

# Influence of age on response to new generation blood-thinning medicines

<b>Submission date</b> 10/05/2016	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 20/05/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 22/08/2022	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Current plain English summary as of 21/09/2020:

### Background and study aims

Oral anticoagulant (blood-thinning) drugs are very useful for treating and preventing blood clots. However, with them comes a risk of bleeding if the blood gets too "thin" (too slow to clot). Currently, warfarin is the most commonly used drug for treating/preventing blood clots, however dosages must be closely monitored as it can cause several severe side effects, such as making people more prone to bleeding. A new generation of anticoagulant drugs has become available which are believed to be safer than warfarin. It is already known that older people, who are normally frailer and have other concurrent diseases, are very sensitive to the blood-thinning effect of warfarin. However, it is unknown whether these people would also more sensitive to the new drugs. This study is looking at whether the blood-thinning activity of a new drug (rivaroxaban) is influenced by age.

### Who can participate?

Thirty patients over the age of 65 and thirty patients under the age of 65 who are healthy.

### What does the study involve?

A sample of blood is then taken through a vein which is tested in the laboratory for how much clotting factor is present (proteins that control bleeding) so that the clotting time between the two groups of patients can be compared.

### What are the possible benefits and risks of participating?

There are no direct benefits involved for those taking part in this study. There is a small risk of pain, bruising or bleeding during and after blood samples are taken.

### Where is the study run from?

Royal Victoria Infirmary (Newcastle)

### When is the study starting and how long is it expected to run for?

September 2013 to April 2018

Who is funding the study?  
NIHR Newcastle Biomedical Research Centre (UK)

Who is the main contact?  
Professor Farhad Kamali  
farhad.kamali@ncl.ac.uk

Previous plain English summary:

Background and study aims

Oral anticoagulant (blood-thinning) drugs are very useful for treating and preventing blood clots. However, with them comes a risk of bleeding if the blood gets too "thin" (too slow to clot). Currently, warfarin is the most commonly used drug for treating/preventing blood clots, however, dosages must be closely monitored as it can cause several severe side effects, such as making people more prone to bleeding. A new generation of anticoagulant drugs has become available which are believed to be safer than warfarin. It is already known that people who eat little vitamin K (a vitamin mainly found in green leafy vegetables which plays a key role in blood clotting), are very sensitive to the blood-thinning effect of warfarin. However, it is unknown whether these people would also more sensitive to the new drugs. Tests in animals have shown that those with little vitamin K in their diets were more sensitive to the new drugs, however as yet, no one has checked whether this is the same in humans. This study is looking at whether the blood-thinning activity of two new drugs (dabigatran and rivaroxaban) is influenced by how much vitamin K we eat.

Who can participate?

Thirty patients over the age of 65 suspected of even little vitamin K and thirty patients under the age of 65 with healthy, balanced diets.

What does the study involve?

All participants are asked to complete a questionnaire about the foods that they have eaten over the last week. A sample of blood is then taken through a vein which is tested in the laboratory for vitamin K levels and how much clotting factor is present (proteins that control bleeding) so that the clotting time between the two groups of patients can be compared.

What are the possible benefits and risks of participating?

There are no direct benefits involved for those taking part in this study. There is a small risk of pain, bruising or bleeding during and after blood samples are taken.

Where is the study run from?

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When is the study starting and how long is it expected to run for?

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Who is the main contact?

Professor Farhad Kamali  
farhad.kamali@ncl.ac.uk

**Contact information**

**Type(s)**  
Scientific

**Contact name**  
Prof Farhad Kamali

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## **Additional identifiers**

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
2.0

## **Study information**

**Scientific Title**  
Investigation of the effect of age on anticoagulant response to novel oral anticoagulants (direct thrombin inhibitors and FXa inhibitors) ex-vivo

**Acronym**  
KOALA

**Study objectives**  
Current study hypothesis as of 21/09/2020:  
Age enhances anticoagulation response to a new generation of oral anticoagulants.

Previous study hypothesis:  
Vitamin K deficiency enhances anticoagulation response to a new generation of oral anticoagulants.

**Ethics approval required**  
Old ethics approval format

**Ethics approval(s)**

**Study design**

Single-centre observational cohort study

**Primary study design**

Observational

**Secondary study design**

Cohort study

**Study setting(s)**

Hospital

**Study type(s)**

Other

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet.

**Health condition(s) or problem(s) studied**

Anticoagulation response

**Interventions**

Current interventions as of 21/09/2020:

The study will recruit 30 elderly inpatients not on warfarin and 30 young medically stable subjects not on warfarin.

A sample of 20 ml fasting venous blood is then taken for later laboratory tests. Activated partial thromboplastin time (aPTT), prothrombin time (PT) and modified PT will be measured in plasma incubated with rivaroxaban (100-500 ng/ml). The kinetics of thrombin formation in plasma in the presence of drug will be determined using the endogenous thrombin potential (ETP) test.

Previous interventions:

The study will recruit 30 subjects suspected of low dietary vitamin K intake (elderly inpatients not on warfarin), 30 elderly medically stable subjects (inpatients not on warfarin) with healthy diets, and 30 healthy younger subjects with adequate dietary vitamin K intake.

All subjects will complete a validated simple questionnaire (FFQ) which records their food intake of vitamin K containing foods on average and over the past week. A sample of 20 ml fasting venous blood is then taken for later laboratory tests Plasma fasting vitamin K levels will be measured as an indication of subjects' dietary status. Activated partial thromboplastin time (aPTT), prothrombin time (PT) and modified PT will be measured in plasma incubated with rivaroxaban (100-500ng/ml). The kinetics of thrombin formation in plasma in the presence of drug will be determined using the endogenous thrombin potential (ETP) test.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Rivaroxaban

**Primary outcome measure**

Clotting time

**Secondary outcome measures**

No secondary outcome measures

**Overall study start date**

01/09/2013

**Completion date**

01/04/2018

## **Eligibility**

**Key inclusion criteria**

Current inclusion criteria as of 21/09/2020:

Older subjects:

1. >65 years old
2. Medically stable
3. Without liver dysfunction
4. Able to give informed consent

Younger subjects:

1. <65 years of age
2. Healthy

Previous inclusion criteria:

Older subjects:

1. >65 years old
2. Medically stable
3. Without liver dysfunction
4. Able to give informed consent
5. Suspected of vitamin K deficiency as evaluated by the use of dietary questionnaire

Younger subjects:

1. <65 years of age
2. Healthy
3. Having a normal healthy diet as evaluated by the dietary questionnaire

**Participant type(s)**

Mixed

**Age group**

Adult

**Sex**

Both

**Target number of participants**

60

**Total final enrolment**

66

**Key exclusion criteria**

1. Less than 18 years of age
2. Liver dysfunction
3. Receiving anticoagulation therapy

**Date of first enrolment**

01/10/2013

**Date of final enrolment**

01/10/2016

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Royal Victoria Infirmary**

Victoria Road

Newcastle upon Tyne

United Kingdom

NE1 4LP

## **Sponsor information**

**Organisation**

Newcastle upon Tyne Hospitals Foundation Trust

**Sponsor details**

Royal Victoria Infirmary

Newcastle upon Tyne

England

United Kingdom

NE1 7RU

**Sponsor type**

Hospital/treatment centre

**Website**

[www.newcastlejro.org.uk](http://www.newcastlejro.org.uk)

**ROR**

<https://ror.org/05p40t847>

## **Funder(s)**

**Funder type**

Government

**Funder Name**

NIHR Newcastle Biomedical Research Centre

## **Results and Publications**

**Publication and dissemination plan**

Research output (publications, conferences and presentations), and educational materials for patients and health professionals involved in anti-coagulation management, including GPs and hospital doctors.

**Intention to publish date**

31/12/2020

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

The datasets generated during and/or analysed during the current study are/will be available upon request from Farhad Kamali ([farhad.kamali@ncl.ac.uk](mailto:farhad.kamali@ncl.ac.uk)).

Type of data: continuous data of haematological assay results and subject demographics.

When the data will become available and for how long: data may be available upon request after the publication of the study and without limit in the length of time after publication.

By what access criteria data will be shared including with whom: access will be granted at the discretion of the principal investigator detailed above upon request via email, only if it is impossible to acquire the data from the publicly available report and on the basis of the reason for the request and the expected use of the data. No publication of the data should occur and data should not be shared with anyone else without the consent of the principal investigator. For what types of analyses, and by what mechanism: any types of analysis can be agreed in advance with the principal investigator to determine the minimum amount of data that should be shared.

Whether consent from participants was obtained: participants have consented for their data to be used for data analysis and anonymous publication of the results.

Comments on data anonymisation: data have been manually anonymised and as such may be provided at the discretion of the principal investigator.

Any ethical or legal restrictions: the principal investigator may refuse to provide the data in case their expected use is against the sponsor's requirements, or if there are any other restrictions.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>		21/09/2020	21/09/2020	No	No
<a href="#">Results article</a>		17/10/2021	22/08/2022	Yes	No