Economic evaluation of the introduction of rotavirus vaccine in Hong Kong

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ABSTRACT

Background: Rotavirus is a common cause of severe gastroenteritis in young children in Hong Kong (HK) with a high economic burden. This study aimed to evaluate the cost-effectiveness of introducing rotavirus vaccination into the HK Government's Childhood Immunisation Programme (CIP) and to include the potential protective effect of the vaccine against seizures.

Methods: A decision-support model was customised to estimate the potential impact, cost-effectiveness and benefit-risk of rotavirus vaccination in children below 5 years over the period 2020–2029 in HK. Two doses of Rotarix® and three doses of RotaTeq® were each compared to no vaccination. Rotavirus treatment costs were calculated from a governmental health sector perspective (i.e., costs of public sector treatment) and an overall health sector perspective (both governmental and patient, i.e., costs of public sector treatment, private sector treatment, transport and diapers). We ran probabilistic and deterministic uncertainty analyses.

Results: Introduction of rotavirus vaccination in HK could prevent 49,000 (95% uncertainty interval: ~44,000–54,000) hospitalisations of rotavirus gastroenteritis and seizures and result in ~50 (95% uncertainty interval: ~25–85) intussusception hospitalisations, over the period 2020–2029 (a benefit-risk ratio of ~1000:1), compared to a scenario with no public or private sector vaccine use. The discounted vaccination cost would be US$51–57 million over the period 2020–2029 based on per-course prices of US$72 (Rotarix®) or US$78 (RotaTeq®), but this would be offset by discounted treatment cost savings of US$70 million (government) and US$127 million (governmental and patient health sector). There was a greater than 94% probability that the vaccine could be cost-saving irrespective of the vaccine product or perspective considered. All deterministic 'what-if' scenarios were cost-saving from an overall health sector perspective (governmental and patient).

Conclusions: Rotavirus vaccination is likely to be cost-saving and have a favourable benefit-risk profile in HK. Based on the assumptions made, our analysis supports its introduction into CIP.

1. Introduction

Diarrhoea was the fifth leading cause of death in children younger than 5 years globally in 2016 [1]. Almost 30% of diarrhoea mortality in this age group was attributable to rotavirus [2]. Rotavirus gastroenteritis (RVGE) causes significant morbidity in young children [3,4] and a high economic burden [5] in Hong Kong, a metropolitan region of approximately 7 million people. An estimated 1 in 33 Hong Kong children are hospitalised for RVGE by the age of 5 years [4]. There is no compulsory health insurance system in Hong Kong. Hong Kong residents can use the government

funded public healthcare service with only a small co-payment or they can use the private sector where they will usually pay out-of-pocket if they do not have their own health insurance. More than half of inpatient care under 5 years (56.7% in 2016/17) is in the public sector and needs referral through outpatient or Accident and Emergency (A&E) services.

There are two licensed rotavirus vaccines available in Hong Kong. The monovalent vaccine (*Rotarix*®) is a 2-dose rotavirus vaccine given at 2 and 4 months of age. The pentavalent vaccine (*RotaTeq*®) is a 3-dose rotavirus vaccine given at 2, 4 and 6 months of age. *Rotarix*® has been shown to be highly efficacious with 96–97% efficacy in high-income Asian countries including Hong Kong [6] and both *Rotarix*® and *RotaTeq*® were reported to be safe and highly efficacious in Europe and the United States in two seminal clinical studies [7,8]. A recent test-negative case-control study has confirmed 89–95% effectiveness against rotavirus hospitalisations in Hong Kong children younger than 5 years [9]. In addition, rotavirus vaccination has the potential to provide indirect herd protection to unvaccinated individuals [10] and reduce the risk of seizures [11–13].

The World Health Organization (WHO) recommends that all national immunisation programmes include rotavirus vaccines [14]. Despite rapidly growing evidence of the public health benefits of rotavirus vaccine and WHO's recommendation, rotavirus vaccine has not yet been included in the Hong Kong Government's Childhood Immunisation Programme (CIP). Guardians who would like their children vaccinated with rotavirus vaccine are required to take their children to the private sector and pay out-of-pocket. The private sector price is very high compared to the anticipated tender price of the vaccine should it be included in the CIP. Unpublished data in 2015 indicated that lower-income families in Hong Kong are less likely to go to the private sector for rotavirus vaccination than higher-income families. There is no published data on private sector rotavirus vaccine uptake in Hong Kong. From personal communication with the Department of Health (DH), 33.3% of 8723 Hong Kong children born between 2009 and 2012 received rotavirus vaccines in the private sector. This low uptake rate compares to the immunisation coverage rate of over 95% for vaccines included in the CIP such as combined Diphtheria-Tetanus-Pertussis (DTP) vaccines [15].

A previous study published in 2008, using 2002 data, showed that rotavirus vaccination would be cost-saving to the Hong Kong Government if the full-course vaccine cost was less than US$40–92 [16]. However, updated evidence is now available for several inputs and it is possible to calculate additional outcomes, including the costs that could be saved by households, the number of seizures that could be prevented and the expected ratio of vaccine benefits (RVGE and seizures hospitalisations prevented) to vaccine risks (intussusception hospitalisations caused). This study aimed to evaluate the cost-effectiveness of *Rotarix*® and *RotaTeq*® vaccination in Hong Kong from both a governmental health sector and overall health sector (governmental plus patient) perspective, by comparing each vaccine to a scenario without rotavirus vaccination.

2. Methods

A scenario with rotavirus vaccination (either *Rotarix*® or *RotaTeq*®) included in the CIP was compared to a scenario without rotavirus vaccination. In order to capture the changes in time-dependent parameters, we evaluated 10 successive annual birth cohorts from 2020 to 2029, i.e., we calculated the lifetime costs and benefits associated with vaccinating all 10 birth cohorts. All monetary costs and effects were discounted at 3% per year, as sug-

gested in the WHO's guide [17]. All monetary units were adjusted to 2018 United States dollars (US$).

The primary outcome measure was the discounted cost (US$) per disability-adjusted life-year (DALY) averted. We also calculated the ratio of benefits to risks (number of RVGE and seizures hospitalisations averted per one intussusception hospitalisation caused) and other indicators, e.g., numbers of cases, outpatient and A&E visits, hospitalisations and DALYs prevented, costs of vaccination and treatment costs averted.

2.1. Model

We used the UNIVAC model (version 1.4), a transparent Excel-based decision-support model with a universal framework for evaluating the potential impact and cost-effectiveness of different vaccines. This is a deterministic static cohort model with a finely disaggregated age structure (weeks of age between birth and age 5.0 years). The methods used to calculate the potential benefits and risks of vaccination are described in detail elsewhere [18,19].

UNIVAC was customised to evaluate the protective effect of the vaccine on community cases, clinic visits and hospitalisations caused by RVGE. In addition, we evaluated the protective effect of the vaccine on hospitalisations associated with seizures. We also evaluated the potential increase in the number of intussusception hospitalisations (a rare bowel disorder) that could be caused by the vaccine.

2.2. Model parameters

The model input parameters included: demographics, burden of disease, vaccine schedule and coverage, vaccine efficacy, vaccine programme costs, health services utilisation and costs, non-healthcare costs, vaccine safety and possible vaccine-associated risks (intussusception), and potential vaccination benefits (seizure). Table 1 lists the estimates and uncertainty ranges of all input parameters in the model.

2.2.1. Demographic data
The number of live births per year and life expectancy at birth were obtained from the United Nations World Population Prospects 2017 revision [20].

2.2.2. Burden of disease
2.2.2.1. RVGE. Rotavirus disease burden was estimated from the event rates of inpatient, outpatient and A&E visits to publicly funded government clinics/ hospitals (Hospital Authority, HA) and private sector clinics and hospitals. RVGE requiring hospitalisation was classified as severe RVGE. Those with outpatient or A&E visits only were regarded as non-severe RVGE. To be conservative from an overall health sector perspective (both governmental and patient), we assumed no symptomatic RVGE cases treated at home, i.e., all cases not seen in a health facility were considered as subclinical. All severe RVGE cases were assumed to have had a prior outpatient or A&E visit before hospitalisation and we assumed no death from RVGE given its very low mortality rate in high-income countries (HICs) [21]. However, we did consider a very low rate of RVGE mortality in the sensitivity analyses.

We assumed the incidence rate of outpatient and A&E visits for non-severe RVGE in Hong Kong to be the same as that in Taiwan before the introduction of rotavirus vaccination (taking the difference between rates of outpatient/ A&E and hospitalisation) [22], given Hong Kong and Taiwan are both high-income regions in Asia and geographically close to each other. The incidence of rotavirus hospitalisation in children younger than 5 years was obtained from a previous surveillance study undertaken from 1997 to 2011, which used adjustment factors derived from laboratory

Table 1
List of parameters, point estimates in base-case analysis and ranges used in probabilistic sensitivity analysis.

Input parameter[a]	Point estimate	Uncertainty range[b]	Source or assumptions
Disease events per 100,000 per year, <5 years, Non-severe RVGE			
Community cases	7791	(5728–9851)	Assumed that all symptomatic community cases have access to care
Clinic and A&E visits	7791	(5728–9851)	[21]
Disease events per 100,000 per year, <5 years, Severe RVGE			
Community cases	1029	(863–1093)	–
Clinic and A&E visits	1029	(863–1093)	Assumed all severe RVGE cases have a prior outpatient or A&E visit before hospitalisation
Hospitalisations[c]	1029	(863–1093)	[4]
Deaths	0.00	(0.00–0.00)	Assumed no rotavirus-associated deaths
Disease events per 100,000 per year, <5 years, Seizures[d]			
Community cases	1800	(1418–1980)	–
Clinic and A&E visits	1800	(1418–1980)	Assumed all seizure cases have a prior outpatient or A&E visit before hospitalisation
Hospitalisations	1800	(1418–1980)	Derived from local database [4]
Deaths	0.00	(0.00–0.00)	Assumed no seizures-associated deaths
Disease events per 100,000 per year, <5 years, Intussusception[e]			
Community cases	38.00	(34.20–41.80)	–
Clinic and A&E visits	38.00	(34.20–41.80)	Assumed all intussusception cases have a prior outpatient or A&E visit before hospitalisation
Hospitalisations	38.00	(34.20–41.80)	[26]
Deaths	0.00	(0.00–0.00)	Assumed no intussusception-associated deaths
Age distribution scale parameter[f]			
RVGE	75.42	(56.56–94.27)	[4]
Seizures	558.38	(418.78–697.97)	Derived from local database [4]
Intussusception	16.26	(12.19–20.32)	Derived from local database [4]
Disability-Adjusted Life Year (DALY) weight			
Non-severe RVGE	18.8%	(12.5–26.4)	[23]
Severe RVGE	24.7%	(16.4–34.8)	[23]
Seizures	26.3%	(17.3–36.7)	[23]
Intussusception	32.4%	(22.0–44.2)	[23]
Mean duration of illness (days)			
Non-severe RVGE	3.0	(3.0–3.0)	[62]
Severe RVGE	4.0	(3.0–5.0)	Assume equivalent to length of hospital stay [3,4,9,25]
Seizures	3.0	(2.0–4.0)	Assumed equivalent to length of hospital stay (derived from local database [4])
Intussusception	4.0	(3.0–5.0)	Assumed equivalent to length of hospital stay [27-29]
Vaccine coverage (2020–2029)[g]			
Dose 1	95.0%	(90.0–100.0)	[14]
Dose 2	95.0%	(90.0–100.0)	[14]
Dose 3	95.0%	(90.0–100.0)	[14]
Vaccine timeliness scale parameter (median age in weeks)[h]			
Dose 1	11.37	(8.53–14.21)	Data from MCHCs
Dose 2	21.76	(16.32–27.20)	Data from MCHCs
Dose 3	34.36	(25.77–42.95)	Data from MCHCs
Relative risk of intussusception in the 1–7 day risk period			
Dose 1	6.62	(3.91–11.20)	Meta-analysis of 7 studies from high-income countries (refer to Appendices for details)
Dose 2	2.17	(1.48–3.17)	Meta-analysis of 7 studies from high-income countries (refer to Appendices for details)
Dose 3	1.00	(1.00–1.00)	Assumed no risk
Relative risk of intussusception in the 8–21 day risk period			
Dose 1	2.02	(1.13–3.62)	Meta-analysis of 7 studies from high-income countries (refer to Appendices for details)
Dose 2	1.51	(1.04–2.18)	Meta-analysis of 7 studies from high-income countries (refer to Appendices for details)
Dose 3	1.00	(1.00–1.00)	Assumed no risk
Vaccine efficacy 2 weeks after vaccination, *Rotarix*®, 2 doses			
Non-severe RVGE[i]	75.90%	(72.40–86.80)	[30]
Severe RVGE[j]	99.60%	(99.40–99.73)	[28]
Seizures	29.50%	(21.00–38.00)	[12,31]

(continued on next page)

Table 1 (*continued*)

Input parameter[a]	Point estimate	Uncertainty range[b]	Source or assumptions
Vaccine efficacy 2 weeks after vaccination, *Rotarix*®, 1 dose			
Non-severe RVGE	68.31%	(65.16–78.12)	Assumed same proportion of full-course efficacy as severe RVGE
Severe RVGE	89.64%	(89.46–89.75)	[29]
Seizures	26.55%	(18.90–34.20)	Assumed same proportion of full-course efficacy as severe RVGE
Vaccine efficacy 2 weeks after vaccination, *RotaTeq*®, 3 doses			
Non-severe RVGE[i]	75.90%	(72.40–86.80)	[30]
Severe RVGE[j]	99.60%	(99.40–99.73)	[28]
Seizures	29.50%	(21.00–38.00)	[12,31]
Vaccine efficacy 2 weeks after vaccination, *RotaTeq*®, 2 doses			
Non-severe RVGE	65.27%	(62.26–74.65)	Assumed same proportion of full-course efficacy as severe RVGE
Severe RVGE	85.65%	(85.48–85.77)	[29]
Seizures	25.37%	(18.06–32.68)	Assumed same proportion of full-course efficacy as severe RVGE
Vaccine efficacy 2 weeks after vaccination, *RotaTeq*®, 1 dose			
Non-severe RVGE	63.76%	(60.82–72.91)	Assumed same proportion of full-course efficacy as severe RVGE
Severe RVGE	83.66%	(83.50–83.77)	[29]
Seizures	24.78%	(17.64–31.92)	Assumed same proportion of full-course efficacy as severe RVGE
Mean duration of protection (months), 1, 2 or 3 doses [j]			
Non-severe RVGE	176.80	(114.70–268.0)	Assumed to be the same as severe RVGE
Severe RVGE	176.80	(114.70–268.0)	[28]
Seizures	176.80	(114.70–268.0)	Assumed to be the same as severe RVGE
Vaccination costs, *Rotarix*®			
Price per dose	36.00	(31.00–46.00)	From PCV experience and manufacturers
Incremental cost to the health system per dose (2020–2029)	3.29 (Extra manpower cost: 3; Annualised capital cost of refrigerators and recurrent maintenance cost: 0.29)	(2.46–4.11)	Finance Department of a HA hospital and company selling refrigerators
Vaccination costs, *RotaTeq*®			
Price per dose	26.00	(23.00–34.00)	From PCV experience and manufacturers
Incremental cost to the health system per dose (2020–2029)	3.19 (Extra manpower cost: 3; Annualised capital cost of refrigerators and recurrent maintenance cost: 0.19)	(2.39–3.99)	Finance Department of a HA hospital and company selling refrigerators
Mean cost per clinic and A&E visit (Governmental health sector perspective)[k]			Refer to Appendices for details
Non-severe RVGE	9.00	(7.00–11.00)	
Severe RVGE	83.00	(62.00–103.00)	
Seizures	83.00	(62.00–103.00)	
Intussusception	83.00	(62.00–103.00)	
Mean cost per clinic and A&E visit (Governmental and patient health sector perspective)[k]			Refer to Appendices for details
Non-severe RVGE	56.00	(42.00–70.00)	
Severe RVGE	171.00	(128.00–213.00)	
Seizures	171.00	(128.00–213.00)	
Intussusception	171.00	(128.00–213.00)	
Mean cost per hospitalisation (Governmental health sector perspective)			Refer to Appendices for details
Severe RVGE	1702.00	(1277.00–2128.00)	
Intussusception	1748.00	(1320.00–2176.00)	
Seizures	1277.00	(851.00–1702.00)	
Mean cost per hospitalisation (Governmental and patient health sector perspective)			Refer to Appendices for details
Severe RVGE	2888.00	(2166.00–3611.00)	
Seizures	2164.00	(1443.00–2885.00)	
Intussusception	3317.00	(2593.00–4041.00)	

A&E, Accident and Emergency; HA, Hospital Authority; MCHC, Maternal and Child Health Centre; PCV, pneumococcal conjugate vaccine; PSA, probabilistic sensitivity analysis; RVGE, rotavirus gastroenteritis.

[a] All costs are in 2018 United States dollars.

[b] For each probabilistic simulation, parameters were drawn from a distribution with a mean equal to the point estimate and range equal to the low and high values of the uncertainty range. A PERT-Beta distribution was assumed for all parameters [45].

[c] The three adjusted incidence rates in the previous local study were taken as base-case estimate and uncertainty range.

[d] Base-case estimate was derived from local database with any Clinical Management System seizure diagnosis in any diagnostic position over 14-year period (1997–2011), the low value of the uncertainty range in PSA was derived using seizure cases as primary diagnoses only, and the high value was + 10% of the base-case estimate.

[e] Base-case estimate was varied by ±10% in PSA.

[f] All age distributions were fitted to a three-parameter Burr distribution using non-linear least squares minimisation [22]. The scale parameter was varied by ±25% in PSA. Other parameters were fixed for rotavirus (shape 1 = 1.76, shape 2 = 1.07), intussusception (shape 1 = 4.83, shape 2 = 0.14) and seizures (shape 1 = 1.69, shape 2 = 10.47).

[g] Base-case estimate was varied by ±5 percent-points in PSA.

[h] The timeliness of vaccination (coverage by week of age) was fitted to a two-parameter Log Logistic distribution using non-linear least squares minimisation. The scale parameter (median age in weeks) was varied by ±25% in PSA. The shape parameter was fixed for dose 1 (18.05), dose 2 (21.01) and dose 3 (13.14).

[i] The reported estimate from developed countries on effectiveness 86.8% (95% CI: 60.7–95.6) was taken as the high value of the uncertainty range, and the reported efficacy 75.9% (95% CI: 72.4–78.9) was taken as the base-case estimate and its lower bound of the 95% CI was taken as the low value of the uncertainty range in PSA.

[j] A two-parameter cumulative gamma distribution was used to estimate vaccine efficacy against severe RVGE by duration of follow-up. The parameters were based on the median and 95% credible intervals generated by a Bayesian meta-regression of all randomised trials in high-income settings [28]. The same duration of protection was assumed for non-severe RVGE and seizures. The alpha parameter (0.93) was fixed in PSA.

[k] Base-case estimate was varied by ±25% in PSA.

surveillance conducted in one HA hospital and linked to passive discharge diagnosis information (Clinical Management System, CMS) from all HA hospitals to compensate for under-reporting, with estimates made for private hospital admissions [4]. Despite the availability of rotavirus vaccines in the private sector since 2006, there was no reduction in the incidence of hospitalisation for either rotavirus or all-cause gastroenteritis observed in Hong Kong children younger than 5 years over the 14 rotavirus seasons. Therefore, we assumed that the admission rates from 1997 to 2011 were reflective to 'no vaccination' despite the availability of vaccine in the private sector since 2006.

The age distribution of RVGE cases was estimated from that of RVGE hospitalisation [4] which was fitted with a Burr distribution using non-linear least squares minimisation [23]. The disability weights for DALYs were taken from the Global Burden of Disease study [24]. The gastrointestinal symptoms of a RVGE patient generally resolve in 3–7 days [25]. We assumed the duration of illness of non-severe RVGE be the minimum of this range. The length of hospital stay for severe RVGE was estimated to be 4 days [4] (3 [3,4,9] – 5 [4,26]). Assuming no recovery period, the duration of illness of severe RVGE was assumed to be equal to the length of hospital stay.

2.2.2.2. Seizures. All seizure cases were assumed to be hospitalised with a prior outpatient or A&E visit. Using HA data from 1997 to 2011, as in the study by Chiang et al. [4] and the same methodology, the unadjusted incidence rate of hospitalisation for seizures in public hospitals, of children younger than 5 years, was estimated to be 1800 per 100,000 person-years as a reasonable estimate of pre-vaccination incidence. The mortality rate from seizures was assumed to be 0. From the same database [4], among children younger than 5 years, 15.7% was younger than 1 year and 84.3% was aged from 1 to 5 years, and the median length of hospital stay for seizures was 4 days for infants and 3 days for children aged from 1 to 5 years. The weighted median length of hospital stay (3 days) was taken as the base-case estimate, with an uncertainty range of 2–4 days. Assuming no recovery period, duration of illness for seizures was assumed to be the length of hospital stay. The disability weight for DALYs was estimated at 0.263 (95% CI: 0.173, 0.367) [24].

2.2.2.3. Intussusception. All intussusception cases were assumed to be hospitalised with a prior outpatient or A&E visit. The hospitalisation rate of intussusception in children younger than 5 years was estimated to be 38 per 100,000 person-years [27]. We calculated the number of expected vaccine-related hospitalisations following introduction of the vaccine. We did not calculate the number of vaccine-related intussusception deaths because intussusception is a very rare event and case-fatality ratios (CFRs) have been estimated to be very low locally and in high-income settings [18,27]. However, we did consider a very low rate of intussusception mortality in the sensitivity analysis.

A local study reported that intussusception surgical rate was 26.5% and the median length of post-reduction hospital stay for non-surgical patients was 3 days and 7.5 days for surgical patients [28]. Assuming no recovery period, duration of illness was assumed to be the weighted average of length of hospital stay. The disability weight for DALYs was estimated at 0.324 (95% CI: 0.220, 0.442) [24].

2.2.3. Vaccine schedule and coverage

Coverage of rotavirus vaccination after introduction was assumed to be the current coverage for vaccines included in the CIP (95%) for all doses of vaccination over the 10 successive annual birth cohort since vaccines included in the routine universal CIP rapidly attain high coverage as shown following the introduction

of pneumococcal conjugate vaccine (PCV) [15]. Data on the timeliness (coverage by week of age) of DTP vaccination was obtained from the Maternal and Child Health Centre (MCHC) based on a birth cohort born in 2011. The observed timeliness data was fitted with a two-parameter Log Logistic distribution using non-linear least squares minimisation. Combining data on coverage by week of age with estimates of disease burden by week of age allowed for more precise estimates of the potential direct effects of vaccination.

2.2.4. Vaccine efficacy
2.2.4.1. RVGE. Estimates of vaccine efficacy by duration of follow-up were taken from a recent meta-analysis of randomised controlled trials in settings with low under-five mortality [29]. We used the pooled estimates (and 95% credibility intervals) of vaccine efficacy against severe RVGE after a full course of either *Rotarix®* or *RotaTeq®*. Efficacy of one dose of *Rotarix®* was estimated to be 90% of the efficacy value estimated for 2 doses (full-course) [30]. For *RotaTeq®*, one-dose and two-dose vaccine efficacy were assumed to be 84% and 86% of the efficacy value estimated for 3 doses (full-course) [30]. The duration of vaccine efficacy was obtained from the same meta-analysis [29] and all doses were assumed to have the same duration of vaccine efficacy.

Vaccine efficacy against non-severe RVGE was estimated to be 75.9% based on the efficacy of rotavirus vaccination in preventing rotavirus diarrhoea of any severity in developed countries [31].

2.2.4.2. Seizures. A full course of rotavirus vaccination was shown to reduce the risks of seizure-associated hospitalisation or emergency care by 21% in the United States [12] and to have vaccine efficacy of 38% against hospitalisation [32]. These percentages were used as the uncertainty range of vaccine efficacy against seizures and the average of this range was taken as the base-case estimate. However, there is also a study showing no significant association between rotavirus vaccine introduction and seizure admission [33]. A sensitivity analysis was conducted in the absence of this potential benefit.

2.2.5. Intussusception

Both *Rotarix®* and *RotaTeq®* have been associated with an elevated risk of a rare bowel disorder (intussusception) in some settings [34,35]. We estimated the expected number of intussusception hospitalisations that could be caused by the vaccine as well as the costs of treating these cases.

The overall background intussusception rates for Hong Kong children younger than 1 and 5 years were previously reported to be 108 and 38 per 100,000 children respectively [27]. A meta-analysis has been performed on the relative risk of intussusception within different periods post rotavirus vaccination in HICs. Among the six studies included, three studies reported for *Rotarix®* [34,36,37], one study for *RotaTeq®* [38] and two studies for both vaccines [35,38]. Appendix Fig. 1 illustrates the relative risks of intussusception within 1–7 days and 8–21 days after first and second doses of rotavirus vaccine.

2.2.6. Vaccine programme costs

Potential tender prices of *Rotarix®* and *RotaTeq®* were requested and received from the manufacturers. We used a 'symbolic' price of US$92 (US$46 per dose) for a full course of *Rotarix®* as suggested by the manufacturer, where the price was based on the upper bound of the cost-neutral vaccine cost (i.e., the price at which the vaccine would be cost-saving from a governmental perspective) of a previous study by Ho et al., 2008 [16], and a private market price of *RotaTeq®* in Hong Kong of US$34 per dose (US$102 per course) provided by the manufacturer. These were taken as the upper bound of the uncertainty range. The vaccine price in the base-case analy-

sis was based on the experience of PCV in Hong Kong. The percentage reduction in the tender price from the market price was obtained by using the market price used in two previous economic analyses of PCV before its introduction in Hong Kong (US$65 per dose) [39,40] and the 2019 tender price of PCV (US$50.7 per dose); this was 22%. An additional 10 percentage-points of reduction was taken as the lower bound of the uncertainty range. The per-course prices of *Rotarix*® and *RotaTeq*® were estimated to be US$72 (US$36 per dose) and US$78 (US$26 per dose) respectively in the base case and US$62 (US$31 per dose) and US$69 (US$23 per dose) in the lower bound of the uncertainty range. No additional cost for international handling and delivery and vaccine wastage were assumed in the base case but 5% of vaccine wastage was considered as the upper bound of the uncertainty range.

Extra time cost for MCHC nurses to explain and administer one rotavirus vaccine dose was estimated to be US$3 for 5 min, based on the nominal annual mid-point salary for a registered nurse in 2018/19 from the Finance Department of Prince of Wales Hospital. We assumed no additional costs for extra staff, advertising, invitation letter, phone call, surveillance and monitoring or indirect costs of the vaccination programme such as loss of productivity of caregivers since rotavirus vaccination could be fitted into the existing schedule of childhood vaccination. We also assumed no additional cost incurred from vaccination side effects except intussusception.

The model of refrigerators being used in the MCHCs was obtained from the DH. The rotavirus vaccine storage volume required was calculated using a WHO guidance document [41]. It was estimated that one additional refrigerator would be installed for rotavirus vaccine storage for each of the 31 MCHCs. A quotation for the refrigerator was obtained and its cost was annualised with a 10-year expected useful lifetime. We also estimated the recurrent maintenance cost of refrigerators to be 10% of its cost.

2.2.7. Health services utilisation and costs

Among children younger than 5 years, the proportion of patients using health services from public or private sectors are 56.7% and 43.3% respectively for inpatient and 16.3% and 83.7% respectively for outpatient services [42]. For patients with mild illness using public services, 90.9% would go to an outpatient clinic and 9.1% to A&E [43]. For hospitalised RVGE patients in the public sector, 16.7% would have had a prior visit at the government outpatient clinic and 83.3% had a prior A&E visit (unpublished data [5]). Fig. 1 shows a flowchart of health service usage for RVGE in Hong Kong. To provide conservative results, we assumed there were no private A&E and traditional Chinese medicine consultations.

Health service costs were calculated for non-severe RVGE (outpatient and A&E visits) and for severe RVGE (outpatient and A&E visits and inpatient). From the governmental health sector perspective, costs were calculated as the cost to the Government (HA or DH) subtracting the cost paid by the patient to the Government, which was then multiplied by the percentage using the public service. From the overall health sector perspective (both governmental and patient), costs were calculated as the weighted average of cost to the Government plus cost to patients using the private service. Average cost for hospitalisation was calculated as cost per patient day multiplied by length of hospital stay in days.

Health service utilisation for intussusception and seizures was assumed to be the same as that of severe RVGE. Table 1 lists the cost inputs in the model and detailed calculations of health service costs are shown in the Appendix Tables 1–6.

2.2.8. Non-healthcare costs

To provide conservative results, only costs of transportation and additional diapers for RVGE children were considered in the model. Other miscellaneous costs such as food supplements or non-

prescription remedies and indirect costs such as loss of productivity of parents or other caregivers were not considered.

Transportation costs for a sick child and an accompanying caregiver for an outpatient or A&E visit in public and private sectors were estimated. A round-trip travel cost by taxi was assumed to be US$13 by estimating a round-trip distance of 5 km between home and a health service facility. No additional travel cost was assumed from outpatient clinics to hospitals.

An additional two diapers per day was estimated to be required for each RVGE child aged from 0 to 3 years [44]. The cost per diaper was estimated to be US$0.39 (obtained from the Consumer Council). The cost of additional diapers was the product of additional daily cost and duration of illness in days. Given the cumulative proportion of RVGE cases aged from 0 to 3 years was 87% [4], the additional daily cost was estimated at US$0.65 per case.

2.3. Model analyses

2.3.1. Cost-effectiveness analysis

For each vaccine product, we calculated the discounted cost per DALY averted compared to no vaccination:

$$\frac{\text{Incremental costs of including rotavirus vaccination into CIP}-}{\text{Costs averted by rotavirus vaccine}}$$
$$\overline{\text{DALYs averted by rotavirus vaccine}}$$

A negative value of the numerator indicates introduction of rotavirus vaccine is cost-saving. Hong Kong does not have an accepted willingness-to-pay threshold [45] but in the previous study a discounted cost per DALY averted of less than one times Gross Domestic Product (GDP) per capita was considered to be cost-effective [16].

2.3.2. Cost-benefit analysis

We did not convert DALYs averted into monetary values, as this process is often controversial and based on uncertain assumptions. However, we did calculate the proportion of probabilistic simulations that led to a cost-saving result.

2.3.3. Probabilistic sensitivity analyses

Probabilistic sensitivity analyses were conducted to quantify the level of confidence in the output, in relation to the uncertainty in the model inputs; 1000 probabilistic simulations were run for each vaccine. For each probabilistic simulation, parameters were drawn from a distribution with a mean equal to the point estimate and range equal to the low and high values of the uncertainty range. For simplicity, a PERT-Beta distribution was assumed for all parameters [46]. A benefit-risk ratio for hospitalisation was calculated for each simulation by dividing the number of RVGE and seizure hospitalisations prevented by the number of intussusception hospitalisations.

2.3.4. Deterministic scenario analyses

A series of deterministic scenario analyses were conducted to evaluate the impact of different input parameters on the results. We ran one-way scenarios based on the low and high values of the uncertainty range of each input parameter, and multi-way scenarios with several inputs were varied at the same time to generate favourable and unfavourable scenarios for rotavirus vaccine introduction. All scenarios are listed in Table 2.

2.4. Ethics approval

Ethics approval was granted by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (Ref.: CRE-2016.717).
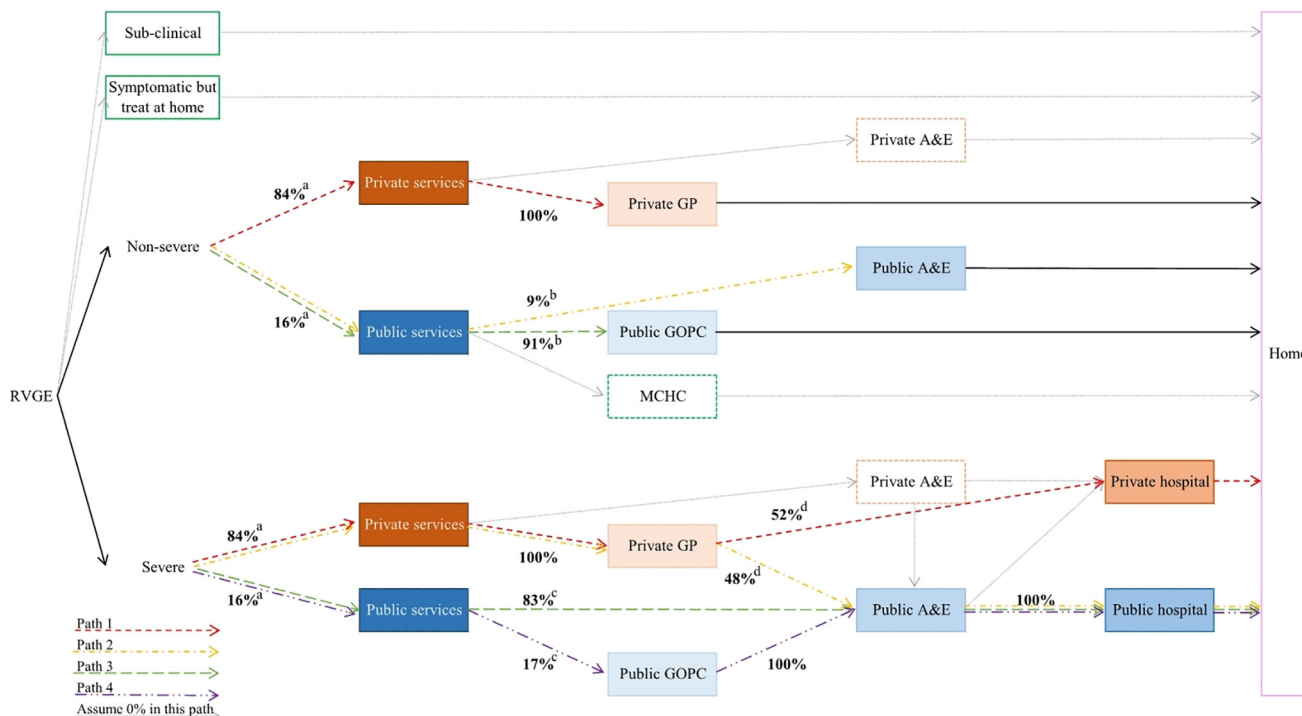
Fig. 1. Flowchart of health service usage for rotavirus gastroenteritis in Hong Kong. [a][41]. [b][42]. [c][3]. [d]Overall 56.7% and 43.3% [41] admitted to public and private hospitals respectively. A&E, Accident and Emergency; GOPC, general outpatient clinic; GP, general practice clinic; RVGE, rotavirus gastroenteritis For both non-severe and severe RVGE, we multiplied the total number of visits (outpatient visits and A&E visits) by the average cost per visit, calculated by taking into account whether visits were in outpatient clinics or A&E departments, whether visits were public or private and the costs and probabilities associated with each. For the average cost per severe RVGE hospitalisation, we multiplied the length of hospital stay in days by the cost per day. The average costs per visit and per hospitalisation were calculated separately for both of the perspectives considered. Detailed calculations can be found in the Appendices.

3. Results

3.1. Cost-effectiveness

From the base-case scenario, over the period of 2020 to 2029, the discounted costs of rotavirus vaccination would be US$51 million and US$57 million based on per-course prices of US$72 (*Rotarix*®) or US$78 (*RotaTeq*®), but this would be offset by discounted treatment cost savings of US$70 million to the Hong Kong Government and US$127 million to both the government and patient, making the introduction of rotavirus vaccine into the Hong Kong CIP a cost-saving intervention. With rotavirus vaccination in the CIP, US$13–20 million and US$70–77 million could be saved from the governmental alone and the governmental plus patient health sector perspectives respectively over a 10-year period.

3.2. Health impacts

We estimated in the base-case scenario that there could be 190,000 non-severe and 33,000 severe RVGE cases prevented by rotavirus vaccination in Hong Kong over the period 2020–2029 (Table 3). In addition, we estimated that 17,000 seizures could be prevented and that 47 additional cases of rotavirus vaccine-associated intussusception could be caused. The total numbers of outpatient and A&E visits and hospitalisations with and without rotavirus vaccine over the 10-year period are shown in Fig. 2. Over the 10-year period, around 350 DALYs could be averted by rotavirus vaccination (Table 3).

3.3. Probabilistic sensitivity analyses

The probabilistic sensitivity analyses showed that there was 100% probability that the two rotavirus vaccines were cost-

saving from the overall health sector perspective (governmental plus patient), when each were independently compared to no vaccination. From the governmental health sector perspective, *Rotarix*® was 99.2% and *RotaTeq*® was 93.5% likely to be cost-saving. 100% of the runs had a cost-effectiveness ratio that was lower than the GDP per capita in Hong Kong in 2018 (US$48,717 [47]). Figs. 3a and 3b show the discounted incremental cost (costs of vaccination programme less costs averted by vaccine) and DALYs averted by universal rotavirus vaccination of the 1000 probabilistic simulations.

3.4. Benefit-risk analyses

We estimate that rotavirus vaccination could prevent 49,000 (95% uncertainty interval [UI]: ~44,000–54,000) RVGE and seizure hospitalisations and cause ~50 (95% UI: ~25–85) intussusception hospitalisations over the period of 2020–2029. This results in a benefit-risk ratio of ~1000:1 (95% UI: ~550–2000:1).

3.5. Deterministic scenario analyses

40 scenarios were evaluated for each vaccine and for governmental alone and overall health sector (governmental plus patient) perspectives, including best-case and worst-case scenarios. For *Rotarix*®, all scenarios were cost-saving except the worst-case scenario from both governmental alone and the overall health sector (governmental plus patient) perspectives. For *RotaTeq*®, the worst-case scenario was not cost-saving from both governmental alone and the overall health sector (governmental plus patient) perspectives, and scenarios with high vaccine price and low costs of health services were also not cost-saving to the Government.

Since most of the scenarios were cost-saving, the tornado diagrams in Figs. 4a–4d illustrate the discounted incremental cost

Table 2
List of scenarios performed in the deterministic scenario analyses.

	Scenarios favourable to rotavirus vaccine introduction	Scenarios unfavourable to rotavirus vaccine introduction
Disease event rates of RVGE	1. High	2. Low
Disease event rates of seizures	3. High	4. Low
Disease event rates of intussusception	5. Low	6. High
Relative risk of intussusception	7. Low	8. High
Vaccine coverage	9. High	10. Low
Duration of vaccine protection	11. Long	12. Short
Vaccine efficacy against RVGE	13. High	14. Low
Vaccine efficacy against seizures	15. High	16. Low
Vaccine price	17. Low	18. High
Incremental cost to the health system	19. Low	20. High
Healthcare costs	21. High	22. Low
Non-healthcare costs (only applicable to governmental and patient health sector perspective)	23. High	24. Low
Disability weights for RVGE	25. High	26. Low
Disability weights for seizures	27. High	28. Low
Disability weights for intussusception	29. Low	30. High
Duration of illness of RVGE	31. Long	32. Short
Duration of illness of seizures	33. Long	34. Short
Duration of illness of intussusception	35. Short	36. Long
Discount rate	37. Low (1%)	38. High (5%)
	39. Best-case scenario with all scenarios favourable to vaccination considered	40. Worst-case scenario with all scenarios unfavourable to vaccination considered, and high vaccine wastage

A&E, Accident and Emergency; RVGE, rotavirus gastroenteritis.

(costs of vaccination programme less costs averted by vaccine), instead of the discounted cost per DALY averted, of rotavirus vaccination introduction for each vaccine and for both governmental alone and overall health sector (governmental plus patient) perspectives. The amount of costs saved by universal vaccination was most influential by the RVGE healthcare cost; and DALYs averted was the most influential by the disability weights for RVGE. The highest combination of DALYs averted and costs saved was found in the scenario with high disease event rates for RVGE.

4. Discussion

This analysis provides a timely update and an expanded perspective to a previous study published in 2008 [16] showing that rotavirus vaccination would likely be cost-saving from both a governmental alone and combined governmental and patient health sector perspective. Deterministic scenario analyses also confirmed the previous findings that healthcare costs and vaccine price are the most strongly influential on the amount of costs saved. Probabilistic sensitivity analyses additionally confirmed that both vaccines would have a high probability of being cost-saving when independently compared to no vaccination. We assumed that both vaccines would generate similar health benefits and risks. Thus, we assumed the product with the lowest negotiated price per course will ultimately be the dominant/ preferred product. We assumed a per-course price of US$72–78, after applying the same discount of market price from the experience of PCV in Hong Kong. However, several new rotavirus vaccines have recently been licensed for global use, including much cheaper Indian vaccines (*ROTAVAC*® and *ROTASIIL*®) [48,49]. Several other rotavirus vaccines are also in the pipeline, including injectable vaccines [48]. Therefore, an even better reduction in tender price obtained by the Government might be expected.

Our analysis also suggested that the benefits of rotavirus vaccine introduction are likely to far outweigh any potential increases of intussusception. Approximately 700 RVGE and 300 seizures hospitalisations could be prevented for each extra intussusception hospitalisation caused. The benefit-risk ratio on RVGE hospitalisation versus intussusception hospitalisation in Hong Kong is higher than 6 out of 7 low-mortality countries (190–571:1) [34,35,50–54] with the United States having a higher ratio (1093:1) [55].

The cost-saving results from the overall health sector perspective (governmental plus patient) are in line with other prospective cost-effectiveness studies in HICs in the same region [22,56,57]. However, one study from South Korea which also used the UNIVAC model showed rotavirus vaccine introduction is cost-effective, rather than cost-saving, from the societal perspective [58]. This could be because of the difference in the estimate of vaccine price used in our models and that protection from seizures was not included in the South Korea analysis. Vaccine prices, which were reported as being 'confidential' in the South Korean study, could vary a lot among countries and influence the results since vaccine price is one of the main drivers of the analysis. From the governmental health sector perspective, prospective cost-effectiveness studies in Australia [56] and Japan [57] showed cost-effective results, but a retrospective economic evaluation of the Australian rotavirus vaccination programme showed cost-saving results for a full-course rotavirus vaccine at AUS99.52 (~US$84.84) in 2008 over 6 years after the implementation of the programme [59].

Introduction of rotavirus vaccine in Hong Kong, a high-income region, would have different economic impacts compared to low-income countries (LICs) and lower-middle-income countries (LMICs). A systematic review [60] showed that rotavirus vaccine introduction would be cost-effective or highly cost-effective in most of these LICs and LMICs. Preventing rotavirus mortality is

Table 3

Health and economic impacts under base-case scenario (10 cohorts vaccinated over the period of 2020–2029).[*]

	Rotarix®			RotaTeq®		
	No vaccine	With vaccine	Averted	No vaccine	With vaccine	Averted
Total cases [#]	412,332	172,755	239,577	412,332	174,771	237,561
Non-severe RVGE	301,414	111,538	189,876	301,414	113,340	188,075
Severe RVGE	39,809	6,901	32,908	39,809	7,214	32,596
Seizures	69,638	52,799	16,839	69,638	52,701	16,937
Intussusception	1,470	1,517	− 47	1,470	1,517	− 47
Total outpatient and A&E visits	412,332	172,755	239,577	412,332	174,771	237,561
Non-severe RVGE	301,414	111,538	189,876	301,414	113,340	188,075
Severe RVGE	39,809	6,901	32,908	39,809	7,214	32,596
Seizures	69,638	52,799	16,839	69,638	52,701	16,937
Intussusception	1,470	1,517	− 47	1,470	1,517	− 47
Total hospitalisations	110,917	61,217	49,700	110,917	61,431	49,486
Severe RVGE	39,809	6,901	32,908	39,809	7,214	32,596
Seizures	69,638	52,799	16,839	69,638	52,701	16,937
Intussusception	1,470	1,517	− 47	1,470	1,517	− 47
DALYs	616	260	356	616	263	353
Total governmental healthcare and non-healthcare costs [^]	144,525,144	73,796,558	70,728,586	144,525,144	74,228,014	70,297,130
Total outpatient and A&E visit costs[^]	10,075,603	5,116,851	4,958,752	10,075,603	5,149,793	4,925,810
Total hospitalisation costs[^]	134,449,541	68,679,707	65,769,834	134,449,541	69,078,221	65,371,320
Total governmental and patient healthcare and non-healthcare costs[^]	258,804,713	130,972,297	127,832,416	258,804,713	131,779,187	127,025,527
Total outpatient and A&E visit costs[^]	30,387,629	14,100,651	16,286,978	30,387,629	14,231,121	16,156,508
Total hospitalisation costs[^]	228,417,084	116,871,646	111,545,438	228,417,084	117,548,065	110,869,019
Vaccine programme costs[^]		51,074,141			56,921,915	

A&E, Accident and Emergency; DALYs, disability-adjusted life-years; RVGE, rotavirus gastroenteritis.

[*] Any estimates of a difference in impact of the two vaccine products should be interpreted with caution as they reflect our uncertain assumptions about the dose-specific efficacy and waning associated with each product.

[#] Assumed no symptomatic RVGE cases treated at home.

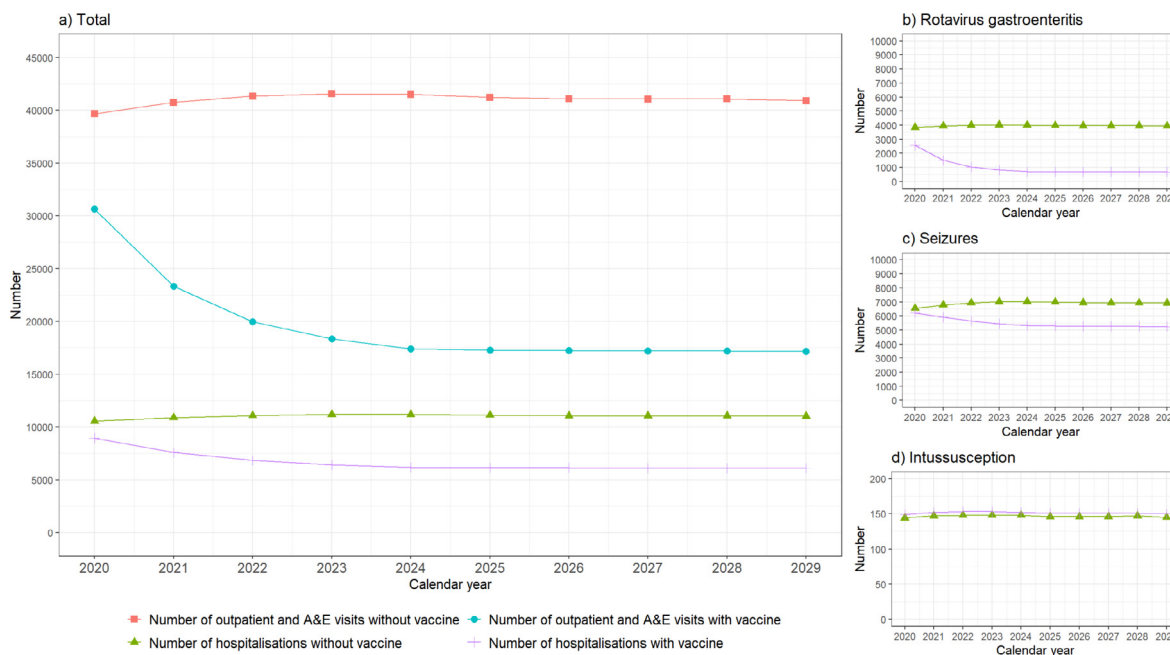[^] All costs are discounted and in 2018 United States dollars.

Fig. 2. Numbers of outpatient and A&E visits and hospitalisations with and without rotavirus vaccine over the first 10 years of introduction. A&E, Accident & Emergency.

one of the most influential factors impacting on cost-effectiveness in LICs and LMICs but as in Hong Kong vaccine price and vaccine efficacy are also very influential on the cost saved in these countries.

We considered the potential protection from seizures in our economic evaluation since this impact has been observed in the United States, Australia, Spain and England [11–13,32,61]. Since the burden of seizures in children younger than 5 years is not low in Hong Kong, 27% of treatment cost savings would be attributed to the protection from seizures, and 8% of DALYs averted

would be due to prevention of seizures. Considering this protection in the model will provide the Government with a more comprehensive perspective when evaluating the potential impact of rotavirus vaccine introduction. However one study from England examining shorter pre- and post-vaccination time periods has shown no significant association between rotavirus vaccination and seizure hospitalisations [33], and there is no data in Hong Kong showing a reduction in seizure incidence. A sensitivity analysis was also conducted without the consideration of the protection from seizures. Both products would still be 100% cost-saving to the
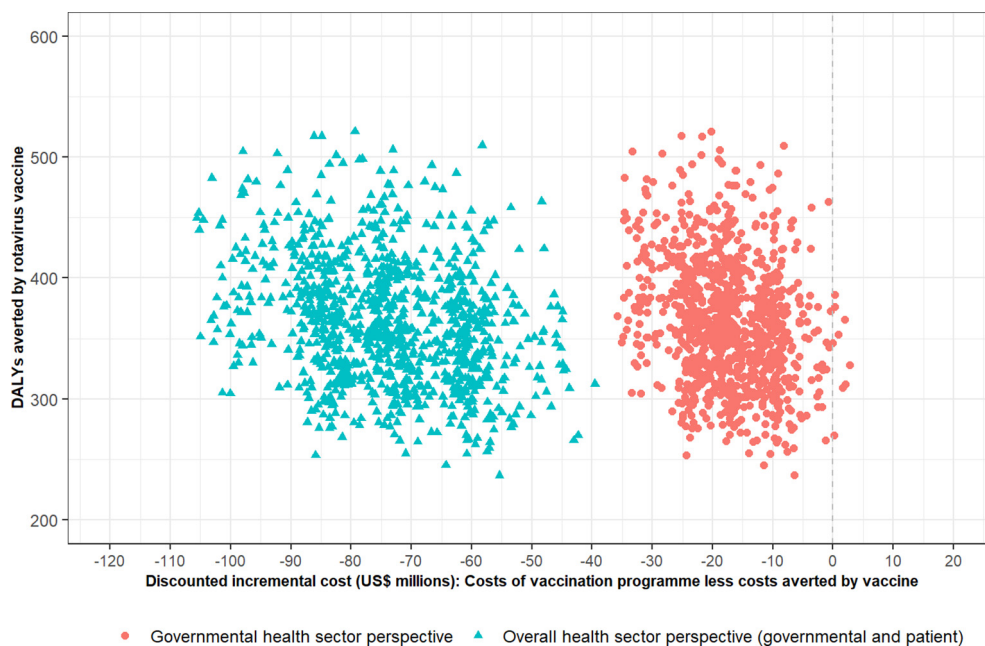
Fig. 3a. Discounted incremental costs versus disability-adjusted life-years (DALYs) averted from a probabilistic sensitivity analysis for monovalent rotavirus vaccine (*Rotarix*®).
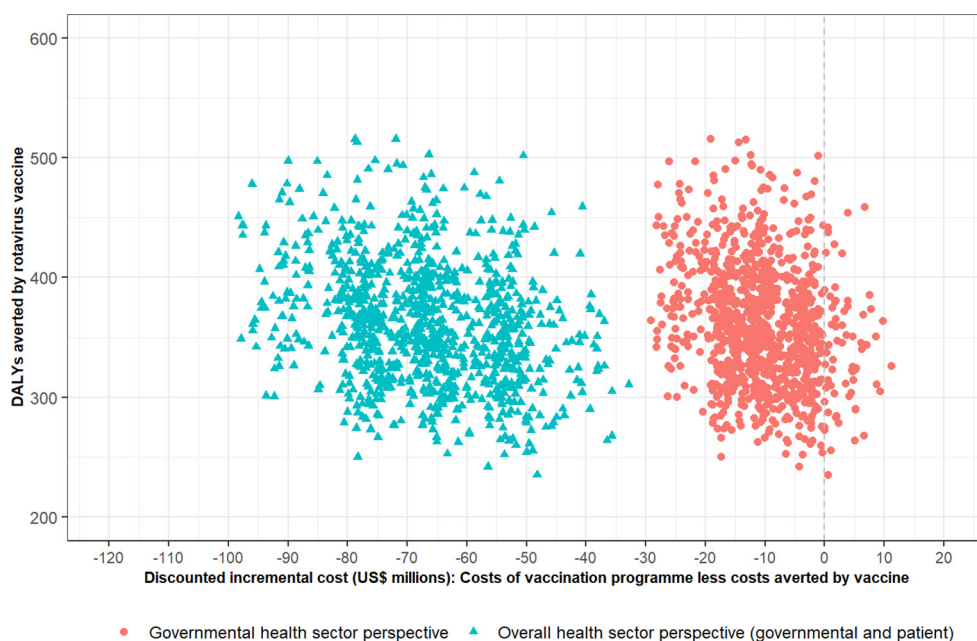

Fig. 3b. Discounted incremental costs versus disability-adjusted life-years (DALYs) averted from a probabilistic sensitivity analysis for pentavalent rotavirus vaccine (*RotaTeq*®).

society from an overall health sector perspective but would be 6–40% likely to be cost-saving to the Government alone. This lower probability compares to the 94–99% probability when the protection from seizures is included. Excluding the potential protection from seizures, the full-course vaccine prices leading to cost-saving results to the Government are close to that estimated from the previous economic evaluation in Hong Kong [16].

The two vaccine products evaluated in this analysis have not been compared head-to-head in a randomised controlled trial, and there is limited evidence to suggest a meaningful difference in real-world impact or safety when both vaccines have been used concurrently in the same country [62,63]. For this reason, we did

not calculate the incremental cost-effectiveness of one product compared to the other, and instead present the cost-effectiveness of each vaccine compared to no vaccination. In addition, any estimates of a difference in impact should be interpreted with caution as they reflect our uncertain assumptions about the dose-specific efficacy and waning associated with each product.

A PERT-Beta distribution was assumed for all parameters in the probabilistic sensitivity analyses. It is a flexible distribution that can be easily incorporated into decision-support models where there is uncertainty about the shape of the distribution and what the appropriate range should be. We acknowledge that it is a simplified approach with skewing and smoothing on the basis of the
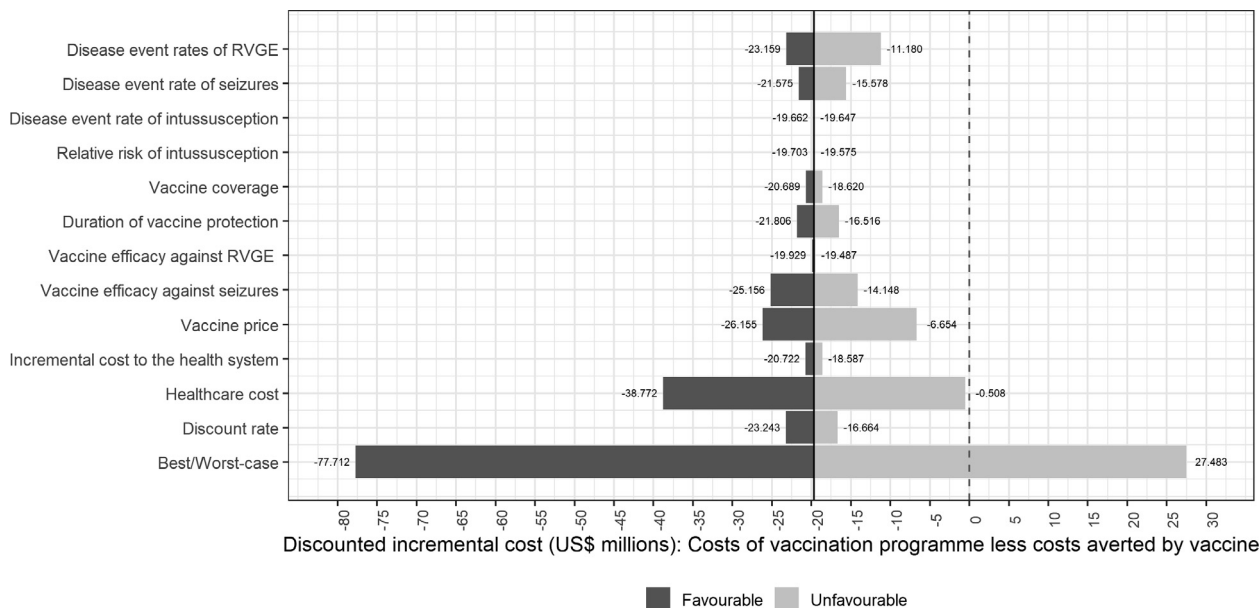
Fig. 4a. Tornado diagram for monovalent rotavirus vaccine (*Rotarix®*) introduction in terms of discounted incremental cost to the government from deterministic scenario analyses (discounted incremental cost in the base-case analysis = −US$19.654 million). A&E, Accident and Emergency; RVGE, rotavirus gastroenteritis.
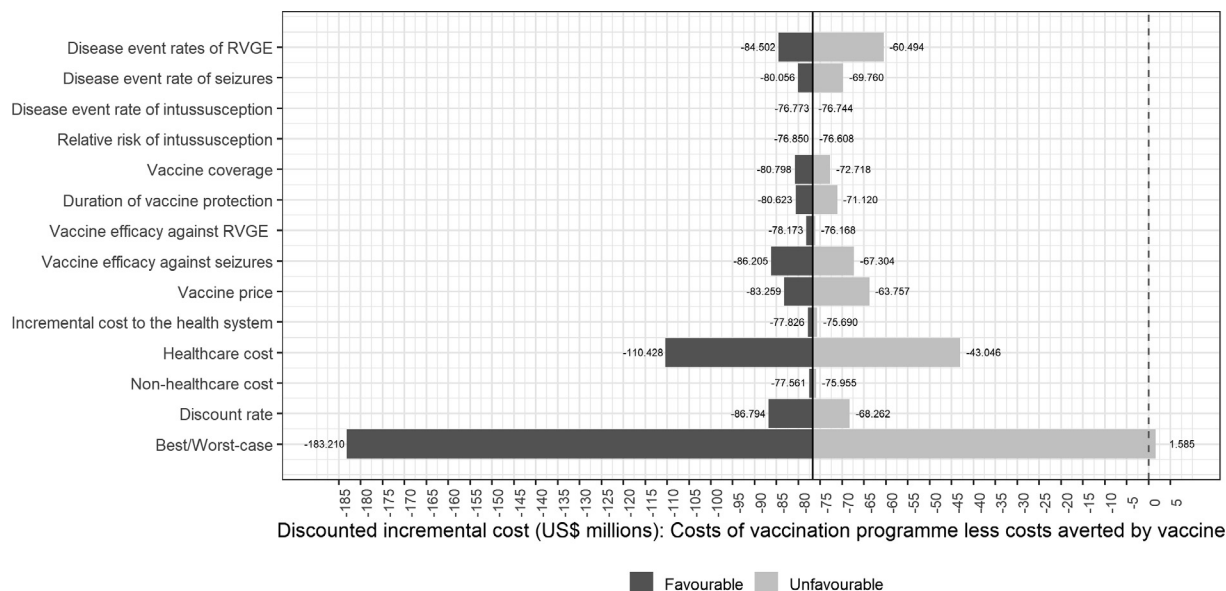

Fig. 4b. Tornado diagram for monovalent rotavirus vaccine (*Rotarix®*) introduction in terms of discounted incremental cost to the society from an overall health sector perspective (governmental and patient) from deterministic scenario analyses (discounted incremental cost in the base-case analysis = −US$76.758 million). A&E, Accident and Emergency; RVGE, rotavirus gastroenteritis.

mid, low and high values of inputs. There are other approaches that could have been used to improve the probabilistic sensitivity analyses but this would require more data than was available, and we do not believe this would alter the main conclusions or recommendations of the analyses.

UNIVAC is a deterministic static cohort model that can be used to generate estimates of the direct effects of vaccination. Indirect vaccine benefits such as herd protection, cross-protection against non-vaccine rotavirus genotypes and reduction of nosocomial infections were not considered in this analysis, so estimates should be regarded as conservative. Developing and calibrating a transmission dynamic model to the Hong Kong context would be an option to account for the indirect vaccine benefit [64] but this would be difficult to justify given the favourable cost-

effectiveness and benefit-risk results based on the direct effects of vaccination alone. A scenario with very high vaccine efficacy (scenario 13) provides an indication of the potential impact of herd effects on the results. However, given the high coverage and high efficacy of vaccines in Hong Kong, the indirect benefits are anticipated to be minimal once the vaccine has been introduced for several years, and all birth cohorts younger than 5 years are participating in the programme.

Also, we used the estimates of RVGE hospitalisation incidence from 1997 to 2011 [4], where rotavirus vaccine has been available in the private market since 2006. This data reflects the rotavirus disease burden before increased uptake of the vaccine in the private sector. We assumed no vaccination during the period of 2006–2011 in the private sector as no reduction in the incidence
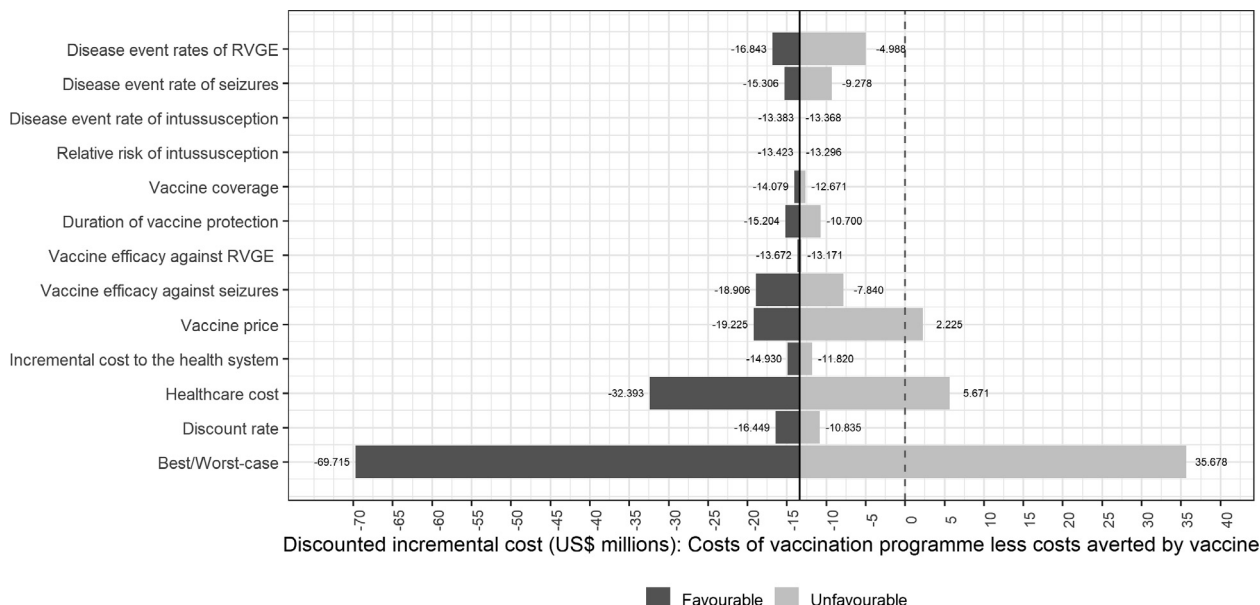
Fig. 4c. Tornado diagram for pentavalent rotavirus vaccine (*RotaTeq®*) introduction in terms of discounted incremental cost to the government from deterministic scenario analyses (discounted incremental cost in the base-case analysis = −US$13.375 million). A&E, Accident and Emergency; RVGE, rotavirus gastroenteritis.
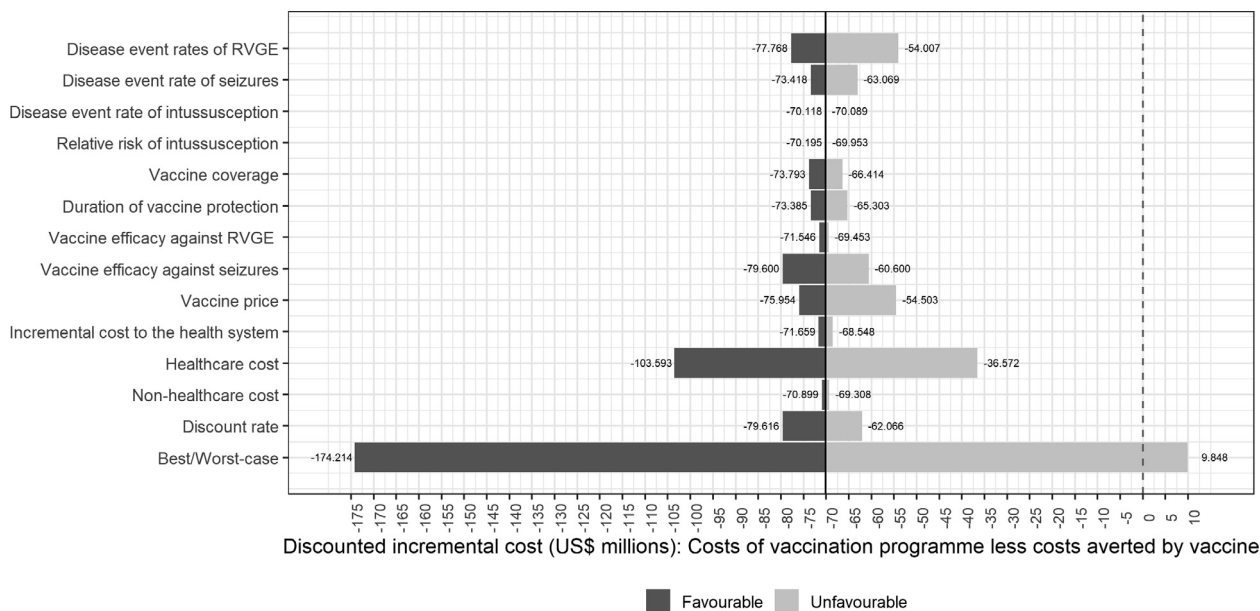

Fig. 4d. Tornado diagram for pentavalent rotavirus vaccine (*RotaTeq®*) introduction in terms of discounted incremental cost to the society from an overall health sector perspective (governmental and patient) from deterministic scenario analyses (discounted incremental cost in the base-case analysis = −US$70.104 million) A&E, Accident and Emergency; RVGE, rotavirus gastroenteritis.

of hospitalisation for either rotavirus or all-cause gastroenteritis was observed in Hong Kong children younger than 5 years over the 14 rotavirus seasons. However, the impact of 49,000 RVGE and seizure hospitalisations prevented should be interpreted with caution as this reflects our uncertain assumption about the baseline burden. A sensitivity analysis was conducted with the best estimate of pre-vaccination RVGE hospitalisation incidence, using the surveillance data from 2001 to 2003 based on the WHO Generic Protocol [3,4]. By estimating the RVGE hospitalisation to be 845 (810–880) per 100,000 person-years, rotavirus vaccination would still be 100% cost-saving to the society from an overall health sector perspective and <94% cost-saving to the Government; and there would be 43,000 (95% UI: 40,000–47,000) RVGE and seizure hospitalisations prevented.

In addition, we were conservative when making assumptions on the input parameters. We assumed no traditional Chinese medicine consultations, miscellaneous costs and loss of productivity of caregivers associated with RVGE. We also assumed no costs for mild RVGE cases treated at home which would result in a more conservative estimate from an overall health sector perspective. We assumed no death from and no private A&E consultation for both RVGE and intussusception, providing an overall conservative estimate due to the higher burden of RVGE than intussusception. Mortality from either RVGE or intussusception is very rare in Hong Kong, so excluding deaths from both diseases from our analyses would not alter the conclusions of our analysis. Had we applied our known but highly uncertain (due to small numbers of deaths) CFRs for RVGE and intussusception [18,27], there would have been

<10 RVGE deaths prevented, and no intussusception deaths caused over the 10-year period of the analysis.

We estimated the disability weights for DALYs from the Global Burden of Disease study [24]. Rather than using DALYs to estimate the quality of life for each episode of RVGE, we could have used quality-adjusted life years (QALYs) based on detailed question-naires administered to individuals in Hong Kong. However, since treatment cost savings outweighed vaccination costs in most of our probabilistic simulations, the choice of using QALYs versus DALYs would not be influential to the outcome, i.e., that the vaccine is likely to be cost-saving in Hong Kong.

As revealed by the deterministic scenario analyses, the highest combination of costs saved and DALYs averted is the scenario with high disease event rates of RVGE. We believe that our findings will be of interest to HICs that have not yet introduced rotavirus vaccine and have a high disease burden of rotavirus in terms of rates of hospitalisation, as seen in Hong Kong.

In conclusion, rotavirus vaccine, which has been shown to be effective in preventing RVGE and reducing morbidity, is likely to be cost-saving to the Hong Kong Government and payers. Its incorporation into the CIP would reduce the burden of disease of RVGE and the associated healthcare and non-healthcare costs and would provide more equitable healthcare access to the community. This economic evaluation can guide policy makers to formulate informed decisions on whether to incorporate rotavirus vaccine into the CIP.

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CRediT authorship contribution statement

Karene Hoi Ting Yeung: Methodology, Soft ware, Formal analysis, Investigation, Writing - original draft, Project administration, Validation, Writing - review & editing. **Shi Lin Lin:** Methodology, Software, Formal analysis, Investigation, Visualization, Validation, Writing - review & editing. **Andrew Clark:** Methodology, Software, Formal analysis, Validation, Writing - review & editing. **Sarah M. McGhee:** Validation, Writing - review & editing. **Cara Bess Janusz:** Validation, Writing - review & editing. **Deborah Atherly:** Validation, Writing - review & editing. **Kate Ching Ching Chan:** Validation, Writing - review & editing. **E. Anthony S. Nelson:** Conceptualization, Methodology, Formal analysis, Investigation, Supervision, Funding acquisition, Validation, Writing - review & editing.

Declaration of Competing Interest

EASN participated in Scientific Input Engagement meeting on dynamic transmission modeling of rotavirus transmission and the impact of rotavirus vaccination organized by Merck Sharp & Dohme (Asia) Ltd. in September 2019. Honorarium paid to EASN's Institution.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2020.10.052.

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