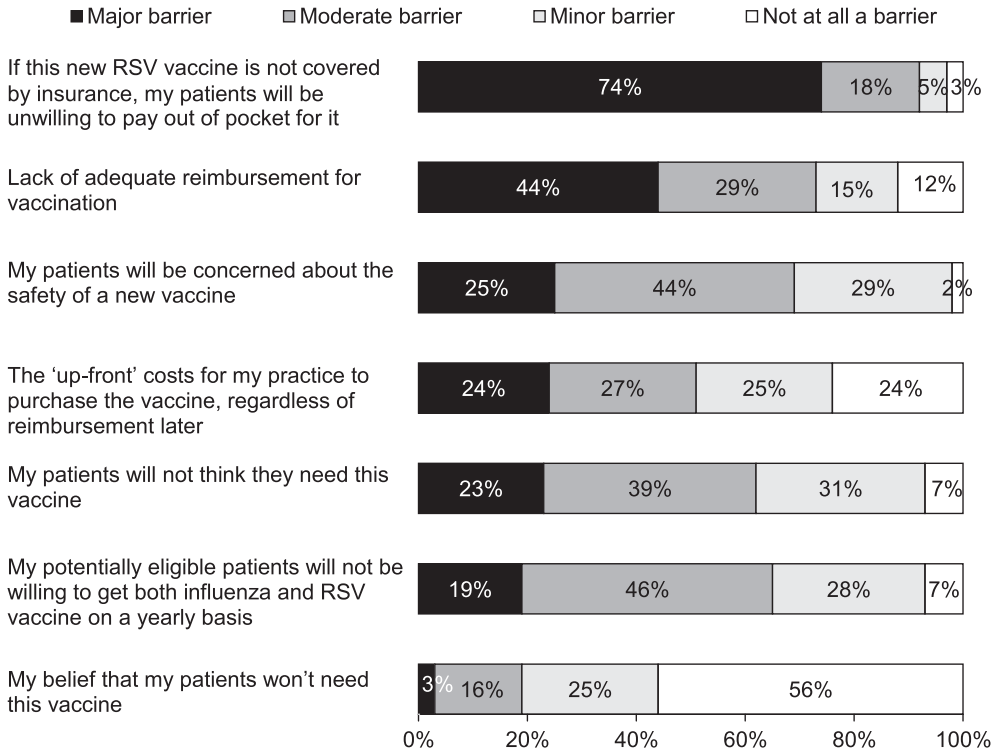

Fig. 3. Physician Anticipated Barriers to an Adults RSV Vaccine, United States, 2017 (n = 317).

adult patients with RSV agreed they needed more information about the burden of disease in adults. But these physicians did seem to believe that RSV is a more important pathogen in older individuals and those with cardiopulmonary disease and immunocompromising conditions, which has been substantiated in the literature [4–8]. Most believed influenza disease is generally more severe than RSV in adults $\geq$ 50 years of age, even though this is not necessarily true [21,22], and reported they rarely consider RSV in patients of this age group with respiratory disease. In light of these findings, educational campaigns regarding RSV disease burden in adults, possibly conducted by national public health and medical professional organizations, would be helpful.

These survey results indicate that physicians are often not testing for RSV disease in adults in outpatient settings, which is not unexpected given the lack of treatment options and adults potentially presenting with mild illness. The minority of physicians who order these tests are most often requesting rapid tests, specifically PCR testing. PCR is the diagnostic test of choice for RSV in adults with 85% sensitivity [23] compared to point-of-care rapid antigen tests, like DFA testing, which are widely used for infants and have poor sensitivity in adults [24]. Only one physician reported using this type of testing.

Lack of lab confirmation of RSV infections likely contributes to the lack of awareness among physicians regarding the true impact of RSV in older adults. The most recent IDSA guidelines for community acquired pneumonia (CAP) in adults do not specifically address RSV testing and state that routine diagnostic tests to identify an etiologic diagnosis are optional for outpatient adults with CAP [25]. In addition, RSV is not a disease that is nationally notifiable [26] These factors combine to create a lack of knowledge of RSV disease in adults. CDC has recently implemented surveillance activities for RSV in hospitalized adults [27].

According to the physicians surveyed, the greatest barrier to patient acceptance of a RSV vaccine is if it was not covered by insurance. If licensed by the Food and Drug Administration and recommended by the Advisory Committee on Immunization Practices, this vaccine would be covered by Medicare Part D for Medicare beneficiaries, in which case individuals would likely have to pay a copay to receive it. Depending on the tiering of the vaccine, the copayment could be substantial, and this may be particularly difficult for older adults with fixed incomes or those who end up in the "donut hole" [28]. This vaccine has the potential to experience financial barriers similar to those that zoster vaccine live has faced as a result of Medicare Part D coverage [29]. More than half of the physicians thought that patients being unwilling to get both a RSV and an influenza vaccine on a yearly basis would be a potential barrier to RSV vaccine, and influenza vaccines are already frequently refused [30].

Our study has strengths and limitations. Results were generated from primary care physicians from across the nation, and we achieved an excellent response rate for a physician survey, but many physicians reported not caring for a person with RSV and were excluded from most of the analysis which may have biased the results to those who think RSV is more important. Although our sample was designed to be representative of ACP and AAFP memberships, the attitudes, experiences, and practices of sentinel physicians may not be fully generalizable. Non-respondents may have held different views than respondents. The survey relied on self-report of practice rather than observation of practice, and respondents reported perceptions and beliefs about a vaccine that is not currently in use. Later respondents answered survey questions in a different order than those who initially received the survey, although our analysis indicates there was no difference in responses regardless of which version of the survey the physician responded to.

The results presented here indicate a RSV vaccine would face significant initial challenges with respect to acceptance and use. A RSV vaccine has the potential to reduce morbidity and mortality associated with adult RSV disease that many primary care physicians are not aware of. Raising physician awareness of RSV disease in adults will require greater dissemination of current knowledge, possibly through educational campaigns spearheaded by national public health and medical professional organizations, but continued surveillance to collect data about incidence and burden of RSV disease in adult populations will also be important. Some forethought to anticipated barriers, particularly financial ones, may ease implementation when a RSV vaccine eventually becomes available.

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Conflict of interest

The authors have no conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.12.031.

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