Melbourne Mobile Stroke Unit and Reperfusion Therapy
Greater Clinical Impact of Thrombectomy Than Thrombolysis

Henry Zhao, MBBS; Skye Coote, MN; Damien Easton, PhD; Francesca Langenberg, DCR; Michael Stephenson, BHLthSc; Karen Smith, PhD; Stephen Bernard, PhD; Dominique A. Cadilhac, PhD; Joosup Kim, PhD; Christopher F. Bladin, PhD; Leonid Churilov, PhD; Douglas E. Crompton, PhD; Helen M. Dewey, PhD; Lauren M. Sanders, PhD; Tissa Wijeratne, MD; Geoffrey Cloud, MBBS; Duncan M. Brooks, MBBS; Hamed Asadi, PhD; Vincent Thijs, PhD; Ronil V. Chandra, MMed; Henry Ma, PhD; Patricia M. Desmond, PhD; Richard J. Dowling, MBBS; Peter J. Mitchell, MD; Nawaf Yassi, PhD; Bernard Yan, DMedSci; Bruce C.V. Campbell, PhD; Mark W. Parsons, PhD; Geoffrey A. Donnan, MD*; Stephen M. Davis, MD*

Background and Purpose—Mobile stroke units (MSUs) are increasingly used worldwide to provide prehospital triage and treatment. The benefits of MSUs in giving earlier thrombolysis have been well established, but the impacts of MSUs on endovascular thrombectomy (EVT) and effect on disability avoidance are largely unknown. We aimed to determine the clinical impact and disability reduction for reperfusion therapies in the first operational year of the Melbourne MSU.

Methods—Treatment time metrics for MSU patients receiving reperfusion therapy were compared with control patients presenting to metropolitan Melbourne stroke units via standard ambulance within MSU operating hours. The primary outcome was median time difference in first ambulance dispatch to treatment modeled using quantile regression analysis. Time savings were subsequently converted to disability-adjusted life years avoided using published estimates.

Results—In the first 365-day operation of the Melbourne MSU, prehospital thrombolysis was administered to 100 patients (mean age, 73.8 years; 62% men). The median time savings per MSU patient, compared with the control cohort, was 26 minutes (P<0.001) for dispatch to hospital arrival and 15 minutes (P<0.001) for hospital arrival to thrombolysis. The calculated overall time saving from dispatch to thrombolysis was 42.5 minutes (95% CI, 36.0–49.0). In the same period, 41 MSU patients received EVT (mean age, 76 years; 61% men) with median dispatch-to-treatment time saving of 51 minutes (95% CI, 30.1–71.9, P<0.001). This included a median time saving of 17 minutes (95% CI, 7.6–26.4, P=0.001) for EVT hospital arrival to arterial puncture for MSU patients. Estimated median disability-adjusted life years saved through earlier provision of reperfusion therapies were 20.9 for thrombolysis and 24.6 for EVT.

Conclusions—The Melbourne MSU substantially reduced time to reperfusion therapies, with the greatest estimated disability avoidance driven by the more powerful impact of earlier EVT. These findings highlight the benefits of prehospital notification and direct triage to EVT centers with facilitated workflow on arrival by the MSU. (Stroke. 2020;51:922-930. DOI: 10.1161/STROKEAHA.119.027843.)

Key Words: aged ■ hospitals ■ humans ■ stroke ■ workflow

Received September 28, 2019; final revision received December 13, 2019.
From the Department of Neurology, Melbourne Brain Centre (H.Z., S.C., D.E., L.C., N.Y., B.Y., B.C.V.C., M.W.P., G.A.D., S.M.D.) and Department of Radiology (F.L., P.M.D., R.J.D., F.I.M., B.Y.), Royal Melbourne Hospital, Victoria, Australia; Department of Medicine and Radiology, Faculty of Medicine, Dentistry and Health Sciences (H.Z., S.C., D.E., L.C., N.Y., B.Y., B.C.V.C., M.W.P., G.A.D., S.M.D.), Stroke Division, The Florey Institute of Neurosciences and Mental Health (D.A.C., J.K., C.F.B., V.T., N.Y., G.A.D.), Department of Medicine, Austin Health, Melbourne Medical School (L.C.), Department of Neurology, Northern Health, Faculty of Medicine, Dentistry and Health Sciences (D.E.C.), Department of Neurology St. Vincent’s Hospital, Melbourne, Faculty of Medicine, Dentistry and Health Sciences (L.M.S.), Department of Neurology, Western Health, Faculty of Medicine, Dentistry and Health Sciences (T.W.), and Department of Radiology (D.M.B., H.A.), Austin Health, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria, Australia; Ambulance Victoria, Melbourne, Victoria, Australia (H.Z., M.S., K.S., S.B., N.Y., B.C.V.C.); Department of Epidemiology and Preventive Medicine (K.S.), Department of Community Emergency Health and Paramedic Practice (K.S.), Translational Public Health Research Division, Stroke and Ageing Research Group, School of Clinical Sciences Department of Neurology (D.A.C., J.K.), Eastern Health, Faculty of Medicine, Nursing and Health Sciences (C.F.B., H.M.D.), Alfred Health (G.C.), Department of Clinical Neurosciences, Central Clinical School (G.C.), and Department of Neurology (H.M.) and Department of Radiology (R.V.C.), Monash Health, Department of Medicine, School of Clinical Science, Monash University, Melbourne, Victoria, Australia; Discipline of Emergency Medicine, University of Western Australia, Australia (K.S., S.B.).

*Drs Donnan and Davis are joint senior authors.
The online-only Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.119.027843.
Correspondence to Stephen M. Davis, MD, Melbourne Brain Centre at Royal Melbourne Hospital, Royal Melbourne Hospital, Parkville, Australia. Email stephen.davis@mh.org.au

© 2020 American Heart Association, Inc.
Stroke is available at https://www.ahajournals.org/journal/stroke
DOI: 10.1161/STROKEAHA.119.027843

922
Mobile stroke units (MSUs) are being increasingly deployed worldwide to provide prehospital stroke care and thrombolysis, following their initial introduction in Homburg, Germany.\textsuperscript{1,2} The MSU model involves a specialized ambulance with an inbuilt computed tomography (CT) scanner and multidisciplinary stroke team trained to assess, scan, and treat patients in the community. This approach has the potential to significantly reduce the time to treatment compared with standard in-hospital diagnosis and treatment. Accurate prehospital diagnosis including CT angiography also allows identification of the need for specialized hospital-based services such as endovascular thrombectomy (EVT) for large vessel occlusion, or neurosurgical management for selected cases of intracerebral hemorrhage, allowing triage to the nearest appropriate comprehensive stroke center.

While previously published data from MSU services in Europe and North America show substantial reductions in time to thrombolysis of \textasciitilde 30 to 45 minutes,\textsuperscript{3,4} little is known about the clinical impact on EVT. Despite the theoretical advantage of improved prehospital triage with CT angiography and prenotification of EVT services, only minor time savings have been reported for hospital arrival to EVT commencement for MSU patients.\textsuperscript{5} Given the greater efficacy of EVT for ischemic stroke compared with thrombolysis alone, reducing time to EVT would be expected to have a major impact on reduction of disability.

The Melbourne MSU was launched in November 2017 as the first in Australia. The MSU is based at a large comprehensive stroke center and operates with a 20-km radius, servicing \textasciitilde 1.7 million people within the city of Melbourne, Victoria. Melbourne is a fast-growing city of \textasciitilde 5 million people, with a mix of comprehensive stroke centers (providing EVT and neurosurgical services), primary stroke centers (thrombolysis only), telemedicine-enabled thrombolysis centers, and non-stroke centers, making accurate prehospital triage critical to ensuring timely treatment for acute stroke. We aimed to describe the impact of the Melbourne MSU within the first 365 days of operation on prehospital treatment and acute reperfusion therapies with a focus on the clinical and health impact of EVT services. We also aimed to determine the effect on estimated disability avoidance by earlier provision of thrombolysis and thrombectomy.

**Methods**

The data that support the findings of this study are available from the corresponding author on reasonable request.

**MSU Operation**

The Melbourne MSU is built with a Mercedes Sprinter 5 series (Mercedes-Benz Australia) chassis with custom long wheelbase box body that incorporates a self-mobile CereTom CT scanner (Samsung Neurologica Corp, MA) and 4G mobile transmission and telemedicine hardware. A contrast power injector, contrast warmer, and inbuilt refrigerator allow CT angiography and medication management. The MSU is currently staffed with an onboard neurologist or senior stroke fellow providing primary assessment and treatment decisions, stroke advanced practice nurse providing clinical support and treatment administration, CT radiographer (nonmedical clinician) performing MSU imaging, and advanced life support and mobile intensive care (capable of intubation and advanced cardiac resuscitation) paramedics providing transport logistics and paramedicine support. We are currently investigating options for telemedicine consultation to replace the onboard neurologist. The MSU carries alteplase, anticoagulant reversal agents (idarucizumab, prothrombin complex concentrate, vitamin K), and antihypertensive and anticonvulsant medications. Tenecteplase and tranexamic acid are also carried for use in interventional drug trials. During the initial phase, the MSU operates Monday to Friday from 8 AM to 6 PM.

The operation of the Melbourne MSU generally follows an integrated dual dispatch model. The MSU is centrally dispatched by Ambulance Victoria as a secondary service to all suspected stroke cases within 12 hours of symptom onset in the designated central Melbourne region, using the Advanced Medical Priority Dispatch System (Priority Dispatch Corp, UT). This does not consider pre-morbid function. Alternatively, the MSU may be requested by attending paramedic crews or dispatched by request of the MSU staff who monitor radio traffic for possible cases. The MSU is able to rendezvous with the primary paramedic crew on-scene or at a secondary location after transport to hospital has commenced. The automatic co-dispatch boundary was set at 20 km of the Royal Melbourne Hospital (RMH) in central Melbourne (Figure 1), designed to align the MSU travel time to the historical ambulance on-scene time (\textasciitilde 20 minutes), which minimizes delays between patient extrication and MSU attendance. Rendezvous can occur outside the 20-km radius for requests initiated by paramedic crews. Paramedic crews can cancel the MSU service should their initial assessment suggest a nonstroke diagnosis. For patients who are reviewed, the MSU generally transports patients requiring prehospital treatment or facilitation for EVT. In our dual dispatch system, the primary ambulance crew will transport those patients who are not planned for reperfusion therapy or who have a nonstroke diagnosis. Patient transport standardly follows Ambulance Victoria guidelines to the nearest thrombolysis stroke center, but the MSU will bypass to the nearest comprehensive stroke center if neurointerventional or neurosurgical services may be required.

Patients presenting with ongoing stroke symptoms within 4.5 hours of symptom onset receive a noncontrast CT brain on the MSU. Patients with onset of symptoms >4.5 hours, wake-up symptoms, and presentation suspicious for large vessel occlusion <24 hours of onset may also be scanned at the discretion of the MSU neurologist. Subsequent MSU intracranial CT angiogram may be performed to detect large vessel occlusion when clinically suspected.

**Cases and Controls**

Data for all MSU dispatched cases were systematically collected prospectively in the Melbourne MSU clinical registry, including all time metrics relating to dispatch, arrival, and treatment. All MSU patients receiving reperfusion therapy, either thrombolysis or EVT, were compared with non-MSU patients receiving EVT without reperfusion therapy presenting via standard ambulance transport to hospital (control cases) within MSU operating hours.

Control data for thrombolysis first ambulance dispatch-to-treatment times were calculated from 2 components: ambulance dispatch to hospital arrival and arrival to thrombolysis. Ambulance dispatch-to-arrival times were prospectively collected for consecutive patients receiving thrombolysis at the RMH in a clinical registry linked with Ambulance Victoria data. For calculating arrival-to-thrombolysis times, we used prospectively collected data from consecutive patients across all 9 metropolitan Melbourne thrombolysis-capable hospitals participating in the Australian Stroke Clinical Registry.\textsuperscript{6} Symptom-onset-to-thrombolysis time differences were compared directly between MSU and Australian Stroke Clinical Registry control cases. Thrombolysis control cases were drawn from 2016 to 2017 as the immediate years before MSU commencement and restricted to patients presenting within MSU operating hours.

Control cases for EVT consisted of consecutive patients with available prehospital linked data presenting to the RMH, the largest EVT service in Melbourne, either directly or via interhospital transfer from 10 metropolitan health services within MSU operating hours. The 2017 to 2018 period was chosen for EVT controls, as the more recent data were thought to better reflect evolving EVT workflows.
Ethics approval for this study was provided by the RMH Research Ethics Committee with waiver of patient consent.

Outcomes
The primary outcome of this study was to evaluate the effect of the MSU on intravenous and endovascular reperfusion therapies compared with standard ambulance and hospital workflows. Median time differences for first ambulance dispatch to commencement of thrombolysis or arterial puncture between MSU and control data were selected as the primary measures of time to reperfusion therapy. Translation to disability-adjusted life years avoided for time savings were then calculated using published estimates for earlier provision of thrombolysis and EVT.

Data are expressed as median and interquartile range (IQR) except where specified. Time differences between MSU and controls were analyzed using quantile regression modeling because of assumed lack of normality, with prespecified 25th, 50th, and 75th quantiles selected. Quantile regression models the association between a set of input variables and specific percentiles (or quantiles) of the outcome variable and estimates differences in the quantiles of the outcome variable between 2 groups. The primary outcome of median time difference between MSU and control groups was, therefore, determined by the 50th quantile of the model, with a P of <0.05 considered significant. Analyses were not adjusted for baseline characteristics.

Time differences were compared between MSU and control groups directly except for thrombolysis first ambulance dispatch to treatment, which were estimated as a sum of the first ambulance dispatch to hospital/scene and hospital/scene to thrombolysis. The median times and respective CIs for this latter composite calculation were estimated using 1000 bootstrapped replications. Statistical analysis was conducted using Stata IC15 software (StataCorp, College Station, TX).

Results
Service Summary
The Melbourne MSU was launched on November 20, 2017, and completed 365 days of full or partial (n=33; 9%) service in August 2019. The MSU was dispatched to a total of 2348 cases (6.4 cases per service day), of which 2089 cases (90%) were from automatic co-dispatch within the 20-km central zone and the remainder from paramedic crew request (n=188; 8%) or MSU self-dispatch (n=70; 2%). Data from the first calendar year showed the MSU attended 65% (1179 of 1804) of the total suspected stroke caseload in the 20-km automatic co-dispatch zone during operational times.

Of total dispatched cases, 1409 cases (60%) were canceled by the initial paramedic crew attending before the MSU arrival, with the vast majority due to absence of, or resolving, stroke symptoms. Of the remaining 939 cases attended by the MSU, 437 (46.5%) underwent MSU imaging with a noncontrast CT brain and 219 (23.3%) underwent intracranial CT angiogram. A provisional diagnosis of stroke was given to 491 patients (52.2% of reviewed), of whom 311 were suspected acute ischemic strokes (63.3%), 33 transient ischemic attack (6.7%), 44 intracerebral hemorrhages (9%), and 12 extra-axial hemorrhages (2.4%), while 91 suspected stroke cases were given a clinical diagnosis of stroke but did not receive a scan because of clear ineligibility for prehospital treatment (18.5%; Figure I of the online-only Data Supplement). Overall, 214 patients (22.8% of attended) were transported to hospital by the MSU.

Impact on Thrombolysis
In the first 365 days of operational service, the MSU provided prehospital thrombolysis to 100 patients (48.3% of all suspected ischemic stroke reviewed <4.5 hours of onset). Of these, 39 received tenecteplase as part of 2 clinical trials (https://www.clinicaltrials.gov; unique identifiers: NCT03340493 and NCT04071613). Dabigatran was reversed with idarucizumab in 5 patients before thrombolysis. Thrombolysis patients were 62% male with a mean age of 73.8 years (SD, ±14.4) and median National Institutes of Health Stroke Scale score of 10 (IQR, 5–18).

Figure 2A shows the time epochs from onset to thrombolysis for MSU compared with metropolitan Melbourne control data. Of MSU tPA cases, 15 patients (15%) received...
thrombolysis <60 minutes from the last known well time, while 47 (47%) patients received thrombolysis <90 minutes from the last known well time. A further 8 patients (8%) received thrombolysis between 3.5 and 4.5 hours, representing cases that would likely have missed the 4.5-hour window by the time of hospital arrival. Post-thrombolysis, 2 patients (2%) met the definition for symptomatic intracerebral hemorrhage according to the Safe Implementation of Treatments in Stroke criteria.12

Time metrics for onset, alarm, and scene to thrombolysis for MSU patients are shown in Tables 1 and 2 in comparison to local controls. Logistic regression P<0.001.

Impact on EVT
In the same period, 57 MSU patients were diagnosed with anterior or posterior circulation large vessel occlusion. Of these, 36 received prehospital thrombolysis and 41 received EVT at the nearest comprehensive stroke center. Bypass of the local stroke center to transport to a comprehensive stroke center was required in 27 cases (47.4% of all large vessel occlusion). Those receiving EVT <6 hours of onset represented 16.5% (36 of 217) of all ischemic strokes within this time frame. EVT patients were 61% male with a mean age of 76 years (SD, ±11.1) and median baseline National Institutes of Health Stroke Scale score of 18 (IQR, 15–22). Of 41 patients receiving EVT, 33 patients received baseline MSU CT angiogram (80%), of whom 10 were directly taken to the endovascular suite on hospital arrival. The 31 remaining EVT patients

Table 1. Treatment Time Saving for Melbourne Mobile Stroke Unit Cases in Comparison to Local Controls

<table>
<thead>
<tr>
<th></th>
<th>25th Quantile</th>
<th>50th Quantile</th>
<th>75th Quantile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference</td>
<td>95% CI</td>
<td>P Value</td>
</tr>
<tr>
<td>tPA: first ambulance dispatch to hospital/scene arrival, min</td>
<td>22.0</td>
<td>17.8 to 26.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>tPA: hospital/scene arrival to tPA, min</td>
<td>5.0</td>
<td>–0.6 to 10.6</td>
<td>0.08</td>
</tr>
<tr>
<td>EVT: first ambulance dispatch to arterial puncture, min</td>
<td>18.0</td>
<td>–1.8 to 37.8</td>
<td>0.075</td>
</tr>
<tr>
<td>EVT: EVT center arrival to arterial puncture, min</td>
<td>16.0</td>
<td>3.2 to 28.8</td>
<td>0.015</td>
</tr>
</tbody>
</table>

EVT indicates endovascular thrombectomy; and tPA, tissue-type plasminogen activator.

Figure 2. Time epochs from onset to thrombolysis and thrombectomy for Melbourne mobile stroke unit (MSU) compared with local controls. *Includes only patients with thrombectomy <6 h from onset. A and B, Comparison to metropolitan Melbourne control cases within MSU operating hours. Logistic regression P<0.001.
Stroke March 2020

Table 2. Melbourne MSU Thrombolysis Time Metrics and Comparison to International Services

<table>
<thead>
<tr>
<th></th>
<th>Melbourne</th>
<th>Berlin13</th>
<th>Houston14</th>
<th>Cleveland15</th>
<th>Hamburg16</th>
<th>Colorado17</th>
<th>Illinois18</th>
<th>Oslo19</th>
<th>New Jersey20</th>
<th>New York21</th>
<th>Toledo22</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=100</td>
<td>n=305</td>
<td>n=12</td>
<td>n=124</td>
<td>n=12</td>
<td>n=13</td>
<td>n=18</td>
<td>n=23</td>
<td>n=16</td>
<td>n=29</td>
<td>n=10</td>
</tr>
<tr>
<td>Onset to tPA, min; median (IQR)</td>
<td>95 (69–128)</td>
<td>73 (53–120)</td>
<td>98 (47–265)*</td>
<td>72 (53–108)</td>
<td>97†</td>
<td>98 (72–184)</td>
<td>78 (±12)</td>
<td>101.0 (SD, 46.5)*</td>
<td>105 (52.0–128.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSU dispatch to tPA, min; median (IQR)</td>
<td>60 (50–69), first ambulance dispatch: 65 (54–80)</td>
<td>48 (39–53)</td>
<td>38 (34–42)</td>
<td>39 (35–45)</td>
<td>62 (52–71)</td>
<td>61.20 (SD, 15.27)*</td>
<td>53 (42–59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scene arrival to tPA, min; median (IQR)</td>
<td>41.5 (34.0–47.3)</td>
<td>25*</td>
<td>29 (29–38)</td>
<td>26 (20–29)</td>
<td>48.3 (SD, 13.7)*</td>
<td>34.7*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scene arrival to CT start, min; median (IQR)</td>
<td>18 (14–23)</td>
<td>14 (9–18)</td>
<td>4 (4–5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPA ≤60 min onset</td>
<td>15/100 (15%)</td>
<td>112/305 (37%)</td>
<td>4/12 (33%)</td>
<td></td>
<td>5/18 (27%)</td>
<td></td>
<td>3/10 (30%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPA ≤90 min onset</td>
<td>47/100 (47%)</td>
<td>187/305 (62%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time saving onset to tPA, min; median (95% CI)</td>
<td>49.0 (33.3–64.7)†‡</td>
<td>39.0</td>
<td>81.0</td>
<td>39.0†</td>
<td>22.5</td>
<td>11.0</td>
<td>42.9*</td>
<td>27.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time saving dispatch to tPA, min; median (95% CI)</td>
<td>42.5 (36.0–49.0)†‡</td>
<td>35.0*</td>
<td>35.0</td>
<td>26.0</td>
<td>29.5</td>
<td></td>
<td>30.4*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT indicates computed tomography; IQR, interquartile range; MSU, mobile stroke unit; and tPA, tissue-type plasminogen activator.

*Reported in mean only.
† Did not report whether mean or median.
‡50th quantile from unadjusted quantile regression analysis using first ambulance dispatch.

(including 23 who had received prior MSU CT angiogram) received further multimodal CT imaging on hospital arrival before EVT. There was a small difference in time to EVT of an additional 23 minutes for those who did not receive MSU CT angiogram, but this was difficult to interpret because of small numbers and significant baseline clinical imbalance. Reasons for not proceeding with EVT included improving symptoms or vessel recanalization with thrombolysis (n=6), unfavorable clinical characteristics on hospital arrival (n=9), and family refusal (n=1).

Time metrics for MSU patients receiving EVT are shown in Tables 1 and 3. Time epochs from onset to EVT commencement for MSU and control data for patients intended for EVT <6 hours of onset are shown in Figure 2B. Comparison control data during MSU operating hours for 2017 to 2018 (n=140 cases) show overall first ambulance dispatch-to-arterial-puncture time of 170 minutes (IQR, 120.5–227.5) for metropolitan Melbourne (direct presentation and interhospital transfer) cases, compared with 119.5 minutes (IQR, 103.3–137.3) for MSU patients. Median onset-to-puncture times were 234.5 minutes (IQR, 157.8–287.5) for control cases and 148 minutes (IQR, 120.3–210.5) for MSU cases. Median time from EVT center arrival to arterial puncture was 52 minutes (IQR, 39.8–71.0) for controls (n=60 cases presenting directly) and 33 minutes (IQR, 23.3–39.8) for MSU patients.

The overall median (50th quantile) time saving for MSU patients from first ambulance dispatch to arterial puncture was 51 minutes (95% CI, 30.1–71.9; P<0.001), with all but 25th quantiles reaching P<0.05 (Figure 3; online-only Data Supplement). Subanalysis of patients located outside the catchment of an EVT center showed a median time saving of 71 minutes (95% CI, 46.3–95.7, P<0.001, all quantiles <0.05), whereas the median time difference for those located within was 6 minutes (95% CI, −18.6 to 30.6, P=0.628; all quantiles >0.05). Median time saving for EVT center arrival to arterial puncture was 17 minutes (95% CI, 7.6–26.4, P=0.001; all quantiles <0.05).

Estimate of Disability Avoided

In previous studies, authors have estimated that for every minute of treatment delay, a median of 1.8 days of healthy life are lost for thrombolysis,7 and a median of 4.3 days of healthy life are lost for EVT (in addition to thrombolysis).8

Table 2. Melbourne MSU Thrombolysis Time Metrics and Comparison to International Services

<table>
<thead>
<tr>
<th></th>
<th>Melbourne</th>
<th>Berlin13</th>
<th>Houston14</th>
<th>Cleveland15</th>
<th>Hamburg16</th>
<th>Colorado17</th>
<th>Illinois18</th>
<th>Oslo19</th>
<th>New Jersey20</th>
<th>New York21</th>
<th>Toledo22</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=100</td>
<td>n=305</td>
<td>n=12</td>
<td>n=124</td>
<td>n=12</td>
<td>n=13</td>
<td>n=18</td>
<td>n=23</td>
<td>n=16</td>
<td>n=29</td>
<td>n=10</td>
</tr>
<tr>
<td>Onset to tPA, min; median (IQR)</td>
<td>95 (69–128)</td>
<td>73 (53–120)</td>
<td>98 (47–265)*</td>
<td>72 (53–108)</td>
<td>97†</td>
<td>98 (72–184)</td>
<td>78 (±12)</td>
<td>101.0 (SD, 46.5)*</td>
<td>105 (52.0–128.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSU dispatch to tPA, min; median (IQR)</td>
<td>60 (50–69), first ambulance dispatch: 65 (54–80)</td>
<td>48 (39–53)</td>
<td>38 (34–42)</td>
<td>39 (35–45)</td>
<td>62 (52–71)</td>
<td>61.20 (SD, 15.27)*</td>
<td>53 (42–59)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scene arrival to tPA, min; median (IQR)</td>
<td>41.5 (34.0–47.3)</td>
<td>25*</td>
<td>29 (29–38)</td>
<td>26 (20–29)</td>
<td>48.3 (SD, 13.7)*</td>
<td>34.7*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scene arrival to CT start, min; median (IQR)</td>
<td>18 (14–23)</td>
<td>14 (9–18)</td>
<td>4 (4–5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPA ≤60 min onset</td>
<td>15/100 (15%)</td>
<td>112/305 (37%)</td>
<td>4/12 (33%)</td>
<td></td>
<td>5/18 (27%)</td>
<td></td>
<td>3/10 (30%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tPA ≤90 min onset</td>
<td>47/100 (47%)</td>
<td>187/305 (62%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time saving onset to tPA, min; median (95% CI)</td>
<td>49.0 (33.3–64.7)†‡</td>
<td>39.0</td>
<td>81.0</td>
<td>39.0†</td>
<td>22.5</td>
<td>11.0</td>
<td>42.9*</td>
<td>27.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time saving dispatch to tPA, min; median (95% CI)</td>
<td>42.5 (36.0–49.0)‡</td>
<td>35.0*</td>
<td>35.0</td>
<td>26.0</td>
<td>29.5</td>
<td></td>
<td>30.4*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT indicates computed tomography; IQR, interquartile range; MSU, mobile stroke unit; and tPA, tissue-type plasminogen activator.

*Reported in mean only.
† Did not report whether mean or median.
‡50th quantile from unadjusted quantile regression analysis using first ambulance dispatch.

Estimate of Disability Avoided

In previous studies, authors have estimated that for every minute of treatment delay, a median of 1.8 days of healthy life are lost for thrombolysis,7 and a median of 4.3 days of healthy life are lost for EVT (in addition to thrombolysis).8
Using ambulance dispatch-to-treatment time savings for MSU patients, we estimated an overall median of 20.9 disability-adjusted life years saved through providing thrombolysis 42.5 minutes earlier for 100 patients, while an estimated median 24.6 disability-adjusted life years were saved through providing EVT 51 minutes earlier for 41 patients.

**Discussion**

In the first operational year, the Melbourne MSU has demonstrated substantial time savings for both intravenous and endovascular reperfusion therapies for ischemic stroke. After accounting for the absolute number of patients treated and the estimated disability avoidance from earlier treatment, the clinical impact on disability avoidance was greater for patients receiving earlier EVT compared with earlier thrombolysis alone. This was driven primarily by the more powerful effect of EVT compared with thrombolysis, rather than the small difference in absolute time saving between the 2 therapies.

The benefit in EVT patients was primarily driven by prehospital MSU diagnosis of large vessel occlusion, which enabled bypass of a local non-EVT center directly to a comprehensive stroke center in almost 50% of patients with large vessel occlusion. Even when patients were located close to an EVT center, MSU prenotification and facilitated workflows achieved a reduction in hospital arrival to arterial puncture by one-third. Furthermore, the time saving was seen despite the majority of EVT patients receiving repeat imaging in hospital to visualize the extracranial circulation. This need for further imaging is diminishing with increasing familiarity of the service and improved prehospital selection of patients appropriate for direct transfer to the angiography suite.

Previous studies that estimated disability avoidance have solely reported the impact of earlier thrombolysis. Given the high proportion of large vessel occlusion managed by the Melbourne MSU and the discordance between peripheral population growth and centrally located EVT services, earlier provision and improved triage for EVT is likely to be a major driver of clinical effectiveness for our service. This, however, may not be translatable to other regions worldwide with different locations and concentrations of EVT services.

Prehospital clinical tools are also used in some regions for EVT triage. However, MSU CT angiogram provides definitive identification of large vessel occlusion and is superior for this purpose. Comparative cost-effectiveness of the 2 approaches would be of interest for future research.

For thrombolysis cases, compared with reported worldwide time metrics, the Melbourne MSU showed slightly longer time from dispatch and scene arrival to commencement of thrombolysis. This may be attributable to differences in our local practice, including relatively high baseline severity of our MSU thrombolysis cases who often have difficult on-scene extrication, coupled with strict no lift manual handling policies used by Ambulance Victoria, which demands lengthy slide techniques for immobile patients and possible engagement of a separate manual handling ambulance. Almost all thrombolysis patients also received CT angiography for confirmation of vessel occlusion and trials recruitment, but this was often done in parallel with thrombolysis administration. These factors, however, did not influence the overall time savings for thrombolysis compared with local controls, which appear similar to published worldwide time metrics. We also used the time from first ambulance dispatch, rather than the more commonly reported MSU dispatch, to better reflect true time savings, as the latter will overestimate time difference if the MSU receives delayed activation by an attending paramedic crew.

The time savings for thrombolysis achieved by the MSU are undoubtedly strongly influenced by prehospital treatment but additionally may be influenced by MSU staffing of a neurologist or senior fellow, who differ in experience and potential adherence to treatment guidelines compared with a typically more junior in-hospital team. The MSU may also have triaged treated patients away from non–thrombolysis-capable sites, which are not included in controls, thereby underestimating time savings.
Our study has several limitations. Overall numbers are still small given data were analyzed only for the first operational year and our analyses could be considered exploratory in nature. We extrapolated dispatch-to-hospital-arrival (prehospital only) times for thrombolysis patients and dispatch-to-arterial-puncture times (prehospital and in hospital) for EVT based on cases presenting to the RMH, due to ambulance-linked hospital data being unavailable from other centers. While we acknowledge that this may not be fully representative of our region, the RMH performs the most EVT cases in our state and controls due to the prehospital environment of the MSU.

We have identified a number of lessons and challenges for MSU interventions. The flexibility to change ambulance dispatch algorithms may be limited depending on local systems, so a multitiered approach may be required, including greater self-triage autonomy for the MSU to attend or decline cases, education of emergency call-takers, and familiarization of paramedics with the MSU service to initiate activation as soon as possible for cases where the MSU is not co-dispatched. Second, the current lack of CT perfusion capability on MSU scanners worldwide also limits some management options, including diagnostic confirmation of stroke where the clinical features are unclear, thrombolysis for wake-up stroke and patients in the 4.5- to 9-hour window, selection for EVT beyond 6 hours, and ability to recruit for trials using CT perfusion selection. The Ceretom MSU CT angiogram also does not cover the aortic arch and carotid bifurcation that would allow the assessment of proximal vascular access for EVT planning. We anticipate that the increasing uptake of MSU services worldwide will generate interest in developing such capabilities for scanners able to be utilized by MSUs.

Third, the workload of the Melbourne MSU in the first year was high but could only cater for ≈65% of all stroke dispatches within the 20-km radius during MSU operating hours, which covers only around a third of the metropolitan Melbourne population. This indicates that a sufficient caseload exists that would support additional MSU services in our region. There are 3 MSU services operating in Berlin, Germany, with a population of ≈3.8 million.

Our study has several limitations. Overall numbers are still small given data were analyzed only for the first operational year and our analyses could be considered exploratory in nature. We extrapolated dispatch-to-hospital-arrival (prehospital only) times for thrombolysis patients and dispatch-to-arterial-puncture times (prehospital and in hospital) for EVT based on cases presenting to the RMH, due to ambulance-linked hospital data being unavailable from other centers. While we acknowledge that this may not be fully representative of our region, the RMH performs the most EVT cases in our state and receives EVT transfers from a broad range of hospitals. Because of association of EVT volume with workflow, it is possible that this might have underestimated time savings had we compared all EVT centers across Melbourne. The RMH is also centrally located in Melbourne and ambulance transport times could potentially be shorter than outer metropolitan stroke centers where living density is lower, again resulting in a potential underestimate of time savings. Our control cases were also largely historical rather than contemporaneous. This was a deliberate decision as the clinical characteristics and in-hospital workflow of the control group may be altered by concurrent operation of the MSU within the same geographic region. Such comparisons may, therefore, be affected by evolutions in workflow practice, although we have attempted to mitigate this for EVT cases by using more recent data. The randomized BEST-MSU (Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit) and B_PROUD (Berlin Prehospital or Usual Delivery of Acute Stroke Care) trials are ongoing and prospectively compare the effect of MSUs with standard of care in emergency departments. Finally, we were not able to ascertain stroke mimics that received thrombolysis in our study but note that treated mimic cases are likely to be present in both MSU and control cohorts, as well as the previous literature used to estimate disability-adjusted life years. We acknowledge that there may be imbalances in the rates of treated mimics between cases and controls due to the prehospital environment of the MSU.

We have identified a number of lessons and challenges for MSU operations. First, dispatch algorithms have limited sensitivity and specificity, with around 60% of MSU dispatches stood down by the first paramedic crew before MSU arrival, due to a low likelihood of stroke. Poor specificity increases running expenses and limits the ability of the MSU to respond to concurrent cases that may be more appropriate for MSU interventions. The flexibility to change ambulance dispatch algorithms may be limited depending on local systems, so a multitiered approach may be required, including greater self-triage autonomy for the MSU to attend or decline cases, education of emergency call-takers, and familiarization of paramedics with the MSU service to initiate activation as soon as possible for cases where the MSU is not co-dispatched.
Finally, we are also actively exploring telemedicine options for remote assessment and management by a neurologist. Telemedicine validation studies in Houston\textsuperscript{3} and Berlin\textsuperscript{4} provide evidence that remote video assessment is reliable. However, while for the Houston experience few connection issues were reported, the Berlin team experienced ≥17% telemedicine failure rate using similar hardware to the Melbourne MSU. In addition, although telemedicine hardware exists within the vehicle, most of our clinical assessments are completed outside the MSU, making further exploration of reliable and portable telemedicine hardware necessary to provide telemedicine-led treatment delivery on the MSU in future.

Conclusions
The first operational year (365 days) of the Melbourne MSU has shown substantial time savings to commencement of both thrombolysis and EVT. Based on estimated disability avoidance, the greatest clinical impact was from earlier provision of EVT, due to the more powerful treatment effect compared with thrombolysis. This indicates that accurate prehospital diagnosis, triage, and provision of faster EVT is a major benefit of MSU operation in our locality.

Sources of Funding
The Melbourne Mobile Stroke Unit and associated projects received funding from the Australian Commonwealth Government, Victorian State Government, Royal Melbourne Hospital Neurosciences Foundation, Stroke Foundation, The Florey Institute of Neurosciences and Mental Health, the University of Melbourne, Boehringer Ingelheim, and private donation.

Disclosures
H. Zhao discloses grants from the Australian Commonwealth Government and the University of Melbourne and personal fees from Boehringer Ingelheim. Dr Cadilhac discloses grants from the National Health and Medical Research Council, Melbourne Health, Boehringer Ingelheim, Medtronic, and Shire. D.M. Brooks discloses grants from Stryker and personal fees from Microvention and Cook. Dr Thijs discloses personal fees from Boehringer Ingelheim, Pfizer/BMS, Medtronic, and Bayer. Dr Mitchell discloses grants from Stryker and Medtronic and personal fees from Microvention. Dr Parsons discloses being on the advisory boards of Allergan, Amgen, Bayer, Boehringer Ingelheim, and Servier. Dr Davis discloses grants from the National Health and Medical Research Council and personal fees from Boehringer Ingelheim and Medtronic. The other authors report no conflicts.

References


