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- ViroNovative BV is a limited liability company established under Dutch Law as a spin-out from the Department of Virology Erasmus Medical Center Rotterdam, The Netherlands

- The company was started by Eric Claassen and Prof. Dr. Ab Osterhaus as a dedicated vehicle for expanding and commercializing the patent portfolio concerned with the human meta-pneumo virus (hMPV)

- ViroNovative BV is co-developing diagnostics, vaccines, antibodies and antivirals for the detection, prevention and treatment of hMPV infection. Since its inception the company has licensed out technology for diagnostics to over 14 major diagnostic companies

- Furthermore, new IP concerning vaccines, antibodies and the use of hMPV as a viral vaccine vector (e.g. for RSV) was developed and filed, for this we are actively looking for co-development partners. All relevant background and foreground IP is owned by ViroNovative BV

Fields of Use and Subjects of the Patent Estate:

- Diagnostic use of hMPV for all types of assays (multiple licensors)
- Development of an hMPV vaccine
- Development of an hMPV therapeutic antibody (passive immunization)
- Development of an anti-viral specific for hMPV
- Use of hMPV as a respiratory viral vaccine vector (for e.g. RSV/PIV/Flu)

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- Globally, infectious diseases are responsible for nearly 30% of all deaths worldwide; more than 15 million people die every year

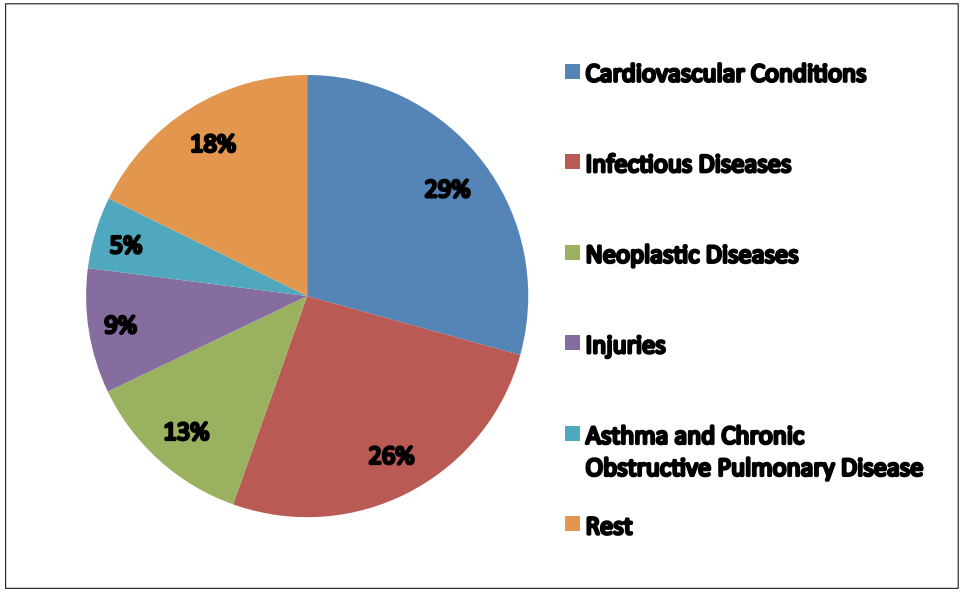

Fig. Global causes of death
Source: WHO (2009)

Infectious Diseases (Millions)	
Respiratory Infections	3,96
HIV/AIDS	2,77
Diarrhoeal Diseases	1,80
Tuberculosis	1,56
Vaccine Preventable Childhood Diseases	1,12
Malaria	1,27
STD	0,18
Meningitis	0,17
Hepatitis B and C	0,16
Tropical Parasitic Diseases	0,13
Dengue	0,02
Other	1,76

- Acute respiratory infections (ARI) continue to be the leading cause of acute illnesses worldwide and remain the most important cause of infant and young children mortality

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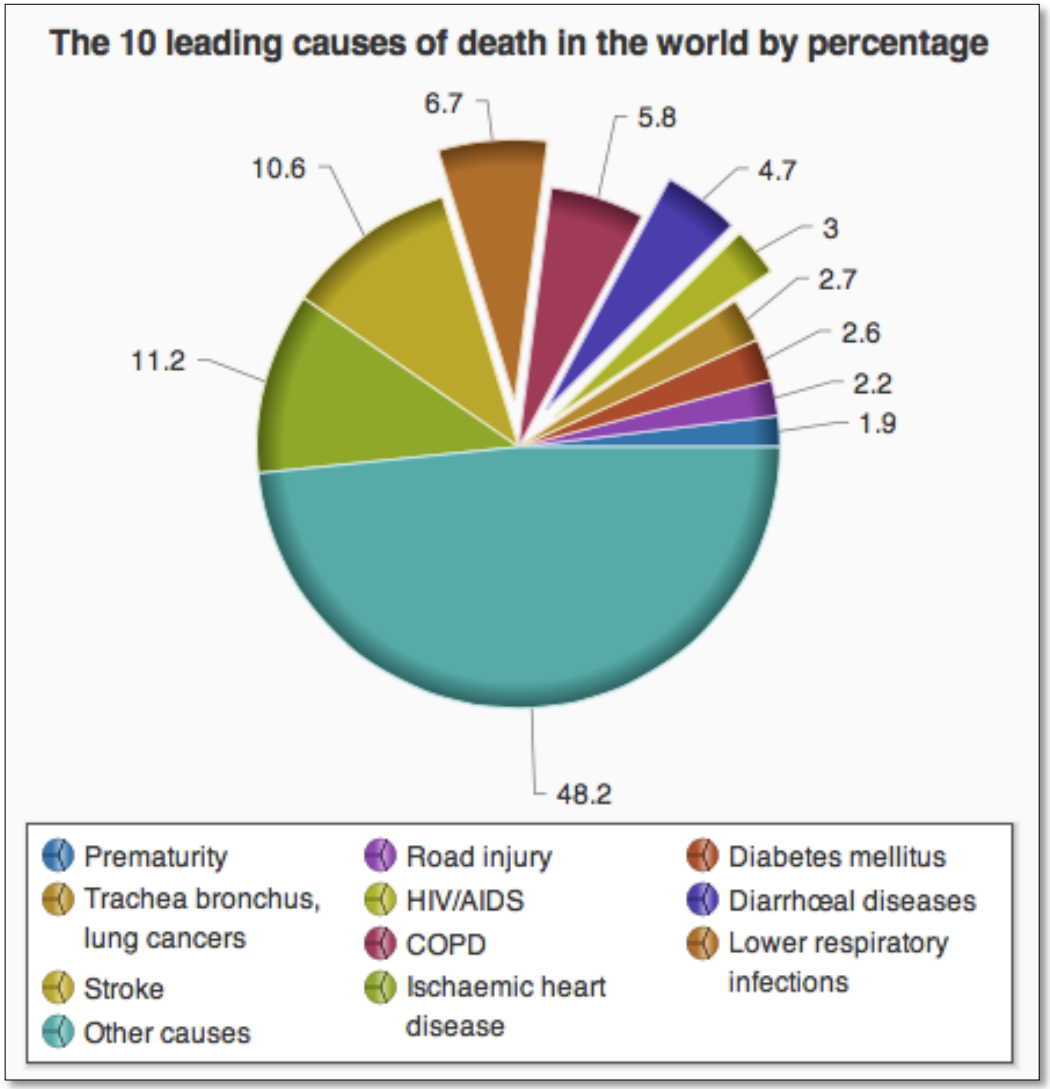

Top 10 causes of death worldwide 2011
Source: WHO

Infectious diseases are responsible for 3 out of 10 leading causes of death in 2011

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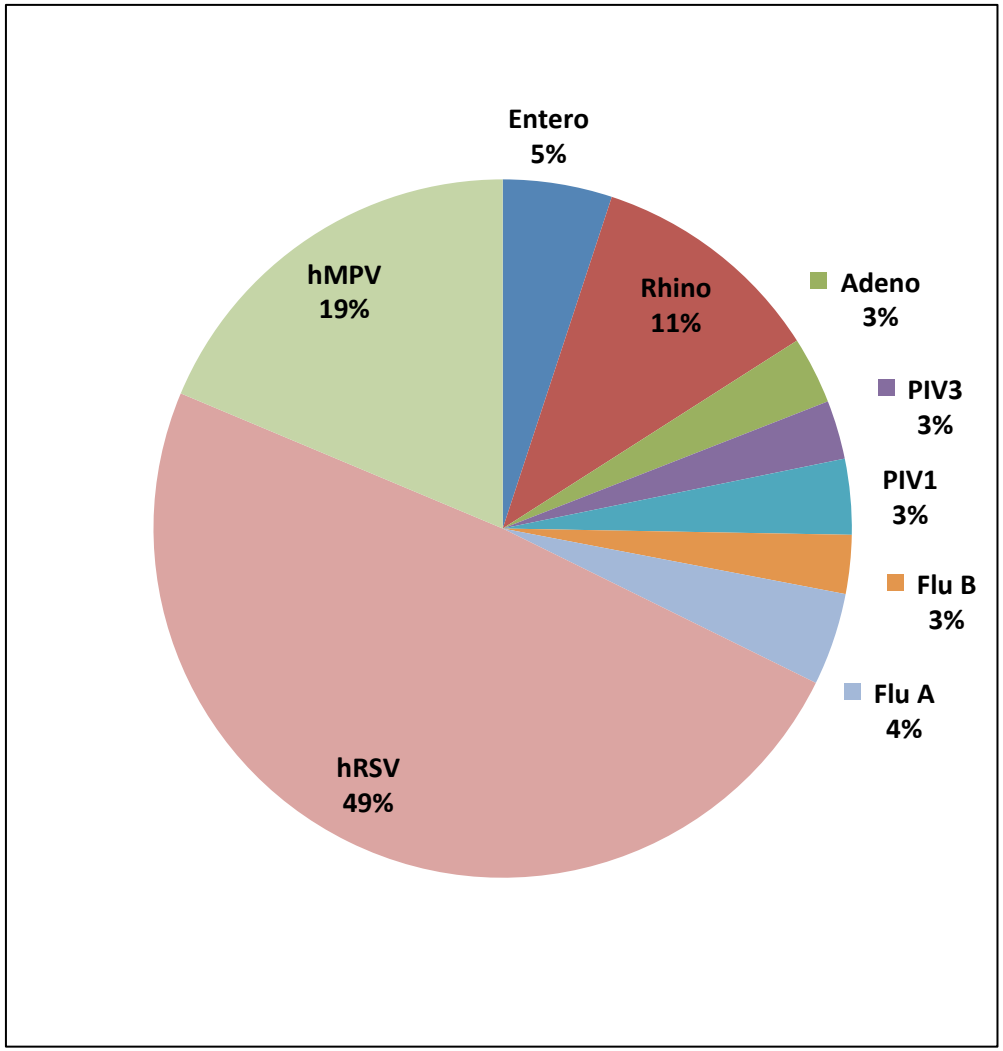
hMPV + RSV form majority disease burden (68%!) in respiratory viral infections



Notable change in significance recognition of HMPV:

- ~19 % of RTIs caused by known viruses
- Classically hMPV was (and is) mistaken for RSV
- This emphasizes the importance of various diagnostic tools
- Virus Specific treatment is essential and will lead to:
  - Clinical cost reduction
  - Less disease (vaccine)
  - Larger and emerging markets

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Diagnostics market: Some Current Licensors

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Therapeutic Market: Estimated

- Annual cost for treatment of viral respiratory tract infections (vRTI) in USA and EU estimated at 50 billion USD

- hMPV accounts for 5-10% of vRTI
- Incidence:
  - 6% in children and healthy adults and elderly
  - 10% (regional differences) in at risk groups
- Sales could exceed 1B USD annually at full market penetration in USA and EU

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hMPV

- While hMPV has traditionally been associated with upper respiratory tract infection, it is now also recognized as a major cause of lower respiratory tract infection in children in several geographical regions

- Recent studies have shown that hMPV accounted for 5-15% of all hospitalizations for acute respiratory infection, while in acute respiratory tract infection (ARTI) in young children, infants and other high-risk populations hMPV is the leading cause of with underlying medical conditions such as prematurity, asthma, cardiopulmonary disease, and immune-compromised patients

hMPV and RSV Facts

- In the past few decades, many etiological agents of respiratory tract illnesses (RTI) have been identified, however a proportion remains with unknown causative pathogen.
- HMPV was uncovered in 2001 by van den Hoogen, BG. Jong, JC. Groen, J. Kuiken, T. de Groot, R. Fouchier, RA. And Osterhaus AD as published in Nature Medecine; *A newly discovered human pneumovirus isolated from young children with respiratory tract disease*
- Initially 28 epidemiological unrelated RTI nasopharyngeal aspirate samples, collected over a 20 year period, contained hMPV isolates.
- HMPV is a newly discovered respiratory virus of the family Paramyxoviridae.
- Genetic and phylogentic research has shown that hMPV is closely related to respiratory syncytial virus (RSV). Further research indicates they are also related in the clinical setting.
- Clinical signs and symptoms are typically non-specific, and may include rhinorrhea, sore throat, sneezing, cough, fever, aching muscles and limbs, headache, and malaise.
- Although the highest burden of hMPV is in young children, it has become clear that hMPV and RSV infections are responsible for an important proportion of RTI across all age groups. In a prospective cohort of nearly 1.400 adult hospitalisations for RTI, hMPV and RSV accounted for 8.0% and 10.5% of the illnesses respectively. Moreover, the proportions of hMPV-and RSV-infected patients requiring ICU admission (13% and 15%) or dying (7% and 8%) were similar for both viruses
- HMPV can be distinguishable from RSV and other RTIs …
  - …

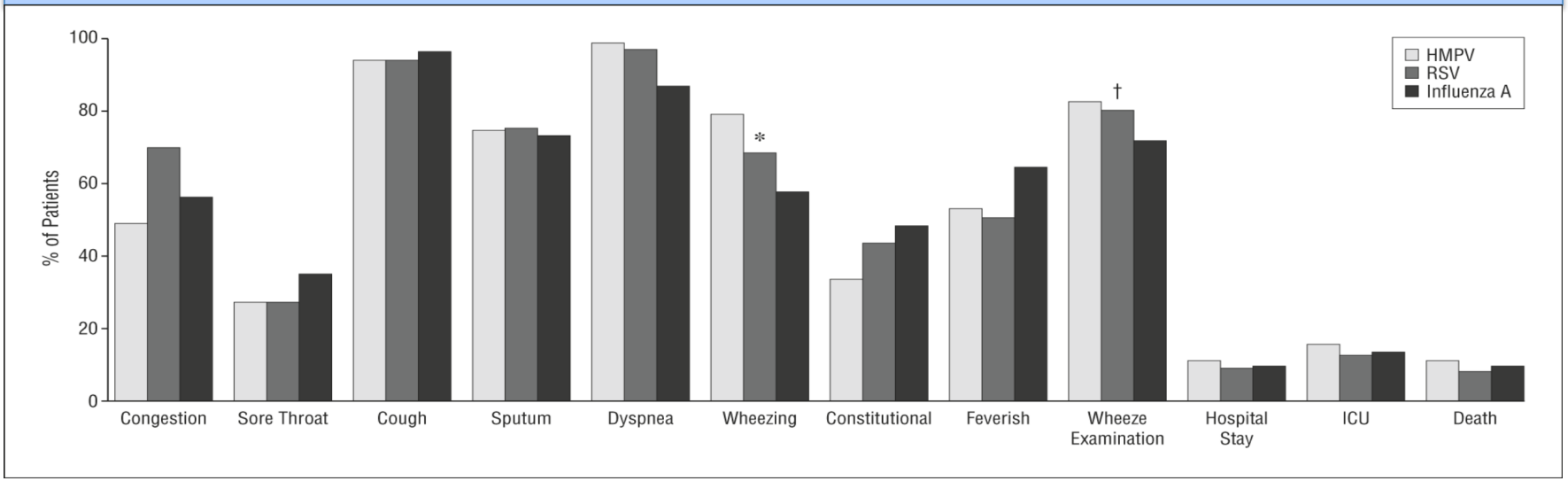

Fig. Comparing clinical symptoms and frequency for hMPV, RSV and Influenza
Source: Walsch (2008) and Falsey (2003)

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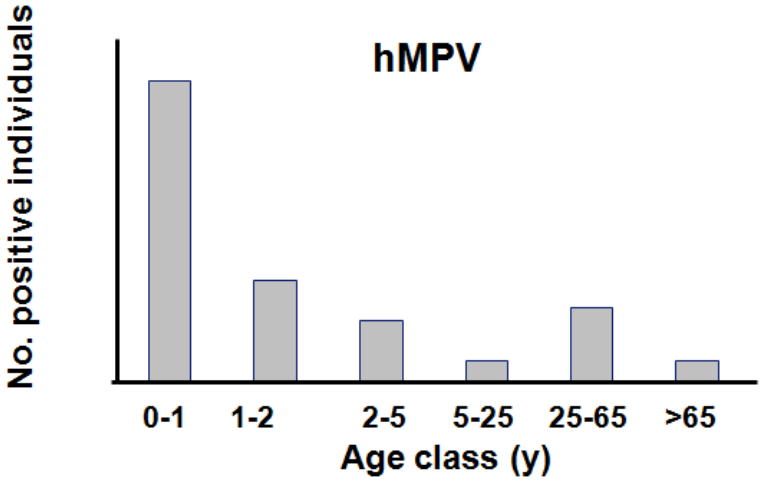
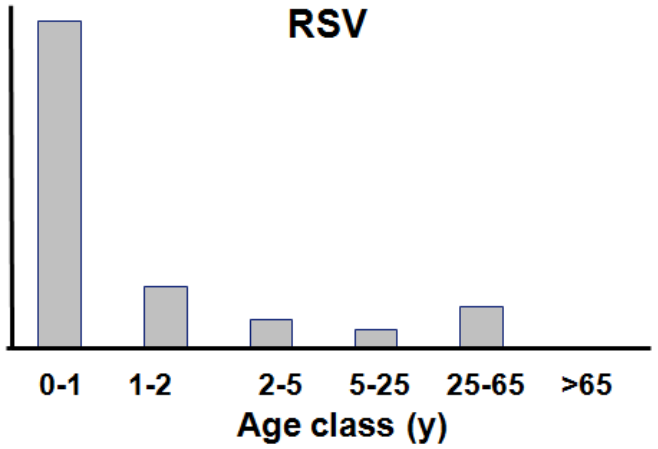
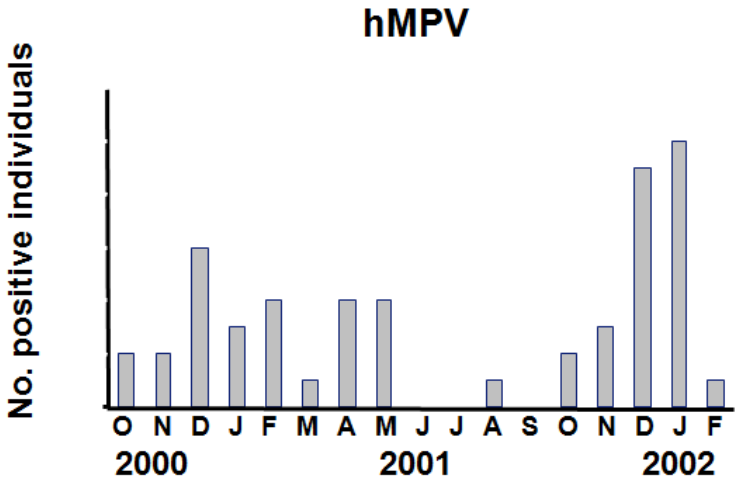
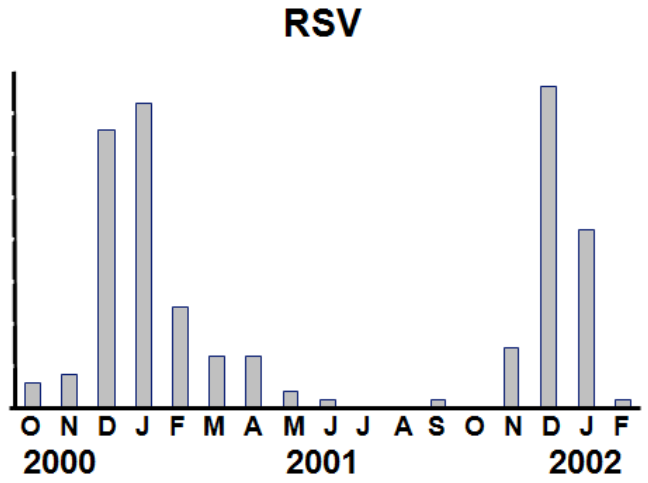
hMPV and RSV: Benchmark





AGE DISTRIBUTION OF hMPV PATIENTS SIMILAR TO THAT OF RSV PATIENTS





SEASONAL DISTRIBUTION OF hMPV INFECTIONS IS SIMILAR TO THAT OF RSV

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hMPV in adults

- In adults of all ages, hMPV is a common infection, and can result in serious infection that requires hospitalization due to; acute bronchitis, COPD exacerbations, and pneumonia
- Average lengths of hospitalization for hMPV-infected younger adults was 9 days, with 13.2% requiring ICU. Elderly adults remain ill for an average of 17 days
- Studies indicate the association of hMPV infection with hospitalisation for acute respiratory tract symptoms in elderly adults
- HMPV infection was similar to 5.5% annual average infection rate for RSV, and greater than that of influenza A (2.4%)
- Several documented outbreaks of hMPV have occurred in long term care facilities, with mortality of up to 50%

Annual Incidence/ %	Study Cohort
13.1	Adults aged 19-40 with acute RTI during winter
5.9	Healthy adults >65 with acute RTI during winter
9.1	High risk adults with acute RTI during winter
8.5	Adult patients hospitalized with acture RTI during winter

Table. Incidence of hMPV in elderly in the US
Source: Walsch et al (2008)

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hMPV in children

- Among infants and children aged less than 3 years in Northern Spain, the incidence rate of hospitalization for hMPV was calculated at 2.6 per 1,000 children, which was higher than the incidence of influenza and PIV
- Infection with hMPV in children varies between 5-37% incidence in patients with respiratory tract symptoms

Author	Country	% children with RTI infected with hMPV	Reference
Sung	Taiwan	27.1	J Microbil, Immun and Infect 2011; 44: 184-190
Boivin	Canada	6	Emerg Infect Dis 2003; 9: 634-40
Esper	USA	6.4	Pediatrics. 2003; 111: 1407-10
Freymouth	France	6.6	Pediatr Infect Dis. 2003;22:92-4
Jartti	Finland	8	Lancet. 2002;360:1393-1394
Maggi	Italy	37, 7, 43	J Clin Microbiol. 2003;41:2987-2991
Peiris	Hong Kong	5.5	Emerging Infect Dis. 2003;9:268-33
Van den Hoogen	Netherlands	7	J Infect Dis. 2003;188:1571-7
Viazov	Germany	17.5	J Clin Microbiol. 2003;41:3043-5

Table. Incidence of hMPV in children

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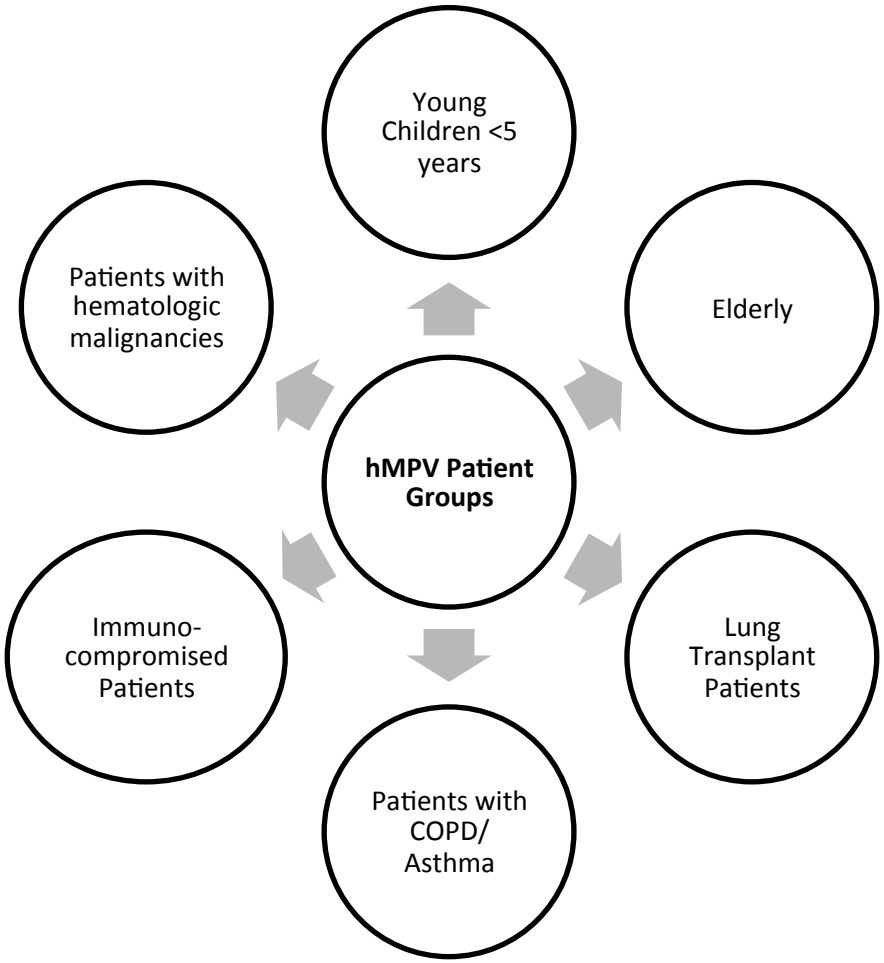
hMPV, major pathogen in respiratory complications



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Huge Economic Impact leads to Value

- Potential value of vaccination for hMPV is significant due to high medical costs
- Given that the clinical manifestations and supportive treatment of hMPV is closely related to those of RSV, literature of hospitalizations costs as a result of RSV was analysed
- Mean costs are estimated at € 2,929 per hospitalization for RSV
- Some studies have estimated the cost of a paediatric hospitalization for influenza at between $3,000 and $4,000 which includes all medical costs regarding to treatment of influenza clinically
- In Europe, there are around 31.000 children hospitalized annually due to hMPV-associated disease
  - Mean hospital duration: 6.5 days
  - This means that the annual economic burden of hospitalized children due to hMPV infections is (6.5* €3,000-4,000) * cases in EU/US = total burden hospitalized children due to hMPV infections
- Total economic impact of non–influenza related vRTI approaches $40 billion annually in the United States (direct costs, $17 billion per year; and indirect costs, $22.5 billion per year)
- The next assumptions are:
  - When vRTIs in the US costs around 17 (300 mln people) billion per year on direct costs, the burden for the EU is (700 mln people) approximately twice as much as those for the US (> 34 billion)
  - This means that the burden of disease of vRTI in the EU and US market is 51 billion
  - HMPV accounts for 5-10% of the viral respiratory diseases
  - The burden of disease per year is € 2.5 - € 5.1 billion per year

Region	Annual Economic Impact	Per Patient Costs Hospitalization	Study Design	References
USA	$ 500 Mln (admission cost)	€ 3799	Bronchiolitis-related hospitalizations	Pellier *et al.* 2005
USA	$ 700 Mln (total burden)	-	Annual RSV burden	Paramore *et al.* 2004
Germany	€ 213 Mln (LRTI burden)	€ 2579	LRTI hospitalizations	Ehlken *et al.* 2005
The Netherlands	€ 2,7 Mln (RSV burden)	€ 3110	Annual RSV burden	Rietveld *et al.* 2004

Table showing estimation of RSV hospitalization burden

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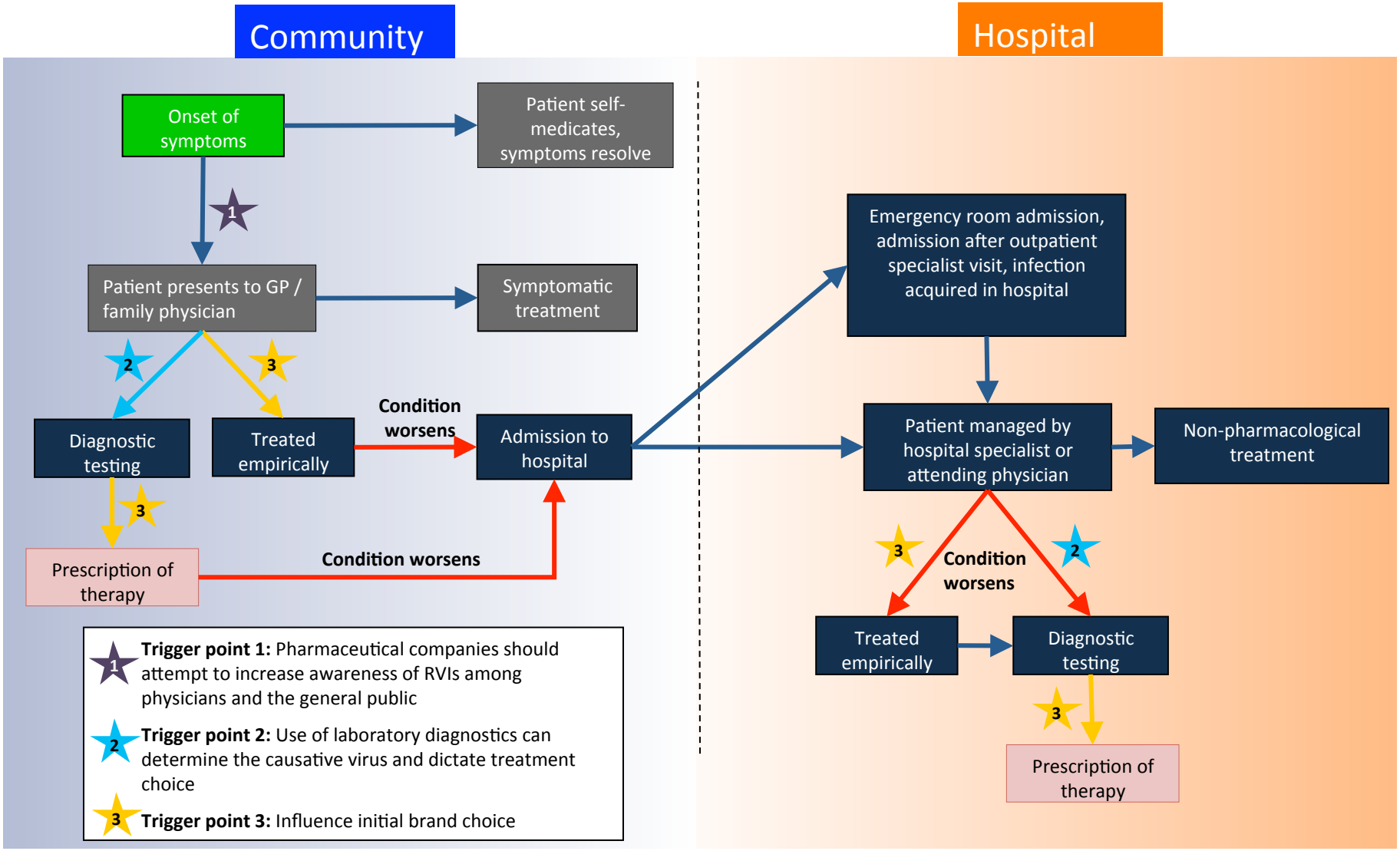
Point of Care diagnostics open up other and larger markets!



Source: DMHC2601

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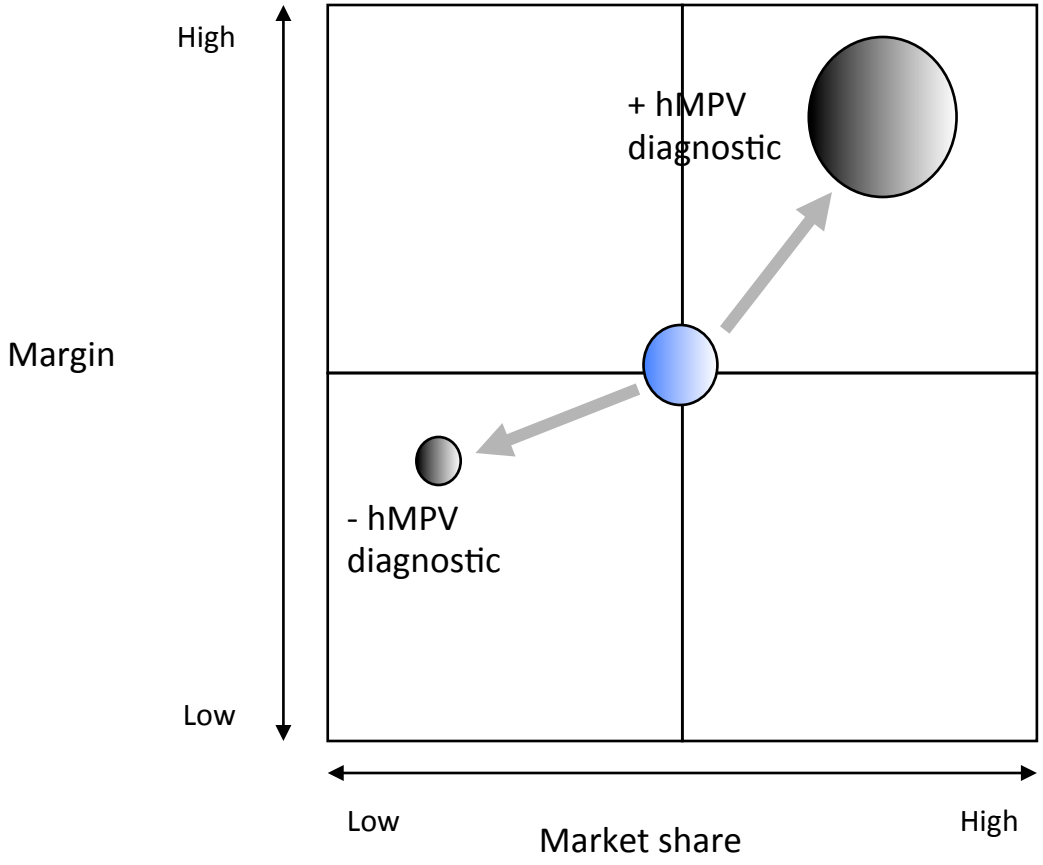
- Competitive advantages and point of care testing will result in significant gain in value of respiratory portfolio (prevention)



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Value of hMPV diagnostics business stems from multiple sources

Control of Market

- Control of hMPV market: value €?m
  - Market size potential equivalent to that of RSV at €30-40m with ~5-10% CAGR
  - Broad protection from competing diagnostics for hMPV
  - Control of licensing
    - Significant licensing revenues

Synergies

- Synergies: value = €?m
  - Development, manufacturing, marketing and sales

Competitive Advantage

- Competitive advantage in respiratory pathogens market: value €?m
  - ***No other respiratory virus subject to broad protection from competing diagnostics***
  - Leverage hMPV to gain share of diagnostics to other respiratory pathogens
    - eg RSV (market size €30-40m with ~5-10% CAGR)
    - Influenza (market size considerably greater than RSV)

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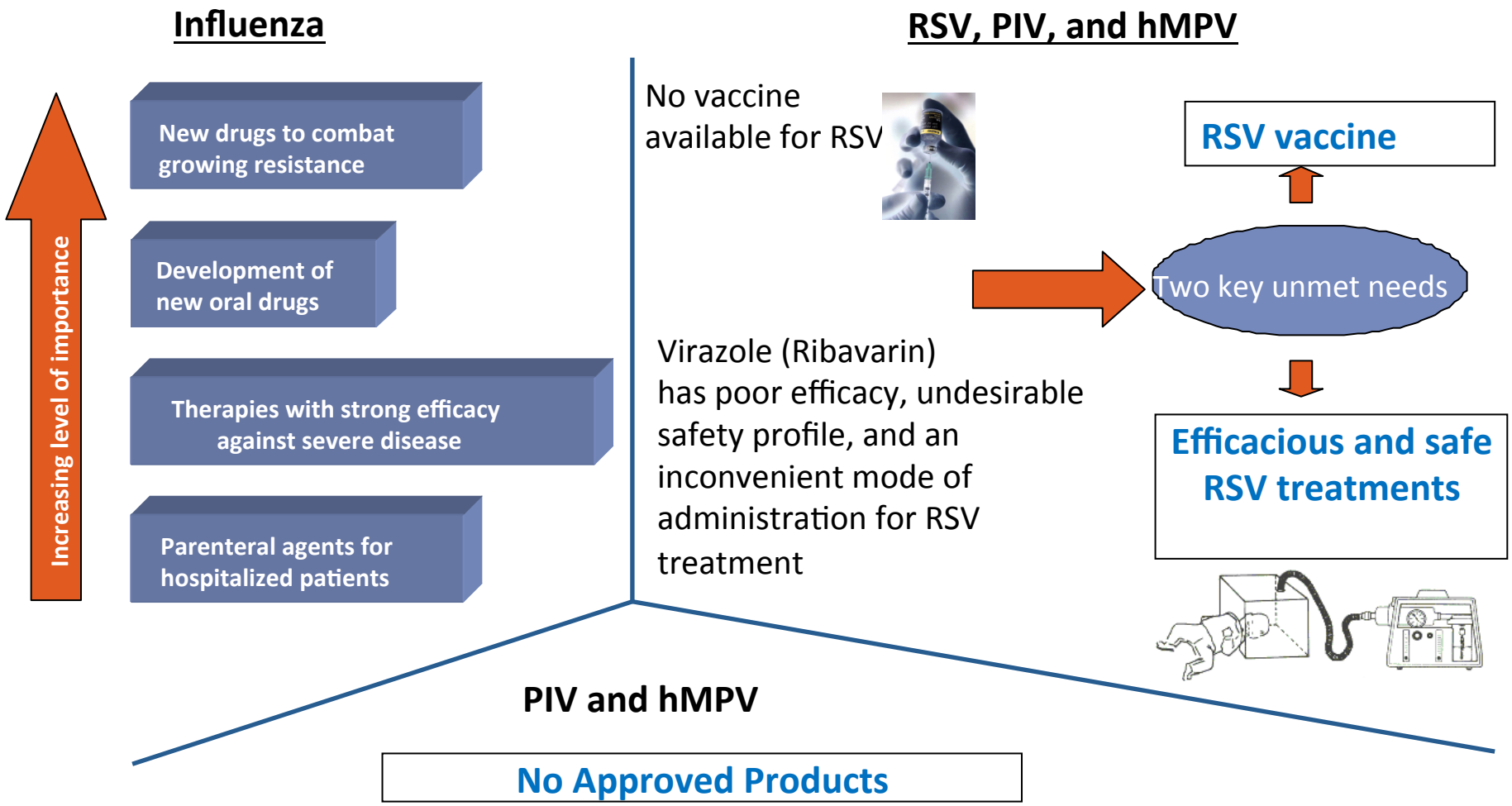
- Currently, there are no approved therapeutics or vaccines for PIV or hMPV infections, despite a high burden and strong unmet need.



Mis-diagnosis of hMPV results in mis-prescription of antibiotics and corticosteroids

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