**Environmental routes of SARS-CoV-2 from production and emission to exposures**

**Physical Industrial Ecology methods for focused pandemic control**

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**Summary**

SARS-CoV-2 infected persons produce virions and emit a share to the environment. There, transport, build-up, decay, and dilution result in concentrations with next exposures and infections. These linked physical phenomena, lacking in SARS-CoV-2 research, connect medicine and virology with epidemiology. Models of Industrial Ecology are applicable, using mass balancing of Substance Flow Analysis. Primary production in the body-factory results in quantified emissions. Different environmental scenarios connect emissions to concentrations, potential exposures, and infection. The analysis is virus-specific, different for other viruses and bacteria.

The emission-concentration-exposure scenarios cover all airborne, fluid, and solid emissions, where possible modelled and quantified. The airborne scenarios distinguish closed spaces with various concentrations, as stocks; exhale flows from breathing, singing, and cough-sneezing; and open-air flows, with always some wind. The fluid scenarios cover small droplets evaporating to airborne status and larger ones settling on objects and persons. The solids scenario also covers SARS-CoV-2 virions production in the small intestines (30m2), the second main production site after the alveoli (50m2).

The scenario outcomes show extreme divergence in potential exposures, often counterintuitive. A full cough blasted in the face at 1 meter distance hardly poses a risk as compared to having dinner with that ill person, not well-ventilated. Common situations differ by five orders of magnitude (Table 3). Deep gaps in current modelling and data are indicated. IE may fill the gap with a new subject: Viral Substance Flow Analysis. SARS-2 results can inform medical-virologic sciences and epidemiology and inform citizens and governments on results-oriented measures.

## Introduction on SARS-CoV-2 virion stocks and flows[[3]](#footnote-3)

### The aim of modelling environmental transmission routes

Age-old knowledge is used to control epidemics, with prime measures including quarantine (*quaranta giorni*), social distancing, mask wearing, and direct physical contact avoidance, all applied since the 14th century, already as a public reaction to a public danger (Foucault, 1975). The Black Death nor SARS-CoV-2 have been contained, however. With modern knowledge, modelling, and data, a more detailed and quantified picture of possible infection routes can be developed, distinguishing the relative risk levels of different circumstances. They are specified here for SARS-CoV-2 (short: *SARS-2*, long: *Severe Acute Respiratory Syndrome Corona Virus 2*), leading to COVID-19 illness, with a pneumonia and secondary infections, in severe cases leading to long-term impairment or death. On that basis, more focused measures may emerge. In between virology and medicine at a micro level and the global pandemic, the macro-level of epidemiology, there must always be a physical route bringing the SARS-2 virions from an infected person to a still healthy person. A toxic infection must have a source and a route.

The WHO advice to the public regarding SARS-2[[4]](#footnote-4) includes physical distancing, wearing a mask, avoiding crowds, cleaning your hands, and coughing into a bent elbow or tissue. Quantified models for supporting these measures for SARS-2, or establishing their relative importance, are fully absent. At a cases level, direct hand contact or fomites transmission leading to COVID-19 pneumonia has never been established. But how strong is that sort of indirect proof? Current lack of knowledge also shows in diverging advises of country CDCs. The US-CDC advised ‘have your Thanksgiving party outside’, while at the same time most European CDCs advised on closing parks, with police control. Terraces and sports fields were closed in many European countries, while US cities closed roads to create space for outside dining. The analysis of such potential measures is not a subject of this study, though gently touching on them in the conclusions.

Before endeavoring in applied modelling, we show major gaps in knowledge ideally to be filled. The model outcomes of the physical analysis model have two related functions. First, they connect medicine and virology on the one hand with epidemiology and medicine on the other. Next, they form a basis for citizens and governments to evaluate measures, combining relative risks with options for measures, in their broader juridical-administrative and socio-economic contexts.

The *goals* of this study are to lay the modelling framework for the quantified analysis of the SARS-2 virion flows from primary production to potential infection; to preliminary fill in sub-models; and to specify gaps in models and data remaining.

### To which scientific domain does this subject belong?

The outside links to the subject are clear. There is input from virology and cell biology and physiology. But it does not belong to either of these subjects. There is a slight link to epidemiology and more general to health sciences, but it certainly is not part them. The interfaces between production and exposure have several applied technical sciences, such as building sciences, ventilation sciences, and there are behavioral sciences, and ultimately ethics and normative political science. All of them have several specialized and more general journals. Nowhere would this broader subject fit in. The scientific development of this interface is broadly seen as a necessity. (Qu, Li, Hu, & Jiang, 2020) (ES&T, with 213 references) advocate the development of such a framework. So do (Huang et al., 2020) (acsNANO, 110 res) and (Mittal, Ni, & Seo, 2020) (Focus on Fluids, 283 refs) who focus directly on their specialized domains however. More recently (Morawska et al., 2021) (Science, 14 refs, with 39 authors) advocated this subject but with a focus on all airborne infections together, not SARS-2 specifical, and on ventilation as a measure only.

Industrial Ecology may be defined in different ways. As *the science of the material basis of the economy*, this subject would not be part, see in this sense the Wikipedia item with broad references[[5]](#footnote-5). Taken as *the science of the physical aspects of society* it might be part, covering emissions more directly. We take that position, based on using an IE modelling structure which directly connects to SFA and elements of LCA. There is primary SARS-2 virions production with partial emission, airborne, fluid, and solid; there are environmental routes with concentrations; and there are airborne, fluid, and solid exposures, with potential health consequences.

The subject of the physical fate modelling of virions deviates from the usual materials and substances covered in Industrial Ecology. There is a direct overlap with toxic substances however, with their source, fate, exposure, and effect modelling. First, there is the analogy with processes analysis in LCA. The basic sequence there is, next to functional aspects, that substances are created, partially emitted, diluted/concentrated transformed/broken down in the environment, and next having their impacts, including health effects. Several IE studies cover biotic emissions, as in cows emitting methane, for example (aan den Toorn, Worrell, & van den Broek, 2020; Vergé, VanderZaag, Desjardins, & McConkey, 2018). Next, in the toxicity analysis of airborne pollutants there has been a shift from PM10, which includes large SARS-2 containing droplets; to PM2.5, smaller airborne evaporating droplets with SARS-2 virions; to UFPs, the often most harmful Ultra Fine Particles (<100nm), in the size order of single SARS-2 virions (140nm, 100nm without spikes). There is a structural similarity in the case analysis of COVID-19 ill persons and that of 3D printers, see (Azimi, Fazli, & Stephens, 2017). Finally SFA, as one main method in Industrial Ecology, can also specify stocks resulting from flows, essential for specifying environmental concentrations and then potential exposures. Mass balances must hold, also for short-lived toxics.

The routes from primary production, different emission routes, different environmental fate routes, and from there to exposures and potential infections seems best linked to the subject of Industrial Ecology taken broadly, and then with a prime choice for this Journal.

## Method

### The nature of the study

Though viruses are not a core issue in Industrial Ecology yet, we use the general methods of industrial ecology in the domain of viral replication, emission, environmental routes to exposures, and their impacts. As the current SARS-2 pandemic will last for longer, and as there will be more epidemics and pandemics, the subject might develop into a new subdomain of Industrial Ecology: Viral Substance Flow Analysis.

As there is no overall model for SARS-2 emissions and exposures yet, and as partial models do not cover the full field, there is a triple task ahead. We first fill in number one, the overall conceptual design, an overarching modelling architecture. The second task concerns the survey of available partial models, required to fill in the sequences from primary production of SARS-2 virions to exposure and infection. Available partial models are combined and developed into more coherent models where possible, organized in the three main modeling stages: from primary production to emissions; from emissions along several routes to exposure; and from exposure to COVID-19 illness. Quantification is possible to some extent regarding the steps from primary production to airborne emissions, in the spread sheet model we develop. Though substantially assumption based, outcomes can be aligned with empirical data. Quantification is also possible for the stage from airborne emissions to concentrations and exposures, partly developing new models and partly using available models and data from other domains. For fluid and solid flows this is not well possible, with only incidental and partial measurements. The stage from exposure to illness cannot be filled in quantitively, due to the basic lack of partial models and data. For all routes in the overall conceptual model, an outline of specific modelling requirements is made.

The third task would have been the independent validation of the models. As we used available knowledge extensively already, this would require new data gathering, a prime task for society, and broader statistical analysis at the physical level. We indicated gaps remaining, many. There has not been any primary data gathering in the project.

### Gaps in SARS-2 knowledge surveyed and partially filled

What should be known is how and how many virions infected persons produce and emit, how the different emission modes are transformed and dispersed in different environments, and how exposures and infections may then result. This overall model is fully lacking in the literature. This lack of empirical modelling also holds for most of the constituting parts. The knowledge gap regards both the structure of the model, reckoning with different types of SARS-2 particles, and the connected partial models and their quantification. The quantification of primary production is lacking, the route from alveoli to alveolar sacs and higher airways has not been modelled, nor are possible internal routes within the body to blood, other organs and especially the intestines. The reverse route of particles into the respiratory systems has been investigated in the literature, not for COVID-19 pneumonia but for administering medicines to the deep level, up to below UFP-size for effective alveolar application. Emission data are scanty as well. At emission, most analyses take only droplets into account, not linked to primary production. Gravity-based separation apparatus can gather these droplets while the virions (140nm) and virion containing clusters below 1000nm (at best below 500nm) leave in their exhaust, unmeasured. There are a few quantified single virion measurements, with methods in development and not yet standardized. Anal swabs show emissions but are hardly quantified.

There is no systematic quantified modelling available of environmental routes of emitted SARS-2 towards potential exposures. And after human exposure, there is no physical model of how the alveoli are reached, required for viral pneumonia in the alveoli, the *Severe Acute Respiratory Syndrome*. How to deal with this dire situation? This is not just a historical issue. The SARS-2 virus is here to stay with us, as several other corona viruses (for example involving the common cold); influenza; and dozens of other viruses did before.

There are many interesting case studies, as on exposures during singing events. A thorough example is (S. L. Miller et al., 2021). Their reverse modelling to required emissions for infection is multi-assumptions based however, including that virions in droplets are the only source; that aerosolized droplets spread homogenously; that the source was one person only; that stay for different times in different spaces made no difference; that 50% of infected persons remain symptomless; that a share of persons becomes symptomatic within 24 hours after exposure; and more. The required exposure for infection is then expressed in *quanta/h*, as the number of airborne droplets. A singing exhaler may produce more droplets than one just sitting quietly. But that would hardly relate to its primary production; the mass balance is fully lacking. This holds for all other case studies as well.

The generic approach required, as indicated above, must just be that: an encompassing framework with provisional quantifications to start with. We specify three consecutive main sub-model stages: production and emission; environmental routes to exposure; and from exposure to illness. For each of these stages we start with a survey of available models and data, and the gaps therein, in chapter 4, 5 and 6 respectively.

### Method for model design

The method is a first approach towards quantified modelling, requiring a conceptual model and next quantifications. The quantifications are preliminary and do not cover all flows, due to scanty data for many flows and transformations. Where quantified, a broad sensitivity analysis covers potential spread.

The method links to parts of LCA and SFA. In LCA the model for individual processes links production, use, and end-of-life processes to their emissions, reckoning with control measures, and next links emissions to environmental impacts, including health impacts. Similar does Environmentally extended Input-output Analysis at a higher level of aggregation. SFA can specify sequences of stocks and flows of a substance, through connected media, here toxic SARS-2 virions. Elements of these basic industrial ecology models are combined. Concentrations belong to the stocks domain of SFA, here filled in for primary production and for different closed and open spaces after emission.

The first step in modelling is the conceptual overview: which stocks and related flows are involved, summarized in Figure 1. Three main stages are distinguished: from primary productions to different emissions; next from these emissions through different environmental routes to different exposures; and from these to different forms of infection. This third modelling stage is not yet quantified here but a few qualitative considerations are given.

As data are scanty, for the moment the structure of the model is most relevant. The implementation of partial models can be aided by lab research and by substantial partial knowledge, not just from SARS-2 times. Most basically: virions that are present somewhere must have been produced and must not have gone astray on the way there: mass balances must hold.

### Sub-models per stage

The first stage regards primary production and emission. The primary production development, from the replicating stock in an infected person, with many variables not yet covered even in partial research, ranging from personal health characteristics, buildup of defenses by previous corona infections, to broader environmental issues where UFPs may damage the defense functions in the lungs. Together they determine the different forms of emissions. The airborne emission is set at a fixed number for modelling after emission, the standard person. That person represents a not yet hospitalized COVID-19 person.

The second modelling stage regards the fate of the SARS virions in the environment. Again, an overall model structure is lacking, which we develop. This environmental fate model first distinguishes two main situations: closed spaces and open spaces. For closed spaces, the novelty of the fate modelling here is that it reckons simultaneously with the emission inflow per m3 room, rising in time; the half-life of SARS-2 virions; and the ventilation rate, with all three exponential processes combined. The empirical support for the half-life is limited so we assume a broad range of values. For the ventilation in closed spaces, we basically use the most reliable ventilation method, instantaneous mixing, and a variable ventilation rate. The ventilation rate is varied in the empirical domain. Instantaneous mixing based ventilation is an ideal, see (CDC, 2003 (last update 2019)) in the healthcare domain, with half-lives quantified based on that assumption. Without it, some parts of the room will have a higher ventilation rate and other parts a lower rate, with corresponding higher or lower concentrations. Especially with low rates mixing may be very limited, requiring an air ventilator. Open windows create a ventilation rate, highest with strong wind and with large differences between inside and outside temperature. These rates are not constant and not predictable. Also, windows are not opened when it is too cold; too windy; or too hot, then often with non-ventilating air conditioners on. Even in temperate zones (Berkeley CA) people tend to open their windows only 35% of the time (Luo, Hong, & Pantelic, 2021). We reckon with well mixed air ventilation only. The model outcomes can be linked to many usual situations.

Some partial measurements are available. There are inside still-air measurements of the normal exhale flow dynamics of persons, coming to a near halt below half a meter, and slower diffusion thereafter. With real-life air flows and air mixing that type of analysis loses significance but it first aids in conceptual understanding.

For outside exposure there are models available only at a spatial scale level well beyond the personal exhales, covering city blocks and more. There are few experimental flow models with dispersion under variable wind speeds covering smaller distances. For virion exhales there are no models available at the scale level between one and twenty meters. We set up a base model covering a situation where people are in a dense group that size, at 1m distance. We use the individual exhales experiments mentioned, we assume very low wind speeds, and place several emitting persons in a row in the wind. The dispersion time is so fast that rising emissions per person and the half-life of SARS-2 virions do not play a role. The model cannot cover specific situations, such as in half-open stadiums, which also are half-closed.

The third stage is the exposure model, potentially leading to infection. The exposure depends on the concentration developing in air and the time of exposure. These simple models are available and may be varied according to characteristics of the individual and levels of activity. As a reference we assume a person at rest, with estimated inhale-exhale time of 3.6 seconds and a volume of 0.5 liter , resulting in one cubic meter per hour. The amount of exposure required for alveolar infection is mostly unknown, as viable virion concentrations in air are hardly measured and persons might differ substantially in this respect, due to airways quality and pre-infection viral defense mechanisms. For illustrative reasons we take a number from the COVID-19 literature, a low and a high estimate, roughly fitting with our illness development model.

Finally, the full triple-stage model for airborne transmissions is applied to many practical situations, defined in terms of possible inflow amounts, their volumes, typical ventilation rates, and exposure times. Though the model quantifications are preliminary, the structure of the outcome may give insights already, as exposure volumes diverge by over five orders of magnitude between situations considered.

The full model structure and the model parts, the linked sub-models, have all been newly constructed. They certainly cannot be found in the literature.

### Sub-models design

The model design starts with an alveolar infection, the pneumonia that is typical for SARS-2, and for SARS-1 and MERS as well. In infected person’s rising infection and primary production leads to several in-body flows and emission types, all rising. Each type of emission flow is followed through main environmental routes, resulting in potential exposures and infections. The flow scheme is in Figure 1, using the customary distinction between airborne, fluid, and solid emissions and exposures. Quantified modelling is approached for all subsystems separately. Some may be quantified within reasonable boundaries, the airborne emissions primarily, with main environmental routes and resulting exposures. Exposures result quite simply from environmental concentrations, by integration over the exposure duration. For other routes, solid and fluid, quantification with some realism was one step too far, with a qualitative modelling structure as main result.

The three main stages are in one chapter each, followed by the chapter application to specific situations and the conclusions.

## Overall modelling framework

The overall modelling framework follows all routes from primary production to infection. It brings together general knowledge on the viral illness, where it replicates, and the airborne, fluid, and solid emissions resulting, the upper part in Figure 1. The middle part follows the emission flows to exposures. The third part constitutes the final part from exposure to ultimately new infections. This third part will not be detailed and quantified. For airborne exposures there is some reverse similarity with the airborne emissions, as airborne virions flow up and down the airways at exhalation and inhalation.

**Figure 1. Mass flows of SARS-2: productions, emissions, transformations, and exposures**



## Models from primary production to emissions

### Available partial models and data, and gaps

SARS-2 (and SARS-1 and MERS similarly) can only reproduce in cells with ACE2 receptors. The distribution of these cells in the body is highly concentrated. They are in the alveoli, the gas-blood exchange chambers in the lungs, with around 50m2 surface (Ochs et al., 2004), and in the small intestines, with a food related exchange surface to blood of around 30m2 (Helander & Fändriks, 2014). These are the two main factories for primary SARS-2 production, ultimately resulting in emissions. Only alveolar emissions are well researched, with some preliminary quantifications.

In addition, there are smaller numbers of such cells in the nose in the cm2 domain (> 3 orders of magnitude smaller than the alveoli) and some in diverse places in the body with small arteries, such as in heart muscles, kidneys, brain, and some sweat glands, see the detailed analysis in (Hamming et al., 2004) and with some additions (Bourgonje et al., 2020) pp.229-231, and some probable exceptions such as in bone marrow (Zheng et al., 2021).

Virions from the alveoli and small intestines may enter the blood stream. There they can infect other tissues with ACE2 receptors. Blood flows, the circulatory system, link all possibly infected tissues, including the alveoli and small intestines themselves. Positive virions tests in the airways are closely linked to positive tests in stool. The latter may last for weeks and up to months after the end of the lung infection (He, Wang, Li, & Shi, 2020; van Doorn, Meijer, Frampton, Barclay, & de Boer, 2020; Xiao et al., 2020; JingCheng Zhang, Wang, & Xue, 2020), with viable virions found in stool (Papoutsis et al., 2021). Quantified data on stool emissions are lacking. Blood-based infections of others have not been documented. Sweat glands might be a research candidate for emissions with infections (J. Liu et al., 2020), without any quantifications yet, and probably not semen (Paoli et al., 2021).

### Stocks and flows detailed

SARS-2 virion production with Covid-19, the primary flow, is from infected pneumocytes, the stock. As the production infects other cells newly, the stock increases, and the flows increase, for given but different defence mechanisms of persons. This increase is halted when SARS-2-specific defences and medicines become active.

SARS-2 readily reproduces in the gut enterocytes as well (Guo, Tao, Flavell, & Zhu, 2021; Lamers et al., 2020), possibly a second primary source. In SARS-2-infected persons the outflow in stool is substantial as indicated by PCR tests on stool, comparable to swabs in their nose and throat, see (Miura, Kitajima, & Omori, 2021), with viable virions in stool (Miura et al., 2021). But viable virions as spread from stool have not been measured. Next, PCR-tests in sewers lead to PCR-based quantified results, see early (Medema, Heijnen, Elsinga, Italiaander, & Brouwer, 2020), but did never involve viable virions.

### Dynamics of respiratory stocks and flows

In lab-based replication using defenceless Vero E6 cells, production and emission starts within hours and halts at around 14 hours at cell death, with new cells infected (Ogando et al., 2020). In humans there are varying estimates of the period of exposure till replication with positive PCR test, from asymptomatic illness to symptomatic illness, hospitalization, ICU, and death. Up to half of positive tests are asymptomatic, especially with younger persons, see the survey analysis in (Rasmussen & Popescu, 2021). We developed a growth model that roughly fits these time periods, see the model in SI-2.a, and see SI-1.a&b for basic assumptions and nomenclature (including for ‘COVID-19’). Before onset of specific defences there is exponential growth in in-body stocks and primary production, and in emissions, of in the order of 2.5% per hour, doubling in slightly over a day.

The model allows for different starting infections, the lowest linked to Day 1. However, severe exposures could start the infection at ‘Day 10’, with a much shorter time to possible symptomatic illness and next hospitalization. The time between exposure and symptomatic illness is virtually always less than 14 days (Bar-On, Flamholz, Phillips, & Milo, 2020) or 10 days (Ivorra, Ferrández, Vela-Pérez, & Ramos, 2020). There is a strong relation between high (PCR based) virion tests and later severeness of illness (Y. Liu et al., 2020), in line with this illness-development model.

The production in the alveoli is in the two flattened-cells thick layer between air and blood. Each pneumocyte cell has a thickness between 100 and 200nm, the size of a SARS-2 virion, while the total barrier has a thickness between 500 and 700nm. The produced virions leave partly towards the blood, in unknown quantities. Towards air, the virions first pass the surfactant-rich watery layer, <100nm thick but with substantial local variation (Siebert & Rugonyi, 2008) and similar and (Fröhlich, Mercuri, Wu, & Salar-Behzadi, 2016) and (Bastacky et al., 1995) on rats. The alveolar sacs (~20 alveoli per sac) are connected to the alveolar ducts and from there to the lower and upper airways (Talaat & Xi, 2017). Outside air flows into the alveoli with each tidal breath and virions-infected air goes into the airways at exhalation. Alveoli and airways are never empty (Residual Volume >1L; inhale at rest ~0.5L), see details in (Ménache et al., 1997). So, a part of virions leaving the alveoli returns to other alveoli, as self-infection. In the smallest airways virions may become small watery droplets at inhalation when the small airways open after collapse at deep exhalation. The already surfactant-wetted virions then become more water-covered (Malashenko, Tsuda, & Haber, 2009), with the water composition also medically relevant (Bake, Larsson, Ljungkvist, Ljungström, & Olin, 2019). A part will re-enter the surfactant-rich surface layer. All airways are covered with epithelial cells where the wetted virions can be caught in mucus, most of them being de-activated there. Mucus with virions and virion parts is transported by the epithelial cells to the throat (~20cm/hour) and mostly swallowed. Mucal droplets can be created and exhaled by cough/sneeze bursts and the trembling of epithelial cells while breathing, singing, and speaking, with shares in quantities lacking. See Figure 2, and a general description of the respiratory system in (Carbrey, 2015).

**Figure 2. SARS-2 virions flows: from primary alveolar production to emissions**

### Reference emitting person quantified

The reference person has the model infection of around Day 17, set at emitting 100 000 virions per hour, not yet hospitalized. Before onset of specific defenses its emission will continue to rise. One order of magnitude smaller or higher exposures are empirically possible, see the PCR-based survey in (J. Ma et al., 2020), who measures between 6000 and 600 000 thousand virions per hour in a group of partly hospitalised patients, with some even larger peaks. Peaks tend to be just before symptomatic illness starts. At day 17, around 0.2% of the alveoli would have been infected, ~1m2, a severe burden for the body already. The reference person has 1000 tidal flows per hour, of half a litre each, half a cubic meter.

## Modelling environmental concentrations and exposures: main routes in closed and open spaces

### Available partial models and data, and gaps

Empirical measurement of single viable airborne SARS-2 virions is very seldom. After SARS-1 a first bubbling-based air filtration system has been developed (Agranovski et al., 2004). Viable airborne SARS-1 virions were measured already in Toronto (Booth et al., 2005), but not yet quantified. Newer measurement apparatus has been developed (Pan et al., 2016). Data on SARS-2 are by (Lednicky et al., 2020), Table 2, focused on particles below 500nm. Quantified measurements, also for droplets, remain by necessity highly diverging due to many confounding circumstances and lack of standardization (also personal communication Lednicky). See the comparison with their air measurements and our mass balance-based modelling outcomes in SI-5.f.

SARS-2 virions decay in the environment, in closed spaces with HalfLifes between 1 and 3 hours and in open spaces down to 15 minutes (Lelieveld et al., 2020) and similar (Smither, Eastaugh, Findlay, & Lever, 2020). In watery suspension in lab situations, droplets of >2000nm may decay much slower (Fears et al., 2020).

In terms of modelling in open spaces, for non-persistent micro-pollutants a more regional meso-level approach has been developed, with ozone formation and destruction as one example (Jian Zhang & Rao, 1999). Large scale vertical mixing and time of day play a major role there.

There is substantial partial analysis for example on pedestrian level exposure by UFPs from combustion engines (Zhu, Ranasinghe, Chamecki, Brown, & Paulson, 2021), there related to cardio-pulmonary health effects. The scale level is still that of city regions however, way beyond where dispersion of SARS-2 virions may be relevant.

There is some empirical measurement of dilution at shorter distances. (Wu, Zhu, Zhen, Zhang, & Lu, 2018) give peak concentrations of gas leaks from storage tanks at distances up to 120 meters, with different wind speeds. Their data indicate a constant dilution per distance, independent from wind speed.

However, the spatial level relevant for SARS-2 is in the meters domain, up to 15 meters at most, as there is no concentration build-up and always some dilution by air mixture.

The gap in quantified outside measurement and modelling is clear: it does not exist. We fill in the gap with several independent modelling approaches.

### Closed and open spaces

Closed spaces and open spaces cover all environments. In closed spaces all three types of emission occur, airborne, watery, and solid, and all five types of exposure (see flows **❶** to **❺** in Figure 1). Airborne emissions cover all forms together here: virions and droplet-nuclei and minidroplets with virions, mucal or watery based (flow ❶ and ❷). Droplet-nuclei result from evaporation, with the non-water part of the mucus-based droplet around 3% (Fröhlich et al., 2016), p.6. Exposures considered are as build up in different closed spaces, and less so in open spaces, and as face-to-face concentrations. Larger droplets may infect the nose directly (flow **❸**) or by first passing to fomites. Stool and stool-droplet fomites may be brought to the nose for infection (flow **❹**) and to the mouth then swallowed towards intestine infection (flow **❺**).

Infections in China were mostly concentrated and contained in Wuhan, Hubei. So, in rare single new cases outside Hubei, individual outbreaks could well be traced, with analysis of the location of secondary infection of a new case (Qian et al., 2020). Of the 1245 cases covered just one infection was probably not indoors, with only one person secondarily infected then. Outside modelling has serious challenges remaining, with different modelling approaches developed here. Fluid and solid exposures have mostly rudimentary conceptual modelling only, with limited and mostly just partial quantifications. We model a few worst cases.

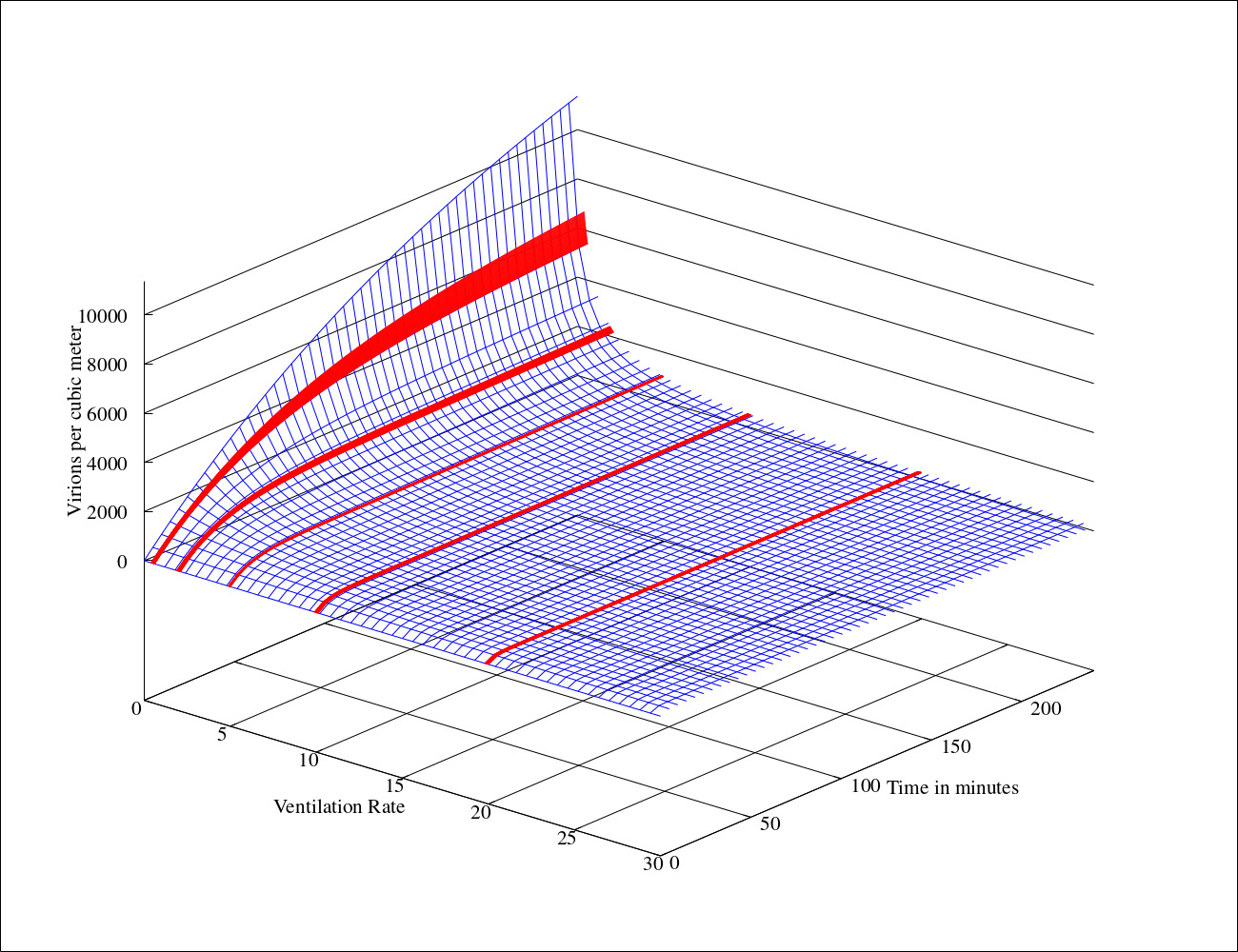
### Closed spaces airborne concentrations (time dependent)

A reference closed space for modelling is set at 100m3, 30m2, with five emitting standard persons, with exponentially rising emissions. Distanced at 150cm ten persons easily fit in; at 1 meter (examples: well-filled restaurant or bar, birthday party) 30 persons fit in. The continuing inflow, exponentially rising, is countered by two concentration-dependent exponential outflows: decay and ventilation. Decay is set at 120 minutes HalfLife, with a sensitivity analysis at 60 and 120 minutes (and for outside spaces also 15 and 30 minutes). Concentrations increase in time, with ventilation dominant over decay long-term, see figure 3. The model description is in SI-4 and the stocks and concentrations in SI-5, the exposures in SI-6, and the results-approaching spreadsheet, for easy sensitivity analysis, in SI-7. The in-house developed new model combines the three exponential mechanisms, with the ventilation part following US CDC (CDC, 2003 (last update 2019)).

A recent survey by (Allen & Ibrahim, 2021) indicates the importance of ventilation for infection prevention also for SARS-CoV-2 but lacks specifics on inflows and concentrations. It gives little support on when which ventilation rates (VRs, US: Air Change rates per Hour, ACHs) are relevant: there is no mass balancing involved and no decay rates used. In ventilation analysis well-mixed ventilation is usually assumed, as we do. At low ventilation rates mixing may be limited however, possibly leading to inversion layers, with locally then much higher concentrations (Zhou, Qian, Ren, Li, & Nielsen, 2017). For larger spaces flow ventilation can be more efficient, if well-designed and executed. In practice, some spots may have high and other low ventilation rates, with locally high concentrations resulting. In spaces with only passive natural ventilation, it is the density (humidity-temperature) difference between inside and outside air that drives the ventilation, aided by wind kinetics. There will be situations over the year that natural ventilation is close to zero, even with opened windows. For virions removal, air filtration can be equivalent to ventilation, saving on energy costs. Air conditioning may cool or heat but normally does not ventilate or filter virions, and then can transport them also to connected rooms (Lu et al., 2020). A ventilation rate of 0.1 is quite common in private housing. School classrooms investigated in England showed VRs down to zero (new schools, all windows closed) and VR0.84 on average (Coley & Beisteiner, 2002), though norms are in the order of VR5. Private sleeping rooms in China vary depending on outside temperature and window closing. If closed, the median VR tends below VR0.45 (Hou et al., 2019). In a study relating dilution to infections for the more infectious SARS-1 (Jiang et al., 2009) found for hospital situations that VRs below 25 still gave a serious chance on infection. Only VR above 250 (!) proved inhalation risk free for long-durations.

We cover the VR range from 0.1 to 40 (in cars (Ott, Klepeis, & Switzer, 2008)) and 60 (high room open window). The resulting range of room concentrations is wide. For VR0.1 the concentrations per cubic metre are at minute 60 (one hour) is 4036 virions and at minute 720 (12 hours) 14052. For VR20 these numbers are 248 virions at t60 and 326 virions at t720. See the full results in SI-5, also for different HalfLifes. Ventilation makes an extreme difference.

**Figure 3. Concentrations rising in time with different ventilation rates**

(red lines: VR0.1; VR2; VR5; VR10; VR20)

### Closed spaces airborne room exposures (time & duration dependent)

The concentrations in closed spaces build up in time. Duration of stay over the concentration determines the exposure. Staying periods are 1, 5, 15, and 120 minutes, while entering at minute 1, 60, 240, 480, 600, 1320, and 2760, covering two full days after 2 hours stay. Entering a sick room and staying there for 6, 12, 24 hours and 48 hours is added as relevant for a long-term care facility. Following (Lelieveld et al., 2020), we use exposure with 350 virions as indication of probable infection, 100 as a minimum, and above 1000 as a high chance on infection.

Exposures differ widely, see the full results in SI-6.Table 1. At a one-minute stay, exposure to infection is never reached, except in fully non-ventilated rooms, entering 24 hours after the infected person, for HL120 (the standard) and HL180. The 5 minutes stay at HL120 may reach infection with VR0.1, entering at minute 240. With higher VRs the entering time for relevant infection recedes, to minute 1320 for VR0.5 and minute 2760 for VR1. At higher VRs exposures are too low for infection.

The 15 minutes stay leads to infectious exposure when entering at minute 60 already, also for other ventilation rates (except HalfLife 15 minutes, relevant outside). That risk drops starting from VR2 and VR5, with hardly risks at higher VRs.

The 120 minutes staygives high exposures, already when entering at minute zero together with the infected person. It requires the still unusual ventilation rate of at least VR20 to reduce the exposure below infection level. At VR0.1 the exposure is 100 times the 350 virions threshold for infection.

Staying together with the emitting person for 8 hours or for one or two days always reaches an exposure of well over 350 virions. At VR0.1 the two-day exposure reaches 470-thousand virions, nearly 1200 times the threshold of 350. This exposure corresponds to an alveolar infection of around 18-thousand virions, starting well into Day 11 in the alveolar infection model in SI-2.a. Newly infected persons will start to contribute to the room concentration.

**Table 1. Potential exposures depending on time of stay of the infected person at entering of not-infected person (t) and the duration of stay (period) following**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **[t,period]** | **VR0.1** | **VR0.5** | **VR1** | **VR2** | **VR5** | **VR10** | **VR20** | **VR40** | **VR60** |
| [0,1] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| [60,1] | 34 | 28 | 23 | 16 | 8 | 4 | 2 | 1 | 1 |
| [240,1] | 82 | 51 | 33 | 19 | 8 | 4 | 2 | 1 | 1 |
| [480,1] | 104 | 58 | 37 | 21 | 9 | 5 | 2 | 1 | 1 |
| [600,1] | 111 | 60 | 38 | 22 | 10 | 5 | 3 | 1 | 1 |
| [1320,1] | 151 | 81 | 52 | 30 | 13 | 7 | 3 | 2 | 1 |
| [2760,1] | 273 | 148 | 94 | 54 | 24 | 12 | 6 | 3 | 2 |
| [0,5] | 8 | 8 | 8 | 8 | 7 | 7 | 5 | 4 | 3 |
| [60,5] | 174 | 145 | 117 | 81 | 39 | 20 | 10 | 5 | 3 |
| [240,5] | 411 | 253 | 165 | 96 | 42 | 22 | 11 | 6 | 4 |
| [480,5] | 521 | 288 | 183 | 106 | 47 | 24 | 12 | 6 | 4 |
| [600,5] | 555 | 303 | 192 | 111 | 49 | 25 | 13 | 7 | 4 |
| [1320,5] | 753 | 408 | 259 | 150 | 66 | 34 | 17 | 9 | 6 |
| [2760,5] | 1365 | 738 | 469 | 271 | 120 | 62 | 32 | 16 | 11 |
| [0,15] | 75 | 72 | 69 | 64 | 52 | 38 | 24 | 14 | 10 |
| [60,15] | 554 | 455 | 363 | 249 | 118 | 61 | 31 | 16 | 11 |
| [240,15] | 1243 | 763 | 497 | 288 | 127 | 66 | 34 | 17 | 11 |
| [480,15] | 1567 | 866 | 550 | 318 | 141 | 73 | 37 | 19 | 13 |
| [600,15] | 1669 | 910 | 578 | 334 | 148 | 76 | 39 | 20 | 13 |
| [1320,15] | 2265 | 1225 | 778 | 450 | 199 | 103 | 52 | 26 | 18 |
| [2760,15] | 4103 | 2219 | 1410 | 815 | 360 | 186 | 95 | 48 | 32 |
| [0,120] | 3812 | 3079 | 2445 | 1695 | 857 | 465 | 243 | 124 | 83 |
| [60,120] | 6577 | 4784 | 3460 | 2146 | 966 | 500 | 255 | 129 | 86 |
| [240,120] | 10698 | 6323 | 4070 | 2357 | 1041 | 539 | 274 | 138 | 93 |
| [480,120] | 12899 | 7080 | 4500 | 2603 | 1149 | 595 | 303 | 153 | 102 |
| [600,120] | 13679 | 7442 | 4729 | 2735 | 1207 | 625 | 318 | 161 | 107 |
| [1320,120] | 18517 | 10017 | 6364 | 3681 | 1625 | 842 | 428 | 216 | 145 |
| [2760,120] | 33543 | 18145 | 11529 | 6667 | 2943 | 1524 | 776 | 392 | 262 |
| [0,240] | 12263 | 8681 | 6240 | 3935 | 1847 | 978 | 504 | 256 | 171 |
| [0,960] | 91126 | 52286 | 34012 | 19998 | 8939 | 4651 | 2374 | 1199 | 802 |
| [0,1440] | 159990 | 89542 | 57684 | 33688 | 14982 | 7781 | 3967 | 2003 | 1340 |
| [0,2880] | 471052 | 257805 | 164597 | 95515 | 42278 | 21917 | 11164 | 5635 | 3768 |
| **Color explanation** | |  |  |  |  |  |  |  |  |
|  | No infectious exposures ('< 350' virions) | | | | |  |  |  |  |
|  | For 5 minutes stay, infectious dose only with very low VRs | | | | | | |  |  |
|  | For 15 minutes stay, serious chance on infection except for VR10 and higher | | | | | | | | |
|  | For 120 minutes stay, serious chance on infection except for VR20 and higher | | | | | | | | |
|  | Long stay, high chance on severe infection, up to 1000 times infective dose | | | | | | | | |

Consider a larger number of emitters per 100m3 than five, each with emissions >100 000 virions/h, present with a longer emitting time, and longer stay-together period than two hours, with many to-be-infected persons. This will lead to many persons infected, each with a very high dose: a superspreading event. Empirical analysis with only partial analytics is in (X.-K. Xu et al., 2020), and similar for SARS-1 (Lloyd-Smith, Schreiber, Kopp, & Getz, 2005; Shen et al., 2004).

### Closed spaces airborne exhale concentrations & exposures (distance & duration dependent)

Exhales are relatively warm and humid, hence have buoyancy, and they have kinetic energy when leaving the nose and mouth. Their speed is reduced very fast when the exhale expands (try and blow out a candle with your nose). The nose/mouse exhale cone, upward curved, is variously estimated with a ~40 degrees opening (Gupta, Lin, & Chen, 2010; Olmedo, Nielsen, de Adana, Grzelecki, & Jensen, 2010; C. Xu, Nielsen, Liu, Jensen, & Gong, 2017). Mouth exhales diffuse faster while nose exhales start more downward. At 45cm distance the speed is down below 25cm/s (Xu et al., 2020). Modelling can be approached most simply by a sphere expanding in the cone (as used for still air inside) but better by a wisp, as the duration of a typical exhale is 1.6 seconds. Single exhales (0.5L) of the 100 000 virions per hour person contain around 100 virions. The first part of the exhale then has reached the low-speed-high-dilution front while the last breath part still enters the cone, see Figure 4a and 4b in (C. Xu et al., 2017), copied in SI-9.a. as Figure 1. Air disturbances determine further dilution, while the warm and humid virion cloud still rises somewhat. After diluting to 50cm distance the one-sphere model gives a volume of 200L, a dilution by a factor 400, with 0.25 virions per 1/2L inhale. This first approach is a substantial overestimate. The wisp model would show a more realistic longer duration of dilution of an exhale. Being in the exhale for a longer period (100 inhales, 6 minutes and longer) would better be approached with the room model.

The burst exhale by cough-sneeze is approached as depicted in lab situation in (Bourouiba, 2020), taken as having 5 times the normal exhale virion load. The dilution at 1m has a radius 50cm, and from there dilutes further, at least following the narrow cone at around 10degrees. Five times inhale in the full cough, highly unusual, leads to an exposure of 7.5 virions at 100cm, and 6 and 5 virion at 150 and 200cm. The 40-degrees cone model would lead to 6.2, 1.8 and 0.75 virions respectively. See the excel sheet results, open to making variants, in SI-10.b.

### Closed spaces fluid droplet concentrations & exposures (distance & frequency)

Droplets can be exhaled normally by breathing, speaking, and singing, and in bursts as by coughing and sneezing. Smaller droplets (<5-10µm) evaporate and remain airborne for inhalation, see above. Basics are by (Duguid, 1946). Before evaporation, kinetics rule and for the larger droplets gravity takes over.

On the way down, droplets may hit persons directly, see (Stadnytskyi, Bax, Bax, & Anfinrud, 2020); (W. Wang et al., 2020); (P. Z. Chen et al., 2020); and (Niazi, Groth, Spann, & Johnson, 2020), with (X. Chen et al., 2020) discussing the option of infection of the eyes. Droplets may hit objects, then with fomite-based indirect exposure.

Bursts of sneeze and cough have been analysed by (Bourouiba, 2020; Bourouiba, Dehandschoewercker, & Bush, 2014; Redrow, Mao, Celik, Posada, & Feng, 2011; Scharfman, Techet, Bush, & Bourouiba, 2016). See for conceptual issues on ‘droplets’ the definitions and assumptions in SI-1.a.

**Direct exposure**

There are five element to model and specify on the way to direct exposure and alveolar infection.

1) The number of viable virions per droplet size and size distribution.

These numbers have not been established, only totals, and those quite rudimentary only. A survey on concentrations in exhale fluids and size distribution of droplets is in (Anand & Mayya, 2020), and similar but not SARS-2 specific in (Buonanno, Stabile, & Morawska, 2020). Using the median concentrations from the survey list of Anand et al. Table 1, we take the five high peak concentrations with a mean of 86\*106 copies per mL, PCR-based, leaving out one extreme outlier. The mean median peak is a factor 3 lower, with extreme variations. The 10µm droplet, the standard droplet diameter cough-sneeze-song based, results in a viral load of 0.045 virions per such droplet. Cough-sneeze droplets may also be larger. In a 50µm droplet there are 5.65 virions, in 100µm droplet, falling fast, there are 45 virions. See SI-8 for details. Song-speak droplets are set at 50µm,

2) Frequency of the droplet-laden exhales.

That number is taken as 100 exhales, 6 minutes. Coughs and sneezes short distance directly in the face are highly unusual, taken as a one-time event. Evaporating droplets are treated in airborne exposure. Alveolar SARS-2 production is not influenced by breathing, singing, or coughing. However, forced exhales may emit mucal droplets that otherwise would have been swallowed, thus adding to total emissions.

3) Spatial spreading of droplets before touching the ground.

Published camera pictures indicate a relevant floor area of 0.5m2, with around 25 visible falling droplets in a cough-sneeze burst, estimated from Figure 1 in (Bourouiba, 2020). In normal breathing and singing they may be smaller and fewer.

4) Nose position of a receiving person.

That position determines the chance of in-nose exposure. The lack of research data is filled with some extreme scenarios. Key is that the opening of the nose must be in the direction of the falling droplet. The receiving person must lye head down, nose-up to the exhaler. This is not a normal situation. Next, the surface of the nose opening is around 2.5cm2 of the 5000cm2 of drop-falling area, a chance of 1:2000 of receiving one.

Twenty-five droplets of 50µm (not 10µm) per exhale result in 2500 droplets, a chance of 1.25 per six minutes lying nose up under a singing person. The virion intake then would be seven. A full hit with a large droplet of 100µm would deliver 45 virions to the nose. These outcomes certainly are unrealistically high estimates.

5) From nose to alveoli.

When hitting the nose opening, transport from nose to the alveoli must follow, for SARS-2 pneumonia. Direct entry to the alveoli is impossible for larger droplets. There is however an area in the nose with ACE2 receptor cells, supporting the olfactory nerves in the upper nasal cavity. Part of the seven SARS-2 virions of a large direct hit might arrive and replicate there, and similar the 45 virions from a cough-sneeze. They then could produce airborne virions, inhaled to the alveoli. There exists no modelling, and certainly no data, on this route to COVID-19 pneumonia. The infection of the nose may be by airborne virions, not fluid, a different route.

Overall, the low chance on a full hit into the nose, the low number of virions involved in a full hit into the nose, and the lacking route to the alveoli make this a highly improbable route for infection, set at ‘1’ to give it a number.

**Exposure through fomites**

The fomite route has the same droplets at its starting point. A droplet may hit an object spreading and decaying there. Next the virions are taken up by hand and placed in the nose. The step-by-step model in (Li, Xu, Cai, Hu, & He, 2021), Table 1 and 2, is not linked to sources and lacks empirical data. Real-life measurements may show positive PCR tests on fomites. But viable virions could not be produced in Italian hospital settings (Mondelli, Colaneri, Seminari, Baldanti, & Bruno, 2020) and similarly (Kanamori, 2021), who also could not find any demonstrated fomite infection in the literature. Even the mobile phones of hospitalized COVID-19 patients were mostly virion-free, 20 out of 22 (J. Ma et al., 2020). (Guo et al., 2021) conclude that information showing relevant concentrations of viable SARS-2 virions on fomites is fully lacking (p.321). The recently changed position paper on this subject by (CDC.Gov, 2021) states that the fomite route can hardly play a role in SARS-2 infections.

A rough quantification: a substantially wet 100µm (0.1mm) droplet, containing 45 virions (high peak, median peak 1.7 virions) may get onto a finger by 10%, a high estimate, while effectively reaching the nose with 10% effectiveness again. That is 0.5 (0.02) virions brought to the nose, still requiring transport to ACE2 cells, replication, and transport to the alveoli for causing COVID-19 pneumonia. We give again a score of ‘*1*’.

This route has serious modelling shortcomings and has mostly missing and some highly variable only indirect data. The numbers constitute a first very rough extreme worst-case approximation. They indicate zero risk.

### Closed spaces solids to nose: stool and fomites (transport & frequency)

Solids to nose may be from stool directly (Lamers et al., 2020) and indirectly through fomites (Li et al., 2021), both well established as potentially relevant, with partially overlapping environmental routes. The conceptual model for direct stool exposure starts with 1) the virion concentration in stool emitted, 2) amount of stool to hands, 3) from hands to nose, next multiplied by frequency, and (4) from nose to alveoli. The fomite route inserts an additional step, to the object and then from fomite to hand. A survey of the literature and remaining questions on the orofecal route is in (Guo et al., 2021) and extensively, covering 59 studies, in (Heneghan, Spencer, Brassey, & Jefferson, 2020). They see limited evidence for viable virions in stool, as opposed to virion-parts measured by PCR, see in this sense also (W. Wang et al., 2020) and (Xiao et al., 2020). Modelled stool concentrations are in (Miura et al., 2021), Figure 1. They vary widely, between 102 and 107 per gram (= ~mL), decreasing with time after symptom onset. Their data result from PCR measurements, not measures of viable virions in stool. For a worst-case stool concentration, we use their near highest score of one million copies per ml, assumed all viable. Next, how much stool could remain on a fingertip? Larger amounts of somebody’s stool on one’s hands will be cleaned directly. A hand surface of 100mm2 thick 0.02mm (20µ), well visible by color, smelly, and with tangible parts, could be a rough first estimate. That layer of 2mm3 contains 200 virions, decaying with unknown speed. The next step is smearing part of that layer into the entry of the nose. Passing 10% seems a very high estimate, 20 virions. As the finger-virions are not airborne, they first move into the mucal defence layer and some fall victim to the non-specific immunological defences, see (Fokkens & Scheeren, 2000). There are ACE2 receptor cells in the nose supporting the olfactory bulb, in the upper nasal cavity (Bilinska, Jakubowska, Von Bartheld, & Butowt, 2020), where some virions might arrive. There are suggestions that these cells form a first stage of immunological defence development (Boscolo-Rizzo et al., 2020; Spinato et al., 2020; Yan, Faraji, Prajapati, Boone, & DeConde, 2020; Yan, Faraji, Prajapati, Ostrander, & DeConde, 2020), with infection there possibly indicating a milder course of SARS-2 illness. The final step, from nose infection to alveolar infection would again require transport of airborne virions. The spreading of infection by consecutive adjoining cells in the upper and lower airways (Cevik, Kuppalli, Kindrachuk, & Peiris, 2020; Mason, 2020) seems dubious, lacking ACE2 cells. It fits however with how the influenza virus may spread. There is no real information on this to-be-modelled step. We set a high estimate at ‘*5*’. Adding an in-between fomite step, from stool-to-*object*-to-hand, would reduce the number of stool virions-to-nose substantially, say 0.1, leading to ‘*0*' exposure of the nose.

xxx

### Closed spaces solids to mouth: stool, fomites, and food (transport & frequency)

Virions to mouth are swallowed, with possibly small intestine infections (30m2 ACE2 cells) and virions production there. A substantial share of the population is in contact with stool from babies and from persons in care situations, while hands rub the mouth very frequently. Next, the route from mouth to intestine must pass the esophagus and stomach, which is possible for many viruses and bacteria. Some break-down may take place. The first step is stool to hands, possibly through fomites, the same as with stool solids to nose regarding the stocks and flows involved. However, while only fingertips can transport into the nose, broader surfaces of the hand can reach the mouth, set at 10cm2, with 2000 virions if indeed viable. Direct mouth contact with contaminated solids may be possible as well, as also in or on foods. This in-between step might very incidentally be substantial, in non-cooked foods, with other illnesses coming up as well. Replication in the small intestines is highly probable given the well-established near certain co-infection with alveolar infection. However, this connection might also be through the circulatory system, potentially bi-directionally. Would there be cases where the intestine infection precedes the alveolar infection? The number of virions swallowed, 10% from hand, can be in the order of 200, see SI-9.a, and may be repeated several times. This supposes viable virions reaching the mouth, not established empirically, and next the small intestines, neither established empirically.

### Open spaces airborne concentrations and exposures (location and time dependent)

The situation considered is 100 persons at a terrace, or other gathering, with a surface of 100m2. Scenarios are based on a long stay of 4 hours and density of emitting persons at 5%, 5 persons. At population level the share of infectious persons in a US state was 1.7% (Menachemi et al., 2020) but in groups it can be higher. In open spaces wind creates transport and turbulence. We specify results for 1m/s (Beaufort 1-0, Light Air to Calm). At 5m/s (Beaufort 3, Gentle Breeze) exposures would be much lower. Temperature differences may lead to substantial vertical transport. Vertical rising and mixing at micro, meso, and macro level, are major factors in ground-level dilution (Jian Zhang & Rao, 1999). They are left out of account, depicting maximum concentrations in this sense. Fluid dynamics might model the transport and dilution of exhales but cannot be reduced to generic situations and mechanisms. Empirical models at this scale level of up to 15m distance are absent. Empirical data are hardly available for other toxics. (Wu et al., 2018) give peak concentrations of VOC leaking from storage tanks at 60 and 120 meters from source, see results of a secondary analysis of their data in SI-9.c. They show an interesting constant dilution over distance, with varying wind speeds.

We developed 3 parallel outside models, see SI-10.a&b. The first is a continuous exposure model with two exhalers standing at 1 meter distance in line with the wind of 1m/s. The second, also a cone model, is an extension of the inside exhale exposure model introducing wind in large cones sections. The third is an extension of the ventilated room model with different ventilation rates. All depict worst-case situations with hardly vertical transport. The results for the most refined continuous model of long-term exposures are in Table 2, with the full set in SI-11.a. Figure 4 shows exposure depending on distance and duration of stay. The other two models function as a check on the levels of exposure, with same order of magnitude results. We abstract from the rising emission levels per person, a few percent, hardly relevant for the 4-hours period. We also abstract from vertical mixing around persons, that are always warmer than the surrounding air.

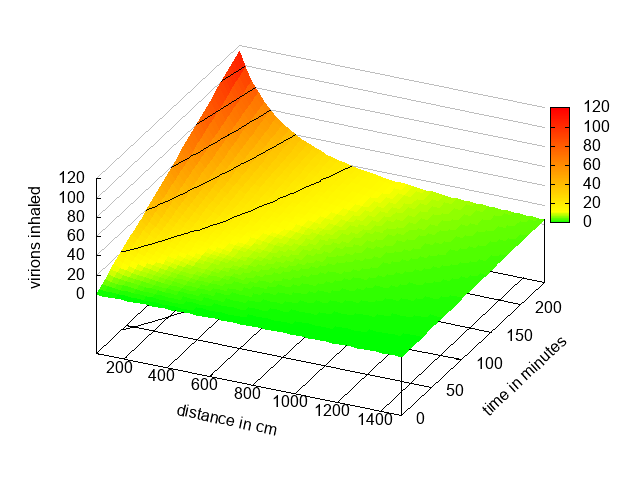
**Table 2. Exposures at different distances on 100m2 terrace two emitting persons in line.**

Exhaler 2 stands 100cm downwind from Exhaler 1. Windspeed 1m/s. Exposure period 4 hours.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Inhaler from Exhaler 1 in cm | *175* | *200* | *500* | *1000* | *1500* |
| Virions inhaled from Exhaler 1 | 48 | 44 | 20 | 8 | 5 |
| Virions inhaled from Exhaler 2 | 70 | 63 | 25 | 10 | 5 |
| **Total Exposure Person X** | **118** | **108** | **45** | **18** | **10** |

The highest exposure is with the inhaler mid-head at 75cm from exhaler 2, 118 virions. Face-to-face that corresponds to an unusually close ~50cm distance. Other persons on the terrace will have a lower exposure than those standing in the two persons-in-row-in-line-with-wind exhales.

**Figure 4. Exposures on a terrace depending on distance and duration**

Two persons in line, distance from the first. Iso-exposure lines in black.

### Other sources of exposure

There are several more incidental routes. Frozen food and its packaging may remain contaminated for a long time, as found several times in China, with a chance on infection especially by the mouth-to-intestines route. The source then is human or animal emissions elsewhere. Animal-to-human infection has been documented in the vicinity of mink farms (Koopmans, 2021), with mink farms in Northern Jutland constituting a main source of human infections, see the broad survey in (Fenollar et al., 2021), also covering ferrets. Ferrets, widely held as pets, can be infected with SARS-2, experiencing broad also alveolar infection (Fenollar et al., 2021). At around 1.5kg, ferrets constitute 0.02 person-equivalent. At VR1 in 20m3 bedroom, a one-night intake may reach 680 virions, with 1823 virions at not uncommon VR0.1. Quantified measurements to support this route are lacking, however.

Next to minks and ferrets, there is a broad range of captive and wild animals already carrying the SARS-2 virus (Opriessnig & Huang, 2020; Shi et al., 2020). Quantified risks from their exhales as from using them as pets or treating and using them for food seem lacking and are assumed by these authors to be low.

## Modelling from exposure to infection

### Available partial models and data, and gaps

There is some knowledge on replication of SARS-2 virions in the upper nose cavity, where ACE2 cells are present in the supportive lining, with fast ACE2 cell replication after infection. also to the small amounts of ACE2 cells in the back of the mouth and in the throat, and in conjunctival parts of the eyes. For COVID-19 pneumonia the eye infection will have to advance through the nose. No data are available, let alone quantified modelling.

The core question remains how the virions produced in nose, mouth, and throat can access the alveoli, The answer is not easy as the exposures causing the nose infection may cause the alveolar infection at the same time. This problem is compounded by multiple infection events. It is not just one inhale that makes one ill. Also, the composition of exposures may be highly variable.

The nose may be infected at airborne inhalation; by a droplet hit towards the upper nose cavity; or indirectly by infected finger contact, requiring an in-nose model for infection. There is a fast reaction there increasing the number ACE2 cells, possibly as an early start of specific defences, and possibly leading to a less serious illness (Sungnak et al., 2020) and see also related to loss of smell (Boscolo-Rizzo et al., 2020; Spinato et al., 2020).

There is substantial knowledge on the physical filtering capacity of the airways, and on the transport of caught particles to the throat, mostly followed by swallowing. The epithelial cells also de-activate virions, so PCR measurements cannot give a reliable indication on the number of viable virions coming up. Quite certainly most in mucus will be swallowed. As there is a near full co-infection of the small intestines with alveolar infection, the swallowing route seems probable though not even proven. The route through blood to the intestines might be as probable, as the blood connected surface there is high, in the order of 30m2. The many smaller spots in the body with ACE2 cells get infected as well, ranging from heart muscles to small arteries and salivary and sweat glands. Human challenge trials with quantified droplet infection in the nose, currently ongoing (Rapeport et al., 2021), might shed some light on this issue, if the intestine infection would be integral part of the research project.

SARS-2 virions can be exhaled and inhaled in several sizes, in droplets larger than 10µm falling fast, and below 10µm remaining airborne after evaporation, increasingly so if smaller. Main lines in inhalation are clear, see (Zuo, Uspal, & Wei, 2020), p.16509. Larger still airborne droplets, 5-10µm may be deposited in nose and upper airways. Medium size particles, 1-5µm, don’t pass to the small airways, taken out by mass inertia in the upper airways as well. Only small particles, below 1µm and smaller more effectively, may reach the alveoli. (Conversely, larger particles if they were produced there, cannot leave the alveoli.) The mass of a 1µm (5µm) diameter sphere is 364 (45554) times the mass of a single SARS-2 virion at 140nm, including its spikes.

A detailed treatment of the tidal flows to the alveoli is in (B. Ma & Darquenne, 2011), and see our Figure 2. What is inhaled will partly move upwards again at exhalation. That volume of breath will partly leave the exposed person and will partly go down again towards other alveoli, in the next inhale.

A given exposure to nose-mouth may work out differently in different persons. This relates to a higher health risk, see the survey on UFPs and health in (Hong & Jee, 2020). Persons with airways obstruction, also by other UFP air pollution, may receive a substantially higher amount of UFPs in their alveoli than healthy persons (Brown, Zeman, & Bennett, 2002). Similarly, medicine application in the lungs are to be UFP-size and smaller for most effective up to alveolar application (Fröhlich et al., 2016) and in more detail (Talaat & Xi, 2017). The SARS-2 pneumonia requires the full route through the airways, with only sub-micron particles passing the ~25,000,000 finest bronchioli to the ~500,000,000 alveoli, see (Lednicky et al., 2020), p.477), and preferentially smaller, towards the UFP size.

The figures for influenza exposure and infection would substantially differ from those of SARS-2. The flu virus does not replicate in the alveoli but in nose, throat, and airways, and may then accommodate a bacterial pneumonia in the alveoli as with pneumococcus variants. Neither does influenza replicate in the intestines cell linings but causes injury and illness there only indirectly (J. Wang et al., 2014). The influenza virus starts replicating where droplets get caught, in throat-mouth-nose and the upper airways. Airborne infection with droplets may therefor play a main role for influenza (Cowling et al., 2013), and see an early case study (Moser et al., 1979), with ¾ of all persons infected within 3 hours. The age distribution of infected persons in an epidemic is extremely different for current SARS-2 and influenza, with influenza dominating in younger persons and much less so in older persons, as these have developed defenses in earlier epidemics already, see (E. Miller et al., 2010).

Conclusion here is that the relation between oral-nasal exposure and alveolar infection has not been established for droplets. Single virions and small virions containing clusters can reach the alveoli directly. The required dose for alveolar infection is not really known.

For illustrative reasons we follow (Lelieveld et al., 2020) with 350 as middle value, and use 100 virions as a lower boundary for a relevant chance on infection, and 1000 virions as high chance.

## Results for quantified exposure scenarios

### Descriptions of situations linked to modelling outcomes, with scenarios.

Real life situations are linked to modelling outcomes, with a broad range of relevant combinations selected for all exposure flows. The concentration development in closed space situations is scalable to volume and number of emitters. One emitting person in 20m3 (~8m2) gives the same concentration build-up as 5 emitters in 100m3 (~35m2). The start of an inhaling stay is specified per situation, as is the duration. If the standard person of 100 000 virions per hour is replaced by an exhaler of 10 000, all figures divide by 10. The range from VR0.1 to VR60 covers almost all situations. Concentrations do not relate linearly to VR changes. The basic data are in Table 1, with extensive sensitivity analysis in SI-6.

Inhaling persons are at least 75cm apart from exhalers. Regular exhale exposures are 100 times. A cough-sneeze burst directly in the face is a one-time event only.

Outside situations refer to 100m2 square with 1 person per m2 and five persons infectious. Duration of stay is four hours. Exposures are linearly scalable with duration concentration build and virion breakdown are negligeable. The location of emitters and exposed persons determines potential exposure, see Figure 4. Wind displacement is taken very low at 1m/s. superimposed on the exhale dilution, while disregarding other causes of turbulence and dilution, especially as related to vertical transport.

### Exposures in selected situations and scenarios quantified.

Table 3 gives the outcomes in terms of potential virion exposures. Colors indicate severeness of potential exposures. Dark green is the not yet infectious dose of below 100 SARS-2 virions and light green a low chance in infection, still below 350 virions. Light red is some real chance on infection, between 350 and 1000 virions and red, above 1000 virions, a substantial chance on infection.

Short exposures (15 minutes) in closed spaces with a standard density of 5 emitting persons in 100m3 poses a negligible risk, even at very low VRs. Very high VRs preclude a serious exposure except with a high density of emitting persons and a longer period of stay.

With longer durations in a room where emissions have led to high concentration risks rise dramatically. Even in a reasonably well-ventilated room (VR5) where one ill person (per 20m3) had been for 1 hour, there is a substantial exposure for the person remaining there for another 2 hours: 966 virions. With larger numbers of emitting persons, as in sick rooms in care situations, infectious exposure is near inevitable, with stringent measures due.

Incidental cough-sneeze exposures remain well below 100 virions even with some repetition.

In outside gatherings with 5 emitting persons per 100m2 and hardly any wind an infectious exposure seems near impossible.

A qualitative evaluation of all treated situations reckoning with key scenarios is in SI-11.c.

**Table 3. Exposures in selected situations and scenarios**

Full tables in SI-11, with evaluation.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Situations:** | **Exposure scenarios:** | |  |  |  |  |  |  |
|  | **ill ratio** | **Maximum density (or distance)** | **Emitting persons** | **Start time, period** | **VRs/ volume** | **Exposure to virions** | **Relative to Ref. 350 virions** | **Ref. Super-market 15 min.** |
| **Bedroom, private, low VR** | 50% | 2/8m2;h2.5m | 1/20m3 | t0,960 | 0.1 | **91126** | **260** | **11506** |
| **Patient ward, sleeping, low VR** | 50% | 10/30m2;h3.3m | 5/100m3 | t0,960 | 0.1 | **91126** | **260** | **11506** |
| **Train compartment long distance** | 33% | 6/8m2;h2.5m | 2/20m3 | t0,960 | 2 | **39996** | **114** | **5050** |
| **Bus long distance** | 5% | 60/80m2h;2.5m | 3/100m3 | t0,960 | 2 | **11999** | **34** | **1515** |
| **Office room** | 25% | 5/30m2;h3.3m | 2.5/100m3 | t0,960 | 2 | **9999** | **29** | **1263** |
| **Bar** | 16.7% | 30/30m2;h3.3m | 5/100m3 | t240,120 | 1 | **4070** | **12** | **514** |
| **Coffee room (choir, clubs)** | 6.7% | 30/30m2;h3.3m | 5/100m3 | t60,120 | 1 | **3460** | **10** | **437** |
| **Pets, ferrets in sleeping room** |  | 2/20m3 | 0.02/20m3 | t0, 960 | 0.1 | **1823** | **5** | **230** |
| **Minks farm, person-equivalent** | 50% | 20/25m2; 4m | 10/100m3 | t2760,120 | 20 | **1552** | **4** | **194** |
| **Restaurant inside full** | 6.7% | 30/30m2;h3.3m | 2/100m3 | t60/120 | 1 | **1384** | **4** | **175** |
| **Long Term care dining room** | 50% | 10/30m2;h3.3m | **5**/100m3 | t60,120 | 5 | **966** | **3** | **122** |
| **Patient ward visitor morning** | 10% | 10/30m2;h3.3m | 1/100m3 | t600,120 | 1 | **946** | **3** | **119** |
| **Bus, metro commuting, busy, long** | 12.5% | 40/40m2;2.5m | 5/100m3 | t0,120 | 5 | **857** | **2** | **108** |
| **Sitting room** | 20% | 5/30m2;h3.3m | 1/100m3 | t240,120 | 1 | **814** | **2** | **103** |
| **Person car ventilation low, not off** | 50% | 4/10m3 | 2/10m3 | t0,240 | 20 | **806** | **2** | **102** |
| **Airplane cabin long distance (SI-3)** | 10% | 10/3m2;2.2m | 1/20m3 | t0,960 | 60 | **802** | **2** | **101** |
| **Dining room, guests, full** | 20% | 15/30m2;h3.3m | 3/100m3 | t0,120 | 5 | **514** | **1** | **65** |
| **Church** | 2% | 50/200m2;10m | 1/100m3 | t0,240 | 1 | **374** | **1** | **47** |
| **Train compartment** | 3.3% | 6/8m2;h2.5m | 0.2/20m3 | t0,240 | 5 | **369** | **1** | **47** |
| **Airplane cabin (short distance)** | 10% | 10/3m2;2.2m | 1/20m3 | t0,120 | 20 | **243** | **0.69** | **31** |
| **Office room** | 2.5% | 5/30m2;h3.3m | 2.5/100m3 | t0,960 | 10 | **233** | **0.67** | **29** |
| **Shop, ill ventilated** | 50% | 5/30m2;h3.3m | 2.5/100m3 | t60/15 | 0.5 | **228** | **0.65** | **29** |
| **Bar** | 6.7% | 30/30m2;h3.3m | 2/100m3 | t60/120 | 10 | **200** | **0.57** | **25** |
| **Dining room, small family** | 20% | 5/30m2;h3.3m | 1/100m3 | t0,120 | 5 | **171** | **0.49** | **22** |
| **Sitting room** | 20% | 5/30m2;h3.3m | 1/100m3 | t0,120 | 5 | **171** | **0.49** | **22** |
| **Coffee room (choir, clubs)** | 6.7% | 30/30m2;h3.3m | 5/100m3 | t60/15 | 5 | **118** | **0.34** | **15** |
| **Terrace outside, exhales & wind** |  | 2 exhalers, row | 75cm after nr2 | 240 min. | 1000L | **118** | **0.34** | **15** |
| **Restaurant inside full** | 3.3% | 30/30m2;h3.3m | 1/100m3 | t60,120 | 10 | **100** | **0.29** | **13** |
| **Shopping mall,** | 4% | 5/30m2;h3.3m | 0.2/100m3 | t60/120 | 2 | **86** | **0.25** | **11** |
| **Dressing room (sport, etc.)** | 33% | 15/30m2;h3.3m | 5/100m3 | t0,15 | 1 | **52** | **0.15** | **7** |
| **Church (high building)** | 2% | 50/200m2;10m | 1/100m3 | t0,120 | 5 | **51** | **0.15** | **6** |
| **Terrace outside, exhales & wind** |  | 2 exhalers, row | 5m after nr2 | 240 min. | 1000L | **45** | **0.13** | **6** |
| **Meeting room** | 2.5% | 10/30m2;h3.3m | 2.5/100m3 | t0,120 | 5 | **43** | **0.12** | **5** |
| **Bus, metro commuting, few** | 5% | 40/40m2;2.5m | 2/100m3 | t60,15 | 2 | **40** | **0.11** | **5** |
| **Terrace outside "room model"** | HL30 | 100/100m2 | 5/500m3 | t0,240 | 60 | **33** | **0.094** | **4** |
| **Exhales normal face-to-face** | better use room model | | 100cm | 100x, 6 min. | | **25** | **0.071** | **3** |
| **Person car ventilation medium** | 50% | 4/10m3 | 2/10m3 | t0,15 | 40 | **22** | **0.064** | **3** |
| **Health club, groups** | 8% | 25/250m2;h4m | 2/1000m3 | t0,120 | 10 | **19** | **0.053** | **2** |
| **Terrace outside, exhales & wind** |  | 2 exhal. in row | 10m after nr2 | 240 min. | 1000L | **18** | **0.051** | **2** |
| **Supermarket, well-ventilated** | 6% | 10/30m2;h3.3m | 2.5/100m3 | t60/15 | 10 | **8** | **0.023** | **1** |
| **Train compartment** | 3.3% | 6/8m2;h2.5m | 0.2/20m3 | t0,15 | 20 | **5** | **0.014** | **0.63** |
| **Exhale cough-sneeze full inhale** | burst + 10 degr. cone | | 100cm | 5x |  | **1.47** | **0.0042** | **0.19** |
| **Platform railway/bus, exhales** |  | 50/100m2 | 75cm distance | 6 min. | 25L | **0.18** | **0.0005** | **0.023** |
| **Legenda** |  |  |  |  |  |  |  |  |
| below low infectious dose (< 100) | high infectious dose (350 - 1000) | | |  |
| low infectious dose (100 - 350) | extreme infectious dose (> 1000) | | |  |  |  |  |  |

## Conclusions

### Gaps in physical models and empirical quantifications, and preliminary results

* Most dearly lacking models first regard the infected person, its primary production, internal cleaning, transport, and composition of the airborne emissions, the fluid emissions, and the emissions in stool, all to be viable virions based. We developed a preliminary respiratory model which fits in with case data on durations between exposure, emissions development, and illness sequences. It allows to differentiate between severeness of exposure and the stage of development of emissions and illness. The internal virion flows between the main production sites, alveoli, and small intestines, is substantially unknown. One route is by swallowing virions caught in the mucus of the airways and then infecting the small intestines (30m2 ACE2 cells). As also other organs and muscles in the body get infected, the reverse direction might be possible as well, from the small intestines to the alveoli.
* For most generic environmental situations conceptual modelling and applied quantified modelling are dearly lacking, as are the data needed for model operationalizations. The only exception is the room ventilation model based on continuous mixing, fit for not too large spaces. We newly developed a model integrating the growth rate of emissions, the decay rates of the virions, and the outflow rates by ventilation. Only one empirical data set, for one specific situation, could be linked to this model, showing a clear lack of measurement data.
* For potential infection from droplets and stool, conceptual environmental models don’t cover specific transformation steps involved in droplets and stool. How many viable virions are there in falling droplets and stool, how do they fix to objects, for how long, and how can they be scraped off, and how can they be deposited in nose and mouth? And how may they next lead to infection in the alveoli and small intestines? Measurements for these steps are also lacking, with few partial exceptions, mostly regarding lab situations.
* The measurements of airborne virion concentrations have severe limitations mostly. Gravity separation misses out all particles below 1000-500nm, including single (wetted) virions and smaller droplet-nuclei, in line with (Gralton, Tovey, McLaws, & Rawlinson, 2011). These near UFP particles tend to come deepest into the lungs, to the alveoli where the viral pneumonia of SARS-2 develops. The presence of airborne viable virions is well established, also for SARS-1. But quantified measurement of exhales and concentrations is only now developing, with full-flow bubbling or wet-deposition. It is complex and expensive still and has not yet been standardized.
* Models for outside dispersion empirical models at the relevant scale level are lacking, even conceptually. Dispersion measurement is available incidentally, at ten times the required scale level at least. We made first quantifications using four different modelling approaches. They tend to roughly the same outcomes, of extremely low exposures.
* Finally, a positive general result. Though absolute exposure levels and infection risks have highly preliminary quantifications, the relative exposures are more robust. Even if five orders of magnitude difference would reduce to four, the lower scores are quite irrelevant and the middle to higher scores remain the main source of risk on infections.

### Results for Industrial Ecology

* The domain of short-lived toxic substances can be expanded to include short-lived toxic biotic substances, such as virions, and possibly protista and biotic toxins like prions, see exemplary (Smith, Booth, & Pedersen, 2011). SARS-CoV-2 will not be the last pandemic to reckon with.
* The factory-to-exposure structure will differ in its details per virus type, as is the case with other short-lived toxic substances. Their decay characteristics must be developed. Some more case studies, including for influenza, would be useful, with improved measurements and modelling steps. The header could be Viral Substance Flow Analysis, or broader: Biotic Substance Flow Analysis (BSFA).
* IE could fill the gap in knowledge which now leaves the relative and absolute importance of preventive measures unsubstantiated.

### Results for medical science and epidemiology

* The daily development model of alveolar infection and emissions (SI-2.a.) gives a framework for assessing the effect of light versus severe exposures. It can help explain the phenomena of super-spreaders and super-spreading events. High exposures lead to high emitters and more severe illness, and probably to more such emitters for a next round of high exposures as well. This link between medical science and epidemiology can be more firmly established.
* Given the duration between infectious exposure and the build-up of specific defences, it can also help explain the difference in the rate and seriousness of infection of similar groups and regions at different times.
* Infection of the small intestines by swallowing virions seems a viable option for infection. As blood-based SARS-2 infections of internal organs are common, there might also be a relevant infection route from the small intestines to the alveoli, not just the other way around through swallowing virus laden mucus.
* There is a clear urgency for improved and standardized measurement of viable virions, from their emission volumes by different persons at different stages and their concentrations and exposures in a broad range of situations.

### Results for citizens and governments

* Potential exposure situations differ by over four orders of magnitude. The highest exposures will have a substantial chance on infection while the lowest are irrelevant.
* In term of personal prevention, results indicate a low to zero risk on infective exposure in open air and in well ventilated places, and through contact with droplets and fomites. One cough full in the face at one meter distance delivers on average less than 1 single virion into the nose, let alone to deep in the lungs to the alveoli. Having dinner with that person in its reasonably ventilated (VR5) 7m2 kitchen, gives a one thousand times higher exposure, at any distance. The inhalation there is with airborne virions, deep into the lungs.
* Very high exposures result virtually only in ill-ventilated spaces with larger numbers of emitting persons per cubic meter and a long duration of stay. Preventive measures can focus on these high-risk situations. Short-term, such situations can be avoided or can be reduced by prevention measures, as by effective ventilation with outside air and with inside filtering devices.
* In a high concentration situation a 70% effective medical mask, would reduce intake to one third, with mostly a substantial risk of infection remaining. In low exposure situations masks, any, are not relevant. Similar holds for social distancing, fully ineffective in well-mixed contaminated spaces and in well ventilated and outside spaces.
* The focus on singing and speaking cannot be justified. Larger droplets and more of them may be exhaled but the primary production in the alveoli is not influenced. The number of virions produced will be diluted over more exhale volume and more fluid. The number of free virions exhaled will hardly be influenced.
* Hand washing and surface cleaning do not reduce COVID-19 risks as these infection routes are not relevant for SARS-CoV-2, in contrast to possibly the common cold and some bacterial infections.
* Medium-term and long-term measures are to focus on reducing high risk situations, with a prime role for improved ventilation and for equivalent filtering systems covering all airborne virions. Adequate air filtering systems are commercially available now already but require control and maintenance.
* High but perfectly feasible ventilation rates can reduce exposures to an infection risk of virtually zero. This is possible even in collective transport, as now already in short-haul modern airplanes. However, long duration transport, for example intercontinental air travelling, requires probably higher ventilation rates than VR17 now assumed enough for airplanes. That is no problem for modern airplanes and neither for other modern transport systems.
* In terms of public policy, the responsibility to create a non-infectious surrounding might be placed with those responsible for the spaces they manage, possibly with public certifications and checks on maintaining effective ventilation. In times of high infection rates, the few higher-risk spaces remaining might become more amenable to focused short term policy measures, replacing, or adapting, the current generic ones of lockdowns, curfews, social distancing, and non-medical masks. Situations of longer stay with ill persons, as in care situations, would be of prime importance. Ill-ventilated private homes would have to be approached with technical and behavioral advice now and with building regulations long term, as already present in Scandinavian countries.
* From a broader political philosophy perspective strategically different measures become available with better quantitative insight on how infections come about. The main alternative for forced vaccination, mask wearing, distance/density rules, travel restrictions and ultimately lock-downs is adequate ventilation. The responsibility to create a non-infectious surrounding might be placed with those responsible for the spaces they manage, possibly with public certifications and checks on maintaining effective ventilation. This is very similar to fire and accident prevention. The responsibility then resides with the persons and organizations who effectively control publicly accessible places. The responsibility for private homes is first with builders, aided by regulations, and in use with householders.

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## SI-0. List of Supporting Information Items

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2. CML, Leiden University: ruben.huele@xs4all.nl [↑](#footnote-ref-2)
3. Supporting information is for now available at https://www.scienceforstrategies.com/sars-covid. The survey table SI-0 there has links to all detailed subjects, SI-1 to SI-1.a. to SI-11.c. [↑](#footnote-ref-3)
4. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks [↑](#footnote-ref-4)
5. https://en.wikipedia.org/wiki/Industrial\_ecology [↑](#footnote-ref-5)