

Supplemental Material

Drip ‘N Ship Versus Direct to Endovascular Thrombectomy: The Impact of Treatment Times on Transport Decision Making

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Supplemental Methods

Tables:

Table I. Model Variables, Definitions, Values, and Data Sources

Table II. Model Parameters

Table III. Mothership and Drip and Ship Models

Figures:

Figure I. Impact of Reduction in Door To Needle and Door In Door Out Times

Figure II. Impact of Reduction in Door To Needle and Door To Groin Puncture Times

Figure III. Impact of Reduction in Door In Door Out and Door To Groin Puncture Times

Supplemental References

Supplemental Methods

For full methodology see Holodinsky et al. Drip and Ship Versus Direct to Comprehensive Stroke Center: Conditional Probability Modeling. *Stroke*. 2017;48(1):233-238. doi:10.1161/STROKEAHA.116.014306.¹ The models were generated using a physiological approach, considering the probability of achieving reperfusion with each given treatment strategy in combination with the probability of good outcome as a function of time to reperfusion, and including the possibility of good outcome without reperfusion. The probability of achieving reperfusion given endovascular therapy was estimated from the ESCAPE trial at 0.74.² The probability of good outcome given successful reperfusion decreases by 0.0006 for every minute delay.³ As the time of reperfusion for patients receiving alteplase is unknown, we assume the same rate of decay applies. The probability of early reperfusion given alteplase therapy was estimated at 0.18.^{4,5} The probability of good outcome given no reperfusion was estimated from the ESCAPE trial to be 0.30.² The door to needle time (A), alteplase bolus to departure for EVT centre time (B), door to groin puncture time (C), travel time from the patient to the thrombolysis centre (X), travel time from the thrombolysis centre to the EVT centre (Y), and travel time from the patient to the EVT centre (Z) are incorporated. It is assumed first reperfusion is achieved 30 minutes into the endovascular procedure. A constant 30 minutes has been added to represent the average time from first medical contact to ambulance arrival and ambulance scene time. Table I displays the model variables, definitions, and data sources. Table II displays the time parameters used in the models, and Table III shows how these elements combine to form the conditional probability models.

Table I. Model Variables, Definitions, Values, and Data Sources

Model Variable	Definition	Value	Data Source
Time X	Travel time from patient to thrombolysis centre	Variable	Using Google's Distance Matrix API drive time from the geographic centre of each Eircode routing key region to the nearest thrombolysis centre was estimated.
Time Y	Travel time from thrombolysis centre to thrombectomy centre	Variable	Using Google's Distance Matrix API drive time from each thrombolysis centre to the nearest thrombectomy centre was estimated.
Time Z	Travel time from patient to thrombectomy centre	Variable	Using Google's Distance Matrix API drive time from the geographic centre of each Eircode routing key region to the nearest thrombectomy centre was estimated.
Door to Needle Time (Time A)	Time from arrival at thrombolysis centre to alteplase administration	Actual thrombolysis centre median door to needle time.	Irish National Stroke Register, years 2014 – 2015.
Door in Door Out Time (Time A + B)	Time from arrival at thrombolysis centre to departure for thrombectomy centre	Actual thrombolysis median door to needle time + 60 minutes.	Irish National Stroke Register, years 2014 – 2015 (door to needle time). Beaumont Hospital (EVT Centre 1) thrombectomy registry. The difference in time from arrival at the thrombectomy centre and alteplase administration was taken for all patients, this was then stratified by thrombolysis centre and the travel time from the appropriate thrombolysis centre to the thrombectomy centre was subtracted to obtain the time from alteplase administration to departure for the thrombectomy centre. The median of these times was taken (time from alteplase administration to departure for thrombectomy centre).
Door to Arterial Access Time (Time C)	Time from arrival at thrombectomy centre to beginning of endovascular procedure.	100 minutes (mothership) 10 minutes (drip and ship)	Beaumont Hospital (EVT Centre 1) thrombectomy registry, years 2014 - 2015
Time from first medical contact to ambulance arrival and ambulance scene time	Time from 999 call to ambulance leaving scene with patient	30 minutes	Representative of response and scene times in major Canadian cities.
P(reperfusion thrombectomy)	The probability that endovascular thrombectomy results in reperfusion (TICI 2b/3 flow)	0.74	The ESCAPE trial. ²
First reperfusion after endovascular thrombectomy	Time from groin puncture to first reperfusion (TICI 2b/3 flow)	30 minutes	The ESCAPE trial. ²
P(early reperfusion alteplase) a. Time B+Y ≥ 70 b. Time B+Y < 70	The probability that alteplase therapy results in the patient achieving reperfusion before they reach the thrombectomy centre.	a. 0.18 b. 0.18[(B+Y)/70]	a. Angiography studies have shown that 1.6% of ICA, 23.9% of M1, and 38.9% of M2 occlusions recanalized after alteplase administration (median 70 minutes), the prevalence of these occlusion locations for patients with a positive LAMS screen and LVO are 28%, 65%, and 5% respectively. ^{4,5} In combination, it is estimated that 18% of patients with proven LVO will achieve early reperfusion. b. Preclinical studies have shown that alteplase clot dissolving rates progress linearly with time in the initial treatment phase. ^{6,7}
Early reperfusion after alteplase administration a. Time B+Y ≥ 70 b. Time B+Y < 70	Time of early reperfusion, should patient achieve reperfusion with alteplase before reaching the thrombectomy centre	a. 70 minutes b. Time B + Y	a. We have defined early reperfusion as 70 minutes post alteplase administration as angiography studies have shown that 1.6% of ICA, 23.9% of M1, and 38.9% of M2 occlusions recanalized a median of 70 minutes after alteplase administration. ⁸ Additionally, this is a relevant time point when considering inter-facility transport times. b. If time B+Y < 70 minutes, then there is not 70 minutes available for early reperfusion to occur before the patient reaches the thrombectomy centre. In these cases, the time of early reperfusion has been adjusted to be equal to B+Y.
P(good outcome reperfusion at time ϕ)	The rate per minute at which probability of good outcome (mRS 0 – 2 at 90 days) given successful reperfusion decreases	0.75 – 0.0006 ϕ	Estimated using endovascular therapy data from The ESCAPE trial and HERMES collaboration. ^{2,3,9} As the exact time of reperfusion is unknown for patients receiving alteplase the same rate of decay is assumed.
P(good outcome no reperfusion)	The probability the patient achieves a mRS 0 – 2 at 90 days given they did not achieve reperfusion.	0.30	The ESCAPE trial. ²

Table II. Model Parameters

Model	Thrombectomy Centre(s)	Median Door to Needle Time	Median Door In Door Out Time	Median Door To Groin Puncture Time
1(base)	EVT Centre 1	Actual centre median	DTN + 60 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
2	EVT Centre 1	30 minutes	DTN + 60 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
3	EVT Centre 1	Actual centre median	DTN + 30 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
4	EVT Centre 1	Actual centre median	DTN + 60 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
5	EVT Centre 1	30 minutes	DTN + 30 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
6	EVT Centre 1	Actual centre median	DTN + 30 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
7	EVT Centre 1	30 minutes	DTN + 60 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
8	EVT Centre 1	30 minutes	DTN + 30 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
9	EVT Centre 1 and EVT Centre 2	Actual centre median	DTN + 60 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
10	EVT Centre 1 and EVT Centre 2	30 minutes	DTN + 60 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
11	EVT Centre 1 and EVT Centre 2	Actual centre median	DTN + 30 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
12	EVT Centre 1 and EVT Centre 2	Actual centre median	DTN + 60 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
13	EVT Centre 1 and EVT Centre 2	30 minutes	DTN + 30 minutes	Mothership: 100 minutes Drip and Ship: 10 minutes
14	EVT Centre 1 and EVT Centre 2	Actual centre median	DTN + 30 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
15	EVT Centre 1 and EVT Centre 2	30 minutes	DTN + 60 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes
16	EVT Centre 1 and EVT Centre 2	30 minutes	DTN + 30 minutes	Mothership: 60 minutes Drip and Ship: 10 minutes

*bold indicates change from base model

Table III. Mothership and Drip and Ship Models

Model	Conditional Probabilities	Time Considerations	Conditional Probability Estimates
Mothership	$P(\text{good outcome}/\text{mothership model})= P(\text{reperfusion} EVT) \cdot P(\text{good outcome} \text{reperfusion at } \phi\text{mins}) + P(\text{no reperfusion} EVT) \cdot P(\text{good outcome} \text{no reperfusion})$	$P(\text{good outcome}/\text{mothership model})= P(\text{reperfusion} EVT) \cdot P(\text{good outcome} \text{reperfusion at } 30+Z+C+30\text{mins}) + P(\text{no reperfusion} EVT) \cdot P(\text{good outcome}/\text{no reperfusion})$	$P(\text{good outcome}/\text{mothership model})=0.74 \cdot [0.75 - 0.0006(30+Z+C+30)] + 0.26 \cdot 0.30$
Drip and Ship	$P(\text{good outcome}/\text{drip and ship model})= P(\text{early reperfusion} \text{alteplase}) \cdot P(\text{good outcome} \text{reperfusion at } \phi\text{mins}) + P(\text{no early reperfusion} \text{alteplase}) \cdot [P(\text{reperfusion} EVT) \cdot P(\text{good outcome} \text{reperfusion at } \phi\text{mins}) + P(\text{no reperfusion} EVT) \cdot P(\text{good outcome} \text{no reperfusion})]$	$P(\text{good outcome}/\text{drip and ship model})= P(\text{early reperfusion} \text{alteplase}) \cdot P(\text{good outcome} \text{reperfusion at } 30+X+A+70\text{mins}) + P(\text{no early reperfusion} \text{alteplase}) \cdot [P(\text{reperfusion} EVT) \cdot P(\text{good outcome} \text{reperfusion at } 30+X+A+B+Y+C+30\text{mins}) + P(\text{no reperfusion} EVT) \cdot P(\text{good outcome} \text{no reperfusion})]$	$P(\text{good outcome}/\text{drip and ship model})=0.18 \cdot [0.75 - 0.0006(30+X+A+B+70)] + 0.82 \cdot [0.74 \cdot [0.75 - 0.0006(30+X+A+B+Y+C+30)] + 0.26 \cdot 0.30]$

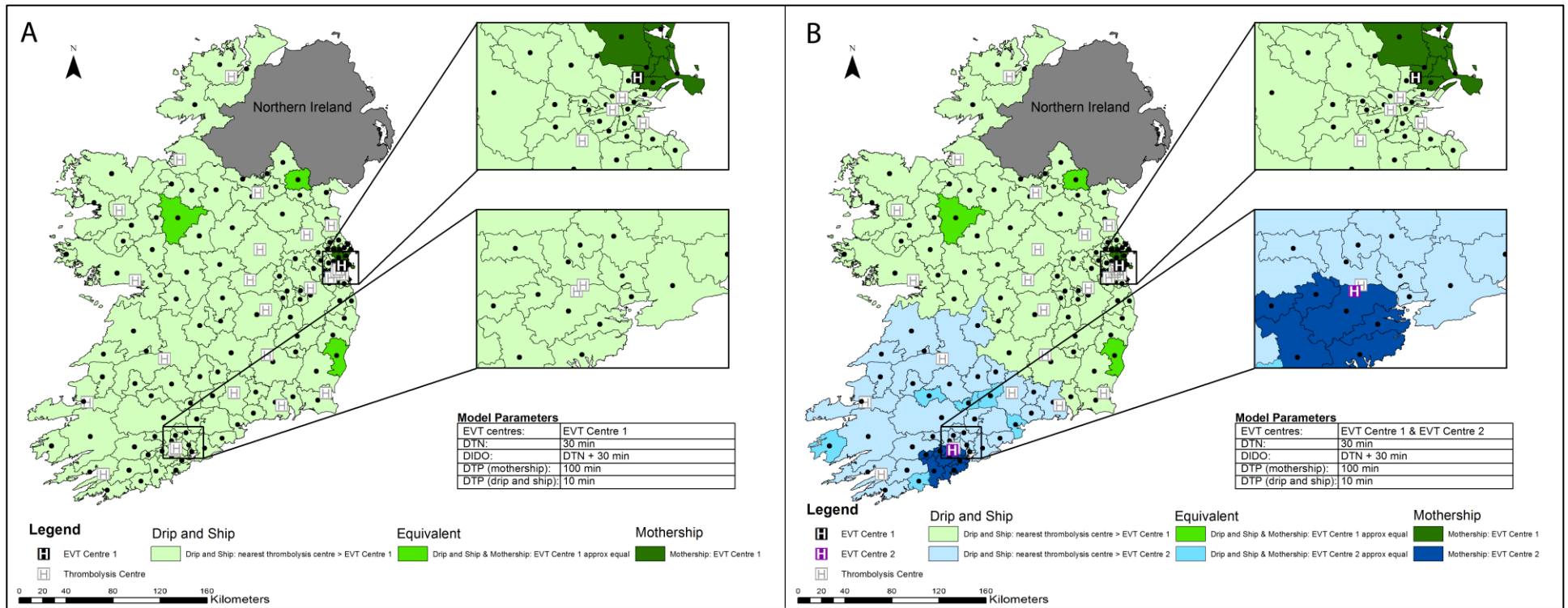


Figure I. Impact of Reduction in Door To Needle and Door In Door Out Times. This map shows the country broken into 139 geographic regions with the geographic centre plotted. In this model, door to needle time is reduced to 30 minutes, time from alteplase administration to departure for the endovascular thrombectomy (EVT) centre is reduced to 30 minutes, door to groin puncture time is 100 minutes in the mothership scenario and is 10 minutes in the drip and ship scenario. Panel A displays one EVT centre; panel B shows the addition of a second EVT centre. Each geographic region is color coded to show the transport method that provides patients with the greatest probability of good outcome.

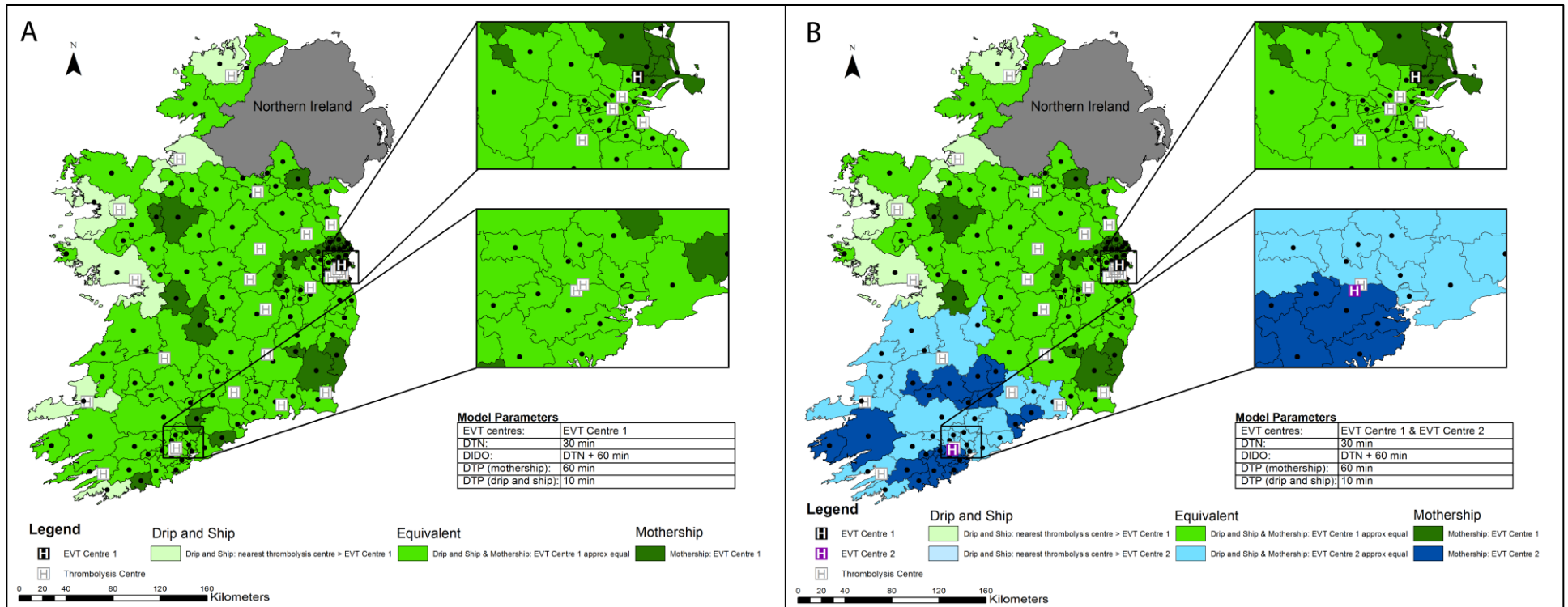


Figure II. Impact of Reduction in Door To Needle and Door To Groin Puncture Times. This map shows the country broken into 139 geographic regions with the geographic centre plotted. In this model, door to needle time is reduced to 30 minutes, time from alteplase administration to departure for the endovascular thrombectomy (EVT) centre is 60 minutes, door to groin puncture time is reduced to 60 minutes in the mothership scenario and remains at 10 minutes in the drip and ship scenario. Panel A displays one EVT centre; panel B shows the addition of a second EVT centre. Each geographic region is color coded to show the transport method that provides patients with the greatest probability of good outcome.

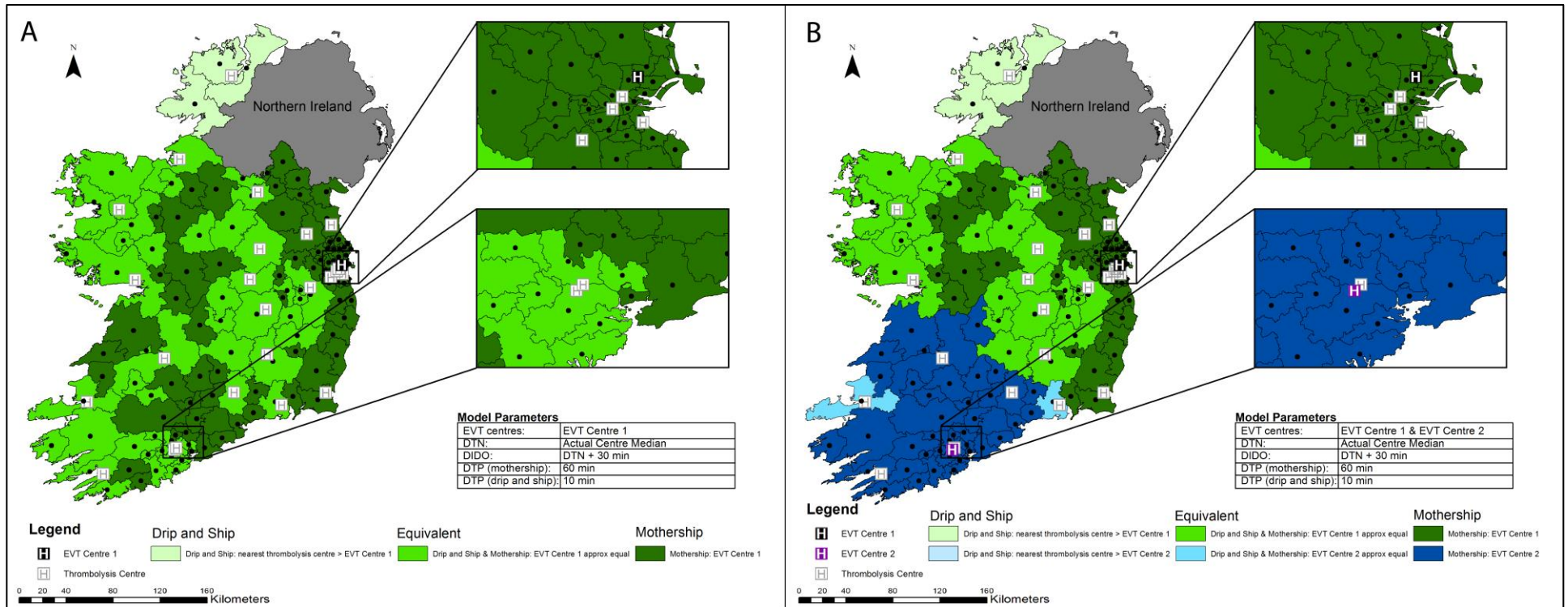


Figure III. Impact of Reduction in Door In Door Out and Door To Groin Puncture Times. This map shows the country broken into 139 geographic regions with the geographic centre plotted. In this model, actual median door to needle time from each centre is used, time from alteplase administration to departure for the endovascular thrombectomy (EVT) centre is reduced to 30 minutes, door to groin puncture time is reduced to 60 minutes in the mothership scenario and remains at 10 minutes in the drip and ship scenario. Panel A displays one EVT centre; panel B shows the addition of a second EVT centre. Each geographic region is color coded to show the transport method that provides patients with the greatest probability of good outcome.

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