START OF THE PANDEMIC PREPAREDNESS PROGRAM BY VENTILATION

Knowledge Gaps and application of the results

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SUMMARY

Ventilation and air cleaning of interior spaces are promising methods for the reduction of airborne pathogen spread and may reduce the number of (airborne) infections. With this in mind, and in response to the 2020-2022 COVID-19 pandemic, the Dutch Ministry of Health, Welfare and Sport (VWS), in collaboration with TNO have initiated this research program focusing on ventilation (P3Venti) as part of the larger Pandemic Preparedness Program of VWS (300 million Euros, annually). In the P3Venti program the importance of aerogenic transmission in total viral transmissibility will be researched, and how ventilation and air cleaning can mitigate this airborne transmission in the long-term healthcare sector and the social sector more broadly. In support of this, research on dose-response relationships, indoor environmental conditions and the cost/benefits across a variety of use cases in these sectors will be performed across 6 program lines. The results will inform ventilation strategies to better combat the spread of SARS-CoV-2; they will also be extrapolated to apply to possible future pandemics. Finally, a 7th program line will collect these results into a knowledge base and network, where information, knowledge and ideas can be generated, collected exchanged, and disseminated, both nationally and internationally.

KEYWORDS

COVID19, Pandemic Preparedness, research program, knowledge gaps, ventilation, air purification, healthcare, aerogenic transmission

1 INTRODUCTION

Airborne or aerosol transmission plays a role in the spread of many infectious diseases and other pathogens. This transmission route is defined by the Word Health Organization as transmission of infection through very small droplets that are able to stay suspended in the air for longer periods of time; it plays a role in COVID-19, but also for example in influenza. The replacement of contaminated air with fresh outdoor air by means of ventilation reduces the number of virus particles present in a room and can thus help reduce the risks related to airborne transmission. Upgrading ventilation systems – whether in combination with air purification or not – may help in ensuring the accessibility of societally important facilities – such as healthcare facilities, and public spaces such as libraries and schools – and help safeguard continuity and quality of service provision during a pandemic. Research is needed to be able to use ventilation effectively.

2 KNOWLEDGE GAPS

Based on available literature, six knowledge gaps with regard to the role of ventilation have been defined by the Dutch National Institute for Public Health and the Environment (RIVM). The RIVM defined these knowledge gaps specifically for SARS-CoV-2, but they are generally applicable to infectious diseases (and indeed other pathogens) where airborne transmission potentially plays a role. Bridging these knowledge gaps is essential in the effective deployment of ventilation and air purification measures. For example, as long it is unclear what proportion of infections is attributable to airborne transmission, the potential preventative value of ventilation measures cannot be assessed.

The knowledge gaps defined by the RIVM are:

1. The contribution of aerogenic transmission to the total transmission of the SARS-CoV-2 virus
2. The dose-response relationship in air. In other words, how many virus particles (viral load) are needed in aerogenic transmission to cause an infection?
3. What is the contribution of ventilation and the use of air purifiers etc. to the prevention of Covid-19?
4. In which social sectors is (investing in) ventilation as a prevention measure most needed and most effective? (Prioritization)
5. What are the proportionality and costs/benefits of applying ventilation?
6. What is the influence of indoor environmental conditions such as humidity and temperature?

The following paragraph offers a brief examination of each knowledge gap.

2.1 Contribution of aerogenic transmission to total transmission

There are two main reasons for the current lack of understanding of the contribution of aerogenic transmission.

1. Current detection methods do not provide sufficient insight into the virulence of aerogenic virus particles, as most detection methods only use RNA typing. Detection methods do provide insight into the virability of virus particles, but not whether they are also virulent after a longer period of time in the air.
2. Under operational conditions, it is very difficult to categorically exclude non-aerogenic transmission routes. Only a few case studies are known in the research literature and review articles point to methodological bottlenecks in these case studies.

2.2 Dose-response relation in air

1. This is the most fundamental knowledge gap. Based on the current state of research, there is no good insight into this. This applies not just to airborne transmission, but to all transmission routes.
2. The question is complicated: whether someone becomes infected depends not only on the amount of virus emitted by a carrier, but also on the circumstances, the duration of exposure, the variant of the virus that is involved, the state of health and underlying pathologies of the recipient, other physiological details of the recipient that do not affect health but in one way or another affect vulnerability to the virus, as well as possible other variables that are not yet (well) understood.
3. Fundamental multidisciplinary and interdisciplinary research is necessary. The most logical candidates to carry out this research are specialized medical knowledge institutes and university medical centres. As far as the authors are aware, this fundamental research is currently getting into gear at the national and international level, for example through research lines and programs within the Horizon Europe program.

2.3 Contribution of ventilation and air purification to prevention

It is currently insufficiently well understood how airborne particles spread through different types of indoor spaces under operational circumstances. Measurement and modelling methods do not take adequate account of the influence of room dimensions, technical building and installation specifications, ventilation system characteristics, placement of system components and other functional and technical elements potentially affecting particle spread and ventilation system performance. Measurement and modelling methods generally assume the presence of a single, continuous or one-time emission source and instant or near-instant homogeneity of particle distribution through the indoor space. On the basis of emerging research it is increasingly likely that virus particle emission varies over time, and that the spread patterns of airborne particles in the early phases of emission play a role in transmission risk. Equally importantly, better and more sophisticated understanding of utilization patterns of different types of indoor spaces is needed, to better gauge exposure risk (a factor of proximity of contact, duration of contact and activity intensity) and to be able to assess the feasibility and impact of utilization on prevention measures.

2.4 In which sectors is (investing in) ventilation as a prevention measure most needed and most effective?

Under pandemic outbreak conditions, or more generally when there is an actual or likely large-scale outbreak of infections, governments are under pressure to deploy public funds towards prevention and mitigation. Since public funds are limited and cannot be deployed indiscriminately, which sectors and sub-sectors to prioritize and why requires decision-making that is both complex and politically fraught.

Compounding this, the knowledge base for responsible and accountable decision-making is under-developed. Whether or not to allocate public funds requires insight into three distinct issues:

I. The potential impact of infections (e.g. in terms of expected excess mortality, adverse health effects, loss of continuity and/or quality of service provision, follow-on effects such as unemployment).
II. The likelihood that deploying or upgrading ventilation and/or air purification measures will be effective in reducing risk (e.g. in terms of utilization patterns, availability of technical solutions, suitability of buildings and spaces for deployment).
III. The extent to which sector or sub-sector organizations are able or unable to finance ventilation and/or air purification measures.

2.5 Proportionality and costs/benefits of ventilation

Investing in ventilation systems and/or air purification technologies comes at a cost. It involves investments in purchase, implementation and maintenance of systems as well as costs associated with operational and organizational adjustments required for the effective functioning of prevention measures. Additionally, up-front investment may well be required to enable research and innovation to develop new and improved, more fit-for-purpose ventilation systems. Costs will need to be borne not just by the public purse, but also by individual for-profit and not-for-profit actors in the sectors and sub-sectors involved. To enable decision-making on whether or not investment is justified, improvements to the current state of the art are needed in the application of cost/benefit[1] analysis models and methodologies to the issue of ventilation as an infection prevention measure. This build-up of knowledge is required, not just to inform public sector policy development and decisionmaking, but also to incentivize private sector actors to commit to appropriate investment levels.

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[1] economic, health and social

2.6 Influence of indoor environmental conditions

Current methods for measuring and modelling particle behaviour and ventilation and/or air purification system performance do not take adequate account of the influence of indoor environmental conditions, particularly relative humidity and air temperature. There is research to suggest that extremes in these parameters affect both particle characteristics over time (such as degradation and dehydration) and system efficacy. There is as yet insufficient knowledge how these factors apply specifically to potentially virus-bearing particles. Further research and analysis is also needed to establish how these indoor environmental conditions interact with the particle- and system-affecting parameters that are addressed under knowledge gap 3 (see paragraph 2.3 above).

3 P3VENTI - A RESEARCH PROGRAM DESIGNED TO HELP ADDRESS THE KNOWLEDGE GAPS AND PROVIDE ACTIONABLE KNOWLEDGE

A research program has been initiated under the acronym P3Venti with the objective of addressing the aforementioned knowledge gaps identified by the RIVM. P3Venti, short for the Pandemic Preparedness and Ventilation program, has been initiated by the Dutch Ministry of Health and is carried out on behalf of the Ministry of Health, Welfare and Sport (VWS) by a flexible consortium of universities and knowledge institutes. These work in varying constellations on research projects that have been or are still being defined within the program.

An outline project plan with an expected duration of 3 years (August 2022 – July 2025) has been drawn up for the program, as well as a detailed annual plan for each calendar year. Each annual plan describes the projects to be carried out in that year, and for each project, it also states which program participants are involved, and it provides a budget estimate, broken down per partner.

3.1 Program lines

The research program is organized into six substantive program lines (PLs) and one PL addressing networking and knowledge sharing. Each PL serves one or more research areas, with projects defined and implemented under them.
Administration and technical management of the program are provided by TNO.

The seven program lines of the P3Venti program are defined as follows:

I. Inventory and analysis of operational conditions
II. CFD analysis
III. Experimental research on ventilation and particle behaviour
IV. Risks, impact and market
V. Costs and benefits
VI. Infectivity and dose-response relationship
VII. Networking and knowledge assurance

The six substantive PLs I-VI represent three distinct methodological research domains, or Blocks. PLs I-III (Block 1) comprise technological research; PLs IV-V- (Block 2) address social and policy research; PL VI (Block 3) is focused on microbiology and virology.

3.2 Block 1 – Technology-based research

PLs I-III carry out technology-based research. This research aims to take steps in knowledge building and concept development on the following issues:

- Aerosol particle behaviour in indoor environments
- Possible differences in behaviour between bioaerosols containing virus particles and inert aerosols of equal size
- The role of functional and technical features of spaces, and the influence of human presence and interactions between persons (staff, clients, visitors)
- The role and importance of human presence and interactions on the quality and effectiveness of processes (such as care delivery) that take place in indoor environments
- The performance of fixed and mobile air handling systems in a variety of room types and under differing usage patterns
- The specific influence of the indoor environment (temperature humidity) on both particle behaviour and performance of air handling systems

This research does not need to start from scratch as there is an existing knowledge base. However, this knowledge base relies on the use of highly simplified model-based assumptions for particle behaviour and equipment performance and falls short in the following areas:

- Most importantly, an adequate understanding of the spread of particles and the effects of ventilation under sector-specific operational conditions is still lacking.
- For healthcare, in particular long-term care, there is still insufficient insight into the influence of variation in the following operational conditions:
    - Room typologies
    - Use of space
    - Applied ventilation systems
    - Other characteristics of the indoor environment that can realistically be expected to vary in practice, but have not yet been systematically identified.

Exposure is used in Block 1 as an – initially relatively crude – proxy for infection risk. Insights into the infectivity and dose-response relationship of aerogenic pathogens, built up in other PLs and research programs, will be used in Block 1 for the technical research lines to refine this proxy relationship.

The following knowledge, expertise and experience is mobilized in the P3VENTI program for the implementation of the research in Block 1:

- Domain knowledge of the sector domains, primarily (long-term) care
- Functional and technical descriptions and characterizations of (care) buildings
- Insight into the current state of buildings and equipment in (long-term) care
- Observation and classification of human behaviour and interactions
- Particle measurement in high-risk environments
- Research into particle emission and particle behaviour in practical settings for SARSCoV-2 research
- In-depth knowledge of installation technology, ventilation systems and equipment, and Indoor Air Quality
- Modelling behaviour and performance of physical systems and devices • CFD modelling and simulations
- "State of the art" test facilities

3.3 Block 2 – Social sciences and policy sciences research

The research in PLs IV and V is aimed at building up and facilitating the access to knowledge which supports decision making by e.g. governments, other actors in the public sector and social and not-for-profit organizations in the effective and proportional use of ventilation as a virus transmission mitigation measure. In other words, the deployment of measures according to clear, specific and measurable objectives, with a clear idea of expected effects and effectiveness, and with a keen awareness of economic and social costs and benefits. Block 2 (PLs IV and V) will address knowledge gaps 4 and 5 as described in sections 2.4 and 2.5:

- In which sectors (and possibly segments within sectors) is investing in ventilation most useful and necessary? (knowledge gap 4)
- What level of investment is feasible and responsible and what negative and positive side effects occur, for business operations within the sector but also on the broader social playing field? (knowledge gap 5)

In order to be able to bridge these knowledge gaps, Block 2 brings together the following areas of knowledge and expertise, in addition to the expertise mentioned for technical research:

- Business management issues and priorities in the sectors the research focuses on
- Risk and process analysis
- Cost/benefit and business case analysis
- Health impact analysis
- SCBA analysis
- Foresight

Block 2 initially focuses on care (long-term care and primary care and/or paramedical care) as an application domain, but have the ambition to broaden research and applicability of research outcomes to other sectors over the course of the implementation of the P3Venti program.

3.4 Block 3 - Microbiology and virology research

The research in PL VI, focuses on knowledge gaps 1 and 2, as identified by the RIVM. A key objective for this is to make sure that the research results are not just relevant for SARS-CoV-2, but also offer actionable knowledge for other pandemic threats. This poses a major methodological challenge as virus properties that influence infectivity and the dose-response relationship can vary greatly from virus to virus or even from variant to variant. Nevertheless, methodological principles and approaches from the research in these PLs can feasibly be distilled to accelerate and improve specific research on other pathogens. Also, from specific findings regarding SARS-CoV-2, more broadly applicable principles for prevention and mitigation can be derived, which can have value as guidelines for policy and implementation, especially in the early phases of future pandemics. Given the potential value of such broadly applicable knowledge, generalizability of research outcomes will be a major focus of the PL.

For example, the 2020-2022 Corona pandemic has shown, among other things, that contamination from person to person via the ambient air is a very important factor in the spread of disease (Figure 1). It also became clear that many parameters play a role in this, but that factual knowledge is often lacking.

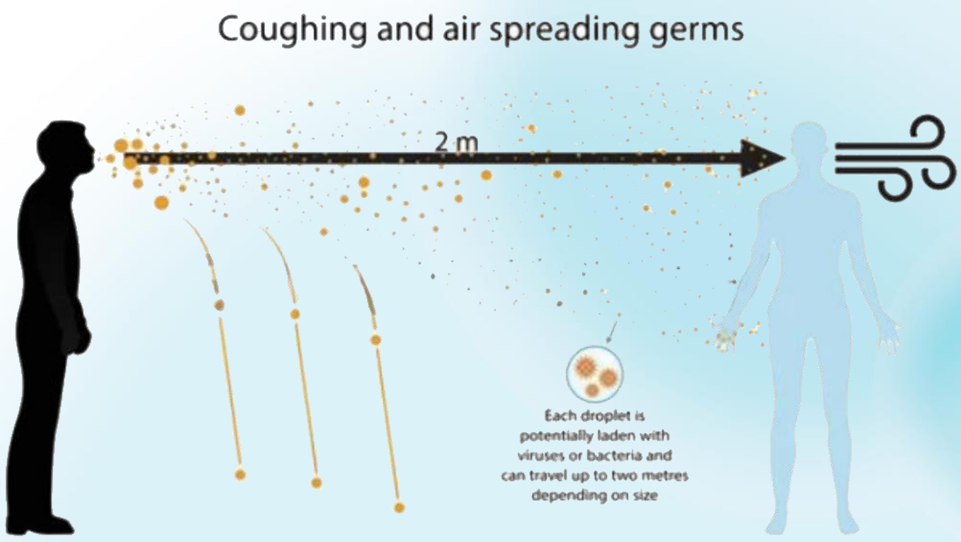

Figure 1 Example of person-to-person spread of disease.

By conducting research on the areas described in section 3.2 with a variety of different virus strains, it may be possible to discover characteristics of the virus and its relationship with the infectivity of emitted particles, under the influence of the environmental parameters mentioned. Identifying characteristics can then contribute to the possibility of predicting the virability of those viral particles in new outbreaks and to what extent these can be influenced by distance, hygiene and ventilation. This in turn builds knowledge in regard to the current Corona pandemic, but also for a possible novel future outbreak.

3.5 PL VII – Networking and knowledge assurance

In addition to the substantive research lines, an important aim of the program is to strengthen and develop the available knowledge base and research capacity in the field of ventilation and pandemic preparedness. To this end, PL VII aims to set up a knowledge network that, over the course of the P3Venti program, should develop into a knowledge platform:

- Where relevant knowledge (in and outside the program) is brought together and connected
- Where ideas and priorities for research and innovation are generated
- That generates collaborations and research and knowledge-sharing alliances
- That forms a basis for the exchange of knowledge and data with institutes and networks abroad
- That provides an easy-to-locate, easy-to-access source of information which (mainly) public sector organizations, but also companies and citizens can use as a resource for practical knowledge, methods and instruments

In this way, the research program not only provides answers to the specific research questions that have been defined for this program, but it also contributes to the strengthening and growth of the knowledge base. Through this, new research questions and needs can in turn be identified in a timely and effective manner.

3.6 Governance of the program

In order to properly shape the program, a governance structure has been set up consisting of a coordination meeting, an advisory board and a general assembly consisting of all parties from the adaptive consortium. The coordination meeting and advisory board have an independent chair who facilitates the consultation.

Decisions in principle about the program (program annual plans, project plans) are made by the coordination meeting. The Ministry of VWS endorses this decision or deviates from it. A schematic representation of the governance structure is shown in Figure 2.

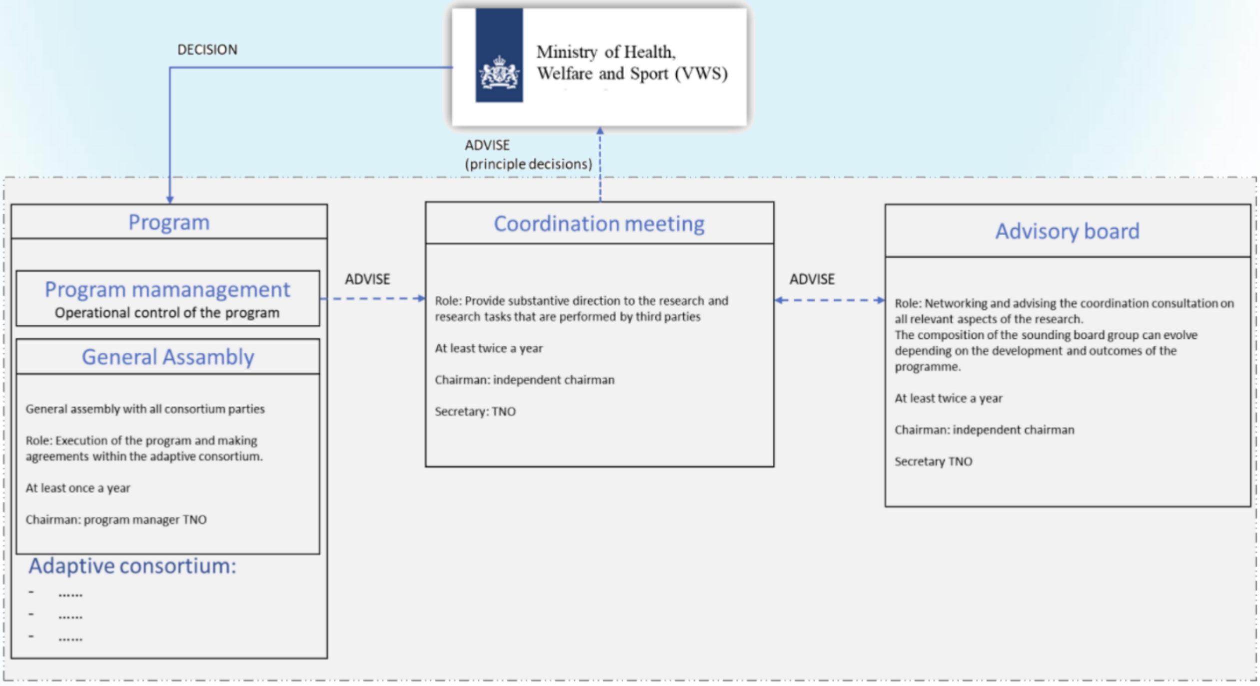

Figure 2 Schematic overview of the organizational structure (as an indication).

4 ACKNOWLEDGEMENTS

The program has so far been established with the support of the Ministry of Health, Welfare and Sport (VWS), Dutch National Institute for Public Health and the Environment RIVM, Eindhoven University of Technology and Utrecht University