# Vitamin K therapy to improve vascular health in patients with chronic kidney disease

Submission date 12/02/2015	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered		
		[_] Protocol		
<b>Registration date</b> 24/02/2015	<b>Overall study status</b> Completed	Statistical analysis plan		
		[X] Results		
Last Edited 24/08/2020	<b>Condition category</b> Urological and Genital Diseases	Individual participant data		

## Plain English summary of protocol

Background and study aims

Chronic kidney disease is a long-term medical condition where the kidneys do work properly. It is a common disease, and particularly so in older people. Kidney problems affect the kidney, and also the health of blood vessels and the heart, leading to an increased risk of heart disease or strokes. Kidney problems lead to blood vessels becoming stiffer than usual, due to a build-up of calcium in the wall of the blood vessel. So finding ways to stop or reverse this stiffening of the blood vessels is really important, and we don't have good treatments for this problem at the moment. Some recent research suggests that vitamin K—a vitamin present in vegetables and dairy foods—might be able to slow down or stop this build-up of calcium in blood vessels. Before we can recommend this as a treatment though, it is important that giving extra vitamin K is tested properly in controlled trials such as this one.

Who can participate?

Patients with chronic kidney disease (stages 3b and 4 - so does not include those on dialysis)

#### What does the study involve?

Participants are randomly allocated into one of two groups. One group takes 400mcg of vitamin K once a day. The other group takes a placebo once a day. Each participant is asked to go to their study centre first for a screening visit, to see whether they are suitable for the study. They then visit the centre a further three times – at the start of the study, 6 months later and, finally, 12 months later. They undergo a number of tests during these visits including blood pressure measurements when lying down and when stood up, walking speed, strength and balance tests and an x-ray of their abdomen. Investigators also take samples of blood and ask participants to provide a urine sample. A small pencil-like device is also placed over the blood vessel of each participant to measure their pulse to test how stiff their blood vessels are. The electrical activity of their heart is also monitored with a heart tracing. At the end of each visit, participants are asked to take home a diary to record any falls they might have over the next six months. They are also given a blood pressure cuff to wear for the next 24 hours and a supply of the study medication they have been allocated to receive.

What are the possible benefits and risks of participating? This dose of vitamin K has been used before and is known to be safe but as with all medications there is a small possibility of side effects. These can include sickness, diarrhoea and dizziness. Having blood taken can cause some bruising. The blood pressure cuff causes mild discomfort to some people. We allow participants to have plenty of rest in between the walking and strength tests so that they are not made overly tired by the tests.

Where is the study run from? University of Dundee and the University of Glasgow, Scotland (UK)

When is the study starting and how long is it expected to run for? June 2015 to August 2017

Who is funding the study? The British Heart Foundation (UK)

Who is the main contact? Dr Miles Witham m.witham@dundee.ac.uk

# **Contact information**

**Type(s)** Public

**Contact name** Dr Miles Witham

#### **Contact details**

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**Type(s)** Scientific

**Contact name** Dr Miles Witham

#### **Contact details**

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# Additional identifiers

### EudraCT/CTIS number

## IRAS number

ClinicalTrials.gov number

Secondary identifying numbers 2014CV03

# Study information

## Scientific Title

Vitamin K therapy to improve vascular health in patients with chronic kidney disease: a randomised controlled trial

#### Acronym

K4Kidneys

#### **Study objectives**

That 1 year of vitamin K2 supplementation (400mcg per day) improves pulse wave velocity compared to placebo in patients with CKD stages 3b and 4

**Ethics approval required** Old ethics approval format

**Ethics approval(s)** East of Scotland Research Ethics Committee, 16/06/2015, approval number: 15/ES/0085

**Study design** Two-centre parallel-group placebo-controlled randomised trial

**Primary study design** Interventional

**Secondary study design** Randomised controlled trial

**Study setting(s)** Other

**Study type(s)** Treatment

**Participant information sheet** Not available in web format; please use contact details to request a patient information sheet

#### Health condition(s) or problem(s) studied Chronic kidney disease stages 3b and 4

#### Interventions

400 mcg once daily oral vitamin K2 (MK7 subtype) vs matching placebo

#### Intervention Type

Supplement

#### Primary outcome measure

Between-group difference in carotid-femoral pulse wave velocity (PWV) at 12 months using the Sphygmocor system

#### Secondary outcome measures

All measured at 0,6 and 12 months except for aortic radiography:

- 1. Vascular health:
- 1.1. Office and 24 hour blood pressure
- 1.2. B-type natriuretic peptide
- 1.3. Central systolic blood pressure and augmentation index derived from applanation
- tonometry at the radial artery using the Sphygmocor system.
- 1.4. Pulse wave velocity at 6 months (in addition to the primary outcome measured at 12 months)
- 2. Insulin and glucose levels to calculate insulin resistance using HOMA-IR
- 3. Marker of effect of vitamin K: dp-ucMGP levels.
- 4. Calcium and bone metabolism and turnover:
- 4.1. Osteocalcin
- 4.2. Tartrate resistant acid phosphatase-5b
- 4.3. Parathyroid hormone
- 4.4. Fetuin
- 4.5. Fibroblast growth factor-23
- 4.6. 25-hydroxyvitamin D
- 4.7. 1,25-hydroxyvitamin D

5. Renal function: We will measure serum creatinine, and urinary protein/creatinine ratio on a spot urine sample at each timepoint

6. Radiological calcification: We will perform lateral abdominal radiography at baseline and 12 months to assess aortic calcification.

7. Physical function:

- 7.1. Short physical performance battery
- 7.2 Grip strength at each timepoint
- 7.3. Monthly falls diary to prospectively record falls

#### Overall study start date

01/06/2015

#### **Completion date**

31/03/2019

# Eligibility

#### Key inclusion criteria

1. Age >18 years

2. CKD stages 3b or 4 (eGFR of >15 ml/min and <45 ml/min by MDRD4 equation)

## Participant type(s)

Patient

## Age group

Adult

Lower age limit 18 Years

Sex

Both

**Target number of participants** 166

Total final enrolment

159

#### Key exclusion criteria

1. Atrial fibrillation

- 2. Taking warfarin (which antagonises vitamin K) or other coumadin derivatives.
- 3. Taking vitamin K
- 4. Unable to give written informed consent
- 5. Currently enrolled in another trial, or within 30 days of completing another trial
- 6. Pregnant or (if female and pre-menopausal) not using reliable contraception

#### Date of first enrolment

01/06/2015

## Date of final enrolment

31/05/2016

# Locations

**Countries of recruitment** Scotland

United Kingdom

Study participating centre Ninewells Hospital and Medical School Ageing and Health Division of Medicine and Therapeutics Ninewells Avenue Dundee United Kingdom DD1 9SY **Study participating centre University of Glasgow** Institute of Cardiovascular and Medical Sciences Glasgow United Kingdom G12 8TA

## Sponsor information

**Organisation** Tayside Academic Science Centre (NHS Tayside and University of Dundee)

**Sponsor details** TASC, Level 3, Ninewells Hospital Dundee Scotland United Kingdom DD1 9SY 01382 383900 tasctayside@nhs.net

**Sponsor type** University/education

Website http://www.ahspartnership.org.uk/

ROR https://ror.org/049x86d03

# Funder(s)

**Funder type** Research organisation

**Funder Name** British Heart Foundation

Alternative Name(s) the\_bhf, The British Heart Foundation, BHF

**Funding Body Type** Private sector organisation

#### Funding Body Subtype

Trusts, charities, foundations (both public and private)

**Location** United Kingdom

## **Results and Publications**

#### Publication and dissemination plan

To be confirmed at a later date

#### Intention to publish date

30/09/2019

#### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Anonymised, individual-participant data from the current study will be available to bona-fide researchers upon request from Professor Miles Witham (Miles.Witham@newcastle.ac.uk), subject to submission of a data access request outlining the planned analysis, purpose of the analysis, data required and publication plan, and subject to approval by the Sponsor

#### IPD sharing plan summary

Available on request

Study outputs					
Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	results	27/09/2019	27/09/2019	No	No
Results article		01/10/2020	24/08/2020	Yes	No
HRA research summary			28/06/2023	No	No