OPEN ACCESS

Transient Ischaemic attack Emergency Referral (TIER): randomised feasibility trial results

Alan Watkins ,[1] Jenna Katherine Jones ,[2] Khalid Ali,[3] Richard Dewar,[4] Adrian Edwards,[5] Bridie Angela Evans ,[1] Lyn Evans,[6] Gary A Ford,[7] Chelsey Hampton,[8] Roger John,[6] Charlene Jones,[9] Chris Moore ,[10] Michael Obiako,[4] Alison Porter ,[1] Alan Pryce,[11] Tom Quinn,[12] Anne C Seagrove,[1] Helen Snooks,[1] Shirley Whitman,[11] Nigel Rees[13]

Handling editor Ellen J Weber

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/emermed-2021-212230).

For numbered affiliations see end of article.

Correspondence to
Dr Jenna Katherine Jones; J.k.jones@swansea.ac.uk

Received 13 December 2021
Accepted 12 September 2024

To cite: Watkins A, Jones JK, Ali K, *et al*. *Emerg Med J* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/emermed-2021-212230

ABSTRACT

Background Early assessment of patients with suspected transient ischaemic attack (TIA) is crucial to provision of effective care, including initiation of preventive therapies and identification of stroke mimics. Many patients with TIA present to emergency medical services (EMS) but may not require hospitalisation. Paramedics could identify and refer patients with low-risk TIA, without conveyance to the ED. Safety and effectiveness of this model is unknown.

Aim To assess the feasibility of undertaking a fully powered randomised controlled trial (RCT) to evaluate clinical and cost-effectiveness of paramedic referral of patients who call EMS with low-risk TIA to TIA clinic, avoiding transfer to ED.

Methods The Transient Ischaemic attack Emergency Referral (TIER) intervention was developed through a survey of UK ambulance services, a scoping review of evidence of prehospital care of TIA and convening a specialist clinical panel to agree its final form. Paramedics in South Wales, UK, were randomly allocated to trial intervention (TIA clinic referral) or control (usual care) arms, with patients' allocation determined by that of attending paramedics.

Predetermined progression criteria considered: proportion of patients referred to TIA clinic, data retrieval, patient satisfaction and potential cost-effectiveness.

Results From December 2016 to September 2017, eighty-nine paramedics recruited 53 patients (36 intervention; 17 control); 48 patients (31 intervention; 17 control) consented to follow-up via routine data. Three intervention patients, of seven deemed eligible, were referred to TIA clinic by paramedics. Contraindications recorded for the other intervention arm patients were: Face/Arms/Speech/Time positive (n=13); ABCD2 score >3 (n=5); already anticoagulated (n=2); crescendo TIA (n=1); other (n=8). Routinely collected electronic health records, used to report further healthcare contacts, were obtained for all consenting patients. Patient-reported satisfaction with care was higher in the intervention arm (mean 4.8/5) than the control arm (mean 4.2/5). Health economic analysis suggests an intervention arm quality-adjusted life-year loss of 0.0094 (95% CI −0.0371, 0.0183), p=0.475.

Conclusion The TIER feasibility study did not meet its progression criteria, largely due to low patient identification and referral rates. A fully powered RCT in this setting is not recommended.

Trial registration number ISRCTN85516498.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with transient ischaemic attack (TIA) are at risk of stroke; one large international study (n=3565 across 61 sites) reported a rate of 6.4% of cardiovascular events including stroke at 1 year.

⇒ However, many patients with TIA do not require ED visits, while TIA mimics may account for more than a third of patients with suspected TIA.

⇒ Prehospital pathways that direct patients with TIA to specialty clinics may allow patients to avoid the ED, but have not been formally evaluated in a randomised controlled trial (RCT).

WHAT THIS STUDY ADDS

⇒ This feasibility study conducted in Wales did not meet its progression criteria to support an RCT of paramedic referral of patients with TIA to clinic compared with standard care.

⇒ The primary issues were low patient identification rate and a low referral rate of eligible patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There remains uncertainty as to whether a fully powered RCT of alternative TIA referral pathways from the community is justified. TIA referral pathways that have already been implemented should be evaluated for safety and cost-effectiveness.

INTRODUCTION

Transient ischaemic attack (TIA) is a neurological event with resolution of symptoms within 24 hours with limited associated sequelae.[1 2] The exact incidence of TIA is unknown, but estimated at 35 per 100 000 people in the UK annually, with cases at increased risk of further TIAs, stroke or death.[3] However, some patients presenting with TIA to emergency medical services (EMS) may not need emergency clinical care in a hospital setting, but should be assessed promptly by a specialist doctor so that treatments to lower the risk of subsequent events can be commenced.[4–6]

Table 1 Outcomes tested for inclusion in full trial in Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial

Primary outcomes: up to 3 months	► Time to subsequent emergency contact (EMS call or ED attendance for any reason) or death. ► Relative risk of emergency event or death between trial arms.
Secondary outcomes: at index call and up to 3 months	Routinely collected: ► Time to specialist assessment by a stroke consultant. ► Outcome of EMS attendance: patient taken to hospital; left at scene; referred to TIA clinic; referred elsewhere. ► Job cycle time (from EMS call to ambulance free time) and episode of care time (from EMS call to discharge of patient from ED or time patient left at scene). ► Healthcare utilisation in 1 and 3 months following contact. ► Costs of implementation, and costs of care and consequences per patient. ► Compliance with intervention, for example, completion of ABCD2 score for intervention arm patients.
	Patient-reported outcomes: ► Patient-reported satisfaction with care received (Quality of Care Monitor).[29] ► Health-related quality of life (SF-12).[30]

EMS, emergency medical services; SF-12, 12-item Short Form Survey; TIA, transient ischaemic attack.

Within a context of EMS providers worldwide adapting models of care provision to cope with increasing demand for emergency care, and with on-scene triage and referral now provided by many services for callers who do not need immediate clinical care in hospital, guidance on prehospital treatment of TIA continues to evolve.[7–11]

At the time of this feasibility study, the UK National Institute for Health and Care Excellence (NICE) guidelines indicated that a patient with an ABCD2 score of 4 or more was at high risk of stroke, and should be seen in a specialist clinic within 24 hours; while a patient with an ABCD2 score below 4 was at low risk of stroke, and should be investigated and treated in a specialist clinic within 7 days.[12] Although this scoring system is no longer recommended, it suggests that, within a triage paradigm, paramedics could have a role in identifying and referring patients with TIA to designated TIA clinics, without conveying them to hospital. This would avoid patients at low risk of subsequent stroke having a healthcare contact at the ED of limited use, only to be discharged home with a referral to TIA clinic and no other immediate care management.

In 2012, the Royal College of Physicians (RCP) found insufficient evidence to make recommendations concerning the management of TIA and the use of risk tools by prehospital clinicians.[13] The RCP called for more training and further research to validate safe and appropriate care pathways; however, at the time of this study, some UK ambulance services had introduced a TIA pathway, without evaluation of safety or effectiveness.

Our aim was to assess the feasibility of undertaking a fully powered multicentre randomised controlled trial (RCT) to evaluate the clinical effectiveness and cost-effectiveness of referral by emergency ambulance paramedic of patients with low-risk TIA (as assessed using the Transient Ischaemic attack Emergency Referral (TIER) clinical pathway) directly to a specialist TIA clinic for early review, instead of immediate transfer to an ED.

METHODS

Study design

TIER was designed as a pragmatic cluster randomised feasibility trial in South Wales, UK, with paramedics randomly allocated to study arms, a 12-month recruitment window in 2016–2017 and patients' allocation defined by the status of attending paramedics.

Our objectives were to develop the intervention, test the feasibility of the intervention and test the feasibility of the trial design and methods.

Intervention development

The TIER intervention was developed in three stages. First, we surveyed all UK ambulance trusts (n=13) about TIA management initiatives.[14] Second, we undertook a scoping review of evidence related to prehospital care of TIA.[15] Finally, we convened a specialist clinical panel to draw together findings from the first two stages, and to finalise the intervention to be tested. The resulting intervention included a treatment protocol (assessment, risk stratification, medications, referral, documentation), training, referral flow chart, patient information leaflet for those who were left at home with a clinic appointment and follow-up (including informing their primary care provider). This protocol was to be used for those randomised to the intervention arm; control arm care comprised initial assessment, immediate care and transfer to ED, unless the patient refused to travel to hospital. (See the online supplemental materials for full protocol.)

Setting

TIER was based in the catchment areas of two study hospitals in South Wales, UK: Prince Charles Hospital, Merthyr Tydfil (Cwm Taf University Health Board), serving a population of approximately 60 000 (18.9% aged 65 or older in 2021 census); and Morriston Hospital, Swansea (Swansea Bay University Health Board), served by ambulance stations in Neath and Port Talbot with population of approximately 80 000 (21.2% aged 65 or older in 2021 census).

Participants

Paramedics

Paramedics based in ambulance stations serving one of the participating EDs were eligible to participate in the study. All eligible paramedics were invited to participate.

Patients

Patients were included if they were resident in the catchment area of a study hospital, attended by a study paramedic during the recruitment period in that catchment area and were subsequently diagnosed with TIA in ED, hospital or TIA clinic.

Patients were excluded if they were unable to give informed consent, including those with apparent or known cognitive impairment, or if they had already been approached to take part for a previous TIA episode within the study period.

Patient consent

It may not be appropriate to obtain consent from patients in a medical emergency, as they cannot be given adequate time to

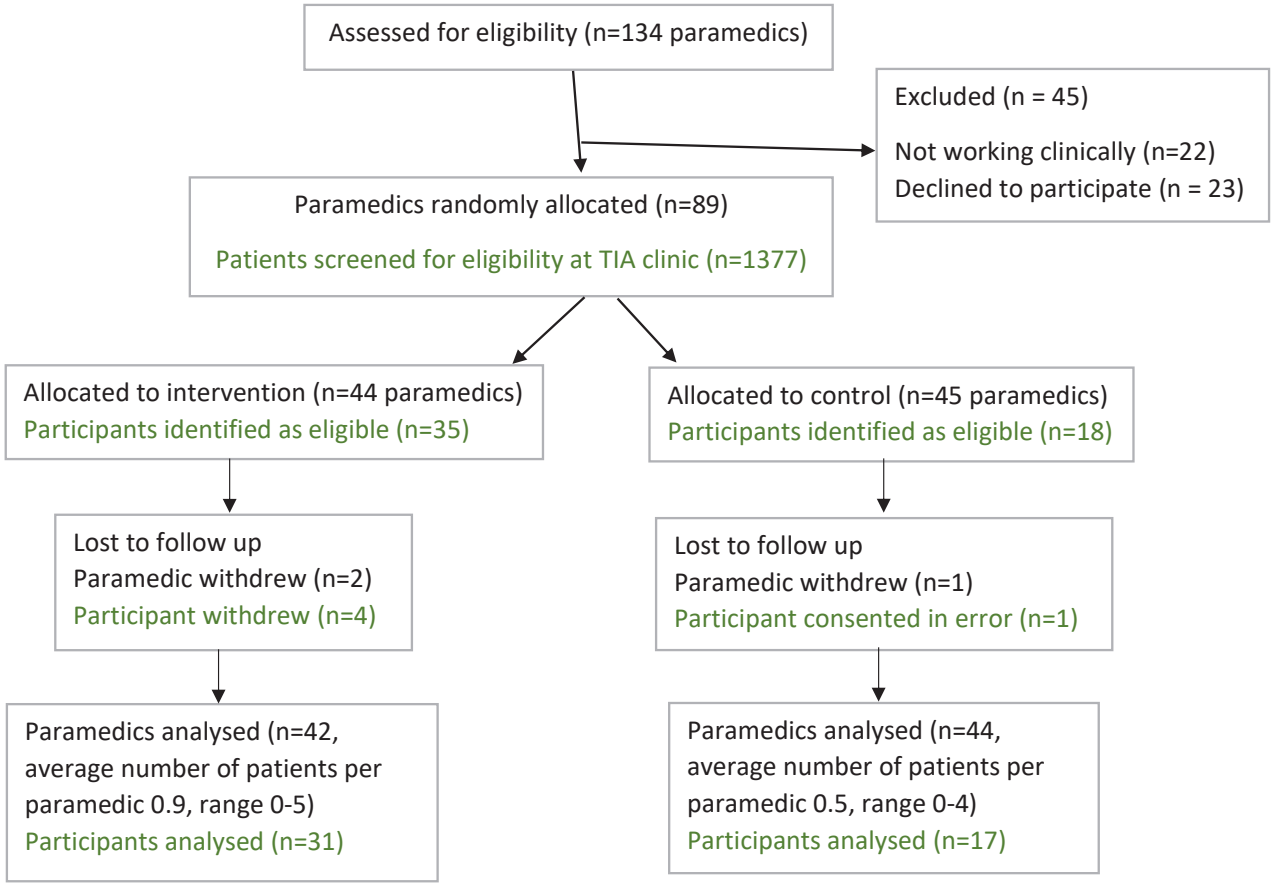

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow chart for Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial. TIA, transient ischaemic attack.

consider their decision. Therefore, we sought patient consent to follow-up in TIER in the 7–10 days after their emergency call.[16–18] The TIER Paramedic Research Support Officer, after checking that patients had not died, sent letters to home addresses of eligible patients. We did not propose to approach relatives or friends of any decedents.

Data collection

We collected routine data for each patient from their hospital notes (ED, inpatient, TIA clinic) and Wales Ambulance Service Trust (WAST) clinical records. We collected self-reported outcomes through questionnaires posted to patients with a return address stamped envelope. All outcomes to be reported are shown in table 1.

Safety reporting

We collected data about serious adverse events (SAEs) through routine data sources (WAST, Health Board); incident reporting; and complaints and coroners' inquests. We classed as SAEs: further EMS calls, ED attendances, emergency admissions to hospital or death within 72 hours; stroke or death within 1 month; and other safety incidents as reported by EMS personnel or patients.

Sample size considerations

As we did not intend to measure effects of the intervention in this feasibility study, we did not conduct a power calculation for TIER, but planned the patient recruitment period using WAST data. We estimated that 86 patients would meet our inclusion criteria over a 12-month period.

Randomisation

Participating paramedics were randomly allocated to one study arm (control or intervention) on a 1:1 basis, stratified by ambulance station, gender and experience level. There was no blocking. The random allocation sequence was produced by Swansea Trials Unit.

Blinding

Due to the nature of the intervention, patients and paramedics could not be blinded to allocation. Hospital clinicians were not blinded to the fact that the patient had been referred by a paramedic.

Progression criteria

Progression criteria to inform discussion on whether to proceed to a fully powered RCT were defined by the research team and agreed by the independent TIER Trial Steering Committee (TSC):

- At least 50% of eligible patients (those subsequently diagnosed with TIA in ED, hospital or TIA clinic) in the intervention arm referred to the TIA clinic or refused referral.
- Routinely collected electronic health records on subsequent health service use available in the Secure Anonymised Information Linkage (SAIL) Databank[19] for at least 80% of patients.

- Mean patient satisfaction score in intervention arm at least 80% of that in the control arm.
- Intervention potentially cost-effective in the NHS using a quality-adjusted life-year (QALY) threshold of £20 000–£30 000.

Analysis

After linking anonymised clinical records, an integrated data set was available for analysis in the SAIL Gateway.[19] The statistical analysis addresses progression criteria and summarises potential outcomes for inclusion in a fully powered RCT. This analysis is therefore mainly descriptive in nature, with inferential methods (including logistic and Cox regressions, summarised by ORs and HRs with 95% CIs, respectively) used sparingly, since this feasibility study was not powered to detect differences that might be judged clinically important.

Exploratory health economic analyses were undertaken from an NHS and Personal Social Services perspective with all costs expressed in 2016/2017 UK pounds sterling. Intervention implementation costs included paramedic and clinical desk staff time (for training, using unit costs; assessment; and referral to TIA clinic), job cycle length and consumables/medication.[20] Healthcare resource use following baseline ambulance call-out was established from linked SAIL data (initial ED visit and inpatient stay, subsequent TIA clinic visits, ED visits, hospitalisation and primary care provider events), using standard unit costs.[21] The 12-item Short Form Survey (SF-12) responses yielded Short Form-Six Dimension scores and QALYs at 1 and 3 months, with incremental costs and QALYs then used to estimate the costs per QALY gained in the two arms.

Analyses were undertaken using Stata V.14 and SPSS V.26.

Changes after the trial began

Amendments were approved to allow us to follow-up the consent letter with a telephone call to ensure receipt and answer any questions the patient may have; and to send reminder letters 2 and 4 weeks after patients received their questionnaire, and offer the option of completing the questionnaire over the telephone.

Table 2 Baseline patient characteristics for Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial

Variable	Intervention (n=31)	Control (n=17)
Gender, n (%)		
Male	22 (71)	8 (47)
Female	9 (29)	9 (53)
Age (years), mean (SD)	73.5 (13.1)	73.0 (15.7)

There was a setback to the planned start of the recruitment period due to delays in gaining research permissions (we were given an unfavourable opinion from the first Health Research Authority Research Ethics Committee meeting that we attended). Due to this, the fixed funding period, and there being no formal basis for our sample size calculation, we recruited for as long as possible, while allowing us to undertake follow-up within our trial period. Recruitment was stopped after 10 months.

When TIA guidelines were updated in 2017, NICE stated that anyone with suspected TIA should be assessed within 24 hours of symptom onset regardless of risk score ('Do not use scoring systems, such as ABCD2, to assess risk of subsequent stroke or to inform urgency of referral for people who have had a suspected or confirmed TIA').[12] On release of these updated guidelines, the study was paused for review by clinical research members of the TIER study team, who judged that the changes would not affect care for the prehospital trial population. This assessment was ratified by the TIER TSC.

Patient and public involvement

People with experience of emergency care for TIA, as patients or carers, were involved in developing, delivering and reporting this study. They attended Trial Management Group meetings and provided experience-based expertise to discussions about the research question, data collection tools including patient-facing information and on synthesis and reporting of findings including preparing this paper.[22 23]

Table 3 Outcomes at index event and up to 3 months for Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial

Outcome	Intervention (n=31)	Control (n=17)
Subsequent emergency event (EMS call or ED attendance) or death, n (%)	9/31 (29.0)	9/17 (52.9)
Time (days) to subsequent emergency contact (EMS call or ED) or death, mean (SD) (n)	41.1 (32.3) (9)	37.2 (24.7) (9)
Time (days) to specialist assessment by a stroke consultant or specialist*, mean (SD)	4.8 (5.1)	3.0 (3.6)
Outcome of EMS call, n (%)		
Conveyed to ED	29 (93.5)	17 (100.0)
Referred to TIA clinic	2 (6.5)	0 (0.0)
Job cycle time (hour:min), mean (SD)		
Time from EMS call to ambulance free	1:58 (0:37)	1:59 (0:40)
Length of episode of care (hour:min), mean (SD)		
Time from EMS call to (1) discharge of patient from ED or (2) time patient left at scene	6:57 (4:19)	6:07 (2:54)
Healthcare utilisation (£) in 3 months following index event, mean (SD)	2419 (4039)	7051 (11 630)
Patient-reported outcomes, mean (SD) (n)		
Quality of Care Monitor score (consent)	4.8 (0.4) (14)	4.2 (1.3) (8)
SF-12 Mental Health component (1 month)	33.5 (14.4) (12)	37.7 (18.2) (5)
SF-12 Physical Health component (1 month)	29.1 (8.5) (12)	39.1 (11.8) (5)
SF-12 Mental Health component (3 months)	38.1 (8.7) (8)	33.3 (7.4) (4)
SF-12 Physical Health component (3 months)	26.0 (10.4) (8)	38.7 (6.4) (4)

*Time to specialist assessment <24 hours for patients admitted to hospital wards. (n) refers to the number of participants with this outcome measure recorded.
EMS, emergency medical services; SF-12, 12-item Short Form Survey; TIA, transient ischaemic attack.

Table 4 Routinely recorded outcomes (SAIL Databank; WAST records) for Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial

Outcome	Intervention	Control
No further ED attendance within 1 month, n (%) No further ED attendance within 3 months, n (%)	27 (87.1) 23 (74.2)	14 (82.4) 9 (52.9)
No hospital admission within 1 month, n (%) No hospital admission within 3 months, n (%)	24 (77.4) 21 (67.7)	13 (76.5) 9 (52.9)
Primary care provider event days within 1 month: min, max, mean (SD) Primary care provider event days within 3 months: min, max, mean (SD)	1, 9, 5.4 (2.2) 1, 26, 13.4 (5.5)	0, 12, 5.5 (2.9) 0, 25, 11.9 (6.0)
Alive at 1 month, n (%) Alive at 3 months, n (%)	31 (100.0) 28 (90.3)	17 (100.0) 16 (94.1)
Number of subsequent EMS calls within 3 months, n (%)		
0	25 (80.6)	11 (64.7)
1	4 (12.9)	4 (23.5)
2	2 (6.5)	1 (5.9)
3	0 (0)	1 (5.9)

EMS, emergency medical services; SAIL, Secure Anonymised Information Linkage; WAST, Wales Ambulance Service Trust.

RESULTS

We report the results of this feasibility study in accordance with the relevant Consolidated Standards of Reporting Trials checklist.[24]

Recruitment and consent

Paramedic allocations commenced in April 2016, followed by training for intervention arm paramedics; patient recruitment started in December 2016 and ended in September 2017 (figure 1).

Paramedics

Of 134 paramedics across Cwm Taf and Swansea Bay, 112 were identified as eligible to participate in TIER, and 89 of these consented to do so. In Cwm Taf, 28 paramedics were allocated to each trial arm. Following lower than anticipated patient recruitment rates in Cwm Taf, further paramedic randomisations were undertaken for Swansea Bay, with 16 paramedics allocated to the intervention arm, and 17 paramedics allocated to the control arm. In Cwm Taf, two intervention paramedics subsequently withdrew consent; in Swansea Bay, one control paramedic withdrew.

Patients

53 patients were identified as eligible for TIER. Five of the 53 eligible patients withdrew, leaving 48 patients consenting to follow-up via routinely collected electronic health records; 25 of these also consented to receive questionnaires. Patient recruitment was higher in the intervention arm, despite similar numbers of paramedics and random allocation. The mean patient age was similar in the two arms, but the proportion of male patients was higher in the intervention arm (table 2).

Of the 86 paramedics who participated in TIER, 37 attended one or more trial patients, with 24 each attending a single patient.

Outcomes

Outcomes at baseline, 1 month and 3 months were similar in the two arms (table 3). Observed differences in primary outcomes did not achieve statistical significance, with unadjusted p values

Table 5 Summary of fulfilment of progression criteria for Transient Ischaemic attack Emergency Referral (TIER) randomised feasibility trial

Progression criterion (whether achieved)	Outcome
1. At least 50% of eligible patients in the intervention arm referred to the TIA clinic or refused referral. (Not achieved)	36 patients were attended by intervention arm paramedics. Three were directly referred to the TIA clinic. In four further cases: one appeared to be a missed referral; one had no prehospital record of TIA; one was attended by a paramedic who was not TIER trained; one patient record was missing. All others were recorded with contraindications: FAST positive (n=13); ABCD2 score >3 (n=5); already taking warfarin (n=2); crescendo TIA (n=1); other clinical factors (n=8). Only 3 of 7 (43%) eligible patients were referred.
2. Data on subsequent health service use available in SAIL for at least 80% of patients. (Achieved)	We submitted to NHS Wales Informatics Service (NWIS) identifying data (including NHS numbers) for 48 patients who consented to follow-up of medical data. All 48 patients were matched and linked with routinely collected electronic health records held in the SAIL Databank, yielding outcomes from the Emergency Department Data Set, Patient Episode Database Wales, Welsh Longitudinal General Practice Dataset and Annual District Death Extract data sets.
3. Mean patient satisfaction in intervention arm at least 80% of patient satisfaction in the control arm. (Achieved)	Mean patient-reported satisfaction with care score in the intervention arm was higher than that in the control arm (4.8/5 and 4.2/5, respectively).
4. Cost/QALY has potential to achieve the NICE criterion of £20 000–£30 000. (Not achieved)	Patients in the intervention group who returned two complete SF-12 questionnaires (n=6) accrued 0.0909 QALYs between 1 and 3 months of follow-up compared with 0.1003 QALYs in the control group (n=4). This results in a QALY loss of 0.0094 (95% CI −0.0371 to 0.0183; p=0.475) in the intervention group, which means that the intervention is both less costly but also less effective than the control in the exploratory analysis.

FAST, Face/Arms/Speech/Time; NICE, National Institute for Health and Care Excellence; QALY, quality-adjusted life-year; SAIL, Secure Anonymised Information Linkage; SF-12, 12-item Short Form Survey; TIA, transient ischaemic attack.

of 0.106 for risk of emergency event (logistic regression: OR=0.365, 95% CI 0.106, 1.242), and 0.099 for the time to an emergency event (Cox regression: HR=0.458, 95% CI 0.181, 1.159). Mean job cycle time was similar in trial arms; mean length of episode of care was longer in the intervention arm, although with large variation within each arm. A total of n=10 patients returned *two* complete SF-12 questionnaires (at 1 and 3 months): n=6 in the intervention arm; n=4 in the control arm.

Healthcare cost considerations were dominated by the heavily skewed costs attributable to inpatient stays. Training costs for the 44 paramedics in the intervention arm and 19 clinical desk staff were estimated to total £4174, including trainee and trainer costs. Intervention delivery cost an incremental £20 per patient transferred directly to a TIA clinic, reflecting the additional paramedic and clinical desk staff time and aspirin cost in making the referral.

Table 4 provides further details on the routinely recorded outcomes available on study patients; these outcomes contributed to the definition of primary and secondary outcomes, and also feature in assessment of progression criteria, as summarised in table 5.

Assessment against progression criteria

Safety

One SAE was observed—a patient in the intervention group was admitted to hospital the same day as their EMS call for TIA with leg cellulitis (unrelated to their neurological presentation).

DISCUSSION

Recruitment

Recruitment of paramedics was good, with 89/112 agreeing to participate in this feasibility study, but patient numbers were lower than expected. Based on local WAST data, we estimated that 86 patients would meet inclusion criteria over a 12-month period; however, during 10 months of recruitment, 53 patients (36 intervention; 17 control) were identified as eligible, with 48 followed up via routinely collected electronic health records. Reasons for this imbalance remain unclear, but may include performance bias, with intervention paramedics more interested or engaged in the trial which involved a change to usual practice. With small patient numbers, it is not possible to determine definitively whether this imbalance was statistically significant.

Use of intervention pathway

Usage of the referral pathway was much lower than expected; only three patients, out of seven eligible, were referred to TIA clinic by intervention paramedics.

Possible reasons for this include: (1) the TIA population which presents to the EMS and is suitable for non-ED pathways is smaller than previously thought; (2) the TIER protocol and pathway were overly restrictive; (3) paramedics were cautious or resistant to change—we know there is a lack of confidence among paramedics about who carries risk when patients are not conveyed to ED.[25]

We are unable to conclude from our study data whether any of these reasons were dominant, and there is a lack of other prehospital literature focusing only on TIAs (as opposed to TIA and stroke) for comparative data.

Outcomes

Our results show that patients in the intervention group waited longer for specialist review but, again, with small patient numbers, we cannot determine definitively whether this was statistically significant. The point of the intervention was not for participants to see a specialist more quickly, but, rather, to avoid an unnecessary healthcare contact in the ED, where they are likely to be discharged home with a referral to TIA clinic and no other immediate management. This is especially important now when there are major delays in ambulance handover with some patients waiting outside EDs for many hours.[26]

Health economics

Our intervention was found not to be cost-effective, as assessed using the standard NICE threshold (cost/QALY has potential to achieve the NICE criterion of £20 000–£30 000). We used this threshold as it would inform the design of a future RCT; however, it could be argued that no change in QALY but resource saving through diversion to clinic (rather than ED attendance which can seem inexpensive but has hidden and opportunity costs) is worthwhile.

Other study design limitations

The hospital clinics were not blinded to which patients were referred by paramedics; effective blinding measures would have been difficult to implement as paramedic referral is not a usual referral route.

Patients who did not attend the TIA clinic may have been missed because they did not receive a diagnosis of TIA. Although we were aware of this throughout the trial, it was not possible to close this loophole, and although we expect this to represent small numbers, it is possible that some patients were not included because of uncertainty about final diagnosis.

Progression criteria

The TIER feasibility study did not meet all its progression criteria. We do not intend to develop a funding application for a fully powered RCT, although it is possible that our progression criteria were too stringent or local system factors were at play in South Wales that would not translate to other areas.

The need to direct care away from EDs remains. Patients with TIAs in some areas of the UK can currently be referred to a same day emergency care unit (which deals with a range of emergency conditions that can be rapidly treated without admission), or EMS triage could communicate with specialist services directly, so patients receive the care they require but do not have to wait for management in the ED.[27 28] There is little evaluation of such alternatives available in the literature, and certainly no randomised trials.

Future research should reflect the continuing evolution of guidance on TIA management and the extent of convergence across geographies.

CONCLUSION

The TIER feasibility study did not meet its progression criteria largely due to low patient identification and referral rates. A fully powered RCT in this setting is not recommended.

Author affiliations
[1]Swansea University Medical School, Swansea University, Swansea, UK
[2]Swansea University, Swansea, UK
[3]Brighton and Sussex Medical School, Brighton, UK
[4]Cwm Taf University Health Board, Abercynon, UK
[5]Cardiff University, Cardiff, UK
[6]Welsh Ambulance Services NHS Trust, Saint Asaph, UK
[7]Radcliffe Department of Medicine, Oxford University, Oxford, UK
[8]Welsh Ambulance Services NHS Trust, Cwmbran, UK
[9]Welsh Ambulance Services NHS Trust, Swansea, UK

[10]Medical and Clinical Services Directorate, Welsh Ambulance Services NHS Trust, Cwmbran, UK
[11]Public Contributor (c/o Swansea University Medical School), Swansea University, Swansea, UK
[12]Faculty of Health, Social Care and Education, Kingston University, London, UK
[13]Pre Hospital Emergency Research Unit, Welsh Ambulance Services NHS Trust, Cardiff, UK

X Alison Porter @SwanseaAlison and Tom Quinn @proftomquinn

Contributors AW analysed the data, drafted the manuscript and is the guarantor. JKJ coordinated the funding application and submission and editing of the manuscript. KA, RD, AE, LE, GAF, RJ, CM, MO and TQ gave clinical and methodological advice, were members of the RMG and helped interpret the findings. BAE coordinated the PPI in this study. CH and ACS were the study managers. CJ was the PRSO. APo led the qualitative work in this study. APr and SW were the public contributors for this research. Conception of the study was done by NR, who was the chief investigator. HS provided methodological oversight.

Funding TIER was funded by Health and Care Research Wales' Research for Patient and Public Benefit, Award 1053.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and TIER received ethical approval in 2016 from Wales Research Ethics Committee 3 (reference 16/WA/0116) and is registered at the ISRCTN registry (reference 85516498).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Alan Watkins http://orcid.org/0000-0003-3804-1943
Jenna Katherine Jones http://orcid.org/0000-0002-1280-4941
Bridie Angela Evans http://orcid.org/0000-0003-0293-0888
Chris Moore http://orcid.org/0000-0002-2192-3002
Alison Porter http://orcid.org/0000-0002-3408-7007

REFERENCES

1 Albers GW, Caplan LR, Easton JD, *et al*. Transient ischemic attack--proposal for a new definition. *N Engl J Med* 2002;347:1713–6.
2 Castledine G, Close A, eds. In: *Oxford Handbook of Adult Nursing*. Oxford University Press, 2009.
3 Amarenco P, Lavallée PC, Monteiro Tavares L, *et al*. Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke. *N Engl J Med* 2018;378:2182–90.
4 Olson DM, Cox M, Pan W, *et al*. Death and rehospitalization after transient ischemic attack or acute ischemic stroke: one-year outcomes from the adherence evaluation of acute ischemic stroke-longitudinal registry. *J Stroke Cerebrovasc Dis* 2013;22:e181–8.
5 Dolmans LS, Hoes AW, Bartelink M-LEL, *et al*. Patient delay in TIA: a systematic review. *J Neurol* 2019;266:1051–8.
6 Sanders LM, Srikanth VK, Psihogios H, *et al*. Clinical predictive value of the ABCD2 score for early risk of stroke in patients who have had transient ischaemic attack and who present to an Australian tertiary hospital. *Med J Aust* 2011;194:135–8.
7 Clark MJ, Purdie J, FitzGerald GJ, *et al*. Predictors of demand for emergency prehospital care: an Australian study. *Prehosp Disaster Med* 1999;14:167–73.
8 BBC News. Police say ambulance service putting demand on its resources. 2014. Available: www.bbc.co.uk/news/uk-england-essex-25669203. 2014 [Accessed 5 Nov 2021].
9 BBC News. Firefighters step in to aid oxfordshire ambulance demand. 2015. Available: www.bbc.co.uk/news/uk-england-oxfordshire-30724426 [Accessed 5 Nov 2021].
10 Snooks H, Williams S, Crouch R, *et al*. NHS emergency response to 999 calls: alternatives for cases that are neither life threatening nor serious. *BMJ* 2002;325:330–3.
11 Snooks H, Wrigley H, George S, *et al*. Appropriateness of use of emergency ambulances. *Emerg Med J* 1998;15:212–5.
12 National Institute for Health and Care Excellence. NICE clinical guideline 68, 2008, (updated 2017). 2017. Available: www.nice.org.uk/nicemedia/pdf/CG68NICEGuideline.pdf [Accessed 5 Nov 2021].
13 Intercollegiate Stroke Working Party. National clinical guideline for stroke. 2012. Available: www.rcplondon.ac.uk/guidelines-policy/stroke-guidelines [Accessed 5 Nov 2021].
14 Bulger JK, Ali K, Edwards A, *et al*. Care pathways for low-risk transient ischaemic attack. *J Paramedic Pract* 2018;10:256–9.
15 Evans BA, Ali K, Bulger J, *et al*. Referral pathways for patients with TIA avoiding hospital admission: a scoping review. *BMJ Open* 2017;7:e013443.
16 Evans BA, Brown A, Fegan G, *et al*. Is fascia iliaca compartment block administered by paramedics for suspected hip fracture acceptable to patients? A qualitative study. *BMJ Open* 2019;9:e033398.
17 Moore C, Bulger J, Morgan M, *et al*. Prehospital recognition and antibiotics for 999 patients with sepsis: protocol for a feasibility study. *Pilot Feasibility Stud* 2018;4:6.
18 Armstrong S, Langlois A, Laparidou D, *et al*. Assessment of consent models as an ethical consideration in the conduct of prehospital ambulance randomised controlled clinical trials: a systematic review. *BMC Med Res Methodol* 2017;17:142.
19 Jones KH, Ford DV, Thompson S, *et al*. A Profile of the SAIL Databank on the UK Secure Research Platform. *Int J Popul Data Sci* 2019;4:1134.
20 Royal College of Nursing. NHS pay scales 2016-2017. 2017. Available: www.rcn.org.uk/employment-and-pay/NHS-pay-scales-2016-17
21 Personal Social Services Research Unit,. NHS Reference Costs 2016 to 2017. University of Kent & Department of Health, 2017.
22 Staniszewska S, Brett J, Simera I, *et al*. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;358:j3453.
23 Evans BA, Bedson E, Bell P, *et al*. Involving service users in trials: developing a standard operating procedure. *Trials* 2013;14:219.
24 Schulz KF, Altman DG, Moher D, *et al*. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
25 Porter A, Snooks H, Youren A, *et al*. Should I stay or should I go?' Deciding whether to go to hospital after a 999 call. *J Health Serv Res Policy* 2007;12:32–8.
26 Association of Ambulance Chief Executives. Delayed hospital handovers: impact assessment of patient harm. 2021. Available: https://aace.org.uk/wp-content/uploads/2021/11/AACE-Delayed-hospital-handovers-Impact-assessment-of-patient-harm-FINAL-Nov-2021.pdf [Accessed 23 May 2022].
27 Houghton M. Same-day emergency care. *Clin Med (Northfield)* 2023;23:99.
28 Ambulatory Emergency Care Network & NHS Improvement. Same day emergency care: clinical definition, patient selection and metrics. 2018. Available: www.england.nhs.uk/aec-same-day-emergency-care-clinical-definition-patient-selection-metrics.pdf [Accessed 23 May 2022].
29 Carey RG, Seibert JH. A patient survey system to measure quality improvement: questionnaire reliability and validity. *Med Care* 1993;31:834–45.
30 Müller-Nordhorn J, Roll S, Willich SN. Comparison of the short form (SF)-12 health status instrument with the SF-36 in patients with coronary heart disease. *Heart* 2004;90:523–7.