Evaluation of a glaucoma genetic risk score through in-depth phenotyping of ocular traits in high and low genetic risk groups

Published: 31-01-2019
Last updated: 24-08-2024

To evaluate the performance of an optimized glaucoma genetic risk score (GRS) by inviting genotyped individuals from the population-based Lifelines cohort for in-depth ophthalmic examinations.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glaucoma and ocular hypertension
Study type	Observational non invasive

Summary

ID

NL-OMON48818

Source
ToetsingOnline

Brief title
Ocular Phenotyping in Lifelines Participants

Condition

- Glaucoma and ocular hypertension

Synonym
Optic neuropathy; glaucoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W,European Committee

Intervention

Keyword: epidemiology, genetic risk score, glaucoma, phenotyping

Outcome measures

Primary outcome

Presence/absence of glaucoma according to the ISGEO criteria.

Secondary outcome

NA

Study description

Background summary

Glaucoma is an adult-onset ocular disorder which can lead to irreversible blindness if not treated in time; this blindness is due to insidious destruction of the optic nerve as initial symptoms often go unnoticed (Janssen et al. 2013; Bailey et al. 2016). An accurate screening procedure to target at-risk individuals could be clinically valuable, as proactive treatment can slow the progression of this disorder. Currently no nationwide population-based screening program exists in the Netherlands for glaucoma, as it is not a cost-effective procedure currently due to the low prevalence of the disease, ~2% in Caucasians (Stoutenbeek et al. 2008). Tailoring glaucoma screening based on an individual*s genetic risk for the disorder has the capacity to find cases earlier, and the resultant early medical intervention could prolong eye health (Stoutenbeek and Jansonius 2006; de Vries et al. 2012). There are at least five causal genes as well as more than 68 genetic variants that have been identified as being linked to glaucoma in Caucasians - making this a classic example of a complex multifactorial disease (Janssen et al. 2013; Bailey et al. 2016). A glaucoma genetic risk score (GRS) can be applied to a sample, representative of the general population (i.e. the Lifelines genotyped cohort) to stratify individuals as high and low genetic risk for glaucoma (Klijs et al. 2015). The LifeLines genotyped cohort was not involved in any previous glaucoma gene finding (GWAS) or replication studies, thus is an ideal population to assess independently the feasibility to pre-screen based on a glaucoma GRS. Genotyped Lifelines participants identified with sufficiently high/low genetic risk for glaucoma will be invited to come in for an in-depth phenotyping of ocular traits and general eye health; they will not be made aware of their genetic

risk for glaucoma.The GRS will be evaluated via the OR of having glaucoma for the highest quintile of the GRS versus the lowest quintile. The phenotyping will occur within the UMCG and will be set up as a carousel of examinations performed by medical students who will be trained to have ocular examination skills.

Study objective

To evaluate the performance of an optimized glaucoma genetic risk score (GRS) by inviting genotyped individuals from the population-based Lifelines cohort for in-depth ophthalmic examinations.

Study design

cross-sectional, observational

Study burden and risks

Participants will have one visit to the laboratory of experimental ophthalmology (LEO) within the UMCG to undergo ocular phenotyping. The participants do not know their genetic risk, nor do those who assess the participants. The examinations are as follows: Visual acuity and refraction, non-contact eye pressure measurement, Frequency Doubling Technique (FDT) to test visual field, Optical Coherence Tomography (OCT) scan to image structural layers of the eye including cornea and retina, fundus photograph to image the fundus of the eye, and quantification of eye moisture levels. All of the proposed ocular examinations are non-invasive. If abnormal results are found with any examination (in case of perimetry only if also present on retest, which will be performed immediately), an on-site ophthalmologist will confirm/falsify the findings and discuss them with the participant. The participant will be referred to their GP if the disease status is confirmed by thorough review of all examination results by an ophthalmologist, otherwise he/she will be reassured. The total time required for the participants is approximately half an hour for reception and ocular examinations. There may be psychological stress if abnormal results are found. However, this is minimized through quick confirmation/falsification and explanation. Moreover, if glaucoma is found, participants will benefit from earlier treatment, which will preserve eye health for longer. Participants will benefit from a free in-depth ocular examination.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

55 years of age or older
Genotyped within the Lifelines cohort
Responded to the invitation letter
-Agreement to notify GP if abnormal results occur with the examination
Written informed consent

Exclusion criteria

Individuals under the age of 55
The informed consent was not provided
The participant is blind - cause is known and is not glaucoma

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2019
Enrollment:	1600
Type:	Actual

Ethics review

Approved WMO

Date:	31-01-2019
Application type:	First submission
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
Other	201800689

Register	ID
CCMO	NL65947.042.18