Tables and figures

Table 1: Demographics at presentation

	Ischaemic stroke (n=103)	**TIA (n =80)**	**Controls (n=109)**	**TOTAL 292**
Number of patients, **n =292** (% of total cohort)	**103** (35.3%)	**80** (27.4%)	**108** (37.0%)	
Age in years, median (range)	77 (42-97)	75.5 (25-99)	55 (23-100)	**71 (23-100)**
Gender: Male	56	40	45	**147 (48%)**
Female	47	40	64	**159 (52%)**
Pre-admission **Rankin (median)**	**1** (0-15)	**0** (0-4)	**0** (0-5)	
Baseline **Rankin (median)**	**3** (0-5)	**0** (0-4)	**0** (0-5)	
Baseline **NIHSS (median)**	**4.5** (0-28)	**0** (0-16)	**0** (0-15)	
Baseline **GCS (median)**	**15** (10-15)	**15** (14-15)	**15** (9-15)	
Baseline **Factor VIII** (IU/dL) **Median** (range)	**178.6** (43.1- 612.7)	**149.7** (46.6-557.1)	**142.6** (46.3-705.5)	**KW 12.47 (p=0.002)**
Baseline **VWFAg** (IU/dL) **Median** (range)	**196.9** (75.4-538.1)	**167.8** (46.5-403.4)	**160.1** (22.6- 600)	**KW 12.87 (p=0.0016)**
Baseline **VWFAc** (IU/dL) **Median** (range)	**188.8** (65.5-338.4)	**159.8** (43.9-310.8)	**140.4** (26.7-304.2)	**KW 83.3 (p<0.0001)**
Baseline **ADAMTS13Ac Ac** (IU/dL) **Median** (range)	**85.9** (38.8-114.2)	**94.0** (34.5-129)	**95.6** (38.4-137)	**KW 25.2 (p<0.0001)**
Ratio VWFAg/ ADAMTS13Ac Median (range)	**2.42** (0.79-9.53)	**1.89** (0.41-8.14)	**1.69** (0.25-15.63)	**KW 24.65 (p<0.0001)**
Blood group: O (total 149: 48% of total cohort)	52 (50%)	42 (53%)	45 (42%)	Chi squared =3.292 (p= 0.1928)
Non-O (total 151: total 52% of total cohort)	51 (50%)	36 (45%)	64 (48%)	

Unknown, n=2)	0	2 (3%)	0	

Key: KW= Kruskal Wallis testing (non-parametric testing to compare medians of more than 2 groups)

Baseline characteristics of the cohort are outlined above. Patients presenting with similar symptoms to IS and TIA but subsequently found to be negative for ischaemic brain injury were included as controls. This group was subsequently not age and gender matched for the ischaemic brain injury groups, which should be taken into account.

Table 2: Longitudinal changes in ischaemic stroke: comparison

Median in IU/dL	**Baseline (t0)**	**Final follow up (t4, minimum 6 weeks from presentation)**	**Difference in medians (matched pairs n=34) Wilcoxon paired t-test**	**Difference in medians (all data) Unpaired t-test**	**KW testing (is there is a significant difference in medians across all time points?)**
FVIII	178.6	137.7	**-21.2 (p=0.0149)**	**-40.9 (p=0.0038)**	**12.58 (p=0.0135)**
VWFAg	196.9	157.7	**-18.24 (0.0093)**	**-47.5 (p=0.0046)**	**9.568 (p=0.0484)**
VWFAc	188.7	143.7	-11.6 (p=0.0289)	-45.05 (p=0.0783)	5.21 (p=0.2665)
ADAMTS13Ac	85.9	96.8	**4.9 (p=0.0092)**	**10.85 (p=0.0043)**	**11.87 (p=0.0184)**
Ratio VWFAg: ADAMTS13Ac	2.42	1.66	**-0.2775 (p=0.0007)**	**-0.869 (p=0.0008)**	**12.42 (0.0145)**

Figure 1: Comparison of haemostatic markers between groups at presentation

Figure 1a

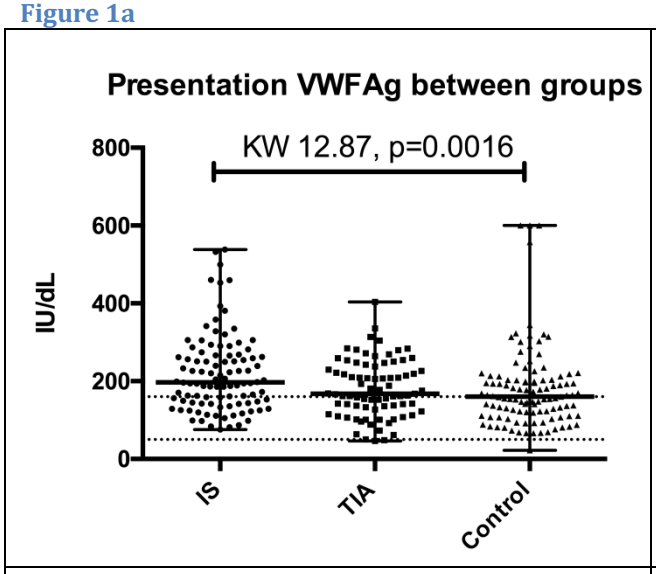


Figure 1b

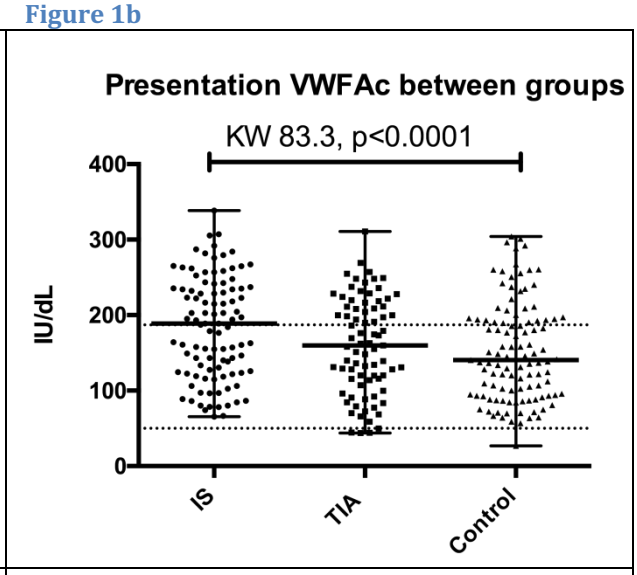


Figure 1c

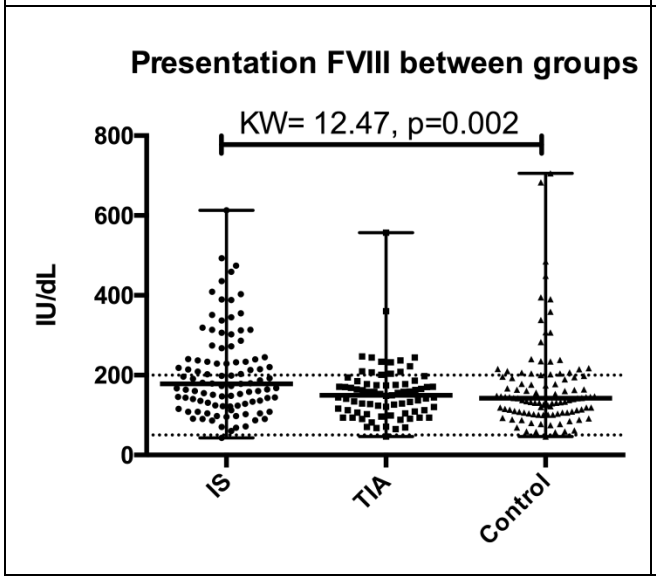


Figure 1d

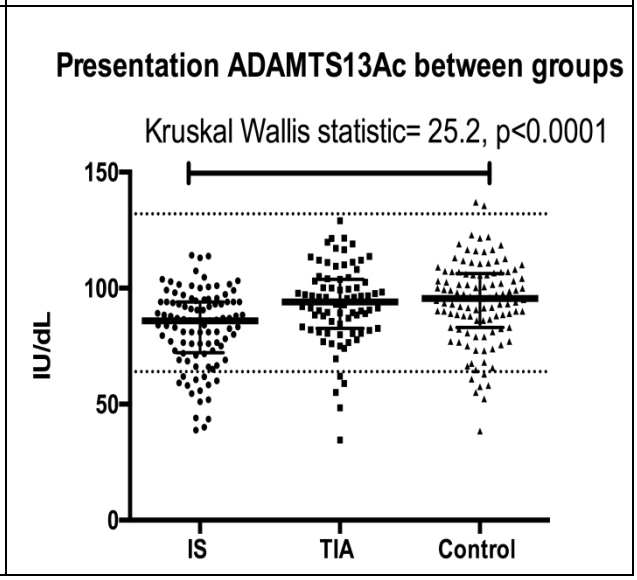


Figure 1 demonstrates Kruskal Wallis testing comparing ischaemic stroke (IS), TIA and control groups at baseline for each haemostatic marker: VWFAg (Fig 1a), VWFAc (Fig 1b), FVIII (Fig 1c) and ADAMTS13Ac (Fig 1d). Figures 1a, 1b and 1c demonstrate significant differences between all groups, with IS demonstrating the highest median VWFAg (196.9IU/dl), Ac (188.8IU/dL) and FVIII (178.6IU/dL), followed by TIA (VWFAg 167.8, VWFAc 159.8, FVIII 149.7 IU/dL) and controls (VWFAg 160.1, VWFAc 140.4, FVIII 142.6IU/dL), in keeping with the known role for VWF and FVIII in arterial occlusion and hence cerebral ischaemia. The reverse trend was seen for ADAMTS13Ac, as illustrated in Figure 1d (ischaemic stroke median 86.0, TIA 94.0, controls 95.6IU/dL). Outliers in the control group with significantly raised VWFAg and FVIII (both circa 600IU/dL) had significant other medical issues; including severe infection.

Figure 2: Longitudinal patterns in ischaemic stroke

Figure 2a

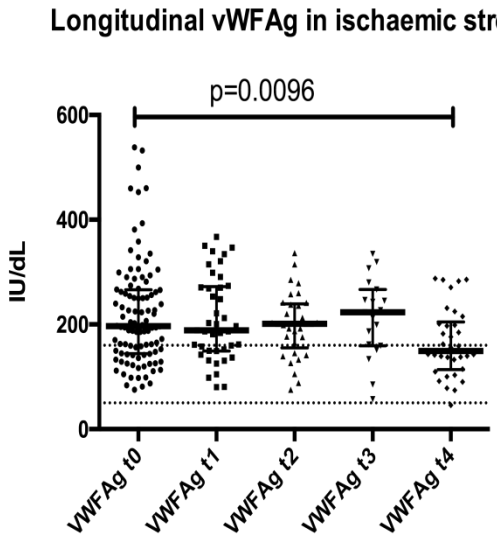


Figure 2b

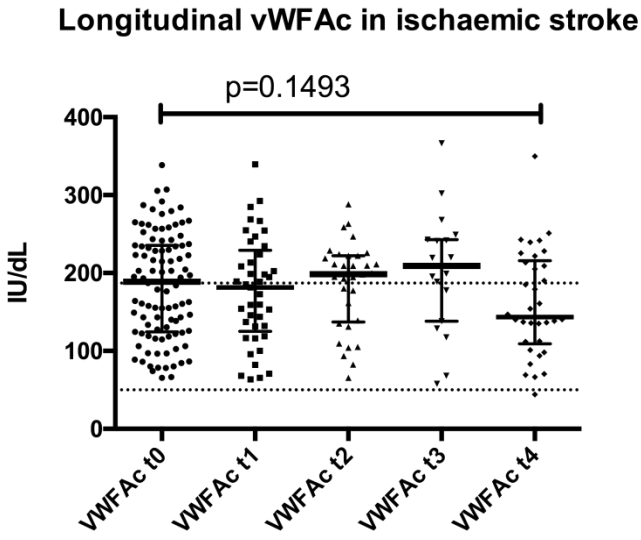


Figure 2c

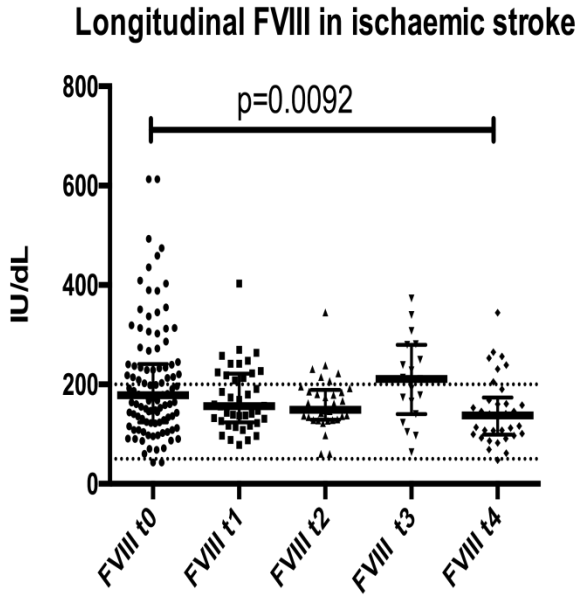
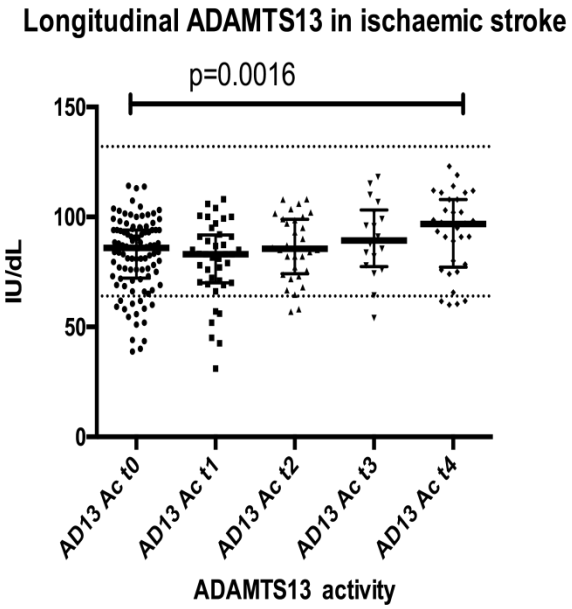


Figure 2d



Longitudinal changes in all haemostatic markers were measured at presentation (t0), 24 hours later (t1), 48 hours post presentation (t2), 5-7 days post presentation (t3) and final follow up from 6 weeks post presentation (t4). Median follow up time for ischaemic stroke specifically was 257 days (range 48-889). Decrease in VWFAg from presentation (median 196.9 IU/dL) to final follow up (median 149.4 IU/dL) was observed (p=0.0046; Figure 2a). The same trend was seen with VWFAc from presentation (median 188.7 IU/dL) to final follow up (median 143.7IU/dL, Figure 2b p=0.0783), and FVIII (presentation median 178.6 to final follow up 137.7 IU/dL; p=0.0038; Figure 2c).

A clear reverse trend was seen with ADAMTS13Ac in ischaemic stroke (Figure 2d), demonstrating a significant increase in ADAMTS13Ac from presentation (median 85.9 IU/dL) to final follow up (median 96.8IU/dL, p=0.0035).

Figure 3: Mortality outcome: difference in presentation haemostatic markers in ischaemic stroke and TIA groups combined

Figure 3a

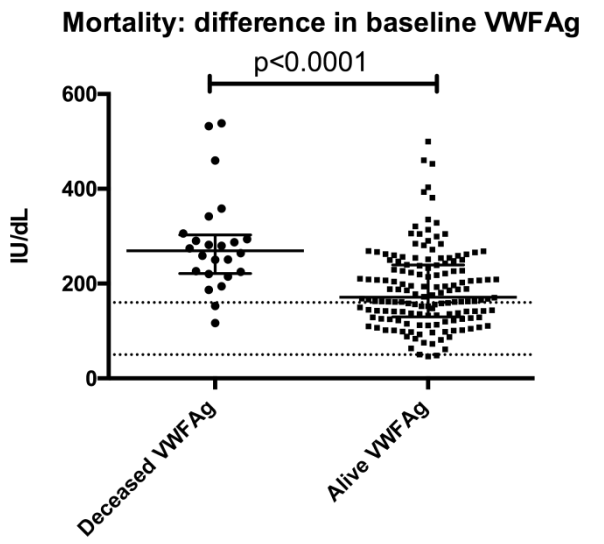
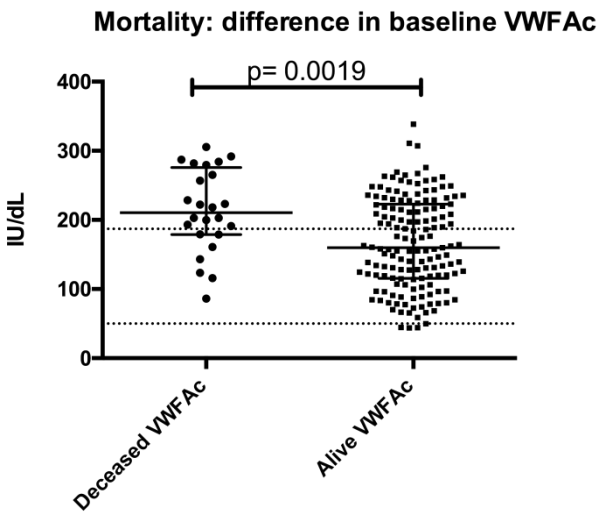


Figure 3b



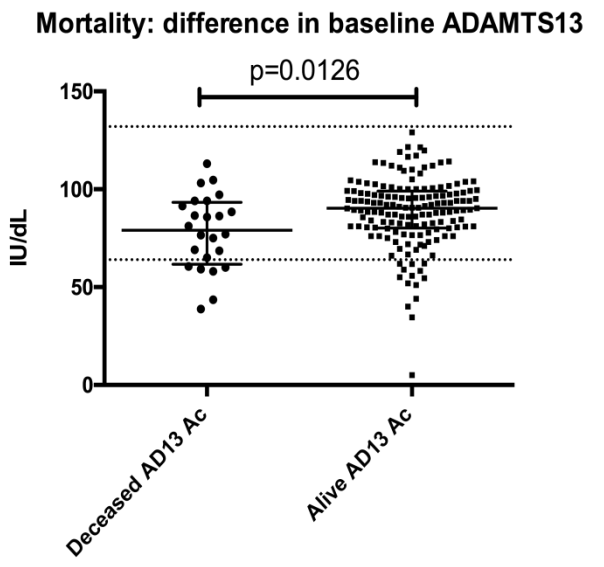


Figure 3c

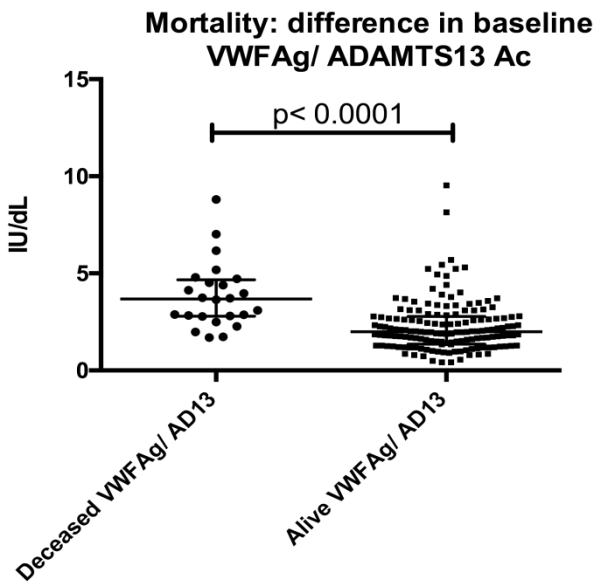


Figure 3d

Figure 3: Significant differences were seen in all haemostatic markers at baseline between those patients whom had subsequently died at final follow up (n=24) versus those whom survived (n=156) at a median follow up time of 152 days post initial presentation (minimum 6 weeks from first presentation). Differences were as follows (died vs survived): VWFAg (269.1 vs 171.2IU/dL p<0.0001; Figure 3a), VWFAc (210.5 vs 159.8IU/dL p=0.0019; Figure 3b), ADAMTS13 activity (79.1 vs 90.3IU/dL, p=0.0126; Figure 3c) and mean VWFAg/ ADAMTS13Ac ratio (3.683 vs 1.988, p<0.0001; Figure 3d).

Table 3: Mortality according to VWFAg-ADAMTS13Ac ratio quartiles in ischaemic stroke and TIA

Quartile	VWFAg-ADAMTS13Ac ratio	Survived (number of patients)	Died (number of patients)	Total number	Mortality rate
1	0.41-1.55	45	0	45	0%
2	1.551-2.11	42	3	45	6.7%
3	2.111-3.09	37	7	44	15.9%
4	3.091-9.53	31	14	45	31.1%