SHORT COMMUNICATION

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FUTURE LANDSCAPE IN THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN CHILDREN

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Introduction

Respiratory Syncytial Virus (RSV) is the leading cause of bronchiolitis in infants and young children. It was first discovered in 1956 and is divided into two major antigenic groups, A and B. Both strains co-circulate during outbreaks [1]. RSV causes a high disease burden for infants globally. Virtually all children will be infected with RSV by two years of age [2]. Every year, RSV causes 33 million episodes of severe respiratory infection in children under 5 years old and 3.6 million hospital admissions [3].

Global and local impact of RSV infection in children

About 101,000 children die from RSV infection each year, and half of them are below 6 months old [4]. The majority of RSV deaths occur among children in Low- and Middle-Income Countries (LMIC) where they never make it to a hospital. Many children die from RSV in the community than in the hospital [5]. No other virus, including influenza, causes this much damage to children

In Malaysia, RSV was the predominant virus, responsible for 70.6% of all laboratory-confirmed viral lower respiratory tract infections (LRTIs) in children aged five years and below over the 26-year study period (1982-2008) [6]. RSV-infected children below two years old had a high hospitalisation rate of 84.5% [7]. A study in Tuanku Jaafar Hospital in Seremban showed 69 out of 450 (15.3%) of the children admitted with RSV in 2008 to 2013 needed intensive care and 1.6% (7/450) died. The case fatality rate (CFR) is five times higher than in developed countries (0.3%) [8].

Seasonality of RSV circulation

Seasonal RSV activity is observed in many regions of the world. Temperate climates have distinct peaks during autumn and winter. Equatorial regions have year-round circulation. Malaysia appears to have a year-round circulation pattern (Figure 1), with seasonal peaks [9-11]. The seasonality of RSV will be an important consideration in developing RSV prevention strategies.

The cost of RSV disease

The healthcare cost of bronchiolitis is five times initially and twice as high in the subsequent six-months, when compared to infants admitted without bronchiolitis. The cost is highest in the first ten days and is due to hospitalisation expenses [12].

There is a wide range of costs of RSV illness in LMICs. The hospitalisation cost of RSV disease ranges from $41 in Malawi to $1,700 and $7,000 in Malaysia and Mexico, respectively [13]. The inpatient RSV cost is equivalent to 24% or 37% of the total monthly household income in Bangladesh and Malawi, respectively [14-15]. Averting this cost through RSV immunisations could have large health impacts and save significant healthcare resources.

Current treatments and future strategies

There is no specific treatment for RSV apart from supportive therapy with intravenous fluids, nutrition, oxygen, empirical antibiotics and respiratory support in the intensive care unit [16]. Since 1960s, researchers have explored various vaccines or options to prevent RSV.

Until 2022, Palivizumab, was the only licensed mono-clonal antibody (mAb) for prophylaxis against RSV. Palivizumab is a short acting mono-clonal antibody and required monthly injections for five months to prevent 55% of RSV disease [17]. It is only indicated for premature infants with chronic lung disease, children younger than two years of age with

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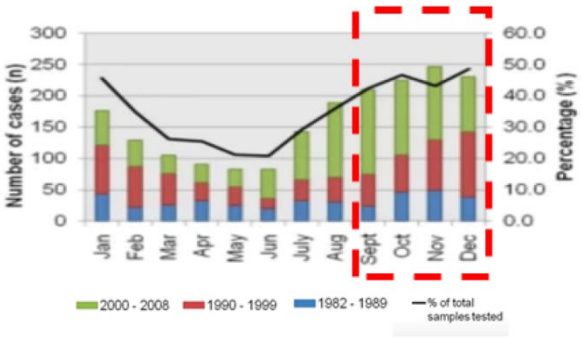
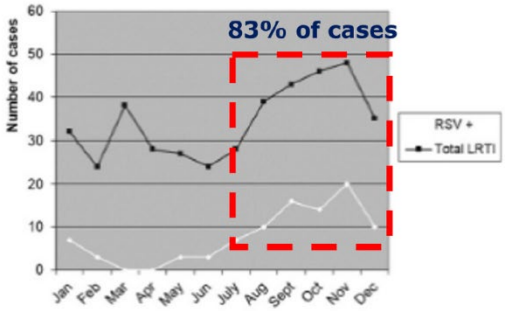
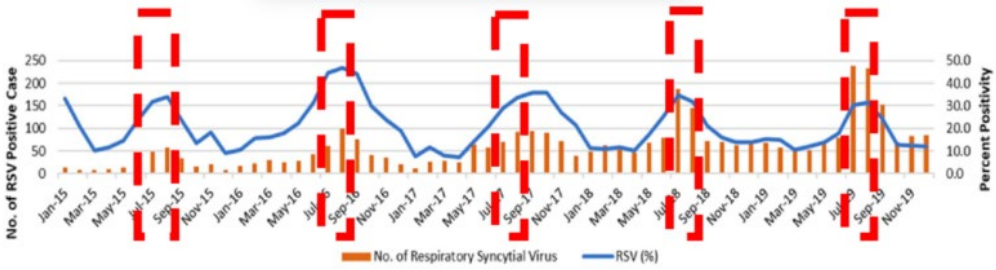


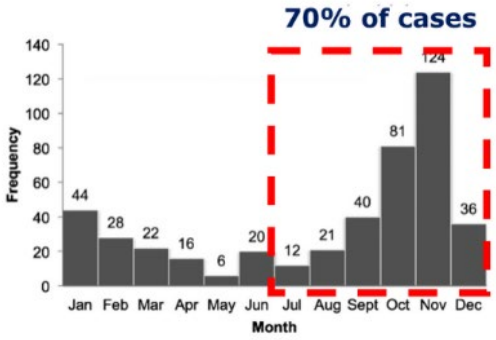
Khor et al (UMMC, 1982-2008)[6]:
RSV season peaks from **September to December**



Teck et al (HRPZII, Kelantan)[11]:
RSV season peaks from **September to December**



Low et al (Pantai Premier Pathology, 2015-2019)[7]:
RSV season peaks from **July to September**



KF Ng et al (HTJ, 2008-2013)[8]:
RSV season peaks from **September to January**

Figure 1. RSV Seasonality in Malaysia with distinct peaks [6-8][11].

hemodynamically significant congenital heart disease, immunocompromised children (particularly transplant patients), and children with severe immunodeficiency diseases [18]. However, evidently most infants with RSV are term infants.

In 2023, Nirsevimab, a long-acting (mAb) was approved by the Food and Drug Administration (FDA) for the prevention of RSV disease in infants and young children [19]. Maternal immunisation confers protection to the foetus through the transplacental transfer of IgG antibodies [20]. It is 83.2% effective in preventing RSV-related hospitalisations in the first five months of life [21]. Real-world experience showed that Nirsevimab is 82-98% effective in preventing RSV-related hospitalisations and 70-90% ICU admissions [22-29]. The safety of Nirsevimab has been proven in both clinical trials and real-world experience. Nirsevimab has shown sustained levels of RSV mAbs through 361 days following a single dose, suggesting that it may offer protection beyond five months [30].

Also, in 2023, a maternal vaccine, given during the third trimester could prevent RSV in the first six months of life, when they are most vulnerable. The vaccine efficacy was 81.8% for the first three months of life and 69.4% for the first six months. The number of maternal participants and infants reporting adverse events within 1 month after birth, was relatively similar for both the RSV vaccine and placebo groups [31].

Cost-effectiveness (CE) of RSV immunization

CE studies have been conducted in 133 LMICs (Figure 2) [32]. RSV maternal vaccine and long acting mAbs have been found to be cost-effective in two-third of the LMICs countries while offering cost-savings in the remainder [32].

Conclusion

The introduction of maternal RSV vaccines and long acting mAbs marks a major advancement in the prevention of RSV disease in infants. These interventions are highly effective, safe, and cost-effective, particularly in low- and middle-income countries where the disease burden is highest.

To maximise public health impact, RSV immunisation should be prioritised in national child health policies, with clear strategies for timely implementation. Early adoption and equitable access will be key to reducing RSV-related hospitalisations, deaths, and economic burden globally.

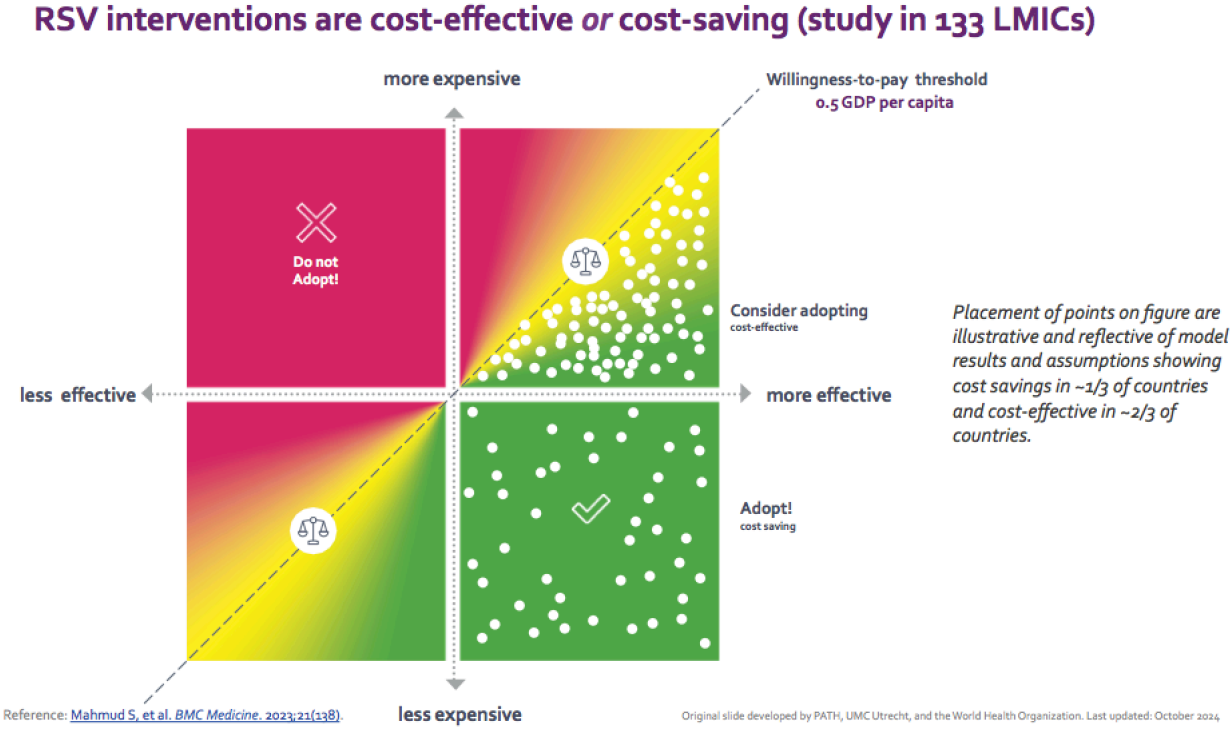


Figure 2. Cost-Effectiveness of RSV Immunization [32]

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