

Algemene gegevens / General Information

Programma / Programme : **COVID-19 Programma**
 Subsidiëronde / Subsidy round : **Bottom-up ronde COVID-19 aandachtsgebied 2**
 Projecttitel / Project title : **SARS-CoV-2 transmission in secondary schools and the influence of indoor environmental conditions**
 Projecttaal / Project language : **Engels / English**
 Geplande startdatum / Planned start date : (10)(2e)
 Geplande duur / Planned duration : 6/2 maanden / months
 Datum indienen / Date of application : **15-06-2020**
 Projecttype / Project type : **Toegepast onderzoek / Applied research**
 Vervolg eerder ZonMw-project / Continuation previously funded project : **Nee / No**
 ZonMw

Projectleden / Project members

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Covid19_digitaal / Covid19_digitaal

Dossier nummer / Dossier number: 50-56300-98-689

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Projectgegevens / Project information**Aandachtsgebieden / Focus****2.1 Thema's aandachtsgebied 2**

- Transmissie en epidemiologie

2.2 Subthema's organisatie van zorg en preventie

- Zorg en preventie op afstand

2.4 Subthema's transmissie en epidemiologie

- Haalbaarheid, effect en effectiviteit van verschillende maatregelen
- Verspreiding van virus in meest getroffen gebieden of bevolkingsgroepen

2.5 Sector

- Andere sector
- Preventie

Samenvatting / Summary

Lifting school closures is one of the first releases considered in 'exit-strategies', given the disruptive effects for society. Yet, the role of schools in SARS-CoV-2 transmission remains largely undetermined. Several conditions in particular in secondary

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schools could favour transmission; Pre- or asymptomatic adolescents may go unnoticed and spread virus via direct or indirect contact (via surfaces), or by exhaled small airborne droplets ('aerosols') in crowded school settings. Of note, airborne transmission is strongly influenced by indoor air quality and ventilation, which are suboptimal in many school buildings.

This project aims to quantify SARS-CoV-2 transmission by various routes within secondary schools and relate transmission rates to indoor environmental conditions and crowding. This project will also investigate the potential for SARS-CoV-2 airborne transmission more specifically

This project combines environmental and virological studies in experimental as well as real-life school settings, studying 1) aerosol concentration, distribution and persistence under various experimental indoor environmental conditions and the biological properties of SARS-CoV-2-containing aerosols; 2) SARS-CoV-2 contamination and transmission along with environmental conditions in schools, supplemented with at least 5 detailed outbreak investigations in school infection clusters including an assessment of prevailing indoor environmental conditions and air circulation patterns, along with extensive environmental air and surface sampling. The outbreak studies will be embedded in a preparedness platform designed for a rapid research response.

Results will help define the importance of secondary schools in the transmission of SARS-CoV-2, quantify the importance of airborne and indirect transmission and the influence of indoor environmental conditions, and provide a road-map to healthy school environments that maximize control of SARS-CoV-2, as well as other respiratory pathogens.

Trefwoorden / Keywords

containment strategies; transmission studies; schools; indoor environmental health; airborne transmission;

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

Nee / No

(10)(2b)

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		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	

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DEFINITIEF

Andere vergunningen / Other permits

**AANVRAAGFORMULIER
UITGEWERKTE SUBSIDIEAANVRAAG
– BOTTOM-UP RONDE
COVID 19 programma**

Deadline voor indiening: 15 juni 2020 (14:00 u)

**LEES ALSTUBLIEFT ALLE INSTRUCTIES IN BIJLAGE "TOELICHTING
INDIENING SUBSIDIEAANVRAAG" 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
(Let op: dit zijn twee verschillende links, gebruik maar 1 van de 2!)

ProjectNet: [Aandachtsgebied 1 \(voorspellende diagnostiek en behandeling\)](#)

ProjectNet: [Aandachtsgebied 2 \(zorg en preventie\)](#)

BASISGEGEVENEN (voorpagina)

NAAM VAN DE HOOFDAANVRAGER:

(10)(2e)

ORGANISATIE:

UMC Utrecht

ENGELSE PROJECTTITEL:

SARS-CoV-2 transmission in secondary schools and the influence of indoor environmental conditions

NEDERLANDSE PROJECTTITEL:

Verspreiding van SARS-CoV-2 in middelbare scholen en de rol van binnenklimaat.

ONDERZOEKSVORSTEL
ma 8 pagina's A4
(inclusief literatuurreferenties)

(voorpagina met basisgegevens niet meegerekend -
font type Arial 10 pts)

1. PROBLEEMSTELLING, URGENTIE EN DOELSTELLING(EN)

Now that the first wave of the COVID-19 epidemic in the Netherlands has been contained and the number of daily new hospitalizations is well below the upper limit of healthcare capacity, government policy is shifting towards gradual reopening of society. Lifting school closures is one of the first releases considered in the 'exit-strategy', given the disruptive effects for society. This is substantiated by results from mathematical modelling that predict a limited effect of school closure in comparison to other social distancing measures on reducing COVID-19 mortality. Yet, the role of schools in transmission of SARS-CoV-2 remains largely undetermined to date as empirical evidence is mostly lacking.

While young children appear to be less susceptible to SARS-CoV-2, and consequently less important in transmission, this is much less evident for adolescents. From several household and seroprevalence studies, SARS-CoV-2 infection rates among adolescent age-groups appear to resemble those of adults more closely, but the infection is usually mild or asymptomatic, which may lower the transmission potential.⁽¹⁾ On the other hand, the much higher contact rates among adolescents attending secondary school could easily make up for the lower infectivity rates. Many school environments accommodate large numbers of students in closely spaced classrooms, while ventilation is often suboptimal. It is known that such conditions favour transmission of respiratory pathogens. In addition, secondary schools generally serve a student population from a wider geographic region compared to elementary schools. In case of an outbreak in a secondary school, there is a realistic potential for wider dissemination across multiple regions. For this reason, minimizing the risk of SARS-CoV-2 transmission in secondary schools is a public health priority and a prerequisite for safe re-opening.

As for most respiratory viruses, direct respiratory droplet transmission from coughing and sneezing has been established as the main route of SARS-CoV-2 transmission. Alternative routes include direct contact, indirect contact (via surfaces), or by small airborne droplets (referred to as 'aerosols'). To what extent these alternative routes are contributing to SARS-CoV-2 epidemic spread is still largely unknown, but observations of large transmission clusters that cannot be explained by droplet transmission, suggest they could be important. Studies suggest that up to 40% of transmission may occur from individuals before they become symptomatic.⁽²⁾ In the absence of coughing and sneezing, this is most likely explained by airborne and (in)direct transmission. Pre- and asymptomatic transmission of SARS-CoV-2 can seriously reduce the effectiveness of containment strategies that center around self-isolation of symptomatic individuals, while asymptomatic infected individuals continue their activities as normal, including school attendance. In such environments, conditions that can favor airborne and indirect transmission should therefore be avoided.

Aerosols ($\leq 5 \mu\text{m}$) are produced during speech and even normal breathing. Singing, loud speech and increased respiration (e.g. from physical activity) increase aerosol generation. Aerosols persist in air for much longer than the larger droplets ($> 5 \mu\text{m}$) typically produced by coughing and sneezing, which settle on surfaces within minutes. Virus containing aerosols can induce infection in the respiratory tract when inhaled by a susceptible person. Both higher concentrations of infected aerosols in the inhaled air and prolonged exposure increase the risk of infection. Importantly, transmission by aerosols can have a much larger radius than the typical 1.5 meters cut-off for droplet transmission, making it particularly relevant in crowded settings. Detection of SARS-CoV-2 RNA in air samples from hospitals containing aerosols in the range of 1-4 μm as well as reports of super-spreader events where subjects were infected beyond a distance of 1.5 meters during indoor gatherings, provide substantive support for existence of this transmission route.^(3,4)

Many studies have shown that indoor air quality affects health, comfort and performance of school children⁽⁵⁾. The effect of indoor air quality, and in particular ventilation, on the transmission of respiratory pathogens is less studied, but has gained substantial attention recently in light of the SARS-CoV-2 pandemic. It should be noted that most secondary schools in the Netherlands have natural ventilation with operable windows, which is often not sufficient to ventilate properly given regular classroom occupancy.

By combining environmental and virological studies in experimental as well as real-life school settings, we will quantify the role of secondary schools in SARS-CoV-2 transmission and establish optimal indoor environmental conditions for its mitigation. More generally, this project will bring in-depth understanding of the airborne transmission route of SARS-CoV-2 and the influence of indoor environmental conditions.

2. LOPEND ONDERZOEK

Evidence thus far on the role of secondary schools in SARS-CoV-2 transmission is scarce and conflicting; In an Australian study with 12 index cases in 10 high schools⁽⁶⁾, only 1 secondary case was identified. In Ireland, 6 notifications of a SARS-CoV-2 case in school settings were examined, two secondary cases were identified from one index case⁽⁷⁾. In an outbreak of SARS-CoV-2 early February at a secondary school in

France, the infection attack rate was 26% among students and staff.(8) In addition, several school clusters have been reported in the media, but these reports lack epidemiological investigations to determine whether transmission occurred in the school environment and under what conditions. To our knowledge, there have been no comparative studies on transmission of SARS-CoV-2 in schools and classrooms with different indoor environmental and crowding conditions. The unique conditions in schools, where up to 32 individuals reside in a closed space with relatively stable indoor conditions, at fixed classroom positions and for prolonged time, offer an ideal setting to quantify exposure-transmission relationships, but requires detailed epidemiological investigation.

While epidemiological data in support of airborne transmission of SARS-CoV-2 is accumulating, members of our group were recently able to confirm the transmission of SARS-CoV-2 via the air over 10cm in the conventional ferret transmission model (9), but also over a longer distance (unpublished data Erasmus MC, S. Herfst et al). From the field of aerosol research, experiments with healthy individuals have recently assessed the size distribution of exhaled aerosols and the distance these droplets travel. Yet, these investigations were done under fixed indoor environmental conditions (10) and the effect of air-currents, ventilation, temperature and humidity on their behaviour is unknown. To ultimately understand the conditions for, and potential of human-to-human airborne transmission, linked investigations are needed as a next step, that 1) assess the size distribution and aerodynamic properties of infectious respiratory droplets obtained from air samples under 2) various indoor environmental conditions.

3. PLAN VAN AANPAK (ONDERBOUWING KEUZES)

THEORETISCHE EN/OF EMPIRISCHE ONDERBOUWING

In combination, the presence of pre- or asymptomatic individuals in crowded indoor environments with poor ventilation could generate 'hot spots' for virus spread via airborne and indirect transmission. Such conditions are easily met in school environments. Secondary schools host a population that appears more susceptible to SARS-CoV-2 compared to primary schools, and that come from a wide geographic region which makes the situation more urgent for secondary schools.

Presence of an airborne transmission route may warrant engineering controls as part of an overall strategy to limit spread of SARS-CoV-2. Appropriate engineering controls include sufficient and effective ventilation, possibly enhanced by particle filtration and air disinfection, avoiding air recirculation and avoiding overcrowding. Often, such measures can be easily implemented and without much cost, but if only they are recognised as significant in contributing to infection control goals.

DESIGN

This project consists of two integrated parts:

- 1) experimental lab studies on infectivity of SARS-CoV-2-containing aerosols, the optimal air sampling techniques, and on aerosol concentration and dispersion under various indoor environmental conditions;
- 2) A prospective observational study and outbreak investigations on SARS-CoV-2 transmission in secondary schools

STUDIE POPULATIE/DATABRONNEN

Part 1) At ErasmusMC, an operational ferret model to study airborne SARS-CoV-2 transmission (11) will be used to determine the size distribution of SARS-CoV-2 containing aerosols, and test the most optimal methods to collect SARS-CoV-2 containing particles from the air. Animals inoculated with SARS-CoV-2 will be housed in a cage in negatively pressurized class-3 isolators. Each cage is connected to an air passage, with a passive airflow running from the infected animal through the air passage. Aerosol particle size distribution and flow will be measured 1) close the infected ferret (exhaled particles) and 2) at various distances from the ferret in the air passage, using spectrometer technology. Air-samples will be taken with different air samplers, which will be compared for their physical (RNA) and biological (viable virus) collection efficiency. The best performing sampler will subsequently be used in Part 2. Upon completion of the ferret experiment we will have;

- 1) Defined aerosol particle size fraction relevant for SARS-CoV-2 transmission, their aerodynamics and biological properties
- 2) Defined optimal air-sampling techniques of particles relevant in SARS-CoV2 transmission

The results will directly feed into the experiments in the Experience room of the SenseLab (Science Centre, TU Delft). A classroom setting will be simulated under different ventilation and indoor environmental settings (natural, mechanical (mixing or displacement)). A technical set-up will be used for a standardized production of aerosol clouds, representing speaking, shouting and singing, will be characterized for particle size distribution at the source and at the point of exposed person(s) at different positions relative to the source. These experiments will help us understand the spatiotemporal dynamics of aerosol dispersion under various indoor and crowding conditions and identify key drivers for aerosol dense environments, where infection risks from virus containing aerosols would be highest. We will particularly focus on concentration, dispersion and persistence of particles sizes relevant for SARS-CoV-2 transmission as determined from the ferret experiments. Upon completion of the SenseLab experiments we will have:

- 1) Characterized aerosol dynamics in class-room settings and key drivers of these dynamics.
- 2) Defined conditions that minimize accumulation and persistence of aerosols, specifically those particle sizes relevant for SARS-CoV-2 transmission

This knowledge will feed into the Part 2 study and optimize assessment of potential aerosol transmission in school settings

Part 2) In a complementary approach, Part 2) will study SARS-CoV2 transmission in real-life school setting along two tracks:

First, we will approach 20 secondary schools in the Netherlands that provide a representative distribution with respect to number of students, building characteristics, education level and degree of urbanization. Selection of these schools will be based on data obtained from the VO-raad (Dutch interest group of school boards and schools in secondary education). Each school will undergo an on-site evaluation of the indoor and outdoor environmental conditions at start of follow-up (Aug-Oct 2020). This includes: type of heating, ventilation and air conditioning systems and settings, possible sources of pollution, floor plan, number of floors, number of students, classroom interior, operable windows, solar screens, etc. Each school will be subsequently equipped with electrostatic dust fall collectors (EDC) that are exposed to classroom air. The EDC consists of a custom-fabricated polypropylene sampler that has electrostatic cloths attached to it to provide a sampling surface. Airborne dust settles on this surface and is captured by the electrostatic properties of the cloth. EDCs will be placed in multiple classrooms and replaced every four weeks until end of follow-up at 6 months. The feasibility of this method to detect SARS-CoV-2 in airborne dust samples was recently validated in studies on mink farms (unpublished data by D. Heederik). The EDC results will provide insights in the level of air contamination with SARS-CoV-2 across classrooms, schools and time and its association with environmental conditions. Whenever a confirmed SARS-CoV-2 case occurs in one of the participating schools, additional information will be collected on the case including age, students or staff, school attendance from one week before symptom onset until start of isolation, classrooms visited, position in the classroom and number of close school contacts put in quarantine. A school questionnaire will detail heating and ventilation regime (including also opening/closing of windows and doors) during the infectious period of the index case. When a secondary case emerges (i.e. any new confirmed case with an epidemiological link to the index case, e.g. shared classroom), information will be collected detailing shared locations with the index case and duration of exposure, proximity in classroom setting etc. All data on infected subjects will be collected anonymously through the school. Jointly, they will provide detailed spatiotemporal mapping of potential infector-infectee pairs within schools and the prevailing environmental conditions. Furthermore, these on-site evaluations provide valuable hands-on 'pilot' experience for the design and conduct of the larger outbreak investigations.

Second, we will set-up a national preparedness platform for detailed outbreak investigations of SARS-CoV-2 clusters in schools. A cluster is defined as at least three cases within two weeks time, where at least two cases have an epidemiological link. The platform includes detailed protocols and action plans that can be immediately called into action whenever a cluster is identified, along with a national infrastructure of prepared schools. For this, we will closely work with the VO-raad and their network that covers all secondary schools in the Netherlands. Through their communication platform secondary schools in the Netherlands will receive information about the preparedness platform and are requested to participate in the outbreak investigations when a cluster emerges. The local outbreak investigation will include on-site assessment of present indoor environmental conditions and air circulation patterns, along with extensive environmental sampling of air (as optimized in Part 1) and surfaces. Virus-containing aerosols and droplets will be collected in the air sampler in virus transport medium. Samples will be aliquoted and subjected to quantitative RT-PCR and virus titration. In addition, all asymptomatic classmates and teachers will be offered SARS-CoV-2 testing. Informed consent will be obtained for sampling of individuals. We plan to conduct the outbreak investigation in at least five outbreak clusters. This will provide detailed outbreak data on air and environmental contamination by the virus as well as asymptomatic transmission.

VERWACHTE UITKOMST (in parameters of beschrijvend)

The primary outcomes of Part 2 include:

- Level, frequency and changes over time of SARS-CoV-2 air contamination, along with number of index and secondary cases as a function of indoor environmental characteristics and heating/ventilation regime in schools
- From outbreak investigations; number and locations of environmental samples positive for SARS-CoV-2, viral load and virus infectivity in relation to outbreak size and in relation to indoor environmental characteristics
- Jointly, these results will be used to quantify the importance of secondary schools in SARS-CoV-2 transmission and epidemic spread under the prevailing containment measures.

DATA-ANALYSE

Next, using indoor air quality and ventilation analysis programs, we will estimate airflows, multizone aerosol contamination and personal exposure of students or groups for the various indoor environments

encountered in the participating schools. The models are parameterized using input from Part 1 as well as Part 2 of the project. In an integrated analysis including virus contamination data for air and surface samples we will simulate observed outbreak patterns and infer the contribution of various routes of transmission. The models will then be used to simulate the effect of various engineering interventions on the indoor environment on transmission of SARS-CoV-2. This results in the identification of a set of modifiable environmental conditions that can help reduce the risk of SARS-CoV-2 transmission in schools.

4. PLAN VAN AANPAK (ONDERBOUW KETES)

TUJDSHEMA (maak daarbij duidelijk wanneer de eerste resultaten worden verwacht)

School inventory: July-September 2020

Experimental studies at SenseLab and Viroscience: July-November 2020

Start school monitoring: Sept 2020

School outbreak studies: Sept 2020- April 2021

Interim evaluation and recommendations: Jan 2021

Final analyses, report writing and recommendations: May-Nov 2021

MOTIVATIE HAALBAARHEID

The infrastructure for the experimental lab studies of Part 1 are fully operational, allowing a rapid start of the project. For Part 2, the school surveillance is set up in a way that harnesses our strong ties with the VO-raad (for school selection) as well as information generated from public health containment measures; as of June 1st 2020, all individuals in the Netherlands with COVID-19 like symptoms are eligible for SARS-CoV-2 testing free of charge. A positive test is followed by contact tracing and 14-day quarantining of all close contacts, defined as individuals who had a contact with the case for at least 15 min within 1.5 meters distance. (12) School-boards are routinely notified of SARS-CoV-2 cases detected among their students or staff. We leverage this source-and-contact tracing system, minimizing required efforts from schools and omitting active recruitment of, and cooperation from students. This makes our project highly feasible.

The creation of a preparedness platform for outbreak investigations highly improves the quality and timeliness of outbreak studies. The importance of mounting a rapid, coordinated deployment of such investigations was recently illustrated during the outbreaks of SARS-CoV-2 at mink farms and slaughter houses. Members of our team involved in the outbreak investigations experienced how the absence of such ready-to-act protocols lead to crucial information being lost (for instance, the slaughterhouse was already cleaned and disinfected before the investigation-team arrived). The creation of the preparedness platform with endorsement by the VO-raad, leveraging their network and communication platform, greatly expands our opportunities to capture (at least) five school outbreaks and studying them in a timely manner as schools reopen in September

Our project group consists of internationally renowned experts from complementary domains to guarantee high scientific standards throughout all phases of the project. With our unique multidisciplinary team, we leverage knowledge, skills, and technical opportunities across virology, epidemiology, population health and engineering the address an urgent public health question in the COVID-19 pandemic.

5. RELEVANTIE

OPROEP SPECIFIEKE RELEVANTIE CRITERIA

The results of this project are highly relevant for public health containment plans as it will:

- 1) help define the importance of secondary schools in the transmission of SARS-CoV-2;
- 2) quantify the importance of airborne and indirect transmission of SARS-CoV-2 and the influence of indoor environmental conditions
- 3) provide insight in the characteristics of airborne route of transmission, such as relevant particle size and biological properties of the aerosols
- 4) provide a road-map to healthy school environments that maximize control of SARS-CoV-2 transmission, as well as other respiratory pathogens.
- 5) Optimize air sampling techniques for the collection of virus-containing aerosols and droplets relevant to future studies on airborne transmission

ZONMW ALGEMENE RELEVANTIE CRITERIA

In the Netherlands, ~1 million students and staff reside and interact on a daily basis in secondary schools.

Herein lies the evident important position of secondary education in the containment strategy. Upon the reopening of schools in September, it will be crucial to closely monitor their effect on the overall epidemic.

Our project offers a detailed assessment of schools, both through planned environmental (including environmental virus contamination) and surveillance studies in schools, as well as through a rapid outbreak response with detailed and timely investigations of SARS-CoV-2 school clusters.

Our project will provide evidence on airborne transmission of SARS-CoV-2 and the influence of indoor environmental conditions that can be directly translated into low-cost and scalable interventions. These may include methods for ventilation, ventilation standards and how to measure these, cleaning and disinfection

practices, etc. While primarily aimed to improve the safe re-opening of secondary schools, these insights and interventions are equally important for other indoor environments like office buildings, primary schools and daycare, shops, nursing homes, etc. We anticipate the results from this project will be highly relevant to COVID-19 policies for other sectors in society.

6. PROJECTGROEPLEDEN EN HUN ROLLEN

(10)(2e) is a Pediatrician and Associate Professor in infectious Diseases Epidemiology at the Julius Center for Health Sciences and Primary Care of the UMC Utrecht. Her epidemiological research focuses on characterizing and quantifying clinical disease and transmission of vaccine preventable and emerging infections to guide clinical and public health policies. She has a specific interest in the role of children in transmitting infectious diseases. In the EU funded RECOVER project, she is scientific coordinator of the European hospital studies on COVID-19 and household transmission studies. She coordinates multicenter pediatric rotavirus, influenza and vaccine studies both clinical and at the community level. She has a key interest in, and pioneers innovative methods for studying disease transmission in the community. She has successfully applied novel methodologies in studies on community spread of respiratory, gastrointestinal, arbovirus and more recently SARSCoV2 infections that she supervised in OneHealth-PACT, SAFARI trial, ZieKA Monitor, ZIKAction and RECOVER. She serves as project leader for the current proposal.

(10)(2e) is professor Indoor Environment at the Faculty of Architecture and the Built Environment, of the Delft University of Technology in Delft. She initiated the SenseLab, a recently opened semi-lab environment partly open to the public, sponsored by 25 companies and organisations. In the past 10 years her research has been focused on the development of a more complex research model to explain symptoms and complaints in specified (exposure) situations, acknowledging other stressors and their integrated effects, interactions, and different needs and preferences of the occupant: a model that includes interactions for both the environment (the situation) and the occupants. For 'The Indoor Environment Handbook: How to make buildings healthy and comfortable', she received the prestigious Choice Outstanding Academic Titles of 2010 Award. She will be heading the experiments at SenseLab and will co-lead the environmental measurements in schools as well as the integrative modeling studies.

(10)(2e) (Assistant Professor, department of Viroscience, ErasmusMC) studies the pathogenesis, virulence and transmissibility of influenza A viruses, with special emphasis on genetic and phenotypic viral factors involved in the emergence of new pandemics. In the last years he extended his research to other respiratory viruses including paramyxoviruses and coronaviruses, including studies on the transmissibility of MERS-CoV and SARS-CoV-2. Other studies involve investigations on the effect of climatic factors on virus stability in the air and the collection and quantification of respiratory virus from the air around hospitalized patients and experimentally infected laboratory animals. He will be leading the ferret experiments at ErasmusMC.

(10)(2e) is professor of Health Risk Analysis and trained as environmental epidemiologist and hygienist. He has performed epidemiological studies in a range of populations focusing on respiratory infectious diseases. He was work package leader of the EU HITEA study. This study focused on the occurrence of respiratory and infectious disease in relation to indoor air quality and involved almost 10,000 schoolchildren from different European countries. He will be leading the air-sampling experiments both in lab and school settings and will co-lead the environmental measurements in schools as well as the integrative modeling studies.

(10)(2e) is Director of the German Dutch Wind tunnels (DNW) and Chief Technology Advisor at the Royal Netherlands Aerospace Centre (NLR). He started his professional career at NLR in the mid-eighties after having graduated from the Technical University of Aachen (Germany) in aerospace engineering. He is president of the board of the 'Nederlandse Vereniging voor Luchtvaarttechniek' (NVvL) and Trustee Board of the Council of European Aerospace Societies (CEAS). He is an expert in the field of applied aerodynamics, flow physics and experimental test techniques. He will be primarily involved in the aerosol size and aerodynamics measurements using nanotechnology at various locations.

(10)(2e) is a pediatric infectious disease and immunology consultant and head of the sub-department of Pediatric Infectious Diseases, Immunology, and Rheumatology at the Erasmus MC- Sophia / Erasmus University Rotterdam. In addition, he is employed at the Department of Viroscience of the Erasmus MC. This unique combination of professional environments has allowed him to set up and implement translational research studies, initiating and coordinating interactions between the scientific and clinical departments. His current research focuses on transmission and (immune-) pathogenesis of emerging and reemerging viruses. He will be involved in the experiments at ErasmusMC as well as design and conduct of the school studies.

(10)(2e) assistant professor at the Institute for Risk Assessment Sciences at Utrecht University, is environmental epidemiologist with a strong emphasis on development and implementation of improved exposure assessment and modelling of bio-aerosols in epidemiological studies. She was PI of the environmental exposure assessment in the VGO studies (Dutch acronym for Farming and Neighbouring

Residents Health study), participated in several European Union (EU) funded studies in the field of environmental and occupational health. She will be responsible for the optimization of methods, implementation of these in outbreak investigations, and integrative modelling.

(10)(2e) is assistant professor in infectious Diseases Epidemiology at the Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht. Her research interests focus on the impact of infectious diseases with (potential) large public health impact (respiratory tract infections, influenza, gastroenteritis and arbovirus infections). As a project leader she is currently involved in two studies to the transmission of SARS-CoV-2 in households. She will be the project coordinator of the school studies.

(10)(2e) is a postdoctoral researcher in the Chair of Indoor Environment at the TU Delft since February 2020. His main research focus is on the behaviours of occupants and the effects of these on energy consumption, with the use of mixed methods data collection and analysis. He earned his PhD in the Faculty of Architecture and the Built Environment in the TU Delft in December 2019 and holds a MSc in Industrial Design Engineering from the TU Delft. He will be responsible for the experiments at SenseLab, environmental school measurements and integrative modeling.

7. KENNISOVERDRACHT, IMPLEMENTATIE, BESTENDIGING

This project has the potential to both substantially advance the science on airborne transmission of SARS-CoV2 and generate societal impact by informing school policies in the COVID-19 pandemic. Moreover, the insights from this study about the role of indoor environmental conditions on the transmissibility of SARS-CoV2 has equal importance for other indoor settings, including offices, elementary schools and daycare, nursing homes, etc. Herein lies evident potential for broader knowledge utilization. Alongside these concrete revenues, the project will also more generally increase our understanding of the link between environmental conditions, aerosols and airborne pathogen transmission.

To achieve maximal knowledge utilization in both science and infection control policies, we plan to disseminate the findings of this research project in the following ways:

First, findings from this research will be shared with the research community and societal stakeholders. COVID-19 is rapidly reshaping the world of bioscience publishing and the way science is currently communicated through rapid sharing of scientific information. Our dissemination strategy will focus on real-time transmission of information through open access preprint scientific publications and webinars simultaneously with peer-review processes. To (rapidly) reach other stakeholders not directly linked to the research community, we will translate our study results into a practical 'blueprint' with concrete recommendations on indoor climate control and ventilation along with engineering solutions to support these. These may include methods for ventilation, ventilation standards and how to measure these, cleaning and disinfection practices, etc. This will be shared with the educational sector, as well as other relevant sectors. Due to the urgency of the situation, we plan to prepare an interim report in January 2021 that will be shared with stakeholders including VWS, RIVM and the VO-raad. This expedited dissemination of relevant study results will enhance the societal value of the research as new findings can be directly incorporated into policy and recommendations.

Second, as stakeholder engagement is one of the cornerstones of this project. We will maximize efforts to reach all parties involved in education. Apart from the VO-raad, this includes individual and collective school boards, regional public health organizations (GGD) responsible for school accommodations, and students. We will disseminate regular newsletters and study results through the network of the VO-raad to all secondary schools. We will interact with local school accommodation boards and VO-raad to facilitate adoption of recommendations and practical solutions.

Third, our consortium highly values the communication of science for the purpose of education. At the TU Science Centre (incl. SenseLab), students from both primary and secondary schools can actively engage with science through on-site experiments and practical exercises. Our project activities will directly feed into these educational efforts. In addition, we plan to develop educational materials that can be shared with secondary schools for application in science classes.

Fourth, our consortium has ample experience in communicating science to the lay public by means of webinars, podcasts, online articles, and twitter. We will use this online media experience to disseminate the main research findings and their implications to the lay community. A study website will support these activities.

8. DEELNAME VAN DE STAKEHOLDER(S)/EINDDOELGROEPEN

Already during the synthesis of this research project, we have involved the VO-raad to synchronize the research objectives with the interests of the key stakeholders. The VO-raad is highly supportive of the project and is willing to facilitate the conduct of this research by offering their network, promoting school participation, and supporting implementation of study results. A continued and robust dialogue between the research team and the VO-raad throughout all stages of the project will guarantee that the research is always aligned with the interests, principles and priorities of secondary education in the Netherlands. We have also contacted the national taskforce indoor environment of the joint municipal health services (GGD-

en) and will involve them the synthesis of the recommendations following from the study results. In addition, members of our team have strong links with the Outbreak Management Team and the National Institute of Public Health (RIVM), as well as national and international engineering associations facilitating instant dissemination of results and recommendations to relevant other stakeholder groups.

9. LITERATUURREFERENTIES:

1. Gudbjartsson DF, Helgason A, Jonsson H, Magnusson OT, Melsted P, Norddahl GL, et al. Spread of SARS-CoV-2 in the Icelandic Population. *N Engl J Med* [Internet]. 2020 Apr 14 [cited 2020 May 14];NEJMoa2006100. Available from: <http://www.nejm.org/doi/10.1056/NEJMoa2006100>
2. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* [Internet]. 2020 May 15 [cited 2020 May 14];26(5):672–5. Available from: <http://www.nature.com/articles/s41591-020-0869-5>
3. Chia PY, Coleman KK, Tan YK, Ong SWX, Gum M, Lau SK, et al. Detection of Air and Surface Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Hospital Rooms of Infected Patients. *medRxiv* [Internet]. 2020 Apr 9 [cited 2020 May 10];2020.03.29.20046557. Available from: <https://www.medrxiv.org/content/10.1101/2020.03.29.20046557v2>
4. Li Y, Qian H, Hang J, Chen X, Hong L, Liang P, et al. Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant. *medRxiv* [Internet]. 2020 Apr 22 [cited 2020 May 14];2020.04.16.20067728. Available from: <https://www.medrxiv.org/content/10.1101/2020.04.16.20067728v1>
5. Bluyssen P. Health, comfort and performance of children in classrooms – New directions for research. *Indoor Built Environ*. 2017;26(8):1040–1050.
6. COVID-19 in schools-the experience in NSW Overview. 2020.
7. Heavey L, Casey G, Kelly C, Kelly D, McDarby G. No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020. *Eurosurveillance* [Internet]. 2020;25(21):2000903. Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.21.2000903>
8. Fontanet A, Tondeur L, Madec Y, Grant R, Besombes C, Jolly N, et al. Cluster of COVID-19 in northern France: A retrospective closed cohort study. *medRxiv* [Internet]. 2020 Apr 23 [cited 2020 May 14];2020.04.18.20071134. Available from: <https://www.medrxiv.org/content/10.1101/2020.04.18.20071134v1>
9. Richard M, Kok A, Meulder D de, Bestebroer TM, Lamers MM, Okba NMA, et al. SARS-CoV-2 is transmitted via contact and via the air between ferrets. *bioRxiv* [Internet]. 2020 Apr 17 [cited 2020 Jun 15];2020.04.16.044503. Available from: <https://www.biorxiv.org/content/10.1101/2020.04.16.044503v1>
10. Bourouiba L. Turbulent Gas Clouds and Respiratory Pathogen Emissions. *JAMA* [Internet]. 2020 Mar 26 [cited 2020 Jun 15];323(18):1837–8. Available from: <https://jamanetwork.com/journals/jama/fullarticle/2763852>
11. Richard M, Kok A, Meulder D de, Bestebroer TM, Lamers MM, Okba NMA, et al. SARS-CoV-2 is transmitted via contact and via the air between ferrets. *bioRxiv* [Internet]. 2020 Apr 17 [cited 2020 May 14];2020.04.16.044503. Available from: <https://www.biorxiv.org/content/10.1101/2020.04.16.044503v1>
12. Landelijk Coördinatiecentrum Infectieziektenbestrijding (LCI). Protocol bron- en contactonderzoek COVID-19 [Internet]. 2020. Available from: <https://lci.rivm.nl/COVID-19-bco>

Specification staff

1.a Staff costs (based on salary scale)

nr	Function / Name	NFU / VSNU member / other staff ruling	Function/Scale	Months	Gross salary - based on table / 1 FTE	Monthly Gross salary (for Other	% fte (for the project)	Salary costs	Gross salary, 40% increment (for Other ruling only)	Overhead % (for Other ruling only)	Total
1	Post-Doc UMCU	NFU	PostDoc	18	(10)/(2b)		80%	(10)/(2b)	€ -		(10)/(2b)
2	Post-Doc TU Delft	NFU	PostDoc	18	(10)/(2b)		110%	(10)/(2b)	€ -		(10)/(2b)
3	Post-Doc IRAS	NFU	PostDoc	18	(10)/(2b)		40%	(10)/(2b)	€ -		(10)/(2b)
4	Post-Doc ViroScience	NFU	PostDoc	18	(10)/(2b)		40%	(10)/(2b)	€ -		(10)/(2b)
5	Research Assistant UMCU	NFU	NWP-H	8	(10)/(2b)		30%	(10)/(2b)	€ -		(10)/(2b)
6	Research Assistant TU Delft	NFU	NWP-H	8	(10)/(2b)		30%	(10)/(2b)	€ -		(10)/(2b)
7	Technician EMC Viroscience	NFU	NWP-H	18	(10)/(2b)		30%	(10)/(2b)	€ -		(10)/(2b)
8					€ 0			€ -	€ -		€ -
9					€ 0			€ -	€ -		€ -
10					€ 0			€ -	€ -		€ -
11					€ 0			€ -	€ -		€ -
12					€ 0			€ -	€ -		€ -
13					€ 0			€ -	€ -		€ -
14					€ 0			€ -	€ -		€ -
15					€ 0			€ -	€ -		€ -

1.b Staff costs (based on hourly rate)

The hourly rate should be acceptable, reasonable and fair

nr	Function	Activity / Actions	Hourly rate	number of hours	Total
1	to be specified		€ -		€ -
2	to be specified		€ -		€ -
3	to be specified		€ -		€ -
4	to be specified		€ -		€ -
5	to be specified		€ -		€ -
6	to be specified		€ -		€ -
7	to be specified		€ -		€ -
8	to be specified		€ -		€ -
9	to be specified		€ -		€ -
10	to be specified		€ -		€ -
11	to be specified		€ -		€ -
12	to be specified		€ -		€ -
13	to be specified		€ -		€ -
14	to be specified		€ -		€ -
15	to be specified		€ -		€ -

DAEB Format

Organisation	Type of organisation	Quoted costs	Quoted co-funding	Requested budget
University Medical Center Utrecht	Knowledge institution			
TU Delft	Knowledge institution			
Institute for Risk Assessment Sciences, UU	Knowledge institution			
Erasmus MC	Knowledge institution			
German-Dutch Wind Tunnels (DNV)	Other	(10)(1c)	(10)(1c)	(10)(1c)
	Total			

Staff costs[illegible]

Material, equipment & consumer goods (itemised)

Material, equipment & consumer goods (remiseu)		Costs	Own contribution / 3rd party co-funding	Requested budget ZonMw
Description	Remarks	Organisation (dropdown menu)		
Lab supplies Senselab and school indoor environment		TU Delft	€	-
Lab supplies airsamples schools		Institute for Risk Assessment Sciences, UU	€	-

[illegible]

The Part 1) experiments will be conducted by staff from ErasmusMC (Viroscience), TUDelft (Senselab) and IRAS. Staff from ErasmusMC will be responsible for the ferret experiments at their lab. The institute of risk assessment of the UU (IRAS) and TU Delft will be involved in these experiments for aerodynamic research and for air sampling experiments for biological measurements. DNW will support the experiments with nanoparticle spectrometry. The Experiments at Senslab will be conducted by TU delft research staff, supported by IRAS and DNW spectrometry.

Part 2) of the project will be coordinated by research staff from UMC Utrecht. Measurements on indoor environmental conditions will be done by TUDelft, air and surface sampling will be conducted by IRAS.

TU Delft will provide the technical equipments and materials for experiments in the Senselab and for school measurements of indoor environment.

IRAS will provide technical equipment and materials for biological sampling.

All samples will be tested for presence and number of viral copies and for infectivity at ErasmusMC.

UMCU will set-up a data collection system and coordinate all project activities.

Research staff from TU Delft and IRAS will be jointly develop and parameterize the statistical and mathematical models. This is supported by UMCU research staff.

All members of the consortium will be involved in synthesis and interpretation of the study results, and in report/manuscript writing.

Checklist

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

Version 1.1 26 May 2020

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 checklist 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 to your grant application.

Requirements & Recommendations	Applicants must report as follows
The preparation phase: grant application	
Who is the data steward who supports the open science and FAIR data planning in your project? Check the website for ZonMw's webinars to inform and support data stewards.	☒ I involve a data steward: Name: (10)(2e) Institute: Julius Center, UMC Utrecht E-mail: (10)(2e)@umcutrecht.nl ☐ I do not have a data steward yet, because <i>Klik of tik om tekst in te voeren.</i>
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: <i>Klik of tik om tekst in te voeren.</i> ☐ Biological materials: <i>Klik of tik om tekst in te voeren.</i> ☐ Research software: <i>Klik of tik om tekst in te voeren.</i> ☐ Other resources, i.e. <i>Klik of tik om tekst in te voeren.</i> ☒ No, I will not use existing resources, because <i>There is no data available that we can use in our study</i> 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 plan (including the protocols, methods, etc).	☒ In case of preregistration: Provide the link or registration code: <i>We haven't preregistered our project yet</i> ☐ For animal studies, the code at the Preclinical Trial Register is: <i>Klik of tik om tekst in te voeren.</i> ☐ No, I do not preregister my research proposal.

Requirement 3: FAIR data within COVID-19 research community Choose the options that suit your project best! 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: Open science in COVID-19 research and 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 (machineactionable) ☐ 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, namely Klik of tik om tekst in te voeren. Comment on your choice(s) We plan to include the data from the project in a data repository (Dataverse.nl) ☐ 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 costs for data stewardship, and – if applicable – costs for additional services from data service providers (e.g. from Health-RI or other providers), 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 - 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 <u>full gold</u> 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.
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