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1 **Full title:** Prognostic risk modelling for patients undergoing major lower limb amputation: an
2 analysis of the UK National Vascular Registry.

3

4 **Running head:** Operative risk after major lower limb amputation

5

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16

17 **Presentation:** The paper was presented at the Vascular Society of Great Britain and Ireland

18 annual scientific meeting in Glasgow in November 2018.

1 What does this study add to the existing literature and how will it 2 influence future clinical practice?

3 This observational study used data from the UK National Vascular Registry to look at risk
4 factors for in-hospital mortality and morbidity following major lower-limb amputation.
5 Eleven independent risk factors were identified including emergency admission, raised
6 white cell count or creatinine, low albumin or patient weight, age, ASA grade, amputation
7 level and prior intervention to the amputated limb. A risk model was developed which had
8 excellent calibration and good discrimination (C-statistic 0.79, 95% C.I. 0.77-0.80). An on-
9 line calculator for the model is available, making it easy to use **in-clinical practice**.

10

11 Abstract

12 **Objective:** Major lower limb amputation is the highest-risk lower limb procedure in Vascular
13 Surgery. Despite this, few high-quality studies have examined factors contributing to
14 mortality. We aimed to identify independent risk factors for peri-operative morbidity and
15 mortality and develop reliable models for estimating risk.

16 **Methods:** All patients undergoing lower-limb amputation above the ankle entered into the
17 UK National Vascular Registry (January 2014–December 2016) were included. Missing data
18 were handled using multiple imputation. Models were developed to evaluate independent
19 risk-factors for mortality (the primary outcome) and morbidity using logistic regression,
20 minimising the Bayesian information criterion to balance complexity and model fit. Ethical
21 approval for the study was granted (Wales REC 3 ref:16/WA/0353).

1 **Results:** All 9549 above ankle joint amputations in the registry were included. Overall, 865
2 patients (9.1%) died before leaving hospital. Independent factors associated with mortality
3 were emergency admission, bilateral operation, age, ASA grade, abnormal ECG and
4 increased white cell count or creatinine ($P < 0.01$ for all). Independent factors reducing
5 mortality were trans-tibial operation, increased albumin or patient weight, and previous
6 ipsilateral revascularisation procedures ($P < 0.01$ for all). A risk model incorporating these
7 factors had good discrimination (C-statistic 0.79, 95% C.I. 0.77-0.80) and excellent
8 calibration.

9 Morbidity rates were high, with 6.6%, 9.7% and 4.3% of patients suffering cardiac,
10 respiratory and renal complications respectively. The risk model was also predictive of
11 morbidity outcomes (C-statistics 0.74, 0.69 and 0.74 respectively).

12 **Conclusions:** Morbidity and mortality after lower limb amputation are high in the UK. We
13 identified several potentially modifiable factors for quality improvement initiatives and
14 developed accurate predictive models that could assist patient counselling and decision-
15 making.

16 **Key words:** Amputation; Peripheral vascular disease; Mortality; Risk modelling

1 Introduction

2 Major lower limb amputation is one of the highest risk surgical procedures in the UK, with
3 in-hospital mortality rates of approximately 6% for below- and 12% for above-knee
4 amputation.¹ It is therefore critical to identify prognostic factors contributing to mortality
5 rates so that quality improvement programmes can be implemented. Although limited
6 work exists for UK populations, the only large studies come from parts of the world with
7 radically different healthcare systems, calling generalisability into question (Supplementary
8 Table 1).²⁻⁷

9 Mortality is not the only negative outcome experienced by this cohort; they face
10 long hospital stays, a high rate of perioperative complications and frequent readmissions.⁸
11 Prognostic risk modelling into leading causes of morbidity is therefore also important.
12 Individualising consent⁹ and risk adjustment of surgeon specific outcome data¹⁰ are also
13 enabled by robust risk models. There is some evidence that the broad adoption of the
14 EUROSCORE¹¹ risk prediction tool in cardiac surgery helped lead to the dramatic
15 improvement in cardiac surgical outcomes which occurred around the turn of the
16 millennium.¹² It is possible that by facilitating appropriate targeting of resources to higher
17 risk patients it may be possible to replicate these results in other fields. Thus development
18 of accurate risk models for patients undergoing major lower limb amputation may have a
19 multitude of benefits.

20 The objectives of this study were therefore to identify the independent risk factors
21 for perioperative mortality and leading causes of morbidity in UK patients and develop

- 1 robust prognostic models. The ability of these models to accurately predict mortality in a
- 2 contemporary UK dataset were then compared to previously published models.
- 3

1 Methods

2 Data

3 All patients recorded in the UK National Vascular Registry (NVR) as undergoing major lower
4 limb amputation (below knee, through knee, above knee, hip disarticulation and hind
5 quarter amputation) from January 1 2014 until December 31 2016 were included in the
6 study. Data were formally requested through and approved by the UK Healthcare Quality
7 Improvement Partnership, who are the data controllers for English and Welsh data within
8 the NVR; and through the Audit and Quality Improvement Committee of the Vascular
9 Society of Great Britain and Ireland, who are the data controllers for Scottish and Northern
10 Irish data within the NVR. Data were retrieved in March 2018 to allow time for completion
11 of the index admission as well as data entry from sites.

12 A list of the variables applied for and their type is given below in Supplementary Table 2.

13 Outcomes

14 The primary outcome was in-hospital mortality. Secondary outcomes were return to
15 theatre during admission, re-admission to a higher level of care, post-operative length of
16 stay and post-operative complications (subdivided into several different categories: cardiac,
17 respiratory, cerebral (stroke), renal failure, haemorrhage and limb ischaemia).

1 Ethical approval and study registration

2 The study was approved by Wales Research Ethics Committee 3 (reference number
3 16/WA/0353), and the protocol was registered in the Australia and New Zealand Clinical
4 Trial Registry (ANZCTR) as ACTRN12618000356268.

5 Statistical methodology

6 All statistical analysis was performed in the R statistical programming environment version

7 3.5.1.¹³ Multiple imputation using the *mice* package version 3.3.0 was used to handle
8 missing data,¹⁴ excluding parameters with more than 50% of values missing from
9 multivariate modelling. Data were imputed using 45 replicates with 45 iterations of the
10 chained equations algorithm for each replicate. In order to explore differences there might
11 be between analysis based on the imputed data and the unimputed data, a sensitivity
12 analysis was done by performing univariate analysis using both complete case analysis
13 compared with the multiply imputed data.

14 Univariate analysis was performed using univariate logistic regression, together with
15 application of Rubin's rules to pool estimates for multiple imputation.¹⁵ Continuous
16 variables were kept as such and odds ratios are given per unit change in value rather than
17 dichotomised into 'high' and 'low' values. Multivariate analysis was performed using
18 multivariate logistic regression analysis to develop models using pre-operative predictors.

19 Parameters were selected for inclusion in prognostic models using stepwise selection and
20 following an Information Criterion based analysis, by minimizing the Schwarz-Bayes
21 Criterion.¹⁶ This was done separately for each of the 45 replicates and terms which were
22 present in at least half of the replicates were retained. ROC curve analysis was used to

1 assess model discrimination using the *pROC* package version 1.12.1.¹⁷ The Delong method
2 was then used to calculate confidence intervals for the area under the ROC curve (C-
3 statistic) and test whether performance was different to the estimated C-statistics of
4 existing models.¹⁸ Comparison with existing models is hampered by the fact that three of
5 the four models we found in a literature search include terms which are not recorded in the
6 National Vascular Registry, so any estimation of the discriminatory power of these models
7 will be hampered by the fact that we can only set these parameters to default values.^{2,5,7}
8 The revised Vascular Biochemistry and Haematology Outcome Model does not suffer from
9 this problem, so comparison with this model can be viewed as 'fair'.³ The Hosmer-
10 Lemeshow goodness of fit test was used to assess calibration of the models.¹⁹

11 ~~Multiple imputation using the *mice* package version 3.3.0 was used to handle missing data,⁴⁸~~
12 ~~excluding parameters with more than 50% of values missing from multivariate modelling.~~
13 ~~Data were imputed using 45 replicates with 45 iterations of the chained equations algorithm~~
14 ~~for each replicate. In order to explore differences there might be between analysis based~~
15 ~~on the imputed data and the unimputed data, a sensitivity analysis was done by performing~~
16 ~~univariate analysis using both complete case analysis compared with the multiply imputed~~
17 ~~data.~~

1 Results

2 Demographics and outcomes

3 There were 12,593 amputations entered into the registry during the study period, of which
4 9549 were above the ankle and so comprised the study population. Of these, 4516 (47%)
5 were trans-tibial, 4369 (46%) trans-femoral, 442 (5%) through-knee, 32 (0.3%) hip
6 disarticulation and 190 (2%) were simultaneous bilateral procedures. Table 1 summarises
7 the baseline characteristics of the study population, together with the amount of missing
8 data for each parameter.

9 Overall, 865 patients (9.1%) died before leaving hospital. The mortality rate for below knee
10 amputations (5.8%) was lower than for above knee procedures (12.0%). There was also a
11 high rate of post-operative morbidity in the cohort, with 6.6%, 9.7% and 4.3% of patients
12 suffering cardiac, respiratory and renal complications respectively. Less than 1% of patients
13 was recorded as having a post-operative stroke or bleeding complication, and 4.4% had a
14 complication relating to limb ischaemia. Ten percent (966/9546) of patients had an
15 unplanned return to theatre, while 4% (363/9545) were re-admitted to critical care. The
16 median post-operative length of stay was 16 days (IQR 9—28 days), with an overall median
17 length of stay of 24 days (IQR 14—42 days).

18 Risk factors for post-operative mortality

19 Univariate analysis revealed that increased patient age; a history of ischaemic heart disease,
20 congestive heart failure, chronic lung disease, chronic kidney disease or stroke; a raised
21 white cell count, raised serum creatinine or low serum albumin; an abnormal ECG; increased

1 American Society of Anaesthesiologists (ASA) grade; emergency admission and pre-
2 operative beta-blocker therapy all increased the odds of in-hospital mortality. Male sex,
3 previous intervention on the same side, below knee amputation, current smoking, statin or
4 ACE inhibitor/ARB therapy, and increased weight all had protective effects (Table 2).

5 Analysis was repeated using complete case analysis to assess sensitivity to the imputation
6 methodology. Results were almost identical to the multiple imputation analysis, giving
7 confidence that the imputation methodology had not introduced significant bias (Table 2).

8 Multivariate regression modelling revealed that independent factors associated with worse
9 in-hospital mortality were emergency admission (Odds Ratio (OR) 2.47, 95% Confidence
10 Interval (C.I.) 1.89-3.24), bilateral operation (OR 2.19, 95% C.I. 1.48-3.25), age (OR per 10
11 year increase 1.21, 95% C.I. 1.13-1.29), ASA grade (OR per unit increase 2.60, 95% C.I. 2.27-
12 2.98), abnormal ECG (OR 1.52, 95% C.I. 1.28-1.79), and increased white blood cell count (OR
13 per 10^9 cells/L increase 1.02, 95% C.I. 1.01-1.03) or serum creatinine (OR per 10 $\mu\text{mol/L}$
14 increase 1.02, 95% C.I. 1.02-1.03).

15 Independent protective factors reducing in-hospital mortality were trans-tibial operation
16 (OR 0.61, 95% C.I. 0.52-0.72), increased serum albumin (OR per g/L increase 0.97, 95% C.I.
17 0.95-0.98), previous procedures to the amputated limb (OR 0.79, 95% C.I. 0.68-0.92), and
18 increased patient weight (OR per 10kg increase 0.95, 95% C.I. 0.91-0.99).

19 [Development of a prognostic model of post-operative mortality](#)

20 A multivariate logistic regression model using the factors identified above to predict the
21 chances of surviving to hospital discharge was constructed. Hosmer-Lemeshow goodness of
22 fit analysis revealed good model fit ($P=0.348$ for evidence of mis-calibration). A calibration

1 table is given in Supplementary Table 3, along with details of the model formula. This is
2 displayed graphically in the Supplementary Figure.

3 ROC curve analysis showed that the model (labelled 'UKAmpRisk') has good (bordering on
4 excellent) discrimination (C-statistic 0.79, 95% C.I. 0.77-0.80). A plot of the ROC curve is
5 shown in Figure 1.

6 Comparison to existing models

7 The C-statistic was 0.59 (95% C.I. 0.56-0.61) for the Vascular Biochemistry and Haematology
8 Outcomes Model (VBHOM),² 0.65 (95% C.I. 0.63-0.67) for the revised VBHOM model
9 (VBHOM2),³ 0.68 (95% C.I. 0.66-0.70) for the Veterans Affairs Model (VAM),⁷ and 0.65 (95%
10 C.I. 0.64-0.68) for the National Surgical Quality Improvement Programme (NSQIP) model.⁵
11 All four models showed inferior discrimination to our model ($P < 0.0001$ for all comparisons).
12 Figure 1 shows all five ROC curves on the same graph for comparison. The NSQIP, VBHOM
13 and VBHOM2 models all failed the Hosmer-Lemeshov goodness of fit test ($P < 0.0001$ in each
14 case), suggesting that they are also poorly calibrated for this patient cohort. The intercept
15 coefficient was not published for the VAM model, so it was not possible to assess the
16 calibration for that model.

17 Risk factors for secondary outcomes

18 Multivariate regression modelling revealed that low serum albumin and high ASA grade
19 were consistent predictors of most morbidity outcomes. Other predictors frequently
20 associated with outcome were amputations done as an emergency and a raised serum
21 creatinine level. Full details of the parameters which were independently associated with
22 the secondary outcomes are given in Supplementary Table 4. The ability of models based

1 on these factors to discriminate between patients who did or did not suffer these morbidity
2 outcomes was again assessed using the C-statistic (Supplementary Table 4).

3 The predictive model for in-hospital mortality was again a good predictor of several of the
4 morbidity outcomes including cardiac, respiratory and renal complications (C-statistics 0.74,
5 0.69 and 0.74 respectively).

1 Discussion

2 We have identified eleven factors which are independently associated with in-hospital
3 mortality in patients undergoing major lower-limb amputation. While some of these factors
4 (principally age and ASA grade) are not modifiable, the majority are potentially amenable to
5 modification through improved clinical care.

6 Many, such as emergency admission and a raised white cell count, are linked to
7 management of patients at a late stage in their disease and may reflect late presentation or
8 recognition. This highlights the critical role of healthcare staff to recognise the deteriorating
9 foot in the community, and robust in-hospital systems and teams to treat patients quickly.

10 Earlier recognition will reduce the number of patients undergoing amputation as an
11 emergency when they are septic, with increased risk of both kidney and cardiac dysfunction,
12 often following a period of chronic low-grade foot sepsis resulting in malnutrition and low
13 albumin. Amputation is often followed by long periods in hospital. In our experience, much
14 of this time is as a result of social or organisational factors, including the need to assess a
15 patient's home for wheelchair suitability and carry out any necessary modifications. Earlier
16 recognition would allow amputation to be handled in a more elective manner, so that this
17 could be done ahead of time, facilitating shorter hospital admissions and thus reduced
18 healthcare costs. Such systems are already in place for many patients in the form of the
19 diabetic foot service and could be rolled out to all patients with chronic limb-threatening
20 ischaemia. -The present work highlights the fact that limb salvage must not be the only
21 measure of the success of 'limb-salvage' clinics, as early recognition that limb salvage is
22 unlikely to succeed will facilitate early discussion about the options and outcomes of

1 amputation, which will in turn improve the outcomes of those patients who decide to have
2 an amputation rather than continuing to pursue further fruitless efforts at limb salvage.

3 We have also developed a model which could be used to aid counselling and decision-
4 making, either in clinic or at the bedside, by quantifying the probability of the patient
5 surviving to hospital discharge. We have developed a web calculator for easy use in clinic
6 which is available from www.ambler.me.uk/Vascular, and could easily be converted into a
7 standalone smartphone app for offline use. By having a model which can more reliably
8 predict mortality, discussions about options can be more fully explored with patients,
9 enhancing shared decision-making.²⁰ Multiple previous studies have shown that surgeons
10 systematically underestimate the chances of a patient surviving an operation.^{21,22} As the
11 choice between amputation and conservative management is sometimes the choice
12 between amputation and palliation, it is critically important that these discussions are
13 conducted in the context of reliable risk estimates.

14 Ten percent of patients returned to theatre during their index admission. This is quite a
15 high proportion, and it would have been useful to examine the reasons for these returns to
16 theatre. Unfortunately, no detail is given in the dataset so some of these patients will have
17 had a minor debridement procedure while some will have had a major revision of
18 amputation level. This may be the reason why it was difficult to generate a model with
19 good discriminatory power for this outcome (Supplementary Table 4).

20 One unexpected factor was that previous procedures to the amputated limb reduced
21 mortality rates. While it is possible that having had previous procedures is simply a
22 surrogate for 'fitness' in some way, it may also be that intervention to facilitate healing at a

1 trans-tibial rather than trans-femoral level might have multiple benefits, both in terms of
2 improved short-term outcomes and also in terms of the improvement in long-term
3 functional outcomes.

4 Strengths of this work include the large, national database used, the rigorous statistical
5 methods used both to handle missing data and also the information criterion approach to
6 reduce the chances of over-fitting. The model we have presented has shown discrimination
7 which improves on the previously published models (Figure 1).

8 Limitations of the study include the fact that the case completion rate in the NVR is known
9 to be only around 60%.²³ This is a dramatic improvement over the situation 10 years ago,
10 when only half this number of cases was entered.²⁴ The UK National Vascular Registry
11 reports for the past two years have highlighted the fact that case ascertainment rates vary
12 widely between Vascular Networks.^{23,25} We can therefore be optimistic that much of the
13 missing data relates largely to institutional and administrative factors rather than patient-
14 related factors, but we must acknowledge the potential that the non-submitted cases might
15 be systematically different from submitted cases, introducing bias into our results. In
16 addition to missing cases, there was also a degree of missing data items within otherwise
17 completed cases. We used multiple imputation to account for these missing data, a
18 rigorous statistical technique which is recommended for this purpose by prominent
19 guidelines.²⁶ Sensitivity analysis using only complete cases gave very similar results (Table
20 2), so there is no evidence that these missing values have introduced significant bias.

21 Validation of data within the NVR is also lacking. This is a general criticism of registry-based
22 studies, as to our knowledge, no national registry of major lower limb amputation cases has

1 ever gone through a rigorous validation procedure. Indeed this is the case for the majority
2 of vascular surgical registries. Two notable exceptions are the SwedVasc registry and the
3 Hungarian registry, although the former included only aortic aneurysm repair and carotid
4 surgery while the latter also included infrainguinal arterial reconstruction. Plans are being
5 put in place for a similar validation exercise of the UK NVR in Spring 2020, but this again is
6 unlikely to include the major lower limb amputation subset.

7 A further weakness of this study is due to the limitations of the data recorded in the NVR.

8 For example it is increasingly recognised that frailty is an important risk factor for peri-

9 operative complications, including mortality.²⁷ Indeed, dependent functional status has

10 been shown in other work to be important for predicting mortality in patients undergoing

11 amputation.^{5,7} Unfortunately, until recently no measure of frailty or functional status was

12 recorded in the NVR. A measure of frailty has recently been added to the NVR dataset,

13 which will allow further investigation of this factor in the future.

14 We have modelled in-hospital mortality, as that is the audit standard within the UK Vascular

15 Registry. Unfortunately, this is different from many other national audit databases such as

16 SwedVasc, which reports 30-day mortality. Inconsistency in outcome reporting is an issue

17 which plagues clinical audit and research, as it makes pooling of information between

18 studies (meta-analysis) challenging or impossible. Efforts are underway to reduce this

19 problem in future, and Core Outcome Sets for patients undergoing major lower limb

20 amputation for complications of peripheral vascular disease are currently in development.²⁸

21 Several of the predictive factors we found are similar to those found in previous work.

22 Increasing age was found to be an independent predictor of mortality in almost all previous

1 studies, including this one. Emergency admission and level of amputation were also found
2 to be predictive of mortality in several other studies, including work from large
3 administrative databases in Japan and the USA.^{6,7} Evidence of systemic sepsis in the form of
4 a raised white cell count has also been identified as a significant factor in previous studies.^{2,5}
5 In contrast, bilateral procedures have not been previously shown in multivariate analysis to
6 have a worse outcome than unilateral procedures, and increased patient weight has never
7 been identified as an independent protective factor previously.

8 Further studies are needed to identify whether attempts to modify any of the factors have a
9 clinically relevant impact on outcomes. Firstly, improvements might be made through
10 quality improvement programmes designed to facilitate earlier identification and treatment
11 of patients for whom further attempts at limb salvage are at high risk of failure. Improved
12 shared decision-making using risk quantified by these data should be encouraged, perhaps
13 supported by a decision aid.²⁹ Secondly, there are more speculative options which would
14 require testing in prospective interventional studies. One of these is a proposed
15 intervention to facilitate healing at a more distal level, as both prior procedures to the
16 amputated limb and below knee operations appear to have a protective role. Increased
17 patient weight and serum albumin have similar protective effects, so it is possible that pre-
18 operative dietary intervention or other 'pre-habilitation' might also be helpful for patients
19 with stable but un-reconstructable arterial disease. There is increasing interest into the
20 putative benefits of 'pre-habilitation', with multiple on-going studies,³⁰ though little
21 concrete evidence of benefit at this time.³¹

22 Further work is also needed to externally validate the predictive model. The importance of
23 this was highlighted within Vascular Surgery recently with the publication of the draft

1 National Institute for Health and Care Excellence (NICE) guidelines for the treatment of
2 Abdominal Aortic Aneurysm,³² which found that none of the models for that patient group
3 which had been subjected to external validation were found to have good discriminatory
4 power. The NICE panel also suggested that the literature on risk scoring in abdominal aortic
5 aneurysm repair reports several un-validated risk scores, and concluded that there is no
6 justification to develop further models in this context, until the external validity of existing
7 ones is assessed. The situation for major limb amputation is somewhat different, with very
8 few available models. Those which do exist are difficult to validate in the UK as they use
9 parameters which are not routinely recorded in the NVR. We are therefore optimistic that
10 the model we have developed has the potential to contribute to improvement of outcomes
11 for patients with chronic limb-threatening ischaemia.

12 In conclusion, we have identified independent risk factors for mortality and morbidity
13 following major lower limb amputation and developed a prognostic model for in-hospital
14 mortality with good predictive power. Important next steps include further external
15 validation, and if supported, the development of quality improvement programmes which
16 focus on modification of the factors we have identified, and adjustment of published
17 surgical outcomes using this model.

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8

9 Disclosures

10 None

11

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17

1 Tables

2

Parameter	Value	Number missing (%)
Age (median (IQR))	70 (60—78)	5 (0)
Sex (Male : Female)	6729 : 2820	0 (0)
Hospital type (teaching : non-teaching)	4544 : 5005	0 (0)
Emergency admission (N (%))	7489 (78.4)	0 (0)
Comorbidities (N (%))		
Diabetes	5065 (53.1)	
Ischaemic heart disease	3788 (39.7)	
Congestive heart failure	1004 (10.5)	
Chronic lung disease	1939 (20.3)	17 (0)
Chronic kidney disease	1968 (20.6)	
Hypertension	5812 (61.0)	
Stroke	1085 (11.4)	
Smoking (Never : Ex : Current)	1948 : 4721 : 2850	30 (0)
Pre-operative blood tests (median (IQR))		
White cell count (10^9 cells/L)	11.7 (9.0—15.4)	14 (0)
Haemoglobin (g/L)	112 (97—148)	3416 (36)
Sodium (mmol/L)	136 (133—139)	38 (0)
Potassium (mmol/L)	4.5 (4.1—4.9)	18 (0)

Creatinine ($\mu\text{mol/L}$)	81 (61—118)	11 (0)
Albumin (g/L)	30 (24—35)	2824 (30)
Abnormal ECG (N# (%))	3672 (42.9)	988 (10)
ASA grade (1 : 2 : 3 : 4 : 5)	90 : 756 : 6164 : 2462 : 75	2 (0)
Indication (N (%))		16 (0)
Acute Limb Ischaemia	1563 (16.4)	
Chronic Limb Ischaemia	1981 (20.8)	
Neuropathy	140 (1.5)	
Tissue Loss	3567 (37.4)	
Uncontrolled Infection	2129 (22.3)	
Trauma	94 (1.0)	
Aneurysm	59 (0.6)	
Pre-operative medications (N# (%))		
Antiplatelet agent	6783 (71.1)	
Statin	6701 (70.2)	3 (0)
Beta-blocker	2560 (26.8)	
ACE-inhibitor / ARB	3035 (32.0)	
Weight (median (IQR))	75 (63—87)	2607 (27)

1

2 *Table 1: Baseline characteristics of patients. ACE – Angiotensin converting enzyme. ARB –*

3 *Angiotensin II receptor blocker.*

Parameter	Multiple Imputation			Complete Case Analysis	
	O.R.	95% C.I.	P-value	O.R.	95% C.I.
Age (per 10 year increase)	0.763	0.720—0.809	<0.0001	0.764	0.721—0.810
Sex (Male vs. Female)	1.241	1.070—1.439	0.004	1.241	1.070—1.439
Hospital type (teaching : non-teaching)	1.034	0.899—1.190	0.637	1.034	0.899—1.190
Emergency admission	0.263	0.203—0.342	<0.0001	0.263	0.203—0.342
Previous intervention on same side	1.617	1.406—1.861	<0.0001	1.618	1.406—1.861
Below knee amputation vs. higher level	2.216	1.907—2.575	<0.0001	2.216	1.907—2.575
Comorbidities (Y : N)					
Diabetes	1.069	0.930—1.230	0.349	1.069	0.930—1.230
Ischaemic heart disease	0.634	0.551—0.730	<0.0001	0.635	0.552—0.731
Congestive heart failure	0.478	0.397—0.576	<0.0001	0.479	0.398—0.577
Chronic lung disease	0.690	0.588—0.810	<0.0001	0.690	0.588—0.811
Chronic kidney disease	0.477	0.411—0.555	<0.0001	0.477	0.411—0.556
Hypertension	0.867	0.750—1.003	0.054	0.868	0.750—1.003
Stroke	0.785	0.640—0.963	0.021	0.785	0.640—0.963
Smoking – Current	1.208	1.031—1.415	0.019	1.206	1.030—1.413
Pre-operative blood tests					
White cell count (10^9 cells/L ↑)	0.968	0.961—0.975	<0.0001	0.968	0.961—0.975
Haemoglobin (per g/L ↑)	1.005	0.996—1.014	0.307	1.005	0.996—1.014
Sodium (per mmol/L ↑)	0.995	0.980—1.010	0.507	0.995	0.980—1.010
Potassium (per mmol/L ↑)	0.993	0.924—1.069	0.860	0.994	0.924—1.069
Creatinine (per 10 μ mol/L ↑)	0.973	0.968—0.977	<0.0001	0.973	0.968—0.977

Albumin (per g/L ↑)	1.061	1.051—1.072	<0.0001	1.062	1.051—1.072
Abnormal ECG	0.411	0.353—0.478	<0.0001	0.400	0.343—0.467
ASA grade (per grade ↑)	0.248	0.219—0.282	<0.0001	0.248	0.219—0.282
Pre-operative medications					
Antiplatelet agent	1.113	0.957—1.295	0.166	1.113	0.957—1.295
Statin	1.258	1.086—1.459	0.002	1.259	1.086—1.459
Beta-blocker	0.718	0.619—0.834	<0.0001	0.719	0.619—0.834
ACE-inhibitor / ARB	1.169	1.002—1.363	0.047	1.169	1.002—1.364
Weight (per 10kg ↑)	1.085	1.042—1.129	<0.0001	1.088	1.043—1.134

1

2 *Table 2: Univariate analysis. Numbers greater than one indicate greater odds of being*

3 *discharged alive. O.R. – Odds Ratio. C.I. – Confidence Interval. ACE – Angiotensin converting*

4 *enzyme. ARB – Angiotensin II receptor blocker.*

1 Caption for Figure

- 2 *Figure 1: ROC curve for UKAmprisk, the prognostic model developed here, with best*
- 3 *estimates of the VAM,⁷ VBHOM^{2,3} and NSQIP models.⁵ Some predictive variables for VAM,*
- 4 *VBHOM and NSQIP models are not available in the NVR.*