Practice Reimbursement
Participating practices will be paid a per-patient fee that will cover the initial practice database search and patient check, and any lab costs incurred as a result of the consent clinics.

INTERESTED?

If you would like more information about the ATTACK study please contact us. We will be happy to answer any questions you may have.

Jennifer Dumbleton
ATTACK Central Trial Office
Nottingham Digestive Diseases Centre (NDDC)
E Floor, West Block
University Hospital
Nottingham NG7 2UH

Chief Investigators:
Prof Hugh Gallagher (Consultant Nephrologist)
Prof Paul Roderick (Prof of Public Health)

UK Trial Manager:
Jennifer Dumbleton
☏ 0115 823 1053
✉ jennifer.dumbleton@nottingham.ac.uk

Regional Principal Investigators:
Prof Mike Moore (Southampton)
Prof David Fitzmaurice (Warwick)
Prof Ahmet Fuat (Newcastle-upon-Tyne)

This project is funded by the NIHR HTA Programme (16/31/127) and the British Heart Foundation.

ATTACK

IRAS ID: 228831
Sponsor ID: 31844

ASPIRIN TO TARGET ARTERIAL EVENTS IN CHRONIC KIDNEY DISEASE (ATTACK)

ATTACK is a pragmatic multicentre open-label randomised controlled trial to determine whether the addition of low-dose aspirin to usual care reduces the risk of major vascular events in people with chronic kidney disease (CKD) who do not have pre-existing cardiovascular disease (CVD).

Background

CKD is a common condition and major risk factor for cardiovascular disease; CVD is the commonest adverse outcome in CKD. Data on primary prevention of CVD with aspirin in people with CKD are limited and inconclusive, and benefit must be balanced against the risk of harm from bleeding which increases with worsening kidney function. NICE have therefore made a research recommendation for a definitive trial in CKD patients.

CKD is defined as any abnormality of kidney function or structure with implications for health that is present for more than three months. It is classified according to the estimated glomerular filtration rate (eGFR) and urine albumin:creatinine ratio (ACR). The presence of an eGFR<60mL/min/1.73m^2 or an ACR>3mg/mmol for more than 90 days is diagnostic of CKD.

CKD is common, particularly in older people; the prevalence of CKD is estimated at 12-13% of UK adults. An important minority of people with CKD will develop end-stage renal disease, but the greatest significance of CKD is as a powerful and potentially modifiable risk factor for CVD. People with CKD are categorised as being at moderate risk, high risk, or very high risk of cardiovascular disease according to the level of both eGFR and ACR.

eGFR (ml/min/1.73m^2)	**ACR (mg/mmol)**			
	<1	**1-2.9**	**3-29.9**	**≥30**
≥105	0.93	1.33	2.46	2.69
90-104		1.63	1.82	4.77
75-89	1.03	1.48	1.73	4.01
60-74	1.09	1.58	2.18	4.23
45-59	1.52	2.38	3.13	4.97
30-44	2.40	3.07	4.12	6.10
15-29	13.51	7.99	5.6	9.49

Pooled estimates of adjusted hazard ratios for cardiovascular mortality according to categories of eGFR and ACR

There is good evidence in the general population that antiplatelet drugs such as aspirin reduce the risk of major vascular events in patients with pre-existing CVD. In lower risk patients without a history of CVD however, the benefits of aspirin are balanced by an increased risk of bleeding.

As the absolute risk of CVD rises both the benefits and bleeding complications of aspirin increase, with the benefits often exceeding the risks in people with an estimated risk of CVD above 1% per year. In CKD however, it is not clear to what extent any benefits may be offset because people with CKD are also at increased risk of bleeding. There is currently insufficient evidence to recommend the use or avoidance of aspirin for the primary prevention of CVD in CKD.

The burden of CVD in CKD is substantial. Overall CVD is responsible for about one-third of all deaths in the UK. It can have a serious impact upon quality of life and cause considerable disability. Our understanding of how to reduce cardiovascular risk in CKD is limited. The results of this trial, whether positive or negative, will provide the evidence to improve clinical outcomes in large numbers of people.

A positive result from this trial would imply that aspirin should be offered to more than 3 million additional people in the UK (excluding those with a contraindication or taking over the counter). If use of aspirin for primary prevention of CVD in people with CKD results in a reduction of 12.5% in the relative risk of CVD, 50,000 additional major vascular events over five years may be prevented in this group. Conversely a negative trial result would provide definitive evidence to stop aspirin in 1 million people who are now taking it for primary prevention.

Trial objectives

The **primary objective** of the trial is to test the hypothesis that low-dose (75 mg non-enteric coated) aspirin reduces the risk of major vascular events in people with CKD who do not have pre-existing CVD.

Patient Recruitment

Patients aged 18 or more with diagnosed CKD will be identified using an automated search of the computer databases of participating GP practices. Patients deemed suitable by their GP and who agree to take part, will be seen by trained CRN or practice nurses at their local GP surgery. The nurses will provide information about the trial, obtain informed consent from the patient, perform a brief health check and obtain blood and urine samples for eGFR and ACR analysis, and baseline haemoglobin. Consenting patients whose screening tests confirm the presence of CKD will be randomised 1:1 to aspirin vs usual care.

Patient Follow-up

Patients will be followed up until 1,827 cardiovascular events have accrued. There will be no face-to-face follow-up visits but patients will be asked to inform their Regional Trial Centre following any hospital admission or change of GP or address. They will also carry a

trial participant ID card which asks admitting hospitals to inform the Regional Centre of admissions. We will contact patients on an annual basis with a brief questionnaire to collect information regarding any hospitalisations they have experienced in the previous year or any cardiovascular or bleeding events.

The trial database will be updated daily by automated interrogation of GP records to identify any hospital admissions, as well as current health and prescribing information. GPs will add an alert to each patient's electronic record to allow easy identification of trial participants.

Pilot Study
An internal pilot study will be conducted during the first 27 months of the trial to assess practice and patient recruitment rates, safety, withdrawal rates and general trial procedures.

Trial Organisation
The Study is sponsored by the University of Southampton.
The trial will initially take place in three geographical areas, the South, the Midlands and the North. The Principal Investigators will be based in Southampton, Warwick and Newcastle-upon-Tyne, and the UK Trial Manager is based in Nottingham.
We are aiming over 3.5 years recruitment to get 25,210 randomised patients. We anticipate an average of 350-400 eligible patients per GP practice and are looking to invite over 195,000 patients to participate. This means that we will need to recruit over 500 GP practices.

To recruit this number of patients we will be assisted by the research networks in England, led by Wessex CRN but:

WE NEED YOUR HELP!