



HOKKAIDO UNIVERSITY

Title	Analyzing Cost-Effectiveness of Allocating Neurointerventionist for Drive and Retrieve System for Patients with Acute Ischemic Stroke
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1 Analyzing Cost-Effectiveness of Allocating Neurointerventionist for Drive and 2 Retrieve System for Patients with Acute Ischemic Stroke

3 4 **Abstract:**

5 **Objectives**

6 There are regional disparities in implementation rates of endovascular thrombectomy due to time
7 and resource constraints such as endovascular thrombectomy specialists. In Hokkaido, Japan,
8 Drive and Retrieve System (DRS), where endovascular thrombectomy specialists perform early
9 endovascular thrombectomies by traveling from the facilities where they normally work to
10 facilities closer to the patient. This study analyzed the cost-effectiveness of allocating a
11 endovascular thrombectomy specialist for DRS to treat stroke patients.

12 **Materials and methods**

13 The number of ischemic stroke patients expected to receive endovascular thrombectomy in
14 Hokkaido in 2015 was estimated. It was assumed that an additional neurointerventionist was
15 allocated for DRS. The analysis was performed from the government's perspective, which
16 includes medical and nursing-care costs, and the personnel cost for endovascular thrombectomy
17 specialist. The analysis was conducted comparing the current scenario, where patients received
18 endovascular thrombectomy in facilities where endovascular thrombectomy specialists normally
19 work, with the scenario with DRS within 60-minute drive distance. Patient transport time was
20 analyzed using geographic information system, and patient severity was estimated from the
21 transport time. The primary outcome was incremental cost-effectiveness ratio (ICER) in each
22 medical area which was calculated from the incremental costs and the incremental quality-
23 adjusted life years (QALYs), estimated from patient severity using published literature. The entire
24 process was repeated 100 times.

25 **Results**

26 DRS was most cost-effective in Kamikawachubu area, where the ICER was
27 \$14,173±16,802/QALY, significantly lower than the threshold that the Japanese guideline
28 suggested.

29 **Conclusions**

30 Since DRS was cost-effective in Kamikawachubu area, the area should be prioritized when a
31 endovascular thrombectomy specialist for DRS is allocated as a policy.

32

33

34 Key words: Cost-effectiveness Analysis, Geographic Information System, Drive and Retrieve
35 System, Endovascular Thrombectomy, Ischemic Stroke

36

37 **Introduction**

38 The cost of stroke treatment accounts for approximately 6% of Japan's national medical
39 expenditure (1), and stroke is the second most common condition, after dementia, that results in
40 a requirement for long-term care. Thus, stroke has a significant impact on society (2). Cerebral
41 infarction accounts for 60% or more of stroke cases (3). Systematic provision of highly equitable
42 and efficient treatment for cerebral infarction is an important policy issue, such as the enactment
43 of the Stroke and Cardiovascular Disease Control Act in December 2018 in Japan, as part of an effort
44 to enhance provision of treatment for cerebral infarction (4).

45 Endovascular thrombectomy is a treatment that endeavors to improve the outcome for acute
46 cerebral infarction patients by early recanalization of occluded arteries by the means of stents,
47 etc., during the acute phase of cerebral infarction. The results of a series of randomized controlled
48 trials were published from 2014 to 2015 (5-8), and meta-analysis of these reports found that

49 endovascular thrombectomy combined with medical treatment significantly improved the
50 therapeutic effect, as compared to medical treatment alone, including intravenous alteplase
51 therapy (recombinant tissue plasminogen activator: rt-PA) (9). Endovascular thrombectomy is
52 thus an extremely important therapy to ensure that patients for whom rt-PA treatment is not
53 feasible can also enjoy favorable outcomes (10).

54 However, there are time constraints for the use of endovascular thrombectomy after cerebral
55 infarction, and resource constraints in terms of facility standards and endovascular thrombectomy
56 specialists who perform the treatment; therefore, there may be regional disparities in
57 implementation rates (11). Hashi et al. have reported regional disparities in the use of rt-PA (12).
58 Hokkaido, the largest prefecture in Japan, is characterized by regional disparities in lifestyle-
59 related services and medical services (13). Fujiwara et al. also reported uneven regional
60 distribution of stroke treatment resources for treatment of cerebral infarction in Hokkaido (14),
61 and Morii et al. reported regional disparities in the geographical accessibility to endovascular
62 thrombectomy treatment (11).

63 The Drive and Retrieve System (DRS) has been proposed in Hokkaido with the aim of
64 eliminating regional disparities in cerebral infarction treatment (15). The DRS is a scheme
65 whereby endovascular thrombectomy specialists perform early endovascular thrombectomies by
66 traveling from the facilities where they normally work (hub facilities) to facilities closer to the
67 patient, which have the equipment required to perform endovascular thrombectomy, such as
68 angiography equipment, but which lack endovascular thrombectomy specialists (spoke facilities).
69 The DRS is currently partially implemented in the suburbs of Sapporo, and it has been reported
70 that the scheme has shortened the time until reperfusion in stroke patients (16).

71 Morii et al. used the geographic information system (GIS) to analyze the effect of the DRS in
72 Hokkaido on accessibility to endovascular thrombectomy and on medical and long-term care

73 costs (11). The Japanese Guideline for Preparing Cost-Effectiveness Evaluation to the Central
74 Social Insurance Medical Council stipulates that although medical and long-term care costs reflect
75 the standard analytical perspectives, it is preferable to include other costs when such costs are
76 expected to create a public burden (17). However, the study by Morii et al. does not consider the
77 costs involved in implementing the DRS, including the labor costs of the doctors, despite the
78 expected need for a sizeable policy intervention. It is also preferable to conduct analysis based on
79 actual introduction of the system, such as analyzing into which specific regions the DRS should
80 be introduced. In addition, the previous study by Morii et al. was a small study that used GIS to
81 investigate the cost-effectiveness of the medical treatment delivery system, but the study was
82 unable to consider the uncertainty of patient distribution, because the virtual patient generation
83 trial was not repeated. Therefore, conducting a repeat trial is necessary to propose a methodology
84 that is able to consider the uncertainty of patient distribution.

85 Thus, the present study simulated a cost-effectiveness of allocating a endovascular
86 thrombectomy specialist for DRS, assuming the additional assignment of doctors based on the
87 policy for the DRS, with a view to improve the system to provide highly equitable and cost-
88 effective treatment for cerebral infarction.

89

90 **Methods**

91 *Subjects and outcomes*

92 The subjects were 1443 virtual patients with cardioembolic infarction in Hokkaido in 2015 who
93 were potentially eligible for endovascular thrombectomy using DRS. The number of these virtual
94 patients was calculated by multiplying the population of Hokkaido (approximately 5.4 million)
95 obtained from the national census (18) by the incidence of cardioembolic infarction on a
96 population basis (26.8/100000 population) as estimated by a previous study, assuming that those

97 patients are potentially eligible for endovascular thrombectomy (19). The regional unit for
98 analysis was set to 21 secondary medical service areas in Hokkaido. Hokkaido Prefecture has a
99 population of approximately 5.4 million people, and its largest city, Sapporo (within the Sapporo
100 secondary medical service area shown in Figure 1), has a population of approximately 2 million
101 people (18), followed by Asahikawa-shi (Kamikawachubu medical service area in Figure 1), with
102 a population of approximately 350,000 people, and Hakodate-shi (Minamioshima medical service
103 area in Figure 1), with a population of approximately 270,000 people. Secondary medical service
104 areas are regional units that provide inpatient medical care within the Japanese healthcare system.
105 The system for providing stroke treatment was considered for each secondary medical service
106 area. During the analysis period, we analyzed the cost-effectiveness of providing DRS for patients
107 with acute cerebral infarction over a 1-year period. The government perspective, which included
108 costs that the government paid, was used as the cost-effectiveness analysis perspective. The
109 analysis included the cost and therapeutic effect within 3 years from onset.

110 The implementation of DRS as a policy is expected to improve patient access to endovascular
111 thrombectomy, but this requires the assignment of specialists to regions with superior cost-
112 effectiveness from the perspective of publicly funded healthcare. Therefore, this study assumed
113 that one endovascular thrombectomy specialist to operate the DRS would be additionally assigned
114 to one hub facility, the labor costs of which the policy would prescribe public funding.

115 Two scenarios were selected: one in which DRS is not implemented (base scenario) and the
116 other in which endovascular thrombectomy specialists travel to spoke hospitals within a 60-
117 minute drive (DRS scenario). The incremental cost-effectiveness ratio (ICER) was calculated as
118 the primary outcome by comparing the two scenarios. The most commonly used metric in cost-
119 effectiveness analyses, the ICER is used by the National Institute for Health and Clinical
120 Excellence in the UK, in Japan (17, 20), and elsewhere. The ICER is usually calculated by taking

121 the difference in therapeutic effect between two treatments as the denominator and the difference
122 in cost as the numerator to provide a ratio of the cost required to attain one unit of therapeutic
123 effect. The ICER calculation scheme used in this study is shown in Figure 2.

124 Quality-adjusted life years (QALYs), a commonly used therapeutic effect metric, was also used
125 in this study. The ICER was calculated for each secondary medical service area from where the
126 doctor traveled (the specialists' working location), i.e. to which secondary medical service area
127 an additional specialist should be assigned for DRS was analyzed from a cost-effective
128 perspective.

129 The cost-effectiveness analysis perspective also included other public expenditures, such as
130 medical, long-term care, and specialist labor costs, for calculating the ICER, based on the
131 government perspective (Figure 2). The ICER evaluation standard was set as Japanese Yen (JPY)
132 5,000,000/QALY (approximately USD 48,146/QALY) based on the Japanese guidelines, and the
133 cost and QALY were discounted at an annual rate of 2%. The currency was converted from JPY
134 to USD using the exchange rate on December 4, 2020 (21). The series of processes used to
135 calculate the ICER from the next section onward was repeated 100 times by operating the GIS
136 using the programming language Python (version 5.7). The random generation of patients with
137 each repetition made it possible to conduct an analysis that considered the uncertainty of the
138 patient distribution.

139

140 Figure 1. Number of hub and spoke hospitals in each medical area

141

142

143 Figure 2. Scheme used to calculate the incremental cost-effectiveness ratio

144

145

146 *Generating virtual patients and identifying target facilities*

147 The generation of virtual patients was based on a previous study on DRS (11). We obtained 1-
148 km² mesh data for the target region from the FY2015 national census (18) and determined the
149 location of the estimated number of patients with cardioembolic infarction in Hokkaido as a whole
150 using the statistical analysis R by The R Foundation (ver 3.5.2). The number of patients generated
151 in each mesh was proportional to the population of each mesh. The number of patients for each
152 determined mesh was generated on each GIS mesh using the GIS random point generation
153 function. ArcGIS Desktop 10 (www.esri.com) was used for the geographical analysis in this study.

154 According to a previous study (11), the identification of target hub facilities and spoke facilities
155 was based on a list of candidate facilities acquired from the Hokkaido branch of the Japanese
156 Society for Neuroendovascular Therapy and the Hokkaido Medical Plan, respectively (13, 22).
157 The criteria for spoke facilities were that they had the ability to perform: 1) blood tests and
158 imaging tests (computed tomography, magnetic resonance imaging, ultrasound, etc.), 2)
159 craniotomy (cerebral aneurysm clipping, removal of intracerebral hematoma, decompressive
160 craniectomy), and 3) thrombolytic therapy with rt-PA. These spoke facilities were also equipped
161 to perform angiography. Next, we searched for hospitals within a 60-minute drive from the 30
162 hub facilities where the specialists were stationed using the ArcGIS Network Analysis Origin-
163 Destination Matrix function. As a result, 30 hub facilities and 74 spoke facilities were identified
164 in Hokkaido. The DRS scenario was set up so that patients would be transported to both hub
165 facilities and spoke facilities for endovascular thrombectomy. The distribution of hub and spoke
166 facilities in Hokkaido are shown in Figure 1.

167

168 *Transport time and doctor travel*

169 Transport time was analyzed using the ArcGIS Search for Find Nearest Facility function based
170 on a previous study (11). The time from the ambulance leaving the fire station to arriving at the
171 patient location and the time from the ambulance leaving the patient location to arriving at the
172 medical facility were analyzed, and the sum of the two times was defined as the transport time.
173 The target patients were classified into time zones depending on the transport time: 0–1 hour, 1–
174 2 hours, 2–3 hours, and 3 or more hours. The 1-hour coverage rate, which is the proportion of
175 patients that could be transported within 1 hour, and similarly the 3-hour coverage rate were
176 calculated as accessibility performance indicators. Additionally, information on the name and the
177 distance to the nearest facility and the arrival facility was acquired from the ArcGIS Search for
178 Find Nearest Facility function to estimate transportation costs and travel routes.

179 It is preferable to perform DRS when an improvement in therapeutic effect can be expected,
180 namely in areas where treatment can be commenced earlier by doctors traveling to the hospital.
181 Therefore, in this study, it was decided that the doctors would travel when the transport time zone
182 was shorter in the DRS scenario than in the base scenario (for example, if a patient's transport
183 time zone would be 1–2 hours in the current scenario but their transport time zone would be
184 shortened to 0–1 h in the 60-minute DRS scenario, then the doctor would travel). In this instance,
185 cases in which the travel time from the hub facilities to spoke facilities was less than 10 min were
186 excluded from the analysis to avoid counting doctors traveling to neighboring hospitals because
187 it was thought that the inclusion of these routes would have little substantial effect. The identified
188 journeys were tabulated by the travel distance and the pair of hub and spoke facilities used for the
189 analysis, while the number of journeys was tabulated by secondary medical service areas based
190 on the original locations of the patient and the traveling doctor.

191

192 *Estimating the severity of the patients' conditions*

193 The severity of the patients' conditions was estimated in accordance with the previous study
194 by Morii et al. (11) and based on the results of the HERMES trial, a meta-analysis of randomized
195 controlled trials (RCTs) (13). The modified Rankin Scale (mRS) at 3 months after onset was used
196 as the cerebral infarction severity index, as it is the most commonly used. The HERMES study, a
197 meta-analysis of the main RCTs on the efficacy of endovascular thrombectomy, demonstrated that
198 the percentage of patients whose prognosis was self-independent at 3 months after stroke
199 significantly declined, and the proportion of patients with a severe condition increased with the
200 delay in the treatment start time. Therefore, we attempted to reflect treatment that achieves better
201 outcomes with an earlier start of treatment using the data on the relationship between the time
202 from endovascular thrombectomy start and the mRS stage prognosis at 3 months after onset from
203 the HERMES study to estimate the severity of the patients' conditions (see Table 1 from the study
204 by Morii et al. (11)). The results of the HERMES study showed that endovascular thrombectomy
205 was significantly effective when reperfusion was achieved before approximately 7 hours. In this
206 study, considering the time to rt-PA treatment and endovascular thrombectomy and time
207 difference between onset time and uncertainty of onset time (23), it was assumed that the subjects
208 transported within 3 hours were eligible for endovascular thrombectomy (11).

209 This simulation also assumed that the severity of the patients' conditions did not change over
210 the target period.

211

212 *QALY analysis*

213 QALYs were calculated by multiplying the time period by the quality of life (QOL) utility value,
214 where death was 0 and perfect health was 1. QOL utility values were assumed to differ depending
215 on the mRS-based severity and were allocated to each patient depending on the severity of their
216 condition (15). The QOL utility values according to severity were acquired from a previous study

217 of Japanese patients with stroke (Table 1) (24).

218

219 *Cost analysis*

220 The costs included the medical, long-term care, labor costs of doctors employed based on this
221 policy, and the doctors' transport costs, as mentioned earlier. The costs of the analysis are
222 summarized in Table 2.

223 Medical costs were assumed to be dependent on the severity, and the total medical costs by
224 severity, published from 2015 in the Stroke Databank, a database of Japanese cases, were used to
225 calculate the medical costs (3). Furthermore, the cost of endovascular thrombectomy is
226 automatically incurred when doctors travel; thus, the cost of one endovascular thrombectomy, set
227 as USD3,192 (FY2018 Medical Service Fee K-178-4) was included in the calculation (25). The
228 fee includes a fee for the angiography inspection. In Japan, the cost of these services does not
229 differ, as official prices are set for all medical and long-term care services.

230 To calculate the long-term care cost, we first converted the severity of the patient's condition
231 estimated based on mRS to the nursing care level used to allocate long-term care services in Japan,
232 based on a previous study (11). Under the Japanese long-term care insurance system, patients who
233 require support to avoid long-term care are classified as Support Level 1 or Support Level 2.
234 Patients who require long-term care services are classified into long-term care levels 1–5. The
235 larger the number, the greater the need for long-term care. The cost of long-term care was based
236 on the converted level of long-term care needed, while the costs were allocated to each patient
237 according to the level of long-term care needed in accordance with the method proposed by
238 Yamaga and Ikeda (Table 1) (26)

239 Labor was set as a fixed cost. Information on the doctors' general wages was obtained from the
240 Basic Survey on Wage Structure conducted by the Ministry of Health, Labour, and Welfare (27).

241 Employment, welfare pension, social, and disaster insurance premiums estimated from the
242 original amount were included in labor costs (28-31). Transport costs were assumed to depend on
243 the distance traveled. Labor and transport costs were subject to a sensitivity analysis, and the
244 ICER was also calculated in the event that there was a 50% increase or a 33% decrease.

245

246

247 **Results**

248 *One- and 3-hour coverage rates*

249 Figure 3a shows the results for each scenario for the 1-hour coverage rate based on patient
250 location, while Figure 3b shows the 3-hour coverage rate. The 1-hour coverage rate was around
251 90% throughout Hokkaido, but the rates were low in medical service areas in Minami Hiyama,
252 Kitaoshimahiyama District, Hidaka, Rumoi, Soya, and Nemuro. In the DRS scenario, the 1-hour
253 coverage rate increased mainly in the medical service areas in Kamikawahokubu, Hokumo,
254 Kitaoshimahiyama, Shiribeshi, and Rumoi. The 3-hour coverage rate was 99% throughout
255 Hokkaido. In the DRS scenario, the 3-hour coverage rate increased mainly in the medical service
256 areas in Rumoi, Soya, and Nemuro, but it remained at around 30% in the Soya medical service
257 area.

258

259 Figure 3. One- and 3-hour coverage rates

260

261

262 *Number of DRS journeys*

263 Figure 4a shows the number of doctors' journeys by patient location in secondary medical
264 service areas. Patients in the Hokumo medical service area had the highest number of doctors'

265 journeys, at 13.9 per year, followed by the Kamikawahokubu medical service area (11.7
266 journeys/year), Rumoi medical service area (4.6 journeys/year), Shiribeshi medical service area
267 (4.5 journeys/year), and Soya medical service area (4.2 journeys/year).

268 Figure 4b shows the number of doctors' journeys based on the travel starting point. Figure 4
269 shows only the secondary medical service areas with hub facilities. The highest number of
270 journeys were in the Kamikawachubu medical service area (20.7 journeys/year), followed by
271 Hokumo (15.4 journeys/year), and Nishiiburi (4.9 journeys/year).

272

273

274 Figure 4. Number of drive and retrieve systems expected in each medical area (a) by patient
275 location and (b) specialist location

276

277

278 *Facilities that performed DRS*

279 This analysis obtained information on the numbers of doctors' journeys and facilities sending
280 doctors. The facilities that sent a comparatively large number of doctors are shown in Figure 5.
281 Figure 5a shows that the largest number of journeys were from the Kamikawachubu medical
282 service area, but it also shows that the treatment routes for patients in the Kamikawahokubu, Soya,
283 Rumoi, and Emmon medical service areas, with doctors traveling from Kamikawachubu to
284 hospitals in the Kamikawahokubu medical service area (Figure 5a). The treatment routes for
285 patients were identified in the Hokumo medical service area with doctors traveling to Abashiri
286 city, which is within the same medical service area, or traveling within the same medical service
287 area and from the Nemuro medical service area (Figure 5b). Figure 5c shows that the DRS was
288 used for several patients in the Shiribeshi medical service area, and treatment routes for patients

289 in the Shiribeshi medical service area were identified as doctors traveling from hospitals in the
290 Sapporo medical service area to hospitals in the Shiribeshi medical service area (Figure 5c), while
291 treatment routes for patients in the medical service areas in Shiribeshi and Kitaoshimahiyama
292 were identified as doctors traveling from Muroran city in Nishiiburi medical service area to Date
293 city (Figure 5d).

294

295

296 Figure 5. Identified drive and retrieve system routes that are expected to be used frequently

297

298

299 *QALY and cost*

300 The mean value of 100 trials of QALY increments obtained from the DRS is shown in Figure
301 6a, while the mean reduction in medical and long-term care costs based on the departure point is
302 shown in Figure 6b. Doctors traveling from the Kamikawachubu medical service area had the
303 highest gain in QALY gain (4.33 QALYs), followed by Hokumo medical service area (1.58
304 QALYs). The reduction in medical costs and long-term care costs based on the departure point
305 were largest in the Kamikawachubu medical service area (USD 115,015), followed by the
306 Hokumo medical service area (USD 39,005).

307

308

309 Figure 6. Gained quality-adjusted life years (a) and medical and reduced nursing care costs (b)

310 in each medical area (based on departure point)

311

312

313 *Cost-effectiveness*

314 The base scenario is being trialed in the Minamioshima, Higashiiburi, and Nakasorachi medical
315 service areas in the 100 trials, which made it impossible to calculate the mean ICER. The ICER
316 for employing a full-time doctor in the Sapporo medical service area is USD 969,766 ±
317 816,293/QALY, USD1,634,635 ± 819,612 in Nakasorachi medical service area, USD 567,511 ±
318 544,292/QALY in the Nishiiburi medical service area, USD 12,572 ± 16,518/QALY in
319 Kamikawachubu Medical Service Area, USD 89,899 ± 51,416/QALY in the Hokumo medical
320 service area, USD 1,078,899 ± 721,417/QALY in the Tokachi medical service area, and USD
321 1,438,215 ± 1,062,089/QALY in the Kushiro medical service area, which means that employing
322 specialists in Kamikawachubu medical service area is the most cost-effective (Table 3). The mean
323 ICERs were calculated excluding trials in which incremental QALY were zero in Minamioshima,
324 Higashiiburi, and Nakasorachi medical service areas (Table 3). The mean ICER in the
325 Kamikawachubu medical service area was significantly lower than the USD 48,146, the
326 evaluation standard based on Japanese guidelines (21). Similar trends were observed in the
327 sensitivity analysis (Figure 7).

328

329

330 Figure 7. Result of sensitivity analysis on specialist personnel and transportation cost

331

332

333 **Discussion**

334 This study conducted a cost-effectiveness analysis by simulation, assuming policy-based
335 introduction of the DRS with the aim of constructing a system to provide highly equitable and
336 cost-effective cerebral infarction treatments. This analysis was added to that of a previous study

337 (11) mainly in that we attempted to conduct a more specific cost-effectiveness analysis by
338 including the costs of the endovascular thrombectomy specialist, transportation, and endovascular
339 thrombectomy, and its geographical analysis was more complete for DRS implementation by
340 acquiring analyzed information on facilities at the departure and destination points rather than by
341 analyzing cost-effectiveness only. The results will be of great importance in considering where an
342 endovascular thrombectomy specialist for DRS should be allocated, where the endovascular
343 thrombectomy specialist should travel, and the cost-effectiveness of the system.

344 Concerning the number of virtual patients, this study used the number of patients with
345 cardioembolic infarction who were potentially eligible for endovascular treatment, while a
346 previous study used the overall number of patients with stroke. We tried to estimate how many
347 patients would benefit from DRS in each medical service area. Furthermore, the entire analytical
348 process was repeated to decrease the extent of uncertainty in the randomly generated patient
349 distributions. Some of the results of geographic accessibility were similar to those of previous
350 research (11), and the results of this study should more comprehensively consider the uncertainty.

351 Although the 3-hour coverage rate was high in almost all medical service areas, it was less than
352 30% in the Soya medical service area, even with the DRS scenario, which is consistent with the
353 trends reported by Morii et al. and Fujiwara et al., indicating regional disparities in accessibility
354 to cerebral infarction treatment in Hokkaido (11,14).

355 The highest number of endovascular thrombectomies performed by traveling doctors was in
356 the Kamikawahokubu medical service area, followed by the Hokumo, Rumoi, Shiribeshi, and
357 Soya medical service areas. Except for the Hokumo medical service area, these medical service
358 areas are characterized by a lack of hub facilities. DRS has been shown to increase accessibility
359 to endovascular thrombectomy in medical service areas without hub facilities (11). The Hokumo
360 medical service area is relatively large. Although there is a hub hospital in Kitami-city, there are

361 none in Abashiri City (Figure 5b). Therefore, even within the same secondary medical service
362 area, there are patients who can be transported within 1 hour, while other patients require 2 or
363 more hours for transportation. Given that the DRS increased the 1-hour coverage rate in the
364 Kitami medical service area, sending specialists from Kitami to hospitals in Abashiri should
365 shorten treatment start times.

366 There are no spoke facilities within a 60-minute drive of hub facilities in the Soya and Rumoi
367 medical service areas. In addition, there are currently patients for whom transport to medical
368 facilities within 3 hours would be difficult. The Stroke and Cardiovascular Disease Control Act
369 and Cardiovascular Disease stipulates that it is important for different regions to collaborate to
370 build a medical provision system when the provision of medical services is difficult within one
371 region (4). DRS is considered an effective scheme for improving regional disparities in regions
372 where accessibility to treatment is not guaranteed, such as the Soya, Emmon, Kamikawahokubu,
373 and Rumoi medical service areas (11). This study set the area for travel to 60 minutes, but it may
374 be possible to investigate a more detailed medical provision system, better suited to the actual
375 situation in the region, by conducting the same analysis using a 90-minute scenario given the
376 geographical characteristics of Hokkaido, which has a large land area. Furthermore, based on the
377 low 3-hour coverage rate in the Soya medical service area, it may be necessary to conduct a
378 comprehensive investigation, including the use of medical helicopters, in addition to the DRS
379 explored here.

380 This study calculated the cost-effectiveness of assigning specialists individually to each
381 secondary medical service area with a hub facility. In this study, the ICER in the Kamikawachubu
382 medical service area was significantly lower than the evaluation criteria of JPY 5,000,000/QALY,
383 and the results were lower than the evaluation criteria after the sensitivity analysis, considering
384 the uncertainty of the doctors' wages. In the previous study, only medical costs (except those for

385 endovascular thrombectomy) and nursing care were included (11), while in this study, costs for
386 endovascular thrombectomy and one endovascular thrombectomy specialist was employed from
387 the public budget. This result suggests that it is cost-effective to assign an additional specialist
388 who is able to perform endovascular thrombectomy for traveling from Kamikawachubu to the
389 Kamikawahokubu medical service area (Fig 5a). One of the reasons for the superior cost-
390 effectiveness is that the labor costs (the annual wage) of the doctors' travels were recorded as a
391 fixed cost, and recouping fixed costs over a number of journeys is thought possible. Profitability
392 may not be ensured if specialists are assigned to hospitals with only a small number of journeys.

393 As mentioned earlier, another reason may be that doctors traveling from Asahikawa would be
394 expected to travel to the Rumoi, Soya, Enmon, and northern Kamikawa medical service areas. At
395 the present time, it takes 3 or more hours for some patients in the Rumoi, Soya, and Enmon
396 medical service areas to travel to medical facilities in Kamikawachubu; thus, implementing DRS
397 in these areas would increase the possibility of endovascular thrombectomy for indicated patients
398 who previously would not have expected a significant therapeutic effect from this procedure,
399 which would in turn be expected to improve the therapeutic effect. Thus, the Kamikawachubu
400 medical service area is a central base for treating patients in northern Hokkaido, making it
401 desirable to enhance the system for endovascular thrombectomy in this region.

402 These results have shown the effect of DRS on improving accessibility and demonstrated that
403 deploying the DRS in the Kamikawachubu medical service area has superior cost-effectiveness.
404 This shows that the Kamikawachubu medical service area is a high priority area for DRS
405 implementation. This study clarified how many travels were expected in each area by DRS and
406 how cost-effective it is to assign an endovascular thrombectomy specialist in each area, including
407 the related costs; therefore, its findings will be of great importance in DRS implementations.
408 Conducting further analyses based on the number of specialists and facility capacity rather than

409 on accessibility alone may provide additional useful information for policy formulations.

410 Although the study found that assigning additional specialists to the Sapporo and Nishiiburi
411 medical service areas was not cost-effective, it demonstrated that there was a certain need for
412 doctors to travel from these secondary medical service areas (Figure 5c and 5d). This result will
413 provide political insight into DRS route implementation. Although it was not cost-effective to
414 assign an additional specialist to these secondary medical service areas, there are a large number
415 of hub facilities and specialists in the Sapporo medical service area (Figure 1). It is preferable to
416 consider the possibility of building a DRS using existing specialists to facilitate equitable
417 treatment accessibility.

418 This study analyzed a sample of Hokkaido, a region in Japan with geographical disparities in
419 accessibility to medical treatment. However, the methodology of using GIS and the existing
420 secondary data implemented in this study could also be applicable to other regions in Japan as
421 well as to other countries. This analysis may be helpful for examining the transportation system
422 for patients with cerebral infarction and formulating policies, including the additional assignment
423 of doctors. This study is one of the few that considers the geographic accessibility and cost-
424 effectiveness of the healthcare provision system. Its methodology considers the accessibility and
425 cost-effectiveness of other situations in which transport time is a determinant of patient outcomes,
426 such as myocardial infarction.

427 Nevertheless, this study has a number of limitations. First, the cost and QALY analysis period
428 was fixed at 3 years due to limited data availability. Alleviating stroke using endovascular
429 thrombectomy would reduce the cost of long-term care over an individual's lifetime; hence,
430 analyzing the effect over a person's lifetime may enable the estimation of a greater number of
431 QALY. Setting a fixed QALY did not allow for consideration of changed circumstances, such as
432 an individual's death, but this type of effect is thought to be equal with or without availability of

433 DRS-type offerings; therefore, it is unlikely that this process would significantly affect the trend
434 of incremental QALY.

435 Second, this analysis followed the standards set out in the Japanese Guideline for Preparing
436 Cost-Effectiveness Evaluation, and the cost analysis was conducted from the government
437 perspective (17). Yamaga et al. calculated the cost of illness due to stroke, including loss of
438 opportunity, given the marked loss of opportunity due to stroke sequelae (26). Further analyses
439 conducted from a social perspective, including loss of opportunity, may provide findings that are
440 more useful for policy decision-making.

441 Third, it did not consider uncertainties associated with the time of day in which the cerebral
442 infarction occurred or the weather. In addition, this analysis does not consider lengthening the
443 time windows for endovascular thrombectomy [32,33]. Therefore, our analysis could have
444 underestimated the benefits of endovascular thrombectomy and DRS, but it did not overestimate
445 them. Further analyses that consider these points may enable a more precise simulation.

446

447 **Conclusion**

448 This study analyzed the cost-effectiveness of assigning an additional specialist who is able to
449 perform endovascular thrombectomies for the DRS in Hokkaido and in the secondary medical
450 service areas of Hokkaido using a GIS, with a view to support the construction of a treatment
451 provision system for acute cerebral infarction patients with superior accessibility and cost-
452 effectiveness in Hokkaido. The results of the study demonstrated that Kamikawachubu medical
453 service area is likely to involve a large number of doctor's journeys and would therefore facilitate
454 the greatest cost reduction effect for medical care and long-term care and attain desirable QALY.
455 It was expected that doctors would travel from Kamikawachubu medical service area to the Soya,
456 Rumoi, Enmon, and Kamikawahokubu medical service areas. The ICER fell below the evaluation

457 criteria of USD48,146/QALY only when additional specialists were assigned to the central
458 Kamikawa medical service area (USD 14,173 ± 16,802/QALY), demonstrating the cost-
459 effectiveness of assignment of additional specialists able to perform endovascular thrombectomy
460 by traveling to Kamikawahokubu medical service area. These results suggest that the central
461 Kamikawa medical service area is a region where the introduction of the DRS should be
462 prioritized.

463

464 **Acknowledgement**

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466

467 **Declaration of interest**

468 None

469

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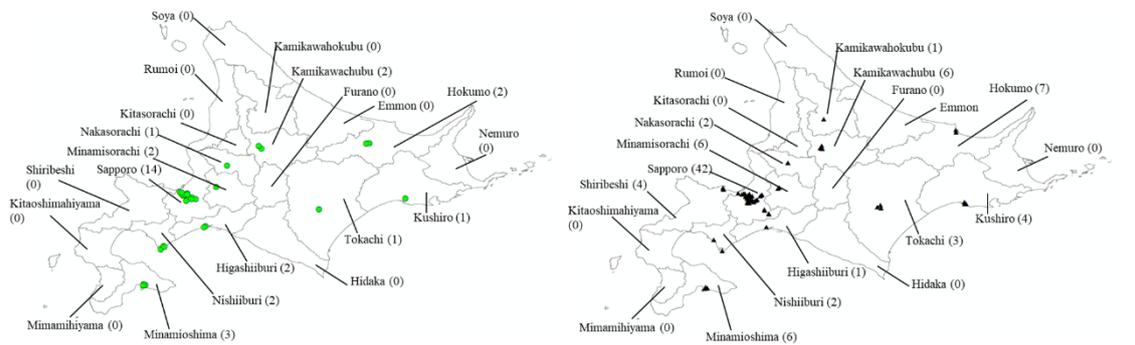
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590 **Figures and figure legends**

a: Hub hospitals

b: Spoke hospitals within 60 minutes from hub hospitals



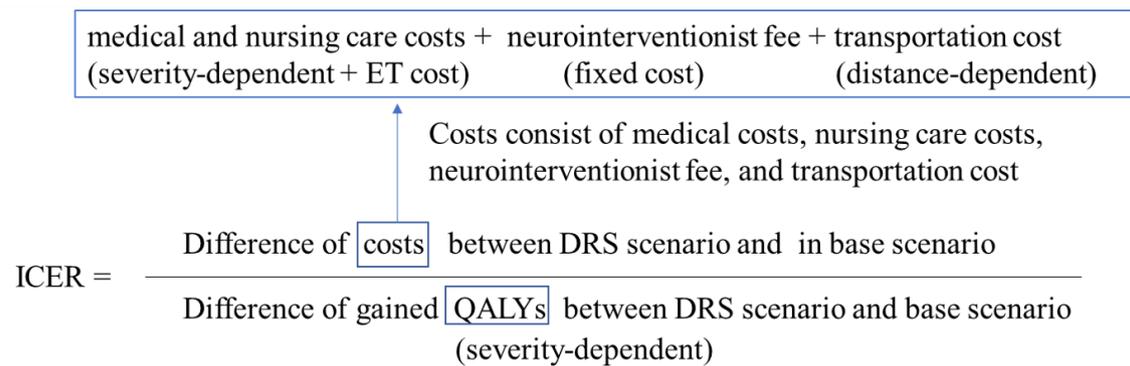
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592 Figure 1. the number of Hub hospitals and Spoke hospitals in each medical area

593 Figure 1 shows the hub Hub hospitals and Spoke hospitals in each medical area identified by

594 “Origin-Destination Matrix” of GIS.

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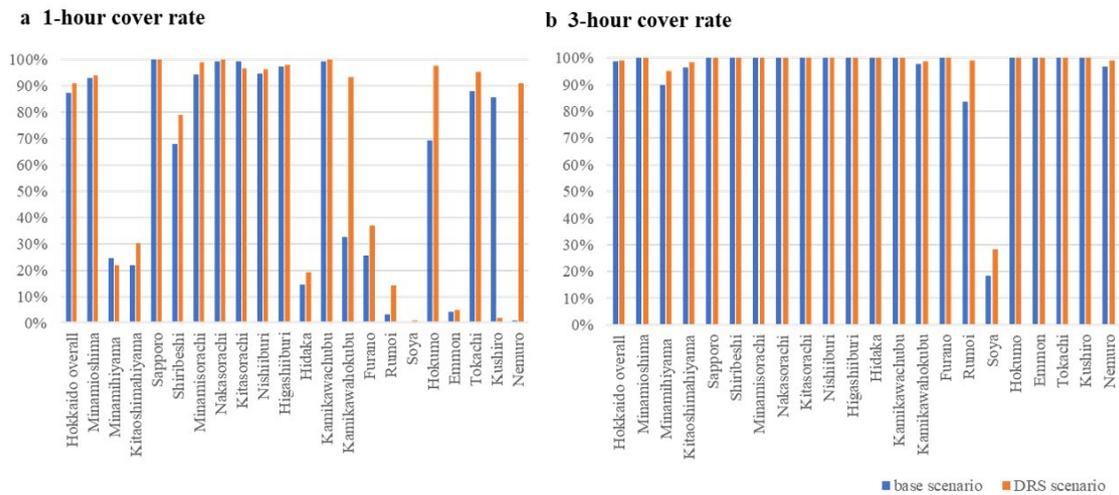
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597 Figure 2: Scheme of calculating ICER

598 Figure 2 shows the scheme of calculating ICER, and what costs was included, and what the

599 drivers of those costs and QALYs

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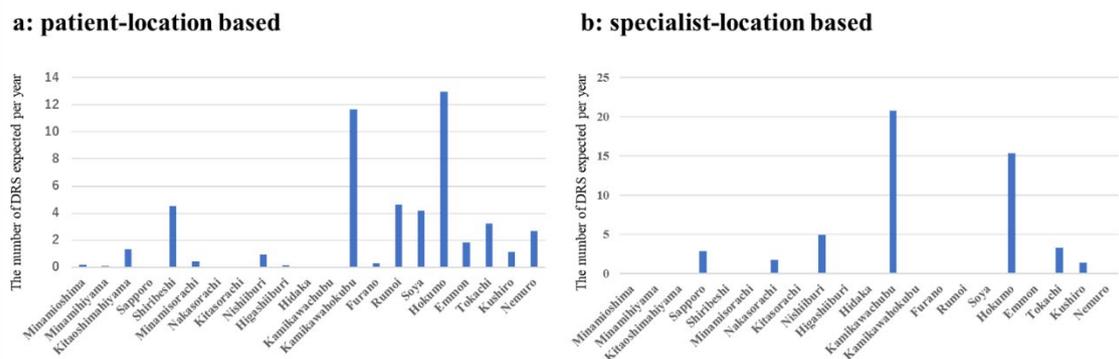


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602 Figure 3: 1-hour cover rate and 3-hour cover rate

603 Figure 3 shows the rate of patients transferred to Hub hospitals or Spoke hospitals within 1 and
 604 3 hours in the 2 scenarios.

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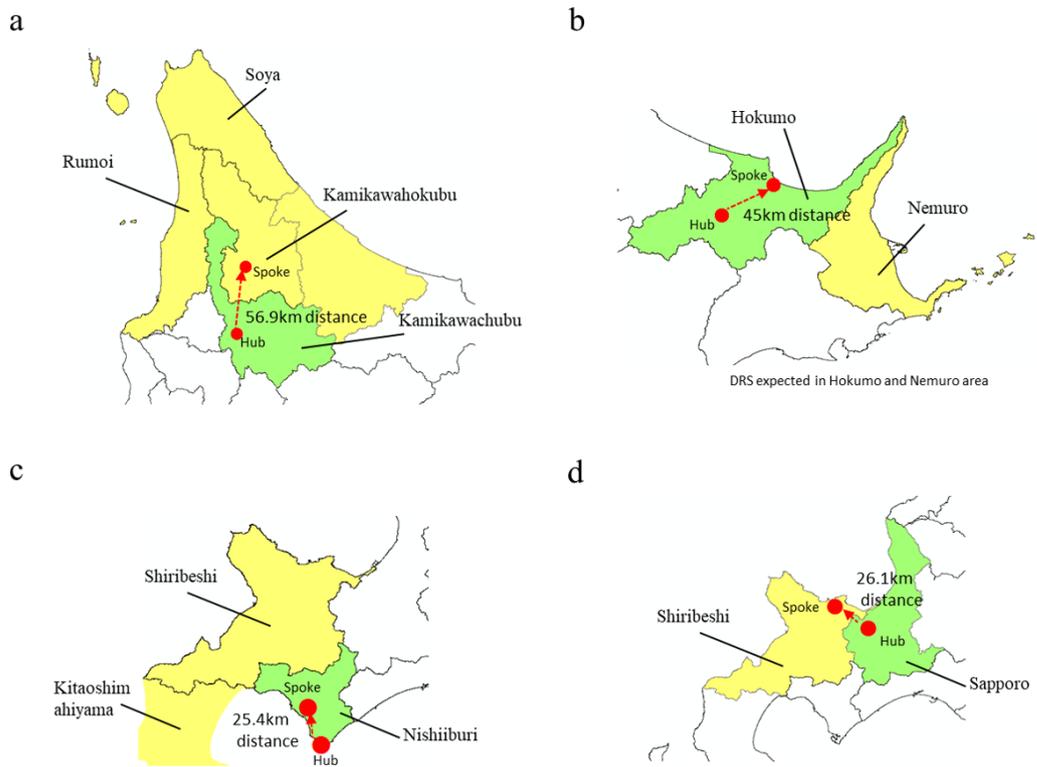
607 Figure 4: The number of DRS expected in each medical area

608 Figure 4 shows the number of DRS expected in each medical area in one year. Figure 4-a is
 609 based on patients-location, while Figure 4-b is based on endovascular thrombectomy specialists'
 610 location.

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615 Figure 5: Identified DRS routes which are expected to be used frequently

616 Figure 5 shows the DRS routes identified by the GIS analysis which are expected to be used

617 frequently.

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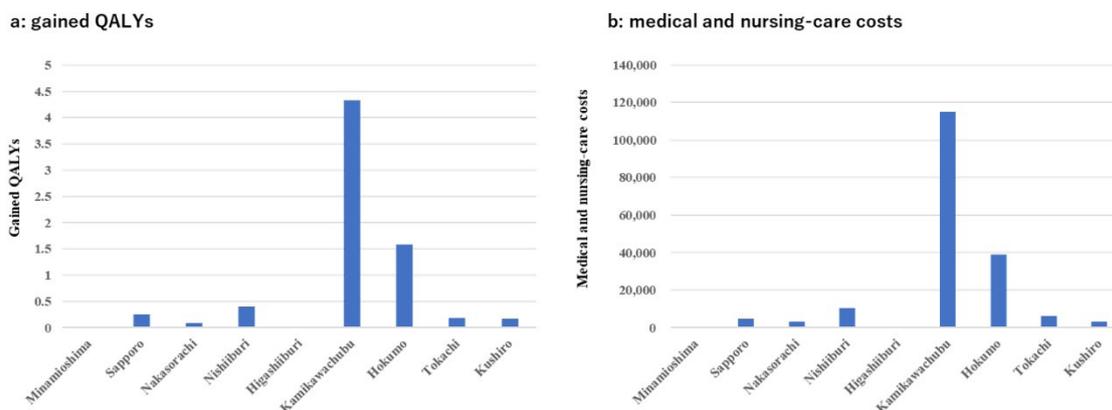
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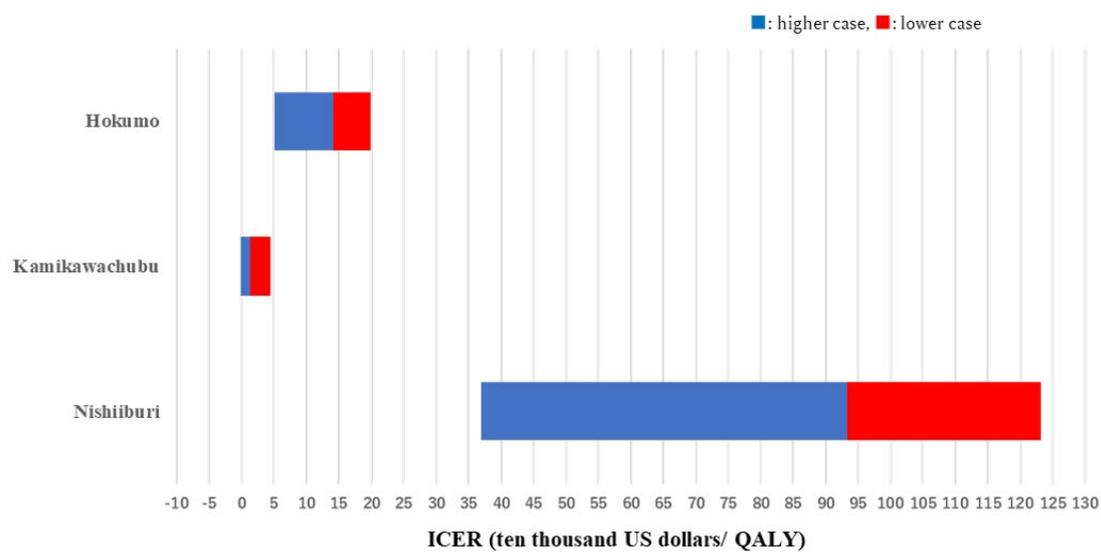


625

626 Figure 6: Gained QALYs (a) and medical and reduced nursing-care costs in each medical area
 627 (specialist-location-based)

628 Figure 6 shows gained QALYs (a) and medical and reduced nursing-care costs in each medical
 629 area (specialist-location-based), which indicate how much costs will be reduced by allocating a
 630 endovascular thrombectomy specialist for DRS in each area.

631



632

633 Figure 7: Result of sensitivity analysis on specialist personnel and transportation cost

634 Figure 7 shows the result of sensitivity analysis of specialist personnel and transportation cost.
 635 The red bar shows the higher case, and the blue bar shows the lower case.