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DEVELOPMENT AND APPLICATION OF A NEW COST-UTILITY MODEL TO ASSESS THE COST-EFFECTIVENESS OF PALIVIZUMAB FOR THE PREVENTION OF SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION IN MODERATE-TO-LATE PRETERM INFANTS

X. Carbonell-Estrany[1], J. Fullarton[2], I. Keary[2], B. Rodgers-Gray[2], J-E. Tarride[3], and B. Paes[3]

[1] Hospital Clinic, Barcelona, Spain; [2] Violicom Medical Limited, Aldermaston, United Kingdom; [3] McMaster University, Hamilton, Ontario, Canada

Introduction

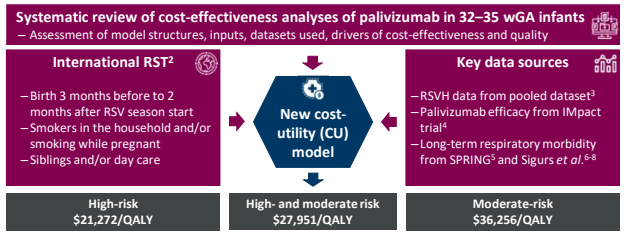
- Palivizumab is the only licensed and effective therapy for preventing RSV hospitalisation (RSVH), but reported cost-effectiveness varies in moderate-to-late preterm (32–35 weeks' gestational age [wGA]) infants[1]
- The 3-variable International Risk Scoring Tool (IRST) can guide prophylaxis for 32–35 wGA infants at greatest risk of RSVH and has the potential to improve the cost-effectiveness of palivizumab[2]

  1: Birth 3 months before to 2 months after RSV season start; **2:** Smokers in the household and/or smoking while pregnant; **3:** Siblings and/or day care

Objective

- To assess the cost-effectiveness of IRST-guided palivizumab *versus* no prophylaxis in Canadian moderate-to-late preterm infants using a new up-to-date cost-utility model

Graphical Summary



Conclusions

- **This new economic analysis demonstrated palivizumab to be highly cost-effective *versus* no prophylaxis in moderate-and-high risk 32–35wGA infants in the Canadian healthcare context**

Results and interpretation

- Palivizumab was highly cost-effective ($27,951/quality-adjusted life year [QALY]) in high- and moderate-risk infants (Table 1) and remained so when assessed only in moderate-risk infants ($36,256)

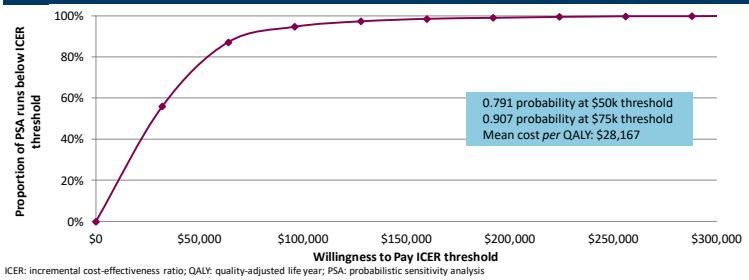
Table 1: Cost-effectiveness† of palivizumab *vs* no prophylaxis using IRST

	High-risk	High- and moderate-risk	Moderate-risk
Cost difference	$3,970	$4,548	$5,086
QALY difference	0.187	0.163	0.140
Cost *per* QALY	**$21,272**	**$27,951**	**$36,256**

†CAN$; discounting at 1.5%; Canadian cost-effectiveness threshold typically stated as $50k, though can be higher (>$75k). IRST: International Risk Scoring Tool; QALY: quality-adjusted life year

- Probabilistic sensitivity analyses (10,000 iterations) resulted in incremental costs of $28,167/QALY, with a 79.1% probability of palivizumab being cost-effective at a $50,000 willingness-to-pay threshold (Figure 1)

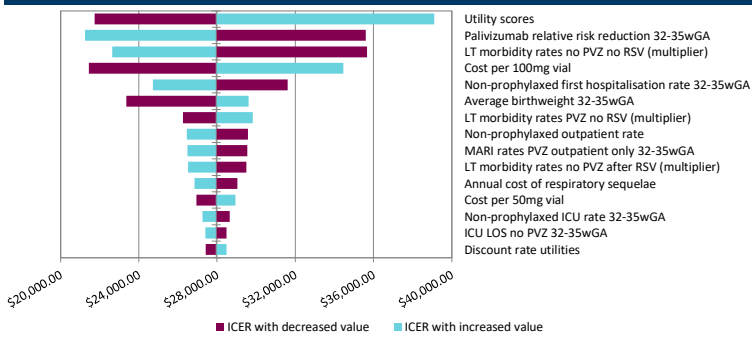
Figure 1: Cost-effectiveness acceptability curve



ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year; PSA: probabilistic sensitivity analysis

- In deterministic sensitivity analyses (±20% on main variables) the model was most sensitive to utility scores, palivizumab efficacy, long-term morbidity rates, and palivizumab cost (Figure 2)

Figure 2: One-way sensitivity analysis ±20% for prophylaxed *vs* non-prophylaxed infants, 15 most sensitive variables



ICU: intensive care unit; LOS: length of stay; LT: long-term; MARI: Medically-attended (emergency room/outpatient) RSV infection; PVZ: palivizumab

- Removing the 1.5% discounting of costs and utilities slightly improved cost-effectiveness
  - High- and moderate-risk, 18 years respiratory morbidity: $24,724/QALY
- Vial sharing (5% wastage) considerably improved cost-effectiveness
  - High- and moderate-risk infants, 18 years respiratory morbidity: $19,582/QALY
- Excluding indirect costs ($27,294/QALY) had a limited impact

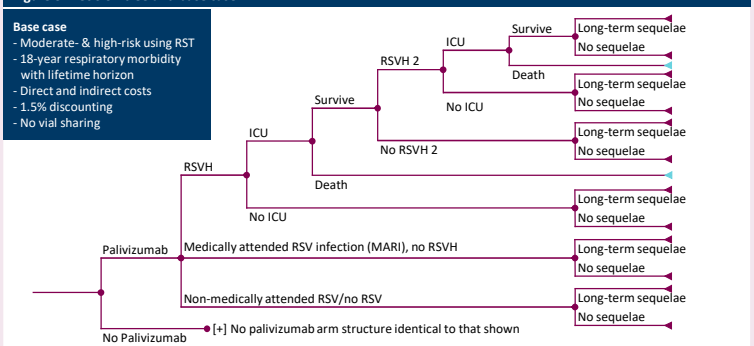
Limitations

- Key limitations of the model relate to the availability of gestational age specific data for utilities and long-term respiratory morbidity beyond 6 years

Methods

- A systematic review of previous economic evaluations of palivizumab in 32–35 wGA infants and expert input informed the structure, inputs and costs
- Infants assessed as moderate- and high-risk of RSVH by the IRST[2] (score ≥20/56) received palivizumab
- Prophylaxed/untreated infants followed a semi-Markov process having either an RSVH, emergency room/outpatient-medically attended RSV infection (MARI), or were uninfected/non-medically attended (Figure 3)

Figure 3: Decision tree and base case



- The IMpact randomised trial[4] was the primary source of palivizumab efficacy (82% reduction in RSVH), with birth data and hospital outcomes derived from the pooled dataset of 7 Northern Hemisphere studies used to develop the IRST[3] (Table 2)

Table 2: Input parameters

Parameter	Palivizumab	No palivizumab
RSVH*		
- Overall rate (for efficacy)	1.8%[4]	10.1%[4]
- Intensive care unit (ICU) rate	17.9%[3]	17.9%[3]
- Ward length of stay, mean days	(In overall cost)	(In overall cost)
- ICU length of stay, mean days	6.8[3]	6.8[3]
- Utility in hospital	0.60[9,10]	0.60[9,10]
- Utility post discharge no sequelae	0.88[11]	0.88[11]
- Utility post discharge long-term sequelae	0.79[12]	0.79[12]
- Mortality (ICU patient only)	0.43%[13,14]	0.43%[13,14]
MARI		
- Rate outpatients only	2.48%[4,15,16]	13.91%[4,15,16]
- Rate outpatients & emergency department	0.42%[4,15,16]	2.38%[4,15,16]
- Rate emergency department only	0.05%[4,15,16]	0.29%[7,15,16]
- Utility	0.95[11]	0.95[11]
No RSVH/MARI		
- Utility no sequelae	0.95[11]	0.95[11]
- Utility long-term sequelae	0.79[12]	0.79[12]

*First and subsequent RSVHs. ICU: intensive care unit; MARI: medically attended (emergency room/outpatient)RSV infection; RSVH: respiratory syncytial virus hospitalisation

- Palivizumab costs were calculated from birth weights defined in Canadian birth statistics[17] in combination with a growth algorithm[18] and Canadian list prices (50mg: CAN$752; 100mg: $1,505)[19] (Table 3)
- Healthcare costs were drawn from the RSV-Quebec study,[20] Healthcare Canada[21,22] and an assessment of childhood asthma costs[23]
- Indirect costs were drawn from Mitchell et al.[24] and national Canadian Statistics[25,26]

Table 3: Direct and indirect costs

Direct		Indirect	
Parameter	**Canadian dollars (CAD$)**	**Parameter**	**CAD$**
Palivizumab*		**Palivizumab administration**	
- 50mg vial	752[19]	- Transport	76.13[25]
- 100mg vial	1,505[19]	- Missed work	176.89[26]
- Nurse administration	14.37[20]		
Pre-admission healthcare contact	214.16[20]	**RSVH**	
		- Missed work	1,213.31[24,26]
RSVH total stay (excl. ICU)	8352.87[20]	- Childcare	116.04[24]
		- Transport	124.86[24]
ICU (per day)	5,747.00[20]	- Other out-of-pocket	341.81[24]
MARI		**MARI attendance**	
- Outpatients appointment	First: 175.40; FU: 91.35[21]	- Transport	18.30[25]
- Emergency department	336.56[22]	- Missed work	42.52[26]
Respiratory morbidity (p.a.)	1,116.45[23]	**Loss of earnings after death**	2,178,497.24[26,27]

FU: follow-up; ICU: intensive care unit; MARI: medically-attended RSV infection; p.a.: per annum; RSVH: respiratory syncytial virus hospitalisation. *Dose calculated using birth data from the source dataset for the IRST[2] with monthly weight gain applied using Narayan et al.[18] algorithm. For moderate- and high-risk infants, the mean number of doses was 4.09

- Respiratory morbidity over 6-18 years across a lifetime horizon was assessed among RSVH, emergency room/outpatient attended RSV-infection (MARI), or uninfected/non-medically attended infants
  - Rates of respiratory morbidity were drawn from the SPRING study[5] up to age 6 years and from Sigurs et al.[6-8] thereafter; the impact of palivizumab was modelled based on data from three studies[28-30]

Table 4: Rates of respiratory morbidity[5-8,28-30]

Year(s)	Palivizumab		No Palivizumab	
	RSVH	No RSVH	RSVH	No RSVH
0-1	18.43%	5.38%	41.43%	12.09%
1-2	18.43%	5.38%	41.43%	12.09%
2-3	11.05%	5.80%	29.27%	15.36%
3-4	6.12%	4.15%	18.55%	12.57%
4-5	4.39%	2.73%	15.00%	9.31%
5-6	3.25%	2.53%	12.39%	9.66%
6-7	2.93%	2.29%	12.39%	9.66%
7-13	2.33%	1.47%	17.39%	10.96%
13-18	1.79%	1.17%	22.39%	14.66%

- Results were expressed as a cost *per* QALY (incremental cost-effectiveness ratio; ICER) *vs* no prophylaxis. RSVH: respiratory syncytial virus hospitalisation

- Scenario analyses included consideration of moderate- and high-risk groups individually, the exclusion of discounting, exclusion of societal costs, inclusion of vial sharing (5% wastage)
- Results are expressed as a cost *per* QALY (incremental cost-effectiveness ratio; ICER) *versus* no prophylaxis

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