

1 **The hidden health and economic burden of rotavirus**
2 **gastroenteritis in Malaysia: an estimation using**
3 **multiple data sources**

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5 **Technical Appendix**

6 This section contains additional material on methodology used to estimate the health and
7 economic burden of rotavirus gastroenteritis in Malaysia.

8 Supplementary Text 1 compares the present study with a previous rotavirus burden estimation in
9 Malaysia. Supplementary Text 2 provides detailed methods and results of the systematic review
10 we conducted of prospective, hospital-based rotavirus surveillance studies in Malaysia.

11 Supplementary Text 3 details the estimation of direct medical costs for rotavirus gastroenteritis
12 using multiple data sources.

13 Supplementary Table 1 compares rotavirus burden estimates of the present study with the 2005
14 study.

15 Supplementary Tables 2 to 3 provide the detailed workings of the estimation of incidence of
16 acute gastroenteritis in Malaysia according to health service utilization.

17 Supplementary Tables 4 summarizes three hospital-based rotavirus studies selected for meta-
18 analysis.

- 19 Supplementary Table 5 details the estimation of unit cost at five tertiary-level public hospitals.
- 20 Supplementary Table 6 shows the estimation of unit costs at healthcare facilities in Malaysia.
- 21 While, supplementary tables 7 to 9 detail the estimation of direct medical, direct non-medical
- 22 and indirect costs for rotavirus gastroenteritis in Malaysia according to health service utilization.

23 **Supplementary Text 1: Comparison of incidence estimates with the** 24 **previous rotavirus burden study**

25 One previous study by Hsu et al[1], estimated the rotavirus (RV) burden in Malaysia. We feel
26 that this study underestimated the burden, due to under-reporting of discharges and inadequate
27 consideration of privately treated episodes. We compare here the estimates of burden of the Hsu
28 et al. study with the present study. (Supplementary table 1)

29 **1.1 Hospital Discharges**

30 Since 1999, electronic records on hospital discharges are captured in a national database
31 administered by the Ministry of Health, Malaysia (MOH). Only MOH public hospitals report to
32 the database. Non-MOH public hospitals, like teaching and army hospitals do not report to the
33 database. Although, discharges from private hospitals were officially collected from 2000, this
34 collection mechanism is not reliable. In 2013, approximately 209 private hospitals were
35 registered in Malaysia, however only 107 hospitals reported hospital discharge data [2]. Also,
36 there is under-reporting in terms of discharges, as diagnostic coding of discharges using
37 International Classification of Disease, tenth revision (ICD-10), is often incomplete in private
38 facilities.

39 **a) Under-reporting of public hospital discharges**

40 In their paper, Hsu et al. reported that during the 2-year study period (1999-2000), there were
41 27,873 children under-five years of age with discharge diagnosis of AG, or an average of 13,937
42 AG hospitalizations annually.

43 This figure is much less than the 21,000 AG hospitalizations reported annually from 2008 to
44 2013. A possible explanation is that in the early years of establishment of the national database,
45 not all discharges were ICD-10 coded, leading to considerable under-reporting.

46 **a) Public hospitals not contributing data not accounted for**

47 Hsu et al. did not account for discharges from MOH hospitals or the non-MOH public hospitals
48 not reporting to the database.

49 In this present study, we adjusted for non response from hospitals by using hospital beds, which
50 takes into consideration both the number and size of the hospitals. Please see Supplementary
51 Table 2.

52 **b) Private hospitals inadequately considered**

53 The Hsu et. al study was unable to collect direct discharge data on private hospitals, and adjusted
54 for an additional 20% of hospitalizations in the private sector, estimating a total of 13,937 AG-
55 related hospitalizations annually in Malaysia (at both public and private hospitals).

56 This estimate is lesser than our current estimate, primarily because it did not directly capture
57 private hospitalizations. From 2010 to 2013, the national database captured an average of 17,000
58 AG private hospital discharges annually, in children under-five years. In our study, we accounted
59 for all diarrheal discharges in the country, including for episodes not reported, by using weights
60 of total hospital beds. Please see Supplementary Table 2.

61

62 **1.2 Outpatient visits**

63 Hsu et al. reported an average of 60,343 AG-related outpatient visits annually to public health
64 clinics between 1998 and 2000. In 2012, 129,424 AG-related outpatient visits in children under-
65 ten years to public facilities were reported.

66 We estimated 82,568 AG-related outpatient visits under-five years, by applying weights based on
67 age-dependent health service utilization from NHMS 2006, to the 2012 data from public
68 outpatient facilities. Again, the difference may be due to improvement in the reporting
69 mechanism to the MOH database over time. (Supplementary table 3)

70 Also, unlike our present study Hsu et al. did not estimate burden of AG outpatient visits to
71 private clinics. We used weights from NHMS 2006 to estimate the number of children who
72 sought treatment at private clinics for diarrheal illness.

73 **1.3 Home-treated cases**

74 The Hsu et al. paper did not consider episodes of diarrhea that did not require formal treatment at
75 healthcare facilities. This is an important burden to society, as children with mild diarrhea still
76 require caregiver's time, and thus incur productivity loss. Our estimates of home-treated episodes
77 is based on health-utilization patterns from the only community-based study in Malaysia[3], and
78 this gives very similar results when compared with two international studies[4, 5].

79 Parashar et al. estimated that for every child requiring medical attention for rotavirus
80 gastroenteritis in developed countries, an additional three to five children develop symptomatic
81 illness requiring only home treatment (or a mild illness) [4]. Our current study findings suggest
82 that in Malaysia, the number of children with rotavirus diarrhoea that were home-treated (145,000)

83 was about 3.5 times the number who sought outpatient care (41,000). This is within the range of
84 estimates of home-treated episodes obtained when using the Parashar et al. expansion factor of
85 four times of outpatient episodes (range of number of home-treated episodes: 124,000 to 206,000).

86 Bilcke et al. estimated the global incidence of symptomatic rotavirus infections at 0.31 (0.19 to
87 0.50) per-person per-year in children under 2 years of age [5]. This would mean 315,000
88 (193,000 to 509,000) symptomatic episodes in children under 2 years annually in Malaysia. Our
89 estimate of 218,000 episodes of symptomatic rotavirus annually in children under-five years of
90 age in Malaysia is well below this estimate.

91 **Supplementary Text 2: Systematic review of prospective, hospital-** 92 **based rotavirus studies in Malaysia**

93 We conducted a systematic search of prospective hospital-based rotavirus (RV) surveillance
94 studies in Malaysia. A meta-analysis was conducted to obtain pooled RV-detection proportions
95 for acute gastroenteritis (AG) hospitalizations.

96 **2.1 Methods**

97 A systematic search was conducted to select studies conducted in Malaysia that comply with
98 WHO recommendations for hospital-based RV surveillance [6]. Criteria for eligibility were as
99 follows: (i) prospective, hospital-based study (ii) at least one year duration, (iii) conducted in
100 Malaysia, (iv) on children under the age of 5 years, (v) stool tested for RV with an enzyme
101 immunoassay test.

102 The literature was searched systematically to locate published articles in three databases
103 (PubMed, Scopus and Web of Science). Search terms used were ‘rotavirus’ AND
104 (‘gastroenteritis OR ‘diarrhoea’ OR ‘diarrhea’) AND ‘Malaysia’. The search was limited to
105 English language publications. Citation search and consultation with experts were conducted to
106 identify additional publications.

107 After removing duplicates, titles and abstracts were screened to identify prospective, hospital-
108 based RV studies. Subsequently, full text articles were read to identify studies meeting the
109 eligibility criteria for inclusion in the meta-analysis.

110 A DerSimonian and Laird random-effects model [7] was used to pool outcomes from each
111 individual study site and calculate the mean and 95% Confidence Interval (CI) for RV-detection
112 proportion.

113 **2.2 Results**

114 The systematic search of three databases provided a total of 94 citations; 39 from Pubmed, 38 from
115 Scopus and 17 from Web of Science. No further articles were identified from citation search or
116 consultation with experts. After duplicates were excluded, 27 articles on rotavirus in Malaysia
117 were screened by title and abstract. Of these, 15 were excluded for not being prospective, hospital-
118 based rotavirus surveillance studies. Three papers were discarded for being results of duplicate
119 primary studies. Full text articles of the remaining nine papers were read, and the eligibility criteria
120 were applied. A PRISMA flow diagram of the review process is shown in Figure 2 of the main
121 text.

122 From 1982 to 2012, there were nine prospective hospital-based rotavirus surveillance studies
123 conducted in Malaysia. The studies were conducted at Kuala Lumpur, the capital city of Malaysia
124 and other locations including Kuching in Sarawak, Kota Kinabalu in Sabah, Johor Baru in Johor
125 and Kuala Terengganu in Terengganu. Only three studies were conducted among children under-
126 five years old. Five of the nine studies used EIA methods to test stool specimens for rotavirus. A
127 total of 9,510 stool specimens were tested for rotavirus, with the rotavirus detection proportion of
128 23% to 50% at each site.

129 A total of three studies met the predetermined eligibility criteria and were included in the meta-
130 analysis [8-10]. These studies were conducted at different time-points between the year 2000 and
131 2010, and at different geographic locations in Malaysia. A total of 5,586 stool samples were tested

132 for rotavirus. The rotavirus detection proportion ranged from 32% to 50% at each individual study
133 site. See Supplementary Table 4 for a summary of the three prospective hospital-based rotavirus
134 surveillance studies selected for meta-analysis.

135 Each of these three studies were conducted at two different locations. For two studies (Hung et al.,
136 2006 and W.S. Lee et al., 2012), results were shown separately for each individual study site [9,
137 11]. The Hsu et al. 2005 paper did not segregate results by study site [9]. Rotavirus detection
138 proportion from 5 individual study sites from the three papers were pooled for the meta-analysis.
139 A random effects model was applied to account for heterogeneity ($I^2 = 86\%$). The pooled estimate
140 of the RV- detection proportion in children under-five years hospitalized for AG was 44.5% (95%
141 CI: 39.6 – 49.4). See Figure 3 in the main text.

142 **Supplementary Text 3: Estimating direct medical costs**

143 The economic burden of RVGE in Malaysia is dependent on unit cost estimates for inpatient and
144 outpatient care at both public and private health facilities in Malaysia. Direct medical costs were
145 calculated based on per bed-day inpatient costs multiplied with the duration of admission for
146 hospitalizations and costs per-visit for outpatient visits.

147 Since unit costs are not readily available in Malaysia, we utilize methods previously used in the
148 estimation of the economic burden of dengue in Malaysia [12, 13]. Multiple data sources were
149 combined for this estimation, including hospital annual reports from five tertiary-level hospitals,
150 local costing studies at six primary-level hospitals and eleven health clinics around the country
151 and World Health Organization-CHOosing Interventions which are Cost-Effective (WHO-
152 CHOICE).

153 **3.1 WHO-CHOICE project**

154 The WHO-CHOICE (World Health Organisation – CHOosing Interventions which are Cost-
155 Effective) project was initiated in 1998 to assist countries in making rational choices based on
156 evidence generated by cost-effectiveness analyses [14].

157 The WHO-CHOICE project allows for estimation of unit cost of inpatient and outpatient care by
158 191 member states, through data collected from 49 countries [15, 16]. Presumably because of the
159 lack of suitable data, Malaysia had not been included in this list of countries contributing data.
160 Using econometric modeling, the WHO-CHOICE project predicts unit costs for countries in
161 which data were not available. In the case of Malaysia, especially since Malaysian data was not
162 obtained for the WHO-CHOICE project, it is preferable to use local data for costing.

163 The facility-types used in the WHO-CHOICE project refers to differences in service
164 characteristics, including difference in case-mix, technical capacity and skills available in
165 facilities [15].

166 In our study, costs for facility levels from WHO-CHOICE project (primary-level, secondary-
167 level and teaching hospitals) were used for estimation of unit-costs for inpatient bed-days at
168 public hospitals. For the estimation of unit-costs for outpatient visits (public hospital and clinics),
169 facility levels used were health facilities with no beds, primary and secondary-level hospitals
170 [15, 17].

171 **3.2 Unit costs at public clinics**

172 A 1995 costing study on the provision of outpatient services in 11 MOH public clinics in Kedah
173 was conducted by Lim KJ provided costs per-visit of US\$ 3.75 in 2013 US\$ [12, 18].
174 Information on costs was collected for personnel, supplies, utilities, maintenance and training,
175 and was derived mainly from the operating budget of the clinics involved. We deemed this unit
176 cost of US\$ 3.75 for public clinics in Malaysia or similar to ‘health facilities with no beds’ from
177 WHO-CHOICE [14, 17].

178 **3.3 Unit costs at primary-level hospitals**

179 A study by Sabrina AR in 2001 estimated unit costs at six primary-level or district hospitals
180 around Malaysia for the year 2001. This study provided us with average costs for primary-level
181 hospitals of US\$ 43 per-visit (range: US\$ 10 to US\$ 78 per-visit) in 2013 US\$.

182 All the selected hospitals in this study were 93 bedded facilities with basic medical and surgical
183 services provided by doctors without specialist qualifications, hospitals which were considered
184 by the MOH as belonging to the category of “district hospitals without specialists” [19].

185 **3.4 Unit costs at tertiary-level hospitals**

186 We conducted top-down costing of five urban, tertiary-level public hospitals in Malaysia. The
187 hospitals selected were University of Malaya Medical Center (UMMC), Hospital Sungai Buloh
188 (HSB), Hospital Sultanah Bahiyah, Alor Setar (HAS), Hospital Melaka (HM) and Hospital
189 Sultan Haji Ahmad Shah, Temerloh (HT).

190 The UMMC is a tertiary-level, teaching hospital administered by the Ministry of Education. The
191 operating expenditure and workload of UMMC was obtained from the 2012 hospital annual
192 report and updated to include salaries of academic clinicians. Academic clinicians are employed
193 by the university, and as such their salaries are not included in the hospital’s operating
194 expenditure. We made the assumption that the academic clinicians spent 60% of their time on
195 clinical service, while the remaining time was spent on academic and research duties. [12] The
196 cost of an outpatient visit was assumed at a fifth the cost of an inpatient day at tertiary-level
197 hospitals.

198 We searched hospital websites individually for annual reports of tertiary-level Ministry of Health
199 (MOH) hospitals. We also hand-searched for annual reports at the MOH library at Putrajaya. The
200 lack of standardized formats and availability of information on admission rates, clinic
201 attendances, bed occupancy rate, hospital expenditure and others limited our selection to 4
202 tertiary-level MOH hospitals.

203 We estimated of unit-costs at tertiary-level hospitals based on the average costs obtained from
204 UMMC and these 4 hospitals (Supplementary table 5). Average costs at tertiary-level hospital
205 was estimated at US\$ 341 per-bed day and US\$ 68 per-visit.

206 **3.4.1 Description of tertiary-level hospitals**

207 **University of Malaya Medical Center (UMMC)**

208 UMMC is a 979 bedded, tertiary-level, teaching hospital administered by the Ministry of
209 Education. UMMC is located in Kuala Lumpur, and is the only public hospital serving the
210 bordering the city of Petaling Jaya, with a population of approximately two million people.

211 **Hospital Sungai Buloh (HSB)**

212 Hospital Sungai Buloh is a 620 bedded, tertiary-level hospital located about 25 km from the
213 capital city of Kuala Lumpur, in the state of Selangor. This hospital serves about approximately
214 2.18 million people or 40% of the population of Selangor. It is known as a center of excellence
215 for the management of infectious diseases, emergency medicine and traumatology, neurosurgery,
216 maxillo-facial surgery, plastic and reconstructive surgery and spinal surgery.

217 **Hospital Sultanah Bahiyah, Alor Setar (HAS)**

218 Hospital Sultanah Bahiyah, Alor Setar is an 870 bedded tertiary-level hospital located in Alor
219 Setar in the northern state of Perlis. . Hospital Sultanah Bahiyah, Alor Setar serves as a regional
220 referral center for 12 clinics in Perlis and 8 state hospitals in the northern region of Malaysia.
221 This hospital provides tertiary-level clinical services in 12 specialties, with 28 clinical
222 consultants providing sub-specialty services including cardiology, nephrology, plastic and
223 reconstructive surgery and maxillofacial surgery.

224 **Hospital Sultan Haji Ahmad Shah, Temerloh (HT)**

225 Hospital Sultan Haji Ahmad Shah, Temerloh is a 500 bedded, tertiary-level hospital serving
226 approximately 900 thousand people in 6 districts in the state of Pahang. In 2012, Hospital Sultan
227 Haji Ahmad Shah, Temerloh employed 2,042 staff, including 31 Clinical Specialists. This
228 hospital provides tertiary-level services in 12 specialties and sub-specialty services including
229 oral-maxillary-facial surgery, pediatric dentistry, and oral surgery.

230 **Hospital Melaka (HM)**

231 Hospital Melaka is a 1,091 bedded, tertiary-level hospital serving approximately 800 thousand
232 people in Melaka and 4 neighboring districts in Johor. Hospital Melaka is second only to
233 Hospital Kuala Lumpur, in number of operational beds among MOH hospitals in Malaysia. It
234 provides services in 17 clinical specialties and sub-specialty services including plastics and
235 reconstructive surgery, oral surgery, dermatology, pediatric dentistry.

236 **3.5 Costing of hospital bed-days**

237 In this current study, we use methods previously utilized in the estimation of dengue burden in
238 Malaysia [12]. In 2010, a two-stage expert workshop, gathered experts from the public and
239 private health sectors and academia to discuss issues arising in the estimation of dengue disease
240 burden and costing, due to insufficient data [20].

241 Two main conclusions from this expert workshop are used in our present study.

242 Firstly, the workshop participants had agreed that the description of tertiary-level or teaching
243 hospitals, as provided by WHO-CHOICE, could refer to the state-level, national referral centers
244 or teaching hospitals in the public sector in Malaysia, including UMMC. The Malaysian district

245 hospitals could be categorized as either primary-level or secondary-level hospitals depending on
246 the services provided. In the case of smaller district hospitals without specialists or with few
247 basic specialties, the participants agreed that they should be categorized as primary-level
248 hospitals. These would include the six district hospitals in the 2001 costing study [21]. The
249 remaining district hospitals could be considered as secondary-level hospitals.

250 Secondly, inpatient care at each hospital-type was assumed to be proportional to the number of
251 beds in these facilities. The expert panel in the dengue study, agreed that the number of tertiary-
252 level beds made up 50% of all hospital beds in the country. The corresponding figures for
253 secondary and primary level hospital beds were 30% and 20% respectively. [12].

254 We assumed that inpatient care for diarrhea at each hospital-type was proportional to the number
255 of beds in these facilities. Distribution of hospitals by number of beds was derived from the
256 expert workshop in the dengue study [12].

257 Cost estimates by facility-type from WHO-CHOICE was used to derive cost-ratios, or the ratio of
258 unit costs for primary and secondary facilities compared to costs at tertiary-level facilities. Unit
259 costs per bed-day for primary-level hospitals are 74% of costs at tertiary-level hospitals (average
260 costs from UMMC and the 4 tertiary-level hospitals).

261 These cost-ratios were applied to unit cost estimates for tertiary-level hospitals and the distribution
262 of healthcare facility by type, to derive average costs per bed-day at public hospitals of US\$ 300.

263 The unit cost estimates for tertiary-level hospitals of US\$ 341 per bed-day and US\$ 68 per-visit
264 (average costs from UMMC and the 4 tertiary-level hospitals), were assumed to be equivalent to
265 costs of private facilities.

266 Duration of admission for an episode of RVGE (3.3 days) was obtained from a 2010 prospective
267 study conducted in two hospitals in Malaysia [11, 22]. (Supplementary Table 6)

268 **3.6 Costing of outpatient visits**

269 Distribution of care to outpatient facilities was based on unpublished data from MOH, Malaysia.
270 Clinic attendances to MOH facilities for childhood diarrhoea in 2012, showed that 56% of
271 outpatient visits were to health facilities with no beds and the remaining were to hospitals [23].
272 We apportioned outpatient care at each hospital type as proportional to the number of beds in these
273 facilities (conclusion of expert panel discussion in Dengue study). As such we distributed the
274 remaining 44% of outpatient visits to tertiary-level (50%), secondary-level (30%) and primary-
275 level (20%) hospitals.

276 Cost estimates by facility-type from WHO-CHOICE was used to derive the ratio of unit costs for
277 secondary-level hospitals compared to costs at primary-level hospitals. Unit costs per outpatient
278 visit for secondary-level hospitals are 141% of the costs at primary-level hospitals (from the
279 Sabrina AR study).

280 Costs per-visit to public health clinics (health clinics with no beds) was derived from the 1995
281 costing study by Lim KJ of US\$ 4. Average costs per-visit from UMMC and 4 MOH hospitals
282 of US\$ 68 was applied to tertiary-level hospitals.

283 Our estimate for the average cost per-visit for outpatient care is US\$ 29 (US\$ 4 for public clinic
284 visits, US\$ 61 for public hospital outpatient visits and US\$ 68 for private clinic visits).

285 See Supplementary Table 6 for estimation of unit costs at healthcare facilities in Malaysia

286 **Supplementary Table 1. Burden of rotavirus gastroenteritis in Malaysia, 2000 and 2013.**

	2000				2013			
	Annual no. of cases of		Events per 1,000		Annual no. of cases of		Events per 1,000	
	diarrhea		children per year		diarrhea		children per year	
	AG	RV	AG	RV	AG	RV	AG	RV
	related	related	related	related	related	related	related	related
Deaths	69	34	0.03	0.01	61	27	0.02	0.01
Hospitalizations	13,937	8,571	5.3	3.3	69,965	31,148	27.5	12.2
Outpatient clinic visits	60,342	14,482	23.1	5.5	233,806	41,260	91.9	16.2
Home Treated			-	-	1,209,128	145,095	475.3	57.0
Total	74,348	23,087	28.5	8.8	1,512,960	217,531	594.7	85.5

287 ^a Results from the estimation of rotavirus burden in Malaysia by Hsu et al. in 2005.

288 ^b By 5 years of age.

289 Birth cohort: 1998: 521,997 live births; 2012^P: 508,774 live births from the Department of Statistics, Malaysia. ^P preliminary data

290 Note: RV: rotavirus; AG: acute gastroenteritis.

291 **Supplementary Table 2. Diarrheal discharges to public and private hospitals in children under-five years in**
 292 **Malaysia**

Row	Item	Source	Public hospitals	Private hospitals
(1)	Diarrheal discharges reported	MOH ^a	23,450	15,886
(2)	No. of reporting hospitals	MOH ^b	96	107
(3)	No. of hospital beds in reporting hospitals	MOH ^b	18,694	12,572
(4)	Total hospitals in Malaysia	MOH ^c	142	209
(5)	Total hospital beds in Malaysia	MOH ^c	41,639	14,033
(6)	Total diarrheal discharges in Malaysia	(1) x (5)/ (3)	52,233	17,732

293 ^a Discharges reported to the national database at the Center for Health Informatics, Planning Division, Ministry of Health, Malaysia.

294 ^b Hospitals reporting discharges to the Center for Health Informatics, Planning Division, Ministry of Health, Malaysia.

295 ^c Total number of hospitals and beds in Malaysia, obtained from Center for Health Informatics, Planning Division, Ministry of Health,
 296 Malaysia.

297 **Supplementary Table 3. Diarrheal outpatient visits at public facilities for children under 10 years and**
 298 **under-five years, 2012**

Row	Item	Source	Public hospitals	Public clinics
(1)	0-9 years	MOH ^a	56,999	72,425
(2)	Proportion of diarrheal attendances	NHMS 2006	71%	58%
(3)	0-4 years	(1) x (2) ^b	40,410	42,158

299 Note: 0-9 years, children under the age of 10 years; 0-4 years, children under the age of five years.

300 MOH, Ministry of Health, Malaysia; NHMS 2006, National Health and Morbidity Survey 2006

301 ^a Annual diarrheal attendances for children under ten years at public clinics obtained from Ministry of Health, Malaysia[23]

302 ^b Annual diarrheal attendances for children under five years are estimated by using age-specific health utilization weights for diarrhea
 303 from National Health and Morbidity Survey 2006.

304 Note: MOH public health facilities provide general outpatient services and/or maternal child health (MCH) services at various levels
 305 of care depending the facilities and the needs of the population (population size etc.). MCH clinics may be located in facilities together
 306 with outpatient services or in separate, smaller clinics close to villages and communities. MCH services are provided by nurses and
 307 midwives at smaller clinics, but also by GPs and Family Medicine Specialists at larger health centres. Returns on outpatient diarrhoeal

308 attendances are not recorded or collected at MCH clinics. MCH clinics provide child health services, mainly Well Baby Clinics,
309 monitoring growth, development, nutrition etc. and administering immunisations. Mild diarrhoeal illness may be treated by nurses
310 especially in smaller community clinics, but more severe episodes would be referred to the outpatient department for treatment by
311 medical officers. We are unable to estimate the number of mild diarrhoea episodes treated at MCH clinics because of the integrated
312 nature of the service provided.
313

314 **Supplementary Table 4. Summary of prospective hospital based studies on rotavirus gastroenteritis selected**
 315 **for meta-analysis**

Author	Study Period	Length of study	Age group	Method of RV-detection	Location	Number of cases tested	Number of RV positives	RV-detection proportion (%)	References
Hsu <i>et al.</i> (2005)	2001-2003	2 years	<5 years	EIA	Kuala Lumpur and Kuching	2260	1130	50%	[1]
Hung <i>et al.</i> (2006)	2002–2003	2 years	<5 years	EIA	Kuala Lumpur	1756	820	47%	[9]
					Kuching	912	445	49%	
Lee <i>et al.</i> (2012)	2008–2010	2 years	<5 years	EIA	Kuala Lumpur	385	161	42%	[11]
					Kuala Terengganu	273	87	32%	

316 Note: RV- Rotavirus; EIA - Enzyme Immunoassay test.

317 **Supplementary Table 5. Estimation of unit costs at tertiary-level, public hospitals in Malaysia**

Row	Item	Source	UMMC, 2012	HSB, 2013	HAS, 2012	HM, 2013	HT, 2012
(1)	Admissions	Hospital Report ^a	53,825	45,372	72,703	74,468	39,849
(2)	Number of registered beds	Hospital Report ^a	979	620	870	1,091	500
(3)	Occupancy rate	Hospital Report ^a	78%	82%	95%	85%	91%
(4)	Occupied beds	(2) x (3)	759	507	826	923	457
(5)	Annual bed days	(4) x 365	276,935	185,000	301,609	336,970	166,659
(6)	Outpatient clinic visits	Hospital Report ^a	800,426	191,077	142,011	305,098	73,347
(7)	Emergency visits	Hospital Report ^a	110,246	150,865	275,009	137,852	69,081
(8)	Total outpatient visits	(6) + (7)	910,672	341,942	417,020	442,950	142,428
(9)	Relative cost: visit/inpatient day	Shepard et al.	0.2	0.2	0.2	0.2	0.2
(10)	Ambulatory bed-day equivalents	(8) x (9)	182,134	68,388	83,404	88,590	28,486
(11)	Total bed-day equivalents	(5) + (10)	459,069	253,389	385,013	425,560	195,145
(12)	Operating expenditure, US\$	Hospital Report ^a	152,513,135	100,435,440	123,091,114	108,541,693	72,961,931
(13)	Estimated salaries of academic clinicians devoted to service	Estimated ^b	11,757,967	-	-	-	-
(14)	Revised operating expenditures, US\$	(12) + (13)	164,271,102	100,435,440	123,091,114	108,541,693	72,961,931

(15)	Cost per bed-day equivalent, US\$	(14)/(11)	358	396	320	255	374
(16)	Cost per outpatient visit, US\$	(15) x (9)	72	79	64	51	75

318 Note: All costs are expressed in 2013 US\$.

319 UMMC, University of Malaya Medical Center; HSB, Hospital Sungai Buloh; Hospital Sultanah Bahiyah, Alor Setar, HAS; Hospital
320 Melaka, HM; Hospital Sultan Haji Ahmad Shah, Temerloh, HT.

321 Table adapted from Shepard et al. and Suaya et al.[12, 13, 24];

322 ^aData from the 2012 UMMC Annual Report, 2013 HSB Annual Report, 2012 HAS Annual Report; 2013 HM Annual Report and the
323 2012 HT Annual Report.

324 ^bData from the Department of Human Resources and Faculty of Medicine, University Malaya. UMMC is an academic teaching
325 hospital and salaries of academic clinicians are paid by the university.

326 **Supplementary Table 6. Estimation of unit cost at healthcare facilities in Malaysia, 2013**

Type of facility ^a	Estimated distribution of facility ^{b,c}	Unit cost (2008 US\$)	Ratio of cost by facility type	Unit cost (2013 US\$)
WHO-CHOICE				
Cost per bed-day				
Primary-level hospital	20%	86.60	0.74	252.93
Secondary-level hospital	30%	90.34	0.77	263.87
Teaching hospital	50%	116.81	1.00	341.19 ^d
Average cost per bed-day				300.34
Cost per outpatient visit				
Health facilities with no beds	56%	7.63	0.48	3.75 ^e
Primary-level hospital	20%	15.93	1.00	43.08 ^f

Secondary-level hospital	30%	22.46	1.41	60.74
Tertiary-level hospital	50%	-	-	68.00 ^d
Average cost per outpatient visit at a hospital				60.84
Average cost per outpatient visit				28.87

327 ^a Definitions of facility levels used in WHO-CHOICE can be obtained from Barnum and Kutzin. Public hospitals in developing
328 countries: resource use, cost, financing, 1993[17].

329 ^b distribution of hospital beds by facility type for estimation of cost per bed-day and cost per outpatient visits at hospitals was adopted
330 from Shepard et al [12]

331 ^c distribution of health facilities with no beds are based on unpublished data from Ministry of Health, Malaysia [23].

332 ^d average cost per bed-day from 5 tertiary-level hospitals in Malaysia is used to represent costs of ‘teaching hospital’ from WHO-
333 CHOICE. Note that there is no equivalent facility-type in WHO-CHOICE, for outpatient visits at tertiary-level facilities.

334 ^e Unit cost per-visit equivalent to ‘health facilities with no beds’ from WHO-CHOICE, obtained from the 1995 costing study on
335 outpatient services in 11 MOH public clinics in Kedah[18].

336 ^f Unit cost for ‘primary-level hospitals’ from WHO-CHOICE, obtained from the 2001 costing study of 6 primary-level or district
337 hospitals[19].

338 **Supplementary Table 7. Estimation of direct medical costs for rotavirus gastroenteritis by health service**
 339 **utilization**

	Rotavirus episodes	Unit costs per	Direct medical costs
	(‘000)	episode^{a,b}	(‘000 US\$)
		(US\$)	
Public hospital inpatients	23	961	22,349
Public hospital outpatients	7	61	434
Public clinic outpatients	7	4	28
Private hospital inpatients	8	1,126	8,888
Private clinic outpatients	27	68	1,815
Home Treated	145	0	
TOTAL	217		33,514

340 Note: All costs are in 2013 US\$;

341 ^a Estimation of unit costs shown in Table 2 of the main text.

342 ^b To obtain cost per episode for a diarrheal admission, average duration of admission (3.3 days) was multiplied with cost per bed-day
 343 [11, 22].

344 **Supplementary Table 8. Estimation of direct non-medical costs for rotavirus gastroenteritis by health**
 345 **service utilization**

	Rotavirus episodes (‘000)	Transport ation costs per- episode ^a (US\$)	Total transport ation costs (‘000 US\$)	Diaper costs per- episode ^b (US\$)	Total diaper costs (‘000 US\$)	Food costs per- episode ^c (US\$)	Total food costs (‘000 US\$)	Direct non- medical costs (‘000 US\$)
Public hospital inpatients	23	15	358	3	75	0.72	17	450
Public hospital outpatients	7	8	55	3	23	0	0	78
Public clinic outpatients	7	3	20	3	24	0	0	44
Private hospital inpatients	8	16	130	3	25	0.72	6	161
Private clinic outpatients	27	4	96	3	86	0	0	182

Home-treated	145	0	0	3	468	0	0	468
TOTAL	217		659		701		23	1,383

346 Note: All costs are in 2013 US\$; RVGE, rotavirus gastroenteritis.

347 ^a One way transportation costs obtained from the National Health and Morbidity Survey 2011. Costs are doubled for outpatient
348 episodes and quadrupled for inpatient episodes.

349 ^b Diaper costs per episode obtained from the average costs for both hospitals used in the 2010 hospital-based study[25].

350 ^c Additional food costs for an episode of diarrhoea hospitalized at University of Malaya Medical Center applied to inpatient episodes .

351 **Supplementary Table 9. Estimation indirect costs for rotavirus gastroenteritis by health service utilization**

	Rotavirus episodes (‘000)	Duration of diarrhea (days)	Average daily wage (US\$)	Total indirect costs (‘000 US\$)
Public hospital inpatients	23	3	25	1,573
Public hospital outpatients	7	3	25	482
Public clinic outpatients	7	3	25	503
Private hospital inpatients	8	3	25	534
Private clinic outpatients	27	3	25	1,805
Home treated	145	3	25	9,815
TOTAL	217			14,714

352 ^a Average monthly wage of RM 2,052 for both sexes in 2013 [26]. All costs are in 2013 US\$.

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355 **References**

- 356 [1] Hsu VP, bin Abdul Rahman H, Wong SL, Ibrahim LH, Yusoff AFH, Chan LG, et al.
357 Estimates of the burden of rotavirus disease in Malaysia. *Journal of Infectious Diseases*.
358 2005;192:S80-S6.
- 359 [2] Health Facts 2013. Health Informatics Centre, Planning and Development Division, Ministry
360 of Health, Malaysia.
- 361 [3] Yap K, Yasmin A, Wong Y, Ooi Y, Tan S, Jegathesan M, et al. A one year community-based
362 study on the incidence of diarrhoea and rotavirus infection in urban and suburban Malaysian
363 children. *The Medical Journal Of Malaysia*. 1992;47:303-8.
- 364 [4] Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths
365 caused by rotavirus disease in children. *Emerging infectious diseases*. 2003;9:565-72.
- 366 [5] Bilcke J, Van Damme P, Van Ranst M, Hens N, Aerts M, Beutels P. Estimating the incidence
367 of symptomatic rotavirus infections: a systematic review and meta-analysis. *PloS one*.
368 2009;4:e6060.
- 369 [6] WHO. Generic protocol for (i) hospital-based surveillance to estimate the burden of rotavirus
370 gastroenteritis in children and (ii) a community-based survey on utilization of health care
371 services for gastroenteritis in children. Field test version.: Department of Vaccines and
372 Biologicals, World Health Organization; 2002.
- 373 [7] DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials*.
374 1986;7:177-88.
- 375 [8] Hsu VP, Abdul Rahman HB, Wong SL, Ibrahim LHJ, Yusoff AFHJ, Chan LG, et al.
376 Estimates of the burden of rotavirus disease in Malaysia. *The Journal Of Infectious Diseases*.
377 2005;192 Suppl 1:S80-S6.

378 [9] Hung L, Wong S, Chan L, Rosli R, Ng A, Bresee J. Epidemiology and strain characterization
379 of rotavirus diarrhea in Malaysia. *International journal of infectious diseases*. 2006;10:470-4.

380 [10] Lee WS, Lim BT, Chai PF, Kirkwood CD, Lee JK. Rotavirus genotypes in Malaysia and
381 universal rotavirus vaccination. *Hum Vaccin Immunother*. 2012;8:1401-6.

382 [11] Lee WS, Lim BTY, Chai PF, Kirkwood CD, Lee JKF. Rotavirus genotypes in Malaysia and
383 Universal rotavirus vaccination. *Human vaccines & immunotherapeutics*. 2012;8:1401-6.

384 [12] Shepard DS, Undurraga EA, Lees RS, Halasa Y, Lum LCS, Ng CW. Use of multiple data
385 sources to estimate the economic cost of dengue illness in Malaysia. *The American Journal of*
386 *Tropical Medicine and Hygiene*. 2012;87:796-805.

387 [13] Shepard DS, Hodgkin D, Anthony YE, Organization WH. Analysis of hospital costs: a
388 manual for managers: World Health Organization Geneva; 2000.

389 [14] World Health Organization-CHOosing Interventions which are Cost-Effective (WHO-
390 CHOICE). WHO.

391 [15] WHO. Note on the Methodology used to predict Unit Costs for Patient Services WHO-
392 CHOICE 2011. 2011.

393 [16] Adam T, Evans DB, Murray CJ. Econometric estimation of country-specific hospital costs.
394 *Cost effectiveness and resource allocation*. 2003;1:3.

395 [17] Barnum H, Kutzin J. Public hospitals in developing countries: resource use, cost, financing:
396 Johns Hopkins University Press; 1993.

397 [18] Lim KJ. Costing of OPD services at main health clinics Kedah Darul Aman. Unpublished
398 report. Ministry of Health; 1995.

399 [19] Sabrina AR. Unit cost of patient care in district hospitals, Ministry of Health, Malaysia:
400 University of Malaya; 2006.

401 [20] Shepard D LR, Ng CW, Undurraga EA, Halasa YA, Lum L, . Burden of dengue in
402 Malaysia: Report from Ministry of Health Workshop. December 6, 2010, Putrajaya, Malaysia.
403 Schneider Institutes for Health Policy, Brandeis University, & University of Malaya; 2011.

404 [21] Sabrina AR. Unit cost of patient care in district hospitals in the Ministry of Health Malaysia:
405 University of Malaya; 2006.

406 [22] Loganathan T, Lee WS, Lee KF, Jit M, Ng CW. Household catastrophic healthcare
407 expenditure and impoverishment due to rotavirus gastroenteritis requiring hospitalization in
408 Malaysia. PLOS ONE (In Press). 2015.

409 [23] Ministry of Health, Malaysia: Outpatient attendences 2012. HIMS Medical Care Sub-
410 System PER-PL206, Center for Health Informatics, Planning Division, Ministry of Health,
411 Malaysia.

412 [24] Suaya JA, Shepard DS, Siqueira JB, Martelli CT, Lum LC, Tan LH, et al. Cost of dengue
413 cases in eight countries in the Americas and Asia: a prospective study. The American Journal of
414 Tropical Medicine and Hygiene. 2009;80:846-55.

415 [25] Loganathan T, Lee W-S, Lee K-F, Jit M, Ng C-W. Household Catastrophic Healthcare
416 Expenditure and Impoverishment Due to Rotavirus Gastroenteritis Requiring Hospitalization in
417 Malaysia. PLoS One. 2015;10:e0125878.

418 [26] Salaries and Wages Survey Report, Malaysia 2013. Department of Statistics, Malaysia.

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