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CALL TO ACTION REDUCING THE BURDEN OF RSV ACROSS THE LIFESPAN

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The recommendations included in this Call to Action are based on discussions at a virtual roundtable convened by the National Foundation for Infectious Diseases (NFID) in November 2021. Participants included a range of multidisciplinary stakeholders and subject-matter experts who explored the burden of respiratory syncytial virus (RSV) across the lifespan and identified key strategic priorities based on prevention, diagnostic, and treatment interventions in the pipeline.

SUMMARY

Respiratory syncytial virus (RSV) is among the most common respiratory infections worldwide, circulating broadly alongside other seasonal viruses, including influenza.¹ In the US, RSV is the **most common cause of bronchiolitis and pneumonia in young children** less than one year of age.² Moreover, RSV is increasingly recognized as a **significant source of respiratory illness among older adults**.^{3,4}

Although RSV is particularly dangerous in premature infants, young children with heart and lung disease, immunocompromised individuals of any age, and older adults all of whom are at increased risk of severe disease—the potential for infection and serious illness is a concern across the lifespan.^{4,5}

Despite these concerning statistics, RSV remains widely underappreciated as a public health threat, even among healthcare professionals (HCPs). Many factors contribute to the lack of awareness of RSV as a cause of serious respiratory infection, including diagnostic challenges, underreporting, and underappreciation of actual disease burden.

There are compelling reasons to prioritize RSV prevention and treatment. New innovations including vaccines, monoclonal antibodies, and other interventions like antiviral medication in various stages of clinical development promise to improve the RSV prevention and treatment landscape in the coming years. The current environment of heightened awareness of the dangers of respiratory virus illness, as a result of the COVID-19 pandemic, also provides a platform to better inform HCPs, policymakers, and the public about the burden of RSV disease, and the need for a strong public health response.

Clear public health messaging is necessary to prepare for therapeutic interventions in development that are designed to reduce RSV-related morbidity and mortality across the lifespan. Additionally, a national commitment to health equity is imperative to successfully address RSV-related health disparities in both children and older adults.

KEY STRATEGIC PRIORITIES



Participants at the NFID roundtable agreed that there is currently a unique window of opportunity to drive progress for RSV surveillance, diagnosis, prevention, and treatment. Key strategic priorities include:

Increase RSV awareness and the sense of urgency to confront the viral infection



RSV continues to receive relatively little attention compared with other respiratory diseases. Specific initiatives are necessary to help raise awareness among HCPs and the public regarding RSV burden, diagnosis, prevention, and treatment.

Strengthen public health responses to RSV

Public health leaders and policymakers need to advance a more robust response to RSV that includes improving public health surveillance, expanding diagnostic capacity, and revisiting public health recommendations. It is imperative to rebuild public health capacity, especially in state and local health departments, which have been operating under unprecedented strain due to the COVID-19 pandemic.8

Pave the way for implementation of new interventions



After decades of limited innovation, the development of new RSV vaccines, monoclonal antibodies, and antiviral treatments could have a tremendous impact on outcomes for those most at risk for RSV infection. These interventions will place new demands including the need for better pediatric and adult surveillance data, health economic assessments, and insurance coverage. Efforts should focus on supporting the rapid adoption and deployment of new evidencebased interventions for RSV prevention and treatment.

THE IMPACT OF RSV IN THE US

The actual burden of RSV is often underappreciated by HCPs, policymakers, and the public. While RSV infection usually results in mild, cold-like symptoms, it is also important to recognize the potential for severe bronchiolitis and pneumonia, particularly among infants, young children, and older adults.5

The impact of severe RSV can be particularly pronounced among individuals with chronic health conditions such as asthma, chronic obstructive pulmonary disease (COPD), or congestive heart failure, which can be exacerbated by RSV infection.⁴ In children, the impact of severe RSV is disproportionate among those with specific identified risk factors, such as younger age, premature birth, and congenital heart disease, yet the majority of children hospitalized with RSV are full-term infants with no underlying conditions.9

The burden of RSV is substantial. Among children in the US age five years or younger, RSV is estimated to cause approximately 1.5 million outpatient visits, 520,000 emergency department visits, and 58,000 hospitalizations each year.^{6,7,10,11} The burden is also substantial in older adults, where the number of RSV-related hospitalizations is estimated at approximately 177,000 annually.³ The actual burden is likely even higher due to underreporting of RSV infections.

RSV-related mortality is concerning.

Among children age five years and younger, RSV is associated with an estimated 100 to 500 deaths per year,¹⁰ while among adults age 65 years and older, RSV is associated with 14,000 deaths each year, suggesting a much larger mortality burden among older adults.³ Additionally, older adults are more susceptible to exacerbation of existing health conditions.13



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The economic burden associated with RSV is substantial, as illustrated by data on charges for care related to bronchiolitis, which is most commonly caused by RSV. In one analysis, nationwide charges for care related to bronchiolitis in children age two years and younger exceeded \$1.7 billion in 2009 dollars.¹⁴ More recent analysis has confirmed the economic impact of RSV and determined that the highest cost burden is in older age groups.¹⁵

Recent studies suggest **disparities in RSV-related hospitalization and disease severity** related to factors including race/ ethnicity, employment status, household income, population density, and crowded living conditions.¹⁶ Furthermore, the COVID-19 pandemic has amplified existing socioeconomic inequalities that precipitate poor health outcomes related to RSV.¹⁷

CHALLENGES IN THE PUBLIC HEALTH RESPONSE TO RSV



Experts at the NFID RSV roundtable discussed challenges in public health response related to HCP perceptions, disease surveillance, testing, prevention, and limited treatment interventions. Key concerns include:

The ongoing COVID-19 pandemic has shifted the focus away from RSV and other causes of serious respiratory illness. Adoption of public health measures to combat COVID-19 altered the normal seasonal incidence of common respiratory infections, such as influenza and RSV. While RSV infections in the US are typically concentrated in the fall and winter, a rapid decrease in cases was noted in early 2020. This was followed by a spike in cases in the summer of 2021 that may be related to easing of pandemic-related restrictions.^{7,18} This underscores the importance of educating HCPs to recognize and diagnose RSV even when "out of season."¹⁹ RSV often goes unrecognized (with delayed diagnosis) because its clinical presentation can be indistinguishable from other respiratory infections.²⁰

While careful collection and analysis of disease data inform prevention and control for diseases such as influenza, surveillance efforts for RSV lag behind. Improved surveillance is needed to collect data about the incidence and burden of RSV, including hospitalizations and intensive care unit (ICU) admissions for all individuals including adults with high-risk conditions. It will be important to collect comprehensive data to allow public health experts to stratify risk by age and by underlying condition to help drive effective vaccination and treatment policies. Local public health departments are challenged to measure the true burden of RSV in affected populations. Although progress is being made, comprehensive surveillance data are necessary to quantify the impact and burden of RSV, particularly as new preventive interventions (e.g., vaccines and monoclonal antibodies) are developed. Additionally, repurposing or leveraging COVID-19-related surveillance

and data systems could potentially provide improved tracking of RSV.

Gaps in diagnostic testing. HCPs need clear guidance on when to test for RSV, particularly as the diagnosis and management of bronchiolitis varies widely from institution to institution.²¹ Currently, diagnostic testing for RSV is infrequent, as clinicians may not suspect RSV as the cause of respiratory disease, particularly among older adults.8 Roundtable participants agreed that RSV testing needs to be widely available, accurate, quick, and inexpensive. A good diagnostic test coupled with access to preventive measures for specific at-risk populations (e.g., infants and young children, pregnant women, and older adults) can help to reduce the burden of RSV disease overall. Furthermore, early diagnosis may be critical to leveraging the full benefits of RSV therapeutics, which could, in turn, drive uptake of testing.



Current limitations of RSV prevention, overall and in at-risk populations. The lack of broadly applicable options for RSV prevention or treatment, is limiting the clinical utility of RSV diagnosis. Palivizumab is approved by the US Food and Drug Administration (FDA) for prevention of serious lower respiratory tract disease caused by RSV in high-risk pediatric patients. However, challenges exist related to the cost of treatment and limitations of current risk-based recommendations, particularly when the majority of RSV-related hospitalizations occur in young children with no underlying risk factors.

In adults, there are no FDA-approved interventions to prevent RSV—as a result, recommendations are generally limited to basic infection prevention practices such as handwashing, cleaning of frequently touched surfaces, and avoiding close contact with others.²² Development of vaccines and monoclonal antibodies will be critical to improved disease prevention. Preventing RSV in adults age 65 years and older could reduce both short- and long-term disability and reduce the burden on the US healthcare system, resulting in:

- Fewer acute illnesses and exacerbation of chronic conditions;
- Less contact with healthcare facilities, especially during the ongoing COVID-19 pandemic;
- Fewer unnecessary antibiotic prescriptions; and
- Decreased economic burden.¹³





Figure 1: RSV Vaccine and Monoclonal Antibodies in Development





EMERGING OPPORTUNITIES

Although research to develop new interventions for RSV prevention and treatment has been challenging, promising candidates are emerging. Recent clinical trials show positive results for traditional vaccines and monoclonal antibodies (Figure 1). New prophylactic interventions on the horizon include products targeted for specific populations maternal, all-infant/newborn, older adult, and immunocompromised individuals.

To support ongoing development of RSV treatment and prevention interventions, public health efforts are needed to help improve understanding of RSV epidemiology and burden, increase awareness of unmet medical needs, and foster novel strategies to prevent, diagnose, and treat RSV.

RSV treatment has been limited primarily to supportive care and the progress in developing novel antivirals for the treatment of RSV-related disease is less certain than development of RSV preventive interventions. Roundtable participants discussed a number of challenges, including the failure to replicate promising results from challenge studies in clinical trials. In some cases, disappointing clinical trial results may be attributed to study participants being treated too late in the course of the disease, at which point the benefit of treatment may be limited. Other challenges include the high level of antiviral activity needed to block RSV-induced, disease-associated responses, and delays in the progress of RSV antiviral drug development due to COVID-19.

There is a need for rapid, inexpensive, highly accurate, and easy-to-use RSV diagnostics at the point of care. These desirable characteristics could support uptake of testing, particularly in primary care practices. Multiplex assays that are able to detect and differentiate between other viruses such as SARS-CoV-2 and influenza can also play a critical role in accurate diagnosis of RSV. Based on experiences with the COVID-19 pandemic, such tests should be adaptable in providing the ability to dynamically add other pathogens. Ultimately, the availability of effective therapeutic options beyond current supportive care practices would increase the benefit of diagnostic testing advances for RSV.

New RSV treatment interventions in development will give HCPs, policymakers, and other stakeholders the opportunity to address key issues related to RSV that may not currently be prioritized due to the COVID-19 pandemic. Insurance gaps and issues of access to new RSV interventions will also be key, particularly among adults, given that a considerable number of adults remain unprotected against influenza, pneumococcal disease, and other vaccine-preventable illnesses.²³





"We need updated epidemiologic information to better characterize the burden of RSV in pediatric and adult populations. Surveillance data are important so we can have a better understanding of the true burden of RSV, including hospitalizations, severe illness, and mortality."

William Schaffner, MD, NFID Medical Director

KEY STRATEGIES TO DRIVE PROGRESS

Roundtable discussions also focused on strategies to capitalize on emerging opportunities for improved prevention, diagnosis, treatment, and surveillance of RSV. In addition to dramatically reducing the burden of RSV, it is also critical to address RSV-related disparities.

Increasing Awareness of the Urgency to Address RSV

Increased awareness is essential to improving diagnosis and treatment of RSV. Developing a baseline understanding of the value of interventions currently in development will help ensure timely adoption once approved and available.

- Offer expanded HCP education to increase disease knowledge and awareness of the impact of RSV across the lifespan among HCPs before prevention strategies, including vaccines, are available. Key stakeholders include internists and HCPs who routinely care for older adults.
- Broaden public understanding of the burden of RSV to help build support for a heightened public health response. Strategies may include media-centered awareness campaigns, consumer and patient educational resources, and innovative digital, storytelling, and influencer campaigns to reach parents of young children as well as older adults and their caregivers.

Strengthening Public Health Capacity

Establish robust RSV surveillance, driven by leadership and investments at the federal level. Priority should be placed on establishing a multi-year baseline of surveillance data to inform public health guidelines and investments, and to monitor their impact on disease transmission and outcomes over time.

Possible approaches include expanding existing Centers for Disease Control and Prevention (CDC) RSV surveillance projects, by repurposing innovations developed for COVID-19, or layering RSV surveillance onto existing influenza surveillance activities. State and local health departments will need to play a central role, requiring dedicated resources and technical support to establish routine RSV surveillance in their jurisdictions.



Expand RSV diagnostic capacity. RSV testing should be used routinely in the differential diagnosis of young children and older adults who present with respiratory illness. Expanded testing capacity will be vital as new treatment options become available. Testing will be necessary to identify those who need treatment and in turn, will provide critical surveillance data.

A combination of actions will be needed: creating more convenient and affordable diagnostic tests; closing gaps in insurance coverage; and addressing logistical and procedural barriers, including delayed or incomplete reporting of test results. HCP education will also be important to increase the uptake of available diagnostic tests, even before new treatment options become available.

Rebuild public health capacity lost due to COVID-19. With public health staff and resources depleted or redirected to confront the pandemic, federal agencies and state and local health departments require the resources to rebuild their capacity to address other, long-standing threats. While RSV is not the only priority to have been overshadowed by COVID-19, many of the strategies discussed depend on a robust and efficient public health infrastructure.

Laying the Foundation for New Interventions

- Prepare regulatory frameworks for future innovations. Some interventions currently in the development pipeline are unique, and may face administration issues, based on the limitations of current regulatory processes focused on vaccines. Regulatory bodies will need flexibility to approve and recommend new interventions to help ensure the broadest possible access.
- Identify funding sources and programs for preventive interventions. Equitable access to new interventions will require reliable reimbursement beyond traditional health insurance. The CDC Vaccines for Children (VFC) program, for example, will likely prove essential for children of under- or uninsured families. Policymakers and public health leaders will need to establish novel pathways to improve access in advance of regulatory approvals for new interventions.
- Establish a cost-effectiveness evidence base, so that insurers and policymakers can make informed decisions about the optimal use of new interventions. Research collaborations between CDC and industry would streamline the development of guidelines and recommendations.



- Identify and implement strategies to manage insurance coverage gaps. Appropriate insurance coverage will be essential to maximizing public health impact and the uptake of new interventions. Payers and policymakers will need to remove potential barriers, such as the cost-sharing requirements that can affect access to recommended vaccines for adults covered under Medicare Part D and Medicaid, or the inclusion of monoclonal antibodies for children covered through VFC. Additionally, changes may be needed to ensure Medicare adequately reimburses HCPs for costs associated with administering RSV vaccines and other preventive interventions.
- Pursue broad-based public health recommendations for evidence-based interventions. Recent evidence and experience—with influenza, COVID-19, and other vaccines—provides a compelling argument that broad, age-based recommendations can maximize uptake.
 While narrower, risk-based recommendations may be appropriate in certain circumstances, CDC and other decision-making bodies should seek the broadest appropriate application of new interventions supported by clinical and economic evidence.

CONCLUSION

There are compelling reasons to prioritize the prevention and treatment of RSV in the US. New and innovative RSV interventions are on the horizon and have the potential to significantly reduce the burden of RSV in children and older adults. Experts anticipate that the continued co-circulation of respiratory diseases along with RSV will make ongoing surveillance even more important to ensuring effective diagnosis and treatment.

HCPs must be familiar with the broad clinical presentation of RSV and the burden across the lifespan to optimize the use of interventions once they become available. Successful implementation of new interventions will rely on raising HCP awareness about RSV and the burden of disease, and on public appreciation of the benefits of prevention. Raising awareness about the burden of RSV infection is an important first step to mitigating RSV as a public health concern in the US, and to help ensure the optimal use of new interventions as they become available.

To learn more, visit www.nfid.org/rsv.



ROUNDTABLE PARTICIPANTS

The following individuals participated in the 2021 NFID virtual roundtable focused on increasing awareness of the burden of RSV across the lifespan:

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NFID MISSION AND VISION

Founded in 1973, the National Foundation for Infectious Diseases (NFID) is a non-profit 501(c)(3) organization dedicated to educating the public and healthcare professionals about the burden, causes, prevention, diagnosis, and treatment of infectious diseases across the lifespan.

As a leader in infectious disease education, NFID collaborates with government, academia, and a wide range of healthcare and other organizations to achieve the vision of healthier lives through the effective prevention and treatment of infectious diseases.

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