出國報告（出國類別：進修）

澳洲Monash Health進修參訪心得

服務機關：成大醫院
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派赴國家：澳洲
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2024/07/04-2024/08/20
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摘要

此次出國進修計畫，我前往澳大利亞墨爾本的 Monash Health，進行於急性中風入院處置與區域轉診系統的參訪研究。主要學習內容包括地理空間分析技術在區域轉診中風救治中的應用，以及移動中風救護車（MSU）的實際運作。Monash Health 透過地理信息系統（GIS）來規劃中風患者的最佳救治路徑，並確定取栓醫院的最佳配置，以縮短患者在黃金時間內接受治療的時間。此外，MSU 提供急性中風患者早期診斷與治療，有效加速了中風病人接受治療的時間。但儘管 MSU 技術成效顯著，但高昂的運營成本和資源需求是重要的挑戰。Monash Health 的中風病人入出院流程，以及針對短暫缺血性中風 (Transient ischemic attack, TIA) 患者的M3T pathway，展示了不同的流程模式可能帶來的影響。這些流程不僅縮短了住院天數或不住院，不但能提升病床利用率，同時並不影響病人的預後表現。這些創新處理流程在中風住院與區域轉診資源配置上提供了寶貴的經驗，同時也為未來在台灣的應用上提供了重要的參考。

關鍵字：急性中風、地理空間分析、移動中風救護車（MSU）

目　次

目的

在本次出國進修計畫中，我前往了**澳大利亞墨爾本的 Monash Health**，這是墨爾本東南部主要的公家急症醫院之一。該醫院同時也是國際知名的教學與研究機構，提供全面的外科、內科、輔助醫療和心理健康服務。

時間與地點

- **訪問時間**：2024 年 7 月 4 日至 8 月 20 日。
- **訪問地點**：**Monash Medical Centre Clayton**，位於墨爾本市郊，是該市提供多專科醫療服務的核心機構之一，主要服務墨爾本東南部社區。

進修主題

此次進修的主題為**急性中風智慧轉診區域規劃參訪研究**。我的主要目的是學習並觀察 Monash Health 的中風診療系統，包括從病患入院前的區域規劃處置、到入院後的檢查及治療流程的特色。

合作對象

在此期間，我與主要的兩位專家進行了密切的合作與交流：

1. **Prof. Henry Ma**：Monash Health 的神經科主任，自 2015 年起擔任此職位，並兼任 Monash University 的醫學教授。他曾擔任 Monash Health 內科培訓主任，並且是澳洲皇家內科醫學會（RACP）全國考試委員會和成人內科基本培訓委員會的資深成員。他的博士論文探討了缺血半影(Ischemic penumbra)的影像學研究，並與知名的 Donnan 教授和 Davis 教授合作，發現了半影可超過傳統的 3 小時時間窗，這為 EXTEND-IV 試驗提供了理論基礎。該試驗的結果在 2018 年世界中風大會上公佈，並成功改變了歐洲和澳洲的治療指南。
2. **Prof. Thanh Phan**：**Monash Medical Centre 的神經科研究主任**，也是國際知名的急性中風治療專家。他的專業背景涵蓋急性中風的影像學分析、轉診系統優化以及地理空間分析技術。Prof. Phan 帶領的研究團隊在急性中風治療領域有著重要的貢獻，尤其在智慧轉診系統和急診醫療資源分配的優化方面。他的研究包括如何運用地理空間技術來優化中風患者的救治路徑，並且通過數據模擬來評估不同醫療設施的服務區域和患者轉診時間。

訪問目標

- 深入了解 Monash Medical Centre 如何在急性中風救治中運用地理分析技術實施區域轉診資源配置。
- 探討急性中風病患的轉診與治療流程，學習其快速處理模式，包括門診與住院管理方式。
- 通過與當地專家的交流，考察急性中風的地理空間分析技術及其在轉診優化中的應用。

過程

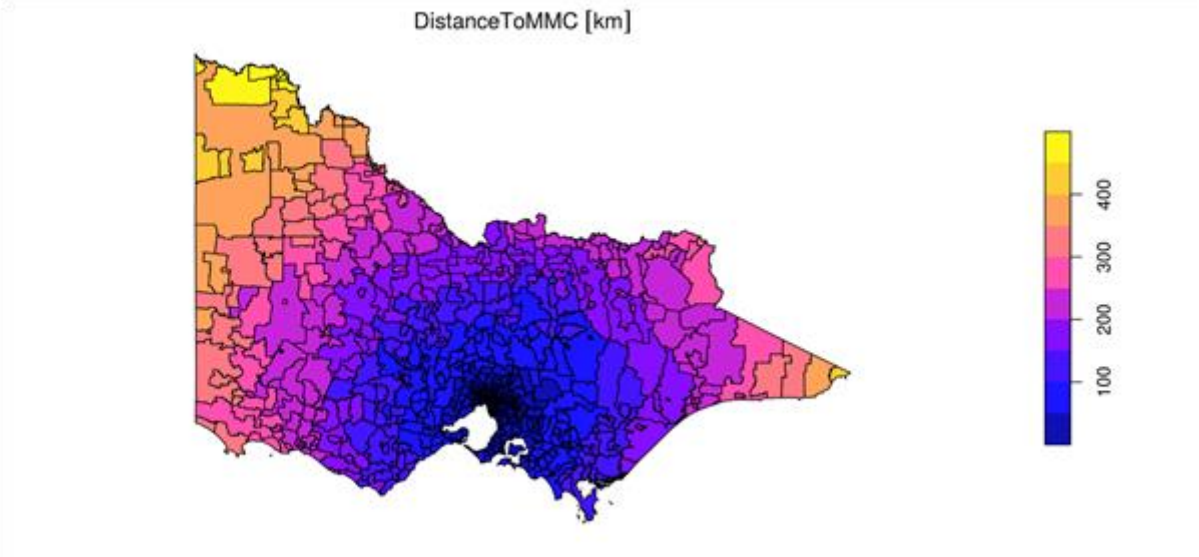
在此次訪問 Monash Health 期間，我主要專注於**急性中風患者的處置流程**，特別是從患者發病到到達急診室、接受治療的整體流程優化，並與當地專家進行了深入交流，探討該系統在台灣的應用可能性。

主要學習內容

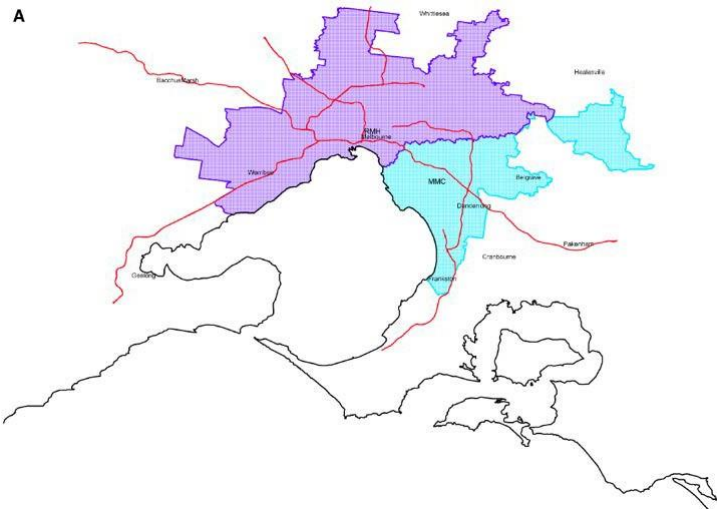
1. **地理空間分析技術**

在中風患者救治中，地理空間分析技術的應用至關重要。Monash Health 運用了地理信息系統（GIS）來計算患者從發病地點到最近醫院的最佳轉診路徑，這些技術有效提高了患者在黃金時間內接受治療的機率。GIS 技術通過分析路況、醫院位置和救護車的反應時間，幫助醫療機構更好地分配資源，優化救護系統。

軟體工具與地理空間分析的實際應用：Monash Health 使用了多種軟件工具來進行地理空間分析。該技術的應用包括利用 **R 和 Python** 等語言來進行分析。具體例子包括基於郵政編碼區域的 **Choropleth 圖**來顯示中風病例的分布(圖一)，以及估算復健中心的服務區域，並基於道路網絡距離計算取栓中心負載的模型（圖二）。這些應用有助於規劃中風患者的最佳救治路徑並優化資源分配。



圖一、維多利亞省各郵遞區號至 Monash Health 之距離



圖二、取栓中心負載模型

表一、於不同時段到取栓中心距離時間模型

	Model 1a					
	RMH			MMC		
Time of Day, h	Coverage, km²	Time to RMH, min	%Cases <30 min	Coverage, km²	Time to MMC, min	%Cases <30 min
0100	1970	20 (IQR 15.2–26.4)	85	959	18 (IQR 13.7–22.2)	94
0815	1765	26 (IQR 19.4–33.7)	66	1164	21 (IQR 15.3–26.1)	85
1230	1909	20 (IQR 16.0–26.0)	87	1020	18 (IQR 13.6–22.1)	94
1715	1802	22 (IQR 17.3–27.4)	82	1126	19 (IQR 14.4–24.1)	90

2. 移動中風救護車（Mobile Stroke Unit, MSU）的應用

移動中風救護車是一種提供急性中風診斷、評估及/或治療服務的救護車。這是一個配備專業人員、成像設備和治療工具的救護車，專門用於在患者發病後的第一時間內進行中風診斷和治療。這一概念最早於 2003 年在德國提出，並於 2010 年在德國 Homburg 首次實施。2014 年，美國休斯頓推出了首個移動中風救護車系統，隨後該技術在挪威、阿根廷、加拿大等國家逐步推廣應用。

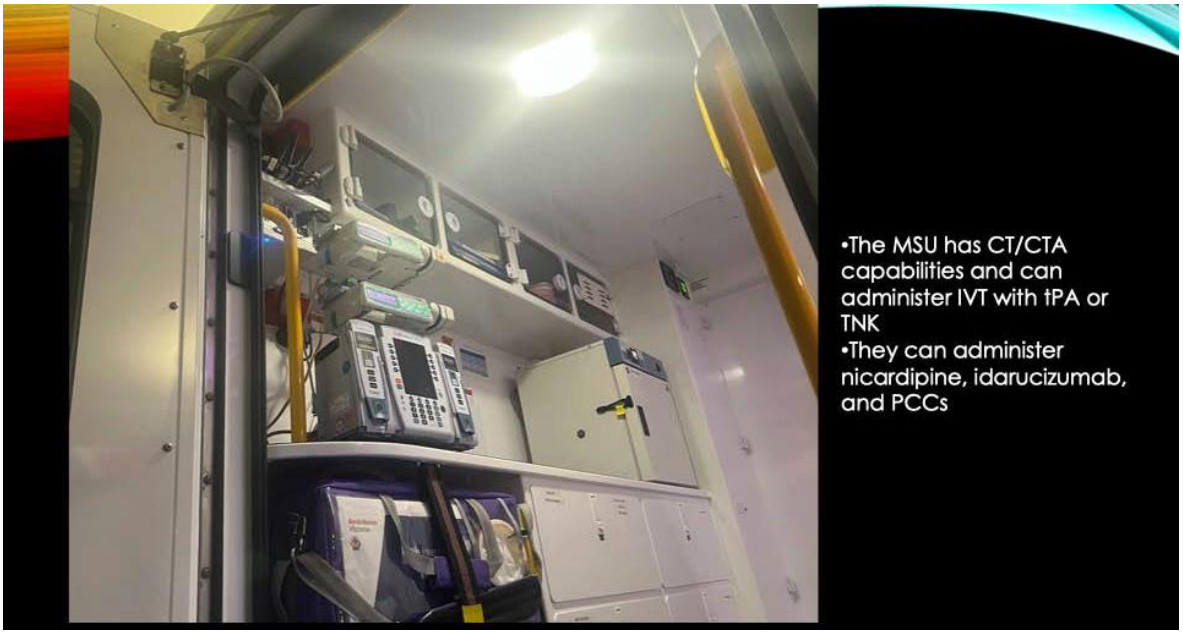
Monash Health 也開展了移動中風救護車（MSU）的研究。MSU 的目標是在患者到達醫院前就提供初步的診療服務，特別是對於需要溶栓或血管內治療的患者，這可以大幅縮短治療延遲。

MSU 的挑戰與成本問題：儘管移動中風救護車（MSU）在提升治療效率方面顯著有效，但運營成本是一個重要的挑戰。每輛 MSU 的運營成本約為 100 萬美元，並且每年需要額外的 100 萬美元來維持運行。MSU 團隊由一名緊急醫療服務（EMS）司機、一名技術員、一名護士、一名放射科工作人員以及一名中風神經科醫生組成(圖三)。在墨爾本，MSU Crew 的工作時長為 10 小時，僅涵蓋星期一到星期五，無法提供全天候的覆蓋。醫院還需承擔管理遠距中風醫療服務的責任，但通常不會額外支付給提供此服務的醫師。

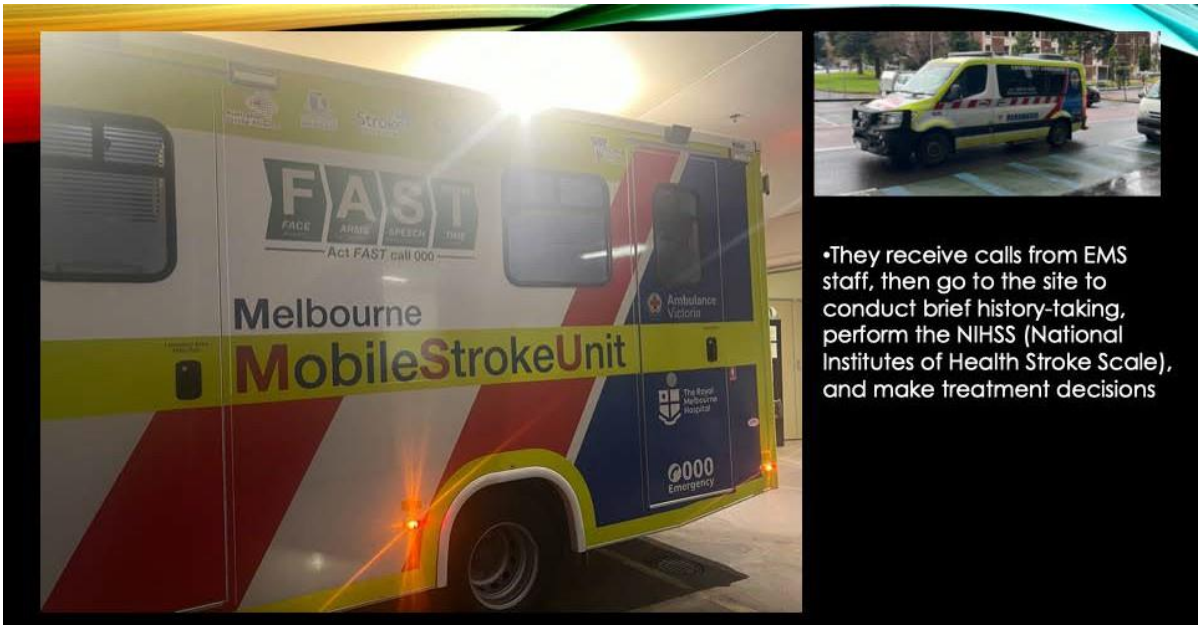
圖三、MSU 團隊

圖四、移動中風救護車（MSU）

圖五、移動中風救護車內 CT/CTA



圖六、移動中風救護車內可執行 tPA 或 THK



圖七、接到 EMS 電話，可立即前往收集病史及評估

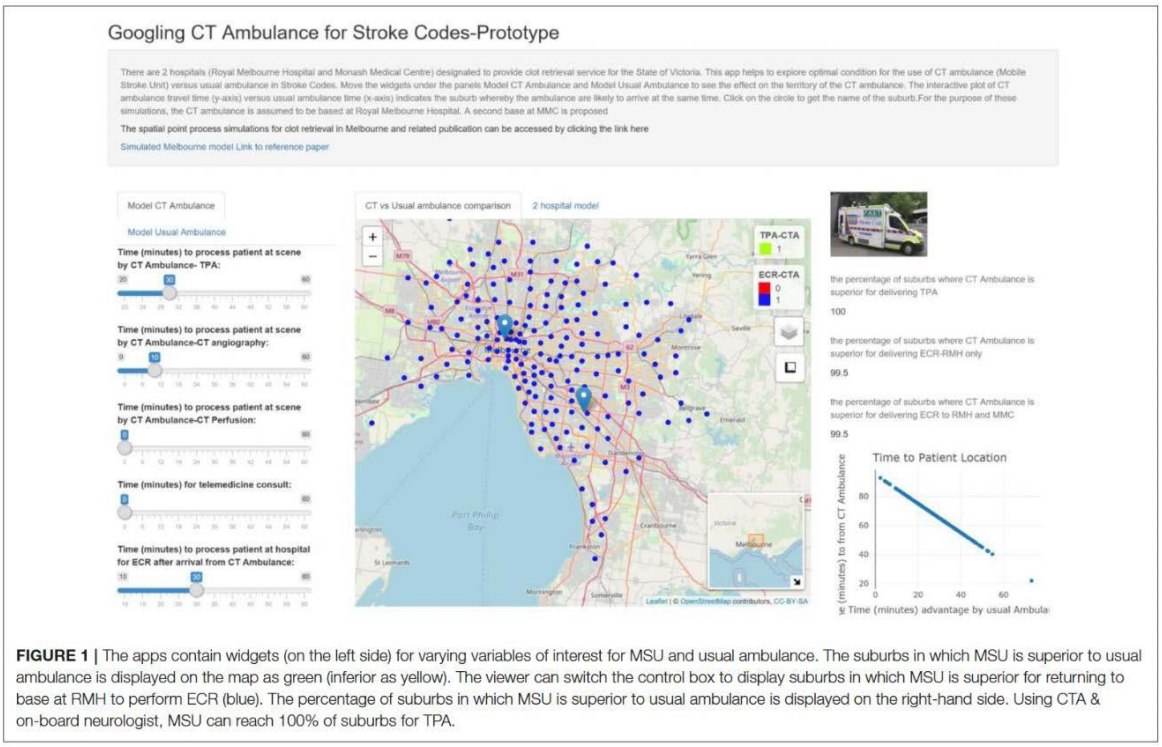


FIGURE 1 | The apps contain widgets (on the left side) for varying variables of interest for MSU and usual ambulance. The suburbs in which MSU is superior to usual ambulance is displayed on the map as green (inferior as yellow). The viewer can switch the control box to display suburbs in which MSU is superior for returning to base at RMH to perform ECR (blue). The percentage of suburbs in which MSU is superior to usual ambulance is displayed on the right-hand side. Using CTA & on-board neurologist, MSU can reach 100% of suburbs for TPA.

圖八、MSU 之地理空間資料分析，分析 MSU 置放位置

除了資金和人力資源挑戰，移動中風救護車在文獻中還面臨以下幾個方面的挑戰：

- **成本效益問題**：目前尚不確定 MSU 的運營是否能夠實現成本效益，大部分研究基於小規模模擬和預測。這需要通過更大規模的臨床試驗來提供更多數據。
- **藥品成本**：例如，每個 tPA 治療成本約為 8000 美元，而一些替代藥物（如 Tenecteplase, TNK）可能有助於降低成本。
- **基礎設施挑戰**：救護車與中風中心之間的協作常常因為溝通和協作不佳而受到影響，需要改進流程。
- **地理因素**：大多數 MSU 項目集中在大城市，然而，偏遠地區的覆蓋仍是一大挑戰。
- **效率問題**：據統計，只有 33%-50%的 MSU 出勤是由中風引起，並且其中一部分患者最終接受溶栓或血管內治療的比例偏低。

MSU 的成效：儘管 MSU 的挑戰眾多，但在某些地區，MSU 已經顯示出顯著的成效。數據顯示，MSU 項目能夠顯著縮短 onset-to-imaging 及 onset-to-treatment 的時間。例如，在美國托萊多、克里夫蘭以及德國柏林等地的 MSU 項目，其從發病到影像檢查（alarm to imaging）及從發病到治療（alarm to treatment）的時間顯著縮短，這有助於提高患者的存活率和治療效果。

3. **中風患者的快速診斷與治療**

在 Monash Medical Centre，**中風患者的住院時間通常較短**，大多數病例的住院時間僅為 3 至 5 天。即使接受了溶栓治療，患者在隨後進行腦部 CT 掃描後，通常

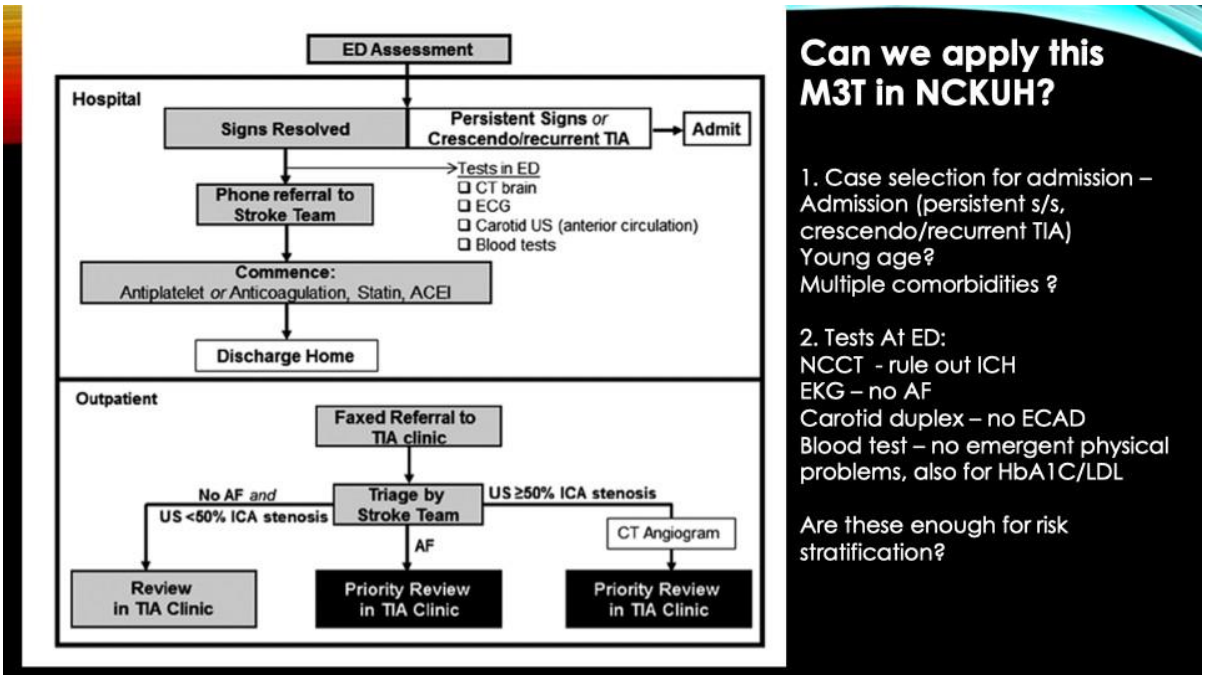
可於第 2 或第 3 天出院。MRI 掃描通常安排在門診進行，並在 1 至 2 週內進行回診。此後，患者通常被轉介至當地家庭醫師處進行進一步的回診和處置。

所有患者在入院時均會進行 CTA（電腦斷層血管攝影）和 CTP（電腦斷層灌注成像），以便快速確定中風類型並制定治療方案，但並不常規進行 MRI 檢查。此外，這些患者不接受靜脈注射液（Intravenous fluids），部分檢查會在門診進行。這一流程強調了快速診斷和僅實施有證據支持的治療的重要性，並能有效縮短住院時間，提高治療效率與病床輪轉率。

4. **M3T（Monash TIA Triaging and Treatment）路徑**

在 2003 年，Monash Health 的 TIA 患者通常會住院治療，只有少數患者會直接從急診室出院。當時，出院患者的管理和轉診主要取決於急診醫師的判斷，並且由急診安排神經科醫師之回診轉診並非常規進行。

隨著 M3T 路徑的建立，所有 TIA 患者在進入急診室後，便會接受快速評估和管理。這些評估包括：**NCCT（非對比電腦斷層掃描）、EKG（心電圖）、頸動脈超音波檢查（Carotid Duplex）以及血液檢查**，並由急診醫師與中風團隊協作進行。隨後，根據再中風風險之血管機制（大血管狹窄或心房顫動患者）優先安排隨後的回診。如果患者出現持續症狀、反復性 TIA 或其他急性醫療問題，則會被收入中風病房，其他患者則進入 M3T 系統的非住院管理流程。這一系統能有效減少住院需求，並確保高風險患者能夠快速接受進一步的診斷與治療。



圖九、M3T（Monash TIA Triaging and Treatment）路徑

M3T 路徑的成效顯著。例如，在 M3T 管理的 TIA 患者中，92.2%的患者在出院時接受了抗血小板治療，相較於之前的模型，該比例為 82.0%（P=0.005）。然而，出院時接受降血脂藥物(Statin)或降壓藥的患者比例則無顯著差異。M3T 還縮短了對於有同側頸動脈狹窄 ≥50% 患者的再血管化治療時間，M3T 系統中，這類患者的再血管化中位時間為 17.5 天（四分位距 4　44 天），而先前模型中為 26.5 天（四分位距 6.5　149.5 天）（P=0.59）。可能基於這些改進，有助於顯著降低 M3T 路徑病患的中風風險。在 M3T

系統中，90 天內的中風發生率為 1.50%（7/468，95% CI, 0.73% 3.05%），而在先前的模型中，該數值為 4.67%（7/150，95% CI, 2.28% 9.32%），呈現差異顯著（P=0.03），風險差異為 3.17%。

5. **臨床試驗與研究的參與**

在此次澳洲參訪中，我有機會觀摩來自不同國家的專家進行合作，特別是在澳洲研究網絡的協助下，建立了與全球多個研究機構的聯繫。同時，我還參與了台澳中風學會的合作項目，這進一步促進了台灣與澳洲在中風治療與研究上的交流與進步。這些合作不僅拓展了國際友誼，還推動了跨國研究的發展。

心得

此次訪問 Monash Health，對我而言是一個極具啟發性的經驗。這不僅是一個了解當地醫療系統如何處理急性中風患者的機會，更讓我深刻體會到創新技術與國際合作對於中風治療的重要性。透過這次的訪問與學習，我對區域轉診系統、地理空間分析技術、M3T pathway 及移動中風救護車（MSU）的應用有了更深入的認識，並思考如何將這些技術和系統運用於台灣的醫療環境中。

1. 區域轉診系統與地理空間分析技術的應用

Monash Health 的區域轉診系統與地理空間分析技術展示了如何利用先進的地理空間分析技術來優化患者救治流程。特別是在中風治療的黃金時間內，GIS 系統通過精確計算最佳路徑，幫助患者快速到達適當的醫療機構，這種精準的調度有助於縮短治療延遲。我認為，這樣的技術對於台灣這樣擁擠且交通複雜的城市也非常具有應用潛力。我期待能將這樣的技術與本地的醫療網絡結合，提升急性中風患者的救治效率。

2. M3T Pathway 的潛力應用

M3T pathway 是 Monash Health 為應對 TIA（短暫性腦缺血發作）患者快速診斷和治療而設計的精確流程，這一系統顯著改善了患者的治療效果並減少了住院需求。M3T 的成功啟示了我，台灣可以引入類似的流程來應對輕度中風和 TIA 患者，特別是在大型醫療中心資源緊張的情況下。具體來說，M3T pathway 強調了在急診室進行快速的影像學診斷（如 NCCT 或 CTA/CTP），並依據血管機制來安排隨後的治療或門診回診。該系統還能識別高風險患者並進行進一步住院觀察，從而確保資源的有效利用。

M3T pathway 不僅能夠縮短診斷時間，還能降低住院率，並通過對高風險患者進行早期干預來預防更嚴重的中風。這樣的模式在台灣的醫療系統中具有很大的應用潛力，特別是針對那些擁有高危因素但症狀輕微的患者。我認為，這樣的流程可以幫助台灣的醫療系統更有效地管理中風風險，並大幅減少由於過度住院導致的資源浪費。

3. 移動中風救護車（MSU）的潛力與挑戰

MSU 技術讓我充分認識到在患者到達醫院之前進行早期診斷與治療的好處。MSU 配備專業團隊及醫療設備，能夠實現院前診斷並進行溶栓治療，這大大縮短了發病到治療的時間（onset-to-treatment time）。在 Monash Health 的實際應用中，這項技術顯著提高了急性中風患者的存活率和預後結果。然而，我也了解到 MSU 在運營成本方面的挑戰，每年約 100 萬美元的運營費用及高額的設備和人力需求使得其推廣面臨困難。這啟發我在考慮台灣是否引入 MSU 技術時，不僅要考慮其治療效果，還需評估其財務可行性和資源配置問題。

4. 臨床試驗與國際合作的價值

我在此次訪問中，最為寶貴的經驗之一是參與了由Henry Ma 教授領導的中風臨床試驗，如隨即即將進行的 EXTERNAL 試驗。這讓我深刻體會到國際合作在提升治療效果和推動學術研究方面的巨大潛力。與澳洲研究網絡及台澳中風學會的合作，進一步深化了兩地在中風治療與研究方面的聯繫，為雙方醫療技術的進步奠定了基礎。我認為這種跨國合作對於解決中風治療中的共通挑戰具有重要意義，並期待將這些學習成果應用於台灣的中風治療系統中。

5. 對未來的展望

此次訪問後，我對如何應用 Monash Health 的成功經驗於台灣的醫療體系有了初步的思考。GIS 技術可以協助我們改進救護車調度系統，縮短急救反應時間；MSU 則可以作為大都市或鄉鎮區域的一種創新解決方案，為中風患者提供早期診斷與治療，但須審慎考慮資源配置；而 M3T pathway 則能夠成為輕微中風和 TIA 患者管理的最佳範例，從而減少不必要的住院和資源浪費。我還認為，台灣與澳洲在中風治療領域的合作將進一步深化，特別是在臨床試驗和醫學教育方面，雙方可以互相借鑒，提升彼此的醫療水準。

總體來說，這次訪問 Monash Health 是一次富有收穫且充滿啟發的學習經驗。它不僅擴展了我對中風治療與流程改善的視野，還啟發了我如何將這些不同的思考視野與國際合作的成果引入台灣，為我們的患者或醫療資源帶來合適的治療流程規劃與配置。未來，我將持續探索如何應用這些新技術於台灣的醫療環境，並期待與更多國際醫療團隊合作，共同推動全球中風治療的進步。

總結建議事項

1、可 revise minor stroke/TIA stroke pathway 以縮短急診留觀時間、住院天數以及調整醫療資源分配

目前輕度中風及 TIA 患者的診療在急診留觀時間和住院天數上仍有優化空間，特別是在資源緊張的醫療環境中。根據 Monash Health 的 M3T pathway 經驗，建議可以透過引入快速診斷及分級治療流程，縮短急診處理時間並減少不必要的住院。具體做法包括：

(1) 加強急診室中影像學檢查的速度（如 NCCT 及 CTA/CTP），確保早期發現中風風險。
(2) 對無重大血管狹窄的輕度中風患者提供出院後的回診和風險評估。
(3) 縮短低風險患者的住院觀察時間，集中資源於高風險患者（如大血管阻塞或心房顫動患者），這不僅能夠提高醫療資源的利用率，還能顯著縮短住院天數，進一步降低醫療成本。

2、持續維持與 Monash Health 之研究聯盟，並維持國際臨床試驗案之參與與促進雙方機構之合作

與 Monash Health 的合作對於提升台灣的中風治療水準具有深遠意義。雙方可以共同參與國際臨床試驗，這不僅有助於引進新的治療策略，也能促進台澳兩地中風學會的合作。具體建議包括：

(1) 定期舉辦雙邊學術交流會議，分享最新的臨床試驗結果和治療進展。
(2) 建立長期的臨床試驗平台，推動中風治療的新技術和新藥物的研發與應用。
(3) 促進研究人員與醫師的定期雙向交流學習，提升雙方在中風治療及臨床試驗上的專業技術和管理經驗。

3、Mobile Stroke Unit 有其實際實行之困難，同時由於兩地醫院密度不同，需進行醫學經濟效益相關評估以確認是否要實際推動

移動中風救護車（MSU）在 Monash Health 的應用證實了其在縮短診斷和治療延遲方面的有效性。然而，由於台灣的醫院密度相對較高，MSU 的需求和效益需要進行更深入的評估。建議如下：

(1) 進行醫學經濟效益評估，計算 MSU 在台灣大都市區（如台北、高雄）的實際運行成本與其對中風救治效率提升的影響。
(2) 根據不同地區的需求，考慮是否需要針對偏遠或醫療資源缺乏地區部署 MSU。
(3) 研究可替代方案，如加強地面救護車的中風診療能力及快速轉診通道，適應不同區域的需求。

4、需持續進行急性中風之 geospatial analysis，以確認於區域內之急性中風處置需是否需持續推動直接到院模式，或仍維持目前部分直接到院、部分轉送模式。

地理空間分析對於優化急性中風患者的轉診和救治模式非常關鍵。台灣現行的部分患者直送專業醫院，部分經由基層醫院轉診的模式需要持續評估。建議如下：

(1) 繼續進行區域內急性中風患者的地理空間分析，評估救護車到院時間、醫療資源分配和各醫院的救治能力。
(2) 基於分析結果，確定是否應該推動更多中風患者直接取栓醫院（Mothership model），還是保持現有的部分患者經轉診模式，以確保資源最優化配置。

評估不同區域的地理條件，針對台灣各縣市的交通與醫院分布，調整救護車和救治策略，確保急性中風患者能夠在最短時間內接受適當治療。

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Stroke

TOPICAL REVIEW

Section Editors: Joseph Broderick, MD, and Michael D. Hill, MD

Mobile Stroke Units: Evidence, Gaps, and Next Steps

Babak B. Navi, MD, MS; Heinrich J. Audebert, MD; Anne W. Alexandrov, PhD; Dominique A. Cadilhac, PhD; James C. Grotta, MD; on behalf of the PRESTO (Prehospital Stroke Treatment Organization) Writing Group

ABSTRACT: Mobile stroke units (MSUs) are specialized ambulances equipped with the personnel, equipment, and imaging capability to diagnose and treat acute stroke in the prehospital setting. Over the past decade, MSUs have proliferated throughout the world, particularly in European and US cities, culminating in the formation of an international consortium. Randomized trials have demonstrated that MSUs increase stroke thrombolysis rates and reduce onset-to-treatment times but until recently it was uncertain if these advantages would translate into better patient outcomes. In 2021, 2 pivotal, large, controlled clinical trials, B_PROUD and BEST-MSU, demonstrated that as compared with conventional emergency care, treatment aboard MSUs was safe and led to improved functional outcomes in patients with stroke. Further, the observed benefit of MSUs appeared to be primarily driven by the higher frequency of ultra-early thrombolysis within the golden hour. Nevertheless, questions remain regarding the cost-effectiveness of MSUs, their utility in nonurban settings, and optimal infrastructure. In addition, in much of the world, MSUs are currently not reimbursed by insurers nor accepted as standard care by regulatory bodies. As MSUs are now established as one of the few proven acute stroke interventions with an effect size that is comparable to that of intravenous thrombolysis and stroke units, stroke leaders and organizations should work with emergency medical services, governments, and community stakeholders to determine how MSUs might benefit individual communities, and their optimal organization and financing. Future research to explore the effect of MSUs on intracranial hemorrhage and thrombectomy outcomes, cost-effectiveness, and novel models including the use of rendezvous transports, helicopters, and advanced neuroimaging is ongoing. Recommended next steps for MSUs include reimbursement by insurers, integration with ambulance networks, recognition by program accreditors, and inclusion in registries that monitor care quality.

Key Words: ambulance ■ emergency medical services ■ evidence-based medicine ■ stroke ■ thrombolytic therapy

Stroke is a common cause of death and disability. While once an untreatable disease, there are now several proven interventions for acute stroke, including specialized stroke units, intravenous thrombolysis, and mechanical thrombectomy.[1–6] The latter 2 are time-sensitive treatments that aim to recanalize occluded cerebral arteries, and the sooner they are administered, the safer and more effective they are.[5,6] For instance, a patient's odds of becoming normal or near-normal is ≈70% higher if they receive intravenous thrombolysis within 60 minutes of stroke onset, the so-called golden hour, than if they receive it 61 to 270 minutes from onset.[7] Stroke systems-of-care have been transformed through prehospital notification by emergency medical services (EMS), individualized patient routing to stroke capable hospitals, and dedicated stroke teams to increase the frequency and speed of these acute stroke recanalization therapies. Unfortunately, in the United States, only about 10% of stroke patients receive thrombolysis or thrombectomy, and only about 1% of those are treated within the golden hour, indicating that current systems-of-care require reexamination.[7,8]

Mobile stroke units (MSUs) are specialized ambulances that include health professionals experienced in acute stroke care that can diagnose and treat stroke patients on scene. These specialized ambulances were first developed in Saarland, Germany in 2008, with the expectation that bringing a stroke unit to the patient

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would lead to quicker thrombolysis times, thereby improving stroke outcomes.[9] Soon thereafter, MSUs spread to Berlin and Houston and have since proliferated to over 25 sites around the world, including Asia and Australia (Figure 1).[10] In 2016, PRESTO (Prehospital Stroke Treatment Organization) was formed.[11] This international consortium aims to improve stroke outcomes, enhance collaborative research, and facilitate MSU distribution.

While different iterations exist, most MSUs contain EMS personnel, a radiology technician, a nurse or nurse practitioner, and a neurologist, either onboard or available by telemedicine. Initially, neurologists rode on MSUs; however, because of time and fiscal constraints and observed inefficiencies, many programs expanded the role of an on-board nurse practitioner or transitioned to a telemedicine approach, especially because one neurologist can then simultaneously staff multiple MSUs.[12] The staffing models for different MSUs are influenced by local ambulance and hospital protocols, regulations, and the availability of specialist staff with stroke expertise.[12]

MSUs are equipped with a computed tomography (CT) scanner, point-of-care laboratory tests, and medicines, including tPA (tissue-type plasminogen activator), labetalol, nicardipine, anticoagulant reversal agents, and benzodiazepines (Figure 2). MSU CT scanners can perform CT angiograms; however, imaging is generally limited to the head and upper neck unless a full-body CT scanner with auto-injection capability is employed, and this configuration generally requires a larger ambulance.[13] Most MSUs operate in densely populated cities; however, MSUs can serve rural areas and can meet and treat patients with stroke who live remotely at intermediate locations by rendezvousing with standard ambulances.[14,15]

MSUs cost about 1 million US dollars to purchase and up to 1 million US dollars per year to operate (costs depend on operating hours, use of telemedicine, personnel wages, and sophistication of ambulance and machinery).[15,16] Larger ambulances with full-body CT scanners cost more, although at the societal level this could be offset by earlier identification and improved prehospital triage of large vessel occlusive strokes.[13] In most of the world, particularly the United States, MSU stroke care, including administered medications, are currently not reimbursed by insurers and the recouped costs are for EMS transport and occasionally physician billing. Therefore, most MSU programs are almost entirely funded by grants and philanthropy.

Besides costs, other hindrances to widespread MSU implementation include lack of recognition by regulators and government agencies, and questions surrounding MSU feasibility in low resource settings and their utility in rural areas. Further, there are several practical considerations that must be overcome to optimize an MSU system, including integration into regional EMS services and collaboration with regional hospitals who do not operate an MSU.

Given the recently published B_PROUD and BEST-MSU trials establishing the effectiveness of MSU care for patients with suspected acute stroke, herein, we provide an evidence-based review on MSU safety, effectiveness, and cost-effectiveness; the barriers for their widespread implementation and potential solutions; alternative approaches to acute stroke care; and the next steps for MSU programs and systems.

EFFECTIVENESS AND SAFETY

MSUs expedite the delivery of intravenous thrombolysis to patients with stroke. PHANTOM-S was a cluster-randomized (by weeks), open-label, clinical trial that evaluated the impact of MSUs in Berlin, Germany between 2011 and 2013.[17] Among 6182 patients for whom an EMS stroke dispatch was activated, 530 received intravenous thrombolysis and alarm-to-thrombolysis treatment times were 15 minutes faster during MSU weeks than non-MSU weeks. Among patients for whom an MSU was deployed, thrombolysis treatment times were even faster with a 25-minute average reduction as compared with usual care. This resulted in a 10-fold greater proportion of golden hour thrombolysis among patients with ischemic stroke.[18] Further, intravenous thrombolysis was administered more often to patients with ischemic stroke with MSU deployment (33%) versus usual care (21%).[17] Supporting the generalizability of these findings, studies from other countries and settings, including densely populated New York City, have shown similarly reduced thrombolysis treatments times with MSU deployment.[19,20]

MSUs improve the prehospital triage of patients with stroke. In a secondary analysis of PHANTOM-S, fewer patients with cerebrovascular events were delivered to hospitals without stroke units when treated by an MSU (5.5%) compared with standard emergency care (11.6%).[21] The discrepancy between groups was most pronounced for patients with intracranial hemorrhage, whereby 11.3% were delivered to hospitals without neurosurgical capability by MSUs versus 43.0% by conventional ambulance. Investigators from Saarland, Germany conducted a randomized multicenter trial that compared prehospital stroke triage between MSU care and standard ambulances with EMS assessments using the Los Angeles Motor Scale.[22] Among 116 total patients, 100% of those managed by MSUs were correctly triaged to the appropriate stroke center (ie, comprehensive for an intracerebral hemorrhage or large vessel occlusion versus primary for other stroke types) as compared with 69.8% of the standard ambulance group. During 365 days of MSU service in Memphis, where prehospital multiphase arch-to-head CT angiography is routinely performed, all MSU patients (n=27) treated with mechanical thrombectomy bypassed the ED and were admitted directly to the catheterization laboratory.[13]

Figure 1. International map of known active mobile stroke unit programs (depicted by orange dots).
Created through Google Maps platform.

MSUs are associated with better functional outcomes in patients with stroke (Table 1). B_PROUD was a prospective, nonrandomized, controlled trial with blinded-end point assessment conducted in Berlin, Germany between 2017 and 2019.[23] At trial start, MSUs had already been integrated into Berlin's standard EMS practice under the auspices of provisional regular care so that EMS triage operators would simultaneously dispatch an MSU and a regular ambulance for suspected patients with stroke within 4 hours of symptom onset. As prior work had suggested that an MSU would be unavailable for 44% of calls, B_PROUD compared outcomes between patients for whom an MSU was dispatched versus those for whom it was not.

The final cohort comprised 1543 patients with ischemic stroke or TIA who lacked absolute contraindications for intravenous thrombolysis. This included 749 (49%) patients for whom an MSU was dispatched and 794 (51%) patients for whom an MSU was not dispatched. Baseline characteristics were similar between groups. The dispatch-to-thrombolysis treatment time was 20 minutes shorter with MSU dispatch than without, and golden hour treatments occurred in 12.8% of patients with MSU dispatch versus 4.0% of those without. More patients with MSU dispatch were treated with intravenous thrombolysis (60.2% versus 48.1%); however, the numbers of mechanical thrombectomies were similar between groups. MSU dispatch was associated with less patient disability at 3 months, with a significant shift in the modified Rankin Scale (mRS) distribution favoring MSU deployment over conventional care (adjusted common odds ratio for worse outcome, 0.71 [95% CI, 0.58–0.86]). In dichotomized analysis, 53.5% of patients with MSU

Figure 2. Interior pictures of regular-sized and large mobile stroke units displaying their essential components.
Images were provided by PRESTO (Prehospital Stroke Treatment Organization) members from The Royal Melbourne Hospital (**A**) and the University of Tennessee Health Sciences Center (**B**).

Table 1. Summary of Pivotal Trials Evaluating the Efficacy and Safety of Mobile Stroke Units

Trial	B_PROUD	BEST-MSU
Design	Prospective, nonrandomized, controlled trial with blinded outcome assessment	Prospective, multicenter, alternating-week, cluster-controlled trial with blinded adjudication of eligibility and outcomes
Setting	Berlin, Germany	7 US cities (2 in the South, 2 in the west, 2 in the Midwest, and 1 in the Northeast)
Sample size	1543 total (749 MSU vs 794 standard ambulance)	1515 total enrolled (886 MSU vs 629 standard ambulance) and 1047 tPA eligible (617 MSU vs 430 standard ambulance)
No. of sites	15 hospitals in Berlin	7 hospital systems within the US
Recruitment	February 2017-May 2019	August 2014–August 2020
Eligibility criteria	Ambulatory patients aged ≥18 y with a final diagnosis of ischemic stroke or TIA with symptom onset-to-dispatch time within 4 h during MSU operation hours and without contraindications to tPA or thrombectomy	Patients with suspected disabling acute stroke presenting during MSU operation hours whose symptom onset was within 4.5 h and had no guideline contraindications to tPA
Interventions	MSU care vs standard ambulance care when MSU unavailable	MSU care vs standard ambulance care according to an alternating week schedule
Primary outcome	Distribution of mRS at 3 mo	Utility-weighted mRS score at 90 days among patients adjudicated as tPA eligible
Clinical parameters	Mean ages 73-74 y, median NIHSS 4, women 46-48%, TIA 17%	Median ages 65-67 y, median NIHSS 10,women 48–53%, Black 39%, TIA 1-4%
Efficacy results	Primary: aOR for worse outcome on mRS 0.71 (95% CI, 0.58–0.96) favoring MSU care Secondary: OR for worse outcome on 3-tiered disability scale 0.73 (95% CI, 0.54–0.99) favoring MSU care	Primary: mean utility-weighted mRS 0.72 in MSU group vs 0.66 in usual care group (pooled difference 0.07; 95% CI, 0.03–0.11) Secondary: mRS ≤1 55% vs 44% with OR 2.43 (95% CI, 1.75–3.36) favoring MSU care
Safety results	SICH: 3.2% with MSU vs 2.8% without MSU Death within 7 days: 1.7% with MSU vs 3.0 without MSU	SICH: 2% in each group Death at 90 days: 8.9% with MSU vs 11.9% in standard ambulance group
Secondary analyses	Sensitivity and subgroup analyses consistent with primary results, QOL measures nonsignificantly favor MSU care	Sensitivity and subgroup analyses consistent with primary results, including an analysis among all enrolled patients
Limitations	Nonrandomized, patients and physicians unblinded, restricted to Berlin, 13% of patients without primary outcome data	Individual patients not randomized, patients and physicians unblinded, different processes for patient identification, mostly urban

mRS indicates modified Rankin Scale; MSU, mobile stroke unit; NIHSS, National Institutes of Health Stroke Scale; QOL, quality of life; SICH, symptomatic intracranial hemorrhage; and tPA, tissue-type plasminogen activator.

dispatch had a favorable 3-month outcome (mRS score 0–2 if age ≤80 years and mRS score 0–3 if age >80 years) versus 46.3% of those without. Quality of life measurements favored the MSU group. Rates of intracranial hemorrhage and death were similar between groups.

BEST-MSU is a prospective, multicenter, cluster-controlled trial conducted at 7 cities in the United States.[24] Patients were enrolled between 2014 and 2020 if they were suspected to have stroke within 4.5 hours of onset and had no obvious contraindications for intravenous thrombolysis. Final eligibility was determined by the medical record review of a single vascular neurologist blinded to group assignment and thrombolysis administration. Study group assignment was determined according to an alternating week schedule whereby MSUs were scheduled as available or not. During MSU on-weeks, emergency call operators would alert both an MSU and a regular ambulance who would then simultaneously deploy to the scene. During MSU off-weeks, only a regular ambulance would deploy to the scene while an MSU nurse would meet the patient and EMS at the destination ED to collect relevant study data.

BEST-MSU enrolled 1515 patients (886 in MSU group and 629 in EMS group), of whom 617 in the MSU group and 430 in the EMS group were subsequently adjudicated as eligible for intravenous tPA. About 39% of enrolled patients were Black and 17% were Hispanic. In addition, 24% had preexisting disability. As site initiation was staggered and recruitment was delayed by the coronavirus pandemic, about three-quarters of patients were enrolled at the primary site in Houston. Baseline characteristics were similar between study groups except the EMS group had more men and less prestroke disability. The median onset-to-thrombolysis time was faster in the MSU group (72 versus 108 minutes) with considerably more golden hour treatments (32.9% versus 2.6%). In the primary analysis, which analyzed patients eligible for tPA, the utility-weighted 90-day mRS score was 0.72 in the MSU group versus 0.66 in the EMS group (pooled difference, 0.07 [95 CI, 0.03–0.11]). In dichotomized analysis, 55.0% of patients in the MSU group achieved a 90-day mRS score of 0 to 1 versus 44.4% in the EMS group. Further, 36.8% of MSU-treated patients became normal versus 25.2% of standard EMS-treated patients. Considering that the brain's ability to withstand ischemia declines with time, tPA's lytic ability inversely correlates with onset-to-treatment time, and tPA was administered much faster to MSU patients with 30%

more treated within the golden hour, a reasonable supposition is that MSU treatment improved functional outcomes by averting permanent strokes.[25,26] In support of this hypothesis, the number of patients adjudicated as nonstrokes (ie, mimics) was the same in the MSU and EMS groups. There were nonsignificantly fewer deaths in the MSU group (8.9%) than the EMS group (11.9%). Rates of symptomatic intracranial hemorrhage and other safety outcomes were similar between groups. Subgroup analyses according to race, site, and time aligned with the primary results.

In secondary analysis of BEST-MSU, when all enrolled (transported) patients were analyzed, including those adjudicated as ineligible for tPA (mimics and hemorrhages), 3-month outcomes still favored the MSU group. In B_PROUD, 26% of patients in the MSU group had MSU dispatches that were later cancelled, and these patients were included in the primary intention-to-treat analysis that found MSU care superior. These data indicate that the benefit of tPA treatment aboard MSUs is of sufficient magnitude that an overall population-level benefit exists even if tPA ineligible patients are included.

B_PROUD and BEST-MSU had notable limitations. First, B_PROUD was conducted solely in Berlin and about three-quarters of BEST-MSU patients were enrolled in Houston. Further, while BEST-MSU did recruit in nonurban settings in Colorado and Northern California, most patients were enrolled in cities. Therefore, the generalizability of these studies to other settings is uncertain. Second, neither study randomly allocated nor blinded individual patients. In B_PROUD, randomization was not performed because local stakeholders believed it was unethical to withhold MSUs if they were available. In BEST-MSU, patients were allocated to study groups according to an alternating week schedule for MSU availability. This design approximated a cluster-randomized approach where the clusters were the days when the MSU was available or not. To address the possibility of bias in group assignment, a propensity score analysis was performed for the BEST-MSU trial, and its results mirrored those of the primary analysis. Blinding of patients and treating providers was not performed because it was impractical to do so; however, blinded outcome assessments were performed. Third, in B_PROUD, 13% of enrolled patients did not have mRS assessments at 3 months (the primary outcome). Baseline characteristics, process indicators, and short-term patient outcomes were similar between patients with and without mRS assessments. Fourth, MSUs did not influence the frequency nor the speed of mechanical thrombectomy. The reasons for this lack of effect are uncertain. Future studies should investigate whether performing CT angiography aboard MSUs could expedite thrombectomy times. Fifth, in BEST-MSU, there were approximately twice as many final diagnoses of stroke reversed by tPA in the MSU group than the ED group, and if these cases were actually mimics or TIAs, then the main results could have been biased in favor of the MSU group. This is unlikely because adjudications were performed by an expert vascular neurologist with access to the entire medical record and imaging. In addition, in a sensitivity analysis restricted to patients with a final diagnosis of definite stroke (420 MSU patients and 311 EMS patients), the 90-day utility weighted mRS (mean 0.67 versus 0.60, P=0.009) and the ordinal mRS shift analysis (odds ratio, 2.46; P<0.001) still favored MSU care.

COST-EFFECTIVENESS

A major concern with MSUs is cost. While B_PROUD and BEST-MSU have demonstrated the superiority of MSUs compared with standard emergency care in terms of functional outcomes, it remains uncertain whether MSUs are cost-effective, particularly given their substantial expense. Then again, compared with a nondisabling stroke, a disabling stroke more than doubles a patient's long-term costs and MSUs have been shown to prevent disability,[23,24,27] so there is clear potential for cost-effectiveness. Ultimately, the B_PROUD and BEST-MSU trials will provide high-quality evidence on the cost effectiveness of MSUs. B_PROUD's health economics evaluation is almost completed, and its publication is expected in the coming months. BEST-MSU's co-primary aim is to determine MSU cost-effectiveness; health care utilization data have been collected in all patients for a year after stroke and will be analyzed and presented in 2022. In the meantime, modeling studies have forecasted the expected cost implications of MSUs.

Researchers from Saarland, a relatively rural region of Germany, used their prospective randomized trial data to estimate benefit-cost ratios for MSU care.[15] They determined that MSU care versus conventional emergency care was monetarily beneficial according to the parameters of their trial and that the benefit-cost ratio markedly increased with reduced staff and higher population density. Their models estimated that MSUs would be cost-effective for population densities of at least 79 inhabitants per kilometer,[2] and that their operating distances for optimal efficiency ranged from 43 to 65 km.

Using data from the PHANTOM-S trial, health economists analyzed the cost-effectiveness of earlier and more frequent thrombolysis aboard MSUs.[28] They estimated that with the Berlin MSU model and an annual net cost of 963954 Euros, faster and more frequent thrombolysis treatment by a MSU would lead to 18 fewer disabled patients each year, equating to an incremental cost-effectiveness ratio of 32 456 Euros per quality-adjusted life year. This cost falls within the 50 000 US dollar threshold many societies use to determine an intervention's cost-effectiveness.[29]

A cost consequence analysis was conducted using data from the Cleveland Clinic's MSU.[16] In this simulated analysis, it was estimated that for 355 MSU transports,

the incremental cost of an MSU compared with standard EMS transport was 70 613 US dollars, but this cost would be balanced by avoiding 76 interhospital transfers, which could result in cost saving from a societal perspective.

Investigators from Melbourne evaluated the costs and benefits of their MSU using an economic simulation model.[30] Using data on 1244 patients treated aboard their MSU in 2018 (their first operational year) and projected benefits from MSU care, they estimated that compared with standard emergency care, a MSU costs 30982 Australian dollars for each disability-adjusted life-year avoided. In probabilistic sensitivity analysis with varied model inputs, over 95% of simulations remained within this acceptable threshold.

Funding models vary by country and therefore there is need for cost-effectiveness evidence from MSU programs of different settings and contexts to support business arguments.[31] A PRESTO initiative is to encourage MSU programs to use standard protocols and questionnaires for economic evaluation to support reliable international comparisons and to permit transparency regarding differences in resource utilization and reported costs and assumptions.

BARRIERS TO IMPLEMENTATION

There are several barriers preventing widespread MSU expansion (Table 2). First are the financial implications of providing these programs/services. Assuming MSUs are confirmed as being cost-effective, who should pay their costs? MSUs cost millions of dollars to purchase and operate, and in much of the world, their only recouped costs are for standard ambulance transportation. Without a sustainable financial model and acceptance by federal and private insurers, MSU care will not spread beyond select sites who can procure their own funding source. Discussions with national health insurance programs by PRESTO members and other stakeholders are underway, and it is reasonable to assume that MSU care will eventually receive its own payment designation like other proven stroke interventions. Special dispensations will need to be considered for rural or low resource settings where lower case volumes will make financial viability challenging even if MSU care were robustly reimbursed.

A second barrier to MSU implementation is inefficiency. Like ED stroke activations, only a proportion of MSU dispatches turn out to be for actual strokes and an even smaller proportion are treated with thrombolysis or thrombectomy. Refining EMS triage systems through advanced education of dispatchers, machine learning strategies to more accurately identify stroke among emergency calls, and the use of screening tools for large vessel occlusive stroke to identify patients most likely to benefit from ultra-early recanalization therapies could improve the efficiency and impact of MSUs. In the United States, despite marketing campaigns, only about 50% of patients with stroke present to the ED via ambulance.[32] Addressing barriers to ambulance use among patients with stroke, including cost, public knowledge about stroke, and access should be intensified. Restricting MSU operations to high-yield daytime and early evening hours when stroke diagnoses are most frequent and tPA eligibility is greatest might also improve MSU efficiency.[33] Further, in settings where the incidence of stroke may be low, adapting MSUs so they can also treat other time-sensitive medical emergencies, such as cardiac arrest, could be considered to better justify costs. Last, discovery of other time-sensitive treatments for stroke, such as hemostatic therapy for intracerebral hemorrhage, could also make MSUs more efficient.

A third barrier to implementation is the variable and sometimes fractured relationship among EMS providers and stroke centers. Ideally, MSU programs would be seamlessly integrated within EMS networks and all local stroke centers and stakeholders would cooperate and contribute to the success of the program. Unfortunately, in many places, several for-profit and privatized EMS systems exist and compete, and many MSU programs, particularly in the United States, are led by individual medical centers that may have minimal communication or collaboration with nearby centers. This barrier is less of an issue in countries with publicly funded health systems.

A fourth barrier is geographic constraints. An MSU can only be effective if it can reach and treat a patient quickly, and in certain rural areas, this may not be possible. Access to high-quality stroke care is already an issue in rural areas, where there are considerably fewer thrombectomy-capable centers. Besides the rendezvous approach for MSUs, a potential solution could be mobile stroke teams who travel by helicopter.[14,34] This approach has been proposed by experts and is being actively piloted in Australia, although it would raise costs and there would be additional safety and practical concerns, including the need for lighter imaging devices.[34]

ALTERNATIVE APPROACHES AND COMPARABILITY TO OTHER INTERVENTIONS

For communities to consider investing in MSUs, several factors need to be reviewed, including whether existing systems could be optimized to outperform MSUs. The first consideration is whether prehospital stroke identification systems can be improved. However, in first-world countries, many, if not most, communities already have established processes to identify stroke patients and preferentially transport them to appropriate stroke centers.[35] This includes use of the Cincinnati Prehospital Stroke Scale and other stroke screening tools.[36,37] Alternatively, prehospital stroke diagnosis and transport could be improved through widened telemedicine coverage by

Table 2. Barriers to Mobile Stroke Unit Implementation and their Potential Solutions

Barrier	Current state	Potential solutions
Finances		
Cost-effectiveness	Uncertain if cost-effective; estimates limited to simulations and projections from small studies	B_PROUD and BEST-MSU trials collected long-term health care utilization data and will determine MSU cost-effectiveness with stronger evidence; cost-effectiveness could be improved by treating other time-sensitive emergencies, modifying the care model, or reconfiguring the interdisciplinary team
Cost of ambulance	About 1 million US dollars; financed by MSU programs, often via philanthropy and grants	Payment by governments, EMS groups, or large health care systems depending on individual community needs and resources
Cost of operations	Annually up to 1 million US dollars for staff, equipment, and maintenance; financed by MSU programs, often via philanthropy and grants	Credential MSUs as acute stroke-ready centers and institute unique payment designations that reimburse MSUs commensurate to their operating costs; stroke and radiology physician professional fees paid by insurance
Cost of medicines	Each tPA vial costs about 8000 US dollars; labetalol, nicardipine, and benzodiazepines cost much less (10–100 s of US dollars depending on agent and dose); often financed by MSU programs	Use tenecteplase instead of tPA; station MSUs in underserved areas to use discounted pricing; institute unique payment designations for MSUs that reimburse commensurate to their operating costs, including medicines administered
Infrastructure	Relationship between EMS and stroke centers often not streamlined with many competing systems and centers with variable communication and collaboration	Integrate MSU programs into municipal EMS systems; require collaboration and quality review from all designated stroke centers; standardize and mandate prehospital best practices according to community factors
Geographic factors	Most MSUs operate in densely-populated cities, though some serve relatively rural (Saarland) or suburban (Colorado) areas	Increase access through helicopter units and intermediate location rendezvous transports; clinical trials could investigate MSU efficacy in nonurban areas
Efficiency	About 33%–50% of MSU dispatches are for actual strokes, and only a proportion of those are treated with tPA or thrombectomy	Refine EMS triage systems through education, screening tools for severe or large vessel occlusive stroke, and machine learning algorithms; reduce barriers to ambulance use; restrict MSU operations to high-yield hours

EMS indicates emergency medical services; MSU, mobile stroke unit; and tPA, tissue-type plasminogen activator.

EMS or hospital-based clinicians. Telemedicine-enabled ambulances are equipped with a 2-way mounted camera, allowing physicians to evaluate prehospital stroke patients before or during ambulance transport. These so-called mini-MSUs have been shown to enhance stroke recognition, improve triage accuracy, and facilitate reperfusion therapies.[38,39] While this approach is less costly than standard MSUs and has considerable merit, particularly in rural settings where transport times may be extensive; such an approach would still require transport to an ED for brain imaging thereby delaying thrombolysis treatment. A second consideration would be refining ED and hospital pathways for acute stroke response. While best practices such as employing acute stroke alarms and response teams, transporting patients directly to the scanner, skipping labs in select patients, and administering tPA in the radiology suite can expedite its delivery, even in the best circumstances, it will take 10 to 15 minutes to transport the patient from scene to ED and another 20 to 30 minutes from ED arrival to administer drug. As indicated in the B_PROUD and BEST-MSU trials, which averaged ED door-to-needle times of 30 and 40 minutes, respectively, even at established stroke programs, MSUs outperform EDs in the frequency and speed of tPA delivery.[23,24] A third consideration would be implementing mobile or "commando" stroke teams that travel between hospitals to administer proven acute stroke interventions.[40] This approach, while promising for its ability to improve the frequency and speed of mechanical thrombectomy at sites lacking neurointerventionalists, has not been shown to expedite tPA delivery as compared with current systems. Therefore, while we certainly advocate for removing any inefficiencies in prehospital and ED stroke pathways, these practices would likely result in minimal incremental gains at most advanced communities and would probably not surpass the benefits provided by MSUs under the settings and contexts they have been evaluated to date.

To fully appreciate the merits of MSUs, the evidence for their benefits should be contrasted with other proven acute stroke interventions. Combining B_PROUD and BEST-MSU data in a crude unadjusted calculation, MSU care resulted in 9.7% more patients with mRS score 0 to 1 than EMS care (number needed to treat=10). When using landmark phase 3 trial data, and while recognizing that patient populations and study designs differed between trials and that MSU's treatment effect relies on tPA, MSU care versus standard emergency care appears to provide more net benefit than aspirin versus placebo, stroke units versus general medical wards, and intravenous tPA 3 to 4.5 hours from stroke onset versus placebo (Figure 3).[1,3,41] In addition, the net benefit of MSU care versus standard emergency care approaches that of tPA within 3 hours of stroke onset versus placebo.[42] The functional outcome effects of MSUs are less than that of mechanical thrombectomy 0 to 6 and 6 to 24 hours from stroke onset, but MSUs, in theory, can be applied to more patients.[4,6] We acknowledge that the indication

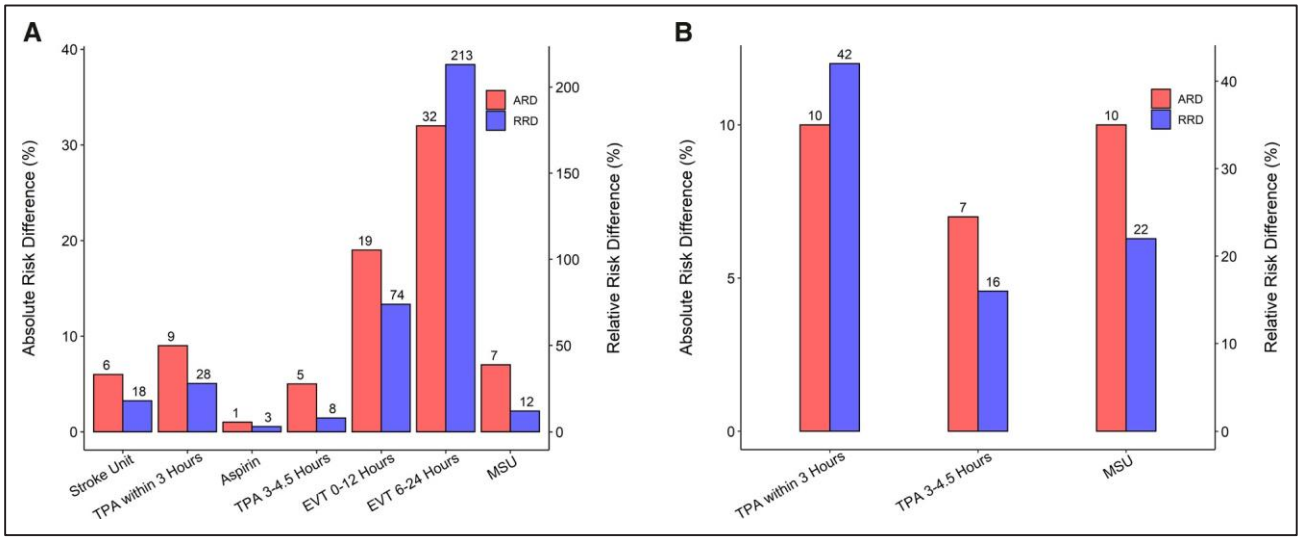

Figure 3. Bar graphs depicting the estimated long-term functional outcome benefits of proven acute stroke interventions as compared with the previous standard-of-care. Interventions are listed chronologically according to when they were proven effective.

Estimated absolute and relative risk differences were obtained from recent high-quality meta-analyses of phase 3 randomized trials or the individual trials themselves. **A**, For all proven acute stroke interventions using a modified Rankin Scale score cutoff of 0 to 2 (independent in activities of daily living). **B**, Limited to intravenous tPA and MSUs using a modified Rankin Scale score cutoff of 0 to 1 (normal or near normal). ARD indicates absolute risk difference; EVT, endovascular therapy; MSU, mobile stroke unit; RRD, relative risk difference; and tPA, tissue-type plasminogen activator.

of each intervention varies and that combined they likely provide the best opportunity for optimizing patient outcomes. Further, MSU care increases patients' likelihood of attending the most appropriate stroke center/unit and thereby increases access to other evidence-based treatments.[21]

NEXT STEPS

For MSUs to become recognized as a standard practice and proliferate, there are several important steps at different levels that need to occur (Table 3). At the local level, EMS and stroke leaders, politicians, and advocacy groups should meet to determine whether their community would benefit from one or multiple MSUs and, if so, how they should be organized and funded. Local stakeholders will also need to determine the optimal MSU infrastructure for their community. Should MSU administration and provisions be controlled by EMS, medical centers, or both? If local MSUs already exist, should their hours be broadened, should currently nonparticipating sites be involved, should large vessel occlusion screening tools be implemented at triage, and should CT angiograms be systematically performed? These questions and others will need to be decided by local stakeholders according to their individual circumstances before MSU standardization and proliferation.

At the regional level, MSUs should be included in quality and academic stroke databases, such as Get With The Guidelines-Stroke. As MSU programs expand, it is important that their scale, reach, quality, and outcomes are closely tracked, so they can be modified, as needed, to benefit the individual needs of local and regional communities. Such data will also enable high-quality research on the real-world effectiveness and impact of MSUs.

At the national level, MSUs should be officially recognized in clinical practice guidelines and considered in the accreditation of stroke programs by regulatory bodies. MSUs are essentially mobile acute stroke-ready centers and, therefore, it is reasonable for them to have comparable designation and performance evaluation. Alternatively, MSU program designation could be enfolded within existing comprehensive stroke centers. However, in that case, unique and standardized MSU performance criteria should be developed and utilized. The quality of care aboard MSUs should be monitored as rigorously as in-hospital stroke care and programs.

A critical step at the national and international level is the creation of a unique diagnosis-related group by federal organizations such as the Centers for Medicare and Medicaid Services. Without an official classification, it is unlikely that insurers and governments will pay for MSU care; and without reimbursement, MSU programs will remain scarce. Given the substantial effect size afforded by MSUs, we encourage medical societies such as the American Heart Association/American Stroke Association and the European Stroke Organization, among others, to help advocate for legislation standardizing MSUs and their reimbursement at the national and international levels.

Several reimbursement models are possible. One possible model would be bundled payments of varying price

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Table 3. Necessary Steps for Mobile Stroke Unit Expansion

Steps	Responsible parties	Action items
Standardized reimbursement	Regional and national governments, health insurers, medical societies	Create unique diagnosis-related groups for MSU care, which insurers agree to pay
Streamlined infrastructure	EMS and stroke leadership, local and regional governments, hospital systems, patient advocates	Determine optimal infrastructure and best practices for local community, including who should control MSU administration and provisions, how they should be integrated within EMS, where and when they should be stationed, and what assessments and treatments they should perform
Regulatory agency recognition	Regulatory agencies, hospital systems, medical societies, EMS and stroke physician leadership	Establish official designation and accreditation process for MSU programs with standardized quality metrics and monitoring
Guidelines endorsement	Guideline committees, medical societies, stroke leadership	Update MSU's level of evidence and class of recommendation to reflect recently published efficacy trials
Database inclusion	Research agencies, medical societies, stroke leadership, national governments, industry	Include MSU care in quality and academic medical registries and databases
Clinical trials development	Research agencies, stroke and EMS leadership, industry, medical societies	Develop MSU research infrastructure and personnel, design MSU focused trials, study MSUs in rural and underserved regions, and include MSU populations in current hyperacute stroke trials

EMS indicates emergency medical services; and MSU, mobile stroke unit.

tiers, based on case complexity and treatments rendered, incorporating personnel, laboratory, imaging, medication, and transportation costs. The converse model would be instituting separate bills for the individual components of MSU care including increased reimbursement for ambulance transportation. A hybrid model would be bundling some components of MSU care such as EMS services, diagnostics, medications, and transportation, while maintaining separate billing for professional services rendered by stroke specialists and radiologists. An additional consideration will be whether MSU renumeration should affect payments to accepting hospitals. The optimal approach for a given country/region will ultimately depend on their individual needs, EMS infrastructure, and existing fiscal models, and will require negotiation and final approval by national health insurance programs based on precedent and internal policy.

After MSUs have been accepted by authorities and proliferate, they could become a cornerstone of prehospital stroke research. The time savings afforded by MSUs provides an excellent opportunity to systematically investigate promising hyperacute stroke treatments that may be exquisitely time-sensitive, including neuroprotectants and thrombolysis enhancers for ischemic stroke and hemostatic agents for hemorrhagic stroke. MSU programs are already being included in stroke clinical trial networks such as the NIH's StrokeNet to harness this unique potential.

CONCLUSIONS

Based on biological plausibility, extensive observational data, and multiple clinical trials, including 2 efficacy trials, MSUs have now been proven superior to conventional emergency care for patients with suspected acute ischemic stroke. We therefore expect that clinical practice guidelines will reflect this new evidence and that elevation of MSU care to a Level of Evidence A, Class 1 Recommendation by relevant guidelines would be reasonable. Level A Evidence classification could be argued through the criteria of high-quality evidence from > 1 randomized controlled trial (the PHANTOM-S and Saarland, Germany trials, and arguably BEST-MSU, which approximated a cluster-randomized design).[17,22,24,43] Class 1 Recommendation classification could be argued through the logic that MSUs are superior to conventional emergency care and therefore they should be chosen over conventional emergency care when available. While this important step may result in more wide-scale proliferation of MSUs, before this occurs, there is urgent need for high-level decisions surrounding MSU infrastructure, logistics, and payment structure. We think that these discussions would be best led and prioritized by stroke leaders and organizations, so that patient outcomes and not bureaucracy or finances drive decisions. Important next steps for MSUs include reimbursement by insurers, integration with ambulance networks, recognition by program accreditors, and inclusion in quality registries. As these initiatives are enacted, we await prospectively collected data on MSU's cost-effectiveness as well as their benefit in hemorrhagic stroke and less populous settings. With MSU expansion, researchers should explore how MSUs can improve the identification and treatment of cerebral large artery occlusions, enrollment in hyperacute stroke clinical trials, and even patient outcomes in other time-sensitive emergencies. MSUs highlight the veracity of the time is brain concept and provide the stroke community a new opportunity to make quantum improvements in patient outcomes.

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附錄二

Googling Service Boundaries for Endovascular Clot Retrieval Hub Hospitals in a Metropolitan Setting
Proof-of-Concept Study

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Background and Purpose—There is great interest in how endovascular clot retrieval hubs provide services to a population. We applied a computational method to objectively generate service boundaries for such endovascular clot retrieval hubs, defined by traveling time to hub.

Methods—Stroke incidence data merged with population census to estimate numbers of stroke in metropolitan Melbourne, Australia. Traveling time from randomly generated addresses to 4 endovascular clot retrieval–capable hubs (Royal Melbourne Hospital [RMH], Monash Medical Center [MMC], Alfred Hospital [ALF], and Austin Hospital [AUS]) estimated using Google Map application program interface. Boundary maps generated based on traveling time at various times of day for combinations of hubs.

Results—In a 2-hub model, catchment was best distributed when RMH was paired with MMC (model 1a, RMH 1765 km^2 and MMC 1164 km^2) or with AUS (model 1c, RMH 1244 km^2 and AUS 1685 km^2), with no statistical difference between models (P=0.20). Catchment was poorly distributed when RMH was paired with ALF (model 1b, RMH 2252 km^2 and ALF 676 km^2), significantly different from both models 1a and 1c (both P<0.05). Model 1a had the greatest proportion of patients arriving within ideal time of 30 minutes followed by model 1c (P<0.001). In a 3-hub model, the combination of RMH, MMC, and AUS was superior to that of RMH, MMC, and ALF in catchment distribution and travel time. The method was also successfully applied to the city of Adelaide demonstrating wider applicability.

Conclusions—We provide proof of concept for a novel computational method to objectively designate service boundaries for endovascular clot retrieval hubs. **(*Stroke*. 2017;48:1353-1361. DOI: 10.1161/STROKEAHA.116.015323.)**

Key Words: endovascular treatment ■ Google ■ hospital ■ mapping

Stroke is a leading cause of disability worldwide and results in significant economic and societal cost.[1] In spite of this, there is now substantial optimism with acute stroke management since the publication of pivotal trials for thrombolysis[2] and endovascular clot retrieval (ECR).[3–8] The latter addition to the stroke armamentarium has generated debate as to how best to deploy this therapy because it requires highly skilled stroke teams, interventional radiologists, support staff, and unrestricted access to angiography suites and beds.[9] In Australia and around the world, this type of service is likely to be located in a major ECR hub hospital, and because of the need for specialized services, the number of such hubs providing a 24-hour service 7 days a week will be limited.

From the perspective of government and health service organizations, there is immense interest in how to design such centralized hyperacute stroke services to optimize timely access to stroke care for the public. Such a model has been shown to increase usage of intravenous thrombolysis.[10] This concept of a centralized hub and spoke model has been embraced in London where stroke services were redesigned to provide intravenous thrombolysis.[11,12] This service was conceptualized such that no Londoner should be >30 minutes (idealized traveling time [TT]) away from a hyperacute stroke service,[11] the number of acute stroke hospitals providing intravenous thrombolysis were reduced, and patients transferred across traditional hospital boundaries to the designated hyperacute stroke hospital. This approach has been shown to lead to lower mortality and length of stay.[13] The London model has not yet been reconfigured for ECR purposes because these trials were published in 2015 and the meta-analysis of the trials published in 2016.[4]

In Australia, the state of Victoria has set up a statewide service protocol[14] for ECR immediately after the publication of the

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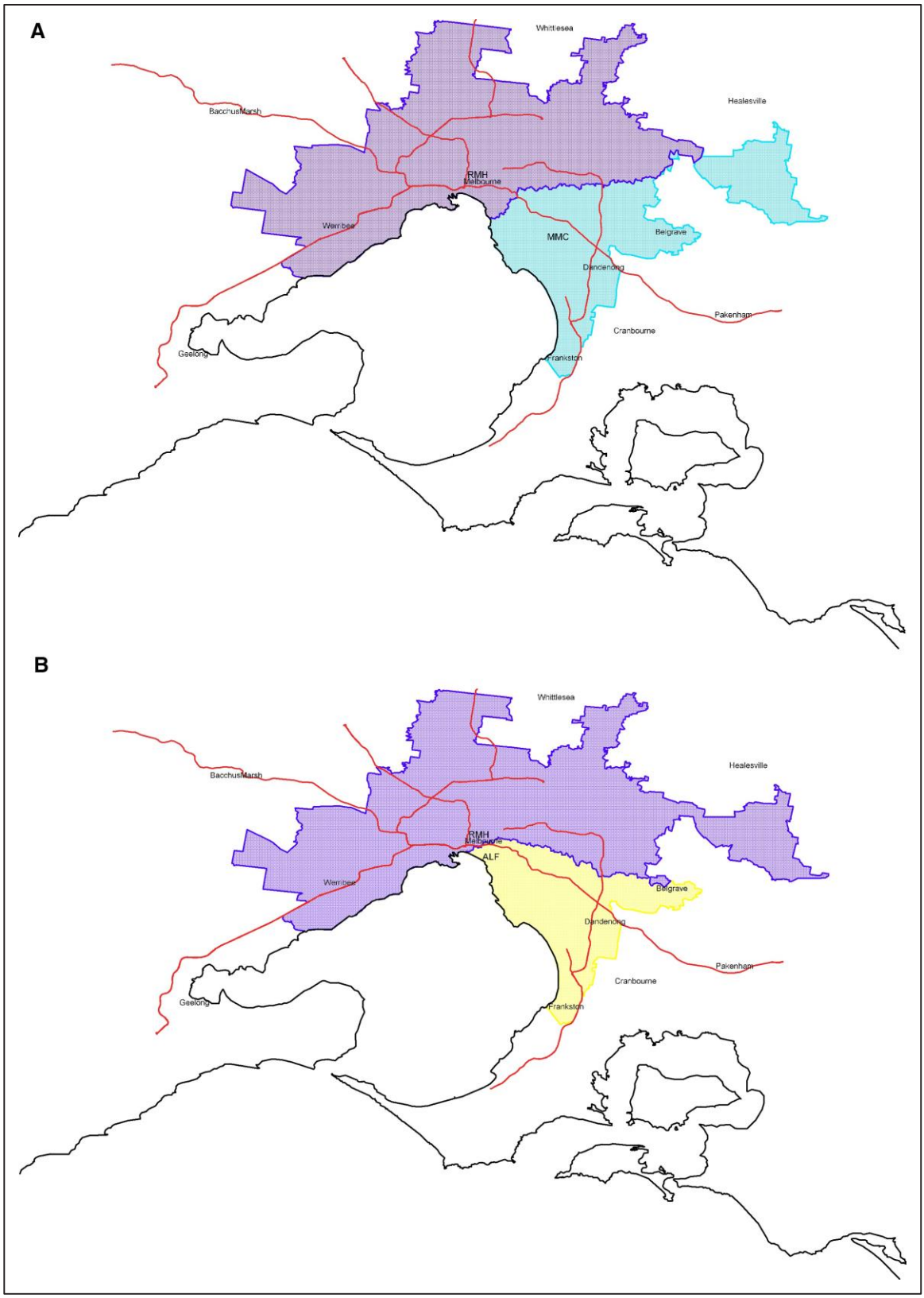

Figure 1. Catchment areas for different permutations of 2-hub model. This is a stylized map of the catchment area for model 1a (**A**, Royal Melbourne Hospital [RMH] and Monash Medical Center [MMC]), model 1b (**B**, RMH and Alfred Hospital [ALF]), and model 1c (**C**, RMH and Austin Hospital [AUS]) in the morning, during peak traffic. RMH has purple icon, MMC has blue icon, AUS has green icon, and ALF has yellow icon. The interactive map can be accessed at https://gntem2.github.io/Google-Map-to-Victorian-ECR-Hospitals/.

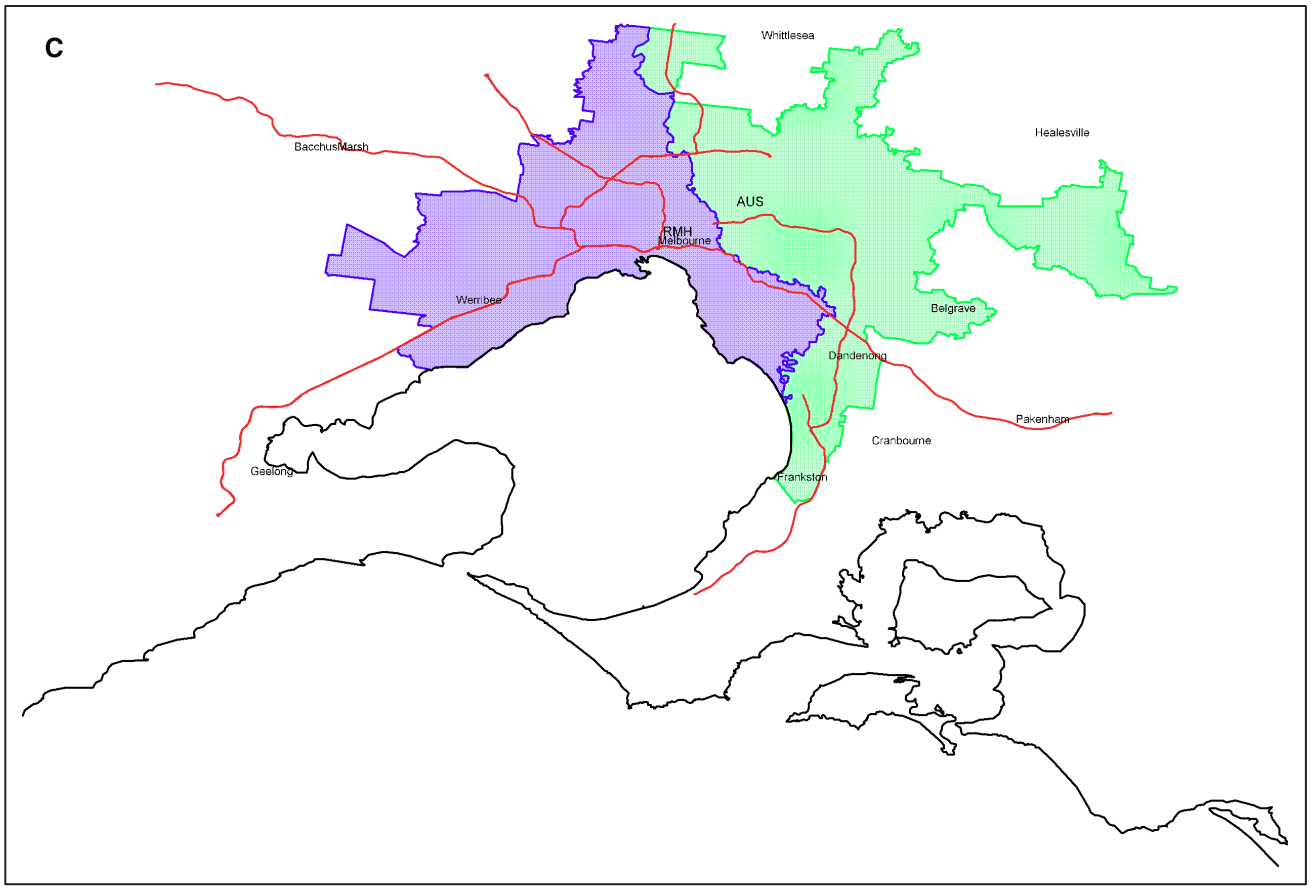

Figure 1 Continued.

ECR trials.[3–8] In this framework, 2 hospitals were designated as ECR hubs with one (Royal Melbourne Hospital/RMH) to be active immediately and a second (Monash Medical Center/MMC) to come on line later. These ECR hubs are required to provide a 24-hour service not just for patients in their immediate local catchment but also for all residents of Victoria. In addition to these 2 centers, there are 2 other Victorian ECR-capable hospitals and 6 non–ECR-capable hospitals providing intravenous thrombolysis in metropolitan Melbourne. By taking advantage of recent developments in the Google Map application program interface (API), we undertook this proof-of-concept study to develop and apply a computational method to objectively establish service boundaries for putative ECR hubs as defined by the traveling time from random locations to the hubs.

Methods

Setting

Melbourne is the capital city of the state of Victoria in Australia with a population of ≈4 million (http://www.abs.gov.au/websitedbs/). The postcodes for metropolitan Melbourne are in the range 3000 to 3207. To estimate the number of strokes in each postcode and hospital catchment area, previously published stroke incidence data in Melbourne was merged with the population census data in each suburb.[1] The 2011 census data for each suburb were obtained from Australian Bureau of Statistics.

ECR-Capable Hospitals in Melbourne

Four of these hospitals (Royal Melbourne Hospital [RMH], Monash Medical Center [MMC], Alfred Hospital [ALF], and Austin Hospital [AUS]) are capable of acting as ECR hubs. Given the status of RMH as the active designated ECR hub, all simulations were performed with this hospital in the model. Each of the other 3 ECR-capable hospitals (MMC, Austin, and Alfred) were considered as a potential ECR hub for the state-wide service in addition to the RMH in varying combinations. Boundary maps were performed for 2 ECR sites (RMH/MMC, RMH/ALF, and RMH/AUS, model 1), 3 ECR sites (RMH/MMC/ALF and RMH/MMC/AUS), model 2), and 4 ECR sites (model 3) using logical comparison of traveling time from each address to the different ECR hospitals. A description of major arterial road networks that service Melbourne and these ECR-capable hospitals is provided in the online-only Data Supplement. The locations of the ECR-capable hospitals relative to these aterial roads can be seen in Figures 1 and 2, and the interactive web display of these figures at https://gntem2.github.io/Google-Map-to-Victorian-ECR-Hospitals/.

Google Map API

We used the functionality of the Google Map API (https://developers.google.com/maps/) and the R (R Project for Statistical Computing, version 3.2.5) interface to Google Map API, ggmap.[15] The Google Map geocoding API describes a location in terms of its geocode (latitude and longitude). Random coordinates were generated in each suburb of metropolitan Melbourne and converted to addresses and their governing postcodes using reverse geocoding. Reverse geocoding was used to check that the randomly generated coordinates lay within a postcode, and if not, the relevant coordinate was removed and another random coordinate generated in its place. This step was repeated until the estimated number of stroke cases in that postcode (based on previously published stroke incidence data)[1] had been reached. Postcode boundaries were obtained from

https://www.data.vic.gov.au/data/dataset/postcode-boundaries-polygon-vicmap-admin.

Table 1. Traveling Time and Coverage Area for Different Combinations of 2 ECR Hub Models in Metropolitan Melbourne

Time of Day, h	Model 1a						Model 1b		
	RMH			MMC			RMH		
	Coverage, km²	Time to RMH, min	%Cases <30 min	Coverage, km²	Time to MMC, min	%Cases <30 min	Coverage, km²	Time to RMH, min	%Cases <30 min
0100	1970	20 (IQR 15.2–26.4)	85	959	18 (IQR 13.7–22.2)	94	2275	22 (IQR 16.3–27.9)	81
0815	1765	26 (IQR 19.4–33.7)	66	1164	21 (IQR 15.3–26.1)	85	2252	29 (IQR 21.8–36.4)	54
1230	1909	20 (IQR 16.0–26.0)	87	1020	18 (IQR 13.6–22.1)	94	2311	23 (IQR 17.1–27.8)	82
1715	1802	22 (IQR 17.3–27.4)	82	1126	19 (IQR 14.4–24.1)	90	2258	25 (IQR 18.6–30.9)	71

(*Continued*)

Estimation of Ambulance Travel Times and Potential Hospital Catchment

The travel time between each simulated address (representing location of a patient with stroke) and each chosen hospital in the study was computed using the ggmap[15] interface to the Google Map directions API. The ggmap[15] package was modified in house to specify the departure time from each address and a traffic model based on the time of travel so that varying traffic conditions could be taken into account. The transport times to each hospital from each simulated address were computed at 4 different times: 0815 (peak morning traffic), 1230, 1715 (peak evening traffic), and 0100 hours for a single chosen day, Wednesday, June, 8, 2016, using the optimistic or best-case scenario traffic model to approximate an emergency ambulance transit. The catchment area for a hospital was determined by collecting all addresses for which the travel time to that hospital was less than the travel time to the others. The use of different times of day allowed exploration of changes in the catchment areas associated with varying traffic conditions.

To compare the catchment distribution between the 2-hub models, we first computed the absolute differences in catchment areas (at different time of the day) between the reference hospital (RMH) against the paired hospital within each model. Next, we compared these differences between models using a Wilcoxon rank-sum test, and comparisons conducted for model 1a versus model 1b, model 1a versus model 1c, model 1b versus model 1c. For comparisons of 3-hub models, we compared the absolute difference between catchment of each hub relative to RMH's catchment within each model using the Wilcoxon rank-sum test. In addition, we compared the differences in proportions of patients arriving within TT between the models using χ^2 tests of proportion.

To display the results of analyses, interactive web-based maps of the different models were generated using R package leaflet using tiles from OpenStreetMap (OpenStreetMap contributors. For copyright, see http://www.openstreetmap.org/copyright).[16] The interactive maps display the travel time within that catchment as contours, and the time to hospital is displayed by clicking on that contour at any specific location. The figures provided in this article are stylized depiction of the boundary catchment of the ECR hubs.

To validate the model with real patient travel time data, we performed a comparison of Google Map API estimates of travel time with actual ambulance travel time for consecutive patients with stroke who attended Monash Medical Center in the calendar year 2015 and who had a stroke a code activated. Absolute differences in travel time were compared such that an earlier or later arrival at destination was treated equally as the time difference between the 2 methods. This validation project was approved by the Monash Health Human Research Ethics Committee.

To establish the applicability of our method in another metropolitan setting, we applied it to estimate traveling time to ECR hubs in the city of Adelaide, the capital of South Australia. Because of its smaller population size (1.29 million) than Melbourne, it has currently one designated hospital as the statewide ECR hub, but there are 2 other ECR-capable hospitals. Therefore, we simulated the scenarios of 1, 2, and 3 hospitals acting as ECR hubs. The maps and data relating to this simulation are provided in the online-only Data Supplement.

Results

The traveling time to the different ECR-capable hospitals under different traffic condition are displayed in Tables 1 through 3, Figures 1 and 2, and Figure I in the online-only Data Supplement. The interactive maps for each model and traffic condition can be viewed on https://gntem2.github.io/Google-Map-to-Victorian-ECR-Hospitals/. The interactive web page allows pan and zoom on the street at the boundary of the catchment. Figures II in the online-only Data Supplement shows plots of time to hospital at different times of day. The travel time to ALF and MMC changed little throughout the different traffic conditions. By contrast, the travel time for RMH and AUS increased during peak traffic.

During the morning peak hour time with a 2-hub model (Table 1; Figure 1), catchment was best distributed when RMH was paired with MMC in model 1a ([RMH 1765 km²,

Table 2. Traveling Time and Coverage Area for Different Combinations of 3 ECR Hub Models in Metropolitan Melbourne

Time of Day, h	Model 2a								
	RMH			MMC			ALF		
	Coverage, km²	Time to RMH, min	%Cases <30 min	Coverage, km²	Time to MMC, min	%Cases <30 min	Coverage, km²	Time to RMH, min	%Cases <30 min
0100	1921	21 (IQR 15.5–26.9)	84	889	18 (IQR 12.9–23.5)	92	118	11 (IQR 7.7–13.4)	100
0815	1726	27 (IQR 20–34.4)	63	1098	21 (IQR 14.2–27.3)	83	104	12 (IQR 8.4–15.9)	100
1230	1861	21 (IQR 16.1–26.6)	85	970	18 (IQR 13.0–22.9)	94	98	12 (IQR 8.3–14.3)	100
1715	1750	23 (IQR 17.3–28.3)	80	1076	19 (IQR 13.6–24.9)	89	102	12 (IQR 8.5–15.3)	100

(*Continued*)

Table 1. Continued

Model 1b Continued			Model 1c					
ALF			RMH			AUS		
Coverage, km²	Time to AUS, min	%Cases, <30 min	Coverage, km²	Time to RMH, min	%Cases, <30 min	Coverage, km²	Time to ALF, min	%Cases <0 min
653	21 (IQR 13.1–27.8)	80	1373	22 (IQR 15.4–27.3)	83	1556	21 (IQR 14.3–30)	75
676	25 (IQR 16.6–33.9)	65	1244	27 (IQR 19.4–35.4)	58	1685	25 (IQR 17.6–33.8)	63
618	22 (IQR 17.1–27.8)	75	1360	22 (IQR 16.4–27.7)	82	1568	21 (IQR 14.9–29.5)	76
670	24 (IQR 15.9–31.8)	69	1453	24 (IQR 17.9–30.8)	72	1474	24 (IQR 16.7 33.3)	67

ALF indicates Alfred Hospital; AUS, Austin Hospital; IQR, interquartile range; MMC, Monash Medical Center; and RMH, Royal Melbourne Hospital.

median traveling time 26 minutes [interquartile range {IQR}, 19–34 minutes], 66% of cases within TT during peak hour and MMC 1164 km², median traveling time 21 minutes [IQR 15–26 minutes], 85% of cases within TT) or with AUS in model 1c (RMH 1244 km², median travel time 27 minutes [IQR 20–35 minutes], 58% of cases within TT; AUS 1685 km², median travel time 25 minutes [IQR 18–34 minutes], 63% of cases within TT). By contrast, RMH had a large catchment when paired with ALF in model 1b (RMH 2252 km², median travel time of 29 minutes [IQR 19–36 minutes], 54% of cases within TT; ALF (676 km², median travel time 25 minutes [IQR 21–34 minutes], 65% of cases within TT). Comparing catchment distributions, there were significant differences between models 1a and 1b (P<0.03) and between 1b and 1c (P<0.03) but not between 1a and 1c (P=0.20). Model 1a (RMH and MMC) had the greatest proportion of subjects arriving within TT, followed by model 1c (RMH and AUS) and model 1b (RMH and ALF; all P<0.001; Table I in the online-only Data Supplement).

For the 3-hub model (Table 2; Figure 2), the combination (model 2b) of RMH (1088 km², median travel time 23 minutes [IQR 16–33 minutes], 69% of cases within TT), MMC (740 km², median travel time 18 minutes [IQR 14–22 minutes], 94% of cases within TT), and AUS (1100 km², median travel time 19 minutes [IQR, 14–25 minutes], 86% of cases within TT) resulted in better distribution of catchment area than the combination (model 2a) of RMH (1726 km², median travel time 26 minutes [IQR 20–34 minutes], 63% of cases within TT), MMC (1098 km², median travel time 20 minutes [IQR 24–27 minutes], 83% of cases within TT), and ALF (104 km², median travel time 12 minutes [IQR 8–16 minutes], 100% of cases within TT). The statistical comparisons for catchment of individual hubs within model 2a against that of RMH did not reach statistical significance (P=0.3), whereas comparisons within model 2b reached significance (P=0.03). Model 2b (RMH, MMC, and AUS) had a greater proportion of cases arriving to hospital within 30 minutes compared with model 2a (RMH, MMC, and ALF; P<0.001; Table I in the online-only Data Supplement).

There was no statistical difference in TT between a 4-hub (RMH, AUS, ALF, and MMC) and a 3-hub (RMH, MMC, and AUS) model (Table 3), but it is worthwhile noting the small catchment for ALF in the former (94 km², median time 11 minutes [IQR 8–15 minutes]) and the other 3 hospitals taking up the most of the coverage for Melbourne in the 4-hub model.

For the validation analysis of the computational method against actual patient travel time at MMC, the mean absolute difference in TT between the actual ambulance transfer and the Google Map API estimate for patients was 3.5±2.5 minutes (n=122).

Results of simulations of TT in Adelaide are presented in Figures III through V and Tables II through V in the online-only Data Supplement. Boundary map generation was demonstrated to be feasible. Simulations suggested that, with the 1-hub model (Royal Adelaide Hospital), 78% of patients arrive in hospital within TT, whereas different combinations of 2-hub models result in higher (88%) proportion of patients arriving within TT (all significantly different from 1-hospital model, P<0.001). With the 3-hub model, 98% of patients arrive in hospital within TT (significantly different from the 2-hub model).

Discussion

In this proof-of-concept study, we have used a novel and objective computational method to map service boundaries for metropolitan ECR hubs based on travel time to the hub.

Table 2. Continued

Model 2b								
RMH			MMC			ALF		
Coverage, km²	Time to RMH, min	%Cases, <30 min	Coverage, km²	Time to MMC, min	%Cases <30 min	Coverage, km²	Time to ALF, min	%Cases <30 min
1162	18 (IQR 13.0–24.5)	89	697	17 (IQR 13.0–20.9)	95	1069	16 (IQR 12.0–21.2)	92
1088	23 (IQR 15.7–33.1)	69	740	18 (IQR 13.7–22.4)	94	1100	19 (IQR 13.8–25.1)	86
1157	19 (IQR 14.0–24.4)	89	719	17 (IQR 13.0–20.7)	97	1053	16 (IQR 12.4–20.8)	94
1230	20 (IQR 15.0–26.6)	82	948	18 (IQR 13.6–21.9)	96	751	18 (IQR 13.5–22.3)	91

ALF indicates Alfred Hospital; AUS, Austin Hospital; IQR, interquartile range; MMC, Monash Medical Center; and RMH, Royal Melbourne Hospital.

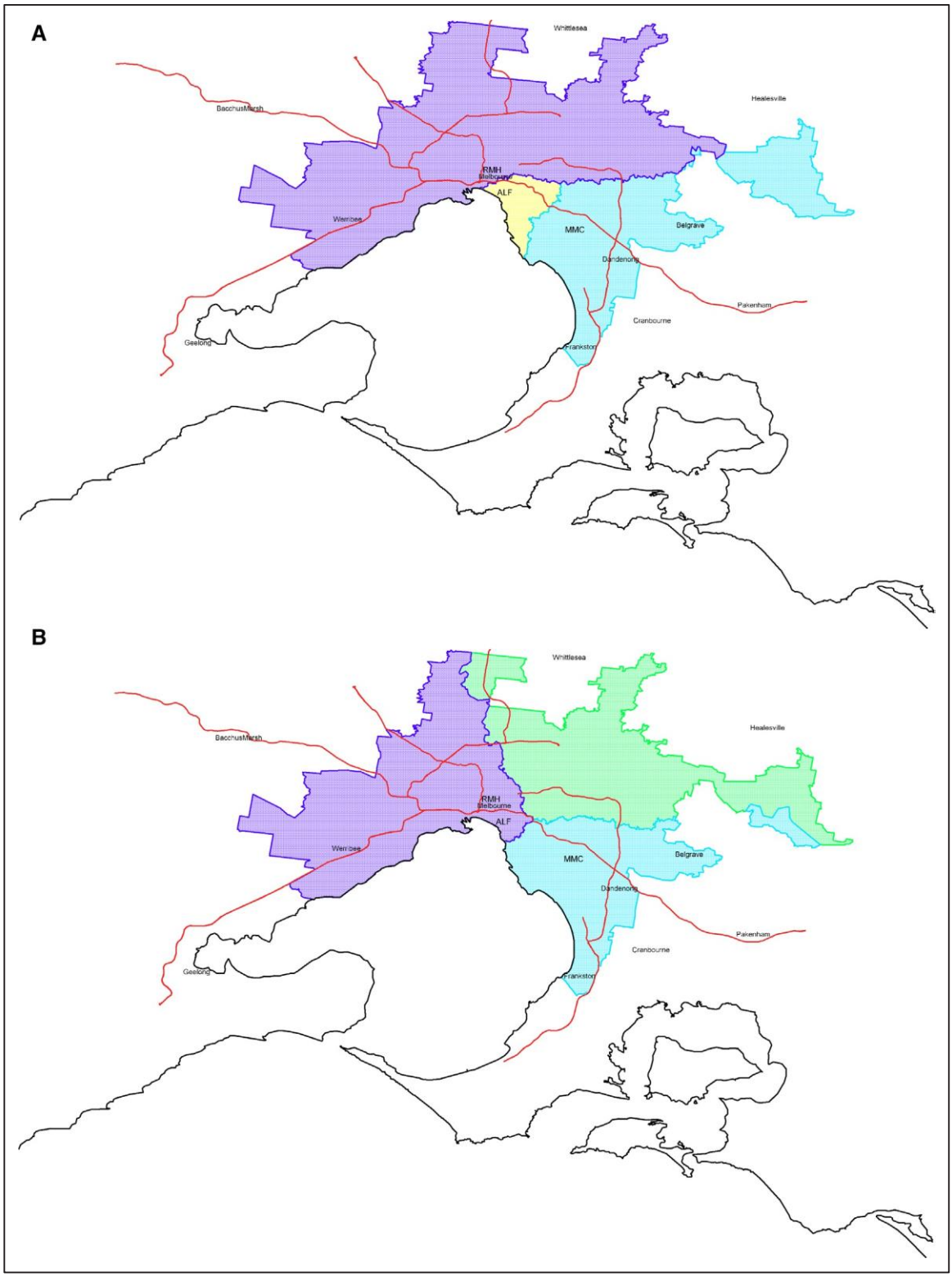

Figure 2. A, This is a stylized map of the catchment area for model 2a (Royal Melbourne Hospital [RMH], Monash Medical Center [MMC], and Alfred Hospital [ALF]) in the morning, during peak traffic. **B**, Catchment areas for different permutations of 3-hub model. This is a map of the catchment area for model 2b (RMH, MMC, and Austin Hospital [AUS]) in the morning, during peak traffic. RMH has purple icon, MMC has blue icon, AUS has green icon, and ALF has yellow icon. The interactive map can be accessed at https://gntem2.github.io/Google-Map-to-Victorian-ECR-Hospitals/.

These simulated models can be used to identify the ideal hub for patient transfer and locations that may be disadvantaged by the current design of ECR services in metropolitan Melbourne. Additionally, we can model and display the impact of traffic condition (time of day) on travel time and the catchment areas to hospital by generating interactive

Table 3. Traveling Time and Coverage Area for 4 ECR Hub Models in Metropolitan Melbourne

Time of Day, h	RMH			MMC			ALF			AUS		
	Coverage, km²	Time to RMH, min	%Cases, <30 min	Coverage, km²	Time to MMC, min	%Cases, <30 min	Coverage, km²	Time to ALF, min	%Cases, <30 min	Coverage, km²	Time to AUS, min	%Cases, <30 min
0100	1121	19 (IQR 12.8–25.6)	87	635	17 (IQR 12.2–22.2)	94	113	11 (IQR 7.6–13.0)	100	1059	16 (IQR 11.8–21.4)	92
0815	1058	25 (IQR 15.7–34.4)	66	684	17 (IQR 12.8–23.1)	93	93	11 (IQR 7.9–15.0)	100	1092	19 (IQR 13.8–25.2)	86
1230	1116	20 (IQR 13.6–25.5)	88	673	17 (IQR 12.4–21.2)	97	93	11 (IQR 8.2–14.2)	100	1046	16 (IQR 12.3–21.0)	93
1715	1183	21 (IQR 14.4–28.1)	79	900	18 (IQR 12.9–22.4)	95	98	12 (IQR 8.4–15.1)	100	747	18 (IQR 13.4–22.3)	91

ALF indicates Alfred Hospital; AUS, Austin Hospital; IQR, interquartile range; MMC, Monash Medical Center; and RMH, Royal Melbourne Hospital.

maps. Our approach is applicable to other metropolitan areas in Australia and potentially applicable in many other international locations when designing services for ECR or indeed other acute time-dependent conditions such as acute coronary syndrome. Additionally, the maps may guide ambulance personnel in real-time identification of routes to the nearest ECR hub.

Geographical information systems have been used to evaluate access to percutaneous coronary intervention[17] and access to thrombolysis in North America[18] but not for generating maps of catchment areas for hospitals. In the context of acute stroke, we were able to harness recent developments in geographical information technology to not only estimate travel times but also generate interactive maps of hospital catchment. Google Map began as a desktop application in 2005, with the mobile phone application added in 2008 and the crowd sourcing Waze App integrated in 2013 (harnessing traffic and incident information). Google Map API, thus, obtains traffic information by crowd-sourcing data from multiple users who enable My Location App or Waze App on their mobile phones.[19] These Apps send anonymous information to Google about their location and speed on the road. When these data from the large online community of users are combined with knowledge of local road speed limits, aided by smart sensors at key locations as well as updates from local authorities, a comprehensive picture of traffic conditions can be generated.[20] The ggmap interface makes it easier to run the request in batches and specifying the traffic time, crucial to ensuring uniform sampling at a point in time. To our knowledge, such an approach has not been previously reported and carries substantial significance for the organization of hyperacute stroke services in the current era of ECR.

Selection of ECR hubs for other cities cannot be empirically inferred directly from the Melbourne model but would require simulation for each city based on their individual geography, arterial roads, and locations of ECR-capable hospitals. It is, therefore, important to establish the feasibility of this mapping approach in settings other than Melbourne, and we have clearly demonstrated this in another metropolitan location. In this respect, it is important to note that Google Map API is designed for estimating time to any destinations including businesses, restaurants, and plotting crime scenes—and is widely and globally available given the advent and use of mobile devices. Here, we have tapped into its potential to map time from any destinations to hospital for patients with stroke, and this requires stroke incidence/prevalence data, population census data per postcode (or similar region), geographical information on shapefiles for each postcode, and a local knowledge of ECR-capable hospitals. In the absence of such data, an alternative approach would be to simulate time to hospitals from all real addresses, rather than random fictitious addresses. Although this alternative method can provide useful information about the potential catchment of ECR hubs, it may not provide data on the number of patients with stroke within a region that the hospital service as the simulation can result in more cases than there are people at risk of stroke.

With respect to metropolitan ECR service design, once a primary hub is identified (as is the case with RMH in Melbourne and RAH in Adelaide), a second and third hub can be identified based on the catchment area maps and time to hub. Using the idealistic notion of a maximum 30-minute traveling time to the ECR hospital, we can assess the ECR hub location that best suits this requirement for models requiring ≥2 hubs. From the perspective of metropolitan Melbourne, it seems that the optimal models are a combination of RMH and MMC (model 1a) or a combination of RMH, MMC, and AUS (model 2b). This latter combination of 3 hospitals working collaboratively would provide the best coverage with the smallest proportion of patients within TT. This approach may be ideal to reduce the impact of overcrowding of ECR hubs resulting from diversion of stroke patients away from smaller hospitals. Overcrowding remains an important potential issue and will require careful monitoring of admission data, strategic planning of extra resources, and a collaborative approach to manage workload. Previously, others have reported that 36% of patients with acute stroke present to hospital within 8 hours from onset.[21] On the basis of this and the extended catchment for ECR, we would expect ≈1890 stroke admissions per year to our center (MMC), which is a more than doubling of current admissions. In strategic planning, additional beds are to be added for our stroke unit (doubling the size of the current unit) and an extra angiography suite commissioned to meet requirements. Although ECR hubs in Victoria are required to have a least 2 angiography suites and a minimum of 3 interventional radiologists, it means that only 2 cases can

be handled simultaneously every 2 hours in a 1-hub model, 4 cases in a 2-hub model, and 6 cases in a 3-hub model. With 3 collaborative hubs, if one hub has reached capacity of 2 ECR cases, then, it can provide an alert to ambulance control that can then use our interactive map to redistribute the next cases to the closest available ECR hubs.

The issue of transport to the most appropriate hospital is also important. In London, 97.5% of patients were transported to sites that offered comprehensive hyperacute stroke services. Although this figure is likely to be lower in the ECR era because not all hyperacute hospitals provide such services,[22] an issue that emerges is whether patients should be transported to their nearest thrombolysis-capable hospital first or to ECR-capable hospitals.[9] It has been proposed that an ECR-hub transfer should be effected if the patient is approximately equidistant in travel time from these 2 different types of hospitals,[9] and our interactive map could play a role in assisting with this decision. To avoid ECR hubs being overwhelmed, such patients should be rapidly transported to a non-ECR hospital nearest to their residential addresses when stable after acute clot retrieval.[11] Stroke experts will need to actively engage with local government including ambulance services to design these aspects of statewide ECR services.

Our study has limitations. We have not yet analyzed the impact of the proposed model on ambulance transport. Ambulance control organizes transport to hospitals using ambulances from multiple ambulance station locations across Melbourne. We have not addressed this issue in our proof-of-concept approach, because it will need to accommodate a large number of variables with respect to ambulance locations. We have also not addressed the impact of having 2 or 3 ECR hubs on ambulance service because a model of 2 hospital hubs has been already considered at our government level and agreed to by Ambulance Victoria.[14] In creating the map, the assumption is that ambulance control is equipped with sophisticated technical equipment or support for call takers to execute these tasks while still providing 000 (911 in North America) response to incoming calls. As such, the model did not take into account the impact on ambulance services when a stroke code has been dispatched by ambulance control. Apart from availability of essential services such as stroke unit, interventional neuroradiologists, and supporting units (including neurosurgery and intensive care unit), we have not taken into account individual ECR experiences or expertise at a potential hub, onset to treatment time, door to needle, and door to groin puncture for ECR. Issues of door to needle and door to groin are important factors in assessing performance of ECR hubs.[23] These variables are a reflection of organization and infrastructure at a hospital, and designated ECR hubs should be able to obtain funding to improve them even further.[13] The success of this strategy was observed in the reconfiguration of hyperacute stroke services in London by the change in Northwick Park Hospital to become a hyperacute stroke hospital.[24] By contrast, placement of an experienced ECR hub in a location that is difficult to access can delay in access to therapy. In the setting of Melbourne, the 3 ECR-capable hospitals estimated by travel time to be ideal because hubs were all experienced centers that had participated in a recent landmark ECR trial.[7] Our simulations were also based only on postcodes for metropolitan Melbourne, not the outer suburbs. However, the outer suburbs of Melbourne are still dependent on the same major arterial roads that service the ECR hubs. Another potential limitation is that we used estimates of travel time from Google Map API. It may, therefore, be assumed that actual travelling time may be greater than these estimates. We were reassured by our local validation analysis that showed small absolute differences between Google Map API times and observed ambulance travel time. Also, it must be borne in mind that ambulances in Melbourne do have the option of using lights and sirens, driving through red lights, or even crossing to the opposite lane against traffic if absolutely necessary—in contrast to the Google Map API that is based on the user strictly abiding by driving regulations.

In summary, we have provided proof of concept that a novel computational approach for estimating the metropolitan service boundaries for ECR hubs that can be used to identify the ideal hub for patient transfer (given their locations). This method can be applied to other metropolitan areas in Australia or potentially around the world (where Google Map API provides coverage) when designing ECR or similar services.

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Figures provided in the web link (https://gntem2.github.io/Google-Map-to-Victorian-ECR-Hospitals/) were created using data OpenStreetMap contributors and tiles from osm.org. The data are available under the Open Database License, whereas the tiles are available under Creative Commons Attribution-ShareAlike 2.0 license. Details are available at http://www.openstreetmap.org/copyright. The maps were created using the OpenStreetMap tiles but do not suggest that the licensor endorses the use of this map.

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附錄三

Stroke
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Monash Transient Ischemic Attack Triaging Treatment : Safety of a Transient Ischemic Attack Mechanism-Based Outpatient Model of Care

Lauren M. Sanders, Velandai K. Srikanth, Damien J. Jolley, Vijaya Sundararajan, Helen Psihogios, Kitty Wong, David Ramsay and Thanh G. Phan

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Monash Transient Ischemic Attack Triaging Treatment
Safety of a Transient Ischemic Attack Mechanism-Based Outpatient Model of Care

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Background and Purpose—Controversy surrounds the need for routine hospital admission for transient ischemic attack. The Monash Transient Ischemic Attack Triaging Treatment (M3T) model adopts rapid management in the emergency department followed by outpatient management prioritized by stroke mechanism. We compared safety and processes of care between M3T and the previous model of routine admission.

Methods—Study cohorts consisted of patients managed with M3T (2004–2007) and the previous model (2003–2004). We determined 90-day stroke outcome using clinical and medical record review and data linkage to the population level statewide hospital discharge morbidity database. We compared models of care using risk difference analysis, followed by logistic regression to adjust for previous indicators of risk. Secondary outcomes were proportions admitted, proportions undergoing carotid ultrasound, times to ultrasound and revascularization, and medication prescription.

Results—In M3T (mean age, 64.7±14.7) 85/488 (17.4%) patients were admitted compared with 117/169 (62.9%) in the previous model (mean age, 72.5±13.9). With near-complete follow-up, 90-day stroke outcome was 1.50% (95% confidence interval, 0.73%–3.05%) in M3T and 4.67% (95% confidence interval, 2.28%–9.32%) in the previous model (P=0.03). Compared with the previous model, the adjusted odds ratio of stroke for M3T was 0.46 (95% confidence interval, 0.12–1.68; P=0.24). M3T was associated with greater proportions undergoing carotid ultrasound (P<0.001) and receiving antiplatelet therapy (P=0.005).

Conclusions—The M3T system was associated with low 90-day stroke outcome in transient ischemic attack patients, providing proof of concept that these patients may be managed safely without routine hospital admission using a closely supervised protocol in the emergency department. **(*Stroke*. 2012;43:2936-2941.)**

Key Words: outpatient ■ stroke ■ transient ischemic attack

There is controversy regarding whether transient ischemic attack (TIA) patients can be managed safely without hospital admission.[1–3] Although it has been proposed that hospitalization may improve access to thrombolysis in the event of recurrent ischemia,[4] recent modeling indicates outpatient management may be more cost-effective.[5] Post-TIA stroke rates are reported to be ≈5% at 7 days[6] and as low as 1% to 3% at 90 days in settings of expedited treatment.[7–12] The before and after study design of EXPRESS[8] provided evidence that rapid clinic-based management was superior to delayed initiation of therapy in TIA patients not referred to an emergency department (ED). Low stroke rates were reported with a rapid nonadmission-based protocol in SOS-TIA (admission rate 26%),[7] and the feasibility of protocol-driven evaluation based in an ED observation unit was later shown in unselected TIA patients presenting to hospital.[12] In the Ottawa study,[9] 98.4% of patients were discharged from ED with medication management at the discretion of the ED physician, Doppler ultrasound was booked as an outpatient, and urgency of follow-up was triaged based on the ABCD^2 score. In the TWO ACES study,[10] patients were discharged from ED based on a low ABCD^2 score[13] (admission rate, 30%). However, a low ABCD^2 score may miss patients with a modifiable high-risk mechanism such as atrial fibrillation or carotid stenosis.[14,15] Management in an inpatient ward vs an ED setting (ED observation unit) has been evaluated in only

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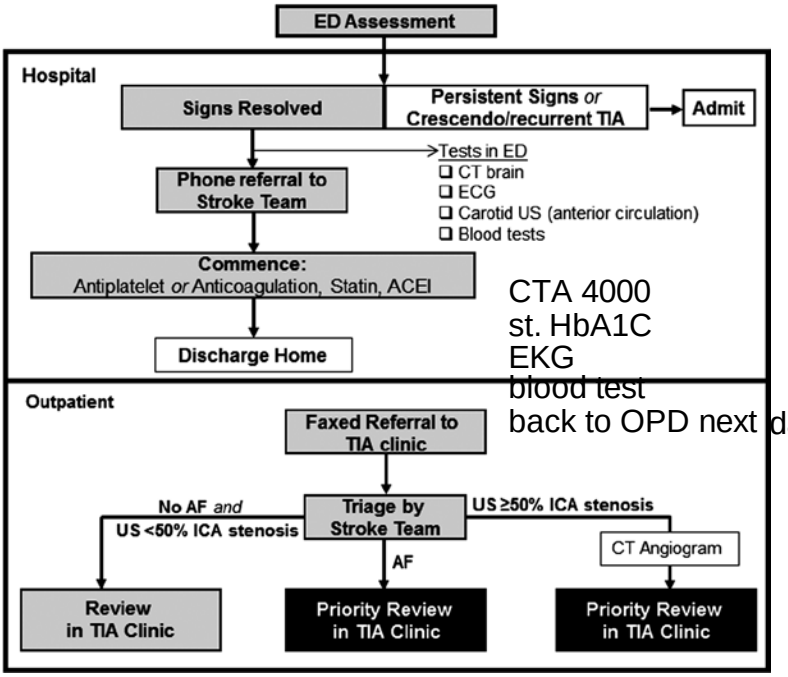

Figure. Flow diagram of the Monash Transient Ischemic Attack Triaging Treatment pathway. ED, emergency department; CT, computed tomographic imaging; US, ultrasound; ACEI, angiotensin-converting enzyme inhibitor; ICA, internal carotid artery; AF, atrial fibrillation.

1 randomized trial, although the primary outcome in this study was length of stay.[11] It is uncertain whether nonadmission is safe compared with routine admission in unselected TIA patients if urgency of management is stratified based on vascular mechanism.

In May 2004, we changed our model of TIA care, replacing an admission-based model with a nonadmission-based protocol, the Monash TIA Triaging Treatment (M3T) pathway. In M3T, rapid evaluation and management are initiated for all TIA patients in ED, in consultation with the stroke team, and urgency of TIA clinic follow-up is prioritized by vascular mechanism. Because the highest 90-day stroke risk is associated with large artery atherosclerosis and cardioembolism,[16] such patients are given urgent clinic appointments. We present our experience of M3T during its first 4 years, comparing performance with the previous admission-based model to provide proof of concept for managing TIA patients safely without routine admission. We evaluated whether M3T would be no worse in safety compared with the previous model, hypothesizing that primary outcome (90-day stroke) would be similarly low for both models.

Materials and Methods

Samples and Descriptive Data

We adopted a before and after cohort design similar to EXPRESS.[8] The primary cohort consisted of all patients with suspected TIA presenting to ED and managed in M3T from May 2004 to December 2007. TIA was defined as "acute loss of focal cerebral or monocular function with symptoms lasting <24 hours and that is thought to be due to inadequate cerebral or ocular blood supply as a result of arterial thrombosis or embolism."[17] We derived the comparison cohort from all patients presenting to ED from January 2003 to January 2004, who were assigned an *International Classification of Diseases*, 10th revision, Australian Modification TIA code G45.8 or G45.9. A stroke neurologist (T.P.) confirmed diagnosis after clinical consultation and/or review of medical records. In addition to presenting features, investigations, and treatment, we extracted data for potential confounding variables (preexisting vascular risk factors, medications before TIA) from hospital and clinic medical records. The Southern Health (Hospital) and Monash University Human Research Ethics Committees approved this study.

M3T Model

The M3T pathway (Figure) first requires emergency physician evaluation of suspected TIA patients, with decisions undertaken in consultation with the stroke team. Patients with persistent signs, recurrent/crescendo TIA, or other acute medical issues are admitted to the stroke unit. All other patients enter the nonadmission arm of M3T.

Our decision-making paradigm is driven by vascular mechanism, without dependence on the $ABCD^2$ score[13] or other risk-stratification tools. All patients receive urgent computed tomography brain imaging, ECG, and baseline blood tests in ED, with request forms marked "TIA Pathway" to expedite results. The radiology department facilitates same-day carotid ultrasound (anterior circulation symptoms) or next-day if patients present after usual working hours. After computed tomography review, antiplatelet therapy is immediately commenced or modified. If AF is identified and no contraindications exist for anticoagulation, then warfarin is commenced and titrated as an outpatient in conjunction with the patient's general practitioner. Guidelines for antihypertensive and lipid-lowering therapies are included in the pathway.

When a patient enters the M3T pathway, ED physicians fax a standardized TIA referral to a daily TIA clinic to facilitate outpatient review. The stroke registrar and nurse triage referrals on a daily basis, with priority appointments for patients with ipsilateral internal carotid artery stenosis ≥50%, a conservative threshold chosen to avoid missing a critical stenosis attributable to ultrasound misclassification.[18] For patients with ≥50% ipsilateral internal carotid artery stenosis, confirmatory computed tomography angiography or contrast-enhanced magnetic resonance angiography is arranged within 24 hours. Immediate referral for surgical intervention occurs for patients with confirmed symptomatic stenosis ≥70%. Patients with AF also receive priority review to assess anticoagulation. Patients without symptomatic internal carotid artery stenosis or AF are allocated less urgent appointments (usually within 4–6 weeks) given that antiplatelet therapy is commenced in ED. Optimization of other vascular risk factors occurs during clinic visits.

Table 1. Patient Characteristics

	All Cases			Confirmed TIA		
	Previous Model (n=169)	M3T (n=488)	*P* Value	Previous Model (n=128)	M3T (n=301)	*P* Value
Age, mean±SD	72.5±13.9	64.2±14.7	<0.001	72.4±14.2	67.7±13.1	0.001
Male (%)	99 (58.6)	267 (54.7)	0.383	73 (57.0)	175 (58.1)	0.832
Hypertension (%)	105 (62.1)	286 (58.6)	0.421	80 (62.5)	203 (67.4)	0.323
Hyperlipidemia (%)	79 (46.7)	256 (52.5)	0.200	65 (50.1)	179 (59.5)	0.096
Diabetes mellitus (%)	34 (20.1)	104 (21.3)	0.743	27 (21.1)	80 (26.6)	0.620
Ever-smoker (%)	69 (40.8)	131 (26.8)	<0.001	53 (41.4)	86 (28.6)	0.009
Atrial fibrillation (%)	40 (23.5)	56 (11.5)	<0.001	29 (22.7)	44 (14.6)	0.043
Carotid stenosis >50%*	19/88 (21.5)	39/417 (9.4)	0.001	19/76 (27.6)	39/372 (14.3)	0.026

M3T indicates Monash Transient Ischemic Attack Triaging Treatment; SD, standard deviation; TIA, transient ischemic attack.
*Patients undergoing ultrasound for anterior circulation symptoms.

Pre-M3T Model of Care

During 2003, most TIA patients were admitted to hospital. For the few patients discharged directly from ED, management and referral for neurologist follow-up were at the discretion of the emergency physician. Outpatient neurology referral from ED was not routine.

Outcome and Follow-Up

Primary outcome was stroke at 90 days. Stroke was defined as "rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting >24 hours or leading to death, with no apparent cause other than of vascular origin."[19] We determined stroke events by face-to-face neurologist consultation for the majority of patients. We used a sensitive and validated telephone questionnaire[20] in patients who declined consultation, or we searched medical records if they were deceased or unable to be contacted. Methods of outcome ascertainment may vary by physician, method of interview, or in recording of data in medical files. To limit this possible bias, we also captured stroke events within 90 days of TIA by data linkage of both cohorts to *International Classification of Diseases*, 10th revision, Australian Modification stroke codes (I63.0–9, I64.0) in the comprehensive population-level hospital morbidity discharge datasets maintained by the Victorian Department of Health.[21] We applied the same definitions and follow-up methods to both cohorts to minimize potential for measurement bias. Secondary outcomes were times to carotid ultrasound and revascularization, proportions admitted, and medication prescription.

Statistical Analysis

We used 2-tailed *t* tests and χ^2 tests to compare groups for baseline characteristics and to assess distribution of potential confounders.[22] We calculated 95% confidence intervals (CI) for observed proportions (p_i) of stroke at 90 days using the Wilson method.[23] To evaluate our hypothesis of similarly low stroke outcome in both models, we calculated the risk difference (risk difference=*Padmission model–PM3T*) and constructed confidence limits using the method of variance estimates recovery.[24] In cases of no true difference between groups, the risk difference CI would be expected to include zero.[23]

We controlled for potential confounding using established methods of multivariable logistic regression.[22] We first evaluated the effect of each potential confounding variable on stroke outcome using univariable logistic regression. Variables with $P \leq 0.20$ were included in multivariable logistic regression to generate an adjusted odds ratio of 90-day stroke outcome for M3T compared with the previous model. We did not adjust for differences in treatment after presentation, because these are components of the model of care undergoing evaluation. We also compared stroke in M3T with proportions reported in other published nonadmission-based TIA management studies[7–11] using χ^2 test.

Additionally, we assessed M3T for noninferiority against the previous model and other rapid-care models (1-tailed; $\alpha=0.10$). We assumed admission to represent "optimal treatment" and proposed that an increase of >3 strokes per annum in M3T would be unacceptable. Based on an average of 84 patients per annum presenting with a definite TIA in M3T, this would equate to 3.6% absolute increase in 90-day stroke rate, which we rounded down to a conservative noninferiority margin (δ) of 3.0%. Noninferiority is inferred if the 90-day stroke rate in M3T is not >3.0% higher than that in the previous model.

Because of skewed distribution of times to carotid ultrasound and revascularization, we evaluated differences in the interquartile ranges using interquantile regression, adjusting for baseline confounding factors. Proportions admitted were compared using χ^2 test. Although we did not use ABCD^2 score[13] to enable decision-making, we compared stroke outcome between those who would have been assigned ABCD^2 scores 0 to 3 vs >3. All statistical analyses were undertaken using Stata (version 11.0; Stata Corporation).

Results

We treated 488 patients in M3T between May 2004 and December 2007. Of these, 187 patients were TIA "mimics," leaving 301 with neurologist-confirmed TIA. We identified 169 patients treated in the previous model between January 2003 and January 2004, with a presenting diagnosis of TIA (based on *International Classification of Diseases*, 10th revision, Australian Modification TIA codes). Of these, 41 were TIA "mimics," leaving 128 with neurologist-confirmed TIA. Table 1 details comparison of patient characteristics between M3T and the previous model. Patients in M3T were younger, less likely to have atrial fibrillation and carotid stenosis, or to be former smokers (all $P<0.05$), but they were similar with respect to sex and other vascular risk factors. There were no significant differences in antiplatelet ($P=0.08$), antihypertensive ($P=0.47$), or statin ($P=0.85$) use before TIA.

We achieved 90-day follow-up in 468/488 (95.9%) patients in M3T and 150/169 (88.6%) patients in the previous model. Stroke outcome at 90 days was 1.50% (7/468; 95% CI, 0.73%–3.05%) in M3T compared with 4.67% (7/150; 95% CI, 2.28%–9.32%) in the previous model ($P=0.03$). All stroke events occurred in patients with neurologist-confirmed TIA: 2.36% (7/296; 95% CI, 1.15%–4.80%) in M3T compared with 6.14% (7/114; 95% CI, 3.01%–12.13%) in the previous model ($P=0.06$). Using data linkage, 90-day outcome was available for 93.3% of cases (M3T: 460/488, 94.3%; previous model: 154/169, 91.1%). This approach identified 17 stroke events overall, and proportions of patients

Table 2. Comparison of 90-Day Stroke Outcome Between Monash Transient Ischemic Attack Triaging Treatment and Previously Published Studies

Study	90-Day Stroke n/N*	90-Day Stroke %	95% CI, %	P†
M3T	7/296	2.36	1.15–4.80	. . .
EXPRESS (phase 1)‡[8]	32/310	10.32	7.41–14.21	<0.001
EXPRESS (phase 2)[8]	6/281	2.14	0.98–4.58	0.85
SOS-TIA[7]	13/770	1.69	0.99–2.87	0.47
Ottawa[9]	31/982	3.16	2.23–4.45	0.48
TWO ACES[10]	2/116	1.72	0.47–6.07	0.69

CI indicates confidence interval; M3T, Monash Transient Ischemic Attack Triaging Treatment; TIA, transient ischemic attack.

*TIA patients with 90-d follow-up.

†χ^2 test of proportions compared with M3T.

‡EXPRESS (phase 1) did not have an associated accelerated protocol for investigation and management.

with stroke were 1.74% (8/460; 95% CI, 0.88%–3.39%) in M3T compared with 5.84% (9/154; 95% CI, 3.1%–10.73%) in the previous model (P=0.007). The absolute risk difference between M3T and the previous model was 3.17% (95% CI, 0.32%–8.17%) among all patients and 3.78% (−0.19% to 9.89%) among those with definite TIA. Using a threshold of $P \leq 0.20$ in univariable logistic regression, age, sex, atrial fibrillation, carotid stenosis, ever-smoking, and previous statin use were considered for adjustment in multivariable logistic regression. The adjusted odds of stroke in M3T tended to be lower than in the previous model when all patients were considered (odds ratio, 0.46; 95% CI, 0.12–1.68; P=0.24) and among only those with definite TIA (odds ratio, 0.43l 95% CI, 0.12–1.59; P=0.21), although neither reached statistical significance. Stroke outcome at 90 days in M3T was similar to that reported in other published rapid TIA management models (Table 2). At the prespecified δ of 3.0%, M3T was noninferior to the previous model, EXPRESS (phase 2),[8] SOS-TIA,[7] and Ottawa[9] studies (Supplementary Table I). However, the noninferiority comparison with the previous model was powered below the recommended 95%,[25] whereas comparison with SOS-TIA[7] was adequately powered at 97% (Supplementary Table I).

In M3T, 417/488 (85.5%) underwent carotid ultrasound compared with 79/169 (47.9%) in the previous model (P<0.001). Median time to ultrasound, adjusted for differences in demographics, was similar in both groups (M3T: 1 day, interquartile range 0–3; prior model: 1 day, interquartile range 0–2; P=0.09). Of the patients with ipsilateral internal carotid artery stenosis ≥50%, 14/39 (35.9%) and 8/19 (42.1%) underwent carotid revascularization in M3T and the previous model, respectively. Median time to revascularization was 17.5 (interquartile range, 4–44) days in M3T and 26.5 (interquartile range, 6.5–149.5) days in the previous model (P=0.59). Compared with the previous model, more TIA patients in the M3T cohort were discharged with antiplatelet therapy (92.2% vs 82.0%; P=0.005), but there were no differences in proportions of patients discharged with statins (42.2% vs 46.3%; P=0.47) or antihypertensive agents (46.1 vs 50.5%; P=0.44). Admission to a hospital bed occurred in 85/488 (17.4%) and 117/169 (69.2%) patients in M3T and the previous model, respectively (P<0.001). Within M3T, there was no difference in stroke outcome between admitted (2/85; 2.35%) and nonadmitted (5/403; 1.24%) patients (P=0.43). Stroke outcome at 90 days in patients with ABCD^2 score >3 was 1.27% (5/297; 0.74%–3.96%) for M3T and 4.76% (4/84; 1.87%–11.61%) for the previous model. In patients with ABCD^2 score 0 to 3, the respective proportions were 1.05% (2/191; 0.29%–3.74%) and 3.53% (3/85; 1.21%–9.87%). There was no significant difference in stroke outcome between those with ABCD^2 score 0 to 3 and >3 within either cohort (M3T: P=0.56; previous model: P=0.68).

Discussion

Our results indicate that the nonadmission-based M3T system is safe when compared with routine hospital admission for TIA patients. Stroke rates in M3T were low and comparable with those observed in other rapid-care TIA models.[7–12] Compared with the previous model, M3T was associated with greater use of antiplatelet medication and carotid ultrasound. The ABCD^2 score did not predict outcome in either M3T or the previous model of care. Our findings suggest that a well-structured and supervised model focused on rapid investigation and initiation of treatment in ED, coupled with prioritized clinic follow-up based on stroke mechanism, is an acceptable alternative to hospital admission for TIA patients.

The stroke rate at 90 days in M3T was low and similar to rates associated with structured nonadmission-based TIA management in EXPRESS,[8] SOS-TIA,[7] and Ottawa[9] studies. However, unlike our study, there was no comparison with admitted patients in these studies. In the TWO ACES study,[10] 30% of patients were admitted based on risk stratification using the ABCD^2 score.[13] The M3T protocol, in contrast, is applied to unselected TIA patients, successfully avoiding admission in the majority of patients. The M3T protocol differs from other published pathways in several components. Unlike SOS-TIA[7] and EXPRESS,[8] it does not require the presence of neurologists at first assessment but requires initiation of treatment by ED physicians based on a structured pathway developed by stroke neurologists. Clinic follow-up urgency, in contrast to Ottawa[9] and TWO ACES,[10] is not based on the ABCD^2 score, but rather on underlying vascular mechanism. We recently have shown in our setting that a low ABCD^2 score may miss a modifiable high-risk mechanism.[15] Importantly, admitting M3T patients based on ABCD^2 score would have resulted in a dramatically higher admission rate (65%) with resultant implications for resource utilization.

A significant advantage of models such as M3T is the ability to improve hospital bed availability with the potential for cost-savings to the hospital system. An Australian survey reported that 96% of TIA patients managed in a hospital setting initially present to ED, and 65% of surveyed hospitals reported a policy of admission for either all or "high-risk" TIA.[26] With a national average of just 2.6 public hospital beds per 1000 population and hospital occupancy commonly >90% capacity, hospital beds are a limited resource.[27] In 2006/2007, the average bed-day cost for TIA in Victoria, Australia, was approximately 1000 Australian dollars (AUD$). Based on the median length of stay for TIA patients

in our study (2 days) and ≈160 TIA presentations per year to our center, the annual bed-cost alone would be as high as AUD$320 000 for 100% admission, AUD$256 000 for 80% admission, and only AUD$64 000 for 20% admission. For a median 4-day admission, as seen in our previous model of care and in SOS-TIA,[7] the respective values would be AUD$640 000, AUD$512 000, and AUD$128 000 per annum. However, these are only estimates, and further detailed cost evaluation with attention to microcosting of elements may be required to determine cost-effectiveness.

Some propose that admission would expedite access to thrombolysis,[4,28] which may confer cost-savings given projected decreases in stroke-associated morbidity and mortality. Authors of a cost modeling study reported borderline cost-effectiveness for 24-hour admission of all TIA patients assuming a 24-hour stroke risk of 4.2% and a presumed higher rate of thrombolytic administration in hospitalized patients.[4] However, results of a more recent decision analysis indicated early stroke rates of 20% were necessary to achieve cost-effectiveness.[5] In our study, 2-day stroke outcome in M3T was only 0.85% with similarly low early rates seen in other rapid assessment pathways.[7–10] To date, clinical evidence is lacking to support the hypothesis that admission of TIA patients leads to timely thrombolysis.

We recognize that different health systems and economic factors may influence TIA care models. For example, other Australian investigators have observed higher stroke rates in patients discharged directly from their ED compared with those admitted, concluding that delay or omission of appropriate investigations and treatment, in the absence of a structured rapid-care pathway, contributed to their findings.[29] In our center, strong collaborative links between ED and stroke and radiology departments were integral to the successful implementation of our M3T protocol. Conversely, a Spanish study reported difficulties implementing timely investigations and treatment, leading the authors to conclude that hospital admission was necessary in their setting.[30]

The strengths of our study include the high rate of follow-up, multiple sources of outcome ascertainment, and comparison with the model of care immediately preceding M3T. To minimize possible measurement bias associated with use of a historical cohort, we applied standardized definitions for TIA and stroke and a neurologist confirmed TIA diagnosis. Beyond searching hospital medical records for stroke outcome, we used data linkage with the Victorian hospital discharge morbidity database to detect patients presenting to another institution with stroke. These data, although dependant on the accuracy of *International Classification of Diseases*, 10th revision, Australian Modification coding, provide another avenue by which the 2 groups could be compared and minimize potential bias attributable to loss of follow-up. In the unlikely event of stroke in all M3T patients lost to follow-up, and no additional stroke in the previous model, there would still be no significant difference in outcome (P=0.48).

There are limitations to this study. We did not perform a randomized comparison of TIA models, but used a before and after study design similar to EXPRESS.[8] However, to design a randomized trial comparing models for noninferiority with conservative δ values of 3%, 2%, and 1%, we would require >600, >1400, and >5600 patients per arm, respectively, posing significant logistic challenges to conduct such a trial in a timely fashion at a single institution. Although the comparison of M3T with the previous Monash model was underpowered to definitively confirm noninferiority, it was clearly noninferior to the SOS-TIA model (a large study with the lowest 90-day stroke rate[7]). Furthermore, we used a conservative noninferiority margin. The low stroke rate (1.50%) in M3T presented with robust and conservative CI[23] along with superior system process indicators (eg, uptake of antiplatelets, proportions receiving ultrasound) add credence to the safety of M3T.

In summary, our study provides proof of concept that a well-organized nonadmission-based TIA model of care such as M3T is likely to be safe. The key component in any TIA model of care probably lies in mobilization of resources to expedite essential investigations and management based on vascular mechanism.

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Disclosures

None.

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Title Page

SUPPLEMANTAL MATERIAL

Monash **T**ransient Ischemic Attack **T**riaging **T**reatment (M3T): safety of a TIA mechanism-based outpatient model of care

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Supplementary Table S1: Non-inferiority comparisons between M3T model and other models (δ=3.0%)

Comparison group*	95%CI for non-inferiority (1 tailed; α=0.10)	Power (1-β)
Prior Monash Model (n=114)	-7.8%, 0.2%	0.60
EXPRESS[1] phase 2 (n=281)	-1.8%, 2.28%	0.88
SOS-TIA[2] (n=770)	-0.96%, 2.32%	0.97
Ottawa study[3] (n=982)	-2.5%, 0.93%	0.92
TWOACES[4] (n=116)	-1.8%, 3.1%	0.72

*TIA patients with 90-day follow-up

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ORIGINAL RESEARCH
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Application of Strategic Transport Model and Google Maps to Develop Better Clot Retrieval Stroke Service

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Background and purpose: Two hubs are designated to provide endovascular clot retrieval (ECR) for the State of Victoria, Australia. In an earlier study, Google Maps application programming interface (API) was used to perform modeling on the combination of hospitals optimizing for catchment in terms of current traveling time and road conditions. It is not known if these findings would remain the same if the modeling was performed with a large-scale transport demand model such as Victorian Integrated Transport Model (VITM). This model is developed by the Victorian State Government Transport has the capability to forecast travel demand into the future including future road conditions which is not possible with a Google Maps based applications. The aim of this study is to compare the travel time to potential ECR hubs using both VITM and the Google Maps API and model stability in the next 5 and 10 years.

Methods: The VITM was used to generate travel time from randomly generated addresses to four existing ECR capable hubs in Melbourne city, Australia (i.e., Royal Melbourne Hospital/RMH, Monash Medical Center/MMC, Alfred Hospital/ALF, and Austin Hospital/AUS) and the optimal service boundaries given a delivering time threshold are then determined.

Results: The strategic transport model and Google map methods were similar with the R^2 of 0.86 (peak and off peak) and the Nash-Sutcliffe model of efficiency being 0.83 (peak) and 0.76 (off-peak travel). Futures modeling using VITM found that this proportion decreases to 82% after 5 years and 80% after 10 years. The combination of RMH and ALF provides coverage for 74% of cases, 68% by 5 years, and 66% by 10 years. The combination of RMH and AUS provides coverage for 70% of cases in the base case, 65% at 5 years, and 63% by 10 years.

Discussion: The results from strategic transport model are similar to those from Google Maps. In this paper we illustrate how this method can be applied in designing and forecast stroke service model in different cities in Australia and around the world.

Keywords: stroke, transport, optimization, Google Maps, endovascular clot retrieval

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INTRODUCTION

The successes of endovascular clot retrieval (ECR) trials in 2015 (1 – 6) have generated optimism in the treatment of stroke and also debate on translating of these trials into clinical practice for both rural and metropolitan patients (7). These issues include whether patients should be transported to transfer directly to "mothership" or treat at the local hospital first, so called "drip and ship" (8, 9). Initial management at the local hospital has been associated with delayed onset to revascularization (10) and poorer outcome (11). Such idea on treatment exist previously in the development of primary stroke center (PSC) and comprehensive stroke center (CSC) (12, 13). Hospitals certified as CSC have faster time to reperfusion than PSC (14); these ideas now have taken center stage given the better outcome for ECR in centers with high volume output of cases. However, transfer of all cases or screened positive LVO cases can impact on capacity of the receiving hospital. The capacity of the "mothership" hospital to handle the diversion of patients has not been evaluated. In 2017, it has been estimated that 10 – 16% of patients would be eligible for ECR. This number will change with the publications of two ECR trials which extend the time window to 16 – 24 h (15, 16).

The State of Victoria had deemed in 2016 that two ECR hubs would be required for this purpose and performed a rigorous process to select the ECR hubs (17). This idea is similar to the concept of CSC but with a difference that the CSC provide care for the catchment and also outlying rural areas (12). Royal Melbourne Hospital (RMH) was selected as the first site with Monash Medical Center (MMC) added in the year 2018. An initial study showed that the combination of RMH and MMC would be optimal in terms of the ability of patients to travel to these hospitals within the idealized time of 30 min (18). This study was performed using an interface to the Google Maps API to query traveling time at different times of the day. A potential drawback of that study is that it cannot assess stability of the transport model in the future given population growth, increasing number of cars on the road and building of new road links and public transport routes. In this study, a trip-based travel demand model developed for the whole state of Victoria was used to obtain the travel time from a random generated address to each of the nominated ECR-capable hospitals in Melbourne. This method of analysis is standard within the transport industry but is not so well known in the medical literature, Historically, models of these systems have been developed to model the movement patterns of passengers and vehicles in cities. These models are used by transport planners and decision makers to understand the travel behavior of travelers over time (19). The aim of this study is to employ a strategic transport model to evaluate the findings from the Google Maps API and assess if the catchment for the two hospitals remain stable into the future. Consistent with the idea developed in the call for paper in this special issue of Frontiers in Neurology, we will spend the next section discussing how investigators can apply similar methods at their local sites.

METHODOLOGY

Setting

Melbourne is the second largest city in Australia and is the capital city of the state of Victoria in Australia with a population of approximately 4 million. The addresses were generated from the postcodes for metropolitan Melbourne are in the range 3,000 – 3,207. This aspect had been described in our earlier paper in 2017 (18).

ECR Capable Hospitals

There are 4 ECR capable hospitals in Victoria: Royal Melbourne Hospital (RMH), Monash Medical Center (MMC), Austin Hospital (AUS) and Alfred Hospital (ALF). At the time of the writing of the Statewide Protocol for ECR in 2017, it was planned to operate with 2 ECR hubs (17). RMH is located near to the center of Melbourne, MMC to the South-East, AUS to the North and ALF is located between RMH and MMC.

Transport Modeling

In this paper, an idealized time of 30 min is used based on the modeling in the redesign of stroke service in London (20). In this section, we explain the VITM model as a transport demand model as well as its functionality to generate the service boundaries of nominated ECR-hub in different combinations based on travel time. The Victorian Integrated Transport Model (VITM) is a large-scale trip-based model known as "four-step" process which has been used by the Victorian Department of Transport (DoT) and VicRoads to evaluate the impacts of alternative transportation and land use investments as well as presenting any changes in travel demand in response to different input assumptions (21). This process has four basic phases as its name implies: trip generation, trip distribution, mode choice and, trip assignment (22). This study consists of two main stages. The first stage is to validate the VITM model by comparing the VITM base case 2016 results with travel time data produced by the Google Maps API from the previous study. To this end, different statistical tests such as R^2, RMSE, and NSE will be applied. Once the validity of the VITM model is confirmed, VITM will then be utilized to predict travel time in projection years of 2021 and 2026.

VITM MODEL

Trip generation predicts the number of trips produced in a certain area of the network by trip purpose and destined for a particular traffic analysis zone. Trip distribution connects trip production and attraction. Mode choice defines if trip is done with personal vehicle or public transport while trip assignment estimates the specific route for each trip. The original VITM was developed based on the travel data collected during 1990 but recalibrated using the Victorian Integrated Survey of Travel and Activity (VISTA) data (23). VISTA is a household survey diary data of randomly selected households (23). In this data, all information about how individuals travel including a simple walk with their dog to the way they travel between states are gathered. The main goal of this survey is to understand the complex

travel behavior of individuals. The model then incorporates the complex interactions within the transport system (e.g., car driving, public transport or other mobility modes) and that with economics, demographic and future land use change. The VISTA data was used in recalibration process to update trip generation, distribution and mode choice modules.

The state-wide version of VITM covers the entire state of Victoria. This model is based on a zone structure which collectively represent the geography of the modeled area. This model consists of 6,973 transport zones (12). The standard outputs from VITM are available at 5-yearly intervals from the latest VISTA data of 2016 year to a 30-year horizon (2046). This model provides travel demand estimates based on trip origin to destination, selected mode of car or public transport for all travel purposes. The car "skim" matrices produced by VITM represent travel time in minutes by time of day period as well as travel distance in form of kilometer by time of day.

Comparison of Different Models

Traffic zones containing the random addresses used in our previous study were identified, and travel time between each traffic zone and each hospital calculated using the VITM model. The catchment area for each hospital was determined by assigning each traffic zone to the closest hospital according to travel time. To estimate the catchment area of each hospital in 2-hub combinations, the number of zones which have travel time to that hospital less than the paired one were collected. The traveling time to 2-ECR combinations extracted from VITM in comparison to the Google Maps API data as well as the proportion of patients arriving to nominated hospital in each model during period are illustrated in **Table 1**. **Figures 1 – 3** show the catchment area of RMH as reference hospital in different combination with other hospitals.

The findings from Google Map were compared to that by VITM model using the R^2, and Nash – Sutcliffe model efficiency coefficient. The base case refers to the travel times extracted using Google APIs for Wednesday, 8th of June 2016 (24). The R-squared (R^2), and Nash-Sutcliffe model efficiency (NSE) are normally employed in model evaluation studies. R^2 values are within the range of 0 and 1 where values close to 0 show a poor fit and values close to 1 represent a perfect fit. The Nash-Sutcliffe model efficiency coefficient ranges from $-\infty$ to 1. An efficiency of 1 ($NSE = 1$) corresponds to a perfect match of the model (13, 14).

TABLE 1 | Proportion of patients arriving within 30 min in 2-hub models over base and future years.

Year \ Model	Model 1-a (RMH-MMC) (%)	Model 1-b (RMH-ALF) (%)	Model 1-c (RMH-AUS) (%)	
2016	82	65	63	Peak
2021	79	61	60	
2026	77	59	59	
Year \ Model	**Model 1-a**	**Model 1-b**	**Model 1-c**	
2016	86	74	70	Off peak
2021	82	68	65	
2026	80	66	63	

Stability of the Model in Future Year 2021 and 2026

Input variables to VITM for future years (2021 and 2016) consist of changes in land use data and generalized highway cost calculation including demographic, income growth, vehicle operating cost, parking cost, and parking boundaries. Following we will present results for the permutation of 2-hub in future years. Average time to each hospital in each combination as well as changes in proportion of patients arriving the hubs in critical 30 min during 10 years from 2016 to 2026 are presented inrea (**Table 1**).

RESULTS

For travel time forecasts, the strategic transport model and Google map methods had similar outputs with an R^2 of 0.86 (peak and off peak) and the Nash-Sutcliffe model of efficiency being 0.83 (peak) and 0.76 (off-peak travel).

Model 1-a (RMH, MMC) had a greater proportion of cases arriving to hospital within 30 min in all 3 years compared with model 1-b (RMH, ALF) and 1-c (RMH, AUS) (**Supplementary Table 1**). In model 1-a, the median traveling time to RMH is 15 min (IQR 17.75 – 23.08 min), 80% of cases within idealized travel time (TT) of 30 min during inter-peak in 2016 which decline to median travel time of 20.5 min (IQR 13.8 – 27.3) with 72% cases within TT. The same trend can be seen in MMC from 2016 to 2026 with increase in travel time from 15 (IQR 13.3 – 18.13) to 18.8 (IQR 14.3 – 23.35) and a decrease in percentage of cases arriving under 30 min from 90 to 85%. In other 2-hub models, the general decreasing trends in coverage of nominated hospital within 30 min are observable (**Supplementary Table 2**). In model 1-b, the median time to RMH was 21 min (IQR 17.75 – 23.08) in the year 2016, 25.84 min (IQR 19.16 – 32.53) in the year 2021 and 26.18 min (IQR 19.43 – 32.92) in the year 2026; the median time to ALF was 20 min (IQR 16.54 – 23.15) in the year 2016, 23.98 min (IQR 16.59 – 31.38) in the year 2021 and 24.09 (IQR 16.65 – 31.53) in the year 2026. In model 1-c, the median time to RMH was 15 min (IQR13.1 – 18.6) in the year 2011, 19.9 min (IQR13.28 – 26.65) in the year 2021 and 20.5 min (IQR 13.8 – 27.3) in the year 2026; the median time to AUS was 15 min (IQR 13.3 – 18.13), 16.13 min (IQR 13.93 – 18.33) in the year 2021 and 18.8 min (IQR 14.3 – 23.35) in the year 2026.

The combination of RMH and MMC has the greatest proportion of simulated cases arriving within ideal time of 30 min, 86% (off-peak) and 82% (peak). This proportion decreases to 82% (off-peak) and 79% (peak) after 5 years and 80% (off-peak) and 77% (peak) after 10 years. The combination of RMH and ALF provides coverage for 74% of cases, 68%

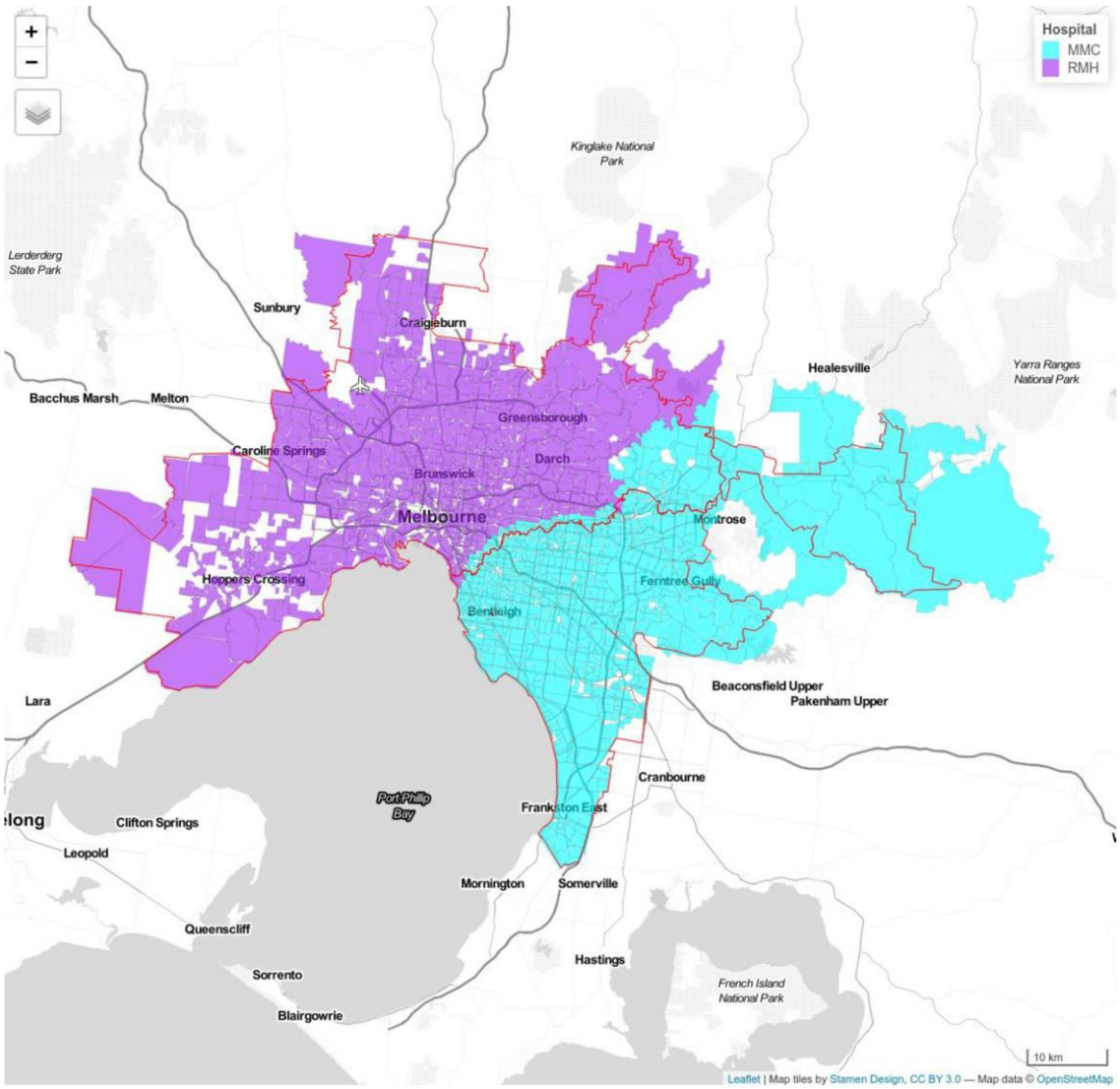

FIGURE 1 | Model 1a Royal Melbourne Hospital (RMH) and Monash Medical Center (MMC). Royal Melbourne Hospital's catchment has purple color and Monash Medical Centre's catchment is displayed with blue color. Red line shows the boundary determined using Google APIs.

by 5 years and 66% by 10 year. The combination of RMH and AUS provides coverage for 70% (off-peak) and 65% (peak) of cases in the base case, 65% (off-peak) and 61% (peak) at 5 year, and 63% (off-peak) and 59% (peak) by 10 year (**Table 1**).

Off peak, the VITM model yields a total of 4,338 patients within MMC catchment and 5,434 patients in RMH catchment. The Google Map model yields a total of 3,854 patients within MMC and 5,958 patients. If 10% of the patients with stroke in this catchment are eligible for ECR then it is estimated from VITM model that the number of cases in the MMC and RMH catchments are 434 and 543 patients, respectively. During peak hour, the VITM model yields a total of 4,253 in MMC and 5,519 in RMH catchments. The Google Map model yields a total of 4,213 in MMC and 5,599 in RMH catchments. In this case and assuming 10% of the patients are eligible them the estimated number of cases are 425 for MMC and 552 for RMH (**Supplementary Table 3**).

DISCUSSION

The key finding from this study is that the travel time forecasts from the Google Maps API is similar to that obtained by a strategic transport model and that the two-hospital model comprising of RMH and MMC provided the optimal solution with respect to inter-peak traveling time into the future. We were able to explore future

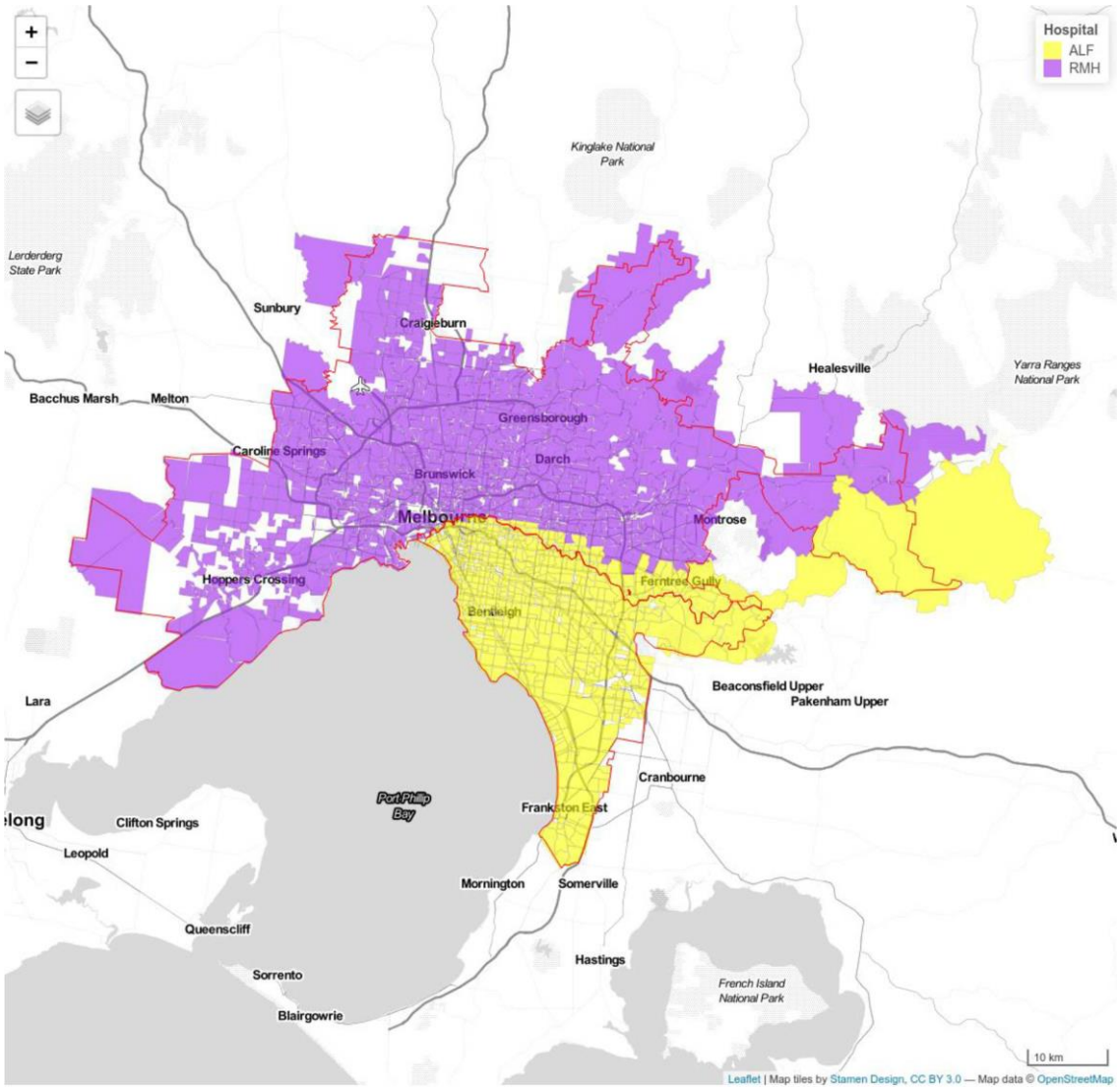

FIGURE 2 | Model 1b Royal Melbourne (RMH) and Alfred Hospitals (ALF). Royal Melbourne Hospital's catchment has purple color and Alfred Hospital catchment is displayed with yellow color.

transport scenarios up to 10 years and found that this combination remains stable suggesting the RMH and MMC combination is robust in both current and future scenarios. We propose that a combination of the two methods should be used to model hospital catchment for stroke or other medical illness.

Strategic Transport Model and the Google Maps API

The strategic transport model requires someone trained in its use and cannot be used easily by someone unfamiliar with the methodology. Running the model can take several weeks whereas the simulation with the Google Maps API can be performed overnight. Further, the license for the use of this model come from the Department of Transport and thus it is not open for public access. By contrast, the Google Maps API is open to the public upon signing up at the Google Developers' website. The two methods differ in that the main objective of strategic transport demand models is to meet long-term mobility needs on the basis of socio-economic scenario and land-use characteristics (25). As such strategic transport models like VITM produce transport metrics at the aggregate level of zone called traffic analysis zone. By contrast, the Google Maps API estimates travel time for a given trip at the specified time to individual addresses within zones. A critical difference between a strategic transport model and the Google Maps API is that the strategic transport model can be used for future travel planning. We were reassured our findings with the Google Maps API were confirmed with the strategic model using the high value on Nash-Sutcliff of model efficiency.

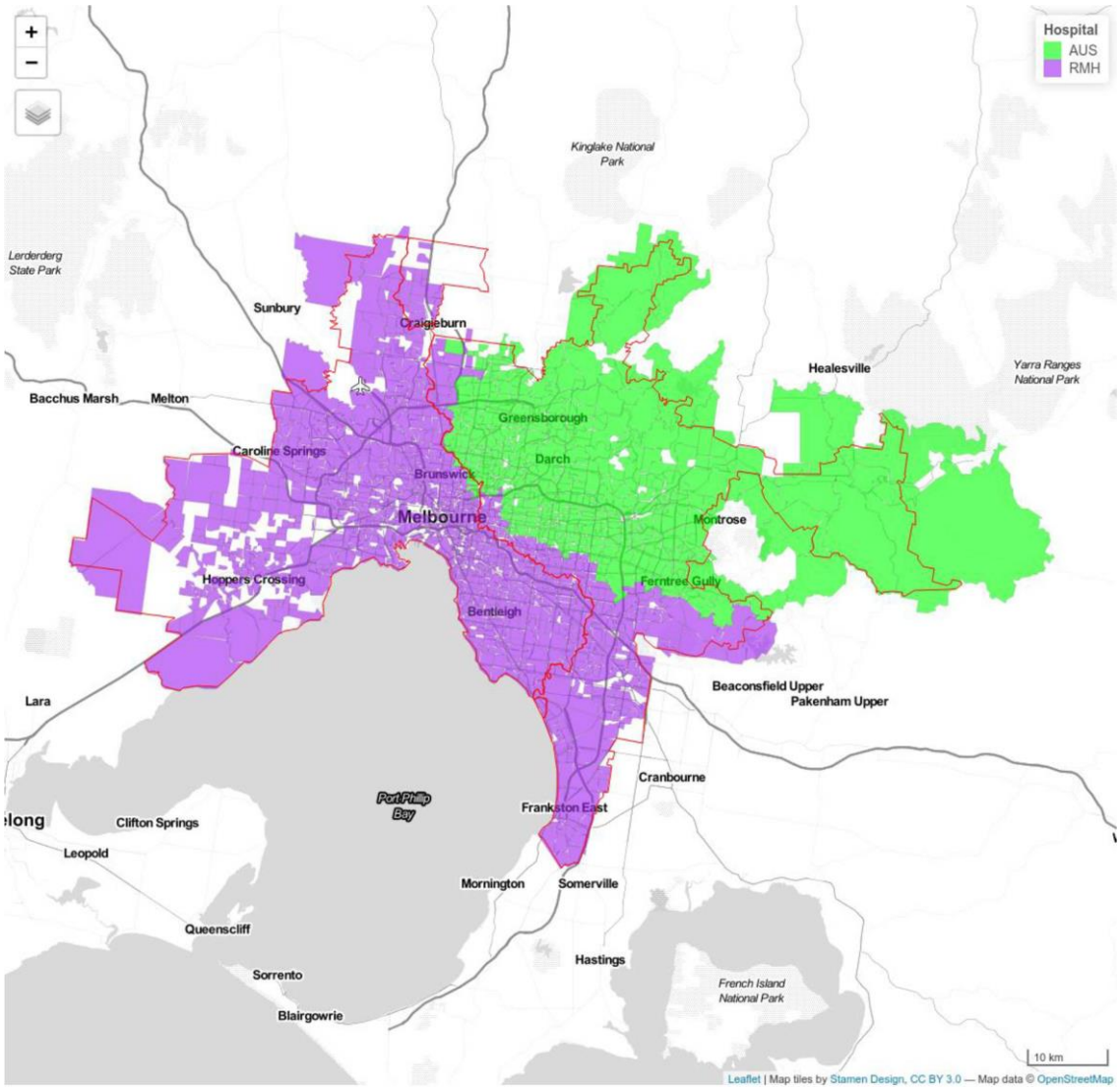

FIGURE 3 | Model 1c Royal Melbourne (RMH) and Austin Hospitals (AUS). Royal Melbourne Hospital's catchment has purple color and Austin Hospital's catchment is displayed with green color.

Strategic Transport Model in Australia and Around the World

Similar research can be conducted for other cities. For example, in Adelaide the MASTEM (The Metropolitan Adelaide Strategic Transport Evaluation Model) (26) and the STM (The Strategic Travel Model) in Sydney can be used in a same way to define the ECR service boundaries in this City (27). In England, the London Transport Studies (LTS) (28) is available while in Zurich and Singapore, an agent based (MATsim) model is available (29).

Our study has several limitations. The focus in this paper and our earlier paper has been on travel time (18). These are other issues to consider such as the government willingness to pay and the allocated budget, the number of available accredited interventional neuroradiologists and stroke (vascular) neurologists and the observed number of stroke cases requiring ECR. For example, the requirements to apply for second designated ECR hub in Victoria included sufficient number of accredited interventional neuroradiologists (4 at MMC) and stroke neurologists (5 at MMC) and 2 angiographic suites. A coalition of 2 ECR hubs would be able to handle 4 cases simultaneously every 2 h. Such a scenario has not yet been reached. The use of VITM for predicting future scenarios are based on a number of inputs to the model and as these scenarios are estimate of future events. In this study, the term "stable" has been used to describe the lack of variation in the catchment over the years for the combination of RMH and MMC. It was 6% change in the peak traffic model for this combination and 8% decrement for the RMH and ALF and 7% decrement for RMH and AUS.

The current study does not address the issue of model of patient care such as treatment at "mothership" or treat at the local hospital first, so called "drip and ship" (8, 9). There are various arguments either way. Proponents of treatment with "direct to mothership" model would point to the better outcome with direct transfer, possibly from avoiding delay from inter-hospital transfer and earlier revascularization (10, 11). A cautious approach would be to evaluate the capacity of the "mothership" hospital to handle the diversion of all patients to the mothership before imaging. Using very conservative estimate of 10% eligible patients, the "mothership" hospital would face a deluge of patients to process to treat in order to perform ECR on 434 patients at MMC or 543 patients at RMH. A variety of tools are now available to screen patients for LVO (30, 31). However, a formal prospective field testing of these tools and the impact on hospital case load has not yet been evaluated. Prior study had suggested that evaluation of models of care should include different type of hospital ability and ambulance transport (7). We would add the use of screen tool for LVO in the modeling approach.

CONCLUSION

In summary, we introduced a trip-based demand model to estimate the catchment area for ECR hubs and assess the stability of the model over time. This method can be applied in designing and planning ECR services not only in different states of Australia but also in Metropolitan cities over the world.

DATA AVAILABILITY

The datasets generated for this study are available on request to the corresponding author.

AUTHOR CONTRIBUTIONS

TP, RB, and HV: design. AT, HV, and RB: analysis. TP, HV, RB, GC, HM, and VS: writing.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.00692/full#supplementary-material

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