Question 42 evidence tables

Question 42: Does assessment and treatment in Mobile Stroke Units (MSU) for suspected acute stroke patients in the out of hospital setting prior to arrival in hospital lead to better functional outcomes, improved thrombolysis and thrombectomy treatment rates with process times and improved survival compared with routine care?

NB Any discrepancies between reviewers in evidence quality and comment were discussed at the corresponding evidence review meeting

REF ID	Source	Setting, design and subjects	intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
446	Thorsen, K., Larsen, K., Jaeger, H. S., Bache, K. G., Solyga, V., Tveit, L. H., et al. (2021). Ultraearly thrombolysis by an anesthesiologist in a mobile stroke unit: A prospective, controlled intervention study. *European Journal of Neurology*, 28(8), 2488-2496.	Norwegian Acute Stroke Prehospital Project (Treat-NASPP) is a single-centre non-randomised, prospective controlled intervention study exploring alternative staffing model using a trained anaesthetist to deliver IVT. Setting: Ostfold county, Norway, 300,000 residents covering 4000km^2	MSU staffed by trained anaesthetist, paramedic nurse and paramedic (with parallel dispatch of standard ambulance) Control – conventional ambulances in the same catchment	Primary: Difference in onset to treatment time (OTT) between MSU and control Secondary: -alarm to treatment (ATT), -rtPA rate, -discharge to home (surrogate as mRS rarely recorded) -3month mRS (blinded -SICH -Mortality	OTT 17 minutes shorter in the MSU group. 166 in MSU group (from 4361 stroke code dispatches), 92 (55%) received rtPA 274 in control ambulance, 107 (39%) received IVT Very mild stroke Median NIHSS 4 and 2 No difference in mRS at 3 months, SICH nor mortality.	0 Unclear how it was decided as to whether a patient would receive MSU or control. Low recruitment rate in control group Inclusion and exclusion criteria referred to in Fig1 [trial flow] are not clear. Baseline imbalance in NIHSS Not generalisable to UK

434	Chowdhury, S. Z., Baskar, P. S., & Bhaskar, S. (2021). Effect of prehospital workflow optimization on treatment delays and clinical outcomes in acute ischemic stroke: A systematic review and meta-analysis. *Academic Emergency Medicine*, 28(7), 781-801.	Design: Systematic Review and Meta-Analysis of mostly cohort studies with 3 randomised trials but varying levels of controls Setting: unclear from Studies included multicentre representation US, Australia, Germany, Europe Participants: (1) aged 18 years or older, (2) patients diagnosed with AIS, (3) studies with a defined prehospital systems change workflow optimization to the standards of care, (4) studies with good methodologic design, (5) studies with an appropriate control group.	Intervention: prehospital systems change/workflow optimizations for IVT, MT and Mobile Stroke Units Control: the existing standards of care for prehospital stroke management in the control group	Primary outcome and secondary outcomes : 1. systems delay and 2. reperfusion delivery efficacy : a. time to treatment and reperfusion rate variables b. clinical outcomes, mortality; c. adverse effects/ safety outcomes. Studies divided into 1. Improved IVT triage 2. LVO Bypass 3. MSU	Data on outcomes limited to a small number of studies eg MRS at 90 only 7/26, mortality n=5, sICH n=10 Note MSU studies n=9, data on MSU part of subgroup analysis MSU intervention was associated with an increased IVT rate (RR = 1.22, 95% CI = 0.98 to 1.52) not statistically significant DTN for MSU MSU— SMD = – 0.87, (95% CI = – 1.57 to – 0.17;) CallTN for MSU (SMD = – 1.41, 95% CI = – 1.94 to – 0.88 which was a significant reduction Onset to needle time MSU subgroup showed statistically significant time reduction (SMD = – 1.15, 95% CI = – 1.74 to – 0.56) MSU subgroup showed statistically significant time reduction in Door to Puncture time for LVO patients (SMD = – 1.17, 95% CI = – 1.48 to – 0.86) 2 MSU studies included in the CTP time meta- analysis showed that there was a significant reduction in DTP time for MSU patients (SMD = – 0.73, 95% CI = – 1.08 to – 0.38;) The three MSU studies included in the CTI time meta- analysis showed a	+ Acceptable but MSU data really only through subgroup analysis not the primary focus of the analysis

					significant reduction in CTI time for MSU patients (SMD = – 1.32, 95% CI = – 2.29 to – 0.36; Functional outcomes overall with PSOW there was no significant difference in good functional outcomes at 90 days. (RR = 1.04, 95% CI = 0.97 to 1.12) MSU subgroup no difference in functional outcomes MSU— RR = 1.01, 95% CI = 0.90 to 1.14; MSU subgroup associated with a non significant reduction in mortality (RR = 0.83, 95% CI = 0.36 to 1.94)	
434	S. Z. Chowdhury et al 2021 Effect of prehospital workflow optimization on treatment delays and clinical outcomes in acute ischemic stroke: A systematic review and meta-analysis	Systematic literature review and meta-analysis. Studies included: 1) patients with acute ischemic stroke; 2) studies with a defined prehospital systems change workflow optimization to the standards of care; 3) studies with good methodologic design and 5) studies with appropriate control group. The studies that used mobile stroke units were conducted in Germany and North America.	Use of pre-hospital workflow optimization pathway vs control The use of pre-hospital workflow pathway was sub grouped in 3 categories: 1) improved intravenous thrombolysis triage; 2) large vessel occlusion bypass and 3) mobile stroke unit	1) Intravenous thrombolysis rate; 2) mRS at 90-day: 3) mortality at 90-day;4) symptomatic haemorrhage rate	Mobile stroke units (n=6 studies) were associated with: 1) A non-significant increased IV thrombolysis rate (RR= 1.22, 95% CI 0.98-1.52) 2) No significant improvement in 90-day functional outcome (n=6 studies) in prehospital workflow optimization as a whole (RR=1.04,95% CI=0.97- to 1.12), neither in the mobile stroke units (RR=1.01, 95% CI=0.90- to 1.14). The overall heterogeneity was low but there was significant publication bias. The mobile stroke units were associated with a	+ Some evidence that mobile stroke units may increase thrombolysis rate, improve 90-day functional outcome and reduces mortality (subgroup analysis) but RCT needed. This systematic review and meta-analysis did not directly address the question.

		Studies included in outcome variable meta-analysis (n=14); studies included in Stroke Workflow Time variable meta-analysis (n=20; 4 RCT with concurrent controls; 13 used historical controls); studies included in Stroke Workflow Rate Variable meta-analysis (n=16)			nonsignificant reduction in mortality risks at 90-days (RR= 0.83, 95% CI=0.36 to 1.94). Overall heterogeneity was moderate and publication bias was fond in tunnel plot.	
437	Grotta, J. C., McCarthy, J., Flanagan, T., Yamal, J. M., Jacob, A. P., Wang, M., et al. (2021). Prospective, Multicenter, Controlled Trial of Mobile Stroke Units. New England Journal of Medicine, 385(11), 971-982.	observational, prospective, multicenter, alternating-week trial.	Thrombolysis in conventional setting against mobile stroke unit.	7.2% increase in patients having a better mRS at 90 days for MSU patients compared to ASU.	Our results show that in the areas served by the trial, patients who received emergency care within 4.5 hours after stroke onset had less disability on a utility-weighted scale at 90 days with MSU management than with management by EMS. Only 2.6 % of EMS patients in the study received t-PA compared to 32.9 in the MSU group.	++
437	Grotta, J. C., McCarthy, J., Flanagan, T., Yamal, J. M., Jacob, A. P., Wang, M., et al. (2021). Prospective, Multicenter, Controlled Trial of Mobile Stroke Units. New England Journal of Medicine, 385(11), 971-982.	Prospective, observational, multicentre cluster-controlled study (alternating weeks). 1047 eligible to receive tPA: 617 MSU and 430 via EMS. 7 urban centres in USA. Outcome assessments blinded to trial-group allocation and whether tPA administered.	Alternating weeks of MSU care versus emergency medical services (EMS). Weeks both discpatched at same time; vs only those who were eligible for thrombolysis	Primary: Utility-weighted mRS $\geq$0.91 (approximating mRS $\leq$1) versus <0.91 (mRS >1) at 90 days in those eligible to receive tPA (whether or not they received tPA). Secondary: (i) 30% reduction in NIHSS by 24h. (ii) 90 day mortality. (iii) Proportion thrombolysed.	MSU associated with higher utility-weighted mRS than EMS care: 0.72 (+/-0.35) versus 0.66 (+/- 0.36) (aOR for $\geq$0.91 2.43, 1.75-3.36). Secondary: (i) 30% reduction in NIHSS occurred more frequently in MSU than EMS: 75% versus 67.8% (aOR 1.45, 1.10-1.93).	++ Large well-designed RCT. Limitation is analysis by tPA eligibility rather than those thrombolysed.

				(iv) Onset-to-tPA time.	(ii) Mortality at 90 days lower in MSU than EMS: 8.9% versus 11.9%. (iii) Higher proportion thrombolysed in MSU than EMS: 97.1% versus 79.5% (iv) Median onset-tPA faster with MSU than EMS: 72 versus 108 min.	
444	Siegerink, B., Ebinger, M., Kunz, A., Wendt, M., Zieschang, K., Schmehl, I., et al. (2021). Association between Dispatch of Mobile Stroke Units and Functional Outcomes among Patients with Acute Ischemic Stroke in Berlin. *JAMA - Journal of the American Medical Association*, 325(5), 454-466.	prospective, nonrandomized, controlled intervention study was conducted in Berlin, Germany, from February 1, 2017, to October 30, 2019. If an emergency call prompted suspicion of stroke, both a conventional ambulance and an MSU, when available, were dispatched	Simultaneous dispatch of an MSU (computed tomographic scanning with or without angiography, point-of-care laboratory testing, and thrombolysis capabilities on board) and a conventional ambulance (n = 749) vs conventional ambulance alone (n = 794).	The primary outcome was the distribution of modified Rankin Scale (mRS) scores (a disability score ranging from 0, no neurological deficits, to 6, death) at 3 months.	Patients with an MSU dispatched had lower median mRS scores at month 3 (1; interquartile range [IQR], 0-3) than did patients without an MSU dispatched. 2; IQR, 0-3; common OR for worse mRS, 0.71; 95%CI, 0.58-0.86; P < .001). In a quarter MSU was cancelled, About 20 minutes earlier thrombolysis, and more thrombolysis in the MSU.	This included only patients with a final hospital diagnosis of stroke, so less relevant to the whole population. The post-hoc diagnosis of stroke makes it difficult to put into practice
444	B. Siegerink et al 2021 Association between Dispatch of Mobile Stroke Units and Functional Outcomes among Patients with Acute Ischemic Stroke in Berlin	Observational study set in Berlin (2017-2019) comparing MSU with conventional EMS for patients with ischaemic stroke and TIA. Control group included patient eligible for MSU but where one was unavailable. 3 mobile stroke units used. Time selection 0700-2300 (Mon-Sun). Blinded outcomes.	MSU with conventional vs conventional ambulance. MSU: CT, CTA, POC, thrombolysis and staffing including neurologist trained in emergency medicine	Modified Rankin Score (0-6). Three tier disability scale Secondary outcomes: thrombolysis rates	749 (MSU) vs 794 (conventional). Overall NIHSS 4 (whole group) MSU lower median mRS (1) vs (2) Conventional with OR for worse outcome 0.71 [0.58 to 0.86]. Sensitivity analyses carried out did not alter direction of odds ratios. ie 26% MSU cancelled (ITT analysis still consistent) I calculated NNT for excellent outcome (mRS 0-1) to be 11. Lower odds for worse outcome across three tiers	Non randomised. Only ischaemic stroke patients and not all suspected stroke Selective time (0700-2300) Mon-Sunday Blinded outcome Metropolitan area only (not rural) ie generalisability

					of disability (OR 0.73:[0.54 to 0.99] favouring MSU Higher rate of thrombolysis 60.2% vs 48.1% favouring MSU with faster onset to thrombolysis (95 mins vs 110 mins favouring MSU)	
438	Grunwald, I., Guyler, P., Perera, S., Menon, N., Haq, M. I. U., Phillips, D., et al. (2020). Mobile stroke unit in the united kingdom health care system: Avoidance of unnecessary a&e admissions for the majority of patients. *International Journal of Stroke*, 15(1 SUPPL), 210.	Prospective audit of UK NHS based MSU over 6 months (or 62 days of service) in Southend-on-Sea, 15 mile radius, circa 180,000 population. MSU comprised 1 paramedic, 1 stroke physician, 1 observer, 1 radiologist for first 50 cases (then remote); use of CTangiography if NIHSS>7, and AI (Brainomix)	MSU No control	Workflow metrics MSU-based stroke management Baseline clinical assessments Safety.	116 patients (mean age 79): -35 to SU -1 cath lab -1 neurosurgery -50 A&E -29 ambulatory setting rtPA for AIS patients was 29% with dispatch to needle time of 42 mins No complications	- Audit/feasibility. No control. First author is co-founder of Brainomix. AI used in the MSU.
449	Weinberg, J. H., Sweid, A., Herial, N., Gooch, M. R., Zarzour, H., Tjoumakaris, S., et al. (2020). The impact of the implementation of a mobile stroke unit on a stroke cohort. *Clinical Neurology and Neurosurgery,* 198, 106155.	Retrospective analysis of a prospective maintained database of mobile stroke unit dispatched cases from August 2019 to March 2020 in Bensalem Township, outside Philadelphia	Mobile stroke treatment use.	This study did not address the outcomes of interest. There was no control group and no patients follow up.	Amongst 195 mobile stroke unit (MSU) responses, 101 patients treated and transported by the MSU. Diagnoses: 41.6% ischaemic strokes, 27.3% TIAs, 3.9% ICH and 27.3% stroke mimics. Data available for 97 patients. Mean NIHSS =3.1; only 7/96 patients had tPA; 12 patients transferred to the main hospital for intervention; mean NIHSS was 15.8; 5 patients received tPA.	Low Very small numbers; patients had very low NIHSS score. Only 7/96 patients had thrombolysis. Only 12 patients transferred for intervention. No follow up data, no functional outcome.

					9/12 had MT; No patients had post-tPA haemorrhage. The mean time of dispatch to arterial puncture was 2:59 ±1:02; the mean time to last known well to tPA administration was 1:28 ±0:48min; with 4 receiving tPA within 60min. Mean NIHSS at discharge (n=12): 5.9 (0-20)	
449	Weinberg, J. H., Sweid, A., Herial, N., Gooch, M. R., Zarzour, H., Tjoumakaris, S., et al. (2020). The impact of the implementation of a mobile stroke unit on a stroke cohort. *Clinical Neurology and Neurosurgery,* 198, 106155.	Setting: US Philadelphia. Mobile Stroke Unit Responses Design: retrospective analysis of a prospectively maintained database of all MSU dispatched cases from August 2019 to March 2020 Participants: Patients with symptoms of acute stroke, within 24 hours of sx onset, patient willing to have telemedicine consult, willing to be transferred to Major Stroke Centre	MSU stroke care – didn't compare to standard care	Outcomes not clearly defined in the text but they collected data on demographics, risk factors, NIHSS scores, mRace scores, TPA or MT given, final diagnosis and time related metrics	101/195 MSU responses were treated and transported by the MSU. 7/96 (7%) received TPA, 12 had MT The mean time (hr:mm) of dispatch to scene arrival was 0:07+0:03, scene arrival to CT start was 0:10+0:03, CT start to teleneuro start was 0:05+0:03, teleneuro start to scene departure was 0:06+0:05, scene departure to hospital arrival was 0:12+0:06, hospital arrival to arterial puncture was 2:59+1:01. The mean time of dispatch to arterial puncture was 3:34+1:02. The mean time (LKW) to tPA administration was 1:28+0:48 with 4 (57.1 %) patients receiving tPA within 60 min of LKW and 5 (71.4 %) patients receiving tPA within 90 min. The mean time of dispatch to tPA was 0:37+0:09	0 Low quality. Descriptive study, no comparison to standard care, showed MSU potential but nothing concrete regarding functional outcomes for patients who received the care. Small sample size n=101

					Mean time of scene arrival to tPA administration was 0:28+0:07.	
443	Parker, S. A., Kus, T., Bowry, R., Gutierrez, N., Cai, C., Yamal, J.-M., et al. (2020). Enhanced dispatch and rendezvous doubles the catchment area and number of patients treated on a mobile stroke unit. *Journal of Stroke and Cerebrovascular Diseases*, 29(8), 104894.	Observational study comparing two MSU service delivery methods depending on distance from MSU base station. 338 individuals thrombolysed: 169 on scene and 169 distant. Sub-study of BEST-MSU study.	Compares treatment 'on scene' by MSU for nearby individuals versus rendezvous between EMS and MSU for more distant patients.	(i) Distance from MSU base station. (ii) Time from MSU alert to tPA bolus. (iii) Proportion of calls thrombolysed.	(i) Median distance from MSU base station: 6.4 (IQR 6.4) miles for on scene, 12.4 (IQR 5.5) miles for rendezvous ($p<0.0001$). (ii) No difference in time from alert to bolus: mean 36 (+/- 10) mins for on scene versus 37 (+/- 10) min for rendezvous ($p=0.65$). (iii) Higher proportion thrombolysed in rendezvous model: 44% versus 13%.	+ Does not address question of MSU-delivered versus hospital-delivered hyperacute treatment, but may inform service models (with rendezvous potentially expanding the coverage of an MSU).
443	Parker, S. A., Kus, T., Bowry, R., Gutierrez, N., Cai, C., Yamal, J.-M., et al. (2020). Enhanced dispatch and rendezvous doubles the catchment area and number of patients treated on a mobile stroke unit. *Journal of Stroke and Cerebrovascular Diseases*, 29(8), 104894.	US region Over a period of 4 years Using a MSU to travel and meet an ambulance outside of their normal radius	Monitored the radio system for possible calls and if the patient was over the normal allotted distance then they would rendezvous with the crew	A rendezvous system significantly expands the range of operations for a MSU in an urban area, doubling the number of patients treated, without incurring delay.	Adding a rendezvous approach to an MSU dispatch pathway doubles the range of operations and the number of patients treated by an MSU in an urban area, without incurring delay	+
436	Fatima, N., Saqqur, M., Hussain, M. S., & Shuaib, A. (2020). Mobile stroke unit versus standard medical care in the management of patients with acute stroke: A systematic review and meta-analysis. *International Journal of Stroke*, 15(6), 595-608.	Systematic review and meta-analysis of 11 studies (7 RCT and 4 Observational studies). RCT's were not blinded. Comparison of MSU versus Conventional ambulance programmes identifying process measures and outcomes. All strokes included although ICH not reported in the	MSU vs Conventional care	mRS [0-2] reported at day 1 and day 7 as primary outcomes performance metrics included: onset to thrombolysis (47.5 minute difference between MSU and conventional) and 24 minutes difference between onset and therapy decision and 13 minutes difference from	OR for primary outcome 1.46 [1.06 to 2.03} at day 7 favouring MSU but with non significant effects on day 1 mRS, in hospital mortality and complications	Acceptable. Analysis combined both RCT and observational and prospective data. RCT studies were not blinded. Clinical outcomes such as mRS at day 1 and day 7 are not clinically relevant and are not practiced in the UK. No outcomes related o ICH reported.

		analysis with regards to outcomes		onset to end of brain imaging all		
436	Fatima, N., Saqqur, M., Hussain, M. S., & Shuaib, A. (2020). Mobile stroke unit versus standard medical care in the management of patients with acute stroke: A systematic review and meta-analysis. *International Journal of Stroke*, 15(6), 595-608.	11 publications, 2 authors extracted data	MSU in US and Germany. No discussion of what is meant by MSU	mRS 0-2 as primary outcome. On average a 26 minute earlier decision with MSU than with standard care; 23 minute faster mean thrombolysis (62 vs 75 from alarm to lysis) which is fast by UK standards. OR 1.46 for better outcome which is greater than explained by the reduction in time to lysis		Meta-analysis of mixed observational and randomised studies
451	Zhao, H., Coote, S., Easton, D., Langenberg, F., Stephenson, M., Smith, K., et al. (2020). Melbourne Mobile Stroke Unit and Reperfusion Therapy: Greater Clinical Impact of Thrombectomy Than Thrombolysis. *Stroke*, 51(3), 922-930.	Reporting the first operational year of the Melbourne MSU, serviing 20km radius and 1.7million peolpe: 100 patients treated with pre-hospital thrombolysis compared to control cases (selected from 2016/17 registry data restricted to those thrombolysed in MSU operating hours)	MSU over 1 year compared to historical controls	Primary: Ambulance dispatch to starting rtPA (or arterial puncture for EVT cases) Secondary: ambulance and hospital workflows Translation to DALYs based on average time differences between MSU and control	MSU: 6.4 cases per service day. 1409 cases, 60% cancelled by initial paramedic crew attending. Of the remaining 939, 46.5% had MSU CT imaging with 23.3% having a CTA. rtPA 100 MSU patients received rtPA (48% of AIS reviewed within 4.5hr). Mean NIHSS 10 MSU Median onset-to-needle 95.5mins (n=100). Compared to 143.5mins in control (n=153). Difference 42.5mins (95%CI 36-49) EVT MSU: 57 had LVO, 36 received pre-hospital IVT and 41 EVT.	0 Evidence suggests faster rtPA and EVT workflow times but no data on clinical outcomes nor the effect on non-stroke cases. Use of historical controls introduces bias Cases and control baseline characteristics not well presented Some parallels probable with large cities in the UK but difficult to generalise.

451	Zhao, H., Coote, S., Easton, D., Langenberg, F., Stephenson, M., Smith, K., et al. (2020). Melbourne Mobile Stroke Unit and Reperfusion Therapy: Greater Clinical Impact of Thrombectomy Than Thrombolysis. *Stroke*, 51(3), 922-930.	Setting: Australia, Melbourne Design: Case Control cohort study Participants: All suspected stroke cases within 12 hours of symptom onset in the designated central Melbourne region	Cases: those who were treated by MSU Controls: those presenting to metropolitan Melbourne stroke units via standard ambulance within MSU operating hours	Median time differences for first ambulance dispatch to commencement of thrombolysis or arterial puncture between MSU and control data Disability-adjusted life years avoided for time savings were then calculated using published estimates for earlier provision of thrombolysis and EVT	Median time saving using MSU: first ambulance dispatch to hosp/scene 26 mins, scene/hosp arrival to TPA 15 mins. First dispatch to puncture for EVT 51 minutes ([95% CI, 30.1–71.9], P<0.001) All statistically significant. Overall time saving from dispatch to thrombolysis: 42.5 minutes (95% CI, 36.0–49.0). Median time saving of 17 minutes ([95% CI, 7.6–26.4], P=0.001) for EVT hospital arrival to arterial puncture for MSU patients. Overall median of 20.9 disability adjusted life years saved by providing thrombolysis 42.5 minutes earlier for 100 patients. Median 24.6 disability-adjusted life years were saved through providing EVT 51 minutes earlier for 41 patients.	0 Acceptable-low quality, definite risks of bias with methods used for control groups “historical rather than contemporaneous” Study exploratory in nature.
435	Ciccone, A., Berge, E., & Fischer, U. (2019). Systematic review of organizational models for intra-arterial treatment of acute ischemic stroke. *International Journal of Stroke*, 14(1), 12-22.	Systematic review of different organizational models for intra-arterial treatment in acute ischaemic stroke. 27 studies included in qualitative analyses (17 observational and 6 RCT of intra-arterial therapy) and 6 studies included in quantitative analyses.	4 organizational models identified: mother-ship, drip-and-ship, mobile interventionist and mobile stroke units. Non-randomized comparisons were performed using data from 8 observational studies and 1 randomized-controlled trial of intra-arterial therapy in mother-	Survival Functional outcome Arterial patency	Only 2 studies on mobile stroke units reporting qualitative data were included. One study (Germany) included 53 patients vs 47 controls. Mobile stroke units reduced the median time from alarm to treatment decision substantially but there was no significant difference in	Low. Larger RCT trials with functional outcome data were needed at the time of this publication.

		Only 2 studies used mobile stroke units as intervention (one study included 53 patients and other study 3213 patients).	ship vs drip-and-ship models.		numbers receiving therapy or in neurology outcome at 7 days. Another study (Germany) Assessed time reduction to thrombolysis in patients with a stroke in whom mobile stroke units was available and deployed (1804 patients) vs control weeks (2969 patients). There was a reduction of 15 minutes (95% CI, 11-19) in alarm-to-treatment times in the catchment area during mobile stroke unit weeks (76.3 min; 95% CI, 73.2-79.3 vs 61.4 min; 95% CI, 58.7-64.0; P < .001). Thrombolysis rates were 29% during mobile stroke unit weeks and 33% after mobile stroke units deployment vs 21% during control weeks (differences, 8%; 95% CI, 4%-12%; P < .001, and 12%, 95% CI, 7%-16%; P < .001, respectively). Mobile stroke unit deployment incurred no increased risk for intracerebral haemorrhage or 7-day mortality.	
447	Tsivgoulis, G., Geisler, F., Katsanos, A. H., Korv, J., Kunz, A., Mikulik, R., et al. (2018). Ultraearly Intravenous Thrombolysis for Acute Ischemic Stroke in Mobile Stroke Unit and Hospital Settings. *Stroke*, 49(8), 1996-1999.	Comparative analysis using STEMO data and SITS-EAST data Identified 117 patient s and 136 where no previous disability had not been noted	No intervention, just looking at the outcomes of the 2 registers	There was no benefit to be had with the use of ultra-early IAT when compared to standard hospital treatment	Although this is the case the percentage of patient accepted into the study were not the same infact in the STEMO arm some 38.4% of all patients were included, but only 0.9 of all	+

					patient entered into the SIT-EAST register were entered The authors acknowledge that there is a time difference between the 2 data sets used with the SIT-EAST data having more than 10 years more data available and they did wonder if this did have some bearing	
447	Tsivgoulis, G., Geisler, F., Katsanos, A. H., Korv, J., Kunz, A., Mikulik, R., et al. (2018). Ultraearly Intravenous Thrombolysis for Acute Ischemic Stroke in Mobile Stroke Unit and Hospital Settings. *Stroke*, 49(8), 1996-1999.	Compared patients from MSU with controls from another dataset treated with alteplase	alteplase	MSU versus hospital		Low
441	Kobayashi, A., Czlonkowska, A., Ford, G. A., Fonseca, A. C., Luijckx, G. J., Korv, J., et al. (2018). European Academy of Neurology and European Stroke Organization consensus statement and practical guidance for pre-hospital management of stroke. *European Journal of Neurology*, 25(3), 425-433.	Systematic review and expert consensus document covering a range of pre-hospital stroke management issues (identified using GRADE method). PICO 10 relates to use of MSUs: - 2 RCTs comparing MSUs to in-hospital intervention. - 1 observational study.	MSU versus hospital-delivered thrombolysis.	(i) Rate of thrombolysis. (ii) Effect on onset-to-treatment time. (iii) Comparison of rates of sICH.	(i) Increase in likelihood of receiving tPA with MSU (OR 1.79, 1.44-2.33). (ii) Median reduction in onset-bolus interval of 24-81 minutes with MSU. (iii) No difference in rates of sICH between MSUs and in-hospital intervention: OR 0.59, 0.25-1.38.	+ Study-level meta-analysis of 2 RCTs.
441	Kobayashi, A., Czlonkowska, A., Ford, G. A., Fonseca, A. C., Luijckx, G. J., Korv, J., et al. (2018). European Academy of Neurology and European Stroke Organization consensus statement and practical guidance for pre-hospital	Consensus [European] statements so really n/a [2018]. I think superseded by ESO 2022 statements	MSU vs Conventional	Treatment decisions	Reduction in time to receive IVT	+ Highlighted two RCT which did not comment on functional outcome

	management of stroke. *European Journal of Neurology*, 25(3), 425-433.					and only of lysis metrics.
433	Bowry, R., Parker, S., Wu, T.-C., Noser, E., Jackson, K., Rajan, S. S., et al. (2015). Benefits of stroke treatment using a mobile stroke unit compared with standard management: The BEST-MSU study run-in phase. *Stroke*, 46(12), 3370-3374.	Setting: US Design: 8 week run in phase before Trial Participants: Stroke patients in the community, last seen normal within 4.5 hrs, hx and exam consistent with stroke, no definite TPA contraindications	Mobile Stroke unit care V Standard care	No real outcome declared but did look at 90 day MRS, EVT times and Times for LYsis	Of the 12 patients treated with tPA on the MSU 4 (33%) were treated between 0 - 60 mins of SX , 4 between 61 -80 min, and 4 between 81 -270 min of onset. Mean time from EMS activation by a 911 call to tPA bolus was 47 minutes (range, 37–60 minutes). MSU on scene to tPA 25 min (18–42) Mean LSN to tPA time 98 min (47–265) Mean Baseline NIHSS, 10 (3–19) 90-day mRS score was 0 or 1 in 4 of the 12 tPA-treated MSU patients 4 MT patients LSN to groin puncture time, 175 (140–224) Door to groin puncture time 101 min (77–124)	Low quality, low numbers descriptive for feasibility
433	Bowry, R., Parker, S., Wu, T.-C., Noser, E., Jackson, K., Rajan, S. S., et al. (2015). Benefits of stroke treatment using a mobile stroke unit compared with standard management: The BEST-MSU study run-in phase. *Stroke*, 46(12), 3370-3374.	10 week pilot/run-in phase for the BEST-MSU trial (see NEJM 2021 Grotta) 10 weeks (8MSU v 2 SM), non-randomised feasibility study testing criteria for patient selection into the mail trial.	MSU versus standard management (SM)	"Lessons of implementation phase"	24 enrolled over 57 MSU days and 2 in the 14 SM days. 12 treated with tPA 4 primary SICH 1 SAH On scene-to-tPA 25mins (median) No CTA on MSU	- Non randomised feasibility study. Can't generalise to the UK Important lessons for their main trial: -No concealment of allocation -Higher baseline level of disability (hence

						move to utility weighted mRS as primary outcome) -careful assessment of mimics and their outcome
442	Kunz, A., Ebinger, M., Geisler, F., Rozanski, M., Waldschmidt, C., Weber, J. E., et al. (2016). Functional outcomes of pre-hospital thrombolysis in a mobile stroke treatment unit compared with conventional care: an observational registry study. *The Lancet. Neurology,* 15(10), 1035-1043.	Observational registry study; Germany between 2011-2015 427 patients treated with mobile stroke unit and 505 patients received conventional care. 305 patients in the mobile stroke unit group and 353 in the conventional care group had lived at home without assistance before the stroke and were included in the analysis.	Ischemic stroke patients receiving thrombolysis within a mobile stroke unit vs conventional care	Proportion of patients who lived at home without assistance before stroke and had a 3-month mRS score of 1 or lower.	161 (53%) of patients in mobile stroke unit vs 166 (47%) in the control group had an mRS score of 1 or lower (p=0.14). Compared with conventional care, adjusted ORs for mobile stroke unit care for the primary outcome (OR 1.40, 95% CI 1.00-1.97; p=0.052) were not significant. Intracranial haemorrhage (p=0.27) and 7-day mortality (p=0.23) did not differ significantly between treatment groups. Dichotomised secondary outcomes (mRs 0-3 and mortality) were more favourable for patients within mobile stroke unit group. Mean onset to treatment time was 33 minutes shorter in the mobile stroke unit group than in conventional care group. Significantly more patients in the mobile stroke unit received tPA within 60 min and within 90 min of onset compared to control group.	++ No significant differences in achieving primary outcome in both groups (mobile stroke unit versus standard care) Pre-hospital start of IV thrombolysis might favour outcome. Patients treated in mobile stroke unit received IV thrombolysis 30 minutes earlier than patients treated with conventional care. Larger scale RCT are needed.

448	Walter, S., Audebert, H. J., Katsanos, A. H., Larsen, K., Sacco, S., Steiner, T., et al. (2022). European Stroke Organisation (ESO) guidelines on mobile stroke units for prehospital stroke management. *European Stroke Journal*, 7(1), XXVII-LIX.	A review of the evidence of MSU within Europe, using the GRADE method the contributors are from what I can see the same people who may have contributed heavily to the roll out of MSU's and as such their objectiveness and impartiality maybe in question	Early intervention of treatment within the scope of practice at that time ie distance and running time to the job	No increased risk better functional outcomes on discharge	MSU use is suggested for the prehospital assessment of patients with suspected stroke. If an ischaemic stroke is diagnosed MSUs can facilitate swift treatment initiation with clot buster infusion and transportation to an appro- priate hospital that can provide potential clot removal through a procedure. Potential benefits for patients with a brain bleed may be possible and no direct harm, especially to those not suffering from a stroke could be detected. Further research is needed to detect further benefits. Local EMS organisations should invest in optimising dispatch quality in order to make MSUs available to as many AIS patients as possible.	++
439	Helwig, S. A., Ragoschke-Schumm, A., Schwindling, L., Kettner, M., Roumia, S., Kulikovski, J., et al. (2019). Prehospital Stroke Management Optimized by Use of	Randomised controlled trial testing the diagnostic accuracy of MSU versus Los Angeles Motor Scale (LAMS) in	MSU (typical architecture of brain imaging, POC, neurologist, telemedicine but not all SU contained CTA)	Statistical analysis included sensitivity, specificity, positive and negative predictive value for identifying LVO and ICH as	116 patient recruited and interim analysis 63 MSU (100% accuracy) 53 OPM (69.8%)	Although RCT Small study Selective population Low numbers of patients with LVO

	Clinical Scoring vs Mobile Stroke Unit for Triage of Patients With Stroke: A Randomized Clinical Trial. *JAMA Neurol*, 76(12), 1484-1492.	patients with LVO and ICH. Study period 2015-2017. Select population analysed (14% of patients screened recruited into the study) Comparison made between MSU and Optimised Pre-hospitalised Management programme (OPM). Randomisation occurred on a weekly basis. Statistical analysis included sensitivity, specificity, positive and negative predictive value		well as LVO (cut of >4) with triage decision in sending patients appropriately to CSC	100% sensitivity, specificity and PPV and NPP for MSU All significantly greater than OPM metrics 42% OPM required secondary transfers to CSC NO difference in outcomes although greater key metrics with thrombolysis timings	Does not answer PICO question.
439	Helwig, S. A., Ragoschke-Schumm, A., Schwindling, L., Kettner, M., Roumia, S., Kulikovski, J., et al. (2019). Prehospital Stroke Management Optimized by Use of Clinical Scoring vs Mobile Stroke Unit for Triage of Patients With Stroke: A Randomized Clinical Trial. *JAMA Neurol*, 76(12), 1484-1492.	Prospective multicentre cluster-randomised (week-wise, with maximum four week blocks) intention-to-treat study. Interim analysis of 116 patients (of planned 232): 53 in optimised prehospital management group versus 63 in MSU group. - Study stopped early having met pre-specified interim analysis criteria. Two non-urban regions in Germany.	Optimised prehospital management (OPM) using Los Angeles Motor Scale versus MSU.	Primary: Accurate triage decision (proportion of patients accurately triaged to either comprehensive stroke centre or primary stroke centre – defined as those with LVO or ICH to nearest comprehensive stroke centre). Secondary: (i) Need for further transfer between centres for those with LVO or ICH. (ii) Call-to-tPA bolus times. (iii) Median mRS for confirmed strokes at day 90.	Higher proportion with a correct triage decision in MSU versus OPM: 63/63 (100%) versus 37/53 (69.8%) respectively. Difference: 30.2%, 95% CI 17.8-42.5%, P<0.001 Secondary: (i) Fewer transfers needed with MSU versus OPM: 0/11 (0%) in MSU group versus 7/17 (41.2%) in OPM group (difference 41.2%, 95% CI 17.8-64.6%), P=0.02). (ii) Faster call-to-tPA bolus times with MSU (mean 50.1 +/- 10.1 minutes) versus OPM (84.9 +/- 30.2), P<0.001. (iii) No difference in median mRS at 90 days for MSU	+ Results not directly relevant to PICO, though potentially some implications for rates and processing times of MT given need for secondary transfers. Likely underpowered for secondary outcomes.

					cohort (3, IQR 1-4) versus OPM (3, IQR 1-5), P=0.12.	
445	Sookram, G., Kim, J., Cadilhac, D. A., Coote, S., W Parsons, M., Yan, B., et al. (2021). Economic evaluation of the Melbourne Mobile Stroke Unit. *International Journal of Stroke*, 16(4), 466-475.	Simulation model. Compared costs/benefits for the treated 2018 cohort with hypothetical counterfactual where this cohort would have received standard care. Cost perspective = healthcare providers of emergency/acute care. Operational costs of MSU obtained from service data. Various one-way and probabilistic sensitivity analyses.	MSU vs simulated standard care	Primary outcome=incremental cost per DALY avoided; DALYs estimated from improvements in provision of thrombolysis and EVT and estimates of DALYs avoided from provision of these therapies, as indicated by literature. Improvements in time to reperfusion therapies was based on difference in medians from the MSU clinical records and standard care estimates in a national stroke registry.	Time savings - resulting in greater provision of time-sensitive treatments - are expected to be associated with an additional 45 DALYs avoided for the 2018 modelled cohort. US$31k per DALY avoided. So within acceptable range.	Fair quality simulation modelling study. However, based on observational data for just one year and one context, and compared to a hypothetical counterfactual. Necessarily relies on various assumptions based on the expert opinion of hospital clinicians etc. and excludes longer term/non-acute costs. Importantly, lacks patient-level outcomes data. So not robust enough to draw conclusions for guideline.
440	Hustey, F. M., Kralovic, D., Reimer, A. P., Zafar, A., Russman, A. N., Uchino, K., et al. (2020). Cost-Consequence Analysis of Mobile Stroke Units vs. Standard Prehospital Care and Transport. *Frontiers in Neurology*, 10, 1422. Cost-Consequence Analysis of Mobile Stroke Units vs. Standard Prehospital Care and Transport. Frontiers in Neurology, 10: 1422.	Similar to the above, performed a model comparing patients served by a MSU (Cleveland Clinic) versus simulated standard care. Decision analytic model. Data from patients served by the Cleveland MSU 2014-2015. Hospital perspective – informed probabilities. Gaps filled with expert opinion and literature. Various deterministic	MSU vs simulated standard care.		MSU cost an additional $71k for 355 patient transports, which is a relatively small additional cost given the initial large investment and maintenance costs required. MSU avoided 76 secondary interhospital transfers and 76 ED encounters. Sensitivity analysis identified 6 variables with measurable impact on the model's variability and a threshold value at which MSU	Modelling study with similar caveats to that reported by Kim et al. Hospital perspective only. Largely local data and opinion so limited generalisbility.

		and probabilistic sensitivity analyses.			becomes the optimal strategy: number of stroke patients (>391), probability of requiring transfer to a comprehensive stroke center (>0.52), annual cost of MSU operations (<$696,053), cost of air transfer (>$8,841), probability initial receiving hospital is a CSC (<0.32), and probability of ischemic stroke with ST (<0.76). MSUs can avert significant costs in the administration of stroke care once optimal thresholds are achieved. But a comprehensive CEA is required to determine not just the operational value of an MSU but also its clinical value to patients.	
450	Yamal, J.-M., Jacob, A. P., Gonzalez, M. O., Tilley, B. C., Rajan, S. S., Lairson, D. R., et al. (2018). Benefits of stroke treatment delivered using a mobile stroke unit trial. *International Journal of Stroke*, 13(3), 321-327.	Ongoing Phase 3 multicentre prospective cluster RCT with ec evaluation. First year+ lifetime CEA from Medicare's perspective using ICER and NB regression. Lifetime costs after first year will be simulated using Markov modeling. Nonparametric	MSU vs standard management weeks	Primary = 90 day utility-weighted mRS. (Utility weights transform the 7 mRS levels to values between 0 and 1 with distances between levels reflecting patient and societal valuation of each disability state); Coprimary=cost-effectiveness based on EQ5D and 1 year post-stroke costs.	N/A THIS PAPER DESCRIBES AN ONGOING TRIAL THAT HAS YET TO COMPELTE RECRUITMENT	Seems like a large and well-designed trial. Standard robust prospective CEA. So could be helpful for informing the guideline when complete.

		bootstrapping/CEACs to assess uncertainty plus deterministic one-way and multiway sensitivity analyses to check robustness of ICER and NBR estimates by varying the study parameters by set percentage points in each direction, determined thorough literature review and expert opinion. (1) Rehospitalizations; (2) other inpatient stays; (3) emergency department visits; (4) QoL; and (5) survival will be compared between groups using logistic regression, linear regression, and survival analysis.				
944	Turc, G., Hadziahmetovic, M., Walter, S., Churilov, L., Larsen, K., Grotta, J. C., et al. (2022). Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis. JAMA Neurol, 79(3), 281-290.	Systematic review and meta-analysis of MSU on management of patients with ischaemic stroke using 14 articles. Combination of observational and RCT included.	MSU vs standard care	mRS 0-1 at 90 days. Process measures: Onset to IVT time IVT < 60 mins of onset sICH 7 and 90 day mortality	Reduced disability excellent outcome OR: 1.64 (1.27 to 2.13) Shorter onset to IVT with MSU (31 minutes) No difference in safety or mortality	+ Included both RCT and Observational studies

944	Turc, G., Hadziahmetovic, M., Walter, S., Churilov, L., Larsen, K., Grotta, J. C., et al. (2022). Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis. *JAMA Neurol*, 79(3), 281-290.	Studies comparing MSU deployment and usual care for patients with suspected stroke were eligible for analysis, excluding case series and case-control studies.	Mobile stroke unit (specialized ambulance equipped with computed tomography scanner, point-of-care laboratory, and neurological expertise) use leads to better functional outcomes compared with usual care).	Primary outcome: mRS 0-1	Compared with usual care, MSU use was associated with excellent outcome (adjusted odds ratio [OR], 1.64; 95%CI, 1.27-2.13; P < .001; 5 studies; n = 3228) 14 articles, 3 RCT	++
945	Chen, J., Lin, X., Cai, Y., Huang, R., Yang, S., & Zhang, G. (2022). A Systematic Review of Mobile Stroke Unit Among Acute Stroke Patients: Time Metrics, Adverse Events, Functional Result and Cost-Effectiveness. *Front Neurol,* 13, 803162.	Systematic review on time metrics, outcomes and cost effectiveness on MSE vs standard care 16 studies included	MSU vs standard care	Time to therapy Time to CT mRS 0-2 at 90 days QALYS and ICR calculated	Faster time to therapy and imaging as well as higher rates of mRS (0-2) with MSU Cost benefit favourable with MSU for QALYS and ICR (cusp of what UK would find acceptable)	+ Good. Studies heterogeneous though and subject to bias with sub group analysis.
945	Chen, J., Lin, X., Cai, Y., Huang, R., Yang, S., & Zhang, G. (2022). A Systematic Review of Mobile Stroke Unit Among Acute Stroke Patients: Time Metrics, Adverse Events, Functional Result and Cost-Effectiveness. *Front Neurol,* 13, 803162.	Comprehensive systematic review of the clinical trial and economic literature.	MSU compared with conventional emergency medical services	No clear primary outcome	16 articles mean reduction of 32.64min (95% confidence interval: 23.38–41.89, p < 0.01) No reported effect on mRS (p value only provided)	Moderate to low quality.