



This is a repository copy of *Evaluating current acute aortic syndrome pathways: Collaborative Acute Aortic Syndrome Project (CAASP)*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/223991/>

Version: Published Version

Article:

Zhong, J. orcid.org/0000-0001-5325-3739, Singh, A.A. orcid.org/0000-0002-9099-4162, Safdar, N.Z. et al. (106 more authors) (2024) Evaluating current acute aortic syndrome pathways: Collaborative Acute Aortic Syndrome Project (CAASP). *BJs Open*, 8 (5). zrae096. ISSN 2474-9842

<https://doi.org/10.1093/bjsopen/zrae096>

Reuse

This article is distributed under the terms of the Creative Commons Attribution (CC BY) licence. This licence allows you to distribute, remix, tweak, and build upon the work, even commercially, as long as you credit the authors for the original work. More information and the full terms of the licence here:

<https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

Evaluating current acute aortic syndrome pathways: Collaborative Acute Aortic Syndrome Project (CAASP)

Jim Zhong^{1,2} , Aminder A. Singh^{3,4,*} , Nawaz Z. Safdar^{2,5}, Sandip Nandhra⁶, and Ganesh Vigneswaran⁷, on behalf of CAASP Collaborators

¹Department of Diagnostic and Interventional Radiology, Leeds Teaching Hospitals NHS Trust, Leeds, UK

²School of Medicine, University of Leeds, Leeds, UK

³Cambridge Vascular Unit, Cambridge University Hospitals NHS Trust, Cambridge, UK

⁴Cambridge Stem Cell Institute, University of Cambridge, Cambridge, UK

⁵Department of Internal Medicine, St. James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK

⁶Northern Vascular Centre, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Trust, Newcastle, UK

⁷Faculty of Medicine, University of Southampton, Southampton, UK

*Correspondence to: Aminder A. Singh, Cambridge Stem Cell Institute, University of Cambridge, Cambridge, UK, and Cambridge Vascular Unit, Cambridge University Hospitals NHS Trust, Box 212, Addenbrookes Hospital, Hills Road, Cambridge CB2 0QQ, UK (e-mail: aminder.singh@nhs.net)

Members of CAASP are co-authors of this study and are listed under the heading Collaborators.

Presented at the Cardiovascular and Interventional Society of Europe (CIRSE) annual conference, September 2023, Copenhagen, Denmark; European Society of Vascular Surgery, September 2023, Belfast, UK; British Society of Interventional Radiology (BSIR) annual scientific meeting, November 2023, Newport, UK, and Vascular Society of Great Britain and Ireland Annual Scientific Meeting, November 2023, Dublin, Ireland.

Abstract

Background: Diagnosis of acute aortic syndrome is challenging and associated with high perihospital mortality rates. The study aim was to evaluate current pathways and understand the chronology of acute aortic syndrome patient care.

Method: Consecutive patients with acute aortic syndrome imaging diagnosis between 1 January 2018 and 1 June 2021 were identified using a predetermined search strategy and followed up for 6 months through retrospective case note review. The UK National Interventional Radiology Trainee Research and Vascular and Endovascular Research Network co-ordinated the study.

Results: From 15 UK sites, 620 patients were enrolled. The median age was 67 (range 25–98) years, 62.0% were male and 92.9% Caucasian. Type-A dissection (41.8%) was most common, followed by type-B (34.5%); 41.2% had complicated acute aortic syndrome. Mode of presentation included emergency ambulance (80.2%), self-presentation (16.2%), and primary care referral (3.6%). Time (median (i.q.r.)) to hospital presentation was 3.1 (1.8–8.6) h and decreased by sudden onset chest pain but increased with migratory pain or hypertension. Time from hospital presentation to imaging diagnosis was 3.2 (1.3–6.5) h and increased by family history of aortic disease and decreased by concurrent ischaemic limb. Time from diagnosis to treatment was 2 (1.0–4.3) h with interhospital transfer causing delay. Management included conservative (60.2%), open surgery (32.2%), endovascular (4.8%), hybrid (1.4%) and palliative (1.4%). Factors associated with a higher mortality rate at 30 days and 6 months were acute aortic syndrome type, complicated disease, no critical care admission and age more than 70 years ($P < 0.05$).

Conclusions: This study presents a longitudinal data set linking time-based delays to diagnosis and treatment with clinical outcomes. It can be used to prioritize research strategies to streamline patient care.

Introduction

Acute aortic syndrome (AAS) encompasses a spectrum of life-threatening emergency aortic conditions including aortic dissection (AD), intramural haematoma (IMH) and penetrating atherosclerotic ulcer (PAU), with dissection accounting for over 90% of cases¹. AAS has an estimated population incidence of 2–16 per 100 000 persons and outcomes remain poor with high perihospital mortality rates^{2–4}. Multiple risk factors exist for AAS including those that increase intimal shear stress, for example hypertension, and those that weaken the vessel wall, for example atherosclerosis or connective tissue disorders⁵. Some patients also have a family history of AAS, with 13–22% having an affected first-degree relative⁵.

There are approximately 2500 cases per year in England, although some have suggested that the condition is under-reported in part due to its varied clinical presentations^{6,7}. Symptoms include chest and back pain that can mimic a range of other more common conditions with successful diagnosis reliant on a high degree of clinical suspicion alongside a low threshold for cross-sectional imaging. Early recognition is key to the successful management of patients with acute AD, however, in 16–40% of cases there is a delay in diagnosis that can lead to an adverse outcome⁷.

At present there is limited understanding of the current pathways used to diagnose AAS. Clinical 'red-flag' symptoms, such as truncal pain and syncope, have historically demonstrated limited accuracy⁸. Although the literature suggests that one of the more sensitive

Received: May 16, 2024. Accepted: July 16, 2024

© The Author(s) 2024. Published by Oxford University Press on behalf of BJS Foundation Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

(62–78%) symptoms for AAS is truncal pain, it is a very common presenting complaint and may represent several other differential diagnoses⁹. A previous study identified several clinical factors that were associated with delays in diagnosis such as female sex, age more than 70 years, diabetes mellitus and painless presentation, however, these studies have not been validated¹⁰. Identifying the interval(s) within a patient's pathway where delay occurs, such as between symptom onset and admission, or time to imaging or treatment, remains challenging to elucidate. Retrospective studies are limited by data availability and prospective studies struggle to recruit suitable numbers of positive AAS patients given the relatively low incidence in comparison to similar presenting pathologies such as myocardial infarction¹¹.

Significant variation exists in AAS diagnostic pathways across regions, with many emergency departments not having a formal work-up pathway for AAS². This likely affects the time to diagnosing AAS, which is time-sensitive given the need for urgent management and potential intervention. These diagnostic delays could impact patient outcomes.

The Collaborative Acute Aortic Syndrome Project (CAASP) was developed with patients to evaluate current pathways and understand chronology of AAS patient care. Further aims were to highlight clinical, diagnostic and management factors that might impact on clinical outcomes through time-based delays.

Methods

Project design

This was a multicentre, retrospective service evaluation pertaining to adult patients diagnosed on imaging with AAS. All hospitals with an accident and emergency unit were eligible to participate. The study was co-ordinated and delivered through collaboration between the UK National Interventional Radiology Trainee Research (UNITE) network and the Vascular and Endovascular Research Network (VERN). Open invitations to participate were circulated via social media, national radiology and vascular surgery society mailing lists, and personal communications. The study protocol has been published¹².

Project approvals

CAASP was approved as a national service evaluation project by the lead organization Leeds Teaching Hospitals NHS Trust (approval date 18 May 2022, ref: CAASP). All participating UK sites were required to locally register the study as a national service evaluation project before data collection. Ethical approval was not required in the UK as no patient identifiable information was collected and there was no impact on routine care.

Participants

All adult patients (age more than 18 years) with a diagnosis of AAS (type A dissection, type B dissection, non-A non-B dissection, PAU, IMH) on imaging between 1 January 2018 and 1 June 2021 were included. Exclusion criteria were non-AAS pathology (for example traumatic or iatrogenic aortic injury) or chronic presentation of aortic disease.

AAS was defined using the European Society of Cardiology guideline¹³. Complicated AAS was defined as the presence of end organ malperfusion or aortic rupture. AAS patients were identified at each enrolled centre (by the local study team) using a focused search strategy on electronic radiology information systems ([Appendix S2](#)). Data were retrospectively collected for AAS patients diagnosed between 1 January 2018 and 1 June 2021 using a template data form. Follow-up data was collected for a duration of

6 months from the first imaging diagnosis of AAS. The start date for centres was variable to allow for local registration and approval, however, the end date for centres submitting data was 31 March 2023. AAS patients were cross-checked against prospectively maintained local databases of AAS patients to ensure identification of all possible patients.

Project outcomes

The primary aim was to capture information on the time taken for patients with AAS to attend hospital from the onset of symptoms, the time from hospital presentation to imaging diagnosis and time from imaging diagnosis to management/treatment instigation.

The primary endpoint was to determine the impact of the total and individual time components on the patient mortality rate within 30 days and 6 months. Secondary endpoints included additional clinical (for example presentation symptoms, signs, observations, vital signs, co-morbidities and blood test results) and demographic (for example age, sex, ethnicity, distance to hospital, deprivation score) variables correlated with time to hospital presentation, diagnosis and treatment and subsequent mortality rate outcomes. The coronavirus disease (COVID)-19 group included all patients who presented on or after 23 March 2020, when the UK national lockdown started. Before this date, the patients were labelled as a 'Non-COVID' group to investigate if this was a significant variable affecting the study outcomes.

Sample size

This project was designed to evaluate current AAS pathways, therefore, no minimum sample size was required to show effect. Centres with fewer than five patients were excluded.

Data management

Deidentified data were transferred to a UK NHS server (based at Leeds Teaching Hospitals NHS Trust, Leeds) as per NHS and Caldicott Guardian principles. Data sharing agreements were adhered to. Each centre was required to record local identifiers on a secure, local, and general data protection regulation compliant database to allow data capture and linkage.

Data analysis

Summary statistics regarding time to presentation, time to imaging diagnosis, time to treatment, mortality rate and complications for AAS patients within the first 6 months of imaging diagnosis are presented. Time outcomes are presented as median time (i.q.r.).

Factors associated with both mortality rate and delay were calculated using multivariable analysis. The choice of variables to include in this model was based on consensus opinion from the steering group. A multiway analysis of variance (ANOVA) was used to calculate individual factors that contributed to timepoint measures, with handling of continuous variables (for example age and distance) with analysis of covariance (ANCOVA). Extreme outliers were examined by plotting raw data and removed if data was greater than the 99th centile. Statistical significance was measured at $P < 0.050$, with post hoc comparisons by Tukey–Kramer. Geometric means, approximate standard deviations and 95% confidence intervals (95% c.i.) are reported for the significant variables by back-transformation to allow for an understanding of reported significant variables rather than reporting normalized log transformed means. Differences in diagnostic pathways between

Table 1 Demographics of study cohort

Demographics	Total	Predictors of time from symptom onset to hospital presentation P	Predictors of time from hospital presentation to imaging diagnosis P	Predictors of time from imaging diagnosis to treatment P
Age (years), median (range), (n = 620)	67 (25–98)	0.459	0.988	0.918
Centre type (n = 620)		0.802	0.665	0.102
DGH	45 (7)			
Tertiary	575 (93)			
Sex (n = 620)		0.385	0.756	0.589
Male	382 (62)			
Female	238 (38)			
Ethnicity (n = 537)		0.887	0.410	0.249
Caucasian	499 (92.9)			
Black	17 (3.2)			
Asian	17 (3.2)			
Other	4 (0.7)			
Index of multiple deprivation decile		0.348	0.707	0.594
1 (most deprived)	68 (11.5)			
2	42 (7.1)			
3	52 (8.8)			
4	54 (9.2)			
5	54 (9.2)			
6	72 (12.2)			
7	66 (11.2)			
8	57 (9.7)			
9	55 (9.3)			
10 (least deprived)	69 (11.7)			
Distance from presenting hospital (miles), median (range)	6.4 (1–199)	0.807	N/A	0.271
Aortic pathology (n = 620)		0.664	0.282	0.059
Type A	226 (41.8)			
Type B	190 (34.5)			
Non-A non-B	13 (2.3)			
Penetrating aortic ulcer	48 (9.4)			
Intramural haemorrhage	60 (12.1)			
Complicated disease (n = 565)	233 (41.2)	N/A	N/A	0.495
Mode of presentation (n = 561)		0.163	0.386	N/A
Direct self-presentation	91 (16.2)			
Ambulance	450 (80.2)			
GP referral	20 (3.6)			

Values are n (%) unless otherwise stated. For each time outcome (symptom onset to hospital presentation, hospital presentation to imaging diagnosis and imaging diagnosis to treatment), the P values for the included variables are presented. DGH, district general hospital; N/A, not applicable.

specialist cardiovascular centres and non-cardiovascular centres, geographical and socioeconomic (using the index of multiple deprivation scores) variation were assessed to provide an insight into the variability of management.

Binomial logistic regression was used to identify factors that were significantly associated with survival metrics (alive at 30 days and 6 months). Significant factors were then used in a multivariable Cox proportional hazards model. Age was dichotomized around 70 years, all timepoints (for example time from symptom onset to presentation) were binarized about the median. The study 'end date' was 31 March 2023 with all sites having to submit data by this date to be included in analyses. Those alive at this date were censored.

Handling missing data

Missing data was highlighted and the number and percentage of individuals in the missing category are presented.

Results

During the study interval, 620 patients from 15 UK sites were enrolled. Baseline demographics are presented in Table 1, clinical presentation symptoms in Table 2 and past medical history factors

in Table 3. Median age (range) was 67 (25–98) years, 62.0% (382 of 620) were male and 92.9% (499 of 537) were Caucasian. The most frequent AAS was type-A dissection (41.8%), followed by type-B (34.5%), IMH (12.1%), PAU (9.4%) and non-A non-B dissection (2.3%), while 41.2% had complicated AAS. The most common presenting symptom was sudden onset pain (79.9%). Mode of presentation included by emergency ambulance transfer (80.2%), self-presentation (16.2%) and primary care referral (3.6%); 60.2% were managed conservatively, 32.2% had open surgery, 4.8% had endovascular aortic repair, 1.4% had a hybrid procedure and 1.4% had palliative management.

AAS factors associated with time

The median time (i.q.r.) from symptom onset to hospital presentation was 3.1 (1.8–8.6) h, time from hospital presentation to imaging diagnosis was 3.2 (1.3–6.5) h and from imaging to initial treatment was 2.0 (1.0–4.3) h. The distribution of the three outcome timepoints is shown in Fig. 1. Deidentified individual centre data are shown in Fig. 2, highlighting the distribution of time points over the 15 UK centres.

A history of hypertension, sudden onset chest pain or migratory pain was significantly associated with the time from symptom onset to hospital presentation. Patients with hypertension had

Table 2 Clinical presentation symptoms and signs of study cohort

Presenting symptoms and signs	Total	Predictors of time from symptom onset to hospital presentation	Predictors of time from hospital presentation to imaging diagnosis	Predictors of time from imaging diagnosis to treatment
		P	P	P
Chest pain (n = 588)	430 (73.1)	0.145	0.519	0.425
*Sudden onset pain (n = 567)	453 (79.9)	0.0001 (↓)	0.597	0.811
Severe intensity pain (n = 532)	405 (76.1)	0.945	0.964	0.201
Back pain (n = 547)	361 (66.0)	0.619	0.125	0.376
Abdominal pain (n = 526)	194 (36.9)	0.869	0.523	0.429
*Migratory pain (n = 499)	219 (43.9)	0.020 (↑)	0.165	0.916
Focal neurology (n = 486)	74 (15.2)	0.115	0.550	0.645
Collapse (n = 539)	107 (19.9)	0.050	0.219	0.573
New murmur (n = 479)	42 (8.8)	0.963	0.173	N/A
Ischaemic limb (n = 511)	50 (9.8)	N/A	0.028	N/A
Hypotension (n = 586)	121 (20.7)	N/A	0.914	N/A
Shock (n = 579)	72 (12.4)	N/A	N/A	N/A
Cardiac tamponade (n = 564)	43 (7.6)	N/A	N/A	N/A
Fever (n = 574)	16 (2.8)	N/A	N/A	N/A
Coma (n = 594)	74 (12.5)	N/A	0.090	N/A

Values are n (%). For each time outcome (symptom onset to hospital presentation, hospital presentation to imaging diagnosis and imaging diagnosis to treatment), the P values for the included variables are presented and significant variables highlighted with *. ↓ indicates significant decrease in time from symptom onset to hospital presentation and ↑ indicates significant increase in time from symptom onset to hospital presentation. N/A, not available.

Table 3 Co-morbidities and past medical history details of study cohort

Co-morbidities/past medical history	Total	Predictors of time from symptom onset to hospital presentation	Predictors of time from hospital presentation to imaging diagnosis	Predictors of time from imaging diagnosis to treatment
		P	P	P
*Hypertension (n = 577)	338 (58.6)	0.025 (↑)	0.847	N/A
Known aortic aneurysm (n = 568)	88 (15.49)	0.481	0.509	N/A
Previous aortic dissection (n = 562)	25 (4.5)	0.919	0.930	N/A
Bicuspid aortic valve (n = 480)	7 (1.5)	0.618	0.453	N/A
History of myocardial infarction (n = 561)	71 (12.7)	0.617	0.218	N/A
Cardiac failure (n = 565)	38 (6.7)	0.566	N/A	N/A
Previous cardiac surgery (n = 562)	50 (8.9)	0.458	N/A	N/A
Prior cardiac catheterization/angioplasty (n = 548)	44 (8.0)	0.808	N/A	N/A
*Familial aortic disease (n = 350)	19 (5.4)	0.320	0.019 (↑)	N/A
Known Marfan or connective tissue disease (n = 487)	23 (4.7)	0.286	0.775	N/A
Diabetes (n = 568)	66 (11.6)	0.489	N/A	N/A
Treatment (n = 580)		N/A	N/A	0.057
Medical	349 (60.2)			
Surgery	187 (32.2)			
Endovascular	28 (4.8)			
Hybrid	8 (1.4)			
Palliative	8 (1.4)			
*Transfer to another centre (n = 606)	181 (29.9)	N/A	N/A	0.012 (↑)
Admission to critical care (n = 558)	436 (78.1)	N/A	N/A	N/A
Presented during COVID (23 March 2020–1 June 2021)	240 (38.7)	0.589	0.397	0.803
Hb (n = 605), median (range)	133 (49–199)	N/A	0.606	N/A
Creatinine (n = 609), median (range)	87 (28–627)	N/A	0.593	N/A
First recorded systolic BP (n = 569), median (range)	141 (49–287)	N/A	0.751	N/A
First recorded diastolic BP (n = 561), median (range)	79 (23–190)	N/A	0.812	N/A
First recorded HR (n = 569), median (range)	75 (30–162)	N/A	0.661	N/A
First recorded RR (n = 539), median (range)	18 (10–96)	N/A	0.299	N/A

Values are n (%) unless otherwise stated. For each time outcome (symptom onset to hospital presentation, hospital presentation to imaging diagnosis and imaging diagnosis to treatment), the P values for the included variables are presented and significant variables highlighted with *. ↑ indicates significant increase in time. N/A, not available; Hb, haemoglobin; BP, blood pressure; HR, heart rate; RR, respiratory rate.

significantly longer times to hospital presentation (geometric mean 4.8 h (95% c.i. 4.1 to 5.6)) than those without a history of hypertension (geometric mean 4.5 h (95% c.i. 3.7 to 5.5)). Patients with sudden onset pain had significantly shorter times to hospital presentation (geometric mean = 3.8 h (95% c.i. 3.4 to 4.3)) than those without (11.6 h (95% c.i. 7.5 to 17.6)). Patients with migratory pain (219 of 499) had slightly longer times to hospital presentation (geometric

mean = 4.8 h (95% c.i. 3.9 to 5.7)) than those without migratory pain (4.4 h (95% c.i. 3.7 to 5.3)).

A family history of aortic disease ($P < 0.01$) or concurrent ischaemic limb ($P = 0.028$) significantly impacted upon the time from hospital presentation to imaging diagnosis. A family history of aortic disease was associated with a longer time to diagnosis (5.7 h (95% c.i. 3.0 to 10.3) versus 3.7 h (95%

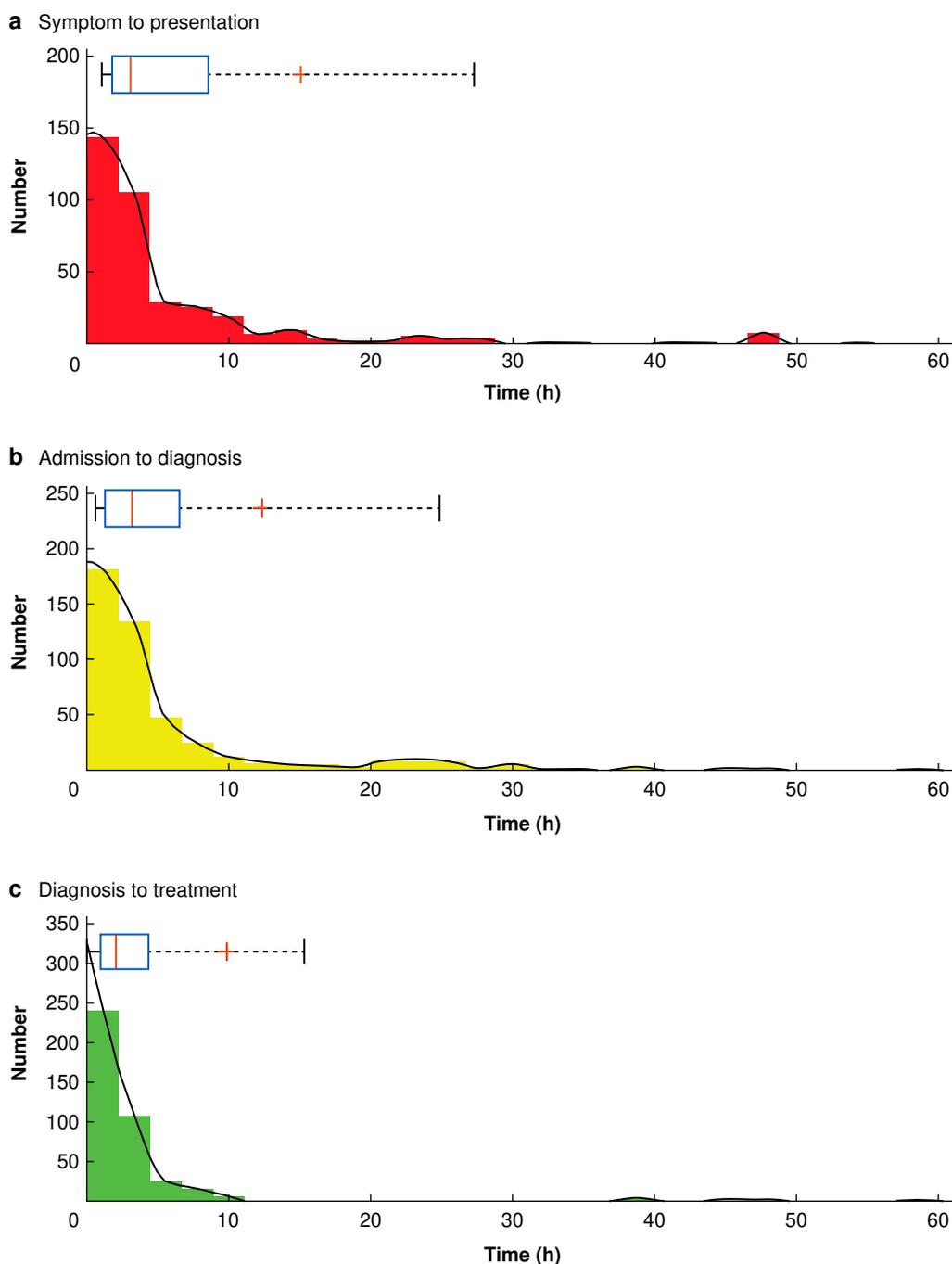


Fig. 1 Histograms demonstrating the distribution for times from symptom onset to hospital presentation a, admission to imaging diagnosis b and diagnosis to treatment c

Smoothed data is plotted in black. Above individual histograms are box and whisker plots with a red line for median, '+' for the mean, a blue box around the 25 and 75% quartiles and whiskers bounding 9 and 91%.

c.i. 3.2 to 4.3)). Patients with concurrent ischaemic limb had much shorter times to diagnosis compared with those without (1.5 h (95% c.i. 1.1 to 2.0) versus 4.4 h (95% c.i. 3.8 to 5.0)).

Patients who were transferred to another centre had significantly longer times from imaging diagnosis to initial treatment (3.3 h (95% c.i. 2.7 to 4.1)), compared with patients who received their care within the same hospital (2.6 h (95% c.i. 2.3 to 3.0), $P=0.01$). Notably, the treatment administered demonstrated a trend ($P=0.056$) for endovascular approach (9.3 h (95% c.i. 4.5 to 18.0)) leading to a

longer time to initial treatment than medical/conservative management (2.7 h (95% c.i. 2.3 to 3.1)), open surgery (2.5 h, (95% c.i. 2.0 to 3.1)), hybrid (2.8 h (95% c.i. 1.2 to 5.5)) or palliative (0.5 h (95% c.i. 0.4 to 0.7)).

Distance from hospital and time from onset to hospital presentation was stratified by index of deprivation (Fig. 3) between low (1–5) and high (5–10) deprivation and demonstrates that those with a high index of deprivation lived a closer distance to the hospital but did not demonstrate a reciprocal decrease in time from symptom onset to hospital presentation ($P=0.001$).

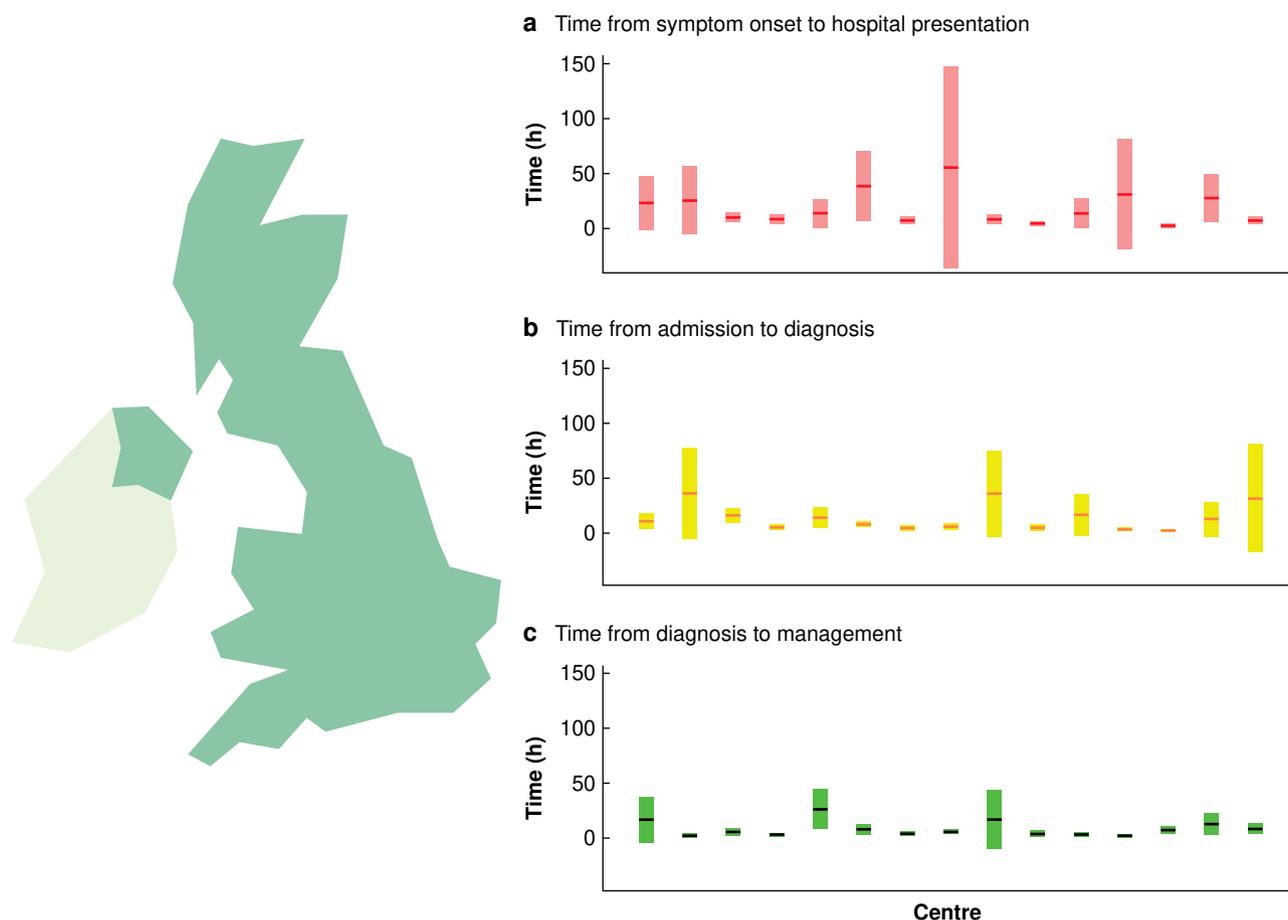


Fig. 2 Distribution of timepoints over the 15 UK centres

Mean time points for each centre are shown as horizontal lines and are placed over a 1.96 \times standard error of the mean (95% confidence interval) in **a** time from symptom onset to hospital presentation, **b** time from admission to imaging diagnosis and **c** time from diagnosis to treatment, expressed in hours.

Factors associated with mortality rate

Predictors of 30-day and 6-month mortality rates are demonstrated in [Table 4](#) with [Fig. 4](#) showing statistical analysis of these variables. A multivariable Cox proportional hazards model was used to investigate whether age, type of AAS, presence of complicated disease, admission to critical care, time from symptom onset to hospital presentation, time from hospital presentation to diagnosis, time from diagnosis to treatment and whether the AAS occurred during COVID-19, were significantly associated with survival. Age more than 70 years (HR 0.51 (95% c.i. 0.37 to 0.70), $P < 0.001$), aortic pathology (HR 0.80 (95% c.i. 0.70 to 0.90), $P < 0.001$) (see [Fig. 4](#) for breakdown of categories), complicated disease (HR 2.2 (95% c.i. 1.6 to 3.0), $P < 0.001$) and admission to critical care (HR 0.41 (95% c.i. 0.29 to 0.56), $P < 0.001$) were all significantly associated with survival. No time variables were significantly associated with survival, and there was no effect found for whether the patient was managed during the COVID-19 pandemic.

Discussion

This contemporary, multicentre data set provides a real-world evaluation of UK AAS care pathways and a longitudinal data set linking time-based delays to diagnosis and treatment with clinical outcomes. Most notable findings include time-associated predictors of symptom onset to hospital presentation, presentation

to imaging diagnosis and imaging diagnosis to treatment, and significant independent predictors of mortality rate (AAS type, complicated disease, no admission to critical care and age more than 70 years).

There are several important messages from the present study. Firstly, CAASP reinforces the importance of early recognition of AAS and prompt referral to secondary care. Before the COVID-19 pandemic, an investigation by the Healthcare Safety Investigation Branch⁷ reported that approximately 20% of patients with thoracic aortic aneurysm and dissection (TAAD) die before reaching any hospital and, alarmingly, half die before admission to a specialist centre, with an estimated number of 2500 cases per year in England. The study found that diagnostic delays occurred in up to 40% of patients, particularly in those who presented to hospital themselves or if the doctors initially suspected a cardiac cause of chest pain. CAASP suggests that mode of presentation and increasing time to hospital presentation may be additional factors as patients not presenting by emergency ambulance faced greater delay.

Interestingly, patients with lower socioeconomic status lived closer to hospitals but did not demonstrate a reciprocal decrease in time to hospital presentation. This is an important finding suggesting disparity in presentation to hospital is disproportionately impacting those of lower socioeconomic status, demonstrating inequality in healthcare, and is in keeping with the published literature¹⁴. Educational initiatives targeting this group of patients

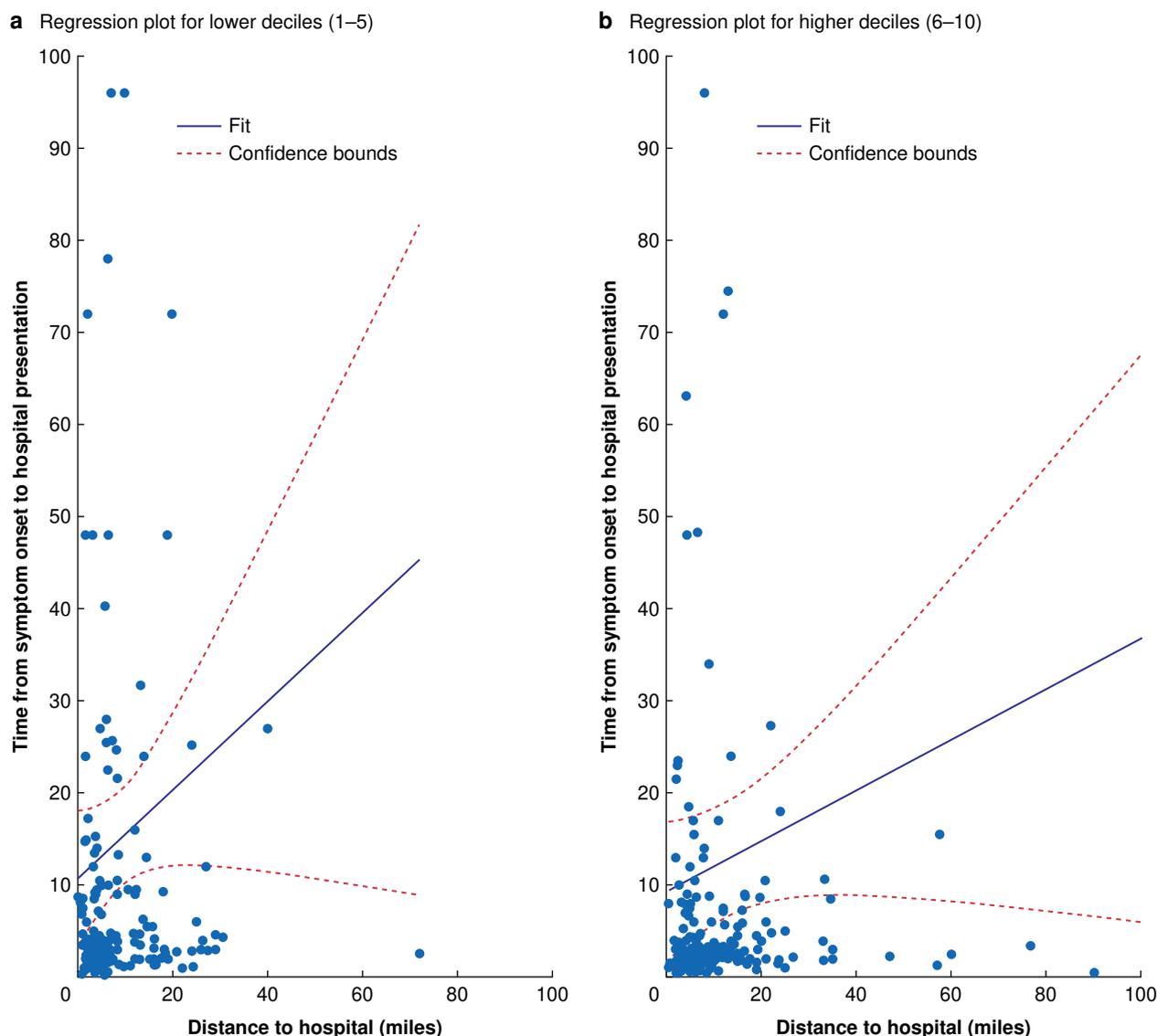


Fig. 3 Distance from hospital and time from onset to hospital presentation stratified by index of deprivation a (low 1–5) and b high (6–10)

Table 4 Binomial logistic regression predictors of 30-day and 6-month mortality rate

Term	Odds ratio of being alive at 30 days (95% c.i.)	Alive at 30 days (P)	Odds ratio of being alive at 6 months (95% c.i.)	Alive at 6 months (P)
Time from symptom onset to hospital presentation (h)	1.01 (0.99,1.02)	0.551	0.99 (0.98,1.01)	0.450
Time from hospital presentation to imaging diagnosis (h)	1.03 (0.98,1.08)	0.214	1.0054 (0.99,1.02)	0.555
Time from imaging diagnosis to treatment (h)	0.98 (0.95,1.02)	0.408	0.99 (0.96,1.02)	0.518
Centre type	3.49 (0.17,72.08)	0.419	N/A	1.000
*Age at presentation	0.93 (0.89,0.97)	<0.001	0.93 (0.89,0.97)	<0.001
Sex	0.51 (0.19,1.36)	0.176	0.45 (0.17,1.23)	0.119
Ethnicity	1.19 (0.33,4.29)	0.787	0.87 (0.20,3.88)	0.858
Index of multiple deprivation decile	0.90 (0.77,1.05)	0.171	0.91 (0.79,1.06)	0.228
*Aortic pathology	1.65 (1.13,2.40)	0.009	1.75 (1.19,2.56)	0.004
Mode of presentation	0.68 (0.32,1.47)	0.329	0.75 (0.36,1.55)	0.436
*Complicated disease	0.19 (0.07,0.49)	<0.001	0.24 (0.09,0.62)	0.003
Treatment	1.15 (0.59,2.25)	0.685	1.10 (0.58,2.10)	0.775
History of previous aortic dissection	0.75 (0.04,13.83)	0.846	0.42 (0.02,7.22)	0.552
*Admission to critical care	3.06 (1.18,7.96)	0.022	3.21 (1.24,8.35)	0.017
COVID-19	1.50 (0.60,3.73)	0.381	1.18 (0.49,2.84)	0.705

Significant variables highlighted with *. N/A, not applicable.

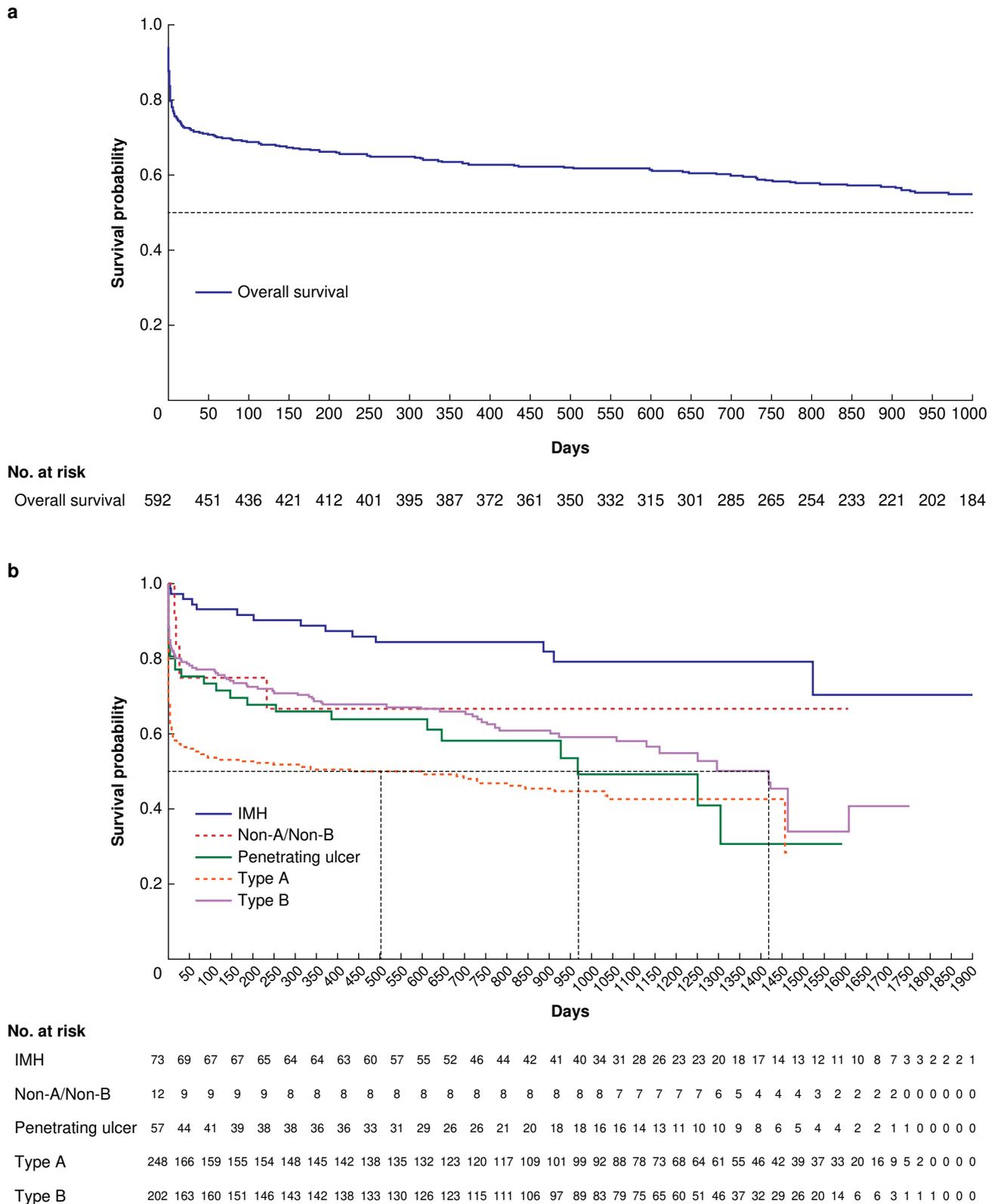
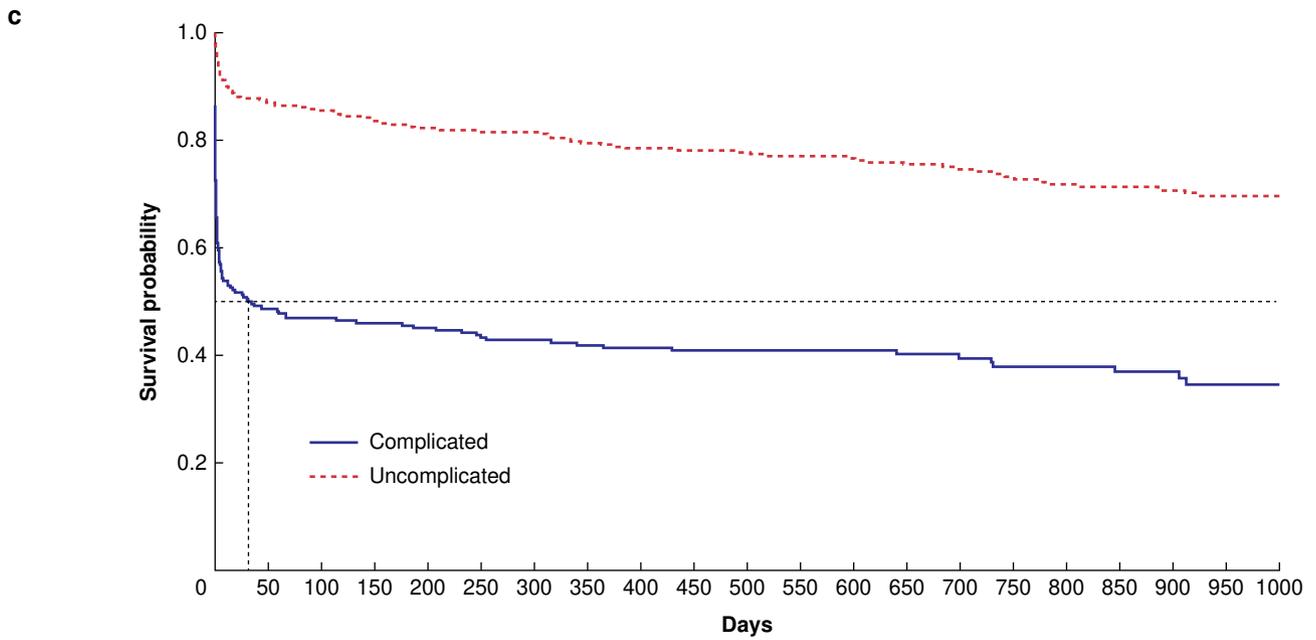


Fig. 4 Kaplan–Meier survival curves: (a) overall; and for each of the independent predictors of mortality rate including: (b) aortic pathology, (c) presence of complicated disease, (d) admission to critical care and (e) age less than 70 years
IMH, intramural haematoma.

may represent one method for improving the time taken for patients to present to hospital.

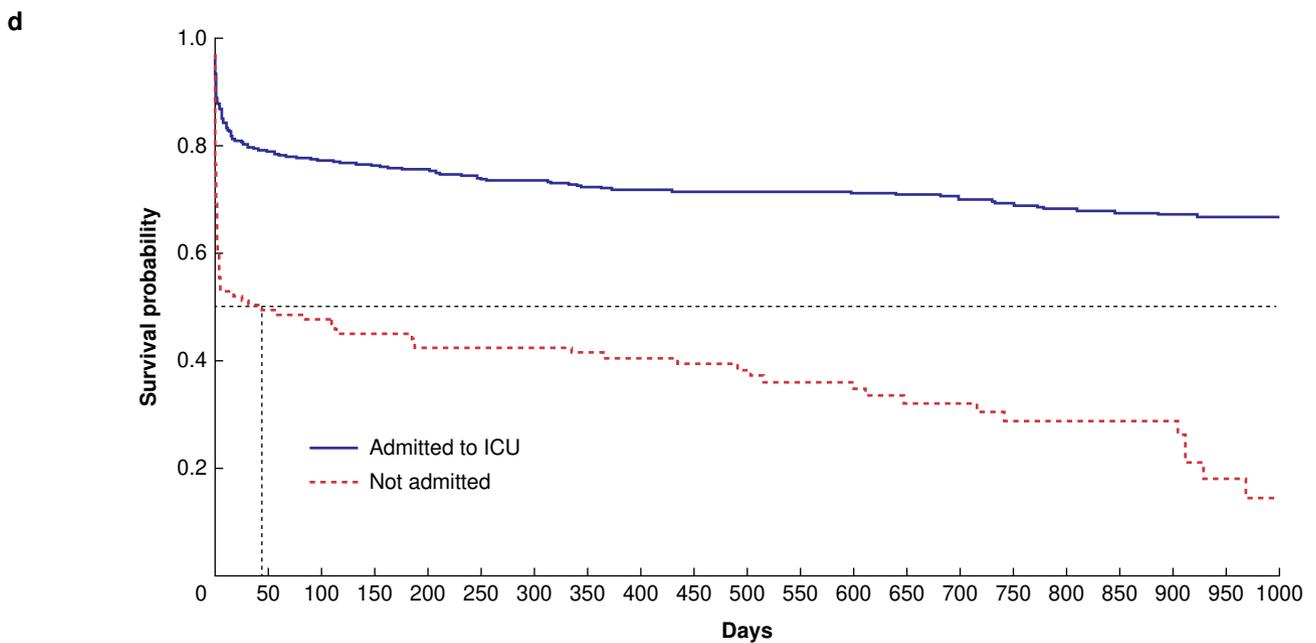
As part of the International Registry of Acute Aortic Dissection (IRAD), an analysis was undertaken to identify variables associated

with delays in diagnosis and treatment in TAAD patients¹⁰. They found delays in diagnosis to occur more frequently in those with atypical symptoms (such as non-abrupt symptoms and when patients did not present with chest, back or any pain) and those



No. at risk

Complicated	230	142	136	133	130	124	121	119	114	110	104	98	94	90	86	78	76	68	63	57	50
Uncomplicated	313	272	266	257	251	247	244	238	228	221	217	207	194	185	173	161	153	140	133	121	112



No. at risk

Admitted to ICU	418	340	331	322	318	309	306	301	291	284	276	263	251	241	230	217	208	193	182	170	155
Not admitted	119	72	68	65	61	60	58	57	53	50	49	45	41	37	35	32	31	27	26	20	18

Fig. 4 Continued

presenting to a non-tertiary centre. Delay in time from diagnosis to surgery in IRAD was associated with a history of previous cardiac surgery, presenting without sudden onset pain and initial presentation to a non-tertiary centre. CAASP identified the presence of migratory pain or hypertension as significant predictors of delay in the time from symptom onset to hospital presentation. A meta-analysis of the Japan-Specific Health

Checkups and UK Biobank¹⁵ suggested that acute aortic dissection events and mortality rate are significantly higher in those with hypertension, which challenges its exclusion from validated risk prediction tools such as the Aortic Dissection Detection Risk Score. Furthermore, chronic hypertension leads to molecular changes within the aortic wall such as elastic fibre loss¹⁶. Atypical factors should be considered when developing new educational and

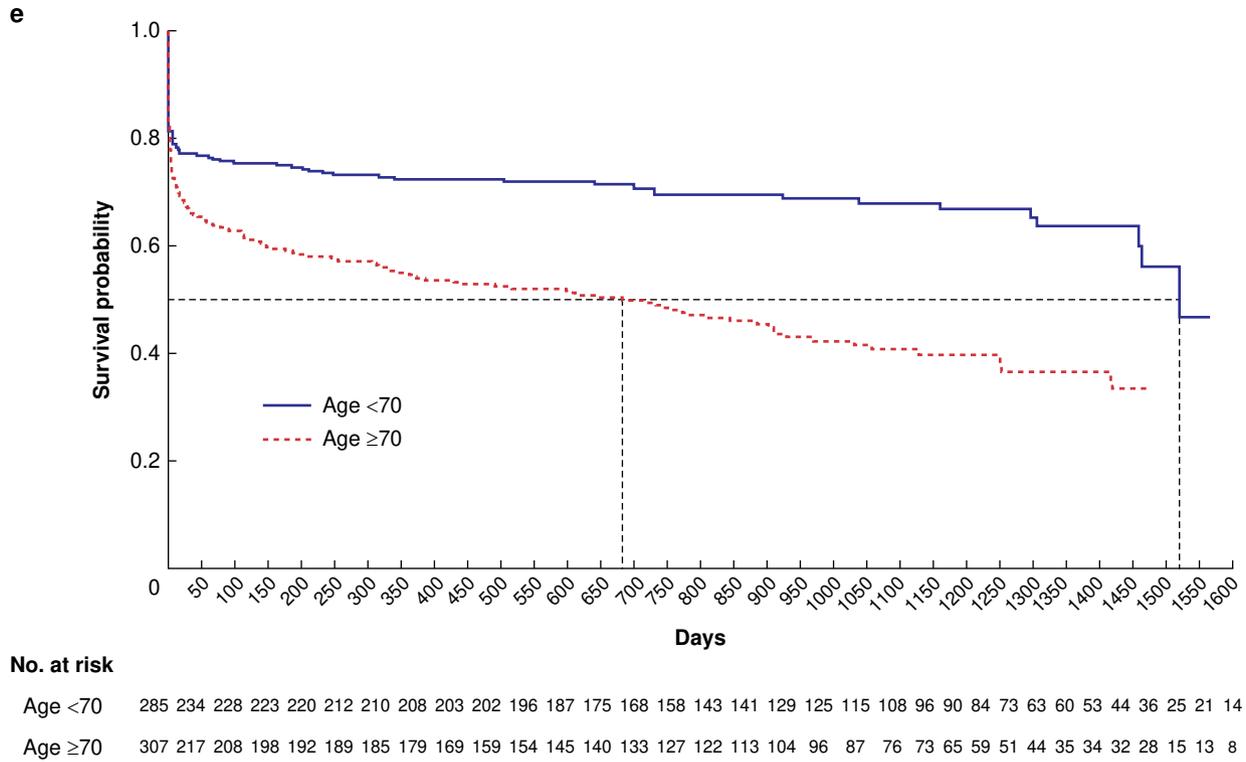


Fig. 4 Continued

training materials as well as diagnostic pathways. Furthermore, abdominal pain was noted in 34% of patients, suggesting that atypical symptoms need to be routinely reviewed as part of a systems enquiry. This is particularly the case in the setting of aortic dissection where concurrent abdominal pain may indicate abdominal aortic and mesenteric vessel involvement¹⁷.

IRAD also demonstrated increased time from presentation to diagnosis in those of non-white ethnicity and those with a history of coronary artery bypass, ultimately resulting in an operative delay¹⁰. In addition, CAASP demonstrated that a requirement for transfer to a specialist unit for initial treatment after imaging diagnosis was significantly associated with delay. This suggests differential access to treatments for patients is dependent on their access to specialist services, which can impact time to treatment. Such access issues need to be addressed by policymakers through robust referral and transfer pathways to ensure AAS patients do not face a ‘postcode lottery’ when it comes to access to definitive treatment. Although not statistically significant there was a trend for delay in management of patients with type B dissection requiring either hybrid or endovascular therapy. This is not surprising as these patients often require an interval of re-evaluation after best medical therapy. This contrasts with type A dissection where the accepted treatment is to proceed with urgent open surgery.

Limb ischaemia can increase the index of suspicion of AAS and urgency of imaging, which can in part explain its significance in reducing the time delay to imaging diagnosis. Conversely, a family history of aortic disease increased time to imaging. Family history suggests a genetic component, increasing the likelihood of familial aortic disease as a differential¹⁸. This finding is surprising given it is standard enquiry during clinical consultation and part of the assessment in patients presenting with sudden onset chest or back pain and may be due to the small cohort of patients with

family history. This challenges the assumption that the presence of a positive family history of aortic disease would lead to a higher index of suspicion of AAS and suggests more work is required in raising awareness of AAS amongst clinicians.

CAASP demonstrated significantly better survival in the patient cohort admitted to a critical care setting. Guidelines recommend aggressive management of blood pressure, heart rate and pain¹⁸, and the optimal setting for this is an intensive care unit (ICU). The factors leading to a worse mortality rate in the non-ICU cohort were not captured by this study and could have been due to patient characteristics such as multimorbidity, but this merits further investigation. Significantly worse survival outcomes for those presenting with complicated AAS are expected, as are the survival outcomes dependent on type of AAS. Both findings place CAASP in line with the published literature¹⁹ and as such timely referral to critical care for AAS patients is essential and should ideally occur soon after diagnosis.

The Oxford Vascular Study²⁰ predicted a significant increase in annual dissection events from 3892 in 2010 to 6893 in 2050, partly due to the growing UK population where the number of those aged above 75 years is projected to double over the same interval, which is particularly concerning given that CAASP has identified age more than 70 years to be associated with a worse mortality rate. This demonstrates the urgent need to improve care and diagnostic pathways and determine the best treatments for this patient cohort.

The present study provides valuable information regarding the characteristics of patients presenting with AAS, which may reflect differences in diagnostic and treatment pathways across the UK. In 2021, a working party comprised of patients and clinicians, formed through a collaboration between the Vascular Society of Great Britain and Ireland and the James Lind Alliance, identified top research priorities in aortic disease, which included ‘What methods can be used to ensure that people with acute aortic

conditions such as dissection are diagnosed quickly and treated without delay²¹, which formed the premise for CAASP. Further, the Acute Aortic Dissection Toolkit was launched in March 2021²². This sets out principles for the management of aortic dissection and aimed to provide practical advice and guidance for commissioners, service providers and clinicians to support system-wide improvement in AAS management. A key part of this work was audit and governance to allow measurement of the incidence and outcomes on a UK-wide basis. CAASP has contributed important information about variations in AAS care pathways, and patient characteristics associated with time and worse outcomes, that should be readily identified to optimize AAS pathways and can aid policy planning on where intervention to improve care quality is required.

The limitations of this work include its retrospective design and, due to several hospitals without electronic patient record systems, information being obtained from physical notes with risk of incomplete data. This contributed to missing variables in the data set, which was mitigated by excluding those patients from linked analyses. There may be geographical bias in the data depending on which centres contributed to the project, which were likely those with more staff and resources to enable them to participate, which could limit the generalizability of findings. However, the high number of centres and patients included reduces this bias. It was only possible to identify patients with AAS who had survived long enough for an imaging study to confirm their diagnosis. Patients who died of AAS before hospital presentation or before scan were not identified, which could bias the patient cohort.

CAASP presents a longitudinal data set linking time-based delays to diagnosis and treatment with clinical outcomes through a multicentre, UK collaborative research methodology. It can be used to prioritize research strategies to streamline patient care by highlighting where in the patient journey delays can occur.

Collaborators

Ishtiaq Aziz (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK), Aseel Abuduruk (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK), Adel Abdallah (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK), Philip Stather (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK), Enrico Mancuso (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK), Ayman Elsayed (Norfolk & Norwich University Hospital NHS Foundation Trust, Norwich, UK) Tom Wallace (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Ryan Laloo (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Steve Tang (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Kelsey Aimar (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Ahmed Al Aafi (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Jim Zhong (Leeds Teaching Hospitals NHS Trust, Leeds, UK) Choong Poon (Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK), Jun-Li Tham (Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK), Weii Jsim Leong (Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK), Ahmed Khalil (Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK), Mohamed Taha (Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK) Bharadhwaj Ravindhran (Hull Royal Infirmary, Hull, UK), Chukwuemeka Igwe (Hull Royal Infirmary, Hull, UK), Elio Plevneshi (Hull Royal Infirmary, Hull, UK), Mustafa Altarqane (Hull Royal Infirmary,

Hull, UK) David C. Bosanquet (Aneurin Bevan University Health Board, Wales), Khaing Khant Oo (Aneurin Bevan University Health Board, Wales), Brenig Gwilym (Aneurin Bevan University Health Board, Wales), Syfe Azooz (Aneurin Bevan University Health Board, Wales), Ayako Niina (Aneurin Bevan University Health Board, Wales) Indrajeet Mandal (John Radcliffe Hospital, Oxford, UK), Abin Varghese (John Radcliffe Hospital, Oxford, UK), Michael Stephanou (John Radcliffe Hospital, Oxford, UK), Ehsan Ghaffari (John Radcliffe Hospital, Oxford, UK), Raman Uberoi (John Radcliffe Hospital, Oxford, UK) Katrina Harborne (University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK), Samuel Walker (University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK), Faizan Nasir (University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK), Niamh Horne (University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK), Benjamin Alam (University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK) Andrew Christie (Queen Elizabeth University Hospital, Glasgow, UK), Linda Watkins (Queen Elizabeth University Hospital, Glasgow, UK), Rebecca Cuthbertson (Queen Elizabeth University Hospital, Glasgow, UK), Lucia Lenart (Queen Elizabeth University Hospital, Glasgow, UK), Neera Chaudhary (Queen Elizabeth University Hospital, Glasgow, UK), Alisa Khalid (Queen Elizabeth University Hospital, Glasgow, UK) Ragai R. Makar (Countess of Chester Hospital NHS Foundation Trust, Chester, UK), Andrew I. Khallaf (Countess of Chester Hospital NHS Foundation Trust, Chester, UK), Chris T. Francis (Countess of Chester Hospital NHS Foundation Trust, Chester, UK), Shady Zaki (Countess of Chester Hospital NHS Foundation Trust, Chester, UK), Ramez Shehata (Countess of Chester Hospital NHS Foundation Trust, Chester, UK), Anwar Al-Kassar (Countess of Chester Hospital NHS Foundation Trust, Chester, UK) Liam Musto (University Hospitals of Leicester NHS Trust, Leicester, UK), Nikesh Dattani (University Hospitals of Leicester NHS Trust, Leicester, UK), Gabriel Lopez-Penna (University Hospitals of Leicester NHS Trust, Leicester, UK), John S.M. Houghton (University Hospitals of Leicester NHS Trust, Leicester, UK) Mathew Pettit (St George's University Hospitals NHS Foundation Trust, London, UK), James Budge (St George's University Hospitals NHS Foundation Trust, London, UK), William Selway (St George's University Hospitals NHS Foundation Trust, London, UK), Barnaby Farquharson (St George's University Hospitals NHS Foundation Trust, London, UK), Mital Desai (St George's University Hospitals NHS Foundation Trust, London, UK), Jack Mcalinden (St George's University Hospitals NHS Foundation Trust, London, UK) Kriti Tripathi (Northampton General Hospital NHS Trust, Northampton, UK), Isaac Kobe (Northampton General Hospital NHS Trust, Northampton, UK), Ramesh Kannan (Northampton General Hospital NHS Trust, Northampton, UK), Charlotte Slee (Northampton General Hospital NHS Trust, Northampton, UK), Reema Munshi (Northampton General Hospital NHS Trust, Northampton, UK), Sriram Kumar Boppana (Northampton General Hospital NHS Trust, Northampton, UK) Sai Wunnava (Newcastle upon Tyne Hospitals, Newcastle, UK), Michael Woodmass (Newcastle upon Tyne Hospitals, Newcastle, UK), Caitlin Nessa Griffith (Newcastle upon Tyne Hospitals, Newcastle, UK), Alexandra Rachel Beth Dalton (Newcastle upon Tyne Hospitals, Newcastle, UK) Yousef Shahin (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK), Victoria Burrows (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK), Saima Ehsan (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK), Joe Kang (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield,

UK), Joni Tan (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK), Thomas Geh (Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK) Drew Maclean (University Hospital Southampton, Southampton, UK), Sohini Chatterjee (University Hospital Southampton, Southampton, UK), Bukola Ogunjinmi (University Hospital Southampton, Southampton, UK), Marina Pearson (University Hospital Southampton, Southampton, UK), Deevia Kotecha (Manchester University NHS Foundation Trust, Manchester, UK), Nikesh Dattani (Leicester Vascular Institute, Glenfield Hospital, Leicester, UK), Ruth Benson (University of Birmingham Clinical Trials Unit, Birmingham, UK), Robert Blair (Belfast Health and Social Care Trust, Belfast, UK), Shian Patel (University Hospital Southampton NHS Foundation Trust, Southampton, UK), Joseph Shalhoub (Imperial College Healthcare NHS Trust, London, UK), Hunain Shiwani (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Avik Som (Massachusetts General Hospital, Boston, USA), Ginny Sun (Harvard University, Cambridge, USA), Manar Khashram (Waikato District Health Board, Hamilton, New Zealand), Graham Cooper (Sheffield Teaching Hospitals, Sheffield, UK), Julie Sanders (St Bartholomew's Hospital, London, UK), Philip Scott (University of Wales Trinity St David, Wales, Lampeter), Sarah Wilson (Wexham Park Hospital Emergency Department, Frimley Health NHS Foundation Trust, Slough, UK), Robin Williams (Newcastle upon Tyne Hospitals, Newcastle, UK), Paul Walker (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Phil Jackson (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Mathew Bromley (Leeds Teaching Hospitals NHS Trust, Leeds, UK), Graeme Ambler (Cambridge University Hospitals, Cambridge, UK), Panagiota Bimpili (Oxford University Hospitals NHS Foundation Trust, Oxford, UK), Louise Hitchman (Hull Royal Infirmary, Hull, UK), Katherine Hurndall (Imperial College London, London, UK), Sarah Onida (Imperial College Healthcare NHS Trust, London, UK), Athanasios Saratzis (Glenfield Hospital BHF Cardiovascular Research Facility, Leicester, UK), Nina Al-Saadi (Black Country Vascular Network, Dudley, UK), Lauren Shelmerdine (Newcastle upon Tyne Hospitals, Newcastle, UK)

Funding

The authors have no funding to declare. For the purpose of open access, the corresponding author has applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission.

Acknowledgements

J.Z. and A.A.S. share joint authorship. S.N. and G.V. share joint senior authorship. We would like to thank The Aortic Disease Charitable Trust for their support of this work.

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

Data availability will be considered on written request.

Author contributions

Jim Zhong (Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing), Aminder Singh (Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing—original draft, Writing—review & editing), Nawaz Safdar (Data curation, Methodology, Writing—original draft), Sandip Nandhra (Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing—review & editing) and Ganesh Vigneswaran (Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Visualization, Writing—original draft, Writing—review & editing).

References

- Baliyan V, Parakh A, Prabhakar AM, Hedgire S. Acute aortic syndromes and aortic emergencies. *Cardiovasc Diagn Ther* 2018; **8**:S82–S96
- Bell R. How do you solve the problem of aortic dissection? *J Vasc Soc GB Irel* 2022; **1**:106–107
- Vardhanabhuti V, Nicol E, Morgan-Hughes G, Roobottom CA, Roditi G, Hamilton MC et al. Recommendations for accurate CT diagnosis of suspected acute aortic syndrome (AAS)—on behalf of the British Society of Cardiovascular Imaging (BSCI)/ British Society of Cardiovascular CT (BSCCT). *Br J Radiol* 2016; **89**:20150705
- Wundram M, Falk V, Eulert-Grehn JJ, Herbst H, Thurau J, Leidel BA et al. Incidence of acute type A aortic dissection in emergency departments. *Sci Rep* 2020; **10**:7434
- Corvera JS. Acute aortic syndrome. *Ann Cardiothorac Surg* 2016; **5**: 188–193
- Albornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA et al. Familial thoracic aortic aneurysms and dissections—incidence, modes of inheritance, and phenotypic patterns. *Ann Thorac Surg* 2006; **82**:1400–1405
- Mahase E. Half of patients with acute aortic dissection in England die before reaching a specialist centre. *BMJ* 2020; **368**:m304
- Morello F, Santoro M, Fargion AT, Grifoni S, Nazerian P. Diagnosis and management of acute aortic syndromes in the emergency department. *Intern Emerg Med* 2021; **16**:171–181
- Ohle R, Kareemi HK, Wells G, Perry JJ. Clinical examination for acute aortic dissection: a systematic review and meta-analysis. *Acad Emerg Med* 2018; **25**:397–412
- Harris KM, Strauss CE, Eagle KA, Hirsch AT, Isselbacher EM, Tsai TT et al. Correlates of delayed recognition and treatment of acute type A aortic dissection: the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2011; **124**:1911–1918
- Camacho X, Nedkoff L, Wright FL, Nghiem N, Buajitti E, Goldacre R et al. Relative contribution of trends in myocardial infarction event rates and case fatality to declines in mortality: an international comparative study of 1.95 million events in 80.4 million people in four countries. *Lancet Public Health* 2022; **7**:e229–e239
- Zhong J, Vigneswaran G, Safdar NZ, Mandal I, Singh AA, Nandhra S. Understanding the current acute aortic syndrome (AAS) pathways—the Collaborative Acute Aortic Syndrome Project (CAASP) protocol. *PLoS One* 2024; **19**:e0297782
- Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H et al. 2014 ESC guidelines on the diagnosis and

- treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The task force for the diagnosis and treatment of aortic diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2014;**35**:2873–2926
14. Lim B, Chauhan D, Schultz ML, Levine D, Loumiotis I, Friedmann P et al. Relation of community-level socioeconomic status to delayed diagnosis of acute type A aortic dissection. *Am J Cardiol* 2022;**170**:147–154
 15. Hibino M, Otaki Y, Kobeissi E, Pan H, Hibino H, Taddese H et al. Blood pressure, hypertension, and the risk of aortic dissection incidence and mortality: results from the J-SCH study, the UK Biobank study, and a meta-analysis of cohort studies. *Circulation* 2022;**145**:633–644
 16. Nienaber CA, Yuan X. Taming hypertension to prevent aortic dissection: universal recognition of a “new normal” blood pressure? *Circulation* 2022;**145**:645–647
 17. Levy D, Goyal A, Grigorova Y, Farci F, Le JK. *Aortic Dissection*. Treasure Island (FL): StatPearls Publishing LLC, 2024
 18. Isselbacher EM, Preventza O, Hamilton Black JIII, Augoustides JG, Beck AW, Bolen MA et al. 2022 ACC/AHA guideline for the diagnosis and management of aortic disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation* 2022;**146**:e334–e482
 19. Tsai TT, Nienaber CA, Eagle KA. Acute aortic syndromes. *Circulation* 2005;**112**:3802–3813
 20. Howard DP, Banerjee A, Fairhead JF, Perkins J, Silver LE, Rothwell PM. Population-based study of incidence and outcome of acute aortic dissection and premorbid risk factor control: 10-year results from the Oxford Vascular Study. *Circulation* 2013;**127**:2031–2037
 21. Lawson JA, Bown MJ, Bicknell CD, Long J, Gronlund TA. Research priorities for aortic diseases: results of the James Lind Alliance/Vascular Society GBI priority setting exercise. *J Vasc Soc GB Irel* 2022;**1**:34–412
 22. The Aortic Dissection Charitable Trust. Acute aortic dissection (AAD) NHS toolkit. 2022. <https://aorticdissectioncharitabletrust.org/acute-aortic-dissection-toolkit/>.