



Algemene gegevens / General Information

Programma / Programme : **COVID-19 Programma**
 Subsidiëronde / Subsidy round : **Bottom-up ronde COVID-19 aandachtsgebied 3**
 Projecttitel / Project title : **Corona effects on behavior and resilience of society and its inhabitants: safely interconnected data from cohort and CBS studies**
 Projecttaal / Project language : **Engels / English**
 Geplande startdatum / Planned start date : **01-11-2020**
 Geplande duur / Planned duration : **24 maanden / months**
 Datum indienen / Date of application : **25-05-2020**
 Projecttype / Project type : **Fundamenteel onderzoek / Fundamental research**
 Vervolg eerder ZonMw-project / Continuation previously funded project : **Nee / No**
 ZonMw

Projectleden / Project members

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COVID19 - Lijn 3 of WiP / COVID19 - Lijn 3 or WiP

Dossier nummer / Dossier number: 50-56300-98-909

DEFINITIEF

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Projectgegevens / Project information**Samenvatting / Summary**

Human behavior is critical in shaping the COVID-19 pandemic. In the absence of vaccination and medical treatment, behavior is crucial in limiting the distribution and consequences of the pandemic. This requires that insights from medicine and biology are combined with those from behavioral and social sciences. Here we bring together scientists from psychology, biology, medicine, epidemiology and Statistics Netherlands (CBS) who collaborate in large research consortia in the Netherlands to realize crucial cross-disciplinary collaboration to understand how social conditions may amplify the impact of biological factors. The list of key questions to address is long and will grow. With respect to behavior the list includes the role of coping with stressful events, solidarity, religion, loneliness, personality, prosocial behavior and its driving factors, intergroup conflicts, where people live and their exposome (e.g. Betsch, Nature Human Behavior, 4, 438, 2020). With respect to biology it includes genetic and genomic background and metabolomics status. We argue that insight into the causes, impact, and mitigation of the pandemic can only be achieved by research that combines data on behavior, as characterized above, with biological data, at the level of the individual and the family, because variation in behavior, or where people live, is shaped by (epi)genetics, just as

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the physiological response of the host is in part shaped by the host genome and the impact of biology is shaped by social conditions.

Databases containing privacy sensitive data often have limited technical and operational options for full, secure data connections and sharing. We will realize solutions based on an existing, safe environment for linkage of cohort data with data from CBS in a high performance computing (HPC) environment and provide a framework to optimally and safely work together in combining multiple existing and new datasets that are already available or are presently collected.

Trefwoorden / Keywords

Cohort; biobank; consortia; CBS; safe record linkage; COVID-19 vulnerability; physiological and mental resilience; societal; behavioral and biological determinants

Samenwerking / Collaboration

Samenwerking tussen onderzoek en praktijk / Cooperation between research and practice:

Nee / No

Financiële gegevens / Financial data

ZonMw budget

Kostenpost	Jaar / Year								Totaal / Total
	1	2	3	4	5	6	7	8	
Personeel	200	200	0	0	0	0	0	0	400
Materieel	50	50	0	0	0	0	0	0	100
Implementatie	0	0	0	0	0	0	0	0	0
Apparatuur	0	0	0	0	0	0	0	0	0
Overig	0	0	0	0	0	0	0	0	0
Totaal / Total	250	250	0	0	0	0	0	0	500

Co-financiering / Cofinancing

Naam co-financier / Name of cofinancier	Bedrag / Amount	Status

Bijzondere gegevens / Additional information

Vergunningen / Permits

	Verklaring nodig / Statement required?		Status verklaring / Statement status		
	Ja / Yes	Nee / No	Verkregen / Acquired	Aangevraagd / Applied	Nog niet aangevraagd / Not applied yet
METC	X		X		
DEC		X			
WBO	X		X		

Onderschrijvingen / Assents

	Ja / Yes	Nee / No	N.v.t. / N.A.
Code biosecurity / Code Biosecurity			X
Code openheid dierproeven / Code Transparency of Animal Testing			X

Andere vergunningen / Other permits

METC: onderzoek met bestaande data gecombineerd met COVID-19 gegevens die per locatie zijn goedgekeurd als WMO of niet-WMO plichtig onderzoek.

WBO: onderzoek met bestaande cohort en CBD data gecombineerd met COVID-19 gegevens die voor cohorten die onder WBO vallen per locatie zijn goedgekeurd als WMO of niet-WMO plichtig onderzoek.

AANVRAAGFORMULIER PROJECTIDEE – BOTTOM-UP RONDE COVID 19 programma

Deadline voor indiening: 25 mei 2020 (14:00 u)

**LEES ALSTUBLIJFT ALLE INSTRUCTIES IN BIJLAGE "TOELICHTING
INDIENING PROJECTIDEE" VAN DE OPROEPTEKST ZORGVULDIG!**

Wanneer u het formulier heeft ingevuld:

1. Zet het formulier om naar een PDF file en controleer de details
2. Upload het complete formulier als een bijlage bij uw indiening in Projectnet
ProjectNet: [Aandachtsgebied 3 maatschappelijke dynamiek](#)

BASISGEGEVENS (voorpagina)

NAAM VAN DE HOOFDAANVRAGER:

Prof. dr. D.I. Boomsma & Prof. Dr. P.E. Slagboom

ORGANISATIE:

Vrije Universiteit, Amsterdam / LUMC, Leiden

PROJECTTITEL:

Het Corona effect op gedrag en veerkracht van de samenleving en haar inwoners: veilig verbonden data uit Nederlands cohort en CBS onderzoek.

Corona effects on behavior and resilience of society and its inhabitants: safely interconnected data from cohort and CBS studies

DATASTEWARD:

Wie is de datasteward die de open science en FAIR data planning in uw project ondersteunt? Zie de webinars op de [ZonMw website](#) om de datastewards te informeren en ondersteunen.

Ik betrek een datasteward bij mijn project:

Naam: (10)(2e)

Instituut: LUMC, Leiden

E-mail: (10)(2e)@lumc.nl

Was aanwezig bij de webinar: Ja Nee

Ik heb nog geen datasteward.

ONDERZOEKSVORSTEL max 3 pagina's A4 (inclusief literatuurreferenties)	(voorpagina met basisgegevens niet meegerekend - font type Arial 10 pts)
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1. PROBLEEMSTELLING EN DOELSTELLING(EN):

Background: In the absence of medical treatment and vaccination, behavior of individuals and groups is the most critical factor in shaping the COVID-19 pandemic. There is a multitude of questions regarding the behavior of diverse groups, their resilience and the resilience of society during and after the COVID-19 pandemic. The ambition of this project is to address these questions based on safe data interconnection and record linkage across the rich multiple databases available from multiple disciplines.

Problem: How can we explore to what extent the psychological, behavioural, biological, social and environmental factors impact physiological and mental resilience as a consequence of the Corona outbreak? This aetiological question relates to the variation in e.g. genetic and genomic background, clinical and mental condition, socioeconomic status, exposome (e.g. exposure risk) of members in society influencing their response to the outbreak, recorded as infection status, disease course and mental health during the outbreak and aftermath and asks which social conditions amplify the impact of biological factors.

Goal: Understand the aetiology of variation in physiological and mental resilience to eventually predict vulnerability and strength, develop interventions and policies to help achieve personal, organisational and societal goals during the Corona outbreak and its aftermath. The resilience depends on the capacity of coping with stressful events, solidarity and protective behaviour as well as the physiological, sociological and economic individual risk. To systematically analyse variation in individual resilience, we will consider the genetic and biological background, social networks, including family structures, the role of religion, tolerance for loneliness, prosocial behaviour, intergroup dynamics, employment and job loss and socio-economic status. These privacy sensitive variables are available from cohorts and biobanks (e.g. genotypes, personality) and Statistics Netherlands (CBS).

Problem: Databases containing privacy sensitive data often have limited technical and operational options for full, secure data sharing.

Goal: To realize solutions based on an existing, safe environment that allows scientists to combine information and link their data with data from CBS enabling them to run analyses in a high performance computing (HPC) environment and to provide a framework to optimally and safely work together in combining multiple existing and new datasets that are already available or are presently collected.

Problem: There is insufficient knowledge how the enormous diversity in data and information on physiological, mental and behavioural effects before and after the Corona outbreak can be best utilized.

Goal: To combine and systematically analyse data on the response to the outbreak in the context of data on genome, metabolome, transcriptome, personality, lifestyle, socio-demographic factors, and exposome existing at CBS and cohort studies. Together the partners and studies that are united in this proposal represent a broad range of scientific disciplines and of societal segments of inhabitants of the Netherlands. To perform the analyses we aim for, studies will be involved that collected data on personal characteristics, the connection of which requires the project to provide a high level of data organization and protection.

We address problems and aim to realize goals in the theme "Onderzoek naar de veerkracht samenleving", focussing on *vulnerable groups (Kwetsbare groepen)*, *Social inequality (Maatschappelijke ongelijkheid)* and *Psychological effects and emotional well-being (Psychologische effecten en emotioneel welbevinden)*.

2. PLAN VAN AANPAK:

There are highly valuable initiatives to collect new data for research into the consequences of the COVID-19 outbreak. Researchers across a large number of disciplines are affiliated to consortia representing population and patient / clinical cohorts, childhood and adult participants, sick and healthy people, biobanks, ELSI expertise, infrastructure and computing facilities. This proposal brings together scientists working within consortia that focus on development, health, social factors and exposome.

- ODISSEI (Open Data Infrastructure for Social Science and Economic Innovations): <https://odissei-data.nl/nl/>
- Health-RI/BBMRI.nl (Health Research Infrastructure /Biobanking and Biomolecular Resources Research Infrastructure The Netherlands) : <https://www.health-ri.nl/>
- CID (Consortium Individual Development) : <https://individualdevelopment.nl/>
- CBS (Centraal Bureau Statistiek) : www.cbs.nl/microdata
- RIVM (Rijksinstituut voor Volksgezondheid en Milieu)
- DTL (Dutch Techcentre for Life Science) : <https://www.dtls.nl/>
- Exposome-Nl
- GECCO (Geoscience and health cohort consortium) : <https://www.gecco.nl/>

Within these consortia a large number of cohorts (please see consortia websites) follow child, adult and elderly participants by longitudinal data collections. New data collections in this period dominated by the Corona outbreak focus on physical and mental health, effects of home schooling, job loss, exposures to risk factors, risk and protective behavior, compliance with social distancing rules, possible COVID-19 infection, hospitalization and functioning after surviving the contamination. Collaborations already take place among cohorts, e.g. by using standardized surveys for new data collection. When the phase of local data collection and studies has been completed, **we aim to have realized a safe interconnected infrastructure with possibilities to combine and analyze cohort data, link these to data from Statistics Netherlands and analyze such datasets on a large scale to answer the question who –given the same exposure- is resilient and whose mental and physical health is compromised.**

By bringing together information from Statistics Netherlands (CBS), cohorts, biobanks and exposome, we can include molecular, health, behavioral and socioeconomic profiles of the host as potential factors that impact the risk of contamination, disease course as well as measures of daily functioning, mental health and school performance in younger and older people. It is the diversity of the characteristics of participants in the numerous cohorts across the lifespan (young, (un-)healthy old, multi-morbidity, obesity) and the new and existing data in all cohorts that enables immediate investigation of the risk factors and consequences of COVID-19, when all of this information is safely interconnected.

Within Health-RI and BBMRI.nl, there is expertise in combining cohort, biological and clinical data and the ethical and legal aspects thereof (see <https://www.elsi.health-ri.nl/welkom-op-de-elsi-website/>); in ODISSEI there is expertise in working with cohorts within demographics and social sciences and in safe linking of data to CBS data. These research consortia have longstanding collaborations with SURF to realize safe data linkage and analyses. One collaborative project is the development of the ODISSEI Secure Super Computer (OSSC), a secure high-performance computing environment, incorporating linkable datasets and advanced analytics tools at the national supercomputer of SURF. This environment allows researchers to link cohort data to data from Statistics Netherlands (CBS: (<https://www.cbs.nl/nl-nl/onze-diensten/maatwerk-en-microdata/microdata-zelf-onderzoek-doen/catalogus-microdata>) and run analyses in a high-performance computing environment (see: <https://odissei-data.nl/nl/odissei-secure-supercomputer/>).

Against this background, we will work with researchers in the Netherlands to optimize the size of datasets for analyses of cases and controls, access safe computing environments, tooling for data integration and analysis, harmonization in procedures and rules for successful engagement in research collaborations. We can address our goal to understand the aetiology of variation in physiological and mental resilience to the outbreak and its aftermath. High or low resilience given a certain exposure level (to contamination, hospitalization, anxiety, social distance) is likely to be a function of genetic and biological makeup, health, social networks, including family structures, religion and political opinion, tolerance for loneliness, prosocial behavior, intergroup dynamics, employment and job loss and socio-economic status.

We offer the following use cases:

- The possibility and conditions of using COVID-19 contamination and hospital admission microdata for research purposes: options are currently explored between CBS, RIVM and GGD. This option if realized will greatly enhance the opportunities for improved research projects, because uniform information will be available for all persons which may be combined with cohort and CBS microdata.
- Genetic association and genotype-by-exposure (GxE) studies linking COVID-19 data to genotypes and CBS microdata to assess which social conditions amplify the impact of genetic factors. A first successful genotypes-CBS microdata linkage and analysis was realized at the OSSC when linking cohort genotype data to health care data from Statistics Netherlands (de Zeeuw et al, to be submitted). Here we will build upon and extend this model and analyze genotype-COVID-19 data including age, sex, exposure, SES and other moderators in GxE modeling.
- Understanding of risk and resilience in response to acute social stress among families with children. The COVID-19 outbreak is a natural experiment to study how children and young people typically react during a crisis. Child physical and mental health longitudinal data have been collected within the CID consortium in multiple large child cohorts, from newborns to young adults. Together the CID child cohorts represent all areas of the country (see e.g. Veldkamp, et al., 2020; Zondervan-Zwijenburg et al., 2019). We will link these data, collected before and after the COVID-19 outbreak, to standardized CBS information and assess the outbreak impact on mental health (problems) of children. Findings may teach parents and other adults how to help children in later waves of the coronavirus or during the next major crisis.
- Which molecular profiles associate with vulnerability to infection and the mild and more severe physical and mental outcomes of COVID-19, the vulnerability to anxiety and depressive illness induced by the social dynamics of the outbreak, and do these profiles also predict? In BBMRI.nl/Health RI, physical and mental health data of surveys across the past 20 years will be analyzed in conjunction with metabolomics data in >25,000 subjects, with transcriptome and methylome data in >4,000 study participants and additional data

on vascular condition and inflammatory and related factors thought to play a role in the vulnerability to severe symptoms. The COVID-19 related data will be/are being collected by through surveys used by multiple cohorts. In an earlier successful project, 25 cohorts have worked together in BBMRI.nl to analyze (e.g. Bot et al. 2020) metabolomics and depression data.

-Network analyses: Social networks can amplify the spread of behaviors that are both harmful and beneficial during an epidemic, and these effects may spread through the network to friends, friends' friends and even friends' friends' friends (see van Bavel et al Nat Human Behavior, 2020). An extensive social network dataset in OSSC is expected to become available from Statistics Netherlands early 2021 (van der Laan et al, to be submitted); see also <https://odissee-data.nl/en/2018/10/analysing-social-network-of-the-netherlands-cbs-ossoc/>.

3. HAALBAARHEID VAN HET PROJECT:

Timeline:

1st year: establish analyses plans enabled by ongoing data collections and the timelines for such analyses (first and second phase opportunities); set up designated data infrastructure at OSSC, enable cohorts to work together on privacy sensitive data. Start executing the first data analyses.

2nd year: execute the analyses; we envision the first phase data analysis to comprise COVID-19 related symptoms (physical and mental health), infection rate and disease course survey studies in the cohorts, combining these of clinical cohorts; the second phase data analysis to comprise longer term functioning after mild contamination, after surviving severe contamination and hospitalization, exposures to risk factors collected in earlier timepoints and compliance with social distancing rules and anxiety, as well as on how this period affects multiple aspects of children's lives.

Feasibility:

The consortia represent groups and cohorts that have successfully worked together exemplified by recent publications. They have a strong wish to collaborate on COVID-19 research at a higher level across consortia to combine social data, mental and physical health information.

4. RELEVANTIE VOOR DE PRAKTIJK:

We deem the following criteria as especially relevant for our proposal: Het onderzoek vindt **niet al elders** plaats: applies to our CBS- cohort collaborations; **Borging**: OSSC and ELSI service desk will fully share experience and knowledge for future project; **Opschaalbaarheid**; **Samenwerking: multi- en interdisciplinair**; **Toegevoegde waarde**. **Diversiteit**: e.g. we include males and females and cover the complete age range; information on SES is available for all; **biologische als sociaal-culturele oorzaken**: this is the cornerstone of our proposal; **Toepassing van ICT**: OSSC

5. DEELNAME VAN DE STAKEHOLDER(S) (e.g. patiënten, zorgprofessionals, etc.):

Maatschappelijke adviesraad van BBMRI (MAB)

6. LITERATUURREFERENTIES (optioneel):

Bavel et al (2020) Using social and behavioural science to support COVID-19 pandemic response. *Nat Human Behavior*.
 Bot M et al (2020) Metabolomics Profile in Depression: A Pooled Analysis of 230 Metabolic Markers in 5283 Cases With Depression and 10,145 Controls. *Biol Psychiatry*.
 Deelen J, et al (2019) A metabolic profile of all-cause mortality risk identified in an observational study of 44,168 individuals. *Nature Comm*.
 Van der Laan et al (to be submitted) An integral social network analysis based on administrative data for the 17 million inhabitants of the Netherlands.
 Veldkamp S et al (2020) Parental Age in Relation to Offspring's Neurodevelopment, *J Clinical Child & Adolescent Psychology*
 De Zeeuw et al (to be submitted) Linking data from a longitudinal twin-family cohort to population-based register data from Statistics Netherlands: A genome-wide association on health care expenditure study.
 Zondervan-Zwijenburg M et al (2019) Parental Age and Offspring Childhood Mental Health: A Multi-Cohort, Population-Based Investigation. *Child Dev*