Measuring the vaccine success index: a framework for long-term evaluation and monitoring of rotavirus vaccination.

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Objective

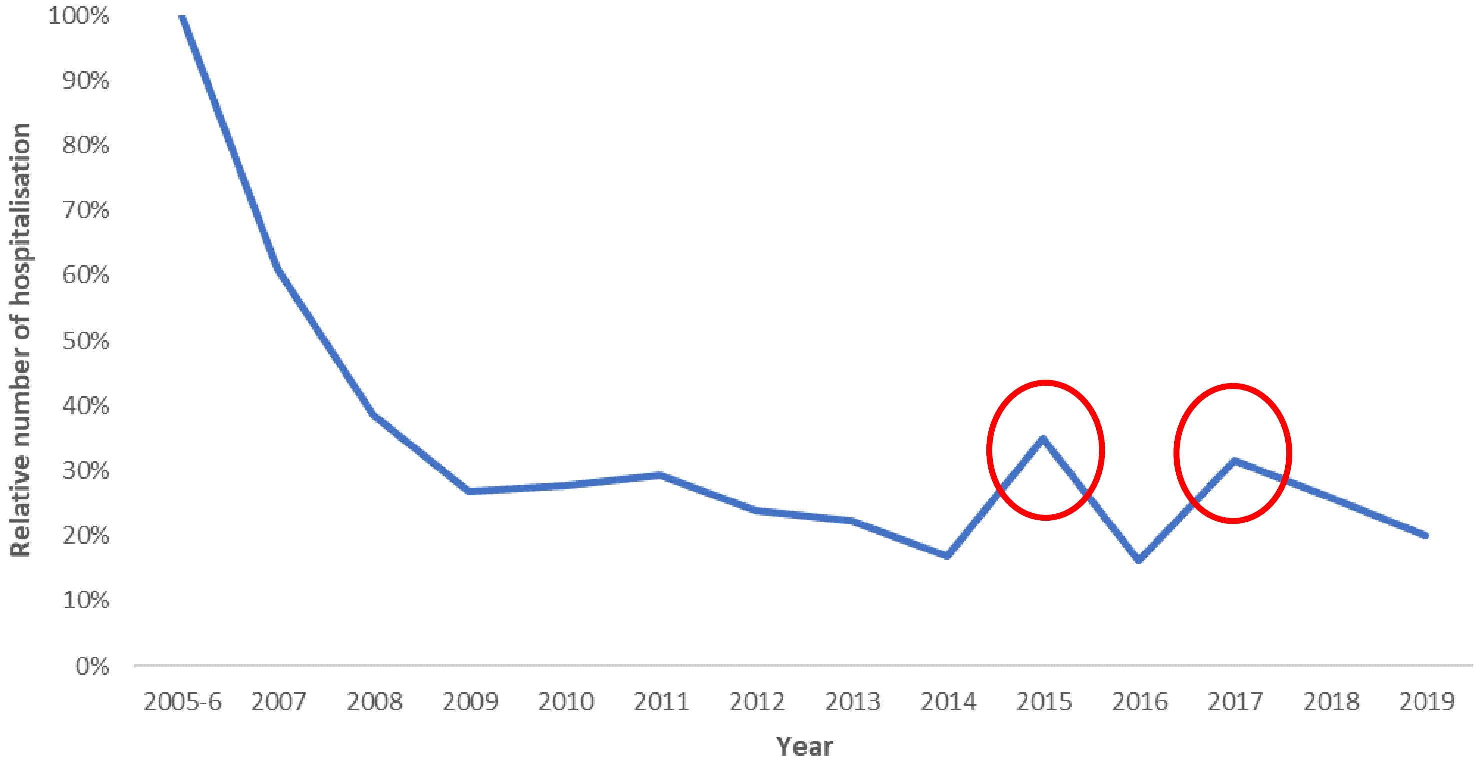
- How to evaluate the economic success of long-term vaccination? The case of rotavirus vaccination in Belgium.

- In other words, can we start vaccinating anywhere anytime after market approval or should we first consider a vaccination strategy to start with?

The issue

- Rotavirus vaccination was introduced in Belgium with reimbursement in Nov 2006
- We followed the decline in hospitalisation of rotavirus diseases every year in a sample of paediatric wards from 2005 until 2019
- The following graph (Figure 1) demonstrates the annual observations made
- The questions we had:
  - Can we explain the observation of small biannual picks appearing over time?
  - Can we express the result in a measure of long-term vaccination success or failure?

Figure 1



100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Relative number of hospitalisation
2005-6
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
Year

Method

- We hypothesized that having biannual peaks appearing over time is caused by a failure of introducing the vaccine using an optimal launch strategy. This leads to poor herd effects first years causing over time the appearance of new primary sources of infection at an older age instigating the new peaks.
- The economic value capturing this failure can be expressed using a ratio of cost-impact analysis (CIA) over cost-effectiveness analysis (CEA) resulting in a value > 1. That ratio is called the vaccine success index.
- To accept that approach, we need to endorse 4 new elements in the assessment:
  - presence of primary and secondary sources of infection
  - presence of a vaccine uptake period and a vaccine post-uptake period
  - understanding the difference between CEA and CIA
  - right interpretation of the success index result
- We may demonstrate with modelling that countries with an optimal vaccination strategy at start will have a success index ≤ 1 with the additional condition of a low CEA result

Result (1)

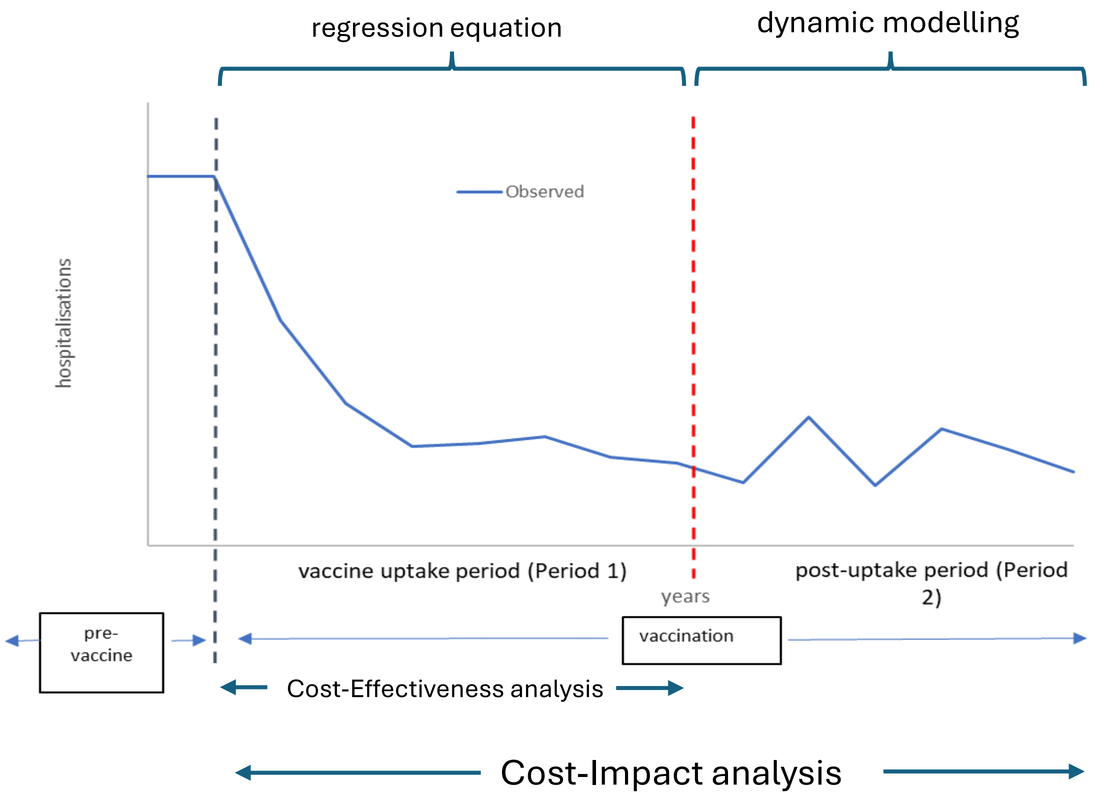
- Rotavirus vaccine was launched in Belgium only 3 months before the next peak season causing no huge nor a sustained herd effect
- Observed RotaBis data on hospitalisation

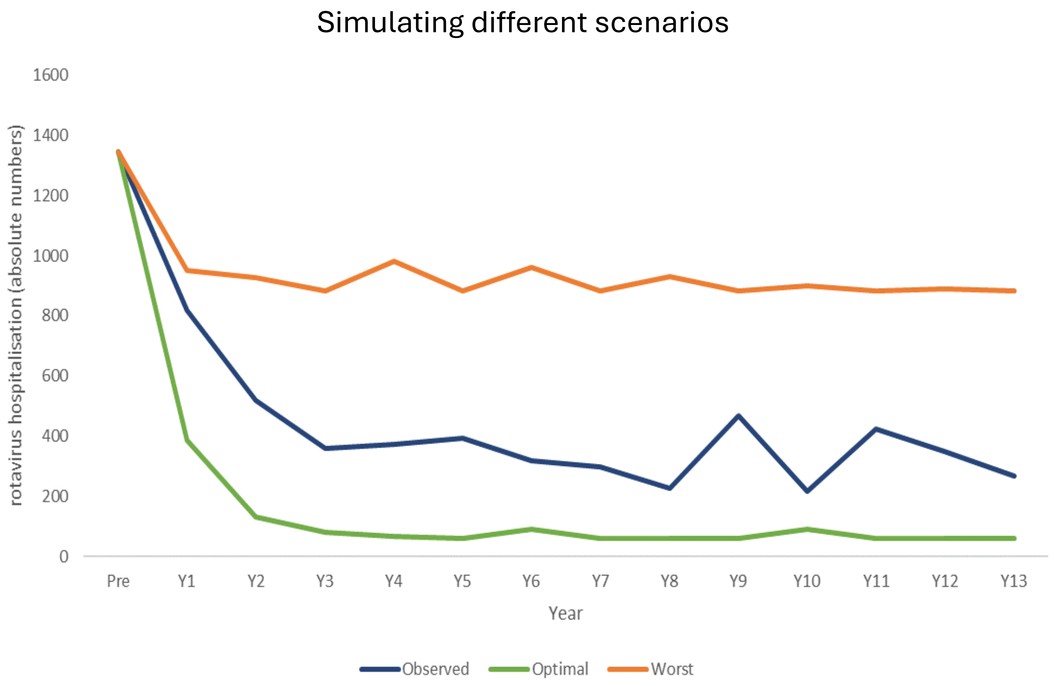
Age-groups	Pre	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}	Y_{11}	Y_{12}	Y_{13}
0-2m	113	94	62	56	44	65	54	44	**48**	56	28	55	52	27
3-12m	678	340	152	129	127	133	103	97	**70**	137	75	123	125	95
13-24m	413	311	208	100	139	134	114	107	**74**	186	85	180	119	96
25-36m	102	56	67	49	33	44	33	33	**31**	67	17	42	37	35
37-48m	27	16	18	19	19	12	9	15	**4**	13	8	18	9	9
49-60m	12	2	12	8	10	7	7	4	**1**	10	4	6	8	6
Total	**1345**	**819**	**519**	**361**	**372**	**395**	**320**	**300**	**228**	**469**	**217**	**424**	**350**	**268**
Relative reduction	100%	61%	39%	27%	28%	29%	24%	22%	17%	35%	16%	32%	26%	20%

- Blue cells: pre-vaccination
- Green cells: vaccine uptake period
- Light brown cells: post-vaccine uptake period
- Pink cells: herd effect primary infection source only
- Yellow cells: herd effect primary & secondary infection source
- Dark brown cells: age-shift in primary source

Result (2)

- Modelling Figure 1





Result (3)

- Cost-Effectiveness of the vaccine uptake period

Item		Undiscounted	
	Age Group	No Vaccination	Vaccinated
Hospital days	0–2 m	904	467
	3–12 m	5424	1151
	13–24 m	3304	1187
	25–36 m	816	346
	37–48 m	216	112
	49–60 m	96	51
	Total	10,760	3314
Cost	Hospital cost	€ 15,784,920	€ 3,472,599
	Vaccine cost		€ 14,219,016
QALY	QALY-loss	−96.99	−21.34
	CEA		**€ 25,204**

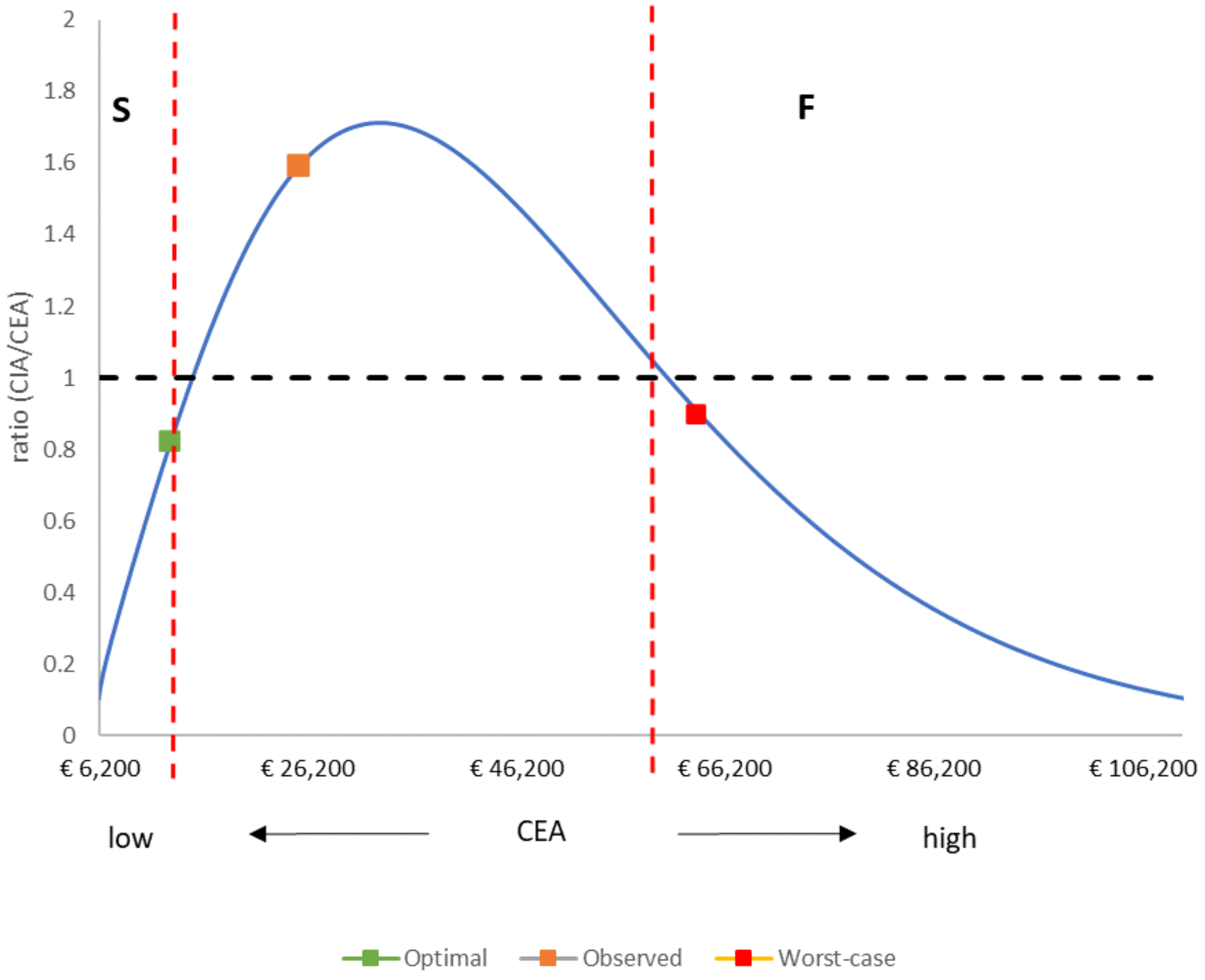
- Cost-Impact of the vaccine uptake + post uptake period

Item		Undiscounted	
	Age Group	No Vaccination	Vaccinated
Hospital days	0–2 m	1469	685
	3–12 m	8814	1706
	13–24 m	5369	1853
	25–36 m	1326	544
	37–48 m	351	169
	49–60 m	156	85
	Total	17,485	5042
Cost	Hospital cost	€ 25,650,495	€ 5,283,296
	Vaccine cost	°	€ 25,403,756
QALY	QALY-loss	-157.60	-32.46
	CIA		**€ 40,247**

Results (4)

	Difference in QALY- loss	Difference in Cost	ICER	Ratio (CIA/CEA)
Observed				
Cost-effectiveness (CEA)	75.65	€ 1,906,695	€ 25,204	
Cost-impact (CIA)	125.14	€ 5,036,557	€ 40,247	1.59
Simulation Optimal launch scenario				
Cost-effectiveness (CEA)	55.94	€ 732,801	€ 12,939	
Cost-impact (CIA)	149.39	€ 1,599,297	€ 10,705	0.83
Simulation Worst-case launch scenario				
Cost-effectiveness (CEA)	26.58	€ 1,874,495	€ 70,523	
Cost-impact (CIA)	50.95	€ 3,224,655	€ 63,290	0.90

Success Index : CIA/CEA



Summary

- The success index indicates the economic result of the vaccination programme long term being successful or not
- Working with ‘impact’ analysis is well-known in epidemiology. It is surprising that HE did not follow that same logic.
- Worst- and best-case scenarios are seen in real life with countries like Spain and UK & Finland as examples
- Answering the introduction question about having a good vaccination strategy in place at start of the program seems obvious in doing so
- The study is a long-time investment, but produced much insightful information about the disease, its spread, the vaccine working, and its economic value (short to long term) (12 peer reviewed publications)

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