ISRCTN47414943 https://doi.org/10.1186/ISRCTN47414943

Are vitamins B12 causally related to cardiometabolic risk factors and disease?

Submission date 15/11/2017	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 17/11/2017	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 10/07/2018	**Condition category** Circulatory System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Low serum levels of vitamin B12 (vB12) have been associated with increased body mass index (BMI) and with increased cardiometabolic outcomes (risk of having diabetes, heart disease or stroke) in several studies. However, it is unclear what the relationship is between vB12 to cardiometabolic risk factors and diseases. This study aims to investigate if there is a relationship between vB12 and indicators of body fat, lipid and glucose (sugar) levels, type 2 diabetes (a condition where blood sugar levels become uncontrolled) and cardiovascular disease (diseases that involve the heart or blood vessels).

Who can participate?
Those who have participants in a previous genome-wide association study (GWAS)

What does the study involve?
This study uses information from a previous genome-wide associate study (GWAS). The researchers take information about serum levels of vB12. The researchers analyse the relationship between vB12 and cardiometabolic risk factors and diseases using publicly available GWAS summary statistics for 15 outcomes.

What are the possible benefits and risks of participating?
There are no benefits or risks of participation

Where is the study run from?
Oslo University Hospital (Norway)

When is the study starting and how long is it expected to run for?
March 2017 to October 2017

Who is funding the study?
Southern and Eastern Norway Regional Health Authority (Norway)

Who is the main contact?
Ms Gunn-Helen Moen
g.h.o.moen@studmed.uio.no

Contact information

Type(s)
Scientific

Contact name
Ms Gunn-Helen Moen

ORCID ID
https://orcid.org/0000-0002-8768-0904

Contact details
Oslo University Hospital
Oslo Universitetssykehus, Aker
Trondheimsveien 235
Oslo
Norway
0586
+47 (0)480 20554
g.h.o.moen@studmed.uio.no

Additional identifiers

Protocol serial number
123

Study information

Scientific Title
Are serum levels of vitamin B12 causally related to cardiometabolic risk factors and disease? A Mendelian randomisation study

Study objectives
Is there a causal relationship between vB12 and indicators of body fat, lipid- and glucose parameters, T2D and cardiovascular disease?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Each of the studies used in this project have their own ethical approval and only publicly available data is used

Study design

Observational cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
The effect of vitamin B12 on cardiometabolic outcomes

Interventions
11 single nucleotide polymorphisms (SNPs) robustly associated with serum levels of vB12 in a previous genome-wide association study (GWAS) of 45 576 individuals are selected. We performed two sample MR analyses of the relationship between vB12 and cardiometabolic risk factors and diseases using publicly available GWAS summary statistics for 15 outcomes in up to 339224 individuals. Robustness of results is tested with sensitivity analyses using MR Egger regression and Weighted Median estimation, and by performing additional analyses excluding a variant in the FUT2 gene which may be pleiotropic.

This data is taken from publically available summary statistics – which means information regarding genotype/SNP, effect SNP, effect size, standard error, p-values, minor allele frequency etc that is available online.

Summary results statistics on the same SNPs from 15 different GWAS of cardiometabolic outcomes are also taken. The cardiometabolic outcomes are selected on the basis of the following inclusion criteria: the outcome having been associated with vB12 level in observational epidemiological studies and the availability of large meta-GWAS analyses with publicly available summary statistics on the outcome.

Intervention Type
Genetic

Primary outcome(s)
1. Fasting glucose is measured using genetic data from available GWAS
2. Fasting blood insulin is measured using genetic data from available GWAS
3. HOMA-IR is measured using genetic data from available GWAS
4. HOMA-B is measured using genetic data from available GWAS
5. HbA1c is measured using genetic data from available GWAS
6. Total cholesterol is measured using genetic data from available GWAS
7. LDL cholesterol is measured using genetic data from available GWAS
8. HDL cholesterol is measured using genetic data from available GWAS
9. Triglycerides is measured using genetic data from available GWAS
10. BMI is measured using genetic data from available GWAS
11. Waist-hip ratio is measured using genetic data from available GWAS
12. Leptin is measured using genetic data from available GWAS
13. Body fat is measured using genetic data from available GWAS
14. Coronary artery disease is measured using genetic data from available GWAS
15. Type 2 diabetes is measured using genetic data from available GWAS

Key secondary outcome(s))

There are no secondary outcome measures

Completion date
15/10/2017

Eligibility

Key inclusion criteria
Participants in the previous genome-wide association study (GWAS)

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
There is no participant exclusion criteria

Date of first enrolment
15/04/2017

Date of final enrolment
29/07/2017

Locations

Countries of recruitment
Norway

Study participating centre
Oslo University Hospital
Oslo Universitetssykehus, Aker
Trondheimsveien 235
Oslo
Norway
0478

Sponsor information

Organisation
Oslo University Hospital

ROR
https://ror.org/00j9c2840

Funder(s)

Funder type
Government

Funder Name
Helse Sør-Øst RHF

Alternative Name(s)
South-Eastern Norway Regional Health Authority, Southern and Eastern Norway Regional Health Authority, helsesorost, Helse Sør-Øst RHF, helse-sor-ost-rhf, HSØ RHF - South-Eastern Norway Regional Health Authority, sorost

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Norway

Results and Publications

Individual participant data (IPD) sharing plan
All data are already publically available. The trialists will include a protocol of how they extracted the data in the publication.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2018		Yes	No