

Door-in-door-out times for patients with large vessel occlusion ischaemic stroke being transferred for endovascular thrombectomy: a Victorian state-wide study

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To cite: Wong JZW, Dewey HM, Campbell BCV, *et al*. Door-in-door-out times for patients with large vessel occlusion ischaemic stroke being transferred for endovascular thrombectomy: a Victorian state-wide study. *BMJ Neurology Open* 2023;5:e000376. doi:10.1136/bmjno-2022-000376

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjno-2022-000376>).

Received 13 October 2022
Accepted 05 January 2023



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ABSTRACT

Background Time to reperfusion is an important predictor of outcome in ischaemic stroke from large vessel occlusion (LVO). For patients requiring endovascular thrombectomy (EVT), the transfer times from peripheral hospitals in metropolitan and regional Victoria, Australia to comprehensive stroke centres (CSCs) have not been studied.

Aims To determine transfer and journey times for patients with LVO stroke being transferred for consideration of EVT.

Methods All patients transferred for consideration of EVT to three Victorian CSCs from January 2017 to December 2018 were included. Travel times were obtained from records matched to Ambulance Victoria and the referring centre via Victorian Stroke Telemedicine or hospital medical records. Metrics of interest included door-in-door-out time (DIDO), inbound journey time and outbound journey time.

Results Data for 455 transferred patients were obtained, of which 395 (86.8%) underwent EVT. The median DIDO was 107 min (IQR 84–145) for metropolitan sites and 132 min (IQR 108–167) for regional sites. At metropolitan referring hospitals, faster DIDO was associated with use of the same ambulance crew to transport between hospitals (75 (63–90) vs 124 (99–156) min, $p < 0.001$) and the administration of thrombolysis prior to transfer (101 (79–133) vs 115 (91–155) min, $p < 0.001$). At regional centres, DIDO was consistently longer when patients were transported by air (160 (127–195) vs 116 (100–144) min, $p < 0.001$). The overall door-to-door time by air was shorter than by road for sites located more than 250 km away from the CSC.

Conclusion Transfer times differ significantly for regional and metropolitan patients. A state-wide database to prospectively collect data on all interhospital transfers for EVT would be helpful for future study of optimal transport mode at regional sites and benchmarking of DIDO across the state.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Shorter transfer time between peripheral hospitals and comprehensive stroke centres has been associated with improved clinical outcomes in patients with large vessel occlusion stroke requiring endovascular thrombectomy.

WHAT THIS STUDY ADDS

⇒ The median door-in-door-out time in Victoria was 107 min for metropolitan sites and 132 min for regional sites. Air transfer may save overall transport time for sites located more than 250 km from the nearest comprehensive stroke centre.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study reveals the value of system-wide databases to capture interhospital patient transfer metrics. Such data will help with the planning of patient transfers by optimising the choice of transport mode and increasing the precision of patient arrival times.

INTRODUCTION

The effectiveness of endovascular thrombectomy (EVT) for large vessel occlusion (LVO) ischaemic stroke is time sensitive. Any delay in transfer would theoretically result in poorer outcomes as infarct size increases. This hypothesis is supported by data which demonstrate worsening functional outcomes with greater reperfusion delays, especially in patients for whom complete reperfusion was not achieved.^{1–3}

In Australia, patients presenting with acute stroke are generally assessed at the nearest regional or metropolitan hospital. Most of

these are hospitals that do not have an on-site EVT service. Victorian Stroke Telemedicine (VST) was first established in 2013 and now provides 24/7 telehealth consultations for patients with suspected stroke. The service operates across 17 Victorian regional hospitals and provides access to a stroke physician.⁴ If appropriate, patients are then transferred to a comprehensive stroke centre (CSC) after discussion between the CSC neurologist, neurointerventionalist and the VST clinician. Victoria has two designated state-wide CSCs and one additional CSC also receives external transfers for EVT. Two additional metropolitan centres provide EVT for patients presenting to their service but do not routinely accept external transfers for EVT. There are no privately funded CSCs in Victoria.

The transfer time from peripheral hospitals without on-site EVT capability to CSCs has not been studied in Victoria. We sought to examine the patient journey for those with LVO stroke, with particular interest in door-in-door-out time (DIDO) and interhospital transfer times from both metropolitan and regional hospitals across the state of Victoria.

METHODS

Patients who were transferred from a public hospital in Victoria, Australia to a CSC for consideration of EVT between January 2017 and December 2018 were included. All sites are guided by the state-wide service protocol for transfers of patients requiring EVT.⁵ The imaging of all transferred patients is reviewed by the neurointerventionalist at the CSC. The final decision to transfer is agreed between the referring and CSC clinicians. Patients transferred between hospitals but who did not ultimately undergo the procedure were also included in the study.

The study was designed to focus on the transfer processes between public hospitals and high-volume EVT centres. The EVT centres included in this study were The Royal Melbourne Hospital, Monash Medical Centre and the Austin Hospital. The following regional sites were included (figure 1): Mildura, Swan Hill, Horsham, Echuca, Bendigo, Hamilton, Warrnambool, Ballarat, Werribee, Shepparton, Wangaratta, Albury, Warragul, Traralgon, Wonthaggi, Sale and Bairnsdale. Metropolitan sites included were Box Hill Hospital, Maroondah Hospital, University Hospital Geelong, Frankston Hospital, Sunshine Hospital, Footscray Hospital and the Northern Hospital.

Data linkage

All patients transferred from an external hospital with ischaemic stroke were identified from the departmental stroke databases at the CSCs. These records were reviewed to confirm the presence of LVO and intention to transfer for EVT. These data were then matched with records from Ambulance Victoria and metropolitan hospitals. VST provided data from their consultation database which is separate from the medical record of the regional hospitals. To maintain patient confidentiality, identifying data were only shared between hospitals involved in the patient's care to match cases for this study. Patients were then assigned study codes for later identification and analysis. The study was registered at the respective ethics and research offices as a quality improvement project and patient consent was not required.

Definitions

LVO was defined as occlusion of the intracranial or extracranial internal carotid artery, M1 or M2 middle

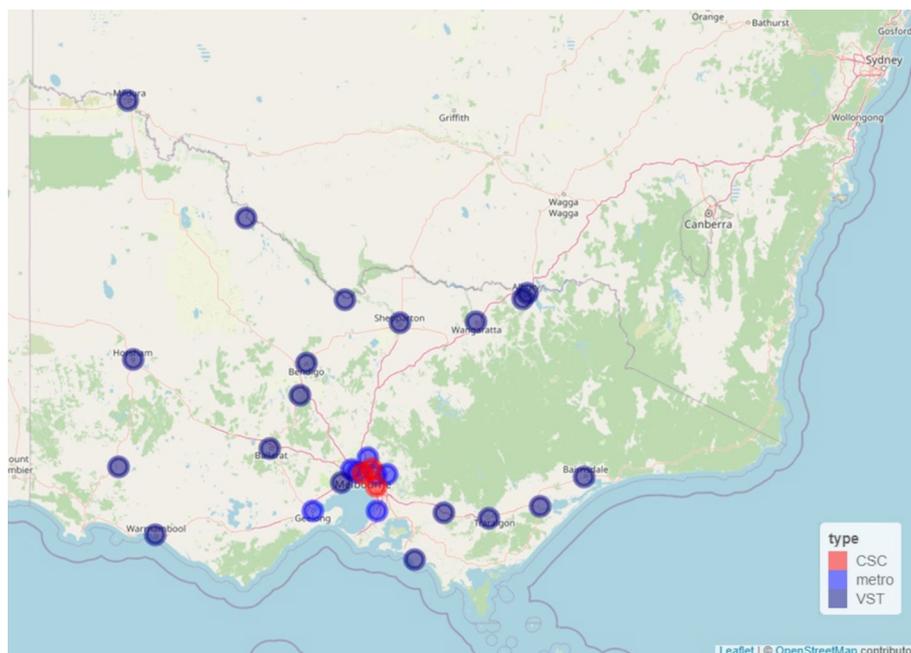


Figure 1 Map showing geographic distribution of all stroke centres included in this study. CSC, comprehensive stroke centre; metro, metropolitan sites; VST, Victorian Stroke Telemedicine sites.

cerebral artery or basilar occlusion. ‘Inbound’ refers to events or transport occurring prior to arrival at the first hospital. ‘Outbound’ refers to events or transport occurring between the referring hospital en route to the CSC. DIDO was calculated as the time between arrival at the first hospital and departure from that hospital as obtained from ambulance records. Arrival and departure times documented by Ambulance Victoria were chosen as they had fewer missing data and were more reflective of the patient’s true arrival and departure times at the emergency department. In cases where these data were missing, the documented triage time obtained from the medical record was used. Door-to-door time (D2D) is defined as the time between patient arrival at the first hospital and patient arrival at the CSC. This represents the sum of the DIDO and travel time between referring hospital and CSC. The CSC arrival time was also obtained from Ambulance Victoria records unless missing from the data.

‘Air transfer’ refers to fixed-wing or helicopter transfers, but this distinction was not available retrospectively in individual case files. Any outbound transfer involving two or more crews was considered a ‘multi-leg journey’. This included air transfers where an additional road crew was required to transport the patient from the referring hospital to the aircraft, and/or aircraft to the CSC.

Statistical analysis

Statistical analysis was performed in RStudio V.4.0.5. Comparisons between groups were assessed using χ^2 or Kruskal-Wallis tests as appropriate. Multivariable analysis with variables of interest was performed using linear regression models with controls for patient age, sex, premorbid function, time of day and time of week. Missing data were excluded from analysis using a pairwise deletion method. Statistically significant variables were further selected using a stepwise forward selection method based on the Akaike information criterion.

RESULTS

Records for 491 patients were found during the 2-year period, with 455 included in the study (figure 2). Records were complete for only 38% of patients. Incomplete records were either missing data from the inbound journey, outbound journey, primary stroke centre (PSC) metrics or a combination of these. Thirteen patients from private hospitals and nine patients from other public hospitals were identified in the study. These transfers were not included in the scope of the study. All of these records were also missing part or all ambulance data.

Three hundred and ninety-five patients (89.8%) underwent EVT after transfer. There was one posterior cerebral artery occlusion, two proximal M3 occlusions and one vertebral artery occlusion included in the final cohort. Baseline demographics of the patients stratified by metropolitan and regional referral locations are shown in table 1. There were no significant differences in patient

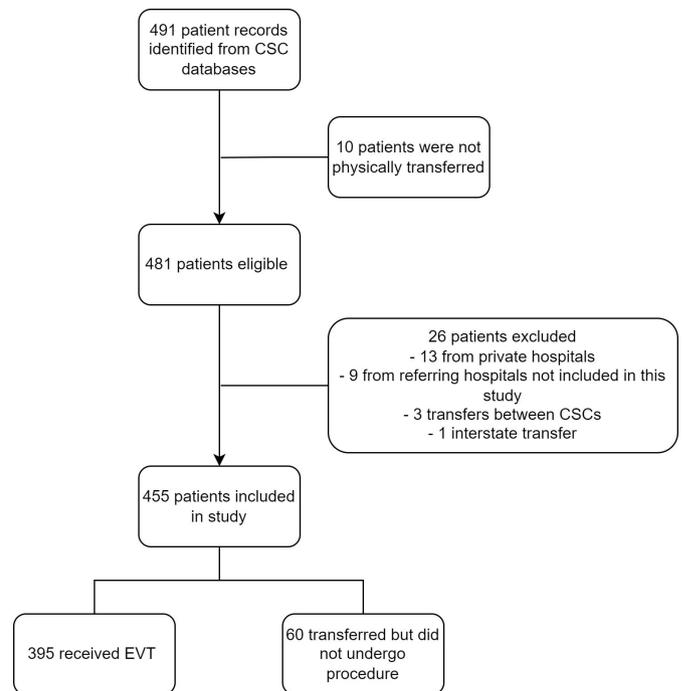


Figure 2 Flow chart summarising the inclusion and exclusion of patients for the study. CSC, comprehensive stroke centre; EVT, endovascular thrombectomy.

baseline demographics between metropolitan and regional sites. A higher proportion of patients in regional centres required transfer by air or had multileg outbound journeys en route to the CSC. The outbound journey was much longer for patients coming from regional centres as expected for the increased distance from CSCs. Inbound metrics for patients arriving by ambulance to the first hospital are shown in table 2.

DIDO and interhospital transport times for individual sites are listed in online supplemental tables 1 and 2. Median DIDO was longer at regional sites than metropolitan sites (132 (108–167) vs 107 (84–145) min, $p<0.001$). DIDO for regional patients transported by air was longer than DIDO for patients transported by road crew only (160 (127–195) vs 116 (100–144) min, $p<0.001$). For regional patients, multivariable linear regression showed an association of shorter DIDO with worse stroke severity by the National Institutes of Health Stroke Scale score, whereas longer DIDO was associated with air transfers and less urgent ambulance dispatch (code ≥ 2 ‘not lights and sirens’) ($R^2=0.347$, $p<0.001$).

At metropolitan sites, univariable analysis showed an association between shorter DIDO and the use of the same transporting crew for the outbound transfer (median DIDO 75 vs 123.5 min, $p<0.001$). However, this association was not seen at regional centres (figure 3). Use of the same crew occurred in 53/189 (28%) of cases at metropolitan PSCs and 20/101 (19.8%) of cases at regional centres. In multivariable analysis of metropolitan transfers, use of the same outbound crew (75 (63–90) vs 124 (99–156) min, $p<0.001$) and patients receiving thrombolysis (101 (79–133) vs 115 (91–155) min, $p<0.001$)

Table 1 Comparison of demographic data and key transfer times within the study cohort

	Regional (N=176)	Metropolitan (N=279)	Overall (N=455)	P value
Sex, n (%)				0.519
Female	72 (40.9)	124 (44.4)	196 (43.1)	
Male	104 (59.1)	155 (55.6)	259 (56.9)	
Age (years)				0.273
Median (Q1, Q3)	72.0 (64.0, 78.0)	73.0 (64.0, 81.0)	73.0 (64.0, 80.0)	
NIHSS score on first assessment				0.151
Median (Q1, Q3)	15.0 (9.00, 19.0)	16.0 (10.0, 20.0)	15.0 (10.0, 20.0)	
Missing, n (%)	16 (9.1)	31 (11.1)	47 (10.3)	
Premorbid mRS, n (%)				0.071
0	131 (74.4)	180 (64.5)	311 (68.4)	
1	17 (9.7)	44 (15.8)	61 (13.4)	
2	8 (4.5)	9 (3.2)	17 (3.7)	
≥3	4 (2.3)	11 (4.0)	15 (3.2)	
Missing	16 (9.1)	35 (12.5)	51 (11.2)	
Arrival mode, n (%)				0.009
Ambulance	164 (93.2)	253 (90.7)	417 (91.6)	
Inpatient	3 (1.7)	20 (7.2)	23 (5.1)	
Self-present	9 (5.1)	6 (2.2)	15 (3.3)	
Thrombolysis, n (%)				0.597
Yes	100 (56.8)	142 (50.9)	242 (53.2)	
No	76 (43.2)	122 (43.7)	198 (43.5)	
Missing	0	15 (5.4)	15 (3.3)	
Transport by air, n (%)				<0.001
Yes	83 (47.2)	3 (1.1)	86 (18.9)	
No	76 (43.2)	271 (97.1)	347 (76.3)	
Missing	17 (9.7)	5 (1.8)	22 (4.8)	
Multileg outbound journey, n (%)				<0.001
Yes	82 (46.6)	2 (0.7)	84 (18.4)	
No	71 (40.3)	256 (91.8)	327 (71.9)	
Missing	23 (13.1)	21 (7.5)	44 (9.7)	
DIDO (min)				<0.001
Median (Q1, Q3)	132 (108, 167)	107 (84, 145)	114 (91.0, 150)	
Missing, n (%)	85 (48.3)	38 (13.6)	123 (27)	
Outbound journey time (min)				<0.001
Median (Q1, Q3)	90.0 (73.0, 105)	26.0 (20.0, 36.5)	33.5 (23.0, 75.0)	
Missing, n (%)	69 (39.2)	56 (20.1)	125 (27.5)	

P values shown for Kruskal-Wallis test. A multileg outbound journey refers to any transfer involving two or more ambulance crews between the referring hospital and comprehensive stroke centre, including any transfers to and from an aircraft.

DIDO, door-in-door-out time; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

were associated with shorter DIDO (multivariable linear regression $R^2=0.13$, $p=0.02$). We did not find any association between DIDO and patient age, sex, severity of stroke, premorbid function, weekday versus weekend, working hours versus after hours or PSC case volume in univariable or multivariable analyses across the overall or metropolitan cohorts. Full detail of the analyses can be

found in online supplemental tables 3 and 4, and online supplemental figure 1.

Data were available for eight sites which used either road transport alone or combined air and road transport (Geelong, Ballarat, Bendigo, Wangaratta, Shepparton, Hamilton, Warrnambool and Bairnsdale). Total DIDO and outbound travel times for these sites

Table 2 Comparison of inbound metrics for ambulance-transported patients at regional and metropolitan centres

	Regional (N=176)	Metropolitan (N=279)	Overall (N=455)	P value
Symptom onset to call (min)				0.369
Median (Q1, Q3)	29.0 (9.00, 82.5)	35.5 (11.0, 110)	31.0 (9.00, 101)	
Missing, n (%)	76 (43.2)	179 (64.2)	255 (56.0)	
Dispatch response time (min)				0.889
Median (Q1, Q3)	10.0 (8.00, 15.0)	10.0 (8.00, 15.0)	10.0 (8.00, 15.0)	
Missing, n (%)	53 (30.1)	75 (26.9)	128 (28.1)	
Extrication time (min)				0.037
Median (Q1, Q3)	21.0 (16.0, 25.0)	18.0 (13.0, 26.0)	19.0 (14.0, 25.8)	
Missing, n (%)	55 (31.3)	78 (28.0)	133 (29.2)	
Inbound travel time (min)				0.077
Median (Q1, Q3)	16.0 (8.00, 34.0)	19.0 (13.8, 26.0)	19.0 (12.0, 29.0)	
Missing, n (%)	55 (31.3)	79 (28.3)	134 (29.5)	

P values shown for Kruskal-Wallis test.

are shown in [figure 4](#). DIDO was longer at all these sites when patients were transferred by air compared with road transport. However, overall D2D was numerically shorter when transferred by air if road transport distance exceeded 250 km (Hamilton, Warrnambool and Bairnsdale) or if the median calculated D2D by road transport exceeded 250 min (Shepparton, Hamilton, Warrnambool and Bairnsdale) based on visual comparison in [figure 4](#).

DISCUSSION

This is the first report of transfer time metrics at a state level in Australia for patients with LVO transferred from a peripheral referring hospital to a CSC. Metrics such as DIDO are an ideal target for quality improvement and have been shown to correlate with stroke outcomes.³

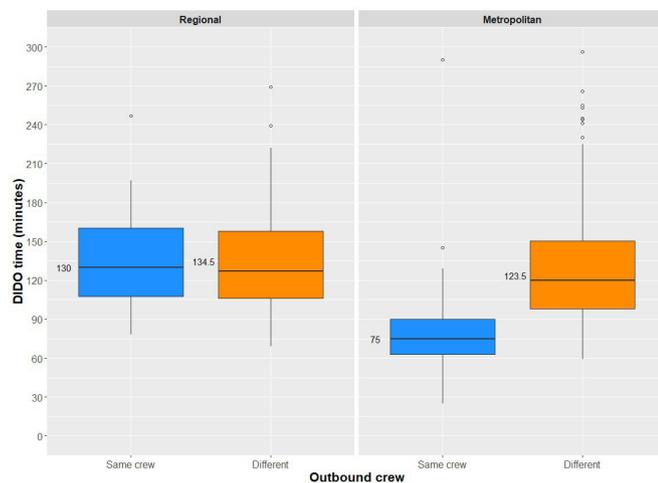


Figure 3 Boxplots comparing DIDO and use of the same outbound crew, stratified by regional and metropolitan sites. The difference was found to be statistically significant at metropolitan sites in univariate and multivariate analyses. DIDO, door-in-door-out time.

These time metrics are important as they serve as objective measures of the overall performance of a complicated process currently involving multiple organisations.^{6,7} In Victoria, air transport of patients may be organised by either Ambulance Victoria or Adult Retrieval Victoria depending on the clinical status of the patient. Regardless of the agency involved, the same pool of aircraft is used for all acute and non-acute transfers of patients within the state. In our cohort, up to four separate ambulance crews may be involved in air transfers between regional sites and CSCs.

The inbound time metrics suggest ambulance performance is similar in metropolitan and regional settings. Importantly, time from crew dispatch to arrival at the scene was similar (median 10 min). There was a small difference observed in extrication time at the pick-up address (median 21 vs 18 min), but this was not statistically significant once applying a Bonferroni correction for multiple comparisons and is probably of little clinical significance. Despite the similar response and arrival times for crews in regional compared with metropolitan areas, there continues to be a discrepancy in DIDO between metropolitan and regional hospitals. However, there is still scope for improvement in DIDO at metropolitan sites. In a cluster-randomised trial involving high-efficiency PSCs in non-urban areas of Catalonia, Spain,⁸ the median DIDO was 78 min between 2018 and 2020, shorter than the best performing metropolitan site in this study (82 min).

In metropolitan centres, use of the same ambulance crew to transport the patient between PSC and CSC reduced DIDO, consistent with previous findings.⁷ This is impractical to replicate in regional sites largely due to crew availability as the regional road ambulance crew would be out of service for a median of 180 min to cover the return journey between regional PSC and CSC. In fact, we did not find the use of the same

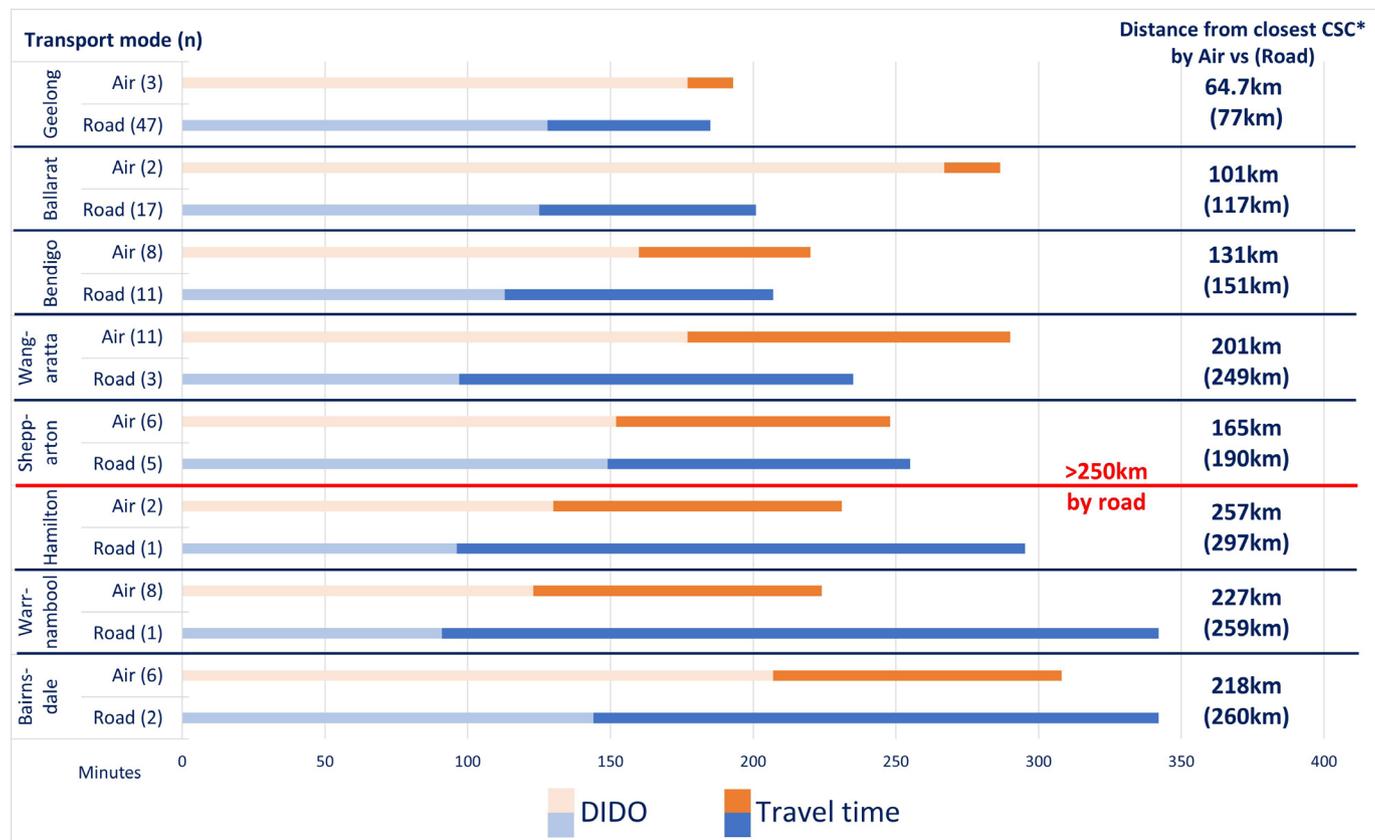


Figure 4 Graph comparing road and air transport at regional sites which used both modes of transport. Not all transfers occurred to the closest CSC for that site and these data were excluded from the graph. University Hospital Geelong is considered a metropolitan primary stroke centre within the Victorian system. It is the only metropolitan site which used air and road transport. CSC, comprehensive stroke centre; DIDO, door-in-door-out time.

ambulance road crew to be associated with shorter regional DIDO, possibly reflective of the additional time required to coordinate such a transfer. Regional patients receiving thrombolysis were not found to have longer DIDO, although patients with more severe stroke were associated with shorter DIDO. Also, ambulances dispatched as less urgent ‘not lights and sirens’ were associated with longer DIDO. This would indicate that other factors within local patient transfer protocols or logistic factors within the state ambulance service, that were not captured within this study, need to be further examined and improved. Although we did not adjust for multiple comparisons, the α levels of the reported statistically significant associations were <0.001 .

DIDO was consistently longer when transporting patients by air, an observation seen elsewhere in Australia.⁹ Our data suggest that for regional Victorian sites located more than 250 km by road from their closest PSC, the longer DIDO spent arranging for air transfer is offset by the saving in outbound travel time. Conversely, sites closer than 250 km should preference road-only transport to avoid prolonging DIDO due to logistical delays of air transfer. We suggest that distance, being a non-modifiable factor, could be used to guide the choice for mode of transport until

sustained improvements in regional DIDO are able to change the equation.

Victoria is the smallest mainland Australian state and the difference between the shortest (Werribee) and longest (Mildura) distances between a regional site and a CSC is 450 km. Given the relatively few transfers from individual regional sites over the study period, our data from individual regional sites are imprecise for clinical or modelling purposes. However, these data can act as a guide for clinicians involved in the care of these patients. At state-wide referral sites, there can often be patients requiring EVT requiring transfer simultaneously. With such data, receiving hospitals can account for DIDO and travel time in preparing for patient arrival. The data can be portrayed in an easily accessible, interactive format as shown in this link (<https://jowo92.shinyapps.io/DIDOMap/>).

The main limitation of this study is the high proportion of missing data. This is despite our best efforts in matching patient identifiers across databases from different health services. Our experience of the current difficulties in identifying patients transferred for EVT from existing routine data and local hospital stroke databases strongly argues for the establishment of a prospective state-wide database with key variables of interest relating to LVO stroke transfers and outcomes. This should include the smaller EVT centres

and private hospitals that were omitted in this study as the uptake of EVT increases. Also, we were unable to assess if DIDO across Victoria has improved since 2019 and the authors acknowledge that more contemporary data may show different findings. Quality improvement initiatives at the PSC level have been shown to dramatically decrease DIDO.^{10–12} At one metropolitan Melbourne PSC, DIDO has improved from 82 min from 2017 to 2018 in this study to 50 min in 2021.¹⁰ The very resource intensive nature of modern stroke interventions should justify the effort and investments of establishing such a database. Monitoring of DIDO at a system level and benchmarking with other sites may assist with local quality improvement initiatives. A shift to an underlying ‘Formula 1 pit stop’ or ‘grab and go’ mentality needs to be instilled while addressing local process-related delays to achieve sustained improvement in DIDO across the state. Such a database could also be linked to the interactive map for up-to-date data of transfer times across the state.

In conclusion, regional sites in Victoria have longer DIDO than metropolitan hospitals. Investment in the development of a state-wide database for patients transferred for EVT will support improvements in overall treatment efficiency of patients with LVO stroke. Such data can further refine DIDO and travel time estimates, which can inform decisions on the optimal mode of transport to ultimately shorten the time to reperfusion.

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Contributors JZWW and PMCC conceived the study. JZWW, HMD, BCVC, PJM, MP, TP, RVC, HM, MB, VT, TW, BC, DC, JR, KS, CB and PMCC designed and planned the data collection and linkage methods. JZWW, BCVC, TP, HM, VT, EL, TW, SJ, BC, MYN, DC, RKS, JR and PMCC were responsible for ethics applications and governance at each site. JZWW, BCVC, TP, AW, EL, SJ, BC, MYN, RKS, KS and CB performed data collection from their respective organisations. JZWW finalised the linkage, and prepared and analysed the data. JZWW and PMCC drafted the manuscript. All authors contributed to editing of the manuscript and approved the final submission. PMCC is the guarantor of the overall study.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Map disclaimer The inclusion of any map (including the depiction of any boundaries therein), or of any geographic or locational reference, does not imply the expression of any opinion whatsoever on the part of BMJ concerning the legal status of any country, territory, jurisdiction or area or of its authorities. Any such expression remains solely that of the relevant source and is not endorsed by BMJ. Maps are provided without any warranty of any kind, either express or implied.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Anonymised individual patient data may be provided upon reasonable request. Summary data from individual sites are uploaded as supplementary information and can also be accessed from <https://jowo92.shinyapps.io/DIDOMap/>.

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occlusion with efficiency of care and patient outcomes. *JAMA Neurol* 2017;74:793–800.

Supplementary table 1. Complete data for individual metropolitan sites.

Metropolitan Sites	Box Hill (N=85)	Frankston (N=17)	Geelong (N=55)	Maroondah (N=1)	Northern (N=48)	Sunshine (N=64)	Western (N=9)	Overall (N=279)
Sex								
Female	40 (47.1%)	8 (47.1%)	26 (47.3%)	1 (100%)	20 (41.7%)	25 (39.1%)	4 (44.4%)	124 (44.4%)
Male	45 (52.9%)	9 (52.9%)	29 (52.7%)	0 (0%)	28 (58.3%)	39 (60.9%)	5 (55.6%)	155 (55.6%)
Age (years)								
Median [Q1, Q3]	74 [65, 82]	77 [72, 80]	71 [62.5, 77]	83 [83, 83]	70.5 [64.8, 81.3]	70 [64, 80]	68 [64, 80]	73 [64, 81]
NIHSS score on first assessment								
Median [Q1, Q3]	17 [11, 22]	16 [11, 19]	14 [70, 18]	NA	12 [9, 18]	17 [10, 20]	14 [11, 17]	15.5 [10, 20]
Missing	0 (0%)	2 (11.8%)	1 (1.8%)	1 (100%)	13 (27.1%)	11 (17.2%)	3 (33.3%)	31 (11.1%)
Pre-morbid mRS								
0	57 (67.1%)	13 (76.5%)	37 (67.3%)	0 (0%)	14 (29.2%)	51 (79.7%)	8 (88.9%)	180 (64.5%)
1	25 (29.4%)	1 (5.9%)	8 (14.5%)	1 (100%)	2 (4.2%)	6 (9.4%)	1 (11.1%)	44 (15.8%)
2	2 (2.4%)	0 (0%)	4 (7.3%)	0 (0%)	3 (6.3%)	0 (0%)	0 (0%)	9 (3.2%)
≥3	1 (1.2%)	1 (5.9%)	1 (1.8%)	0 (0%)	6 (12.5%)	2 (3.1%)	0 (0%)	11 (4%)
Missing	0 (0%)	2 (11.8%)	5 (9.1%)	0 (0%)	23 (47.9%)	5 (7.8%)	0 (0%)	35 (12.5%)
Inbound travel time (mins)								
Median [Q1, Q3]	19 [13.5, 24]	23.5 [19.5, 28.8]	20.5 [12, 28.8]	NA	16 [14, 25.8]	21.5 [13, 27]	22.5 [19.3, 25.8]	19 [14, 26]
Missing	18 (21.2%)	3 (17.6%)	21 (38.2%)	1 (100%)	18 (37.5%)	12 (18.8%)	7 (77.8%)	80 (28.7%)
Door to CT time (mins)								
Median [Q1, Q3]	10.5 [6, 16]	15 [6, 22.5]	22 [16, 32]	38 [38, 38]	17 [12.3, 25.8]	25 [21, 43]	40 [32.5, 62.5]	19 [11, 28]
Missing	3 (3.5%)	1 (5.9%)	2 (3.6%)	0 (0%)	10 (20.8%)	3 (4.7%)	2 (22.2%)	21 (7.5%)

Metropolitan Sites (continued)	Box Hill (N=85)	Frankston (N=17)	Geelong (N=55)	Maroondah (N=1)	Northern (N=48)	Sunshine (N=64)	Western (N=9)	Overall (N=279)
Thrombolysis								
Yes	55 (64.7%)	7 (41.2%)	22 (40%)	0 (0%)	18 (37.5%)	37 (57.8%)	3 (33.3%)	142 (50.9%)
No	30 (35.3%)	9 (52.9%)	32 (58.2%)	0 (0%)	21 (43.8%)	25 (39.1%)	5 (55.6%)	122 (43.7%)
Missing	0 (0%)	1 (5.9%)	1 (1.8%)	1 (100%)	9 (18.8%)	2 (3.1%)	1 (11.1%)	15 (5.4%)
Door to Needle time (mins)								
Median [Q1, Q3]	50 [37, 59.5]	79 [55.5, 89]	75 [57, 107]	NA	57.5 [47.3, 85]	88 [73, 109]	85 [83, 94.5]	62 [50, 88]
Missing	30 (35.3%)	10 (58.8%)	33 (60%)	1 (100%)	30 (62.5%)	27 (42.2%)	6 (66.7%)	137 (49.1%)
Door in Door out time (mins)								
Median [Q1, Q3]	82 [65, 113]	146 [131, 187]	131 [100, 159]	107 [107, 107]	97 [83, 127]	117 [97, 148]	105 [105, 106]	107 [84, 145]
Missing	3 (3.5%)	3 (17.6%)	1 (1.8%)	0 (0%)	9 (18.8%)	16 (25%)	6 (66.7%)	38 (13.6%)
Multi-leg outbound journey, n (%)								
TRUE	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)	0 (0%)	1 (1.6%)	0 (0%)	2 (0.7%)
FALSE	85 (100%)	17 (100%)	44 (80%)	1 (100%)	37 (77.1%)	63 (98.4%)	9 (100%)	256 (91.8%)
Unknown	0 (0%)	0 (0%)	10 (18.2%)	0 (0%)	11 (22.9%)	0 (0%)	0 (0%)	21 (7.5%)
Outbound transport involving air transfer, n (%)								
TRUE	0 (0%)	0 (0%)	3 (5.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.1%)
FALSE	85 (100%)	17 (100%)	47 (85.5%)	1 (100%)	48 (100%)	64 (100%)	9 (100%)	271 (97.1%)
Unknown	0 (0%)	0 (0%)	5 (9.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (1.8%)
PSC to CSC travel time (mins)								
Median [Q1, Q3]	22 [19, 26]	32 [27, 36]	57 [51.5, 62]	33 [33, 33]	30 [27, 34]	22.5 [18.8, 27]	17 [16, 20]	26 [20, 35]
Missing	19 (22.4%)	4 (23.5%)	12 (21.8%)	0 (0%)	15 (31.3%)	8 (12.5%)	0 (0%)	58 (20.8%)

Supplementary table 2. Complete data for individual regional sites.

Regional sites A-H	Albury (N=22)	Bairnsdale (N=9)	Ballarat (N=23)	Bendigo (N=21)	Castlemaine (N=1)	Echuca (N=10)	Hamilton (N=3)	Horsham (N=1)
Sex								
Female	10 (45.5%)	2 (22.2%)	8 (34.8%)	7 (33.3%)	1 (100%)	3 (30%)	1 (33.3%)	0 (0%)
Male	12 (54.5%)	7 (77.8%)	15 (65.2%)	14 (66.7%)	0 (0%)	7 (70%)	2 (66.7%)	1 (100%)
Age (years)								
Median [Q1, Q3]	73.5 [68, 81]	76 [67, 79]	69 [58, 75.5]	76 [68, 79]	89 [89, 89]	72.5 [67.3, 77.8]	77 [65, 79.5]	71 [71, 71]
NIHSS score on first assessment								
Median [Q1, Q3]	16 [11.3, 19]	5 [2, 17]	17 [11, 24]	11 [7, 18]	NA	16 [15, 17]	18 [15, 18.5]	14 [14, 14]
Missing	0 (0%)	0 (0%)	8 (34.8%)	0 (0%)	1 (100%)	1 (10%)	0 (0%)	0 (0%)
Pre-morbid mRS								
0	16 (72.7%)	7 (77.8%)	12 (52.2%)	19 (90.5%)	0 (0%)	6 (60%)	3 (100%)	1 (100%)
1	3 (13.6%)	2 (22.2%)	2 (8.7%)	1 (4.8%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)
2	3 (13.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (10%)	0 (0%)	0 (0%)
≥3	0 (0%)	0 (0%)	1 (4.3%)	1 (4.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	0 (0%)	0 (0%)	8 (34.8%)	0 (0%)	1 (100%)	1 (10%)	0 (0%)	0 (0%)
Inbound travel time (mins)								
Median [Q1, Q3]	12 [7, 13]	28 [14, 36]	16 [8.75, 40.8]	9 [7, 29]	NA	5 [4, 8.50]	17 [14.5, 19.5]	NA
Missing	17 (77.3%)	2 (22.2%)	3 (13%)	4 (19%)	1 (100%)	3 (30%)	1 (33.3%)	1 (100%)
Door to CT time (mins)								
Median [Q1, Q3]	NA	NA	NA	NA	NA	NA	NA	NA
Missing	22 (100%)	9 (100%)	23 (100%)	21 (100%)	1 (100%)	10 (100%)	3 (100%)	1 (100%)

Regional sites A-H (continued)	Albury (N=22)	Bairnsdale (N=9)	Ballarat (N=23)	Bendigo (N=21)	Castlemaine (N=1)	Echuca (N=10)	Hamilton (N=3)	Horsham (N=1)
Thrombolysis								
Yes	13 (59.1%)	3 (33.3%)	9 (39.1%)	11 (52.4%)	0 (0%)	6 (60%)	2 (66.7%)	1 (100%)
No	9 (40.9%)	6 (66.7%)	14 (60.9%)	10 (47.6%)	1 (100%)	4 (40%)	1 (33.3%)	0 (0%)
Door to Needle time (mins)								
Median [Q1, Q3]	NA	NA	NA	NA	NA	NA	NA	NA
Missing	22 (100%)	9 (100%)	23 (100%)	21 (100%)	1 (100%)	10 (100%)	3 (100%)	1 (100%)
Door in Door out time (mins)								
Median [Q1, Q3]	NA	170 [156, 207]	137 [106, 179]	121 [105, 166]	NA	164 [145, 211]	130 [114, 145]	NA
Missing	22 (100%)	4 (44.4%)	8 (34.8%)	9 (42.9%)	1 (100%)	3 (30%)	1 (33.3%)	1 (100%)
Multi-leg outbound journey, n (%)								
TRUE	16 (72.7%)	8 (88.9%)	1 (4.3%)	9 (42.9%)	0 (0%)	8 (80%)	3 (100%)	0 (0%)
FALSE	0 (0%)	1 (11.1%)	18 (78.3%)	10 (47.6%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)
Unknown	6 (27.3%)	0 (0%)	4 (17.4%)	2 (9.5%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
Outbound transport involving air transfer, n (%)								
TRUE	18 (81.8%)	7 (77.8%)	2 (8.7%)	8 (38.1%)	0 (0%)	10 (100%)	2 (66.7%)	0 (0%)
FALSE	0 (0%)	2 (22.2%)	18 (78.3%)	11 (52.4%)	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)
Unknown	4 (18.2%)	0 (0%)	3 (13%)	2 (9.5%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)
PSC to CSC travel time (mins)								
Median [Q1, Q3]	NA	95.5 [84.5, 115]	74 [67.3, 79.8]	92.5 [87.8, 94.8]	NA	80.5 [53.3, 92.8]	105 [101, 152]	NA
Missing	22 (100%)	5 (55.6%)	7 (30.4%)	7 (33.3%)	1 (100%)	0 (0%)	0 (0%)	1 (100%)

Regional sites M-Wa	Mildura (N=3)	Sale (N=6)	Shepparton (N=12)	Swan Hill (N=1)	Traralgon (N=14)	Wangaratta (N=14)	Warragul (N=7)	Warrnambool (N=9)
Sex								
Female	1 (33.3%)	6 (100%)	5 (41.7%)	0 (0%)	5 (35.7%)	9 (64.3%)	2 (28.6%)	3 (33.3%)
Male	2 (66.7%)	0 (0%)	7 (58.3%)	1 (100%)	9 (64.3%)	5 (35.7%)	5 (71.4%)	6 (66.7%)
Age (years)								
Median [Q1, Q3]	64 [59, 67]	75 [67.5, 79.5]	72.5 [56, 80.5]	72 [72, 72]	68.5 [62, 72.8]	74.5 [68.3, 82]	69 [66, 73]	66 [41, 75]
NIHSS on arrival								
Median [Q1, Q3]	19 [9.50, 20]	11 [6.25, 21.8]	7 [2.50, 12.5]	12 [12, 12]	12.5 [7, 22.8]	17 [13, 21]	13 [11, 15]	7 [2, 15]
Missing	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	0 (0%)	3 (21.4%)	0 (0%)	0 (0%)
Pre-morbid mRS								
0	3 (100%)	6 (100%)	8 (66.7%)	1 (100%)	11 (78.6%)	6 (42.9%)	7 (100%)	9 (100%)
1	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	3 (21.4%)	2 (14.3%)	0 (0%)	0 (0%)
2	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	0 (0%)	2 (14.3%)	0 (0%)	0 (0%)
≥3	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	0 (0%)	1 (7.1%)	0 (0%)	0 (0%)
Missing	0 (0%)	0 (0%)	1 (8.3%)	0 (0%)	0 (0%)	3 (21.4%)	0 (0%)	0 (0%)
Inbound travel time (mins)								
Median [Q1, Q3]	50 [50, 50]	5 [4, 17.5]	12 [8, 32]	16 [16, 16]	20 [10, 29]	25 [5, 36]	10 [7.50, 10]	41.5 [19.5, 49]
Missing	2 (66.7%)	3 (50%)	3 (25%)	0 (0%)	1 (7.1%)	1 (7.1%)	4 (57.1%)	1 (11.1%)
Door to CT time (mins)								
Median [Q1, Q3]	NA	NA	NA	NA	NA	NA	NA	NA
Missing	3 (100%)	6 (100%)	12 (100%)	1 (100%)	14 (100%)	14 (100%)	7 (100%)	9 (100%)

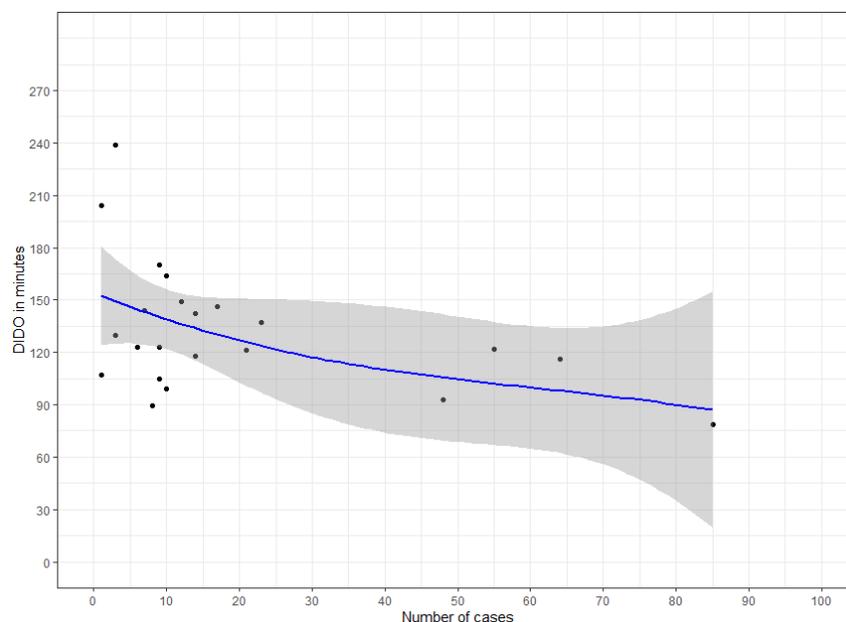
Regional sites M-Wa (continued)	Mildura (N=3)	Sale (N=6)	Shepparton (N=12)	Swan Hill (N=1)	Traralgon (N=14)	Wangaratta (N=14)	Warragul (N=7)	Warrnambool (N=9)
Thrombolysis								
Yes	2 (66.7%)	3 (50%)	8 (66.7%)	1 (100%)	9 (64.3%)	8 (57.1%)	6 (85.7%)	5 (55.6%)
No	1 (33.3%)	3 (50%)	4 (33.3%)	0 (0%)	5 (35.7%)	6 (42.9%)	1 (14.3%)	4 (44.4%)
Door to Needle time (mins)								
Median [Q1, Q3]	NA	NA	NA	NA	NA	NA	NA	NA
Missing	3 (100%)	6 (100%)	12 (100%)	1 (100%)	14 (100%)	14 (100%)	7 (100%)	9 (100%)
Door in Door out time (mins)								
Median [Q1, Q3]	239 [239, 239]	123 [123, 123]	149 [136, 166]	204 [204, 204]	118 [112, 125]	142 [121, 182]	144 [111, 144]	123 [91, 141]
Missing	2 (66.7%)	5 (83.3%)	6 (50%)	0 (0%)	3 (21.4%)	5 (35.7%)	4 (57.1%)	2 (22.2%)
Multi-leg outbound journey								
TRUE	2 (66.7%)	2 (33.3%)	7 (58.3%)	1 (100%)	1 (7.1%)	12 (85.7%)	0 (0%)	9 (100%)
FALSE	0 (0%)	2 (33.3%)	4 (33.3%)	0 (0%)	11 (78.6%)	2 (14.3%)	5 (71.4%)	0 (0%)
Unknown	1 (33.3%)	2 (33.3%)	1 (8.3%)	0 (0%)	2 (14.3%)	0 (0%)	2 (28.6%)	0 (0%)
Outbound transport involving air transfer								
TRUE	3 (100%)	3 (50%)	6 (50%)	1 (100%)	1 (7.1%)	11 (78.6%)	0 (0%)	8 (88.9%)
FALSE	0 (0%)	2 (33.3%)	5 (41.7%)	0 (0%)	12 (85.7%)	3 (21.4%)	5 (71.4%)	1 (11.1%)
Unknown	0 (0%)	1 (16.7%)	1 (8.3%)	0 (0%)	1 (7.1%)	0 (0%)	2 (28.6%)	0 (0%)
PSC to CSC travel time (mins)								
Median [Q1, Q3]	162 [162, 162]	65 [65, 65]	103 [99.8, 111]	115 [115, 115]	90 [82.8, 97.8]	125 [101, 136]	64 [55, 73]	103 [98.5, 123]
Missing	2 (66.7%)	5 (83.3%)	4 (33.3%)	0 (0%)	2 (14.3%)	4 (28.6%)	2 (28.6%)	1 (11.1%)

Regional sites We-Wo	Werribee (N=8)	Wodonga (N=1)	Wonthaggi (N=10)	Overall (N=176)
Sex				
Female	6 (75%)	0 (0%)	3 (30%)	72 (40.9%)
Male	2 (25%)	1 (100%)	7 (70%)	104 (59.1%)
Age (years)				
Median [Q1, Q3]	75 [69.3, 79]	59 [59, 59]	73.5 [67, 75.8]	72 [64, 78]
NIHSS on arrival				
Median [Q1, Q3]	11.5 [4.25, 16.5]	15 [15, 15]	12.5 [8.25, 13.8]	14 [7, 19]
Missing	2 (25%)	0 (0%)	0 (0%)	16 (9.1%)
Pre-morbid mRS				
0	6 (75%)	1 (100%)	9 (90%)	131 (74.4%)
1	0 (0%)	0 (0%)	0 (0%)	17 (9.7%)
2	0 (0%)	0 (0%)	1 (10%)	8 (4.5%)
≥3	0 (0%)	0 (0%)	0 (0%)	4 (2.3%)
Missing	2 (25%)	0 (0%)	0 (0%)	16 (9.1%)
Inbound travel time (mins)				
Median [Q1, Q3]	15 [11, 24.8]	56 [56, 56]	17 [10.5, 24.5]	16 [8, 34]
Missing	4 (50%)	0 (0%)	3 (30%)	55 (31.3%)
Door to CT time (mins)				
Median [Q1, Q3]	NA	NA	NA	NA
Missing	8 (100%)	1 (100%)	10 (100%)	176 (100%)

Regional sites We-Wo (continued)	Werribee (N=8)	Wodonga (N=1)	Wonthaggi (N=10)	Overall (N=176)
Thrombolysis				
Yes	4 (50%)	0 (0%)	9 (90%)	100 (56.8%)
No	4 (50%)	1 (100%)	1 (10%)	76 (43.2%)
Door to Needle time (mins)				
Median [Q1, Q3]	NA	NA	NA	NA
Missing	8 (100%)	1 (100%)	10 (100%)	176 (100%)
Door in Door out time (mins)				
Median [Q1, Q3]	89.5 [78.8, 104]	NA	99 [92.5, 114]	132 [108, 167]
Missing	4 (50%)	1 (100%)	3 (30%)	85 (48.3%)
Multi-leg outbound journey				
TRUE	0 (0%)	1 (100%)	1 (10%)	82 (46.6%)
FALSE	8 (100%)	0 (0%)	8 (80%)	71 (40.3%)
Unknown	0 (0%)	0 (0%)	1 (10%)	23 (13.1%)
Outbound transport involving air transfer				
TRUE	0 (0%)	1 (100%)	1 (10%)	83 (47.2%)
FALSE	8 (100%)	0 (0%)	8 (80%)	76 (43.2%)
Unknown	0 (0%)	0 (0%)	1 (10%)	17 (9.7%)
PSC to CSC travel time (mins)				
Median [Q1, Q3]	28 [26, 43]	NA	77 [73.5, 79.5]	90 [73, 104]
Missing	3 (37.5%)	1 (100%)	3 (30%)	70 (39.8%)

Supplementary Table 3. Univariable analysis (Kruskal-Wallis χ^2) of variables of interest and DIDO

Variable	n	χ^2	p-value
Outbound crew – metropolitan patients only	189	6.869	1.33e-15
Outbound crew – regional patients only	101	0.13966	0.7086
Thrombolysis – metropolitan patients only	264	6.688	0.0097
Thrombolysis – regional patients only	176	0.36086	0.5480
Transport mode (air or ground) – regional patients only	159	16.62	4.566e-05
Outbound ambulance dispatch code – metropolitan patients only	234	11.258	7.926e-4
Outbound ambulance dispatch code – regional patients only	114	7.9584	0.0048

Supplementary figure 1. Association between PSC case volume/site experience and DIDO.

There was a trend towards lower DIDO with higher case volume in univariable analysis (see Figure below), however this did not reach statistical significance (Spearman's rho for non-parametric data = -0.357, $p = 0.102$). PSC case volume was included in the multivariable regression analysis for regional and metropolitan sites (see Supplementary Table 2), but no statistically significant association was found.

Supplementary Table 4. Regression model results after forward selection of significant variables

Variables included in all initial linear regression models were: Age, sex, NIHSS score at PSC, baseline mRS score, thrombolysis, weekday/weekend, time of day (working hours/after hours), ambulance dispatch code, outbound ambulance crew, case volume (total number of transfers made by that PSC during the study period). The models were refined by identifying the most significant variables using the Akaike Information Criterion and included in the final models below.

1. Overall DIDO for all patients

	Estimate	Std. Error	t value	p value	
(Intercept)	51.4792	59.9625	0.859	0.39152	
Outbound crew (different)	53.6718	17.3654	3.091	0.00225	**
mRS score [linear]	-10.1559	67.0592	-0.151	0.87976	
mRS score [quadratic]	9.2704	57.7877	0.16	0.87269	
mRS score [cubic]	-35.2313	75.4497	-0.467	0.64099	
NIHSS score at PSC	-1.5377	1.134	-1.356	0.17646	
Ambulance dispatch code (Category >2 (less urgent))	38.892	22.259	1.747	0.08197	.
Thrombolysis (yes)	-47.5743	16.7369	-2.842	0.00489	**
Patient age	1.1021	0.6968	1.582	0.11517	
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1					
Residual standard error: 118.1 on 224 degrees of freedom (220 observations deleted due to missingness)					
Multiple R-squared: 0.1096, Adjusted R-squared: 0.06986					
F-statistic: 2.758 on 10 and 224 DF, p-value: 0.003164					

This model suggests that using a different ambulance crew to transport the patient between PSC and CSC adds 53.7 minutes to DIDO, while the patient receiving thrombolysis reduced DIDO by 47.6 minutes. Note that 220/455 patients were missing data. This result was not reported in the main manuscript as the model is skewed towards metropolitan patients.

2. DIDO for metropolitan patients only (n=279)

	Estimate	Std. Error	t value	p value	
(Intercept)	13.6487	81.6609	0.167	0.8675	
Outbound crew (different)	71.7545	25.0856	2.86	0.00486	**
mRS score [linear]	-21.265	80.9472	-0.263	0.79316	
mRS score [quadratic]	45.757	78.5526	0.583	0.56114	
mRS score [cubic]	-33.7884	94.4443	-0.358	0.72105	
NIHSS score at PSC	-1.3686	1.738	-0.787	0.43229	
Ambulance dispatch code (Category >2 (less urgent))	25.5126	43.4557	0.587	0.55806	
Thrombolysis (yes)	-68.8786	24.94	-2.762	0.0065	**
Patient age	1.3837	0.9779	1.415	0.15924	
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1					
Residual standard error: 140.8 on 144 degrees of freedom (124 observations deleted due to missingness)					
Multiple R-squared: 0.1334, Adjusted R-squared: 0.07317					
F-statistic: 2.216 on 10 and 144 DF, p-value: 0.01993					

This model using metropolitan patient transfers only suggest that using a different ambulance crew to transport the patient adds 71.8 minutes to DIDO, while the patient receiving thrombolysis reduced DIDO by 68.9 minutes.

3. DIDO for regional patients only (n=176)

	Estimate	Std. Error	t value	p value	
(Intercept)	121.1917	16.8446	7.195	4.00E-10	***
NIHSS score at PSC	-1.9105	0.6709	-2.848	0.00568	**
Ambulance dispatch code (Category >2 (less urgent))	25.3655	12.1908	2.081	0.040876	*
Transport mode (Air transfer)	45.9438	11.6238	3.953	0.000173	***
PSC case volume	1.7071	0.8655	1.972	0.052259	.
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1					
Residual standard error: 42.9 on 75 degrees of freedom (96 observations deleted due to missingness)					
Multiple R-squared: 0.3472, Adjusted R-squared: 0.3124					
F-statistic: 9.972 on 4 and 75 DF, p-value: 1.59e-06					

Mode of transport was included in the multivariable regression analysis for regional patients. There were too few (n=3) air transfers in the metropolitan cohort.