Towards HOMe-based Albuminuria Screening: an implementation study testing two approaches

Published: 21-06-2019
Last updated: 16-11-2024

Primary Objective: To investigate whether population screening for increased albuminuria among the Dutch population can contribute to the early detection of yet undiagnosed risk factors for renal and cardiovascular diseases in an early stage. For...

Ethical review	Approved WMO
Status	Completed
Health condition type	Coronary artery disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50434

Source
ToetsingOnline

Brief title
Towards HOMe-based Albuminuria Screening

Condition

- Coronary artery disorders
- Nephropathies
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Cardiovasular disease, kidney disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: E-Zorg B.V: een dochterbedrijf van KPN, biedt een van de grootste ISO27001- en NEN7510-gecertificeerde particuliere netwerken voor de gezondheidszorg in Nederland. In het huidige project zal E-Zorg de data-infrastructuur en datatransport verzorgen.,Healthy.io Ltd: een Israëlische start-up, die een urine-analysesysteem heeft ontwikkeld voor de diagnose van ziektes, urineweginfecties en zwangerschapscomplicaties. Een test die thuis uitgevoerd kan worden met behulp van een dipstick en een smartphone camera. Voor het huidige project zal Healthy.io hun technologie aanpassen om zo een semi-kwantitatieve analyse van lage niveaus van albuminurie en creatinine mogelijk te maken (ACR | EU-kit).,Topsector Life Sciences & Nutrition (Ministerie van Economische Zaken) en de Nierstichting

Intervention

Keyword: Albuminuria, Cardiovascular disease, Population screening, Renal disease

Outcome measures

Primary outcome

* Participation rate of the two different screening techniques (PeeSpot vs. ACR

| EU).

* Yield of albuminuria screening from both screening methods (PeeSpot vs. ACR |

EU):

- number of subjects with elevated albuminuria,

- number of subjects with elevated albuminuria and with newly diagnosed

risk factors including hypertension, diabetes, hypercholesterolemia, and

impaired kidney function)

Secondary outcome

* Completion rate of the study: number of persons completing the study (ACR

testing, elaborate screening when invited) relative to the number of all

invited persons in the corresponding arm.

* Completion and GP follow-up rate study: the number of persons completing the study (ACR testing, elaborate screening when invited, and visiting GP when recommended) relative to the number of all invited persons in the corresponding arm).

* Usability of the two different screening techniques (PeeSpot vs. ACR | EU):
- User preference: does the participant prefer doing this urine test (either PeeSpot or ACR | EU test) at home or does the participant prefer going to the doctor's office and doing a standard urine test (urinate in cup) there.
- Satisfaction rank: how likely is it that the participant would recommend this test to other for urine testing (5-points Likert scale question: very likely / likely / neutral / unlikely / very unlikely).
- Percentage that described the process as easy (5-points Likert scale question: very easy / easy / neutral / difficult / very difficult).
- Usability success: measured as share or people that tried to do a test that actually succeeded.

* Characteristics of the participants of the two different screening methods (PeeSpot vs. ACR | EU) including differences in age, sex, social economic status, medication use, and history of disease.

* Incremental cost-effectiveness ratio (ICER) in euro per QALY gained for both screening methods (PeeSpot vs. ACR | EU).

* The differences in rate of previously undiagnosed risk factors (hypertension, diabetes, hypercholesterolemia, and impaired kidney function) that were found at the elaborate screening between subjects who have albuminuria and subjects without albuminuria.

Study description

Background summary

Chronic Kidney Disease is a worldwide major public health problem that is associated with an increased incidence of kidney failure resulting in dialysis and/or transplantation, and also an increased risk of cardiovascular events, both accompanied by high costs for society. Symptoms of Chronic Kidney Disease become present only when kidney function drops to below 30%. At that time preventive measures will have only limited efficacy. However, protein excretion in the urine has increasingly been recognized as early marker kidney damage, but it is also associated with the presence of a high blood pressure, diabetes, and/or high cholesterol levels, which are all important risk factors for kidney and cardiovascular disease. Importantly, the prevalence of undiagnosed cardiovascular and kidney risk factors in the Dutch general population is higher than the prevalence of known risk factors. Population screening for urinary protein loss could therefore detect a considerable number of subjects with yet unknown risk factors for progressive kidney and cardiovascular disease who can benefit of early intervention. However, it unclear whether the Dutch population is willing to participate a population screening, which method is suitable for large-scale screening and whether such a screening is cost-effective.

Study objective

Primary Objective:
To investigate whether population screening for increased albuminuria among the Dutch population can contribute to the early detection of yet undiagnosed risk factors for renal and cardiovascular diseases in an early stage. For this, we will investigate:
1. The participation rate of the screening;
2. The yield of albuminuria screening (number of subjects with elevated albuminuria [ACR >30 mg/g] and with newly diagnosed risk factors including hypertension, diabetes, hypercholesterolemia, and impaired kidney function), and;
3. To evaluate the cost-effectiveness of albuminuria screening and compare this

to standard of care.

Secondary Objectives:
1.To assess differences in participation rate, yield, and cost-effectiveness between the two different screening methods (PeeSpot test vs. ACR | EU test).
2.To asses the characteristics of the participants, including differences in age, sex, educational level, estimated social economic status, medication use, and history and presence of disease (obtained by a questionnaire);
3.To asses the characteristics of the non-responders, including differences in age, sex, and estimated social economic status (the latter is based on data of Statistics Netherlands, providing estimated social economic status based on postal codes);
4.To examine differences in characteristics of the responders and non-responders of the two different screening methods (PeeSpot vs. ACR | EU).
5.To assess the usability of the two different screening methods (PeeSpot vs. ACR | EU).
6. To examine the differences in rate of previously undiagnosed risk factors (hypertension, diabetes, hypercholesterolemia, and impaired kidney function) that were found at the elaborate screening between subjects who have albuminuria and subjects without albuminuria.

Study design

Observational study (with an invasive measurement in a small part of the participants)

Intervention

Subjects will be 1:1 randomized using a computer generated algorithm into group A or group B. Participants randomized to group A will receive the PeeSpot urine collection device (Hessels+Grob B.V., Deventer, The Netherlands; Hessels et al. 2011) (see Appendix D). This device consists of a holder containing a urine collection pad, which is an absorption felt containing a dried hygroscopic polymer. When subjects urinate on the pad (midstream urine), it can absorb 1.2 ml urine. The holder can be placed back into the tube and can be easily send to the laboratory by mail for measurement of albuminuria. Because of the dried preservative in the urine absorption felt, the urine has a preservation capacity of 4 days at room temperature. In the laboratory, the urine collecting device can be centrifuged to separate the urine from the pad, and albumin and creatinine can be measured. The results of the test will be sent to the participant by letter. If the test result is positive (which indicates elevated albuminuria), participants will be sent two extra tests for confirmation. When elevated albuminuria is confirmed (at least 1 out of the 2 confirmatory test in accordance with prevailing guidelines), the person in question will be referred for further screening for Chronic Kidney and CardioVascular Disease risk factors (hypertension, diabetes, hypercholesterolemia, impaired kidney

function) to the central screening facility.
Participants randomized to group B will receive the ACR | EU kit (see Appendix E), which consists of a urine test strip, a custom designed urine cup, a color calibrator, and instructions to download the Healthy.io application on their smartphone. For the test, subjects have to collect urine in the cup (midstream urine) and immerse and remove the urine test strip of which the chemical pads will change in color in response to the presence of albuminuria and creatinine. The stick is placed on the color calibrator and scanned with the application with the use of the flash light. Participants then enter the unique participant ID, printed on each kit into the app for anonymous identification. Healthy.io*s system automatically analyzes the semi-quantitative albumin and creatinine levels indicated on the stick and returns an albumin creatinine ratio and level (normal, abnormal, high abnormal). In case the test is positive (abnormal or high abnormal, which indicates elevated albuminuria), participants will be sent two extra tests for confirmation. When elevated albuminuria is confirmed (at least 1 out of the 2 confirmatory test in accordance with prevailing guidelines), the person in question will be invited for further screening for Chronic Kidney and CardioVascular Disease risk factors (hypertension, diabetes, hypercholesterolemia, impaired kidney function) to the central screening facility. When the participant does not perform the confirmatory tests, the participant will receive a push notification via the app as a reminder.

Study burden and risks

This is a study comparing two non-invasive screening techniques (PeeSpot and ACR | EU tests). The participants receive the test via mail and the test (both the Peespot and ACR | EU test) can be carried out at home. Clear instructions regarding the test will be included. When the participant tests positive for albuminuria, this should be confirmed with a confirmation test. The researcher will send an extra tests via the mail to the participant (the same test as the initial test). If this second test result is negative, a third test will be send for deciding the definitieve result. When at least one of these extra tests is also positive, so in total at least two out of two or three test, the participant will be invited to participate a one-time elaborate screening in the Amphia Hospital in Breda. Based on literature, we estimate that approximately 600 participants will be invited for this screening. In this screening, anthropometric measurements will be performed (height and weight), blood pressure will be measured, and blood will be drawn (venipuncture, 7 mL) for assessing traditional risk factors for cardiovascular and renal disease (including HbA1c, glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, and creatinine).

Furthermore, a subset of the participants will, at the end of the study receive a questionnaire including questions on demographics, educational level, disease history, medication use, quality of life, and usability of the screening test.

This subset of participants include: 1) all subjects with an overall positive test for albuminuria (at least 2 out of 3 ACR tests positive) invited to the elaborate screening 2) a subset of subjects with an initial negative ACR test who will be asked to perform a second and third test to examine the false-negative rates (N=500 for both arms) and 3) a subset of the false-negative subset with a second negative test that will be invited for the elaborate screening (N=200 for both arms). The questionnaire will contain questions regarding demographic variables (age, sex, ethnic background, educational level), history of disease (including the presence of albuminuria, hypertension, diabetes, hypercholesterolemia, and decreased renal function), and use of medication. The EuroQol 5D-5L, a standardized questionnaire that provides a score at five health levels (mobility, self-care, daily activities, pain/discomfort and anxiety/depression), whereby a weighted health index can be derived for an individual, will also be included in this questionnaire. Moreover, some questions will be asked about the usability of the urine test. Finally, data about the participants* GP and pharmacy will be asked (together with permission to contact the GP/pharmacy in context of the study in an additional informed consent).

A short questionnaire will be sent to non-responders (of the first 1250 invited participants from both groups). This questionnaire contains some questions about the reasons why people did not participate in the study.

Risks in this study are limited. There are several limitations to screening programs in general, including: 1) confrontation with an unfavorable result, 2) unnecessary anxiety in case of false-positive test results, and 3) unwarranted reassurance in case of false-negative results. We will try to limit these risks as much as possible, by for example the need for confirmation in case of any abnormal finding before action is taken. In case albuminuria is increased in the initial test, it has to be confirmed in at least one out of the two follow-up urine samples that are tested (for ACR | EU as well as for the PeeSpot method) which is in agreement with prevailing guidelines. Only in case there is confirmed increased albuminuria, subjects will be invited to have blood pressure, cholesterol, glucose, and kidney function measured at a screening facility. In case this screening shows any further abnormalities next to the increased albuminuria, patients will be referred to their general practitioner with an advice for confirmation (and potential treatment). In this way the percentage of subjects with false positive findings will be minimized. Moreover, treatment that is advised will be fully based on prevailing general practitioner guidelines (NHG Standaarden CardioVascular Risk Management and Chronic Kidney Disease) to avoid unnecessary treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Individuals aged 45-80 years
- Living in the region of Breda, the Netherlands

Exclusion criteria

- Individuals younger than 45 years or older than 80 years
- Not living in the region of Breda, the Netherlands

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-11-2019
Enrollment:	15032
Type:	Actual

Medical products/devices used

Generic name:	1) PeeSpot urine collection device and 2) ACR | EU test
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	21-06-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65228.042.18