PARTICIPANT INFORMATION LEAFLET
(Please see below for Afrikaans)

Professionals' and patients' perspectives towards disclosing incidental findings of pleiotropic results

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You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you decline participation, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

This study will be conducted at the Faculty of Medicine and Health Sciences at Stellenbosch University. Staff members and students from this faculty, as well as those from the Faculty of Health Sciences at the University of Cape Town will be invited via email to participate in an online survey. Research participants from studies being conducted at the Stellenbosch University Psychiatry department will also be approached to participate.

This study aims to understand the different opinions that researchers, students, and research participants have towards incidental findings in genetics research. We would like to find out what the different attitudes and opinions are regarding the disclosure of incidental findings. We would also like to find out what types of incidental findings should or should not be returned. We also would like to know who should be disclosing these incidental findings to the participants.

We would like you to complete a 30 minute online survey. At the end of the survey you will be asked whether we can interview you about this topic. If you agree we will contact you for a short telephonic interview. Your identity will be kept confidential throughout the study. Identifying details will not be directly linked to the dataset.

Why have you been invited to participate?

You have been invited to participate because either you are a staff member/student at the Faculty of Health Sciences at Stellenbosch University or the University of Cape Town; or you have participated in a previous study at the Faculty of Health Sciences at Stellenbosch University.

What will your responsibilities be?

Please read this information leaflet completely and make sure you understand it before completing the survey. If you do not understand it, please ask one of the researchers to help you before continuing. Once you have finished reading this leaflet, please complete the online survey. The link to the survey was included in the email you received. Ensure that you understand all the questions and the implications of the questions fully. Please ask for help if you do not completely understand a question. Please take the time to complete the survey accurately, ensuring that you reflect your opinions and values. Please do not let you answers be influenced by anybody other than yourself. Do not answer questions based on what you think the researchers would want you to fill in. Please complete the full questionnaire. If you agree to the telephonic interview please provide your email address or telephone number so that we can contact you to arrange the interview.

Will you benefit from taking part in this research?

You will not benefit directly from this research. By completing the full questionnaire you will stand a chance to **win R1500** in a lucky draw. Furthermore, this research will help future participants in genetic research as it will help develop guidelines for disclosing incidental findings in this field.

Are there any risks involved in your taking part in this research?

We do not anticipate any risks in your taking part in this research.

If you do not agree to take part, what alternatives do you have?

If you choose not to participate, you will in no way be disadvantaged.

Will you be paid to take part in this study and are there any costs involved?

No, you will not be paid to take part in the study; however you will stand a chance at winning R1500 in a lucky draw. There will be no costs involved for you if you do take part.

Is there anything else that you should know or do?

You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by the study staff.

IMPORTANT INFORMATION ABOUT GENETICS RESEARCH

What are genes?

Genes are made up of DNA and serve as instruction manuals for our bodies. Each person has a unique genetic make-up. Genes help determine the traits or qualities of an individual. These traits can be physical (e.g. eye colour), mental (e.g. having a good memory), and psychological (e.g. how emotional you get).

Some genes can cause illnesses, like causing one's blood not to clot properly (haemophilia). Other genes can act as risk factors for possibly developing a disease. For example, certain genes can increase one's chances of developing breast cancer, but having these genes does not necessarily mean that you will definitely get breast cancer.

It is important to note that despite genes playing a large role in shaping a person, environmental factors also play a large role. For example, one person's genetic make-up will mean that they have the potential to develop breast cancer but they may never get breast cancer by avoiding risk factors like cigarette smoking. In another case a person may have very healthy genes but have a stroke despite these healthy genes, by living unhealthily and being severely overweight. This interplay between a person's genes and how they live in their environment is crucial to understanding the person's health effectively.

What is pleiotropy?

Genes are not always very simple. One gene does not always cause one specific trait. In some instances one trait is caused by many genes. More relevant to this study is where a single gene causes many different, seemingly unrelated traits. This is called **pleiotropy**.

A good example of pleiotropy is in the disease phenylketonuria (PKU). Here multiple systems are affected by the single gene causing many different traits and the resulting symptoms; e.g. seizures, albinism, and mental disability.

It is important to understand that this is not the same as a disease that has different symptoms in different systems, for example heart failure causes swelling of the legs, kidney failure or shortness of breath. All of these symptoms are caused by the inability of the heart to pump blood effectively. However, in PKU, that single gene causes many different traits that result in the symptoms.

What are incidental findings (IFs)?

Incidental findings (IFs) occur when a previously undiagnosed disease or condition is uncovered while looking for something different. They can occur during imaging investigations, autopsies, and more relevant to this study, during medical research and genetic testing.

While testing for the presence or absence of a specific gene, one might find another gene which could determine a specific trait that may or may not impact the participant's health.

Pleiotropic incidental findings occur when a gene is linked with a new trait or condition that was not initially looked for as part of the research. Genetic research can often involve looking at multiple genes, and some of these genes may be pleiotropic. When these genes, and their traits, are not looked for, it would mean a pleiotropic incidental finding. It is important to note that genetic research is constantly providing new information. New links between traits and genes are continuously being found.

Many factors could influence whether to disclose/reveal the incidental finding to the participant. The incidental finding may or may not be very significant, i.e. it's a minor condition. In another instance, there may not be anything that can be done about the finding; in this case the finding is not **clinically actionable**. If something can be done about the finding then it is clinically actionable. The age of the research participant is also a factor that should be considered. Some diseases may only develop in adulthood (adult onset), whilst others can already develop in childhood (childhood onset).

Now that you have read through the information leaflet, we would like to find out your opinion on the importance of the different factors that influence the return of incidental findings in genetic research. Please click on the link in the email to access the online survey. If you are using a university computer, remember to open your Inetkey.

Thank you in advance for your participation!

DEELNEMER INLIGTINGSBLAD

Professionele persone en pasiënte se perspektiewe aangaande die bekendmaking van toevallige bevindings van pleiotropiese resultate.

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U word uitgenooi om deel te neem aan 'n navorsingsprojek. Neem asseblief die tyd om die inligting wat hier aangebied word, wat die besonderhede van die projek sal verduidelik, te lees. Vra asseblief die studie personeel enige vrae wat u het oor enige deel van die projek wat u nie ten volle verstaan nie. Dit is baie belangrik dat u ten volle tevrede is sodat u duidelik verstaan wat hierdie navorsing behels en hoe u betrek word. U deelname is **heeltemal vrywillig** en u kan weier om deel te neem. As u verkies om nie deel te neem nie, sal dit geensins ‘n negatiewe invloed op u hê nie. U is ook vry om te onttrek van die studie op enige stadoi, selfs al stem u aanvanklik in om deel te neem.

Hierdie studie is deur die **Gesondheidnavorsingsetiekkomitee van die Universiteit van Stellenbosch** goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki, Suid-Afrikaanse riglyne vir Goeie Kliniese Praktyk en die Mediese Navorsingsraad (MNR) se Etiese Riglyne vir Navorsing.

Wat behels hierdie navorsing?

Hierdie studie sal plaas vind by die Fakulteit van Gesondheidswetenskappe by die Universiteit van Stellenbosch. Personeellede en studente van die fakulteit, sowel as dié van die Fakulteit Gesondheidswetenskappe by die Universiteit van Kaapstad, sal genooi word om per e-pos deel te neem in 'n aanlyn-opname. Navorsing deelnemers van studies wat gedoen word by die Universiteit Stellenbosch Psychiatriese departement sal ook genader word om deel te neem.

Hierdie studie het ten doel om die verskillende menings wat navorsers, student, en navorsing deelnemers teenoor toevallige bevindings in genetiese navorsing te verstaan. Ons wil graag uitvind wat die verskillende houdings en opinies is oor die bekendmaking van toevallige bevindings. Ons wil ook graag uitvind watter soort toevallige bevindings moet of moet nie terugbesorg word nie. Ons wil ook weet wie moet hierdie toevallige bevindings bekend maak aan die deelnemers.

Ons wil graag hê u moet 'n 30 minute aanlyn-opnamevoltooi. Aan die einde van die opname sal u gevra word of ons u kan nader vir 'n onderhoud oor hierdie onderwerp. As u instem sal ons u kontak

vir 'n kort telefoniese onderhoud. U identiteit sal vertroulik gehou word gedurende die studie. Identifiserende besonderhede sal nie direk gekoppel word aan die datastel nie.

Hoekom u is uitgenooi om deel te neem?

U is uitgenooi om deel te neem, want óf u is 'n personeellid / student aan die Fakulteit Gesondheidswetenskappe van die Universiteit van Stellenbosch of die Universiteit van Kaapstad; óf u het al deelgeneem in 'n vorige studie by die Fakulteit Gesondheidswetenskappe van die Universiteit van Stellenbosch.

Wat sal u verantwoordelikhede wees?

Lees asseblief hierdie inligtingsblad heeltemal deur en maak seker u verstaan dit voordat u die opname voltooi. As u dit nie verstaan nie, vra asseblief een van die navorsers om u te help voordat u voortgaan. Sodra u hierdie inligtingsblad klaar gelees het, voltooi asseblief die aanlyn-opname. Die skakel na die opname is ingesluit in die e-pos wat u ontvang het. Maak seker dat u al die vrae en die implikasies van die vrae verstaan. Vra vir hulp as u nie heeltemal 'n vraag verstaan nie. Neem asseblief die tyd om die opname akkuraat te voltooi en verseker dat u u menings en waardes weerspieël. Moet asseblief nie toelaat dat u antwoorde beïnvloed word deur iemand anders nie. Moenie vrae beantwoord op ‘n manier wat gebaseer is op wat u dink die navorsers wil hê u moet invul nie. Voltooi asseblief die hele vraelys. Indien u instem om die telefoniese onderhoud te voltooi, verskaf asseblief u e-pos adres of telefoonnommer sodat ons u kan kontak om die onderhoud te reël.

Sal u voordeel trek deur deel te neem aan hierdie navorsing?

U sal nie direk voordeel trek uit hierdie navorsing nie. Indien u die volle vraelys voltooi staan u ‘n kans om R1500 te wen in ‘n gelukstrekking. Die navorsing sal egter toekomstige deelnemers van genetiese navorsing help, omdat die resultate sal help om riglyne vir die bekendmaking van toevallige bevindings in hierdie gebied te ontwikkel.

Is daar enige risiko's wat u sou dra as u deelneem in hierdie navorsing?

Ons voorsien nie dat u enigie risiko’s sou dra as deel van hierdie navorsing nie.

As u nie instem om deel te neem nie, watter alternatiewe het u?

As u kies om nie deel te neem, sal u op geen manier benadeel word nie.

Sal u betaal word om deel te neem in hierdie studie en is daar enige koste aan verbonde?

Nee, u sal nie betaal word om deel te neem aan die studie nie, maar u sal ‘n kans staan om R1500 te wen in ‘n gelukstrekking. Daar sal geen kostes vir u wees indien u sou deelneem nie.

Is daar enigiets anders wat u moet weet of doen?

U kan die Gesondheidnavorsingsetiekkomitee kontak by 021-938 9207 indien u enige probleme of klagtes het wat nie voldoende aangespreek was deur die studie se personeel nie.

BELANGRIKE INLIGTING OOR GENETIESE NAVORSING

Wat is gene?

Gene bestaan uit DNA en dien as handleidings vir ons liggame. Elke mens se genetiese materiaal is uniek. Gene help om die eienskappe of kenmerke van 'n individu te bepaal. Hierdie eienskappe kan fisies (bv. oog kleur), verstandelik (bv. met 'n goeie geheue), en sielkundig (bv. hoe emosioneel u is) wees.

Sommige gene kan siektes veroorsaak, soos om 'n mens se bloed nie behoorlik te laat stol nie (hemofilie). Ander gene kan optree as risikofaktore vir die ontwikkeling van 'n moontlike siekte. Byvoorbeeld, sekere gene kan 'n mens se kanse om borskanker te ontwikkel vermeerder, maar indien ‘n mens hierdie gene het, beteken dit nie noodwendig dat u beslis borskanker sal kry nie.

Dit is belangrik om op tel let dat ten spyte daarvan dat gene 'n groot rol speel in die vorming van 'n persoon, omgewingsfaktore ook 'n groot rol speel. Byvoorbeeld, 'n persoon se genetiese samestelling mag beteken dat hulle die potensiaal het om borskanker te ontwikkel, maar dat hulle ook nooit borskanker ontwikkel nie deur risiko faktore soos sigaret-rook te vermy. In 'n ander geval kan 'n persoon baie gesonde gene hê, maar 'n beroerte kry ten spyte van hierdie gesonde gene, deur ongesond te lewe en hewiglik oorgewig te wees. Hierdie wisselwerking tussen 'n persoon se gene en hoe hulle in hul omgewing lewe, is baie belangrik om die persoon se gesondheid effektief te verstaan.

Wat is pleiotropie?

Gene is nie altyd eenvoudig nie. Een geen veroorsaak nie altyd 'n spesifieke eienskap nie. In sommige gevalle word een eienskap deur baie gene veroorsaak. Meer relevant vir hierdie studie is waar 'n enkele geen baie verskillende, oënskynlik onverwante karaktertrekke veroorsaak. Dit word **pleiotropie** genoem.

'n Goeie voorbeeld van pleiotropie is in die siekte fenielketonurie (FKU). Hier word verskeie stelsels aangetas deur die enkele geen wat die siekte veroorsaak, Die enkele geen veroorsaak die verskillende eienskappe en gevolglik die simptome; bv konvulsies, albinisme en verstandelike gestremdheid.

Dit is belangrik om te verstaan dat dit nie dieselfde as 'n siekte is wat verskillende simptome in verskillende stelsels veroorsaak nie. Hartversaking, byvoorbeeld, veroorsaak swelling van bene, nierversaking of kortasemheid, maar al hierdie simptome word veroorsaak deur die onvermoë van die hart om bloed effektief te pomp. Maar in FKU veroorsaak die enkele geen die baie verskillende eienskappe wat dan lei tot die verskillende simptome.

Wat is toevallige bevindings (TBs)?

Toevallige bevindings (TBs) kom voor wanneer 'n voorheen ongediagnoseerde siekte of toestand ontbloot word terwyl daar gesoek word na iets anders. Hulle kan voorkom tydens beelding ondersoeke, outopsies, en meer relevant vir hierdie studie, gedurende mediese navorsing en genetiese toetse.

Terwyl daar getoets word vir die teenwoordigheid of afwesigheid van 'n spesifieke geen, kan 'n mens 'n ander gene kry wat 'n spesifieke eienskap bepaal. Hierdie geen en sy eienskap mag miskien ‘n impak maak op die deelnemer se gesondheid.

Pleiotropiese toevallige bevindings kom voor wanneer 'n geen gekoppel is met 'n nuwe eienskap of toestand wat nie aanvanklik gesoek word as deel van die navorsing nie. Genetiese navorsing kan dikwels op soek wees na verskeie gene, en 'n paar van hierdie gene kan pleiotropies wees. Wanneer hierdie gene, en hul eienskappe, nie gesoek word nie, is dit 'n pleiotropiese toevallige bevinding. Dit is belangrik om daarop te let dat genetiese navorsing voortdurend besig is om nuwe kennis aan te skaf. Nuwe bande tussen eienskappe en gene word voortdurend gevind.

Baie faktore kan beïnvloed of die toevallige bevinding bekend aan die deelnemer bekend te maak of nie. Die toevallige bevinding mag miskien betekenisvol wees of nie, maw dit kan miskien 'n klein toestand wees. In 'n ander geval is, is daar niks wat gedoen kan word oor die bevinding nie; in hierdie geval is die bevinding nie **klinies uitvoerbaar** nie. As iets gedoen kan word oor die bevinding, dan is dit klinies uitvoerbaar. Die ouderdom van die navorsing deelnemer is ook 'n faktor wat in ag geneem moet word. Sommige siektes kan slegs ontwikkel in volwassenheid (volwasse aanvang), terwyl ander reeds in kinderjare kan ontwikkel (kinderjarige aanvang).

Noudat u deur die inligtingsblaad gelees het, wil ons graag u mening hê oor die belangrikheid van die verskillende faktore wat die bekendmaking van toevallige bevindings in genetiese navorsing beïnvloed. Klik asseblief op die skakel in die e-pos vir toegang tot die aanlyn-opname. As u met op ‘n universiteitsrekenaar werk, onthou om u Inetkey oop te maak.

Dankie by voorbaat vir u deelname!