Delays to revascularisation for patients with chronic limb-threatening ischaemia in England

Short title

Delays to revascularisation for patients with CLTI

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Keywords: chronic limb-threatening ischaemia (CLTI), hub-and spoke network, time to revascularisation, care pathways, postoperative outcomes

ABSTRACT [250 words]

Background

Vascular services in England are organised into regional hub-and-spoke models, with hubs performing arterial surgery. This study examined time to revascularisation for chronic limb-threatening ischaemia (CLTI) within and across different care pathways and its association with post-revascularisation outcomes.

Methods

Three inpatient and four outpatient care pathways were identified for patients with CLTI undergoing revascularisation between April 2015 and March 2019 using Hospital Episode Statistics (HES) data. Differences in times from presentation to revascularisation across care pathways were analysed using Cox regression. The relationship between postoperative outcomes and time to revascularisation was analysed using logistic regression.

Results

Among 16483 patients with CLTI, 9470 had pathways starting with admission to a hub or spoke hospital, while 7013 (42.5%) were first seen at outpatient visits. Among the inpatient pathways, patients admitted to arterial hubs had shorter times to revascularisation than those admitted to spoke hospitals (median 5 days [IQR 2-10] vs 12 days [IQR 7-19], $p<0.001$). Shorter times to revascularisation were also observed for patients presenting to outpatient clinics at arterial hubs compared with spoke hospitals (median 13 days [IQR 6-25] vs 26 days [IQR 15-35], $p<0.001$). Within most care pathways, longer delays to revascularisation were associated with increased risks of postoperative major amputation and in-hospital death, but the effect of delay differed across pathways.

Conclusion

For patients with CLTI, time to revascularisation was influenced by presentation to an arterial hub or spoke hospital. Generally, longer delays to revascularisation were associated with worse outcomes but the impact of delay differed across pathways.

INTRODUCTION

Chronic limb-threatening ischaemia (CLTI) is a severe form of peripheral arterial disease in the lower limbs characterized by rest pain and/or tissue loss, such as ulceration or gangrene (Fontaine classification III or IV)[1,2]. The symptoms result from reduced blood flow in the legs and revascularisation is required to improve blood flow, and reduce the risk of limb loss. Revascularisation may be performed using either endovascular techniques (angioplasty and/or stenting), open surgery (lower limb bypass procedures, endarterectomy) or a hybrid combination of procedures, depending upon the patient's risk, severity of limb threatening ischaemia and anatomic patterns of disease[1-4].

Centralisation has been a common strategy for highly specialised surgery in health care systems in Europe and North America[5,6]. In response to the evidence that greater surgeon and vascular unit volumes improve patient outcomes[7-9], there has been a centralisation of vascular arterial surgical services within the National Health Service (NHS)[10] with a hub-and-spoke model[11] introduced within geographical regions. In these regional vascular networks, arterial hubs provide arterial surgery and complex endovascular interventions. Non-arterial spoke hospitals provide outpatient services including local assessment and diagnostic services, and where appropriate, day case peripheral angioplasty and stenting[10]. Patients admitted to a non-arterial spoke hospital are transferred to the regional vascular arterial hub when requiring an operative procedure[10,12]. Through reconfiguration, the number of NHS acute trusts that perform lower-limb bypass operations in England fell from 110 in 2011[13] to 70 in 2017[14].

There has been a long-standing concern that late presentation and delayed management of CLTI contributes to increased rates of lower limb amputation and mortality[15]. National guidance from the Vascular Society in the Provision of Vascular Services 2018 (POVS 2018)[10] and the Peripheral Arterial Disease Quality Improvement Framework (PAD QIF) in 2019[16] recommend revascularisation within 5

days of hospital admission for patients with severe CLTI, or within 14 days of outpatient referral for those who present with stable disease. To ensure patients have rapid access to both endovascular and surgical revascularisation, vascular networks need to have effective referral pathways. Failure to achieve this could result in extended delays, particularly for patients who first present at a spoke hospital before having revascularisation at an arterial centre. The POVS 2018 guidance[10] states that "equal access to treatment should occur irrespective of where in the network a patient presents". Therefore, the aim of this study was to examine how time to revascularisation for patients with CLTI might vary depending upon their care pathway across NHS hospitals in England. This study also investigated the impact of time to revascularisation on adverse short-term outcomes including in-hospital mortality and the risk of subsequent major lower limb amputation within the same admission following revascularisation.

METHODS

The study used a dataset extracted from the inpatient Hospital Episode Statistics (HES) database held by NHS England. The inpatient database codes the diagnostic information using the International Classification of Diseases, Tenth Revision (ICD-10), and operative procedures using the fourth revision of the UK Office of Population Censuses and Surveys classification (OPCS-4). The study cohort consisted of patients aged 35 years and over, admitted as an emergency with CLTI-related diagnostic codes (Supplementary Table 1 for ICD-10 codes) to a NHS hospital in England for a lower limb revascularisation procedure (Supplementary Table 2 for procedure codes) between 1 April 2015 and 31 March 2019. Because patients who had previous revascularisation procedures may have followed different care pathways with potentially more adverse outcomes, only the first revascularisation procedure for each patient was included. Patients were excluded if they had other lower limb revascularisation procedures recorded within two years prior to the start of the study period (1 April 2015). The OPCS procedure codes were used to distinguish between endovascular (angioplasty / stent), open (bypass / endarterectomy) and hybrid procedures. A hybrid procedure

was recorded where both endovascular and open surgical operations were performed on the same date. Patients with end-stage renal disease and on dialysis were excluded, because special care might be required to accommodate their dialysis requirements and potentially prolong waiting times to revascularisation. Patients who had both revascularisation and major amputation on the date of their first lower limb procedure were defined as patients undergoing a primary amputation and also excluded. The analysis was restricted to NHS hospitals in England which had not changed their status from an arterial centre (hub) to a non-arterial centre (spoke) during the study period due to reconfiguration of vascular services, and to patients who resided in England at the time of revascularisation.

Care pathway definitions

Within the hub-and-spoke network model for vascular services in the UK, patients with CLTI could either be directly admitted to a hospital as an emergency (inpatient pathway) or referred to an outpatient clinic for specialist assessment before a treatment decision was made (outpatient pathway). The first contact with vascular services preceding revascularisation was identified using patient records from both inpatient and outpatient HES datasets. When patients had an outpatient visit with a specialist in vascular surgery, diabetic medicine, podiatry or general surgery, occurring within 30 days prior to the admission for revascularisation, they were classed as following outpatient care pathways. This definition was used due to the multidisciplinary nature of foot care, and that some vascular surgeons were still coded as performing as specialists in general surgery. The earliest outpatient visit was defined as the first contact with vascular services. Otherwise, patients were classed as following inpatient care pathways if they had no vascular-related outpatient visits preceding revascularisation and were admitted as non-elective patients. This included patients who (following the initial admission for CLTI) were transferred to another hospital, and/or discharged and then readmitted for revascularisation. The interval between the discharge and readmission was limited to 30 days.

There were a total of 19 distinct pathways starting with either an admission or outpatient visit to an arterial vascular hub or a non-arterial spoke hospital (Supplementary Table 3). These were collated to form seven pathways that captured the type of first contact (inpatient or outpatient), whether that contact was at a hospital with an arterial hub, and whether or not the patient was discharged from hospital prior to revascularisation. Patients starting with an admission were grouped into three inpatient care pathways, while patients who were initially seen at an outpatient clinic were grouped into four outpatient care pathways - see Table 1 for the pathway definitions. To reduce heterogeneity in the overall cohort and focus on the most common pathways in current clinical practice, a small number of patients were excluded from these seven categories: (a) patients who initially presented to an arterial hub hospital and had their subsequent revascularisation at a different arterial centre, and (b) patients who presented to an arterial hub hospital and had their subsequent endovascular procedure at a non-arterial spoke hospital.

Outcome and explanatory variables

The primary outcome was time to revascularisation from the point of first contact (outpatient visit or inpatient admission, as appropriate). The study adopted the POVS 2018[10] / PAD QIF[16] standards on time to revascularisation, namely, 5 days from a non-elective admission and 14 days from an outpatient visit. The proportion of patients with time to revascularisation beyond 5 days following inpatient pathways or 14 days following outpatient pathways was derived for each care pathway. Secondary outcomes were the proportion of patients undergoing a major lower limb amputation after revascularisation within the same admission, and the proportion of patients that died in hospital after revascularisation. The outcome variable for major amputation included all procedures and did not distinguish between the sides of amputation and revascularisation.

Patient characteristics taken from the admission episode were used for analyses. Patient demographics included age on admission, sex, and region of residence. Socioeconomic deprivation was measured using the English Index of Multiple Deprivation (IMD) of a patient's residential area and converted to quintiles based on a national ranking[17]. The severity of CLTI was categorized into two groups, depending on whether or not patients presented with tissue loss (ulceration, gangrene and osteomyelitis).

A patient's comorbidities were captured using the Royal College of Surgeons (RCS) Charlson score[18], which was derived using primary and secondary diagnostic codes from the index hospital admission (admission for revascularisation) as well as admissions during the 12 months preceding the index admission. Acute conditions (such as myocardial infarction) were included in the number of co-morbidities only if they were present in a record of a hospital admission preceding the index admission. Diagnostic codes for peripheral arterial disease (PAD) and diabetes were excluded from the RCS Charlson co-morbidity score in this study. The PAD codes formed part of the inclusion criteria for the study, while the diabetes status was examined as a separate variable.

Statistical analysis

Descriptive statistics were used to describe the demographic and clinical characteristics of the patient cohort. The distribution of time to revascularisation for each care pathway was summarised using the median and quartiles, and presented graphically in a box plot. Differences of time to revascularisation between patients following different care pathways were examined using the Mann-Whitney U test. Cox regression was used to assess the association between time to revascularisation and patient and clinical characteristics. The NHS trusts performing revascularisation were included as random effects in the multivariable Cox regression models to account for similarities in vascular services received among patients in the same trust compared with the whole population. A half day was applied to time to revascularisation in the Cox regression

models where the first contact was on the same date as revascularisation. A hazard ratio <1 indicated that the time to revascularisation tended to be longer for the subgroup patients compared to patients in the reference group.

An initial exploration of the relationship between time to revascularisation and the short-term risks of postoperative mortality and major amputation within the same admission was performed visually using a symmetric nearest neighbour smoother[19,20]. Multivariable logistic regression model was used to assess their associations with time to revascularisation, adjusting for other covariates of interest. Linear and quadratic terms of log transformation of time to revascularisation were explored in the models. The NHS trusts were included as random effects in the models to account for similarities in the postoperative outcomes among patients treated in the same organisation compared with the whole population.

Separate regression analyses were performed for patients following inpatient and outpatient care pathways. Due to the possibly inaccurate clinical coding in administrative hospital data, sensitivity analyses that included additional patients with a primary diagnostic code for acute limb ischaemia and secondary diagnostic codes for CLTI were performed for all Cox and logistic regression analyses conducted in the main analysis. Sensitivity analyses were also conducted to explore the impact of outpatient specialties and the time limit between the outpatient visit and the admission for revascularisation. The analyses involved using: 1) 15-days limit, 2) 60-days limit, and 3) specialist in vascular surgery only. All statistical tests were two-sided and results were considered statistically significant if the p value was less than 0.05. All analyses were conducted using Stata® MP 15 (StataCorp, College Station, Texas, USA).

RESULTS

The study identified 23 274 patients aged ≥35 years who underwent lower limb procedures with an emergency admission for CLTI between April 2015 and March 2019. From these, 17 623 (75.7%) underwent revascularisation as their first lower limb procedure, while 5 651 (24.3%) underwent primary amputation and were excluded. Of those undergoing revascularisation, the following were excluded: 404 (2.3%) patients who were on dialysis at the time of revascularisation, 458 (2.6%) patients treated at 8 hospitals that had changed their status from an arterial hub to a non-arterial spoke site, 142 (0.8%) patients whose first contact for CLTI was at an arterial hub but who subsequently underwent revascularisation elsewhere, and 135 (0.8%) patients whose time to revascularisation exceeded 70 days. These exclusions left 16 483 patients for analyses.

Patient characteristics

The characteristics of patients included in the analyses are summarised in Table 2. The majority were men (65.3%) and aged 70 years and over (62.3%). More than half of the patients (54.8%) had diabetes, and two thirds (67.1%) had at least one other Charlson comorbidity. At the time of revascularisation, 59% of patients had tissue loss. Overall, 9 470 (57.5%) patients followed care pathways that started with a hospital admission, while 7 013 (42.5%) followed care pathways that started with an outpatient visit. Among those who followed an outpatient pathway, 60% had diabetes, whilst about 51% among those who followed an inpatient pathway were diabetic. A slightly higher proportion of patients had tissue loss at the time of revascularisation among those who followed an outpatient pathway than those who followed an inpatient pathway (62.5% vs 56.5%, respectively). The proportion of patients that followed each care pathway varied across English regions (Supplementary Figure 1).

Time to revascularisation

The summary of time to revascularisation for each care pathway is presented in Table 3 and Figure 1 (see Supplementary Figure 2 for the 19 distinct pathways). Of the seven pathways, patients admitted

to an arterial hub hospital as emergency admissions (pathway 1) tended to have the shortest time to revascularisation, with the 5 560 patients having a median time of 5 days (IQR 2-10 days). The 1 783 patients admitted to a non-arterial spoke hospital (pathway 2) had a median time of 12 days (IQR 7-19 days), well in excess of the target 5 days and more than twice as long as those admitted to an arterial hub hospital ($p<0.001$). However, the 2 127 patients who were discharged after the initial emergency admission (pathway 3) experienced even longer delays to revascularisation, with a median of 20 days (IQR 12-30 days) and only 7% had a procedure within 5 days.

For patients who followed the outpatient care pathways and were subsequently admitted to an arterial hub hospital for revascularisation (3 530 and 1 473 patients on pathways 4 and 5, respectively), the median times to revascularisation were similar, regardless of the type of hospitals (hub or spoke) that patients presented to during their initial outpatient visit (median 13 days, IQR 6-25 days). However, the 634 patients who were admitted to a non-arterial spoke hospital following their initial outpatient visits (pathway 6) tended to experience longer delays to revascularisation (median 26 days, IQR 15-35 days) in comparison to patients following pathways 4 and 5 ($p<0.001$). As previously noted, patients who were discharged in the middle of care pathway (pathway 7) had significantly longer delays to revascularisation, with only 14.6% having a procedure within 14-days (see Supplementary Figure 3 for the distribution of delays for each pathway).

These figures for each pathway (Table 3) highlight a distinct difference between arterial hubs and spoke hospitals, regardless of how patients first attended. For the 10 563 (64.1% of all patients) who first presented to an arterial hub hospital (pathways 1, 4 and 5), just over half of the patients underwent revascularisation within the VSGBI recommended times (5-days for inpatients, 14-days for outpatients). However, more than three quarters of patients missed the time targets among the 2 417 (14.7% of all patients) who first presented to a non-arterial spoke hospital (pathways 2, 6). The proportion of patients meeting the recommended time targets was statistically significantly lower in

patients following pathways 2 and 6, compared to that in patients following pathways 1, 4, and 5 (20.1% vs 52.5%, p<0.001).

Factors associated with time to revascularisation

There were some marked differences across the patient characteristics in the proportion of patients that exceeded the 5-days target (Supplementary Table 4) and the 14-days target (Supplementary Table 5), notably whether or not a patient presented with tissue loss and an increasing number of comorbidities. However, patient factors did not fully explain the differences in the times to revascularisation across the various types of care pathways. Figure 2 shows the adjusted hazard ratios describing the association between time to revascularisation and the various inpatient and outpatient care pathways, as well as the influence of different patient and clinical characteristics. Among the patients that followed the inpatient care pathways, longer delays to revascularisation were associated with increasing age, patients presenting with tissue loss and a greater number of comorbidities (Figure 2, left panel; Supplementary Table 4). Among the patients who followed the outpatient care pathways, the associations with longer times were also statistically significant for patients presenting with tissue loss, a greater number of comorbidities, and a diagnosis of diabetes (Figure 2, right panel; Supplementary Table 5).

Postoperative major amputation and in-hospital death after revascularisation

Overall, 1 018 (6.2%) patients underwent major amputation in the postoperative period within the same admission, while 864 (5.2%) died in hospital after revascularisation. In all, 14 733 (89.4%) were alive and amputation free at discharge (Table 3). The univariate relationships between delays to revascularisation and the risk of each postoperative outcome after revascularisation across care pathways are shown in Supplementary Figures 4 and 5. Generally, within the time interval containing most patients, longer delays to revascularisation were associated with worse postoperative outcomes in most care pathways (Figures 3 and 4), after adjustment for patient and

clinical characteristics. The relationship between the adjusted rate of in-hospital amputation and time to revascularisation was also qualitatively different for inpatient pathways 1 and 2 compared to the others. As the delay increased, the rate of major amputation decreased slightly for pathways 1 and 2, whereas it increased for outpatient pathways and the inpatient pathway 3.

For in-hospital death, the adjusted relationship with longer time to revascularisation was also qualitatively different for the inpatient pathways and outpatient pathways. For the patients who were first admitted (pathways 1, 2 and 3), the risk of in-hospital postoperative death was least when the time to revascularisation was between 3 to 7 days, and increased for both shorter and longer delays (Figure 3), with the change being largest for pathway 1. The risk of in-hospital postoperative death for the outpatient pathways was also estimated to increase with longer delays but these did not have the higher risk associated with the shortest delays (Figure 4). Supplementary Table 6 gives the model regression coefficients for these estimates.

Sensitivity analyses

The results of sensitivity analyses are presented in Supplementary Tables 7 to 10. Overall, the results were similar to those presented in the main analyses. The proportions of patients following outpatient care pathways were changed by varying the 30-days limit to 15 and 60 days, and by changing the outpatient specialties. However, for all scenarios, patients admitted to a non-arterial spoke hospital waited on average about twice as long for revascularisation compared with those admitted to an arterial hub hospital. Results from the Cox and logistic regression models were robust across the sensitivity analyses.

DISCUSSION

This study used a novel approach to describe the complex care pathways to revascularisation for patients with CLTI within the hub-and-spoke models of vascular networks in England. These results

highlight a number of issues. It is of concern that patients with CLTI who were first seen at non-arterial spoke hospitals experienced longer delays to access revascularisation procedures, compared to those who were first seen at an arterial hub hospital. The current study suggested patients admitted to a non-arterial spoke hospital (pathway 2) waited on average more than twice as long for revascularisation compared to patients admitted to an arterial hub hospital (pathway 1). Similar differences were observed in relation to the outpatient pathways when patients were treated only at a hub or spoke (pathways 4 and 6). We found there were almost identical times to revascularisation among patients who had an initial outpatient assessment, regardless if that was at an arterial hub or a non-arterial spoke, prior to their subsequent admission to an arterial hub unit for revascularisation (pathway 4 vs 5). Nonetheless, about 45% of patients missed the target of a 14-days maximum delay for patients following outpatient care pathways 4 and 5. Finally, the study suggests that, after around 7 days, longer delays are associated with a slightly but statistically significantly increased risk of postoperative major amputation and in-hospital death. An additional interesting observation was the higher risk of in-hospital death amongst patients who were admitted as an emergency to an arterial hub (pathway 1) and fairly rapid revascularisation was performed within 3 days, which could reflect the likelihood that those treated soonest were the sickest patients often with the most considerable degree of ischaemia.

Our findings on time to revascularisation across care pathways within the hub-and-spoke vascular networks are in agreement with the findings of previous studies, although there are few studies that investigated the relationship between delays to revascularisation and postoperative outcomes in patients with CLTI. Pankhurst and Edmonds identified the centralisation of UK vascular services as being one of the reasons that patients with diabetes and peripheral arterial disease had difficulty accessing specialist vascular services[21]. An organisational survey of UK vascular units reported that some trusts (32 out of 77) had about 1 in 10 patients waiting longer than 48 hours for transfer from a non-arterial spoke unit to an arterial hub unit[14]. The current study supports the survey findings,

and highlights that patients with CLTI who were transferred from a non-arterial spoke hospital to an arterial hub for revascularisation (pathways 2 and 6) experienced longer delays to revascularisation. An unexpected finding was the longer time to revascularisation among patients presenting with tissue loss. It is possible that these patients could have more severe comorbidity or be more frail, and so needed longer time for investigations and preoperative optimisation.

There has been a long-standing concern that late presentation and delayed management in patients with CLTI could contribute to increased major lower limb amputation rates[15]. A Finnish study reported that a delay of more than 2 weeks from the primary care assessment to revascularisation was identified as an independent predictor for major amputation in patients with diabetes and CLTI presenting with tissue loss (odds ratio 3.1, 95% CI 1.4-6.9), compared with a delay of less than 2 weeks[22]. The UK National Vascular Registry (NVR) Annual Report 2020 also reported higher in-hospital mortality rates in patients admitted as an emergency whose time from admission to revascularisation was >5 days, compared to those whose preoperative length of hospital stay was ≤5 days[23]. The current study found that postoperative outcomes were worse when associated with longer delays to revascularisation, although patterns varied across care pathways. Among the patients who followed the outpatient care pathways, in particular within the care pathways 4 and 6, there were small but positive trends between time to revascularisation and the adverse postoperative outcomes of major amputation and in-hospital death. For patients who were initially directly admitted to an arterial hub hospital as an emergency (pathway 1), the risk of in-hospital death was least when revascularisation was performed between 3 and 7 days, and then increased markedly as delays lengthened. A possible explanation is that inpatients who experienced delayed revascularisation may have a greater burden of comorbidity requiring additional time to optimise concurrent medical co-morbidities (cardiac, respiratory, renal, diabetes or infective) prior to attempting revascularisation. A greater proportion of high-risk patients in this group might also explain the greater risk of death among patients with the shortest times to revascularisation. For the

inpatients who were discharged and subsequently readmitted for revascularisation (pathway 3), longer delays also appeared to be associated with an increased risk of postoperative major amputation after adjusting for other patient characteristics, although only being marginally statistically significant. Further investigations into the reasons for interim discharge and subsequent readmission for revascularisation may be required to improve the postoperative outcomes and reduce the amputation rates among this group of patients.

There is always a risk to life or limb in major arterial surgery, and vascular surgery is classified as an urgent care service in the UK[6,10]. Centres of excellence for amputation prevention have been encouraged world-wide for managing patients with CLTI[1]. The Vascular Society of Great Britain and Ireland in 2018 introduced a Peripheral Vascular Disease Quality Improvement Framework with a 5-days target from referral to revascularisation procedures for patients with CLTI who follow the non-elective admission pathways, and a 14-days target for those who follow the outpatient pathways[10,16]. In this study, the 5-days inpatient target was met in just over 50% of patients who were directly admitted to an arterial hub hospital as an emergency, and in only 19% of patients who were admitted to a non-arterial spoke hospital preceding transfer to the regional arterial hub centre. Similar patterns were found in respect of the 14-days target among patients who followed the outpatient care pathways. There is room to improve the time to revascularisation from specialist health care assessment for patients with CLTI in England. The Leicester Vascular Unit instituted a vascular limb salvage clinic on an outpatient basis in 2018 with the aim to meet the 14-days target, and reported improved 12 month outcomes and reduced amputation rates for patients with CLTI, compared with those managed through traditional clinical pathways[24]. Only about 42% of patients in this study followed the outpatient care pathways which could imply that most patients with CLTI were managed with late presentation, and a further investigation could be of importance.

The main strength of this study is the use of both inpatient and outpatient data for all English NHS hospitals, which enabled the study to capture the complex care pathways in the real world for patients with CLTI in a comprehensive manner. This study included most patients with CLTI in England that required urgent care and underwent their first lower limb revascularisation during the study period within the hub-and-spoke model of vascular networks. This study has several potential limitations. First, there are no explicit diagnostic codes for CLTI in the version of ICD-10 used by the HES database (in contrast to the modifications used elsewhere[25]). Therefore, a combination of emergency admission, ICD-10 diagnostic codes and OPCS-4 procedure codes were used to define the study cohort. We limited the study to emergency admission as the NVR 2021 Annual Report[26] reported more than 95% of non-elective lower limb bypass procedures performed in 2019 were due to CLTI (Fontaine score III/IV). This approach will omit patients with CLTI who had an elective revascularisation, but the study was considered to capture the majority of patients with CLTI and be representative of the whole population. Second, the cohort inclusion criteria relied upon the 30-days limit and the range of outpatient specialties used to define the outpatient pathways. Sensitivity analyses that replaced the 30-days limit by 15 days or 60 days showed that the distribution of time to revascularisation for the outpatient care pathways was dependent upon this limit. However, a 30-days limit was considered a reasonable interval between outpatient visits and the admission for revascularisation. Third, there is a risk of residual confounding due to unmeasured confounding variables. This might explain the increased risk of in-hospital death for the shortest times to revascularisation for patients on care pathway 1. Finally, HES only collects data on secondary care. Delays that occurred in the community between the onset of symptoms and specialist assessment by vascular services were not captured in this study.

Conclusions

Vascular arterial surgical services within NHS hospitals in England are organised in a hub-and-spoke centralised model of care. The study highlights patients with CLTI who were first admitted to a non-

arterial spoke hospital preceding transfer to an arterial hub for revascularisation experienced significantly longer delays to procedures on average, compared to those who were first admitted to an arterial hub hospital. This is of concern because longer delays were associated with a small but statistically significant increase in the risk of postoperative major amputation and in-hospital death following revascularisation. In addition, patients who were discharged during the care pathways with subsequent readmission for revascularisation were likely to experience significant delays to revascularisation and an increase risk of adverse outcomes. Further investigation into the reasons for delays is required to improve the vascular care for those patients. A greater insight into this patient group could be gained if HES adopted an ICD-10 modification that included explicit diagnostic codes for CLTI.

[words=approx. 4646]

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Conflict of interest

None

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FIGURE LEGENDS

Figure 1. Boxplots of median (IQR) time to revascularisation from the point of first contact with vascular services, by care pathway. Note data beyond the upper whiskers (outside values) are not presented; the red line indicates time at 5 days and orange line at 14 days.

Figure 2. Adjusted hazard ratio (aHR) of time to revascularisation for patient characteristics and care pathway, shown with 95% confidence intervals and estimated using multivariable Cox regression models, with NHS trust included as random effects. Note a hazard ratio <1 indicates the time to revascularisation tended to be longer for the subgroup patients compared to patients in the reference group. RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.

Figure 3. Marginal predicted probability of postoperative major amputation (blue line) and in-hospital death (red line) across the inpatient care pathways against time to revascularisation, shaded with 95% confidence interval. Details on the fitted regression models can be found in Supplementary Table 6.

Figure 4. Marginal predicted probability of postoperative major amputation (blue line) and in-hospital death (red line) across the outpatient care pathways against time to revascularisation, shaded with 95% confidence interval. Details on the fitted regression models can be found in Supplementary Table 6.

Table 1. Description of care pathways to revascularisation within the English National Health Service

Care pathway	Label	Description
Inpatient pathway - first contact: emergency admission		
1	Adm(Hub)	Admission to an arterial hub hospital and revascularisation during the same admission
2	Adm(Spoke / transfer)	Admission to a non-arterial spoke hospital and revascularisation at the same spoke unit or transfer to a hub or another spoke unit for revascularisation
3	Adm(Any)-Dis+Readm	Admission to a spoke or hub unit, subsequent discharge and readmission to a spoke or hub for revascularisation
Outpatient pathway - first contact: outpatient visit		
4	OP(Hub)-Adm(Hub)	Outpatient visit at an arterial hub hospital and admission to the hub unit for revascularisation
5	OP(Spoke)-Adm(Hub)	Outpatient visit at a non-arterial spoke hospital and admission to a hub unit for revascularisation
6	OP(Spoke)-Adm(Spoke)	Outpatient visit at a non-arterial spoke hospital and admission to spoke unit for revascularisation or admission to spoke unit then transfer to hub unit for revascularisation
7	OP-Adm-Dis+Readm	Outpatient visit at an arterial hub or a non-arterial spoke hospital and admission, followed by discharge and re-admission to either a spoke or hub for revascularisation

Table 2. Characteristics of patients with chronic limb threatening ischaemia at the time of revascularisation (between April 2015 and March 2019), stratified by type of first contact

Characteristics	**Inpatients** (n=9 470, 57.5%)	**Outpatients** (n=7 013, 42.5%)	**Total** (n=16 483)
Male	6 150 (64.9)	4 619 (65.9)	10 769 (65.3)
Age (years)			
<=49	305 (3.2)	195 (2.8)	500 (3.0)
50-59	1 053 (11.1)	837 (11.9)	1 890 (11.5)
60-69	2 189 (23.1)	1 630 (23.2)	3 819 (23.2)
70-79	2 931 (31.0)	2 217 (31.6)	5 148 (31.2)
80+	2 992 (31.6)	2 134 (30.4)	5 126 (31.1)
Deprivation quintile			
Q1 (least deprived)	1 317 (13.9)	1 087 (15.5)	2 404 (14.6)
Q2	1 700 (18.0)	1 239 (17.7)	2 939 (17.8)
Q3	1 855 (19.6)	1 377 (19.6)	3 232 (19.6)
Q4	2 124 (22.4)	1471 (21.0)	3 595 (21.8)
Q5 (most deprived)	2 474 (26.1)	1 839 (26.2)	4 313 (26.2)
Diabetes mellitus	4 791 (50.6)	4 236 (60.4)	9 027 (54.8)
RCS Charlson score (diabetes not included)			
0	3 106 (32.8)	2 315 (33.0)	5 421 (32.9)
1	2 883 (30.4)	2 147 (30.6)	5 030 (30.5)
2	1 858 (19.6)	1 390 (19.8)	3 248 (19.7)
3+	1 623 (17.1)	1 161 (16.6)	2 784 (16.9)
CLTI indicator			
No record of tissue loss	4 114 (43.4)	2 640 (37.6)	6 754 (41.0)
With record of tissue loss	5 356 (56.6)	4 373 (62.4)	9 729 (59.0)
Procedure			
Endovascular	6 644 (70.2)	5 001 (71.3)	11 645 (70.6)
Open surgery	2 235 (23.6)	1 538 (21.9)	3 773 (22.9)
Hybrid	591 (6.2)	474 (6.8)	1 065 (6.5)
Financial Year			
2015/2016	2 465 (26.0)	1 726 (24.6)	4 191 (25.4)
2016/2017	2 372 (25.1)	1 719 (24.5)	4 091 (24.8)
2017/2018	2 430 (25.7)	1 830 (26.1)	4 260 (25.8)
2018/2019	2 203 (23.3)	1 738 (24.8)	3 941 (23.9)

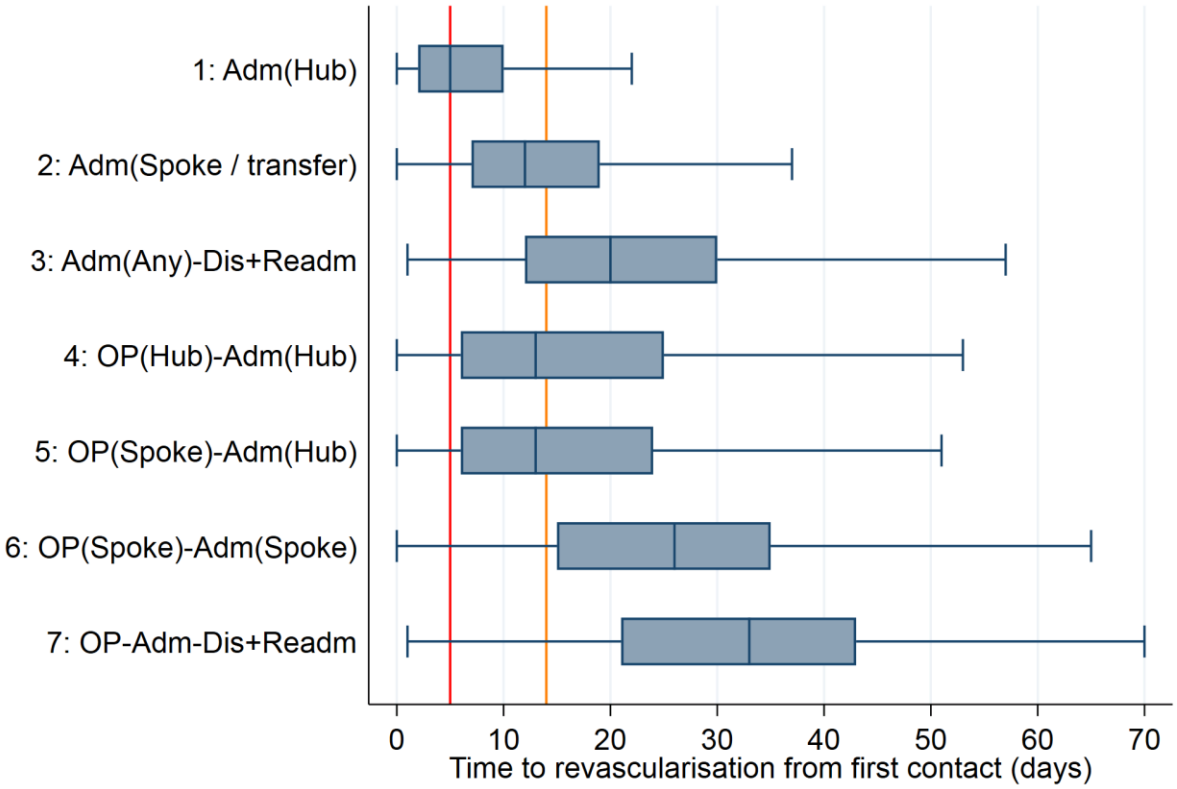
RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.
Financial year runs from 1 April to 31 March next year.

Table 3. Summary of lower limb revascularisation procedures and postoperative outcomes, stratified by care pathway

Inpatients	**1: Adm(Hub)** (n=5 560, 33.7%)	**2: Adm(Spoke / transfer)** (n=1 783, 10.8%)	**3: Adm(Any)-Dis+Readm** (n=2 127, 12.9%)	
Procedure				
Endovascular	3 797 (68.3)	1 374 (77.1)	1 473 (69.3)	
Surgical	1 409 (25.3)	314 (17.6)	512 (24.1)	
Hybrid	354 (6.4)	95 (5.3)	142 (6.7)	
CLTI indicator				
No record of tissue loss	2 705 (48.7)	425 (23.8)	984 (46.3)	
With record of tissue loss	2 855 (51.3)	1 358 (76.2)	1 143 (53.7)	
Time to revascularisation				
Days, median (IQR)	5 (2-10)	12 (7-19)	20 (12-30)	
Beyond 5 days of admission	2 766 (49.7)	1 447 (81.2)	1 978 (93.0)	
Postoperative summary and outcomes				
Hospital stay in days, median (IQR)	8 (3-18)	12 (5-25)	5 (1-14)	
Major amputation	400 (7.2)	124 (7.0)	109 (5.1)	
In-hospital death	336 (6.0)	112 (6.3)	109 (5.1)	
Amputation free survival at discharge	4 877 (87.7)	1 564 (87.7)	1 917 (90.1)	
Outpatients	**4: OP(Hub)-Adm(Hub)** (n=3 530, 21.4%)	**5: OP(Spoke)-Adm(Hub)** (n=1 473, 8.9%)	**6: OP(Spoke)-Adm(Spoke)** (n=634, 3.8%)	**7: OP-Adm-Dis+Readm** (n=1 376, 8.3%)
Procedure				
Endovascular	2 536 (71.8)	1 003 (68.1)	542 (85.5)	920 (66.9)
Surgical	767 (21.7)	352 (23.9)	74 (11.7)	345 (25.1)
Hybrid	227 (6.4)	118 (8.0)	18 (2.8)	111 (8.1)
CLTI indicator				
No record of tissue loss	1 321 (37.4)	592 (40.2)	137 (21.6)	590 (42.9)
With record of tissue loss	2 209 (62.6)	881 (59.8)	497 (78.4)	786 (57.1)
Time to revascularisation				
Days, median (IQR)	13 (6-25)	13 (6-24)	26 (15-35)	33 (21-43)
Beyond 14 days of outpatient visit	1 585 (44.9)	668 (45.3)	483 (76.2)	1 175 (85.4)
Postoperative summary and outcomes				
Hospital stay in days, median (IQR)	7 (3-15)	7 (3-15)	8 (3-18)	4 (1-12)
Major amputation	203 (5.8)	87 (5.9)	35 (5.5)	60 (4.4)
In-hospital death	164 (4.6)	64 (4.3)	33 (5.2)	46 (3.3)
Amputation free survival at discharge	3 185 (90.2)	1 334 (90.6)	576 (90.9)	1 280 (93.0)

CLTI chronic limb-threatening ischaemia; IQR interquartile range.

Figure 1. Boxplots of median (IQR) time to revascularisation from the point of first contact with vascular services, by care pathway. Note data beyond the upper whiskers (outside values) are not presented; the red line indicates time at 5 days and orange line at 14 days.



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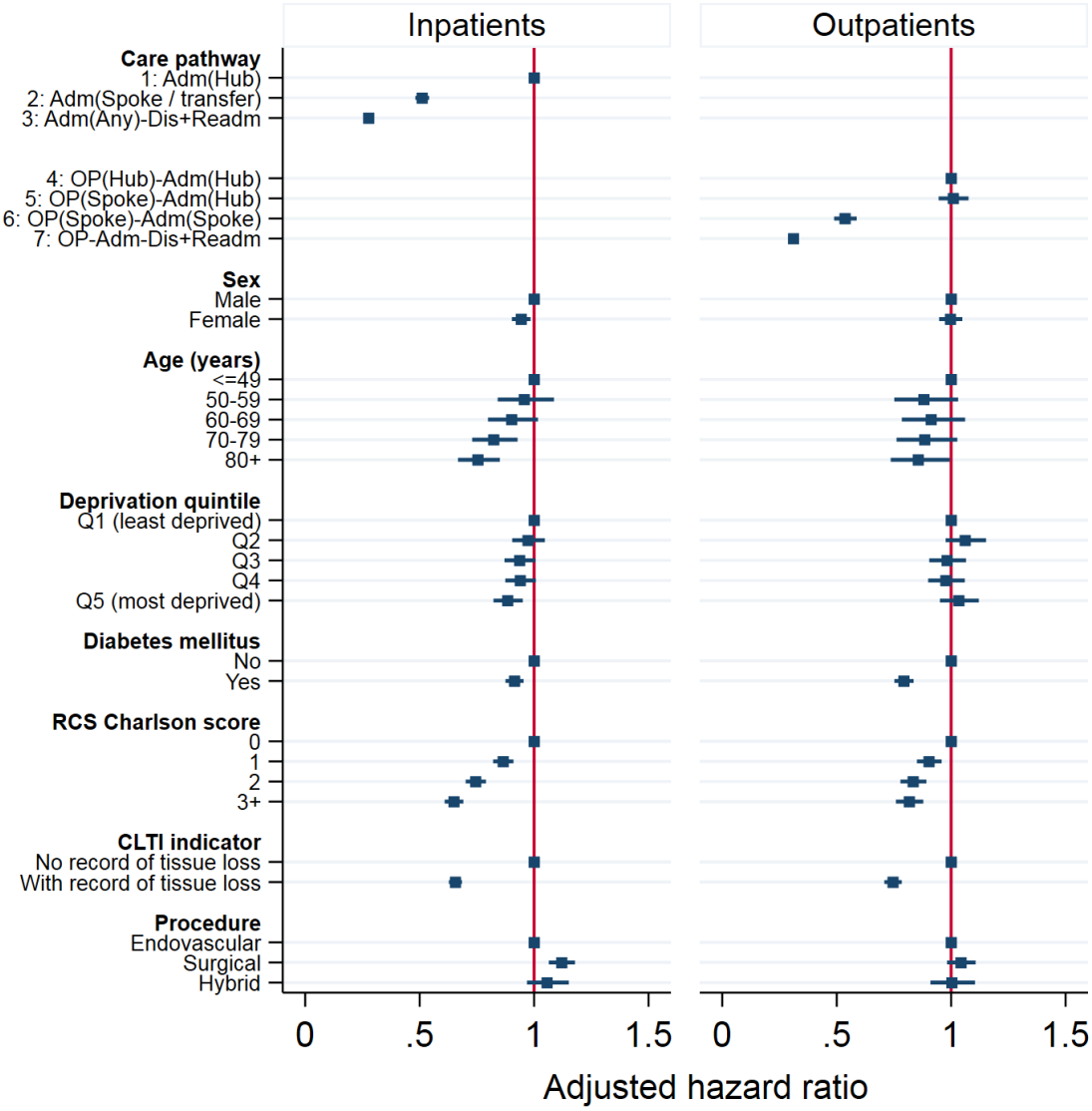

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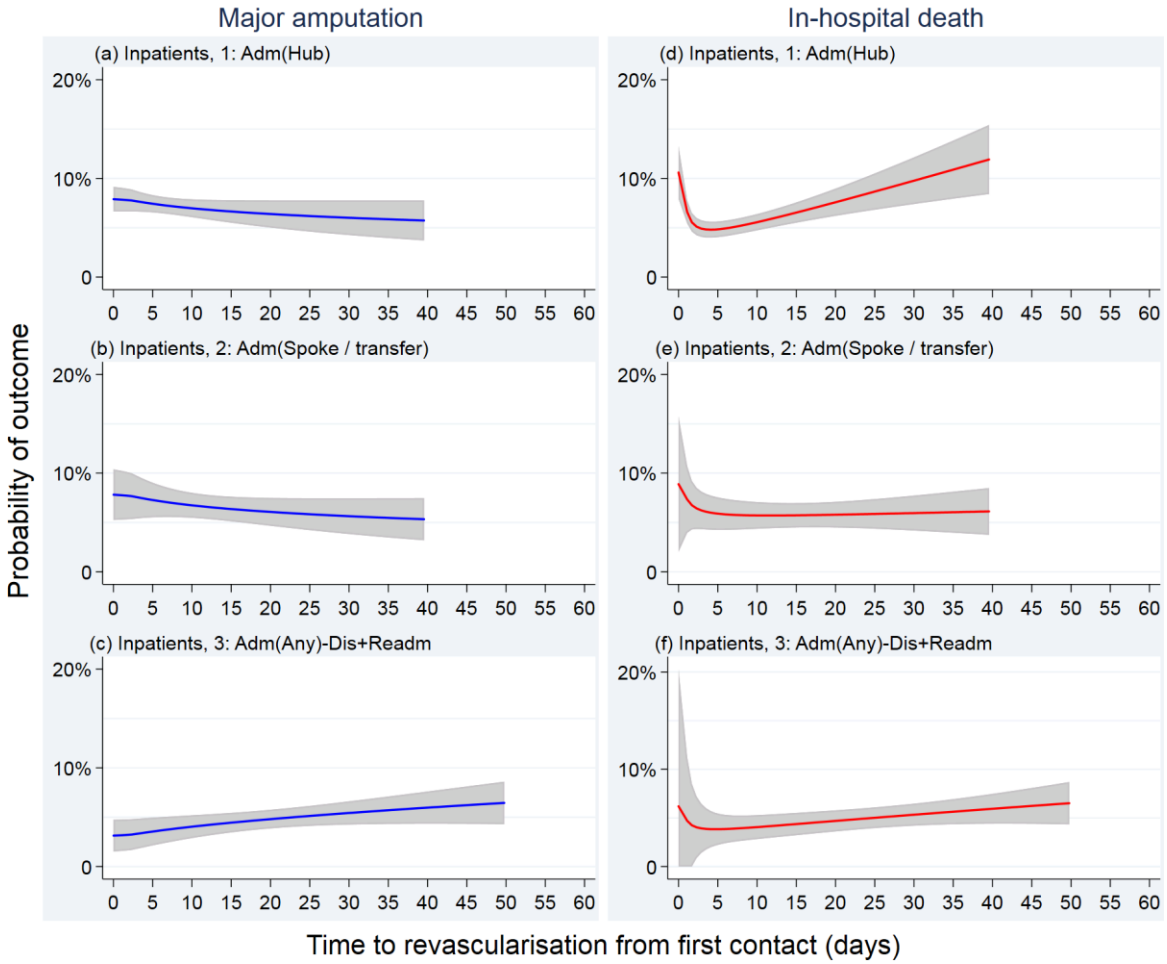

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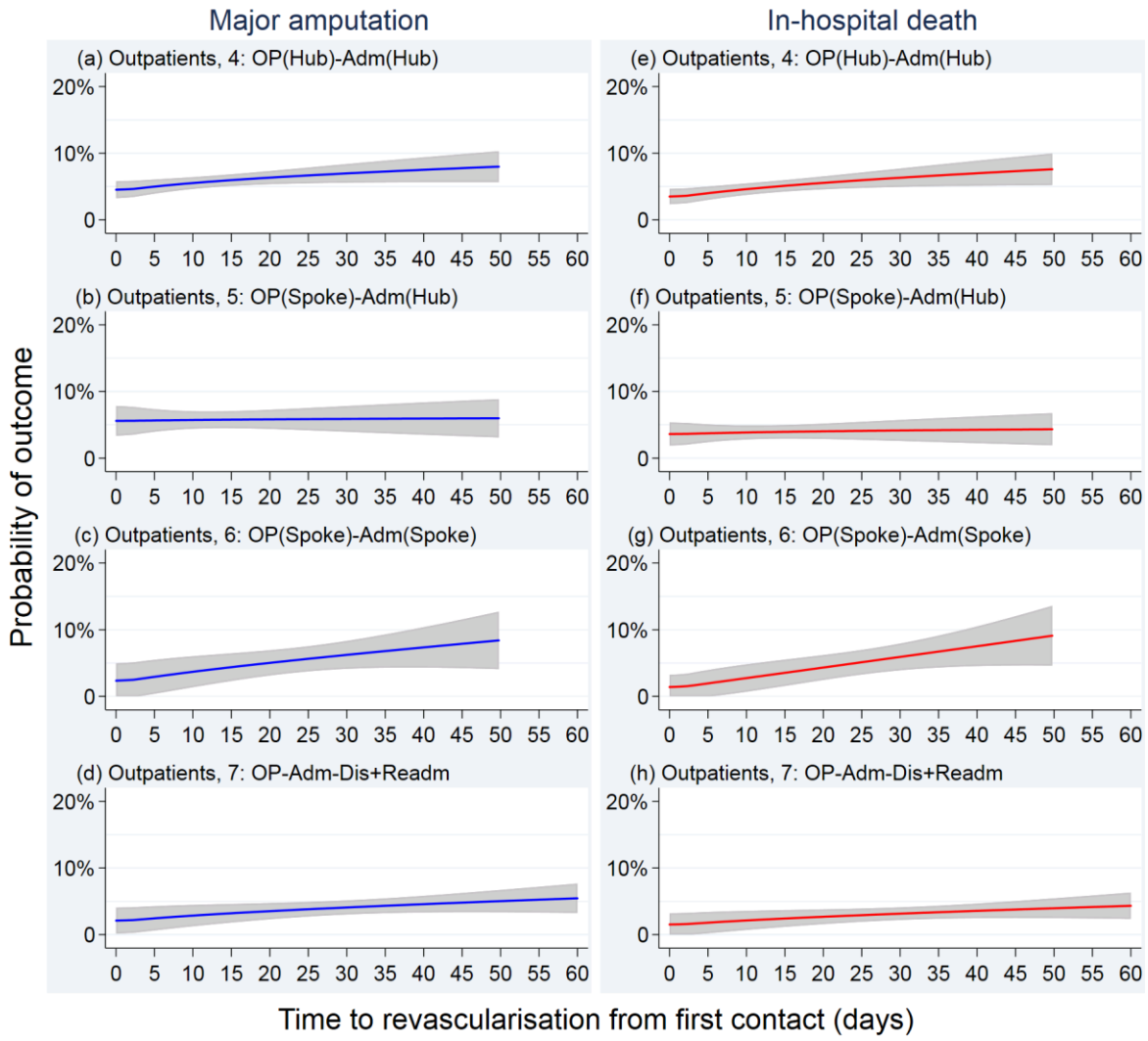


Online Supplementary Material

Delays to revascularisation for patients with chronic limb-threatening ischaemia in England
Q. Li, P. Birmpili, A.S. Johal, S. Waton, A.D. Pherwani, J.R. Boyle, D.A. Cromwell

Supplementary Table 1. ICD-10 codes for chronic limb-threatening ischaemia (CLTI). Note: patients with CLTI were defined using a combination of ICD-10 codes and emergency admission among those undergoing revascularisation procedures.

Disease/condition	ICD-10 code	ICD-10 code description
Intermittent claudication	I739	Peripheral vascular disease, unspecified
Severe limb ischaemia	I702	Atherosclerosis of arteries of extremities I70.02.1 (with gangrene)
	I771	Stricture of artery
	I779	Disorder of arteries and arterioles, unspecified
	L030	Cellulitis of finger and toe
	L031	Cellulitis of other parts of limb
Diabetes with peripheral circulatory complications	E105	Type 1 diabetes mellitus with peripheral circulatory complication
	E115	Type 2 diabetes mellitus with peripheral circulatory complication
	E125	Malnutrition-related diabetes with peripheral circulatory complication
	E135	Other specified diabetes mellitus with peripheral circulatory complication
	E145	Unspecified diabetes mellitus with peripheral circulatory complication
	I792	Peripheral angiopathy in diseases classified elsewhere (diabetic peripheral angiopathy)
Ulceration	L97X	Ulcer of lower limb, not elsewhere classified
	L984	Chronic ulcer of skin, not elsewhere classified
Gangrene	R02X	Gangrene, not elsewhere classified
Osteomyelitis	M860	Acute haematogenous osteomyelitis
	M861	Other acute osteomyelitis
	M862	Subacute osteomyelitis
	M863	Chronic multifocal osteomyelitis
	M864	Chronic osteomyelitis with draining sinus
	M865	Other chronic haematogenous osteomyelitis
	M866	Other chronic osteomyelitis
	M868	Other osteomyelitis
	M869	Osteomyelitis, unspecified

Emergency admissions in the HES data were identified from the admission method with codes of 21, 22, 23, 24, 28, 2A, 2B, 2D.

Lower limb revascularisations with the following primary diagnoses were considered as non CLTI-related and excluded from the study:

- I71*: Aortic aneurysm and dissection
- I723, I724: Other aneurysm
- I743, I744, I745: Arterial embolism and thrombosis – acute limb ischaemia

Supplementary Table 2. Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) version 4 codes to define endovascular and surgical lower limb revascularisation, and major amputation

Location	Code	Description
Endovascular revascularisation for lower limb artery		
Iliac	L541	Percutaneous transluminal angioplasty of iliac artery
	L544	Percutaneous transluminal insertion of stent into iliac artery
femoral	L631	Percutaneous transluminal angioplasty of femoral artery
	L635	Percutaneous transluminal insertion of stent into femoral artery
generic	L662	Percutaneous transluminal stent reconstruction of artery
	L665	Percutaneous transluminal balloon angioplasty of artery
	L667	Percutaneous transluminal placement of peripheral stent in artery
	L711	Percutaneous transluminal angioplasty of artery
Surgical revascularisation for lower limb artery		
Bypass: aorta-femoral arteries	L161	Emergency bypass of aorta by anastomosis of axillary artery to femoral artery
	L162	Bypass of aorta by anastomosis of axillary artery to femoral artery NEC
	L163	Bypass of aorta by anastomosis of axillary artery to bilateral femoral arteries
Bypass: Aorta-iliac artery	L206	Emergency bypass of bifurcation of aorta by anastomosis of aorta to iliac artery NEC
	L216	Bypass of bifurcation of aorta by anastomosis of aorta to iliac artery NEC
Bypass: Iliac-iliac / femoral artery	L501	Emergency bypass of common iliac artery by anastomosis of aorta to common iliac artery NEC
	L502	Emergency bypass of iliac artery by anastomosis of aorta to external iliac artery NEC
	L503	Emergency bypass of artery of leg by anastomosis of aorta to common femoral artery NEC
	L504	Emergency bypass of artery of leg by anastomosis of aorta to deep femoral artery NEC
	L505	Emergency bypass of iliac artery by anastomosis of iliac artery to iliac artery NEC
	L506	Emergency bypass of artery of leg by anastomosis of iliac artery to femoral artery NEC
	L508	Other specified other emergency bypass of iliac artery
	L509	Unspecified other emergency bypass of iliac artery
	L511	Bypass of common iliac artery by anastomosis of aorta to common iliac artery NEC
	L512	Bypass of iliac artery by anastomosis of aorta to external iliac artery NEC
	L513	Bypass of artery of leg by anastomosis of aorta to common femoral artery NEC
	L514	Bypass of artery of leg by anastomosis of aorta to deep femoral artery NEC
	L515	Bypass of iliac artery by anastomosis of iliac artery to iliac artery NEC
	L516	Bypass of artery of leg by anastomosis of iliac artery to femoral artery NEC
	L518	Other specified other bypass of iliac artery
	L519	Unspecified other bypass of iliac artery
Bypass: Femoral – femoral / popliteal / tibial / peroneal	L581	Emergency bypass of femoral artery by anastomosis of femoral artery to femoral artery NEC
	L582	Emergency bypass of femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis NEC

Location	Code	Description
	L583	Emergency bypass of femoral artery by anastomosis of femoral artery to popliteal artery using vein graft NEC
	L584	Emergency bypass of femoral artery by anastomosis of femoral artery to tibial artery using prosthesis NEC
	L585	Emergency bypass of femoral artery by anastomosis of femoral artery to tibial artery using vein graft NEC
	L586	Emergency bypass of femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis NEC
	L587	Emergency bypass of femoral artery by anastomosis of femoral artery to peroneal artery using vein graft NEC
	L588	Other specified other emergency bypass of femoral artery
	L589	Unspecified other emergency bypass of femoral artery
	L591	Bypass of femoral artery by anastomosis of femoral artery to femoral artery NEC
	L592	Bypass of femoral artery by anastomosis of femoral artery to popliteal artery using prosthesis NEC
	L593	Bypass of femoral artery by anastomosis of femoral artery to popliteal artery using vein graft NEC
	L594	Bypass of femoral artery by anastomosis of femoral artery to tibial artery using prosthesis NEC
	L595	Bypass of femoral artery by anastomosis of femoral artery to tibial artery using vein graft NEC
	L596	Bypass of femoral artery by anastomosis of femoral artery to peroneal artery using prosthesis NEC
	L597	Bypass of femoral artery by anastomosis of femoral artery to peroneal artery using vein graft NEC
	L598	Other specified other bypass of femoral artery
	L599	Unspecified other bypass of femoral artery
Endarterectomy or profundaplasty	L521	Endarterectomy of iliac artery and patch repair of iliac artery
	L522	Endarterectomy of iliac artery NEC
	L528	Other specified reconstruction of iliac artery
	L529	Unspecified reconstruction of iliac artery
	L601	Endarterectomy of femoral artery and patch repair of femoral artery
	L602	Endarterectomy of femoral artery NEC
	L603	Profundaplasty of femoral artery and patch repair of deep femoral artery
	L604	Profundaplasty of femoral artery NEC
	L608	Other specified reconstruction of femoral artery
	L609	Unspecified reconstruction of femoral artery
	L681	Endarterectomy and patch repair of artery NEC
Major amputation	X09	Lower limb major amputation

Supplementary Table 3. Description of the 19 distinct care pathways identified using the Hospital Episode Statistics (HES) outpatient and inpatient data between 2015 and 2019

Code	Care pathway description	No.[1] of patients	%
CP01	Admitted spoke->revascularised	782	4.7
CP11	Admitted hub->revascularised	5 576	33.6
CP12	Admitted hub->discharged[2]->readmitted same hub->revascularised	1 287	7.7
CP13	Admitted spoke->transferred to a hub->revascularised	1 010	6.1
CP14	Admitted spoke->transferred to different spoke->revascularised	13	0.1
CP24	Admitted spoke->discharged->readmitted hub->revascularised	704	4.2
CP25	Admitted spoke->discharged->readmitted same spoke->revascularised	129	0.8
CP26	Admitted spoke->discharged->readmitted different spoke->revascularised	31	0.2
CP31	Admitted spoke->same day transferred to hub->discharged->readmitted to same hub->revascularised	21	0.1
OCP01	Outpatient[3] spoke->Admitted same spoke->revascularised	323	1.9
OCP02	Outpatient spoke->Admitted different spoke->revascularised	52	0.3
OCP03	Outpatient spoke->Admitted same spoke->discharged->readmitted same spoke->revascularised	92	0.6
OCP04	Outpatient spoke->Admitted different spoke->discharged->readmitted same spoke->revascularised	11	0.1
OCP21	Outpatient hub visit->Admitted same hub->revascularised	3 533	21.3
OCP22	Outpatient hub visit->Admitted same hub->discharged->readmitted same hub->revascularised	807	4.9
OCP23	Outpatient spoke->Admitted hub->revascularised	1 475	8.9
OCP24	Outpatient spoke->Admitted same spoke->transferred to a hub-> revascularised	267	1.6
OCP25	Outpatient spoke->Admitted hub->discharged->readmitted same hub-> revascularised	284	1.7
OCP26	Outpatient spoke->Admitted same spoke->discharged->readmitted hub-> revascularised	222	1.3
Total		16 619	

[1]Patients included in the table were not limited to ≤70 days of time to revascularisation.
[2]The maximum gap between the discharge date and the subsequent readmission date was defined to be 30 days.
[3]The maximum gap between the outpatient visits and the subsequent revascularisation related hospital admissions was defined to be 30 days, where the first outpatient visit was the earliest visit within the 30-days window with a specialist in vascular surgery, diabetic medicine, podiatry or general surgery.

Supplementary Table 4. Analyses results of time to revascularisation for patients who followed the inpatient care pathways. Hazard ratios (HR)/adjusted hazard ratios (aHR), 95% confidence Intervals (95% CI) and p values were estimated using univariable and multivariable Cox regression models. The multivariable model comprises covariates listed in the table and the NHS trusts as random effects.

	Patients waiting time>5 days	Univariable analysis			Multivariable analysis		
Inpatients	**no. (%)**	**HR**	**95% CI**	**p value**	**aHR**	**95% CI**	**p value**
Care Pathway				<0.001			<0.001
1: Adm(Hub)	2 766 (49.7)	1			1		
2: Adm(Spoke / transfer)	1 447 (81.2)	0.48	0.46-0.51		0.51	0.48-0.54	
3: Adm(Any)-Dis+Readm	1 978 (93.0)	0.30	0.29-0.32		0.28	0.26-0.29	
Sex				0.025			0.008
Male	4 021 (65.4)	1			1		
Female	2 170 (65.4)	0.95	0.91-0.99		0.94	0.90-0.98	
Age (years)				<0.001			<0.001
<=49	185 (60.7)	1			1		
50-59	614 (58.3)	1.03	0.90-1.17		0.96	0.84-1.09	
60-69	1 393 (63.4)	0.94	0.84-1.06		0.90	0.80-1.02	
70-79	1 936 (66.1)	0.86	0.76-0.97		0.82	0.73-0.93	
80+	2 063 (69.0)	0.80	0.71-0.90		0.75	0.67-0.85	
Deprivation quintile				0.427			0.009
Q1 (least deprived)	842 (63.9)	1			1		
Q2	1 101 (64.8)	0.99	0.92-1.07		0.97	0.90-1.05	
Q3	1 204 (64.9)	0.99	0.93-1.07		0.94	0.87-1.01	
Q4	1 372 (64.6)	0.99	0.93-1.07		0.94	0.87-1.01	
Q5 (most deprived)	1 672 (67.6)	0.95	0.89-1.02		0.88	0.82-0.95	
Diabetes mellitus				<0.001			<0.001
No	2 759 (59.0)	1			1		
Yes	3 432 (71.6)	0.83	0.80-0.86		0.91	0.88-0.95	
RCS Charlson score (diabetes not included)				<0.001			<0.001
0	1 785 (57.5)	1			1		
1	1 841 (63.9)	0.84	0.80-0.88		0.86	0.82-0.91	
2	1 313 (70.7)	0.70	0.66-0.74		0.74	0.70-0.79	
3+	1 252 (77.1)	0.58	0.54-0.61		0.65	0.61-0.69	
CLTI indicator				<0.001			<0.001
No record of tissue loss	2 128 (51.7)	1			1		
With record of tissue loss	4 063 (75.9)	0.65	0.63-0.68		0.66	0.63-0.68	
Procedure				<0.001			<0.001
Endovascular	4 545 (68.4)	1			1		
Surgical	1 273 (57.0)	1.26	1.20-1.32		1.12	1.06-1.18	
Hybrid	373 (63.1)	1.14	1.05-1.24		1.06	0.97-1.15	

RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.

Supplementary Table 5. Analyses results of time to revascularisation for patients who followed the outpatient care pathways. Hazard ratios (HR)/adjusted hazard ratios (aHR), 95% confidence intervals (95% CI) and p values were estimated using univariable and multivariable Cox regression models. The multivariable model comprises covariates listed in the table and the NHS trusts as random effects.

	Patients waiting time>14 days	Univariable analysis			Multivariable analysis		
Outpatients	**no. (%)**	**HR**	**95% CI**	**p value**	**aHR**	**95% CI**	**p value**
Care Pathway				<0.001			<0.001
4: OP(Hub)-Adm(Hub)	1 585 (44.9)	1			1		
5: OP(Spoke)-Adm(Hub)	668 (45.3)	1.05	0.99-1.12		1.01	0.95-1.08	
6: OP(Spoke)-Adm(Spoke)	483 (76.2)	0.51	0.47-0.55		0.54	0.49-0.59	
7: OP-Adm-Dis+Readm	1 175 (85.4)	0.34	0.32-0.36		0.31	0.29-0.33	
Sex				0.024			0.901
Male	2 644 (57.2)	1			1		
Female	1 267 (52.9)	1.06	1.01-1.11		1.00	0.95-1.05	
Age (years)				0.773			0.171
<=49	106 (54.4)	1			1		
50-59	464 (55.4)	0.95	0.81-1.11		0.88	0.75-1.03	
60-69	932 (57.2)	0.92	0.80-1.07		0.91	0.78-1.06	
70-79	1 246 (56.2)	0.92	0.79-1.06		0.88	0.76-1.03	
80+	1 163 (54.5)	0.93	0.80-1.08		0.86	0.74-0.99	
Deprivation quintile				0.005			0.161
Q1 (least deprived)	613 (56.4)	1			1		
Q2	678 (54.7)	1.10	1.02-1.20		1.06	0.98-1.15	
Q3	795 (57.7)	1.00	0.93-1.08		0.98	0.90-1.06	
Q4	841 (57.2)	0.99	0.91-1.07		0.98	0.90-1.06	
Q5 (most deprived)	984 (53.5)	1.08	1.01-1.17		1.03	0.95-1.12	
Diabetes mellitus				<0.001			<0.001
No	1 282 (46.2)	1			1		
Yes	2 629 (62.1)	0.71	0.68-0.75		0.79	0.75-0.84	
RCS Charlson score (diabetes not included)				<0.001			<0.001
0	1 167 (50.4)	1			1		
1	1 182 (55.1)	0.88	0.83-0.93		0.90	0.85-0.96	
2	830 (59.7)	0.79	0.75-0.85		0.83	0.78-0.89	
3+	732 (63.0)	0.71	0.66-0.76		0.82	0.76-0.88	
CLTI indicator				<0.001			<0.001
No record of tissue loss	1 275 (48.3)	1			1		
With record of tissue loss	2 636 (60.3)	0.76	0.73-0.80		0.75	0.71-0.78	
Procedure				<0.001			0.386
Endovascular	2 837 (56.7)	1			1		
Surgical	823 (53.5)	1.12	1.06-1.19		1.04	0.98-1.11	
Hybrid	251 (53.0)	1.12	1.02-1.23		1.00	0.91-1.10	

RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.

Supplementary Table 6. Relationship between postoperative outcomes after revascularisation and patient characteristics among inpatients and outpatients. Adjusted odds ratio (OR), 95% confidence intervals (95% CI) were estimated using mixed effects logistic regression models, with NHS trusts as random effects.

		Adjusted OR	95% CI	P value
Inpatients outcome: major amputation				
Care pathway				
1: Adm(Hub)		1	-	-
2: Adm(Spoke / transfer)		0.99	0.67-1.46	0.959
3: Adm(Any)-Dis+Readm		0.37	0.22-0.65	<0.001
Interaction between care pathway and time to revascularisation				
1: Adm(Hub)	Ln(time) ^{2}	0.97	0.94-1.01	0.156
2: Adm(Spoke / transfer)	Ln(time) ^{2}	0.97	0.92-1.02	0.231
3: Adm(Any)-Dis+Readm	Ln(time) ^{2}	1.05	1.00-1.11	0.058
Inpatients outcome: in-hospital death				
Care pathway				
1: Adm(Hub)		1	-	-
2: Adm(Spoke / transfer)		1.09	0.61-1.96	0.765
3: Adm(Any)-Dis+Readm		0.67	0.13-3.42	0.634
Interaction between care pathway and time to revascularisation				
1: Adm(Hub)	Ln(time)	0.57	0.46-0.69	<0.001
	Ln(time) ^{2}	1.22	1.14-1.31	<0.001
2: Adm(Spoke / transfer)	Ln(time)	0.78	0.47-1.30	0.344
	Ln(time) ^{2}	1.05	0.92-1.20	0.447
3: Adm(Any)-Dis+Readm	Ln(time)	0.73	0.22-2.42	0.601
	Ln(time) ^{2}	1.11	0.89-1.39	0.365
Outpatients outcome: major amputation				
Care pathway				
4: OP(Hub)-Adm(Hub)		1	-	-
5: OP(Spoke)-Adm(Hub)		1.25	0.75-2.08	0.386
6: OP(Spoke)-Adm(Spoke)		0.51	0.16-1.64	0.258
7: OP-Adm-Dis+Readm		0.45	0.17-1.21	0.115
Interaction between care pathway and time to revascularisation				
4: OP(Hub)-Adm(Hub)	Ln(time) ^{2}	1.04	1.01-1.08	0.024
5: OP(Spoke)-Adm(Hub)	Ln(time) ^{2}	1.00	0.95-1.06	0.863
6: OP(Spoke)-Adm(Spoke)	Ln(time) ^{2}	1.09	0.99-1.21	0.084
7: OP-Adm-Dis+Readm	Ln(time) ^{2}	1.06	0.98-1.14	0.121
Outpatients outcome: in-hospital death				
Care pathway				
4: OP(Hub)-Adm(Hub)		1	-	-
5: OP(Spoke)-Adm(Hub)		1.04	0.57-1.89	0.91
6: OP(Spoke)-Adm(Spoke)		0.39	0.10-1.54	0.177
7: OP-Adm-Dis+Readm		0.42	0.13-1.37	0.151
Interaction between care pathway and time to revascularisation				
4: OP(Hub)-Adm(Hub)	Ln(time) ^{2}	1.06	1.02-1.10	0.006
5: OP(Spoke)-Adm(Hub)	Ln(time) ^{2}	1.01	0.95-1.08	0.692
6: OP(Spoke)-Adm(Spoke)	Ln(time) ^{2}	1.14	1.02-1.28	0.022

7: OP-Adm-Dis+Readm	Ln(time) ^{2}	1.07	0.98-1.17	0.148

Supplementary Table 7. Summary on frequency, time to revascularisation, postoperative outcomes of major amputation and in-hospital death in four scenarios of sensitivity analyses, by care pathway. The sensitivity analyses are:

1: additionally included patients with a primary diagnostic code for acute limb ischaemia and secondary diagnostic codes for CLTI; the interval between outpatient visit and admission was limit to 30 days

2: the interval between outpatient visit and admission was limited to 15 days

3: the interval between outpatient visit and admission was limited to 60 days; patients with defined time to revascularisation>100 days were excluded

4: limit specialist review to vascular surgery only; the interval between outpatient visit and admission was limit to 30 days

	Sensitivity analysis 1	Sensitivity analysis 2	Sensitivity analysis 3	Sensitivity analysis 4
No. of patients (%)				
Inpatients	11 235 (58.3)	10 464 (63.3)	8 556 (51.7)	12 045 (72.9)
Outpatients	8 043 (41.7)	6 059 (36.7)	7 989 (48.3)	4 471 (27.1)
1: Adm(Hub)	6 745 (35.0)	6 154 (37.3)	5 002 (30.2)	7 193 (43.6)
2: Adm(Spoke / transfer)	2 064 (10.7)	1 889 (11.4)	1 668 (10.1)	2 158 (13.1)
3: Adm(Any)-Dis+Readm	2 426 (12.6)	2 421 (14.7)	1 886 (11.4)	2 694 (16.3)
4: OP(Hub)-Adm(Hub)	4 019 (20.9)	3 123 (18.9)	3 912 (23.6)	2 360 (14.3)
5: OP(Spoke)-Adm(Hub)	1 731 (9.0)	1 299 (7.9)	1 650 (10.0)	1 026 (6.2)
6: OP(Spoke)-Adm(Spoke)	725 (3.8)	534 (3.2)	766 (4.6)	257 (1.6)
7: OP-Adm-Dis+Readm	1 568 (8.1)	1 103 (6.7)	1 661 (10.0)	828 (5.0)
Time to revascularisation, median (IQR) days				
1: Adm(Hub)	5 (2- 9)	5 (2-10)	5 (2-10)	6 (2-10)
2: Adm(Spoke / transfer)	12 (6-19)	12 (7-19)	12 (7-20)	12 (7-19)
3: Adm(Any)-Dis+Readm	20 (12-30)	20 (12-30)	21 (12-31)	20 (12-30)
4: OP(Hub)-Adm(Hub)	13 (6-25)	8 (4-14)	22 (7-46)	9 (4-21)
5: OP(Spoke)-Adm(Hub)	13 (6-24)	8 (5-14)	22 (7-46)	10 (5-22)
6: OP(Spoke)-Adm(Spoke)	25 (15-35)	17 (10-24)	44 (24-60)	22 (13-32)
7: OP-Adm-Dis+Readm	32 (21-43)	24 (15-35)	46 (28-64)	29 (18-41)
Major amputation, no. (%)				
1: Adm(Hub)	478 (7.1)	438 (7.1)	369 (7.4)	501 (7.0)
2: Adm(Spoke / transfer)	142 (6.9)	130 (6.9)	113 (6.8)	152 (7.0)
3: Adm(Any)-Dis+Readm	125 (5.2)	117 (4.8)	97 (5.1)	142 (5.3)
4: OP(Hub)-Adm(Hub)	229 (5.7)	176 (5.6)	220 (5.6)	133 (5.6)
5: OP(Spoke)-Adm(Hub)	109 (6.3)	76 (5.9)	102 (6.2)	57 (5.6)
6: OP(Spoke)-Adm(Spoke)	39 (5.4)	30 (5.6)	47 (6.1)	8 (3.1)
7: OP-Adm-Dis+Readm	66 (4.2)	53 (4.8)	74 (4.5)	29 (3.5)
In hospital death, no. (%)				
1: Adm(Hub)	401 (6.0)	368 (6.0)	307 (6.1)	401 (5.6)
2: Adm(Spoke / transfer)	136 (6.6)	121 (6.4)	106 (6.4)	140 (6.5)
3: Adm(Any)-Dis+Readm	123 (5.1)	122 (5.0)	104 (5.5)	132 (4.9)
4: OP(Hub)-Adm(Hub)	185 (4.6)	141 (4.5)	187 (4.8)	114 (4.8)
5: OP(Spoke)-Adm(Hub)	77 (4.5)	55 (4.2)	70 (4.2)	50 (4.9)
6: OP(Spoke)-Adm(Spoke)	36 (5.0)	25 (4.7)	41 (5.4)	6 (2.3)

7: OP-Adm-Dis+Readm	55 (3.5)	35 (3.2)	57 (3.4)	25 (3.0)

Supplementary Table 8. Analyses results of time to revascularisation for patients who followed inpatient pathways in four scenarios for sensitivity analyses. Adjusted hazard ratio and 95% confidence interval (95% CI) were estimated using multivariable Cox regression models including covariates listed in the table and the NHS trusts as random effects. The cohort settings were the same with that in the main context, except the one(s) specified in each scenario. See Supplementary Table 7 for definitions of sensitivity analysis.

Inpatients	**Adjusted Hazard Ratio (95% CI)**			
	Sensitivity analysis 1	**Sensitivity analysis** 2	**Sensitivity analysis** 3	**Sensitivity analysis** 4
Care Pathway				
1: Adm(Hub)	1	1	1	1
2: Adm(Spoke / transfer)	0.49 (0.47-0.52)	0.51 (0.48-0.54)	0.50 (0.47-0.53)	0.51 (0.49-0.54)
3: Adm(Any)-Dis+Readm	0.27 (0.25-0.28)	0.28 (0.26-0.29)	0.28 (0.27-0.3)	0.27 (0.26-0.28)
Sex				
Male	1	1	1	1
Female	0.94 (0.9-0.98)	0.94 (0.91-0.98)	0.96 (0.92-1)	0.94 (0.9-0.98)
Age (years)				
<=49	1	1	1	1
50-59	0.96 (0.85-1.07)	0.94 (0.83-1.06)	0.86 (0.75-0.99)	0.92 (0.82-1.04)
60-69	0.89 (0.80-0.99)	0.90 (0.80-1.01)	0.85 (0.75-0.97)	0.88 (0.79-0.98)
70-79	0.82 (0.73-0.91)	0.83 (0.74-0.93)	0.8 (0.70-0.91)	0.81 (0.73-0.90)
80+	0.75 (0.68-0.84)	0.75 (0.67-0.84)	0.73 (0.64-0.83)	0.75 (0.67-0.84)
Deprivation quintile				
Q1 (least deprived)	1	1	1	1
Q2	0.96 (0.90-1.03)	0.98 (0.92-1.06)	0.98 (0.90-1.05)	0.99 (0.92-1.05)
Q3	0.93 (0.87-0.99)	0.93 (0.87-1.00)	0.95 (0.88-1.02)	0.96 (0.90-1.02)
Q4	0.92 (0.86-0.99)	0.93 (0.87-1.00)	0.95 (0.88-1.02)	0.95 (0.89-1.01)
Q5 (most deprived)	0.88 (0.82-0.94)	0.89 (0.83-0.96)	0.88 (0.81-0.94)	0.90 (0.85-0.96)
Diabetes mellitus				
No	1	1	1	1
Yes	0.91 (0.87-0.95)	0.91 (0.88-0.95)	0.93 (0.89-0.98)	0.93 (0.9-0.97)
RCS Charlson score (diabetes not included)				
0	1	1	1	1
1	0.87 (0.83-0.92)	0.86 (0.82-0.91)	0.83 (0.78-0.87)	0.87 (0.83-0.91)
2	0.76 (0.72-0.80)	0.74 (0.70-0.78)	0.74 (0.70-0.79)	0.75 (0.71-0.79)
3+	0.67 (0.63-0.71)	0.65 (0.62-0.69)	0.63 (0.59-0.67)	0.68 (0.64-0.72)
CLTI indicator				
No record of tissue loss	1	1	1	1
With record of tissue loss	0.64 (0.61-0.66)	0.66 (0.63-0.68)	0.66 (0.63-0.69)	0.66 (0.64-0.69)
Procedure				
Endovascular	1	1	1	1
Surgical	1.16 (1.10-1.21)	1.13 (1.07-1.18)	1.11 (1.05-1.17)	1.11 (1.06-1.17)
Hybrid	1.07 (0.99-1.15)	1.03 (0.95-1.12)	1.05 (0.96-1.15)	1.06 (0.98-1.15)

RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.

Supplementary Table 9. Analyses results of time to revascularisation for patients who followed outpatient pathways in four scenarios for sensitivity analyses. Adjusted hazard ratios and 95% confidence intervals (95% CI) were estimated using multilevel Cox regression models including covariates listed in the table and the NHS trusts as random effects. The cohort settings were the same with that in the main context, except the one(s) specified in each scenario. See Supplementary Table 7 for definitions of sensitivity analysis.

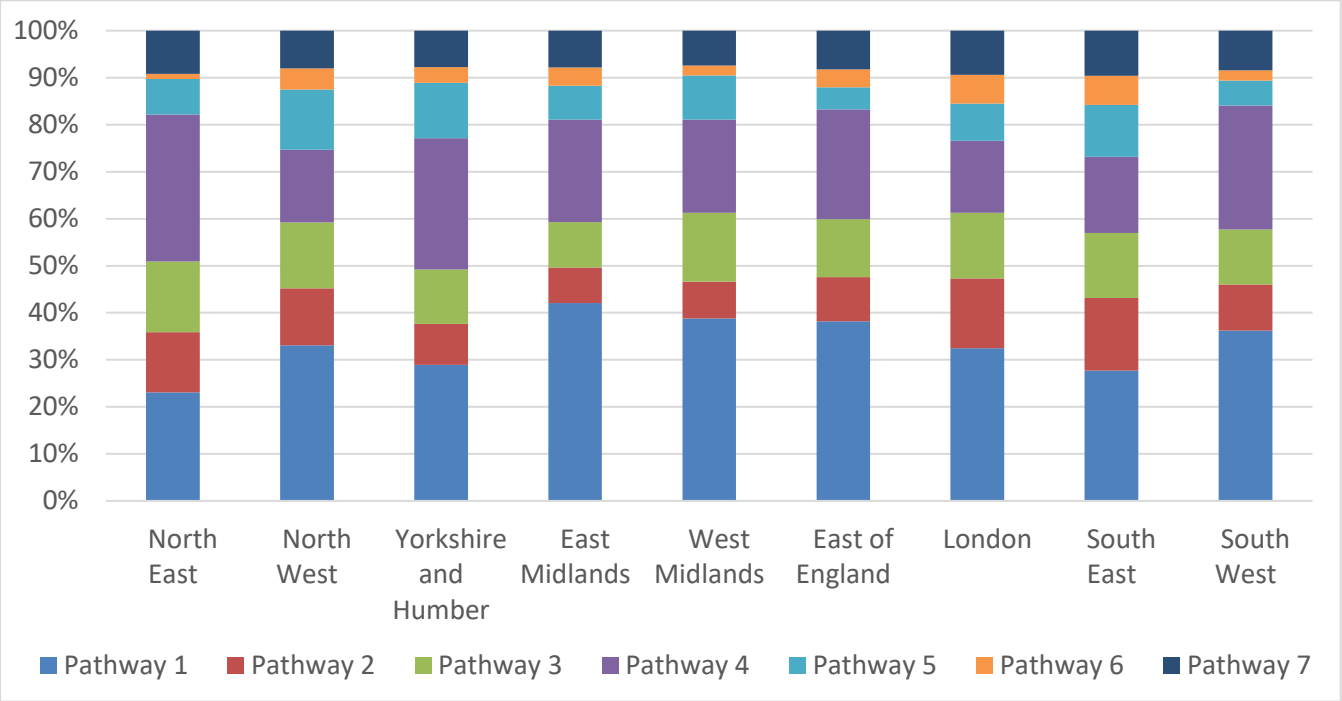
Outpatients	**Adjusted Hazard Ratio (95% CI)**			
	Sensitivity analysis 1	**Sensitivity analysis 2**	**Sensitivity analysis 3**	**Sensitivity analysis 4**
Care Pathway				
4: OP(Hub)-Adm(Hub)	1	1	1	1
5: OP(Spoke)-Adm(Hub)	1.00 (0.94-1.06)	1.02 (0.95-1.10)	1.01 (0.95-1.07)	0.96 (0.89-1.04)
6: OP(Spoke)-Adm(Spoke)	0.53 (0.48-0.57)	0.46 (0.42-0.51)	0.60 (0.55-0.65)	0.50 (0.44-0.57)
7: OP-Adm-Dis+Readm	0.31 (0.29-0.33)	0.26 (0.24-0.28)	0.44 (0.41-0.47)	0.31 (0.28-0.34)
Sex				
Male	1	1	1	1
Female	1.00 (0.95-1.04)	0.96 (0.91-1.02)	1.01 (0.96-1.06)	0.99 (0.93-1.05)
Age (years)				
<=49	1	1	1	1
50-59	0.92 (0.79-1.06)	0.78 (0.66-0.93)	1.02 (0.88-1.18)	0.81 (0.66-0.99)
60-69	0.93 (0.81-1.07)	0.86 (0.73-1.01)	1.06 (0.93-1.23)	0.84 (0.69-1.01)
70-79	0.90 (0.78-1.03)	0.79 (0.67-0.93)	1.00 (0.87-1.15)	0.79 (0.66-0.96)
80+	0.88 (0.76-1.01)	0.77 (0.66-0.91)	1.01 (0.88-1.16)	0.74 (0.61-0.9)
Deprivation quintile				
Q1 (least deprived)	1	1	1	1
Q2	1.04 (0.96-1.12)	1.04 (0.95-1.13)	1.01 (0.93-1.09)	1.05 (0.94-1.16)
Q3	0.97 (0.90-1.04)	0.97 (0.89-1.06)	0.97 (0.9-1.05)	0.96 (0.87-1.07)
Q4	0.96 (0.89-1.04)	0.97 (0.89-1.06)	1.02 (0.95-1.11)	0.98 (0.88-1.09)
Q5 (most deprived)	1.03 (0.95-1.11)	0.99 (0.91-1.08)	1.02 (0.94-1.1)	1.05 (0.95-1.16)
Diabetes mellitus				
No	1	1	1	1
Yes	0.78 (0.75-0.82)	0.77 (0.72-0.81)	0.81 (0.77-0.86)	0.91 (0.85-0.97)
RCS Charlson score (diabetes not included)				
0	1	1	1	1
1	0.91 (0.86-0.96)	0.85 (0.80-0.91)	0.89 (0.84-0.94)	0.91 (0.84-0.98)
2	0.83 (0.78-0.89)	0.78 (0.72-0.84)	0.83 (0.78-0.89)	0.87 (0.8-0.95)
3+	0.81 (0.76-0.87)	0.77 (0.71-0.84)	0.78 (0.73-0.84)	0.82 (0.74-0.9)
CLTI indicator				
No record of tissue loss	1	1	1	1
With record of tissue loss	0.74 (0.7-0.78)	0.75 (0.71-0.79)	0.76 (0.73-0.8)	0.79 (0.74-0.84)
Procedure				
Endovascular	1	1	1	1
Surgical	1.03 (0.98-1.09)	0.96 (0.90-1.02)	1.01 (0.95-1.06)	1.00 (0.94-1.08)
Hybrid	1.02 (0.93-1.11)	0.96 (0.86-1.06)	1.02 (0.93-1.12)	0.93 (0.83-1.05)

RCS Royal College of Surgeons; CLTI chronic limb-threatening ischaemia.

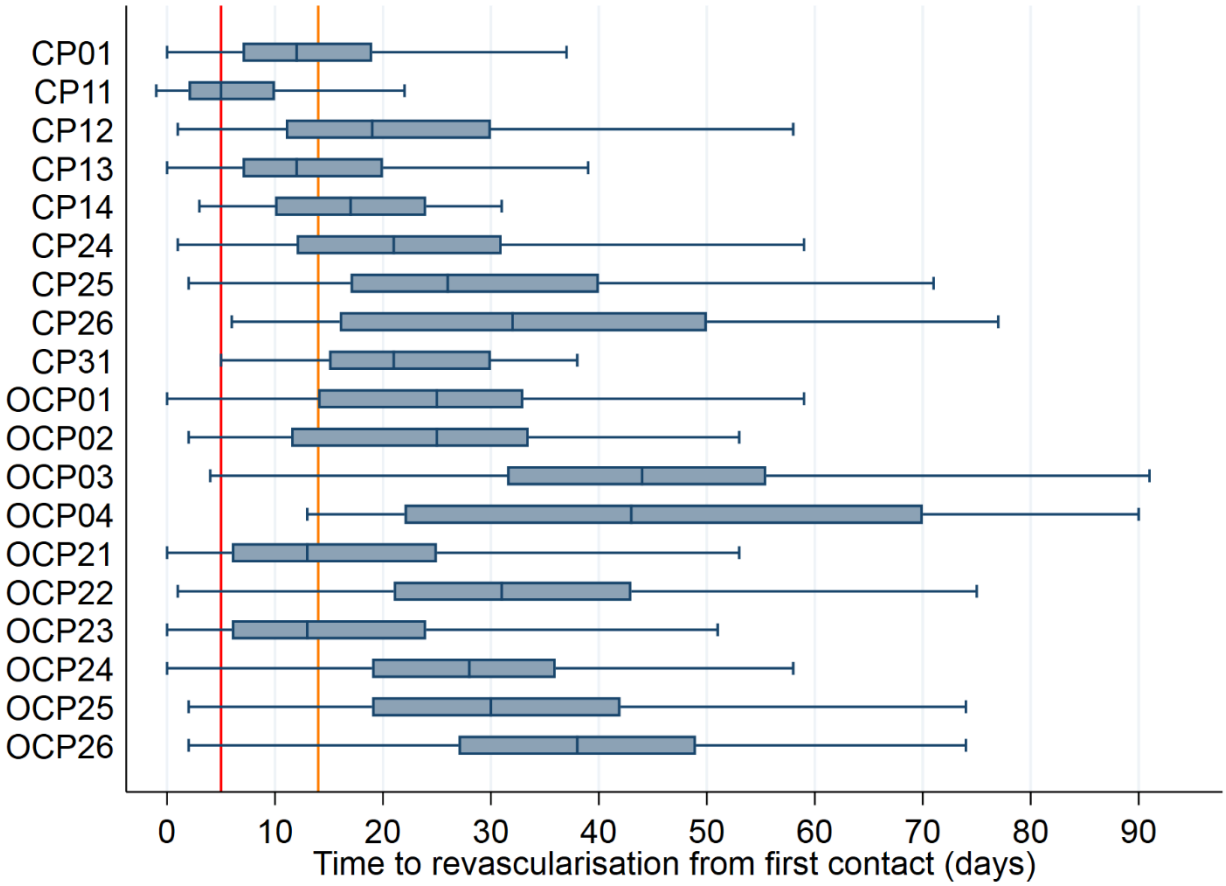
Supplementary Table 10. Analyses results of postoperative outcomes after revascularisation among inpatients and outpatients in four scenarios for sensitivity analyses. Adjusted Odds Ratio and 95% confidence interval (95% CI) of care pathway and their interaction with time to revascularisation were estimated using mixed effects logistic regression models. See Supplementary Table 7 for definitions of sensitivity analysis.

		Adjusted Odds Ratio (95% CI)			
		Sensitivity analysis 1	**Sensitivity analysis 2**	**Sensitivity analysis 3**	**Sensitivity analysis 4**
Inpatients outcome: major amputation					
Care pathway					
1: Adm(Hub)		1	1	1	1
2: Adm(Spoke / transfer)		0.94 (0.65-1.34)	1.03 (0.70-1.50)	0.98 (0.65-1.46)	1.02 (0.72-1.45)
3: Adm(Any)-Dis+Readm		0.40 (0.24-0.66)	0.37 (0.22-0.63)	0.45 (0.26-0.78)	0.42 (0.26-0.67)
Interaction between care pathway and time to revascularisation					
1: Adm(Hub)	Ln(time) ^{2}	0.98 (0.95-1.01)	0.99 (0.95-1.02)	0.97 (0.94-1.01)	0.98 (0.95-1.02)
2: Adm(Spoke / transfer)	Ln(time) ^{2}	0.98 (0.94-1.02)	0.97 (0.93-1.02)	0.96 (0.92-1.01)	0.99 (0.94-1.03)
3: Adm(Any)-Dis+Readm	Ln(time) ^{2}	1.05 (1.00-1.10)	1.05 (1.00-1.11)	1.03 (0.98-1.08)	1.05 (1.01-1.10)
Inpatients outcome: in-hospital death					
Care pathway					
1: Adm(Hub)		1	1	1	1
2: Adm(Spoke / transfer)		1.18 (0.71-1.95)	1.03 (0.58-1.84)	1.00 (0.53-1.88)	1.12 (0.64-1.93)
3: Adm(Any)-Dis+Readm		0.73 (0.16-3.32)	0.49 (0.09-2.65)	0.53 (0.09-3.07)	0.76 (0.17-3.47)
Interaction between care pathway and time to revascularisation					
1: Adm(Hub)	Ln(time)	0.58 (0.48-0.69)	0.59 (0.49-0.72)	0.56 (0.46-0.69)	0.60 (0.50-0.73)
	Ln(time) ^{2}	1.21 (1.14-1.29)	1.21 (1.13-1.29)	1.22 (1.14-1.30)	1.21 (1.14-1.29)
2: Adm(Spoke / transfer)	Ln(time)	0.81 (0.51-1.27)	0.82 (0.50-1.36)	0.84 (0.49-1.45)	0.86 (0.54-1.39)
	Ln(time) ^{2}	1.04 (0.92-1.17)	1.05 (0.93-1.19)	1.03 (0.90-1.18)	1.04 (0.93-1.18)
3: Adm(Any)-Dis+Readm	Ln(time)	0.63 (0.21-1.95)	0.88 (0.26-3.03)	0.73 (0.21-2.49)	0.67 (0.22-2.05)
	Ln(time) ^{2}	1.15 (0.93-1.41)	1.08 (0.86-1.35)	1.13 (0.91-1.40)	1.14 (0.92-1.40)
Outpatients outcome: major amputation					
Care pathway					
4: OP(Hub)-Adm(Hub)		1	1	1	1
5: OP(Spoke)-Adm(Hub)		1.26 (0.80-2.00)	1.38 (0.82-2.32)	1.15 (0.71-1.86)	1.09 (0.60-1.97)
6: OP(Spoke)-Adm(Spoke)		0.52 (0.18-1.53)	0.82 (0.29-2.36)	0.45 (0.15-1.39)	0.70 (0.11-4.47)
7: OP-Adm-Dis+Readm		0.54 (0.22-1.33)	0.47 (0.18-1.22)	0.48 (0.19-1.17)	0.16 (0.04-0.71)
Interaction between care pathway and time to revascularisation					
4: OP(Hub)-Adm(Hub)	Ln(time) ^{2}	1.03 (1.00-1.07)	1.07 (1.02-1.12)	1.02 (0.99-1.04)	1.04 (0.99-1.09)
5: OP(Spoke)-Adm(Hub)	Ln(time) ^{2}	1.01 (0.97-1.06)	1.00 (0.92-1.08)	1.01 (0.97-1.04)	1.01 (0.95-1.08)
6: OP(Spoke)-Adm(Spoke)	Ln(time) ^{2}	1.08 (0.99-1.19)	1.07 (0.96-1.19)	1.08 (1.00-1.16)	0.99 (0.82-1.19)
7: OP-Adm-Dis+Readm	Ln(time) ^{2}	1.04 (0.97-1.11)	1.08 (1.00-1.18)	1.04 (0.98-1.10)	1.13 (1.01-1.26)
Outpatients outcome: in-hospital death					
Care pathway					
4: OP(Hub)-Adm(Hub)		1	1	1	1
5: OP(Spoke)-Adm(Hub)		1.32 (0.78-2.27)	1.13 (0.60-2.10)	0.98 (0.55-1.73)	0.87 (0.44-1.72)
6: OP(Spoke)-Adm(Spoke)		0.36 (0.10-1.31)	0.59 (0.17-2.06)	0.21 (0.05-0.93)	0.06 (0.01-1.84)
7: OP-Adm-Dis+Readm		0.49 (0.17-1.41)	0.46 (0.14-1.52)	0.38 (0.13-1.12)	0.42 (0.10-1.72)
Interaction between care pathway and time to revascularisation					
4: OP(Hub)-Adm(Hub)	Ln(time) ^{2}	1.06 (1.02-1.10)	1.07 (1.01-1.13)	1.03 (1.00-1.06)	1.04 (0.99-1.09)
5: OP(Spoke)-Adm(Hub)	Ln(time) ^{2}	0.98 (0.93-1.04)	0.99 (0.90-1.08)	1.00 (0.95-1.04)	1.03 (0.96-1.11)
6: OP(Spoke)-Adm(Spoke)	Ln(time) ^{2}	1.14 (1.03-1.27)	1.11 (0.98-1.26)	1.14 (1.04-1.25)	1.22 (0.93-1.61)
7: OP-Adm-Dis+Readm	Ln(time) ^{2}	1.06 (0.98-1.15)	1.07 (0.96-1.18)	1.05 (0.99-1.13)	1.04 (0.93-1.16)

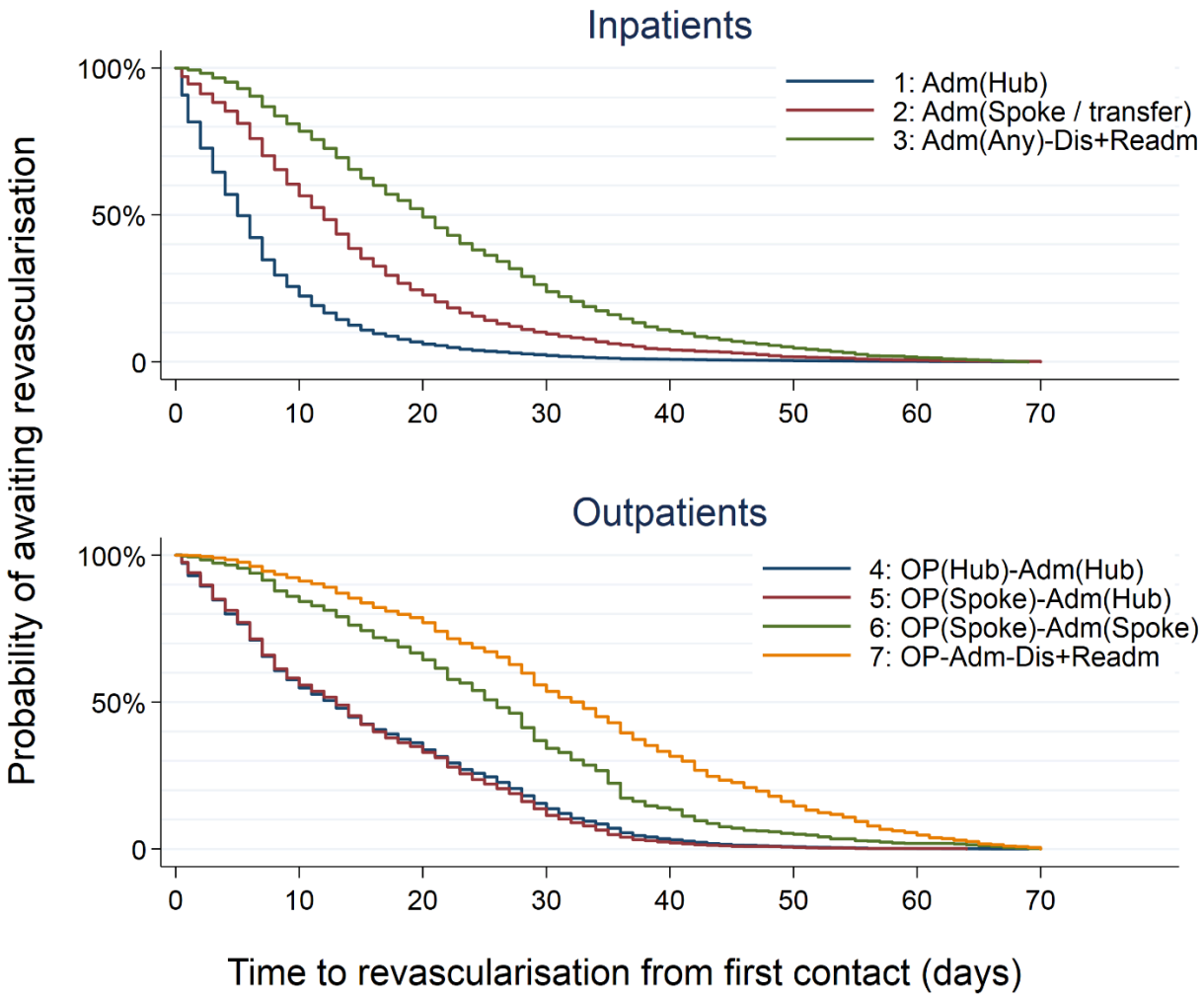
Supplementary Figure 1. Stacked chart of care pathways between April 2015 and March 2019, by residence region in England



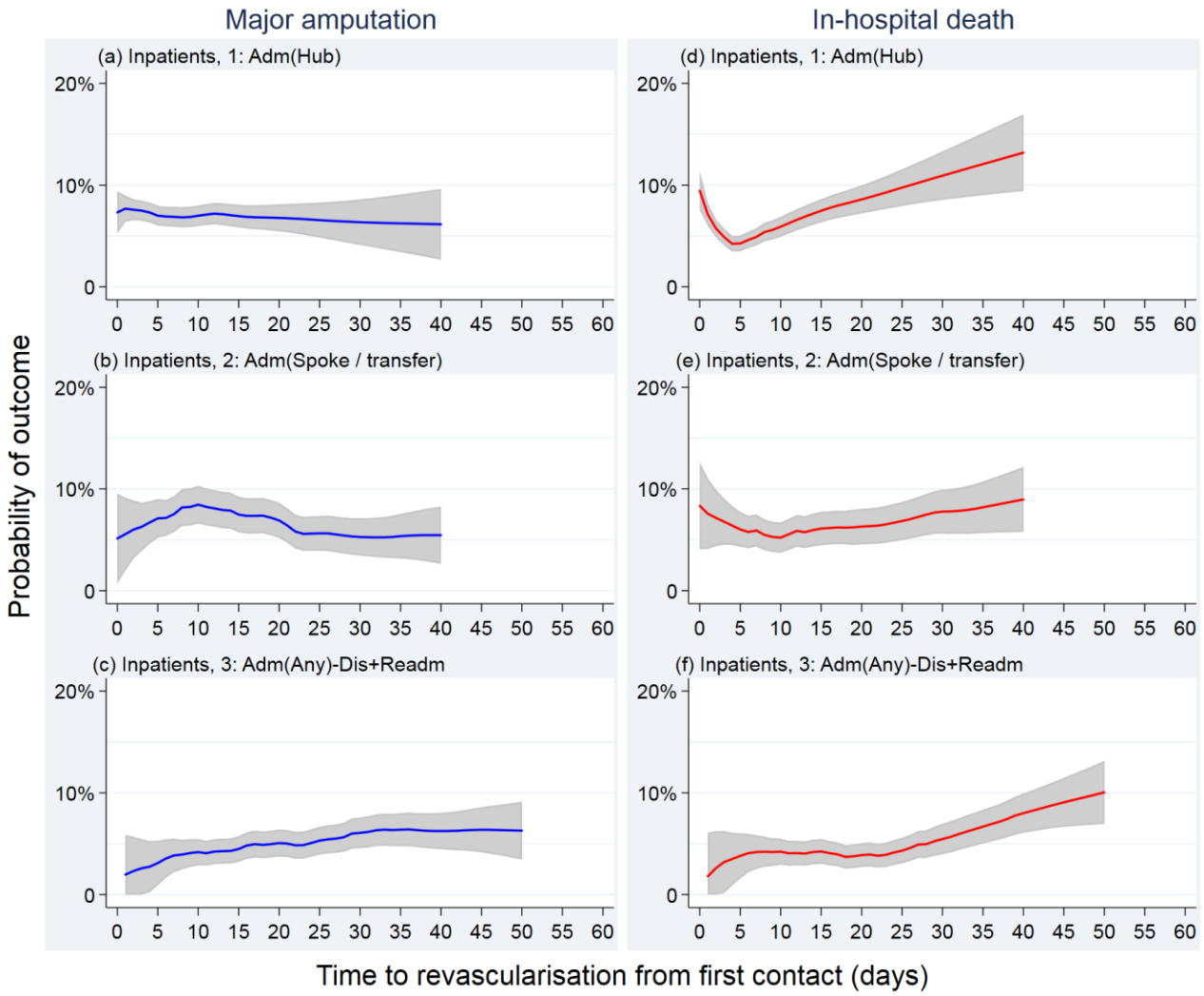
Supplementary Figure 2. Boxplots of median (IQR) time to revascularisation from the point of first contact for the 19 pathways. Note data beyond the upper whiskers (outside values) are not presented; the red line indicates time at 5 days and orange line at 14 days. See Supplementary Table 3 for description of each care pathway code (e.g., CP01)



Supplementary Figure 3. Kaplan-Meier estimator of probability of revascularisation over time (days) from the first contact with vascular services, by care pathway



Supplementary Figure 4. Estimated rates of postoperative major amputation (blue line) and in-hospital death (red line) across the inpatient care pathways against time to revascularisation, shaded with 95% confidence interval. Rates were estimated using a nearest neighbour smoother (RUNNING).



Supplementary Figure 5. Estimated rates of postoperative major amputation (blue line) and in-hospital death (red line) across the outpatient care pathways against time to revascularisation, shaded with 95% confidence interval. Rates were estimated using a nearest neighbour smoother (RUNNING).