

Battle against Respiratory Viruses (BRaVe) initiative

Addressing Unmet Needs

- **Advancing the paradigm**

Since the late 19th century, vaccines, improvements of water and sanitation, and other public health interventions have saved millions of lives annually by preventing a number of infectious diseases. In the mid-20th century, the discovery of antibiotics added the promise of effective treatment for many bacterial infections to the preventive power of vaccines. Together these innovations have constituted the predominant paradigm governing the approach to infectious disease mortality reduction.



In the late 20th century, we have witnessed major breakthroughs in the fight against infectious diseases, in large part because of the development of improved diagnostics and the discovery of antiviral medicines. Progress in molecular biology, genetic engineering, and other disciplines has enabled scientists to design and produce antivirals that target key structures of the virus particles, or else block critical processes involved in viral replication. Examples now include effective antivirals for HIV, herpes, influenza, and hepatitis B and C viruses.

- **Understanding the impact of respiratory viral diseases**

Respiratory infections, exemplified by pneumonia, are the leading cause of death among infectious diseases and account for approximately 20% of mortality in children under five. All ages included, respiratory infections account for around 4 million deaths per year¹. Additionally, lower respiratory infections are the leading cause of burden of disease worldwide, accounting for 94.5 million Disability Adjusted Life Years (DALYs) i.e. 6.2% of total DALYs.

Approximately half of the respiratory infections are due to respiratory viruses. Severe pneumonia is not the only complication of viral respiratory viruses. Respiratory viruses are also responsible, directly or indirectly, of a number of other severe health conditions such as otitis media, sinusitis, acute bronchitis, exacerbation of asthma and chronic lung disorders. These chronic respiratory diseases which can be triggered by respiratory viruses are common problems in all countries, with huge medical and economic impacts. Adults with underlying conditions are particularly at risk for both deteriorations in their co-morbidities and severe infections adding to

¹ The Global Burden of Disease 2004 update, WHO :

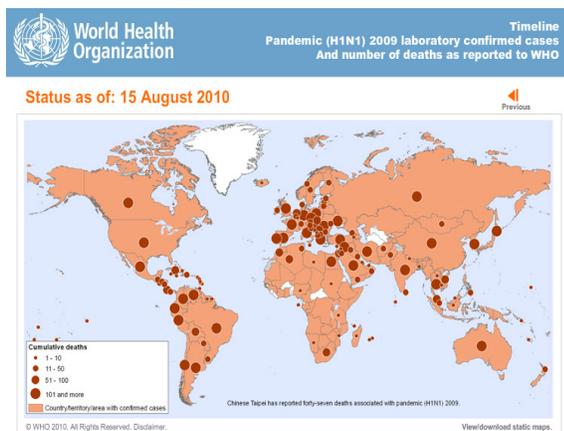
http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf ; accessed July 2012

the burden of respiratory viral infections on health systems. For instance, studies have reported a consistent association between influenza and acute myocardial infarctions.

The burden of respiratory infections is even more disproportionate in developing countries. While efforts to achieve Millennium Development Goal 4 (MDG4)² have been made, the world has not yet seen a significant reduction in such deaths. Advanced diagnostics have revealed that a large proportion of severe infectious diseases in children is due to viruses and that viral infections also act as facilitators of subsequent infection by bacteria.

Therefore, to achieve the MDG 4 and reduce the overall burden caused by respiratory viruses a comprehensive approach tackling bacterial and viral respiratory infections is required.

- **Likelihood of new respiratory virus threats**



Recent global events such as SARS in 2003, re-emergence of avian flu in 2005 and the H1N1 2009 pandemic have alerted the world of the danger of viruses in a globalized world where a dangerous pathogen can emerge and spread to all continents in a matter of days. The large number of viruses in animals and the changing dynamic at the human-animal interface guarantee the emergence of novel respiratory pathogens. Furthermore, the efficient person to person transmission of respiratory viruses makes their control very challenging.

Of note, the IHR pandemic review committee in its report adopted by the World Health Assembly in May 2011³ stated that: *"the world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public health emergency."* The best hope for responding effectively to emergent threats is to improve management of respiratory viral infections and their sequelae in the current inter-pandemic period.

- **Prospects for reducing burden of disease**

With the advance in technology, there is now the prospect of treating viral respiratory infections. Antivirals have been used with success during the influenza H1N1 2009 pandemic and a number of new drugs with broader activity spectrum will be soon licensed. Together with the advance in diagnostic tests and improved clinical management, the possibility to effectively treat viral respiratory infections is not a dream anymore.

The impact of the treatment of viral respiratory infection will be clear on the burden of disease as half of the episodes that are currently not treated will benefit from treatment.

² <http://www.un.org/millenniumgoals/pdf/MDG%20Report%202010%20En%20r15%20-low%20res%2020100615%20.pdf#page=28>

³ http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf



There will also be spill-over effects on other health issues such as the growing resistance to antibiotics. The indiscriminate use of antibiotics for many respiratory illnesses of viral etiology, is likely to foster emergence of resistance in respiratory bacterial pathogens and to cause adverse effects and increased cost of care. In addition, the early treatment of acute viral respiratory infections has the potential to reduce the frequency of apparent bacterial complications.

The treatment of viral respiratory infections will be a useful complement to the vaccination strategy. For many infectious diseases, vaccines remain at the heart of disease prevention and control. Vaccines, when they exist, should be integrated in an overall mitigation strategy against respiratory viruses. Presently, we have only effective vaccines for influenza among the respiratory viruses, and these vaccines have significant limitations, including need for annual administration, limited effectiveness in key risk populations, and very low uptake in most countries. Because there are no effective vaccines for other common respiratory viruses⁴ and it remains uncertain whether and when such vaccines might become available, it makes sense to pursue the development of more effective therapeutics and integrated approaches.

- **What are the challenges?**

There are many challenges for reducing the mortality due to respiratory viral infections.

Healthcare workers, still, tend to think that there is no effective treatment for viral infections. Although antiviral treatment are not yet broadly available it is important to engage the health care work force early on to introduce new practices.

The development of new and better antivirals has not yet increased as much as expected for several reasons:

- the high specificity of the drugs together limits the use for syndromic approach at the primary health care level;
- the inadequate diagnostic capacity reduces the capacity to detect and treat the diseases in a timely manner and therefore obtain more visible benefits;
- the high treatment costs do not allow low-resource countries to access the medicine;
- the lack of distribution systems in many parts of the world and lack of appropriate health infrastructure reduce the use of existing antivirals.

The risk of seeing the emergence of resistant viruses cannot be discarded and having a large number of different drugs would be reassuring as it will allow for the selection of treatment options according to the context.

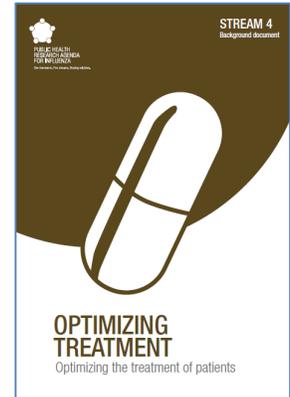
There are already a number of effective measures to improve the clinical management of severe patients. However, these measures such as oxygen therapy are not always properly implemented. A better use of existing resources is critical to achieve sustainable improvement.

⁴ RSV, PIV, hMPV, rhinovirus, human coronaviruses

- **Pre-requisites for success**

More investments in research are needed on :

1. **Defining the "hidden" burden of viral respiratory infections** by a better understanding of disease etiology and epidemiology to help to identifying the most effective management approach in different contexts and situations including emergencies.
2. **Understanding disease pathogenesis and host dynamic** and particularly the interaction between respiratory viral infections and subsequent bacterial complications.
3. **Expanding treatment option for viral respiratory infections** by developing effective antivirals for important acute respiratory pathogens and/or safe and effective biologic response modifiers.
4. **Improving diagnostic and diagnostic tests** to enable clinicians to reliably differentiate viral and bacterial infection at the early stages of the disease.
5. **Improving clinical management** at all levels and in conjunction with primary care, and building on it, improved referral systems must be devised that will connect patients rapidly with hospitals and other higher-level health care facilities so that their cases can be managed appropriately, including better access to oxygen therapy.
6. **Understanding current attitudes and perceptions on respiratory viral infections** by effective communication strategies to facilitate the paradigm shift in the health care workers community, encourage public acceptance of and confidence in respiratory pathogen prevention and treatment programmes.



- **What can be done now?**

To change the current paradigm and implement effective strategies combining vaccines, therapeutics, and enhanced clinical management, efforts are needed in a number of areas:

- A coordinated **global partnership** where partners bring their complementary expertise and strengths;
- **Fundamental and translational** research with application in under-resourced settings to develop guidance and policies;
- **Pilot projects** to improve management of severe respiratory patients in different settings.