Baseline characteristics of the omega-3 fatty acids (Fish oils) and Aspirin in Vascular access

Outcomes in Renal Disease (FAVOURED) study

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Abstract

Aim:

The FAVOURED trial investigated whether three months of omega-3 polyunsaturated fatty acids, either alone or in combination with aspirin, will effectively reduce primary access failure of de novo arteriovenous fistulae. This report presents the baseline characteristics of all study participants, examines whether study protocol amendments successfully increased recruitment of a broader and more representative haemodialysis cohort, including patients already receiving aspirin, and contrasts Malaysian participants with those from Australia, New Zealand and the United Kingdom.

Method:

This international, randomised, double-blind, placebo-controlled trial included patients older than 19 years with stage 4 or 5 chronic kidney disease currently receiving, or planned within 12 months to receive haemodialysis.

Results: Participants (n=568) were overweight ($28.6 \pm 7.3 \text{ kg/m}^2$), relatively young (54.8 ± 14.3 years), and predominantly male (63%) with a high prevalence of diabetes mellitus (46%) but low rate of ischaemic heart disease (8%). Sixty one percent were planned for lower arm arteriovenous fistula creation. Malaysian participants (n=156) were younger (51.8 ± 13.6 years versus 57.1 ± 14.2 years, $p < 0.001$) with a higher prevalence of diabetes mellitus (65% versus 43%, $p < 0.001$) but less ischaemic heart disease (5% versus 14%, $p < 0.01$) compared with the combined Australian, New Zealand and United Kingdom cohort (n=228). Protocol modifications allowing for inclusion of patients receiving aspirin increased the prevalence of co-morbidities compared with the original cohort.

Conclusions:

The FAVOURED study participants, whilst mostly similar to patients in contemporary national registry reports and comparable recent clinical trials, were on average younger and had less ischaemic heart disease. These differences were reduced as a consequence of including patients already receiving aspirin.

Key words: Vascular access outcome; arteriovenous fistula; fish oil; aspirin; haemodialysis

Background

The importance of vascular access for improving clinical care and outcomes in haemodialysis patients is the focus of many quality initiatives around the world (e.g. NKF-KDOQI guidelines¹, KHA-CARI guidelines², Canadian Society of Nephrology³, Fistula First Breakthrough Initiative⁴). The benefits of a native arteriovenous fistula (AVF) compared with synthetic arteriovenous grafts (AVG) or central venous catheters (CVC) include lower rates of thrombosis, infection, interventions to maintain patency and overall mortality⁵⁻⁷. However, native AVF are more difficult to establish and take longer to mature, resulting in a greater need to maintain CVC and a higher primary access failure rate (ranging between 20–60%). Early and late failure has been attributed to early thrombosis and a failure of maturation^{8,9}. Vascular access dysfunction is associated with significant morbidity and mortality and is a major economic burden for health care providers and therefore an important target for therapeutic interventions¹⁰⁻¹².

Although the short-term post-operative use of anti-platelet agents may reduce early thrombosis rates^{8,13-17}, no intervention has been shown to significantly improve the proportion of fistulae that achieve the requirement for sustained regular dialysis, defined as the “usability” of AVF. Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) derived from fish and fish oils not only inhibit platelet aggregation but are anti-inflammatory, anti-proliferative and promote vasodilatation all of which may have a favourable impact on the usability of a de novo AVF¹⁸.

The omega-3 fatty acids (Fish oils) and Aspirin in Vascular access OUtcomes in RENal Disease (FAVOURED) trial investigated whether omega-3 polyunsaturated fatty acids either alone or in combination with aspirin will effectively reduce primary access failure of de novo AVF in patients with stage 4 or 5 chronic kidney disease and, by doing so, increase the proportion that achieve usability. In this paper, the baseline characteristics of the FAVOURED trial patients recruited in Malaysia, the United Kingdom (UK), Australia and New Zealand (ANZ) are described. Characteristics of participants

recruited before and after introduction of study protocol amendments designed to increase recruitment of a broader and more representative dialysis patient group, including recruitment of patients already receiving aspirin, are compared to evaluate the success of the protocol amendments. The Malaysian participants are compared and contrasted with the combined ANZ and UK cohort.

Methods

Participants

The trial included patients with stage 4 or 5 chronic kidney disease aged over 19 years and currently receiving, or planned within 12 months to receive haemodialysis. Participants underwent AVF surgery in the upper or lower arm as their primary haemodialysis access. Patients were excluded if they received a revision of an existing AVF rather than a de novo AVF, had an increased bleeding risk (bleeding disorder, recent or active GI ulcer, platelet count $< 100 \times 10^9 /L$, hepatic insufficiency or anti-coagulation therapy), were taking non-steroidal anti-inflammatory drugs, anticoagulants or anti-platelet agents with the exception of low-dose aspirin (eligible for the expanded protocol using open-label aspirin), had contra-indications for taking the study agents (planned surgery that would require cessation of the study medication, treatment-resistant syndrome of asthma, rhinitis and nasal polyps or a known allergy to the study agents), or were female patients who were breastfeeding, pregnant or intended to fall pregnant during the study period. Local ethics committees approved the study and all enrolled patients provided written informed consent.

Study design

FAVOURED is an international double-blind, randomised placebo-controlled trial (RCT) conducted in 34 haemodialysis centres of ANZ, the UK and Malaysia. This trial is designed to assess the effect of omega-3 PUFAs (Omacor capsules, 2g twice daily, Abbott, UK) and/or aspirin (100mg daily, Bayer Healthcare, United States) on 'AVF access failure', defined as a composite of thrombosis, AVF abandonment or cannulation failure at 12 months following de novo AVF creation. The original protocol was a 2x2 factorial-design trial, whereby participants were randomised to one of four treatment groups formed by aspirin or matching placebo and omega-3 fatty acids or matching placebo.

Patient recruitment started in August 2008 and finished in February 2014. Recruitment to the amended protocol started June 2011 and included suitable patients receiving aspirin and unable or unwilling to cease. In this expanded protocol, participants were allowed to continue with open-label aspirin at their current dose and were randomised to omega-3 PUFAs or matched placebo only. This amendment was implemented in response to the high prevalence of aspirin use and screen failure with selection of a relatively younger and healthier patient cohort. Including patients taking aspirin was expected to enrol a more representative cohort of older patients with a higher prevalence of cardiovascular disease and diabetes. A full discussion of the changes to the study protocol are described in detail elsewhere¹⁹.

Statistical analysis

Results are expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) depending on distribution characteristics for continuous variables and number (percentage) for categorical variables. Comparisons for continuous data were performed using independent-samples t-tests and Wilcoxon rank sum tests, as appropriate. Comparisons for binary measures were performed using Pearson's chi-square tests. Baseline characteristics independently associated with AVF site (upper versus lower arm) were determined using multivariable logistic regression. A p-value less than 0.05 was considered statistically significant. The calculations were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Patient Enrolment

The first FAVOURED study patient was enrolled on the 21st of August 2008, and recruitment concluded on the 28th of February 2014 with a total of 4242 subjects screened from 34 clinical sites. Prior to the start of recruitment to the amended study protocol in June 2011, 21% of patients screened (492 out of 2334) were deemed eligible, with the remaining patients excluded mainly due to the use of anticoagulants or anti-platelet agents such as aspirin (39%). Of the 492 patients deemed eligible, 184 (37%) were enrolled. Following extension of the study protocol to allow inclusion of patients receiving open-label aspirin, 48% of patients screened (909 out of 1908 participants) were deemed eligible and, of these, 384 (42%) were enrolled. Only 10% of the patients screened after the protocol amendments (197 out of 999) were excluded due to concurrent use of other anti-platelet agents or anti-coagulants. In ANZ, 403 participants were randomised from 25 different sites of which 184 were included pre- and 219 post-protocol amendment. Following the protocol amendment, an additional 156 participants were enrolled from 8 Malaysian sites and 9 from a single centre in the UK.

1) Baseline characteristics of all participants

Baseline characteristics of all 568 participants are shown in Table 1. Participants were predominantly male and Caucasian or Asian. The proportion of Indigenous participants was similar to that of the general incident haemodialysis population of Australia and New Zealand ²⁰. Their mean age was 54.8 ± 14.3 years. Most were overweight or obese; almost half had diabetes mellitus and half were former or current smokers, although only a minority had ischaemic heart disease (IHD, 8%) or congestive heart disease (4%). The majority of trial participants had systolic hypertension. The most common causes of chronic kidney disease were diabetic nephropathy (39%), hypertensive nephropathy (14%) and

glomerulonephritis (14%). Half of the participants were not receiving renal replacement therapy and had no other dialysis access at the time of AVF creation, which was predominantly planned for the lower arm. Forty two percent of participants were receiving haemodialysis via a CVC at the time of AVF creation. The mean haemoglobin was $108 \pm 19\text{g/L}$. Platelet counts and coagulation profiles were normal in the vast majority of participants.

2) Comparison of Australian and New Zealand participants pre- and post-amendment of the study protocol

Following protocol modifications to allow for open-label aspirin use in patients committed to aspirin, an additional 219 ANZ participants were enrolled and compared with the 184 participants from the original protocol (Table 2). The average age of the ANZ cohort increased from 54.6 years to 56.9 years. The proportion of Indigenous participants increased (from 13 to 19 %) and that of Caucasians decreased (from 74% to 71%, $p=0.07$). Diabetes mellitus was present in 43% of post-modification participants compared with the original 33% ($p=0.03$), IHD and congestive heart disease increased to 14% and 7%, respectively, compared with 4% ($p<0.001$) and 1% ($p<0.01$), respectively. The mean body mass index (BMI) and waist-to-hip ratio (WHR) but not blood pressure were significantly higher following protocol amendments and diabetic nephropathy as a cause of end-stage kidney disease (ESKD) was more prevalent post-protocol modification (37% versus 22%).

There was an increase in planned creation of lower arm AVF (72% compared with 59%, $p<0.01$) but no significant variation in renal replacement modality or type of dialysis access prior to AVF creation compared with the pre-modification trial cohort.

Whilst the average fasting glucose level and HbA1C were significantly higher in the post-modification cohort (6.8mmol/L and 6.6% compared to 6.1mmol/L and 6%, respectively, $p<0.05$), total cholesterol and LDL-cholesterol levels were reduced.

3) Comparison of combined ANZ and UK participants with Malaysian participants post-protocol amendment

Baseline data comparing the Malaysian cohort (n=156) with the combined ANZ (n=219) and UK (n=9) participants (ANZUK n=228) recruited after protocol modifications are presented in Table 3.

Malaysian participants were significantly younger, shorter and had a lower BMI, but had a similar WHR when compared with the ANZUK group.

Although diabetes mellitus was significantly more prevalent in the Malaysian cohort (65% versus 43%, $p < 0.001$), IHD (5% versus 14%) and smoking (current or former = 40% versus 58%) were less common than in the ANZUK cohort (both $p < 0.01$). At the time of enrolment, Malaysian participants had a significantly lower rate of aspirin use (32%) than ANZUK participants (49%, $p=0.001$).

A lower arm AVF was planned in 48% of Malaysian participants compared to 71% in the combined group. Multivariable regression analysis adjusted for relevant potential confounders indicate that the likelihood of undergoing lower arm AVF surgery was strongly associated with male gender, younger age, and country (ANZUK), but not BMI or diabetes status (Table 4). Sixty percent of the Malaysian cohort required haemodialysis prior to AVF surgery, predominantly via a non-cuffed CVC (83 out of 93 participants). This was in contrast to 35% of ANZUK participants undergoing haemodialysis, primarily via cuffed CVC (68 out of 79), and 43% requiring renal replacement therapy at the time of access surgery.

The average haemoglobin level was significantly lower in the Malaysian cohort compared with ANZUK ($97\text{g/L} \pm 19\text{g/L}$ versus $113 \pm 16\text{g/L}$, $p<0.001$). The proportion of patients using erythropoietin stimulating agents (ESAs) was 17% in Malaysia compared with 44% in ANZUK ($p<0.001$). Malaysian participants had a significantly greater white cell count (8.8 versus $7.5 \times 10^9/\text{L}$, $p<0.001$), platelet count (263 versus $239 \times 10^9/\text{L}$, $p<0.01$) and fibrinogen level (5.9 versus 4.7g/L , $p=0.04$) suggestive of

inflammation. Fasting blood glucose, cholesterol and LDL-cholesterol levels were significantly higher in the Malaysian cohort compared to participants from ANZUK.

4) Comparison between FAVOURED and two recent anti-platelet trials of vascular access outcomes

To date, there has only been one large RCT evaluating the impact of fish oil supplementation on access survival, which was performed in North America and Canada (FISH study)²¹. This study was conducted in participants receiving a de novo arterio-venous *graft* as opposed to a native arterio-venous *fistula*²¹. With regards to native AVF, access failure has so far only been evaluated with short-term (6 weeks) post-operative use of clopidogrel or placebo in a large North American RCT⁸. Patient baseline characteristics of the FAVOURED study, although generally similar to these two North American/Canadian studies, did have some important differences (Table 5). The average age and male predominance was similar in the FAVOURED and the clopidogrel trial, but the average age was higher and gender distribution equal in the FISH study. The prevalence of diabetes mellitus was highest in participants undergoing AVG surgery (53%) compared to participants receiving an AVF (46% and 48% in the FAVOURED and clopidogrel trial, respectively). The rate of IHD was considerably higher in the North American/Canadian studies (34-48%) compared to that of the FAVOURED trial (8%).

Discussion

FAVOURED is the first RCT designed to determine whether the use of omega-3 fatty acids with or without aspirin will improve the usability of de novo AVF. Patients enrolled in FAVOURED were overweight with a male predominance, a high prevalence of diabetes mellitus and current or past smoking history. However, trial participants were on average younger and had lower rates of IHD and congestive heart failure compared with the general haemodialysis population and comparable study cohorts^{8,21-24}. The trial design was modified in response to concerns about slow recruitment due to widespread prevalent aspirin use in order to facilitate recruitment and improve generalizability. Examination of the baseline data confirms that the modified trial protocol was consistent with the intended aims to recruit a more representative trial population by including a broader demographic with participants from Malaysia, Australia, New Zealand and the UK.

The original study protocol had excluded patients that were unable to cease aspirin, which resulted in an unexpectedly high screening failure rate and slow recruitment of a relatively young and healthy study cohort. Following protocol amendments to allow for open-label aspirin use, screening failure rates due to treatment with anticoagulants and antiplatelet agents decreased from 41% to 10%, the proportion of diabetic patients increased by almost one third, the prevalence of IHD more than 3-fold and that of congestive heart disease by almost six times. This is consistent with international data on patients from ANZ, Europe, Japan and North America showing that diabetes mellitus and IHD were significantly more prevalent in patients taking aspirin compared with those not taking aspirin²⁵. Post-protocol amendment, diabetes prevalence in this study (43%) was similar to that reported in incident haemodialysis patients in Australia (47%) and New Zealand (53%)^{22,26}. In contrast, the prevalence of IHD in the trial cohort remained considerably lower (14%) than that reported in incident ANZ

haemodialysis populations (on average 24-32%)^{22,26}. This may in part reflect physicians' concern or patient preference regarding the risk and benefit of participating in FAVOURED based upon their baseline cardiovascular risk.

Patients recruited from Malaysia represent one third of the final trial population and had significant baseline differences compared with participants from the combined ANZ and UK cohort. Malaysians, whilst on average younger and slimmer, had a greater prevalence of diabetes and diabetic nephropathy but lower rates of IHD and aspirin use. These findings are consistent with contemporary data from the Malaysian Dialysis and Transplant Registry reports where diabetes mellitus accounted for 57-61% of primary renal disease and IHD was present in 13% of haemodialysis patients²³. The mean haemoglobin concentration was significantly lower in the Malaysian cohort (97g/L) compared with the ANZUK cohort (113g/L), which may be attributed to variations in the use of ESAs. In Malaysia, 17% of participants were on ESA at enrollment as opposed to 44% of the ANZUK group. This may reflect regional differences in prescribing patterns and funding models. The lower haemoglobin concentration and/or the prevalence of ESA use may influence thrombosis risk and therefore impact on the study outcomes. Use of darbepoetin in the TREAT study was associated with a higher risk of venous and arterial thrombosis compared with no darbepoetin²⁷, and targeting higher haemoglobin concentrations with epoetins significantly increased the risk of vascular access thrombosis²⁸. The haemoglobin levels of the Malaysian cohort are likely to increase following initiation of haemodialysis given that the average haemoglobin of prevalent haemodialysis patients reported by the Malaysian Dialysis and Transplant Registry (111g/L) is similar to that reported by the Australian and New Zealand Dialysis and Transplantation Registry (112g/L) and use of ESA is higher (91% compared to 81-87% in ANZ)^{22,23,26}. Malaysian participants had a significantly higher serum fibrinogen level, white cell and platelet count suggestive of inflammation. Whether this may be due to a higher prevalence of non-

cuffed CVC use compared with the ANZUK cohort (54% versus 8%) or due to other environmental factors is uncertain.

Whilst the average age and male preponderance of FAVOURED participants was comparable to that of the clopidogrel trial⁸, the cohort of the FISH study²¹ was older with an equal proportion of female participants. This may be explained by differences in patient selection for an AVF as opposed to an AVG and regional differences in practice patterns. Older patients with smaller vessels may still be suitable for an AVG but not for a native AVF. Whilst the proportions of patients with diabetes mellitus were comparable across the three studies, the rates of ischaemic and congestive heart disease were considerably lower in the FAVOURED cohort suggesting differences in patient selection. In North America, 47-50% of prevalent haemodialysis patients were reported to have coronary heart disease compared with 13% of haemodialysis patients in Malaysia, and 23-30% of incident and 50-51% of prevalent haemodialysis patients in ANZ^{23,24,26,29}. The clopidogrel trial⁸ and FISH study²¹ are the only two RCTs of interventions targeting haemodialysis access failure of comparable size to date and were conducted in North America and Canada. The FAVOURED trial therefore adds important information on clinical features of patients with ESKD undergoing de novo vascular access surgery in Malaysia, Australia, New Zealand and the UK.

Limitations

Comparison of baseline characteristics between the study population and registry data was limited by differences in data collection. Whilst ANZDATA collects information on incident and prevalent haemodialysis patients separately, Malaysia focuses mainly on characteristics of incident haemodialysis patients and the US registry reports on the entire population with chronic kidney disease and those with ESKD, respectively.

Conclusion

The FAVOURED study successfully enrolled a large number of participants undergoing de novo AVF creation with baseline characteristics that, for the most part, were similar to contemporary registry reports and comparable clinical trials of such individuals. The initial issue of selecting a relatively healthy cohort was managed by modifying the study protocol to allow for open-label aspirin use in patients unable to cease aspirin therapy and did result in enrolment of a more representative cohort of ESKD patients. The enrolment of Malaysian participants enhances the generalizability of this trial whilst providing important information on variations in baseline characteristics of haemodialysis patients and differences in clinical practices.

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Conflict of interests

The authors declare that they have no competing interests.

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Tables:

Table 1: Baseline characteristics of all participants

	Total N=568	Region		
		ANZ (N=403)	Malaysia (N=156)	UK (N=9)
Demographics				
Gender, n (%)				
Male	360 (63%)	264 (65%)	93 (60%)	3 (33%)
Female	208 (37%)	139 (35%)	63 (40%)	6 (67%)
Age (years; mean ± SD)	54.8 ± 14.3	55.8 ± 14.4	51.8 ± 13.6	61.0 ± 12.9
Ethnicity, n (%) [†]				
Aboriginal or Torres Strait Islander	22 (4%)	22 (6%)	0	0
Asian	181 (32%)	26 (7%)	155 (100%)	0
Caucasoid	298 (53%)	289 (72%)	0	9 (100%)
MPI	44 (8%)	44 (11%)	0	0
Other	20 (4%)	20 (5%)	0	0
Clinical history				
Height (cm; mean ± SD) [‡]	166.7 ± 10.2	169.2 ± 10.0	160.2 ± 7.9	166.6 ± 4.6
Weight(kg; mean ± SD) [†]	79.8 ± 23.1	85.0 ± 23.3	66.3 ± 16.5	77.7 ± 21.0
BMI (kg/m ² ; mean ± SD) [‡]	28.6 ± 7.3	29.7 ± 7.5	25.8 ± 5.8	27.9 ± 7.2
Waist measurement (cm; mean ± SD) [§]	99.2 ± 19.4	102.6 ± 18.4	91.3 ± 19.3	93.8 ± 20.7
Hip measurement(cm; mean ± SD) [§]	102.2 ± 18.8	105.2 ± 16.7	94.8 ± 21.5	107.1 ± 16.0
Waist/hip ratio (mean ± SD) [§]	0.98 ± 0.17	0.98 ± 0.10	1.00 ± 0.28	0.87 ± 0.09
Systolic blood pressure (mm Hg; mean ± SD) [†]	146 ± 23	145 ± 23	149 ± 24	152 ± 20
Diastolic blood pressure (mm Hg; mean ± SD) [†]	82 ± 13	81 ± 14	81 ± 13	83 ± 16
Heart rate (beats per minute; mean ± SD) [‡]	76 ± 13	75 ± 13	79 ± 13	78 ± 19
Smoking status, n (%) [†]				
Never	280 (50%)	180 (45%)	93 (60%)	7 (78%)
Former	206 (37%)	161 (40%)	43 (28%)	2 (22%)
Current	79 (14%)	60 (15%)	19 (12%)	0
Diabetes mellitus, n (%)				
Type 1 or Type 2	261 (46%)	156 (39%)	101 (65%)	4 (44%)
Type 1	25 (10%)	19 (12%)	5 (5%)	1 (25%)
Type 2	236 (90%)	137 (88%)	96 (95%)	3 (75%)

Ischaemic heart disease, n (%)	45 (8%)	37 (9%)	7 (5%)	1 (11%)
Congestive heart disease, n (%)	21 (4%)	17 (4%)	4 (3%)	0
Aetiology of renal disease, n (%) [†]				
Diabetic nephropathy	221 (39%)	121 (30%)	97 (63%)	3 (33%)
Glomerulonephritis	77 (14%)	68 (17%)	7 (5%)	2 (22%)
Hypertension/vascular	75 (13%)	46 (12%)	29 (19%)	0
Polycystic kidney disease	40 (7%)	36 (9%)	4 (3%)	0
Reflux nephropathy	27 (5%)	27 (7%)	0	0
Other	125 (22%)	103 (26%)	18 (12%)	4 (44%)
AVF location, n (%)				
Upper arm	223 (39%)	137 (34%)	81 (52%)	5 (56%)
Lower arm	345 (61%)	266 (66%)	75 (48%)	4 (44%)
Renal replacement therapy at time of AVF creation, n (%) [†]				
Transplant	10 (2%)	10 (3%)	0	0
Peritoneal dialysis	35 (6%)	35 (9%)	0	0
Haemodialysis	240 (43%)	145 (36%)	93 (60%)	2 (22%)
Not currently receiving renal replacement therapy	280 (50%)	211 (53%)	62 (40%)	7 (78%)
Principal access currently in use for dialysis, n (%) [†]				
No access currently in use	288 (51%)	221 (55%)	60 (39%)	7 (78%)
Arteriovenous fistula	8 (1%)	4 (1%)	3 (2%)	1 (11%)
Arteriovenous graft - artificial graft	1 (0.2%)	1 (0.2%)	0	0
Central venous catheter (cuffed)	138 (25%)	129 (32%)	8 (5%)	1 (11%)
Central venous catheter (non-cuffed)	94 (17%)	11 (3%)	83 (54%)	0
Peritoneal dialysis catheter	35 (6%)	35 (9%)	0	0
Dialysis duration (months; median [IQR]) ^{††}	4 (2 - 18)	6 (2- 25)	2 (1 - 5)	21 (2 - 39)
Laboratory investigations for pre-dialysis and dialysis participants combined				
Haemoglobin (g/L; mean $\pm$ SD) [‡]	108 $\pm$ 19	113 $\pm$ 16	97 $\pm$ 19	104 $\pm$ 12
Platelets (10 ⁹ /L; mean $\pm$ SD) [‡]	248 $\pm$ 80	242 $\pm$ 79	263 $\pm$ 79	253 $\pm$ 88
White blood cells (10 ⁹ /L; mean $\pm$ SD) [‡]	7.9 $\pm$ 3.2	7.6 $\pm$ 2.3	8.8 $\pm$ 4.9	6.0 $\pm$ 0.7
INR (mean $\pm$ SD) [§]	1.1 $\pm$ 0.3	1.0 $\pm$ 0.1	1.1 $\pm$ 0.5	0.9 $\pm$ 0.1
APTT(seconds; mean $\pm$ SD) [§]	33.3 $\pm$ 15.8	32.7 $\pm$ 17.5	35.2 $\pm$ 10.5	31.4 $\pm$ 3.1
Fibrinogen (g/L; mean $\pm$ SD) [¶]	5.0 $\pm$ 3.9	4.8 $\pm$ 1.3	5.9 $\pm$ 7.9	3.4 $\pm$ 0.7
Sodium (mmol/L; mean $\pm$ SD) [‡]	138 $\pm$ 6	139 $\pm$ 3	136 $\pm$ 11	138 $\pm$ 3
Albumin (g/L; mean $\pm$ SD) [‡]	36.0 $\pm$ 6.2	36.3 $\pm$ 5.7	35.5 $\pm$ 7.3	30.3 $\pm$ 5.1
Fasting glucose (mmol/L; mean $\pm$ SD) [¶]	6.9 $\pm$ 3.8	6.5 $\pm$ 3.1	8.1 $\pm$ 4.9	5.5 $\pm$ 3.5
HbA1C (%; mean $\pm$ SD) [§]	6.4 $\pm$ 2.7	6.3 $\pm$ 2.9	6.7 $\pm$ 1.8	6.0 $\pm$ 1.3

Parathormone (pmol/L; mean $\pm$ SD) [§]	37.3 $\pm$ 35.4	37.9 $\pm$ 37.9	36.0 $\pm$ 28.1	22.0 $\pm$ 5.9
Cholesterol (mmol/L; mean $\pm$ SD) [‡]	4.5 $\pm$ 1.3	4.3 $\pm$ 1.2	5.0 $\pm$ 1.5	4.5 $\pm$ 1.7
Triglyceride (mmol/L; mean $\pm$ SD) [§]	2.0 $\pm$ 1.2	2.0 $\pm$ 1.1	2.1 $\pm$ 1.4	2.1 $\pm$ 0.6
HDL cholesterol (mmol/L; mean $\pm$ SD) [§]	1.1 $\pm$ 0.4	1.1 $\pm$ 0.4	1.1 $\pm$ 0.4	1.6 $\pm$ 1.0
LDL cholesterol (mmol/L; mean $\pm$ SD) [¶]	2.6 $\pm$ 1.1	2.4 $\pm$ 1.0	3.0 $\pm$ 1.2	2.8 $\pm$ 1.6
Laboratory investigations for pre-dialysis participants				
Creatinine (μ mol/L; mean $\pm$ SD) [†]	506 $\pm$ 216	468 $\pm$ 188	652 $\pm$ 249	394 $\pm$ 154
Urea (mmol/L; mean $\pm$ SD) [†]	25.5 $\pm$ 8.0	26.1 $\pm$ 7.8	23.9 $\pm$ 8.6	21.9 $\pm$ 5.7
Potassium (mmol/L; mean $\pm$ SD) [†]	4.7 $\pm$ 0.7	4.8 $\pm$ 0.6	4.5 $\pm$ 0.7	5.1 $\pm$ 0.9
Bicarbonate (mmol/L; mean $\pm$ SD) [‡]	21.0 $\pm$ 4.2	21.7 $\pm$ 3.3	18.6 $\pm$ 6.6	20.0 $\pm$ 3.3
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.2 $\pm$ 0.2	2.2 $\pm$ 0.2	2.2 $\pm$ 0.2	2.2 $\pm$ 0.1
Phosphate (mmol/L; mean $\pm$ SD) [‡]	1.6 $\pm$ 0.4	1.6 $\pm$ 0.5	1.7 $\pm$ 0.4	1.6 $\pm$ 0.4
Laboratory investigations for dialysis participants				
Creatinine (μ mol/L; mean $\pm$ SD) [†]	718 $\pm$ 271	731 $\pm$ 274	700 $\pm$ 263	464 $\pm$ 238
Urea (mmol/L; mean $\pm$ SD) [†]	19.0 $\pm$ 7.7	16.4 $\pm$ 7.6	14.9 $\pm$ 1.6	19.0 $\pm$ 7.7
Potassium (mmol/L; mean $\pm$ SD) [†]	4.5 $\pm$ 0.9	4.7 $\pm$ 0.9	4.2 $\pm$ 0.7	5.1 $\pm$ 0.0
Bicarbonate (mmol/L; mean $\pm$ SD) [¶]	24.0 $\pm$ 3.7	24.6 $\pm$ 3.6	22.0 $\pm$ 3.5	25.0 $\pm$ 1.4
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.2 $\pm$ 0.2	2.3 $\pm$ 0.2	2.2 $\pm$ 0.3	2.3 $\pm$ 0.2
Phosphate (mmol/L; mean $\pm$ SD) [‡]	1.7 $\pm$ 0.6	1.7 $\pm$ 0.6	1.6 $\pm$ 0.5	1.2 $\pm$ 0.2

[†]missing data in <1% of patients

[‡]missing data in 1-4.9% of patients

[§]missing data in 5-9.9% of patients

[¶]missing data in 10-19.9% of patients

^{††} Dialysis patients only (n=275 for all participants on dialysis, n=180 for ANZ cohort, n=93 for Malaysian cohort, and n=2 for UK cohort)

Abbreviations: APTT - activated partial thromboplastin time; AVF – arteriovenous fistula; BMI – body mass index; ESAs – erythropoietin stimulating agents; HDL – high-density lipoprotein; IQR – interquartile range; LDL – low-density lipoprotein; MPI – Maori & Pacific Islanders.

Table 2: Comparison of Australian and New Zealand participants pre- and post-study protocol amendment

	ANZ pre-protocol change (N=184)	ANZ post-protocol change (N=219)	P-value
Demographics			
Gender, n (%)			0.60
Male	118 (64%)	146 (67%)	
Female	66 (36%)	73 (33%)	
Age (years; mean $\pm$ SD)	54.6 $\pm$ 14.4	56.9 $\pm$ 14.3	0.11
Ethnicity, n (%) [†]			0.07
Aboriginal or Torres Strait Islander	6 (3%)	16 (7%)	
Asian	17 (9%)	9 (4%)	
Caucasoid	136 (74%)	153 (71%)	
MPI	18 (10%)	26 (12%)	
Other	7 (4%)	13 (6%)	
Clinical history			
Height (cm; mean $\pm$ SD) [‡]	169.5 $\pm$ 10.3	168.9 $\pm$ 9.7	0.58
Weight(kg; mean $\pm$ SD) [†]	82.9 $\pm$ 24.6	86.8 $\pm$ 22.0	0.10
BMI (kg/m ² ; mean $\pm$ SD) [‡]	28.7 $\pm$ 7.2	30.5 $\pm$ 7.7	0.02
Waist measurement (cm; mean $\pm$ SD) [§]	99.2 $\pm$ 17.8	105.6 $\pm$ 18.6	<0.001
Hip measurement(cm; mean $\pm$ SD) [¶]	103.5 $\pm$ 16.8	106.8 $\pm$ 16.5	0.06
Waist/hip ratio (mean $\pm$ SD) [¶]	0.96 $\pm$ 0.09	0.99 $\pm$ 0.11	<0.01
..... WHR male	0.99 $\pm$ 0.07	1.01 $\pm$ 0.12	
..... WHR female	0.90 $\pm$ 0.08	0.95 $\pm$ 0.08	
Use of ESAs, n (%)	74 (40%)	95 (44%)	0.45
Systolic blood pressure (mm Hg; mean $\pm$ SD) [†]	145 $\pm$ 23	145 $\pm$ 22	0.86
Diastolic blood pressure (mm Hg; mean $\pm$ SD) [†]	83 $\pm$ 13	80 $\pm$ 14	0.09
Heart rate (beats per minute; mean $\pm$ SD) [‡]	76 $\pm$ 13	74 $\pm$ 13	0.06
Smoking status, n (%) [†]			0.14
Never	92 (50%)	88 (41%)	
Former	69 (38%)	92 (42%)	
Current	23 (13%)	37 (17%)	
Diabetes mellitus, n (%)			
Type 1 or Type 2	61 (33%)	95 (43%)	0.04
Type 1	7 (11%)	12 (13%)	

Type 2	54 (89%)	83 (87%)	
Ischaemic heart disease, n (%)	7 (4%)	30 (14%)	<0.001
Congestive heart disease, n (%)	2 (1%)	15 (7%)	<0.01
Aetiology of renal disease, n (%) [†]			<0.01
Diabetic nephropathy	40 (22%)	81 (37%)	
Glomerulonephritis	39 (21%)	29 (13%)	
Hypertension/vascular	22 (12%)	24 (11%)	
Polycystic kidney disease	22 (12%)	14 (7%)	
Reflux nephropathy	12 (7%)	15 (7%)	
Other	49 (27%)	54 (25%)	
AVF location, n (%)			<0.01
Upper arm	75 (41%)	62 (28%)	
Lower arm	109 (59%)	157 (72%)	
Renal replacement therapy at time of AVF creation, n (%) [†]			0.81
Transplant	5 (3%)	5 (2%)	
Peritoneal dialysis	17 (9%)	18 (8%)	
Haemodialysis	67 (36%)	78 (36%)	
Not currently receiving renal replacement therapy	95 (52%)	116 (54%)	
Principal access currently in use for dialysis, n (%) [†]			0.88
No access currently in use	100 (54%)	121 (56%)	
Arteriovenous fistula	1 (1%)	3 (1%)	
Arteriovenous graft - artificial graft	0	1 (0.5%)	
Central venous catheter (cuffed)	61 (33%)	68 (31%)	
Central venous catheter (non-cuffed)	5 (3%)	6 (3%)	
Peritoneal dialysis catheter	17 (9%)	18 (8%)	
Dialysis duration (months; median [IQR]) ^{†††}	6 (2 - 28)	2 (7 - 24)	0.91
Laboratory investigations for pre-dialysis and dialysis participants combined			
Haemoglobin (g/L; mean $\pm$ SD) [‡]	112 $\pm$ 17	113 $\pm$ 16	0.52
Platelets (10 ⁹ /L; mean $\pm$ SD) [‡]	246 $\pm$ 86	238 $\pm$ 72	0.34
White blood cells (10 ⁹ /L; mean $\pm$ SD) [‡]	7.6 $\pm$ 2.2	7.6 $\pm$ 2.3	0.82
INR (mean $\pm$ SD) [§]	1.0 $\pm$ 0.1	1.0 $\pm$ 0.1	0.40
APTT(seconds; mean $\pm$ SD) [§]	34.6 $\pm$ 23.7	31.1 $\pm$ 9.7	0.05
Fibrinogen (g/L; mean $\pm$ SD) [¶]	4.7 $\pm$ 1.3	4.8 $\pm$ 1.4	0.75
Sodium (mmol/L; mean $\pm$ SD) [‡]	139 $\pm$ 3	139 $\pm$ 3	0.03
Albumin (g/L; mean $\pm$ SD) [‡]	36.8 $\pm$ 5.5	35.9 $\pm$ 5.9	0.11
Fasting glucose (mmol/L; mean $\pm$ SD) [¶]	6.1 $\pm$ 2.5	6.8 $\pm$ 3.5	0.05

HbA1C (%; mean $\pm$ SD) [§]	6.0 $\pm$ 1.2	6.6 $\pm$ 3.9	0.04
Parathormone (pmol/L; mean $\pm$ SD) [§]	36.7 $\pm$ 35.5	38.9 $\pm$ 39.8	0.58
Cholesterol (mmol/L; mean $\pm$ SD) [‡]	4.5 $\pm$ 1.2	4.2 $\pm$ 1.2	0.01
Triglyceride (mmol/L; mean $\pm$ SD) [‡]	2.0 $\pm$ 1.0	1.9 $\pm$ 1.2	0.83
HDL cholesterol (mmol/L; mean $\pm$ SD) [§]	1.1 $\pm$ 0.4	1.1 $\pm$ 0.4	0.90
LDL cholesterol (mmol/L; mean $\pm$ SD) [¶]	2.6 $\pm$ 1.1	2.3 $\pm$ 0.9	<0.01
Laboratory investigations for pre-dialysis participants			
Creatinine (μ mol/L; mean $\pm$ SD) [†]	470 $\pm$ 205	467 $\pm$ 174	0.91
Urea (mmol/L; mean $\pm$ SD) [†]	25.2 $\pm$ 7.0	26.8 $\pm$ 8.4	0.12
eGFR (ml/min/1.73m ² ; mean $\pm$ SD) [†]	12.4 $\pm$ 6.8	12.0 $\pm$ 5.3	0.65
Potassium (mmol/L; mean $\pm$ SD) [†]	4.8 $\pm$ 0.6	4.8 $\pm$ 0.7	0.87
Bicarbonate (mmol/L; mean $\pm$ SD) [‡]	21.3 $\pm$ 3.3	21.9 $\pm$ 3.3	0.16
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.2 $\pm$ 0.2	2.3 $\pm$ 0.2	0.47
Phosphate (mmol/L; mean $\pm$ SD) [‡]	1.6 $\pm$ 0.5	1.6 $\pm$ 0.4	0.84
Laboratory investigations for dialysis participants			
Creatinine (μ mol/L; mean $\pm$ SD) [†]	731 $\pm$ 288	730 $\pm$ 263	0.95
Urea (mmol/L; mean $\pm$ SD) [†]	21.1 $\pm$ 7.0	19.8 $\pm$ 8.0	0.25
Potassium (mmol/L; mean $\pm$ SD) [†]	4.7 $\pm$ 0.9	4.7 $\pm$ 0.8	0.99
Bicarbonate (mmol/L; mean $\pm$ SD) [§]	24.3 $\pm$ 4.0	24.9 $\pm$ 3.2	0.33
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.2 $\pm$ 0.2	2.3 $\pm$ 0.2	0.48
Phosphate (mmol/L; mean $\pm$ SD) [‡]	1.7 $\pm$ 0.7	1.7 $\pm$ 0.6	0.91

[†]missing data in <1% of patients

[‡]missing data in 1-4.9% of patients

[§]missing data in 5-9.9% of patients

[¶]missing data in 10-19.9% of patients

^{**}Dialysis patients only (n=84 for pre-protocol amendment cohort, n=96 for post-protocol amendment cohort)

Abbreviations: APTT - activated partial thromboplastin time; AVF – arteriovenous fistula; BMI – body mass index; eGFR – estimated glomerular filtration rate; ESAs – erythropoietin stimulating agents; HDL – high-density lipoprotein; IQR – interquartile range; LDL – low-density lipoprotein; MPI – Maori & Pacific Islanders.

Table 3: Comparison of Australian, New Zealand and UK participants to Malaysian participants post-study protocol amendment

	Post-protocol ANZ and UK cohort combined (N=228)	Malaysian cohort (N=156)	P-value
Demographics			
Gender, n (%)			0.25
Male	149 (65%)	93 (60%)	
Female	79 (35%)	63 (40%)	
Age (years; mean $\pm$ SD)	57.1 $\pm$ 14.2	51.8 $\pm$ 13.6	<0.001
Ethnicity, n (%) [†]			<0.001
Aboriginal or Torres Strait Islander	16 (7%)	0	
Asian	9 (4%)	155 (100%)	
Caucasoid	162 (72%)	0	
MPI	26 (12%)	0	
Other	13 (6%)	0	
Clinical history			
Height (cm; mean $\pm$ SD) [‡]	168.8 $\pm$ 9.6	160.2 $\pm$ 7.9	<0.001
Weight(kg; mean $\pm$ SD) [‡]	86.5 $\pm$ 22.0	66.3 $\pm$ 16.5	<0.001
BMI (kg/m ² ; mean $\pm$ SD) [‡]	30.4 $\pm$ 7.7	25.8 $\pm$ 5.8	<0.001
Waist measurement (cm; mean $\pm$ SD) [§]	105.2 $\pm$ 18.7	91.3 $\pm$ 19.3	<0.001
Hip measurement(cm; mean $\pm$ SD) [§]	106.8 $\pm$ 16.5	94.8 $\pm$ 21.5	<0.001
Waist/hip ratio (mean $\pm$ SD) [§]	0.98 $\pm$ 0.11	1.00 $\pm$ 0.28	0.62
.....WHR male	1.00 $\pm$ 0.12	1.02 $\pm$ 0.27	
.....WHR female	0.94 $\pm$ 0.08	0.96 $\pm$ 0.28	
Use of aspirin, n (%)	111 (49%)	50 (32%)	0.001
Use of ESAs, n (%)	98 (44%)	26 (17%)	<0.001
Systolic blood pressure (mm Hg; mean $\pm$ SD) [‡]	146 $\pm$ 22	149 $\pm$ 24	0.20
Diastolic blood pressure (mm Hg; mean $\pm$ SD) [‡]	81 $\pm$ 14	81 $\pm$ 13	0.52
Heart rate (beats per minute; mean $\pm$ SD) [‡]	74 $\pm$ 13	79 $\pm$ 13	<0.001
Smoking status, n (%) [†]			<0.01
Never	94 (42%)	93 (60%)	
Former	95 (42%)	43 (28%)	
Current	37 (16%)	19 (12%)	
Diabetes mellitus, n (%)			
Type 1 or Type 2	99 (43%)	101 (65%)	<0.001
Type 1	13 (13%)	5 (5%)	

Type 2	86 (87%)	96 (95%)	
Ischaemic heart disease, n (%)	31 (14%)	7 (5%)	<0.01
Congestive heart disease, n (%)	15 (7%)	4 (3%)	0.08
Aetiology of renal disease, n (%) [†]			<0.001
Diabetic nephropathy	84 (37%)	97 (63%)	
Glomerulonephritis	31 (14%)	7 (5%)	
Hypertension/vascular	24 (11%)	29 (19%)	
Polycystic kidney disease	14 (6%)	4 (3%)	
Reflux nephropathy	15 (7%)	0	
Other	58 (26%)	18 (12%)	
AVF location, n (%)			<0.001
Upper arm	67 (29%)	81 (52%)	
Lower arm	161 (71%)	75 (48%)	
Renal replacement therapy at time of AVF creation, n (%) [†]			<0.001
Transplant	5 (2%)	0	
Peritoneal dialysis	18 (8%)	0	
Haemodialysis	80 (35%)	93 (60%)	
Not currently receiving renal replacement therapy	123 (54%)	62 (40%)	
Principal access currently in use for dialysis, n (%) [‡]			<0.001
No access currently in use	128 (57%)	60 (39%)	
Arteriovenous fistula	4 (2%)	3 (2%)	
Arteriovenous graft - artificial graft	1 (0.4%)	0	
Central venous catheter (cuffed)	69 (31%)	8 (5%)	
Central venous catheter (non-cuffed)	6 (3%)	83 (54%)	
Peritoneal dialysis catheter	18 (8%)	0	
Dialysis duration (months; median [IQR]) ^{§§§}	7 (2 - 24)	2 (1 - 5)	<0.001
Laboratory investigations			
Haemoglobin (g/L; mean $\pm$ SD) [‡]	113 $\pm$ 16	97 $\pm$ 19	<0.001
Platelets (10 ⁹ /L; mean $\pm$ SD) [‡]	239 $\pm$ 73	263 $\pm$ 79	<0.01
White blood cells (10 ⁹ /L; mean $\pm$ SD) [‡]	7.5 $\pm$ 2.3	8.8 $\pm$ 4.9	<0.001
INR (mean $\pm$ SD) [§]	1.0 $\pm$ 0.1	1.1 $\pm$ 0.5	0.03
APTT(seconds; mean $\pm$ SD) [¶]	31.1 $\pm$ 9.6	35.2 $\pm$ 10.5	<0.001
Fibrinogen (g/L; mean $\pm$ SD) ^{††}	4.7 $\pm$ 1.4	5.9 $\pm$ 7.9	0.04
Sodium (mmol/L; mean $\pm$ SD) [‡]	139 $\pm$ 3	136 $\pm$ 11	<0.01
Albumin (g/L; mean $\pm$ SD) [‡]	35.6 $\pm$ 6.0	35.5 $\pm$ 7.3	0.86
Fasting glucose (mmol/L; mean $\pm$ SD) [¶]	6.7 $\pm$ 3.5	8.1 $\pm$ 4.9	<0.01

HbA1C (%; mean $\pm$ SD) [§]	6.6 $\pm$ 3.8	6.7 $\pm$ 1.8	0.82
Parathormone (pmol/L; mean $\pm$ SD) [¶]	38.7 $\pm$ 39.7	36.0 $\pm$ 28.1	0.50
Cholesterol (mmol/L; mean $\pm$ SD) [§]	4.2 $\pm$ 1.2	5.0 $\pm$ 1.5	<0.001
Triglyceride (mmol/L; mean $\pm$ SD) [§]	2.0 $\pm$ 1.2	2.1 $\pm$ 1.4	0.44
HDL cholesterol (mmol/L; mean $\pm$ SD) [§]	1.1 $\pm$ 0.4	1.1 $\pm$ 0.4	0.54
LDL cholesterol (mmol/L; mean $\pm$ SD) [¶]	2.3 $\pm$ 0.9	3.0 $\pm$ 1.2	<0.001
Laboratory investigations for pre-dialysis participants			
Creatinine (μ mol/L; mean $\pm$ SD) [†]	463 $\pm$ 174	652 $\pm$ 249	<0.001
Urea (mmol/L; mean $\pm$ SD) [†]	26.6 $\pm$ 8.4	23.9 $\pm$ 8.6	0.04
eGFR ^{††} (ml/min/1.73m ² ; mean $\pm$ SD) [†]	12.1 $\pm$ 5.2	8.0 $\pm$ 3.3	<0.001
Potassium (mmol/L; mean $\pm$ SD) [†]	4.8 $\pm$ 0.7	4.5 $\pm$ 0.7	0.01
Bicarbonate (mmol/L; mean $\pm$ SD) [§]	21.9 $\pm$ 3.3	18.6 $\pm$ 6.6	<0.001
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.3 $\pm$ 0.2	2.2 $\pm$ 0.2	<0.01
Phosphate (mmol/L; mean $\pm$ SD) [‡]	1.6 $\pm$ 0.4	1.7 $\pm$ 0.4	0.77
Laboratory investigations for dialysis participants			
Creatinine (μ mol/L; mean $\pm$ SD) [†]	724 $\pm$ 264	700 $\pm$ 263	0.52
Urea (mmol/L; mean $\pm$ SD) [†]	19.7 $\pm$ 7.9	16.4 $\pm$ 7.6	<0.01
Potassium (mmol/L; mean $\pm$ SD) [†]	4.7 $\pm$ 0.8	4.2 $\pm$ 0.7	<0.001
Bicarbonate (mmol/L; mean $\pm$ SD) ^{††}	24.9 $\pm$ 3.2	22.0 $\pm$ 3.5	<0.001
Total calcium (mmol/L; mean $\pm$ SD) [‡]	2.3 $\pm$ 0.2	2.2 $\pm$ 0.3	0.25
Phosphate (mmol/L; mean $\pm$ SD) [§]	1.7 $\pm$ 0.6	1.6 $\pm$ 0.5	0.35

[†]missing data in <1% of patients

[‡]missing data in 1-4.9% of patients

[§]missing data in 5-9.9% of patients

[¶]missing data in 10-19.9% of patients

^{††}missing data in 20-29.9% of patients

^{†††}Dialysis patients only (n=98 for combined ANZ and UK cohort, n=93 for Malaysian cohort)

Abbreviations: APTT - activated partial thromboplastin time; AVF – arteriovenous fistula; BMI – body mass index; eGFR – estimated glomerular filtration rate; ESAs – erythropoietin stimulating agents; HDL – high-density lipoprotein; IQR – interquartile range; LDL – low-density lipoprotein; MPI – Maori & Pacific Islanders.

Table 4: Multivariable regression analysis for AVF location and covariates post-protocol amendment

Covariates	Odds ratio[†] (95% CI)	p-value
Country (ANZUK)	2.77 (1.67 to 4.60)	<.0001
Gender (male)	2.67 (1.70 to 4.21)	<.0001
Age (years)	0.98 (0.96 to 0.99)	0.01
Body mass index (kg/m ²)	1.01 (0.97 to 1.04)	0.69
Diabetes mellitus	0.96 (0.60 to 1.55)	0.87

[†]Odds ratio shows likelihood of undergoing lower arm arteriovenous fistula (AVF).

Table 5: Comparison of demographic and clinical characteristics: FAVOURED versus two recent anti-platelet trials of vascular access outcomes.

Characteristics	FAVOURED	Clopidogrel Trial	FISH
Regions	ANZ, UK, Malaysia	North America	North America and Canada
Sample size, n	568	877	201
Access type	AVF	AVF	AVG
Anti-platelet agent (dose)	Fish oil (4 g, 46% EPA, 38% DHA)	Clopidogrel (300 mg day 1, 75 mg maintenance)	Fish oil (4 g, 48% EPA, 25% DHA)
Starting date of anti-platelet agent	1 day prior to surgery	1 day after surgery	7 – 10 days after surgery
Age, years	55	54	63
Female, %	37	38	50
Ethnicities, %			
White	53	NA	63
Black	NA	48	16
Asian	32	NA	14
Others	15 [†]	NA	7
BMI, kg/m ²	29	30	
Aetiology of renal disease, %		NA	
Diabetes	39		45
Hypertension	14 [*]		19
Glomerulonephritis	13		25
Polycystic kidney disease	7		4 [§]
Others	27		7 [¶]
Co-morbidities			
Diabetes mellitus, %	46	48	53
Hypertension, %	NA	NA	86
Systolic/diastolic BP, mmHg	146/82	141/79	NA
Ischaemic heart disease, %	8	48	34
Congestive heart disease, %	4	NA	20
Current or former smoking	51	20 ^{††}	55
Access location, %			
Lower arm	61	54	56

Upper arm	39	46	39
Leg	0	0	5

Mean values averaged for placebo and treatment arms, respectively.

†includes Aboriginal, Torres Strait Islander and Maori & Pacific Islander and others

*includes hypertensive and vascular

§includes cystic and other hereditary disorders

¶includes tubulointerstitial disorders and other/unknown

††includes only current smokers

Abbreviations: BP – blood pressure; DHA - docosahexaenoic acid; EPA - eicosapentaenoic acid; FAVOURED indicates The omega-3 fatty acids (Fish oils) and Aspirin in Vascular access Outcomes in Renal Disease; FISH indicates Fish oil Inhibition of Stenosis in Haemodialysis grafts; NA – not assessed.