ZonMw

COVID-19 / COVID-19
Dossier nummer / Dossier number: 50-56300-98-002
DEFINITIEF

Algemene gegevens / General Information

Programma / Programme	:	**COVID-19 Programma**
Subsidieronde / Subsidy round	:	**Urgent traject aandachtsgebied 1 en 2**
Projecttitel / Project title	:	**Evidence-based effective monitoring and control of Covid-19 after the initial outbreak**
Projecttaal / Project language	:	**Engels / English**
Geplande startdatum / Planned start date	:	(10)(2e)
Geplande duur / Planned duration	:	0)(2 **maanden / months**
Datum indienen / Date of application	:	**11-05-2020**
Projecttype / Project type	:	**Toegepast onderzoek / Applied research**

Projectleden / Project members

(10)(2e) (10)(2e) **(Main applicant)**
Functie / Position: (10)(2e) theoretische epidemiologie | *Opleiding / Education:*
Studierichting / Subject:
T: 0)(2 (10)(2e) | *F:* | *E:* (10)(2e) @uu.nl

Universiteit Utrecht
Faculteit der Diergeneeskunde
Gezondheidszorg Landbouwhuisdieren
Postbus 80163
3508 TD UTRECHT

(10)(2e) (10)(2e) **(Projectleader and secretary)**
Functie / Position: Hoogleraar theoretische epidemiologie | *Opleiding / Education:*
Studierichting / Subject:
T: 0)(2 (10)(2e) | *F:* | *E:* (10)(2e) @uu.nl

Universiteit Utrecht
Faculteit der Diergeneeskunde
Gezondheidszorg Landbouwhuisdieren
Postbus 80163
3508 TD UTRECHT

(10)(2e) (10)(2e) **(Administrative responsibility)**
Functie / Position: (10)(2e) faculteit Diergeneeskunde | *Opleiding / Education:* WO
Studierichting / Subject:
T: 10)(2e (10)(2e) *F:* | *E:* (10)(2e) @uu.nl

Universiteit Utrecht
Faculteit der Diergeneeskunde
Faculteitsbestuur
Postbus 80163
3508 TD UTRECHT

(10)(2e) (10)(2e) **(Co-projectleader)**
Functie / Position: (10)(2e) huisartsgeneeskunde | *Opleiding / Education:*
Studierichting / Subject:
T: 10)(2e (10)(2e) | *F:* | *E:* (10)(2e) @lumc.nl

Leiden University Medical Center
Public Health and Primary Care
Postbus 9600
2300 RC LEIDEN

(10)(2e) (10)(2e) **(Executive)**
Functie / Position: (10)(2e) kansrekening | *Opleiding / Education:*
Studierichting / Subject:
T: 10)(2e) (10)(2e) *F:* | *E:* (10)(2e) @tue.nl

Eindhoven University of Technology
Department of Mathematics and Computer Science
Postbus 513
5600 MB EINDHOVEN

(10)(2e) (10)(2e) **(Co-projectleader)**
Functie / Position: Hoogleraar kwantitatieve veterinaire epidemiologie | *Opleiding / Education:*
Studierichting / Subject:
T: (10)(2e) (10)(2e) | *F:* | *E:* (10)(2e) @wur.nl

Wageningen Universiteit
Quantitative Veterinary Epidemiology
Marijkeweg 40
6709 PG WAGENINGEN

(10)(2e) (10)(2e) **(Co-Applicant)**
Functie / Position: (10)(2e) dynamica van infectieziekten | *Opleiding / Education:* WO
Studierichting / Subject:
T: (10)(2e) (10)(2e) *F:* | *E:* (10)(2e) @umcutrecht.nl

Universitair Medisch Centrum Utrecht
Julius Centrum voor Gezondheidswetenschappen en Eerstelijns Geneeskunde
Epidemiologie
Universiteitsweg 100
3584 CG UTRECHT

(10)(2e) (10)(2e) **(Co-projectleader)**
Functie / Position: (10)(2e) infectieziektenmodellering | *Opleiding / Education:*
Studierichting / Subject:
T: (10)(2e) (10)(2e) | *F:* | *E:* (10)(2e) @erasmusmc.nl

Erasmus MC
Maatschappelijke gezondheidszorg
Postbus 2040
3000 CA ROTTERDAM

(10)(2e) (10)(2e) **(Executive)**
Functie / Position: (10)(2e) modellering Cib en (10)(2e) | *Opleiding / Education:*
Studierichting / Subject:
T: (10)(2e) | *F:* | *E:* (10)(2e) @rivm.nl

Rijksinstituut voor Volksgezondheid en Milieu
Centre for Infectious Disease Control (CIb)
Antonie van Leeuwenhoeklaan 9
3721 MA BILTHOVEN

(10)(2e) (10)(2e) **(Executive)**
Functie / Position: (10)(2e) stochastische operations research | *Opleiding / Education:*
Studierichting / Subject:
T: (10)(2e) (10)(2e) (10)(2e) *F:* | *E:* (10)(2e) @cwi.nl

Centrum voor Wiskunde en Informatica
Probability, Networks and Algorithms (PNA)
Postbus 94079
1090 GB AMSTERDAM

Projectgegevens / Project information

Aandachtsgebieden / Focus

Aandachtsgebied
- 2: Zorg en preventie

Samenvatting / Summary

The Netherlands, like many countries in the world, is nearing the phase where the social distancing measures that were imposed to control the outbreak of SARS-CoV-2 (the virus that causes Covid-19) will start to be lifted. As there is unlikely to be anything close to herd immunity even in the most affected areas, there is an acute danger that increased mixing of the population when measures are relaxed, as well as importation of cases from outside the Netherlands, can lead to new clusters of cases and a second major outbreak when uncontrolled. Effective monitoring is essential to find new infections, connected to effective protocols for tracing-testing-isolation/quarantine (to be called TTI here) to prevent the new clusters from growing while

undetected. The fact that in the Netherlands there will be ongoing within-country transmission when measures start to be relaxed brings additional complications and challenges to monitoring and TTI-response. In addition, given the fact that the Netherlands is an important nation for tourism, trade, collaboration and industry, there is very substantial interaction between our country and all citizens of nations around the globe. This is likely to resume (slowly) when 'normal' international travel and mobility is restored. As the Covid-19-pandemic is out of phase across the globe, with nations at the beginning of their outbreaks and nations nearing the end of their first waves, it is likely that we will experience importation of cases from abroad, by air, train, boat and car. As the world is currently dealing with a unique new public health problem and threat for the coming years, it is unclear what an effective strategy of monitoring and response is and whether existing protocols and effort are sufficient to prevent new major outbreaks in the Netherlands until a suitable vaccine becomes available.

The aim of the project is to provide a broad scientific basis for an effective evidence-based system, including uncertainties, of monitoring and TTI response for SARS-CoV-2 that takes into account the characteristics of Covid-19 disease, the status of the outbreak, potential importation of cases, specific risk and core groups, the impact of basic transmission-avoiding measures and human behaviour. This can only be achieved by bringing together a large group of experts from a wide range of quantitative disciplines and medical/public health institutions and organizations and in coordinated concentrated interaction.

The scientific results of the project can be used as input for the RIVM/Cib, GGD, NIVEL and other parties within whose remit it lies to give policy advice on monitoring and control and to implement suitable public health measures in response to Covid-19. On top of that, the methods and models developed during the project will be useful for future outbreaks of newly emerging (respiratory) infections.

Samenwerking / Collaboration

Samenwerking tussen onderzoek en praktijk / Cooperation between research and practice:
Nee / No

Organisaties

GGD Amsterdam
Cluster Infectieziekten
Postbus 2200
1000 CE AMSTERDAM

GGD Rotterdam Rijnmond
Schiedamsedijk 95
3011 EN ROTTERDAM

GGD Zuid Limburg
Het Overloon 2
6411 TE HEERLEN

Maastricht University
Caphri - School for Public Health and Primary Care
Universiteitssingel 40
6211 LH MAASTRICHT

NIVEL
Postbus 1568
3500BN UTRECHT

Rijksinstituut voor Volksgezondheid en Milieu
Centre for Infectious Disease Control (CIb)
Antonie van Leeuwenhoeklaan 9
3721 MA BILTHOVEN

Inhoud / Content

Relevantie / Relevance
The project proposal is very relevant to the call as the emphasis of the call is to contribute to the scientific evidence base for a more solid and improved pandemic response. In the next phase of the outbreak, and until a vaccine becomes available, it is absolutely key to have an effective system of monitoring, together with contact tracing, testing and isolation/quarantine, to track down and efficiently deal with new infections that can (and will) arise and the new clusters of cases these can lead to. Quantitative methods, such as epidemiological and statistical modeling, in combination with data, are essential to obtain insight into how effective monitoring and response needs to be and what type of data need to be collected, given the characteristics of the infection and societal interaction and mobility that will determine transmission of the virus and its epidemiology.

In addition, there may well be specific aspects in common to pathogens that are able to cause devastating pandemics in our present global society. These include easy transmission between all humans without the need for intensive close (or special types of) contact, transmission possible via the environment, common (i.e. non-specific) and variable symptoms, a relatively short latency period, possibly pre-symptomatic infectivity, a substantial infectious period, no prior (cross)immunity, limited but not insubstantial mortality, only non-pharmaceutical interventions available. Respiratory viruses including Influenza-like illnesses broadly speaking fit these criteria. When preparing for the next pandemic, focus on such a combination of criteria seems a sensible idea. Insight from modelling has brought understanding why the above combination of characteristics will spread easily and will be difficult to contain. One can expect that similar issues will be relevant in terms of effective monitoring and contact tracing-testing-isolation/quarantine response. The methods, tools and models we produce in this project and the insight that these bring are therefore expected to be relevant for a wider class of potentially emerging viral pathogens.

Kennisoverdracht, implementatie, bestendiging / Knowledge transfer, Implementation Consolidation

Transfer of knowledge will be achieved in several ways. Although the project has only a short duration, the importance of the work for the public health response is such that close contact and interaction is necessary almost continuously. For this reason, there will be an advisory board consisting of members of the organizations on whose advice, data collection and analytical/ implementation efforts public health response to (human) infectious disease outbreaks depends. These are the RIVM/Cib, GGDs, NIVEL. Direct input of their expertise, ideas and critical assessments will not only improve the project (working on the right questions, with the right context), but will also allow almost immediate transfer of knowledge into practice.

In addition, we aim to publish our scientific results and insight, as well as our methods, tools and models first in preprint archives for quick dissemination and in quality peer reviewed open access journals. We also aim to write a broad review of our findings. All methods, tools and models and the simulation or computational code that accompanies those will be made available in suitable annotated ways, for example on GitHub or similar open websites.

Given the nature of the problem we study, there is likely to be interest in the results and insights from other professionals, the media and the general public. Although the project has been split into connected sub-projects, there is important interaction between all when it comes to addressing practical questions for the general public. We will therefore seek to actively communicate in an open and coordinated fashion. We envisage organizing an open symposium at the end of the project to discuss results with a broader professional and scientific community.

One can certainly envisage that during the project specific new questions arise form the active public health response, directly related to new phases of the outbreak that cannot now be foreseen. Direct interaction with several GGDs and the RIVM/Cib ensures that these questions can be quickly transferred to the wider project team and can lead to specific additional research not yet described in this proposal.

Doelstelling / Objective

The aim of the project is to provide a broad scientific basis for an effective evidence-based system, including uncertainties, of monitoring and contact tracing-testing-isolation/quarantine response for SARS-CoV-2 that takes into account the characteristics of the Covid-19 disease, the status of the outbreak, potential importation of cases, specific risk and core groups, the impact of basic transmission-avoiding measures and human behaviour.

We aim to achieve this in a multidisciplinary collaboration combining a diverse range of relevant quantitative expertise and a diverse range of professionals and researchers from practice.

Plan van Aanpak / Strategy

1. Introduction and background.

The Netherlands, like many countries in the world, is nearing the phase where the social distancing measures that were imposed to control the outbreak of SARS-CoV-2 will start to be lifted. As there is unlikely to be anything close to herd immunity even in the most affected areas, there is an acute danger that increased mixing of the population when measures are relaxed, as well as importation of cases from outside the Netherlands, can lead to new clusters of cases and a second outbreak when uncontrolled (Anderson et al. 2020, Ferguson et al. 2020, Kissler et al. 2020, de Vlas & Coffeng 2020). In China, measures seem to have been relaxed only when the outbreak had run its course. New clusters arose quickly after growing towards normal mobility, mixing and activities (Leung et al. 2020). To prevent a second wave, protocols of tracing-testing-isolation/ quarantine (denoted by 'TTI', hereafter) are operational to prevent the new clusters from growing while undetected. Given the fact that the Netherlands is an important nation for tourism, trade, collaboration and industry, there is very substantial interaction between our country and all citizens of nations around the globe. This is likely to resume (slowly) when 'normal' international travel and mobility is restored. As the Covid-19-pandemic is out of phase across the globe, with nations at the beginning of their outbreaks and nations nearing the end of their first waves, it is likely that we will experience importation of cases from abroad, by air, train, boat and car. The volume of this may change when across the globe outbreaks are slowly brought under control by social distancing, but the new cases arising in recent weeks in China dictate the possible danger. In contrast to China, however, the fact that in the Netherlands there will most likely be ongoing within-country transmission when measures start to be relaxed brings additional complications and challenges to TTI.

Just as at the start of the pandemic, the only control options until an effective vaccine becomes available are measures of social distancing (Hollingsworth et al. 2011). If countries are moving out of (strict or partial) lockdown, ultimately one set of (basic) measures remains when minimizing economic and societal impact. This includes what can be called 'good infection-avoiding behaviour' by the public (i.e. not shaking hands, washing hands effectively, cleaning surfaces, staying at

home when exhibiting specified symptoms) and what has been called the '1.5-meter-society'. Although there has been some research quantifying the impact of these basic measures (Teslya et al. 2020, Prem et al. 2020), it remains unclear what fraction of possible transmissions these measures would prevent. It is clear that the '1.5-meter-society' is an interesting concept in theory, but that it will be difficult to achieve in many situations, for example in public transport or large public events. These can be controlled for a certain period based on governmental restrictions, but at some point, societal and economic pressures will cause restrictions to fade. In addition, one can imagine that, with the passing of time and when only few new cases arise, individual behaviour will be such that these basic measures get watered down and lose effectivity.

A tested approach to case detection is contact tracing around discovered (i.e. symptomatic) cases, together with isolation of that case, quarantine of traced contacts and testing. Covid-19 poses several problems. First, it is likely that a substantial fraction of the infected individuals does not develop the strong symptoms that could be necessary for effective monitoring and to trigger the tracing approach or is asymptomatically infectious (Wölfel et al. 2020,). Second there is most likely pre-symptomatic transmission (He et al. 2020), although it is unclear how much shorter the latency period is compared to the incubation period, or whether the infectivity is similar to that of symptomatic cases. Third, because the incubation period distribution has an average of about 5-6 days (Backer et al. 2020), the uncertainty about pre-symptomatic and asymptomatic transmission not only implies that cases are likely to be missed by regular monitoring, but also that once secondary or tertiary transmissions that do express symptoms are discovered, we could be lagging behind a possibly growing number of cases by one or two weeks.

Research has shown that contact tracing and TTI is difficult as the only way to control outbreaks in cases where there is pre-symptomatic transmission and where the latency and incubation periods are short (Klinkenberg et al. 2006, Ferretti et al. 2020, Sun & Viboud, 2020). Timing is therefore of the essence. The length of these periods for Covid-19 may give more time, but it is unlikely to be more than 2-3 days (Kretzschmar et al. 2020). Another issue is that in regular contact tracing only a fraction of the contacts is found. Particularly the casual contacts with unknown individuals is missed. For a respiratory infection with potentially substantial environmental transmission via contaminated surfaces the fraction of unknown contacts is possibly large. Several technological advances, including various apps, are imaginable, but many have substantial epidemiological problems (apart from important privacy, ethical and technical issues).

2. Aim of the project:

The aim of the project is to provide a broad scientific basis for an effective evidence-based system, including uncertainties, of monitoring and TTI that takes into account the characteristics of SARS-CoV-2, the status of the outbreak, potential importation of cases, specific risk groups and the impact of basic transmission-avoiding measures that are kept in place after lockdown is lifted.

The scientific results of the project can be used as input for the RIVM/Cib, GGD, NIVEL and other parties within whose remit it lies to give policy advice on monitoring and control and to implement suitable measures. It is important to specify what is the aim of the monitoring, as this determines in what sense measures should be "effective", to what degree and how success or failure is assessed. For example, it may matter whether the aim is to minimize the number of cases among specified risk groups that show the highest morbidity and mortality or to minimize the number of new chains/clusters of transmission anywhere in the population. Of course, current practice and protocols for monitoring and TTI in the Netherlands is important input. There are, however, many new dimensions, given the situation and characteristics of Covid-19.

3. Structure of the project:

The project is structured according to the broadly important aspects involved in monitoring and control by TTI for SARS-CoV-2/ Covid-19: i) Mobility and geographical modeling of spread; ii) Syndrome surveillance; iii) Targeted response & core groups; iv) Testing strategy; v) International approaches to monitoring and TTI (best practices and limitations) & criteria for alarm.

There will be five interconnected working groups in the project, combining the above, each led by an epidemiological expert and each working with experts from other quantitative disciplines combining the modeling and statistical expertise needed. The project as a whole involves more experts than can be represented with their roles in the "Project members"-part of the proposal (page 1-2) as the form only allows 10 participants. This is an unusual project, however, demanding active roles for a larger group of scientists. After discussion with ZonMw, it was decided to add everyone group that receives part of the research budget here, represented by the leading group members, and to indicate their roles (and functions when not already mentioned in "Project members"). All groups will involve additional local researchers (post-docs, PhD-students, assistant and associate professors).

Working group 1: Mobility and geographic modeling of spread
Group lead: prof. dr (10)(2e) Erasmus MC)
Group members: prof. dr. (10)(2e) (CWI and TU/e); dr. (10)(2e) (UU; (10)(2e) information and computing science); prof. dr. (10)(2e) TU/e) & Prof. dr. (10)(2e) TU/e & UTwente; (10)(2e) (10)(2e) prof. dr. (10)(2e) (RIVM/Cib and LUMC; (10)(2e)

Working group 2: Syndrome surveillance
Group lead: prof. dr. (10)(2e) (LUMC)
Group members: (10)(2e) (10)(2e) (CWI & VU; (10)(2e) of large-scale analytical data management); prof. dr. (10)(2e) (10)(2e) UU & Animal health Service; professor of monitoring and surveillance) (10)(2e) (10)(2e) LUMC; (10)(2e) (10)(2e)

Working group 3: Targeted response & core groups
Group lead: prof. dr. (10)(2e) (UMCU and RIVM)
Group members: dr. (10)(2e) (RIVM/Cib; senior researcher infectious diseases); (10)(2e) (10)(2e) Maastricht University; (10)(2e) of infectious disease control).

Working group 4: Testing strategy
Group lead: prof. dr. (10)(2e) (10)(2e) (WUR)
Group member: (10)(2e) (TU/e; (10)(2e) of statistics).

Working group 5: International approaches & criteria for alarm
Group lead: prof. dr. (10)(2e) (UU)
Group member: (10)(2e) (10)(2e) (UvA; (10)(2e) of psychological methods (10)(2e) (10)(2e) (CWI; (10)(2e) of numerical analysis and dynamical systems).

All themes are intimately linked, but each theme also has specific questions. The group leads are collectively responsible for links and cross-fertilization and cross-theme interaction. (10)(2e) and (10)(2e) will have the responsibility for the overall project. We will set up a system of very frequent meetings, weekly in the first months of the project. Group members will be involved in more working groups than the one under which they are mentioned.

An Advisory Board will be set up including at least the following experts: dr. (10)(2e) (NIVEL), dr. (10)(2e) (GGD Amsterdam), dr. (10)(2e) (RIVM), prof. dr. (10)(2e) (UMCU), dr. (10)(2e) GGD Rotterdam). Additional members from practice will be approached (GGD Rotterdam, GGD Zuid Limburg).

A consortium agreement will be drawn up. One of the important aspects will be to facilitate use of data that has been, and is being, collected by various project partners. Privacy issues should be dealt with, for example by bringing models to the data rather than the other way around, i.e. by doing specific simulations on location with the holder of the data if no data-exchange is possible because of privacy issues. In a number of cases, aggregated data that cannot be traced back to individuals is sufficient for the analyses we envisage. Another important aspect is the urgency of the work.

4. Project parts in more detail:

Below, we describe the sort of questions to be taken into account for the different aspects, which will be the starting point for the five working groups.

i). Mobility and geographical modeling of spread. Importation of cases from abroad: monitoring travellers (not only by air, but also by train and car), what can be done, what can't be done. Can we say anything about volume of incoming individuals + where they come from under normal circumstances and estimate likely number of incoming cases and possibly likely distribution over the Netherlands? Mixing of people in regions with current active transmission with people in regions with no (or almost no) current transmission. When normal mobility patterns are resumed, taking basic infection-avoiding measures into account, where is infection likely to arise? This does not mean of course that infection can and will not arise elsewhere, but we could look at heat maps of particularly elevated risk for areas with more substantial mixing and mobility to impose more rigorous monitoring. The group of (10)(2e) has experience in applying rare event sampling techniques to construct heat maps. Providing in-silico examples of possible spread post-exit, using mobility data, in fine geographic scale to provide input for others to try out efficacy of testing strategy, contact tracing, surveillance, ...? The working group has been carefully selected to encompass spatial models at three levels of aggregation in the population. This allows multi-scale mobility to connect individual movements to mobility patterns over communities -> cities -> regions -> country. The group of de (10)(2e) uses models at the lowest level of aggregation (individual-based models), the group of (10)(2e) uses models in the form of networks (modeling connections rather than individuals), the group of (10)(2e) uses stochastic compartmental models at the highest level of aggregation to study mobility patterns. An important partner for outsourcing work is the company Mezuro ((10)(2e) who are experts in deriving detailed insight into mobility patterns in the Netherlands from aggregated and anonymous mobile phone data (Vodafone/Ziggo). These data are already available pre-pandemic to show normal mobility in the Netherlands for every day of the year.

ii). Syndrome surveillance. Current practice and innovations in active and passive case finding, use of technology and diverse data sources. Essentially, TTI is passive case finding (in an active way). Can we think of an efficient and effective way of active case finding (other than at Schiphol airport on arrival/departure)? How would you go about this? Citizen based approaches for case finding. Can we make use of citizens who are willing to provide information about possible cases in their social environment? Similarly, to snowball sampling approaches to reach hidden populations, one could make use of people's knowledge of their own social environment to try to find cases and clusters. Other syndromic surveillance tools. Participatory surveillance platform like FluTrend (Grote Griepmeting) and COVID Radar (Chavannes). It has been shown that there was a good correlation between FluTrend and influenza incidence with a time advantage of 1-2 weeks of FluTrend. Reinstalling the website could help with a localized syndromic surveillance. Genetic sequences. Can we use sequence analysis to determine whether there are transmission clusters versus more isolated import cases? Surveillance of public perception. Can we predict when adherence to social distancing will decrease? Are there indications from monitoring social media that something will change/ is changing? Speeding up case finding. Technological solutions: syndrome surveillance in the general population with an app. More effectively, however, seems augmenting the usual flu-surveillance in GP-practices with targeted uses of syndrome-apps in specific groups that are either at greatest risk or can act as sentinels because they have relatively many contacts to a diverse range of individuals (see also 3). Routinely collected surveillance data are available from a small number of sources. Notably, the NIVEL sentinel general practices (40, covering about 0.8% of the Dutch population) provide daily data on acute respiratory problems. Samples of a subset of patients have been tested by RIVM for SARS-CoV-2 since the beginning

of the outbreak. In addition, there are weekly data from 350 general practices provided by NIVEL including information on acute respiratory problems. Reporting is currently on a weekly basis, but could be daily in principle. Delays are in the order of 4-10 days, which is too slow as this means that infections have occurred 10-16 days before, covering more than two generations of transmission. A retrospective analysis against the developing Covid-19-outbreak can inform whether the data are able to track the outbreak well, particularly in areas and time periods with relatively few cases. How can this coverage be improved and how strong should it be to be a useful indicator? Behavioural surveillance. There is a distinct possibility that the adherence to good infection-avoiding behaviour and the 1.5-m-society decreases as time goes by and 'old habits' return. It is a relevant question what behavioural nudging can be used to keep everyone alert and cooperative. However, for the monitoring the question is how diminishing adherence can be measured and how a decrease needs to translate in increased vigilance in the monitoring as more transmission opportunities will arise.

When the lockdown is partially lifted (e.g. by opening schools), the contact network will change (e.g., people otherwise not in contact will become connected through their children, so the shortest path lengths in the contact network will decrease); in response to that change, the value of the reproduction number R will increase, but this will only become visible when people become symptomatic and hospital admissions start to rise. By then, it can be too late to intervene successfully. A possible solution to the problem of the lagging indicators, is to utilize information gathered by the app developers, which may be used to assess the changes in the contact network directly. For example, if an intervention is implemented at time t, and the apps can be used to reconstruct the contact network at time t+1 from the behavioural data gathered, then we should be able to read out global indices like the density of that network. This could be done without requiring sensitive information about individuals. If this is successful, it would allow for a direct measure of the effect of interventions which would allow us to respond faster and monitor policy effectiveness more quickly. We do not currently know whether such a strategy would be feasible or whether it would be sufficiently effective to justify implementation. To investigate this issue, the UvA group led by (10)(2e) plans to utilize epidemiological models constructed by members of the current project group to study the effectiveness of this strategy by means of simulation studies. We will consider the possibility of building a 'dashboard' to allow simulation of various situations and strategies by non-experts. The group of (10)(2e) and the company Ilionx ((10)(2e) have the required expertise for that.

In addition to delivering a faster indicator, reconstruction of the contact network from behavioural data also means that we could set up experimental protocols for assessing the effect sizes of social distancing measures, including subtle interventions like nudging, in small experimental setups. For example, we could investigate the effect of nudging interventions by comparing the structure of the contact network in a group of people subjected to the nudge with that of a control group. In this manner, social distancing interventions would become amenable to systematic experimental research designs.

iii). Targeted response & core groups. Contact tracing. Current practice/protocol for this. What is special about Covid-19 that impacts on contact tracing success and how? How effective does TTI need to be in order to find expected new cases/ chains of transmission and small local clusters quickly, given uncertainty in the frequency with which these arise and in where they arise? How fast do we need to find them given the serial interval? How does effectivity relate to self-reporting of contacts and development of symptoms or active (daily?) follow-up of all contacts? Tracing-app, what are the epidemiological characteristics needed (given that privacy and ethical issues are resolved) and how can this be achieved technically? How to avoid/deal with many false positive alarms (and false negatives) that can arise with such apps? An app gives the possibility for higher-order tracing if records are retained for a longer period (the contacts of the contacts of a suspected case are immediately available). This can potentially speed up case finding, but can also lead to many more false alarms and it should be investigated where the balance lies for effectivity. How to take into account low uptake of an app and (more importantly perhaps) uptake that misses key parts of the population that mix more among themselves than with the overall population? This does not only hold for an app, but also for blind spots in normal tracing. For example, in group immunity by vaccination, it is key whether the people who are unvaccinated mix more among themselves than with the vaccinated part of the population. This is essential for group immunity to work. For tracing, one should also ask the question whether people missed by tracing (or who do not use an app) mix more among themselves than with people who are found by tracing or use of an app. For example, one can think of migrant worker communities, communities in the 'bible belt', nursing homes and homes for the elderly. No matter how high the uptake of an app, it is crucial to find ways of including these special groups.

There are more groups that are special for epidemic spread and targeted response. These core groups are three-fold: those at greatest risk of morbidity and mortality (e.g. nursing homes); those especially well-connected in the population (and therefore at risk of playing a larger than average role in spreading the infection); and those especially well-connected within their group, but not mixing as well with the general population (e.g. 'bible belt', nursing homes, migrants, …). How can surveillance in these groups be set-up effectively? For the first group, it is not only case finding, but also protection. The second group consists of people who potentially play a large role in transmission, should they become infected. The third group could have silent spread before this is picked up and drive a second wave. Vice versa, however, through the unusually high network connectivity of core group-2 members, they also have a higher probability to come into contact with an infected individual and can hence act as sentinels. We cannot find individuals, but could target certain professions, where individuals could be stimulated to actively participate in syndrome surveillance. This could be more effective than syndrome surveillance randomly in the population. Insofar as identifying core groups relies on the construction of a predictive statistical model (i.e., is data-driven), it formulates statistical prediction challenge that the groups at the UvA and CWI (10)(2e) have expertise on.

iv). Testing strategy. Testing capacity and speed (and possibly accuracy) of testing, as part of an effective TTI-response, is also important. Currently, testing is limited in the Netherlands and restricted to severe cases and hospital/care staff. What is the best testing strategy and in what way should we characterize "best" here? How does effectivity depend on epidemiological test characteristics (sensitivity, specificity, ...) and test speed (not only speed until a definite result is obtained, but also speed with which person identified as needing to be tested can actually be tested)? How does the quality of the test relate to the stage of infection (does it pick up infected individuals in latency or in early infectious period when asymptomatic?)? How does antibody

testing for past infection help? Use of sera collected for other purposes? For strategy: advantages/disadvantages and potential impact of targeted testing, e.g. ring-testing (geographic ring or social ring) around detected cases, group testing, individual testing of direct contacts, other variants? What is the optimal sampling strategy for testing (targeted and untargeted or random)?

v). International approaches & criteria for alarm. This consists of making an inventory of current practices in other countries, expressed in qualitative (strategy) and quantitative terms (capacity), successes and problems/failures, relevance to the Dutch situation. It also encompasses modelling and data analysis approaches used abroad to support monitoring decisions and policy. Strong links exist among various project members to the most active and prominent epidemiological groups abroad, as well as to SAGE in the UK. Keeping track of international developments requires constant integration of data as well as updating of statistical models that could be designed to assess the effect of interventions. (10)(2e) group at the UvA has set up the initiative Data versus Corona, a group of data scientists that help investigators doing COVID-19 researchers with statistical modelling and data organization. The Data versus Corona collective is already constructing databases and apps to analyse and visualize the effects of different versions of the lockdown in various countries. Orienting these efforts towards the current proposal, we could accelerate the accessibility of international comparison data in an Open Science platform.

Criteria for alarm. Monitoring purpose and how to measure whether this is being achieved (or is in danger of failing). Up to now, one of the quantifiers of success of measures was the effective reproduction number. This worked fine during the outbreak, as numbers of infected individuals are high (averaging out stochastic and individual variation in infection ability, e.g. superspreaders, and therefore limiting uncertainty) and it is not a problem if there is a delay driven by the type of data that is used (hospital admissions or deaths). In the final phase of the outbreak and after the first wave has ended, however, numbers of cases are likely to be very small, increasing uncertainty bounds. In addition, using hospital admissions causes a delay of two weeks (i.e. more than two generations of infecteds) in picking up any increase in R that may trigger an alarm and the need for more severe regional or national measures. This makes that R is too coarse and uncertain a measure to use, certainly as the only indicator. Spread of infection occurs in a highly complex system that is our society (Heesterbeek et al, 2015) and one cannot rely on a one-dimensional indicator to give an accurate assessment for the danger of new outbreaks in low-transmission settings. A clear advantage of R is that is has a natural dynamical threshold for action, but also there one needs to decide whether a value above 1 should immediately trigger governmental action. What other criterion can be used as a substitute or in addition to it? If this criterion has no natural threshold, what is a level at which alarms should be triggered for more organised governmental intervention? Can this be achieved by regional measures? On what does this depend (tracing results?)? How long should these measures be in place and what monitoring needs to be done in the affected region (if it is limited to one region)? New cases being discovered is not ideal as a measure as it depends on the number of tests and the testing strategy but may be the best alternative. It has no natural threshold so needs criteria (regional increase above certain level? size of region? national increase required? Increase in specific group required and tracked (sentinel group)? Some countries seem to choose a specific number of positive test results per 100.000 inhabitants as a criterion, locally, regionally or nationally. We will investigate the options and their advantages and risks.

Alarms are analysed in terms of the balance that they strike between true/false positives and true/false negatives. This balance is determined by three factors: the degree to which the test is sensitive to the problem it is supposed to detect (typically represented in a Receiver Operating Characteristic (ROC) curve), the threshold at which the alarm is set to go off, and the base rate at which the problem in question occurs. The question is whether we can come up with cleverly constructed variables that perform better than R in minimizing false positives and false negatives. Increases in connectivity of the contact network, specified under point (iv), could be one such detection mechanism; another interesting possibility that may be investigated is the use of Early Warning Signals (EWS) like critical slowing down (Scheffer et al., 2009), which may be visible as the contact network becomes denser and the system as a whole loses resilience. Many other variables could be created and studied for their effectivity for use in alarm systems by using simulation models constructed in the project group and assess robustness using uncertainty quantification techniques. The group of Crommelin (CWI) has developed software for this. We can set up an in silico experimental setup, where investigators can try out different alarm systems to assess their qualities. Up to now, work on early-warning signals, that has led to successes in disciplines such as ecology, has been advocated in many other fields (for example finance and economic analysis, see Battison et al. 2016). A key problem with application to epidemic systems is that, mathematically speaking, the change from a minor to a major outbreak is a different type of bifurcation than those for which the existing early warning indicators have been developed. In addition, there were very few data sets available as most outbreaks are 'n=1' events. The current pandemic, however, will provide a wealth of data for development of indicators. The usefulness of these data, however, will depend on how well monitoring has been performed.

Referenties / References

Anderson, Roy, Heesterbeek, Hans, Klinkenberg, Don & Deirdre Hollingsworth (2020): How will country-based mitigation measures influence the course of the COVID-19 epidemic? The Lancet, 395, 931-934.

Backer, Jantien A and Klinkenberg, Don & Wallinga, Jacco (2020). Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. Eurosurveillance, 25, 2000062, https://doi.org/10.2807/1560-7917.ES.2020.25.5.2000062.

Battiston, S., J.D. Farmer, A. Flache, D. Garlaschelli, A. Haldane, H. Heesterbeek, C. Hommes, C. Jaeger, R. May & M. Scheffer (2016). Complexity Theory and Financial Regulation. Science, 351, 818-819.

Drew, D.A., Long H. Nguyen, Claire J. Steves, Cristina Menni, Maxim Freydin, Thomas Varsavsky, Carole H. Sudre, M. Jorge Cardoso, Sebastien Ourselin, (10)(2e) Wolf, Tim D. Spector, Andrew T. Chan & COPE Consortium (2020). Rapid implementation of mobile technology for real-time epidemiology of COVID-19. Science, 05 May 2020: eabc0473

DOI: 10.1126/science.abc0473.

Ferguson, N., D. Laydon, G. Nedjati-Gilani, N. Imai, K. Ainslie, M. Baguelin, S. Bhatia, A. Boonyasiri, Z. Cucunubá, G. Cuomo-Dannenburg, A. Dighe, I. Dorigatti, H. Fu, K. Gaythorpe, W. Green, A. Hamlet, W. Hinsley, L. Okell, S. van Elsland, H. Thompson, R. Verity, E. Volz, H. Wang, Y. Wang, P. Walker, C. Walters, P. Winskill, C. Whittaker, C. Donnelly, S. Riley & A. Ghani (2020). Impact of Non-Pharmaceutical Interventions (NPIs) to Reduce COVID-19 Mortality and Healthcare Demand (16 March 2020); www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf.

Ferretti, L., C. Wymant, M. Kendall, L. Zhao, A. Nurtay, D. G. Bonsall & C. Fraser, Quantifying dynamics of SARS-CoV-2 transmission suggests epidemic control by digital contact tracing. Science 08 May 2020: Vol. 368, Issue 6491, eabb6936 DOI: 10.1126/science.abb6936.

He, X., Lau, E.H.Y., Wu, P. et al. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med 26, 672–675. https://doi.org/10.1038/s41591-020-0869-5.

Heesterbeek, Hans, Roy M. Anderson, Viggo Andreasen, Shweta Bansal, Daniela De Angelis, (10)(2e), Ken T. D. Eames, W. (10)(2e) (10)(2e), Simon D. W. Frost, (10)(2e), T. Deirdre Hollingsworth, Thomas House, Valerie Isham, (10)(2e), (10)(2e) (10)(2e), James O. Lloyd-Smith, C. Jessica E. Metcalf, Denis Mollison, Lorenzo Pellis, Juliet R. C. (10)(2e), Mick G. Roberts, (10)(2e) & Isaac Newton Institute IDD Collaboration (2015). Modelling infectious disease dynamics in the complex landscape of global health. Science, 347, aaa4339.

Hellewell, J., S. Abbott, A. Gimma, N. I. Bosse, C. I. Jarvis, T. W. Russell, J. D. Munday, A. J. Kucharski, W. J. Edmunds, S. Funk, R. M. Eggo, F. Sun, S. Flasche, B. J. Quilty, N. Davies, Y. Liu, S. Clifford, P. Klepac, M. Jit, C. Diamond, H. Gibbs & K. van Zandvoort, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob. Health 8, e488–e496 (2020). doi:10.1016/S2214-109X(20)30074-7pmid:32119825.

Hollingsworth, D., Klinkenberg, D., Heesterbeek, J.A.P. & R.M. Anderson (2011). Mitigation strategies for pandemic influenza A: balancing conflicting policy objectives. PLoS Comput. Biol. 7(2): e1001076.

Kissler, S.M., Christine Tedijanto, Edward Goldstein, Yonatan H. Grad & Marc Lipsitch (2020). Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. Science Date: 14-Apr-2020 DOI: 10.1126/science.abb5793.

Klinkenberg, D., Fraser, C. & J.A.P. Heesterbeek (2006). The effectiveness of contact tracing in emerging epidemics. PLoS One, Dec 20; 1; e12, 1-7.

Kretzschmar, Mirjam, Rozhnova, Ganna & van Boven, Michiel (2020). Effectiveness of Isolation and Contact Tracing for Containment and Slowing Down a COVID-19 Epidemic: A Modelling Study. Unpublished manuscript available at SSRN: https://ssrn.com/abstract=3551343 or http://dx.doi.org/10.2139/ssrn.3551343.

Leung, K., Joseph T Wu, Di Liu & Gabriel M Leung (2020). First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: a modelling impact assessment. Lancet, 395 (10233), 1382-1393, April 25, 2020.

Prem, K., Yang Liu*, Timothy W Russell, Adam J Kucharski, Rosalind M Eggo, (10)(2e), Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, (10)(2e) & (10)(2e) (2020). The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. Lancet Public Health, 5, e261–70.

Quilty, B.J., Clifford S., Flasche S. & Eggo R.M. (2020). Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV). Eurosurveilance, 252000080.

Roberts, M.G. & J.A.P. Heesterbeek (2007). Model-consistent estimation of the basic reproduction number from the incidence of an emerging infection. J. Math. Biol., 55, 803-816.

Scheffer, M., Bascompte, J., Brock, W. et al. (2009). Early-warning signals for critical transitions. Nature 461, 53–59, https://doi.org/10.1038/nature08227.

Sun, K. & C. Viboud (2020). Impact of contact tracing on SARS-CoV-2 transmission. Lancet Infectious Diseases, April 27, 2020, DOI:https://doi.org/10.1016/S1473-3099(20)30357-1

Teslya, A., Thi Mui Pham, Godijk, N.G., (10)(2e), (10)(2e)., Bootsma, M.C.J. & G. Rozhnova (2020). Impact of self-imposed prevention measures and short-term government intervention on mitigation and delaying a Covid-19 epidemic. Manuscript on MedRXiv, 10.1101/2020.03.12.20034827v2.full.pfd.

Vlas, S. de & Luc Coffeng (2020). A phased lift of control: a practical strategy to achieve herd immunity against Covid-19 at the country level. Manuscript on MedRxiv 2020.03.29.20046011; doi: https://doi.org/10.1101/2020.03.29.20046011.

Wölfel, R., Corman, V.M., Guggemos, W. et al. (2020). Virological assessment of hospitalized patients with COVID-2019. Nature, April 1, 2020. https://doi.org/10.1038/s41586-020-2196-x.

Financiële gegevens / Financial data

ZonMw budget

	Jaar / Year								
Kostenpost	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	**Totaal / Total**
Personeel	415.000	0	0	0	0	0	0	0	415.000
Materieel	85.000	0	0	0	0	0	0	0	85.000
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	**500.000**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**500.000**

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			
DEC		X			
WBO		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

Historie subsidieaanvraag / History grant application

Deze aanvraag is ook ingediend bij organisatie / This grant application has also been submitted to organization:

DAEB Format

Organisation	Type of organisation	Quoted costs	Quoted co-funding	Requested budget
UU	Knowledge institution	91.029,33	-	91.029,33
UMCU	Knowledge institution	40.329,45	-	40.329,45
LUMC	Knowledge institution	35.336,28	-	35.336,28
WUR	Knowledge institution	35.336,28	-	35.336,28
TU/e	Knowledge institution	50.699,88	-	50.699,88
CWI	Knowledge institution	50.699,88	-	50.699,88
UVA	Knowledge institution	25.349,94	-	25.349,94
RIVM	Civil Society Organisation / CSO	25.349,94	-	25.349,94
Maastricht University	Knowledge institution	25.349,94	-	25.349,94
Erasmus	Knowledge institution	35.336,28	-	35.336,28
	Total	414.817,20	-	414.817,20

Staff costs

			Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Function (will be filled based on "staff"sheet)	Remarks	Organisation (dropdown menu)			
H. Heesterbeek		UU	€ 40.329,45	€ -	€ 40.329,45
G. v. Schaik		UU	€ 25.349,94	€ -	€ 25.349,94
D. Panja		UU	€ 25.349,94	€ -	€ 25.349,94
M. Kretzschmar		UMCU	€ 40.329,45	€ -	€ 40.329,45
S. de Vlas		Erasmus	€ 35.336,28	€ -	€ 35.336,28
N. Chavannes		LUMC	€ 35.336,28	€ -	€ 35.336,28
(10)(2b)		WUR	€ 35.336,28	€ -	€ 35.336,28
R. van der Hofstad		TU/e	€ 25.349,94	€ -	€ 25.349,94
E. van de Heuvel		TU/e	€ 25.349,94	€ -	€ 25.349,94
P. Boncz		CWI	€ 25.349,94	€ -	€ 25.349,94
B. Zwart		CWI	€ 25.349,94	€ -	€ 25.349,94
D. Borsboom		UVA	€ 25.349,94	€ -	€ 25.349,94
M. Stein		RIVM	€ 25.349,94	€ -	€ 25.349,94
C. Hoebe		Maastricht University	€ 25.349,94	€ -	€ 25.349,94
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
to be specified			€ -	€ -	€ -
			€ 414.817,20	€ -	€ 414.817,20

Material, equipment & consumer goods (itemised)

			Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Discription	Remarks	Organisation (dropdown menu)			
				€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -

			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€	€ - -	€ -

Other costs (itemised)

			Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Discription	**cost sort (dropdown menu)**	**Organisation (dropdown menu)**			
Publicaties open access en ontsluiting methoden (dashboard)	Open Access publication		€ 25.000,00	€ -	€ 25.000,00
Meeting costs (project + communicatie)	Others, please specify in description		€ 5.182,80	€ -	€ 5.182,80
Outsourcing work (mobiliteitsanalyses Mezuro et cetera)	Outsourcing		€ 50.000,00	€ -	€ 50.000,00
Data ontsluiting en databeheer			€ 5.000,00	€ -	€ 5.000,00
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ -	€ -	€ -
			€ 85.182,80	€ -	€ 85.182,80

Total costs project	€ 500.000,00
Own contribution / co-funding	€ -
TOTAL REQUESTED BUDGET ZONMW	€ 500.000,00

Additional explanation for budget

Approval financial responsible receiving organisation

Receiving organisation
Name:
Function:
E-mail adres:
Date:

Checklist

for Open science & FAIR data elements in the COVID-19 research programme

Version 1.0

This checklist is for the first 4 out of **8 requirements and recommendations** for the **activities for open science and FAIR** data. They relate to the preparation phase of a research project.
The checklists shows a number of options for open science and FAIR data. Please consult **Open science in COVID-19 research** for more information about what you can do, for recent updates on the guidance, new practices, and instructions.

Choose the options that suit your project best!
The purpose of the checklist is to fill in the options that you choose for your project. Discuss with your data steward (or other data expert) the options that suit your project best. If you have options that are not listed below, you may indicate this as well.

Please fill in the form and attach it as a PDF file to your grant application. This is mandatory.

Requirements & Recommendations	Applicants must report as follows
Who is the data steward who supports the open science and FAIR data planning in your project? Check the website ZonMw's webinars to inform and support data stewards.	☐ I involve a data steward: Name: Klik of tik om tekst in te voeren. Institute: Klik of tik om tekst in te voeren. E-mail: Klik of tik om tekst in te voeren. Attended the webinar: ☐ Yes ☐ No ☒ I do not have a data steward yet.
Requirement 1: Alignment and reuse Please show the options for reusing data, biological materials, and/or other resources (from research or from practice) in your project. Check whether it is possible to use resources that are made in the context of COVID-19.	Name the existing resources that you plan to use: ☒ **Data**: publicly available data related to Covid-19; mobility data for the Netherlands; data collected by various project partners ☐ Biological materials: Klik of tik om tekst in te voeren. ☒ Research software: code and software for the analysis of models and epidemiological data ☒ **Other resources**, i.e. mathematical models and methods, and other quantitative and modelling tools, partially produced in the direct context of Covid-19 ☐ No, I will not use existing resources, because Klik of tik om tekst in te voeren. Please mark the resources that you indicated above **in bold** if it is a COVID-19 related resource
Requirement 2: preregistration of all animal studies **(for all other studies, preregistration is strongly recommended)** You are required (for animal studies) and recommended (for all other studies) to preregister your research	☐ I n case of preregistration: Provide the link or registration code: Klik of tik om tekst in te voeren. ☐ For animal studies, the code at the Preclinical Trial Register is: Klik of tik om tekst in te voeren. ☒ No, I do not preregister my research proposal.

plan (including the protocols, methods, etc).	
Requirement 3: FAIR data within COVID-19 research community **Choose the options that suit your project best! (MAATWERK!)** Here you can show the COVID-19 specific standards, technology or infrastructure for FAIR data that you have selected to apply during your project. Once your application is granted, you can use these to fill in your data management plan (DMP) (= requirement 5). Read for more information: 3.Creating FAIR data, tailored to COVID-19	Name the COVID-19 specific FAIR data standards, technologies or infrastructure that are applicable in your study, and you plan to use: ☐ eCRF of the WHO (machine actionable) ☐ A COVID-19 related or other FAIR data point ☐ COVID-19 research platform for data sharing ☐ Data will be recorded in RDF format ☐ I plan to use the metadata scheme that will be developed for COVID-19 research (planned in summer 2020) ☐ Other COVID-19 related standards, etc: Klik of tik om tekst in te voeren. ☐ Collaboration with COVID-19 data collection(s), namely Klik of tik om tekst in te voeren. ☐ A new standard, technology or infrastructure will be developed in the project with the COVID-19 research community. Comment on your choice(s) Klik of tik om tekst in te voeren. ☐ None of the above. Comment: Klik of tik om tekst in te voeren. ☒ I did not decide yet.
Requirement 4: Budget for FAIR data and Open Access Publications You need to plan a budget for open science and research data management during your research project. This budget should include data stewardship, and – if applicable - costs for additional services from data service providers (e.g. from Health-RI), or extra e-infrastructure.	**Explain how you budgeted for open science and FAIR data in your project:** ☐ I specified the costs in the budget form. ☒ I cannot specify the costs right now, and make a reservation of 5% maximum of my research budget for data stewardship. ☐ I did not budget the costs, because Klik of tik om tekst in te voeren. **When you fill in the budget form, you could consider the following aspects:** o Data stewardship o Data services providers (e.g., at Health-RI, other others) o Additional e-infrastructure, exceeding the regular institutional infrastructure. o Other open science and FAIR data related costs. o (Optional) Open access publication(s): ZonMw requires researchers within the covid-19 programme to make all publications resulting from scientific research, that is fully or partially subsidised by ZonMw, immediately (without embargo) open access available with an open license. You are allowed to include costs for full gold Open Access publications in the project budget up to a maximum amount of € 5000,- (specify with 'Open Access'). Immediate Open Access publishing via other routes is

	also permitted, but ZonMw does not provide financial resources for this. For the specific conditions we kindly refer to the programme texts.