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Suppressing indoor pathogen transmission: A Technology Foresight study

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Abstract

Airborne transmission is considered one of the most common ways of transmitting respiratory viruses. The reach of airborne pathogens and persistence of aerosolized particles suspended in the air are a significant concern for the spread of pandemic and seasonal respiratory diseases. This is particularly relevant in indoor spaces where most respiratory infections occur. Controlling the transmission of airborne pathogens is therefore a cornerstone of public health efforts to manage and prevent the spread of infectious diseases, ensuring safety and health for individuals and communities. Technologies that allow such control are essential to address the challenge.

This report is the output of a comprehensive study which evaluates the potential of the current technology landscape for suppressing indoor airborne pathogen transmission. The analysis outlines two main technology groups: those for detecting airborne pathogens and those for decontaminating air and surfaces. It identifies several key technologies in each group, and assesses their maturity, impact, and potential priority for funding. It outlines the drivers, enablers, and barriers for the development and adoption of these technologies, providing insights into factors that may influence their future implementation. It also explores forward-looking perspectives with scenarios for future health crises and offers recommendations for policy and research to address the challenges and leverage the opportunities in the field of indoor air quality.

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Executive summary

Policy context

The COVID-19 pandemic elicited far-reaching actions at EU level to strengthen EU health crises prevention, preparedness and response planning in terms of surveillance capacity and medical countermeasures. It also increased awareness towards airborne pathogens, which present a major concern for public health, especially due to their transmission in indoor spaces and ability to spread globally. For these reasons, enhancing indoor air quality is important to safeguard public health, and to reduce the health impact and the economic costs associated with respiratory diseases. The importance of maintaining healthy indoor environments is recognised at EU level by various directives, even if currently in the EU there is no harmonised regulation addressing indoor air quality relating to biological agents across all Member States.

Key conclusions

Airborne pathogens are a broad class of infective agents that can be transmitted through the air. They are responsible for a variety of bacterial, viral, and fungal infections. Airborne pathogen transmission control can be obtained by technologies allowing their detection and decontamination. This report identifies the most promising technologies in these domains and discusses the drivers, enablers, and barriers that can impact their development and adoption. This study adopts a participatory approach, to draw conclusions through the consultation of expert communities in a Delphi survey and a foresight workshop. It adds a forward-looking perspective through tools such as the "Futures Triangle" and exploring critical uncertainties through scenario evolution.

The following key conclusions are drawn:

- No single technology provides an end-to-end solution for detecting and decontaminating airborne pathogens. For most use cases this is not applicable, but a combined approach is necessary if the goal is to automate decontamination based on immediate detection.
- Indoor air decontamination mostly relies on mature technologies like filtration/ventilation and UV radiation. However, energy consumption and the generation of harmful by-products, respectively, require improvement.
- Air pathogen detection technologies offer a variety of promising options that may benefit from R&D funding:
 - High sensitivity and data-rich methods like nucleic acid amplification and sequencing based techniques are at the basis of public health surveillance programmes for emerging and endemic diseases and hold potential for solutions were non-immediate response to detection are the focus.
 - A technological solution offering an air capturing system with an integrated and autonomous pathogen detection system is not available yet.
- Investment and funding are key to advancing the maturity and impact of various technologies. Defining a research agenda to guide investment priorities and technology development is a must.
- Air quality standards (in terms of pathogen load or similar parameters) need to be defined. A fully decontaminated indoor environment cannot be considered as a realistic standard (similar to a "sterile room") for different reasons (health-related, economic, energy consumption, etc.).
- A strategy for indoor air quality, with clear goals and targets taking into consideration the specificity of the type and function of buildings, should go hand in hand with the technology analysis, as the selection of technologies depends on the strategy and objectives for different types of spaces.
- Developing a comprehensive strategy for indoor air quality can only be achieved through cooperation between multisector communities, including healthcare workers, building architects, scientists, regulators and civil society representatives.
- Advancing towards EU-wide guidelines specifying markers or even concentration limits for indoor air quality, including such for airborne pathogens, would be welcome. Finding consensus regarding the type and levels of microorganisms in air requires further research.

Main findings

Detection technologies include air sampling on one side, and pathogen identification and quantification on the other side, while decontamination technologies range from techniques that remove pathogens from a given environment, like traditional filtration and ventilation, to others that inactivate them through full or partial destruction, like UV radiation or plasma-based inactivation.

The public health goal to be achieved and the physical environment in which the intervention is to take place must be pre-defined for effective communication between stakeholders and meaningful implementation. In some cases, detection and decontamination may be coupled, with detection systems giving feedback for the actuation of decontamination with the objective of decreasing, or eliminating, the health risk posed by aerosolised pathogens. In other use cases, both techniques may be decoupled: pathogen detection may be implemented for surveillance purposes or for the discovery of unknown pathogens, without any decontamination measures implemented. Similarly, decontamination interventions may not always require timely pathogen detection, depending on the specific circumstances.

The mapping and assessment of criteria for evaluating the potential of technologies reveals affordability, i.e. the cost of implementing the technology, and applicability, i.e. user friendliness, as the most important factors.

Technologies that are perceived to provide the most health prevention benefits in the short and medium term include filtration / ventilation, UV radiation, biosensors, direct identification through physico-chemical properties, nucleic acid amplification-based techniques and cyclonic and impactors aerosol samplers.

Once indoor air safety is defined in terms of pathogen concentrations or proxy markers, one technological gap to decrease hazards of the air we breathe indoors is a ready-to-use solution that can perform continuous, long-term or real-time detection of airborne pathogens. Progress in miniaturisation and automation is necessary to manufacture Point-of-Detection devices, i.e. devices that can be used on-site.

The availability of investment and funding is considered the most important factor for pushing developments in decontamination and detection technology fields. Regulatory guidance (European legislation, standards and guidelines), R&D&I efforts and the public perception of cost versus benefit were also perceived as highly relevant. Given that other domains with a health impact (outdoor air quality, water quality, food safety) are highly standardised and regulated, the same needs to be done for indoor air quality (IAQ). Education and public information are necessary to increase technology acceptance.

Related and future JRC work

In the field of detection, a point of attention is given to compatibility between sampling and identification technologies. JRC has prepared a local field study to collect and analyse airborne pathogens by different aerosol capture methods and pathogen detection techniques. The aim is to gain insights into defining the best combinations of air sampling and detection technologies for use cases with different time-to-results, sensitivity and/or molecular characterisation requirements.

Further work supporting technology development and implementation will address real-time *in situ* detection systems that provide continuous monitoring of indoor airborne pathogens. The use of artificial intelligence to recognise pathogen signatures in spectroscopy analyses will be explored as a continuation of exploratory research and proof-of-concept projects.

Quick guide

This work identifies several key technologies for airborne pathogen detection and decontamination, and assesses their maturity, impact, and potential priority for funding. It outlines the drivers, enablers, and barriers for the development and adoption of these technologies, providing insights into the factors that may influence their future implementation. Furthermore, the report offers recommendations for addressing the challenges and leveraging the opportunities in the field of indoor air quality.

A tailor-made technology foresight methodology was used in this exercise, combining quantitative methods such as a Delphi survey with qualitative methods such as scenarios. The purpose of this exercise was to integrate anticipatory insights into the overall research project.

Experts engaged in the exercise came from different types of organisations relevant for this topic, including: academia, research and technology organisations, private companies, business associations, non-governmental organisations, consultancies and public entities, providing therefore a multi-stakeholder perspective on the future-looking development of these technologies and innovations.

1 Introduction

Pollution of indoor and outdoor air has significant deleterious effects on human health and negatively affects social and economic growth. The quality of indoor air is a significant concern since Europeans spend up to 90% of their time inside buildings (Mitova, 2020). Indoor air can be significantly more polluted than outdoor air (Sekar, 2019) and indoor environments are more likely to harbour higher concentration of potentially health-threatening microorganisms. Consequently, the large majority of infections occurs indoors.

Indoor air quality has been the subject of several policy actions to regulate its cleanliness and control pollutants like chemicals, mould or small particles but it continues to impose a significant human health toll. Next to the health burden caused by the exposure to fine particulate matter, the transmission of respiratory viruses and other pathogens indoors is a core driver of the death and illness toll from poor indoor air quality. The vast health impact of the COVID-19 pandemic with more than 20 million lost lives is a clear example of this (Pifarré i Arolas, 2021). Still, the world remains increasingly vulnerable to future respiratory pandemics. Even outside a pandemic, the effects of seasonal respiratory diseases are immense, with ca. 30,000 deaths and economic costs of EUR 6 - 14 billion in the EU each year associated with seasonal influenza alone (Paget, 2022). With COVID-19 now endemic, these numbers are bound to increase or even multiply.

Airborne pathogens are a broad class of infective agents that can be transmitted through the air. These microorganisms are responsible for the transmission of a variety of bacterial, viral, and fungal infections. They include normal or endemic pathogens that are present in the air at a certain baseline concentration and can cause seasonal or regular outbreaks. These could be common respiratory viruses (rhinovirus, influenza) or bacteria such as *Streptococcus pneumonia* or *Haemophilus influenza*, but also special or pandemic-prone pathogens that are extraordinarily present in the air and can cause severe illness. The latter include viruses like SARS-CoV-2 and drug-resistant microorganisms (e.g. *Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter baumannii*, etc.) that cause problematic healthcare-acquired infections.

Airborne transmission is considered one of the main pathogen transmission routes. Its combination with other pathogen attributes like high infectivity, moderate virulence, and high mutation rate delivers the characteristics of the ideal infectious agent. Infectious airborne droplet nuclei can travel several meters inside a room. Exposure to aerosols generated by coughing and sneezing from infected individuals and contact with droplet-contaminated surfaces (plastic, metal, and clothing) have been widely viewed as the dominant modes of transmission of respiratory pathogens (Wang, 2021).

In public health, strategies used for airborne infection control in buildings and enclosed spaces range from reducing transmission and infection probability (e.g. by the use of personal protective equipment or introducing behavioural control measures), to preventing and cancelling out exposure (e.g. by the physical separation of pathogens and their hosts, or by physical removal of pathogens). The interventions differ in their levels of applicability versus efficacy, as well as in the economic and social implications (Morawska, 2020). The implementation of most of these interventions requires appropriate legislation, as well as a set of technologies and products readily available.

1.1 Indoor air quality legislative landscape

The legislative landscape with regard to general indoor air quality can be briefly summarised as follows. WHO has developed guidelines for indoor air quality, relating to a certain number of indoor pollutants, for which scientific evidence of human health effects was robust (Settimo, 2020). The compounds included in the watch list are mostly pollutants of chemical origin, but mention is also made of risks associated with the presence of humidity and airborne biological agents. At European level, indoor air quality is indirectly addressed in various directives and standards, such as the Energy Performance of Buildings Directive (Directive 2010/31/EU), the Eco-Design Directive (Directive 2009/125/EC), Workplace Directives (Directive 89/654/EEC) or the Ambient Air Quality Directive (Directive 2008/50/EC), the latter currently under revision. Pre-legislative initiatives from interest groups have multiplied over the years, together with targeted EU-funded research studies and published EN standards. In this context, it is worth mentioning the methods standardisation efforts carried out by bodies such as ISO and CEN, towards the development of a specific standard "EN ISO 16000: Indoor air". However there is still no integrated EU policy on indoor air quality. Some Member States, such as France, Portugal, Finland, Austria, Belgium, Germany, the Netherlands, and Lithuania, have started to adopt specific guidelines that in some cases are also enforced in their legislative acts (Settimo, 2020).

Looking at the case of waterborne disease control in developed countries, unsafe drinking water was historically a major source of infections until a scientific understanding of waterborne disease transmission, clean water standards and significant infrastructure investment enabled access to safe, non-contaminated drinking water. Targeted changes in indoor air regulations and guidelines, investment in improving our built environment and the adoption of innovative technologies could similarly play a role in reducing the risk and impact of pandemics and the burden of seasonal diseases.

1.2 Technology landscape

Since the COVID-19 outbreak, vast efforts have been carried out worldwide to develop effective countermeasures and reduce airborne pathogen transmission. However, this task is challenging as it is difficult to detect and monitor the concentration and presence of small pathogenic microorganisms. Several novel technological solutions that emerged under the time pressure of the spreading pandemic were implemented together with behavioural solutions. Some of these solutions, such as room ventilation and self-distancing, were initially based on previous knowledge on transmission routes of influenza and other coronaviruses. They helped to decrease transmission, however they showed limitations when it came to eradicating indoor airborne virus exposure and subsequent infections while nonetheless imposing significant social, mental health and economic costs. The challenge is therefore to develop new technological approaches that effectively control air transmission of pathogens, avoid infections and reduce the occurrence of novel pandemics.

In this framework, the present technology foresight aims at:

- identifying existing and emerging technologies for suppressing the spread of pathogens in the air,
- assessing the most promising among those technologies,
- highlighting relevant issues regarding research, development and adoption,
- exploring their potential use in several health crisis scenarios.

Two groups of technologies have been identified: namely, technologies for detecting airborne pathogens, and technologies for the decontamination of air and surfaces. The whole process has been carried out using a foresight approach to bring a future-looking perspective to the use of these technologies for suppressing the transmission of airborne pathogens in indoor environments. This study informs policies, including HERA's countermeasures toolbox, and supports public health initiatives to be better prepared for controlling the transmission of airborne pathogens in public spaces.

2 Methodology

2.1 Technology identification and assessment – Desk research

Peer-reviewed academic journal publications were considered as sources for the initial identification, clustering and assessment of technologies. The databases used to identify the studies were Scopus, PubMed and Medline. To capture the latest evolution of the field, the studies included in the meta-analysis were mainly published after the identification of COVID-19. The list of technologies resulting from this desk research was then assessed and completed in further steps of the foresight process, from expert input gathered through a survey and during a workshop.

- <u>Technologies for airborne pathogen detection</u>: This field was divided into two technological categories: air sampling and pathogen identification and quantification. The air sampling category included all the different technologies that collect airborne particles on different substrates or matrices. The matrix where aerosols have been captured can then be prepared for identification and quantification of the pathogens using technologies belonging to the second category. Not all the technologies of the first category are compatible with the technologies of the second category, and all have advantages and limitations. The list of technologies has been built by screening the scientific literature available in English using the above-mentioned databases and identifying the papers and reviews selected by the keywords "air sampling" or "pathogen detection", for each category.
- <u>Technologies for pathogen decontamination</u>: The search terms and keywords used were "airborne pathogen" AND "decontamination" OR "sterilization" OR "suppression" AND one of the names of the individual technologies described in section 3.3, for example: "UV Radiation" or "Plasma", etc. For harmonisation purposes, in order to define the current taxonomy of the different decontamination technologies, a systematic screening of the existing literature reviews on the topic was performed in parallel to the database search. The inclusion criteria of the search included: the identification of peerreviewed articles in English language included in the above-mentioned databases, and reporting about airborne pathogens (any kind) decontamination strategies independently of their technological readiness level. Studies ranged from clinical studies to preliminary experimental investigations. Patents, letters, editorials and commentaries were not included in the search. Initial screening was conducted via title and abstract analysis and only after preliminary acceptance was the full document reviewed further.

2.2 Technology foresight and future-looking approach

Foresight aims at anticipating future developments by exploring trends, emerging issues and the potential challenges and opportunities accompanying them. Through participatory methods and collective intelligence, it draws useful insights for strategic planning, policymaking and preparedness¹. Technology foresight, a subdiscipline, is a systematic exercise aimed specifically at examining the longer-term future of science, technology, and innovation in order to make better-informed policy decisions (Pietrobelli, 2016). It covers a broad range of technologies and analyses their applications and diffusion as well as the societal context of their development and use (Rader, 2008).

Recent events such as the COVID-19 pandemic have highlighted the critical need to be better prepared for health-related future events that could generate disruptions in most domains of our collective and individual lives. Foresight does not aim to predict if or when a new airborne pathogen might once again have such wide-ranging impact. However, it brings future-looking approaches to research and policymaking, surfacing and supporting discussions on potential actions to avoid it or to address it, if such event unfolds again. In this way, it should lead to greater organisational and societal resilience when such events do occur.

In the context of projects such as the subject of this report, technology foresight brings complementary insights to on-going research, by:

¹ Strategic foresight in the European Commission – retrieved from <u>https://commission.europa.eu/strategy-and-policy/strategic-planning/strategic-foresight_en</u>

- establishing a participatory process and convening internal and external expertise to better assess technologies and innovations through a multiplicity of perspectives;
- structuring a future-looking approach that surfaces drivers, enablers and barriers connected with future technology research, development and adoption.

The purpose of this foresight exercise was not to provide specific outputs that could be presented independently from the overall research project. In that sense, the reader will find the insights captured in the survey and the workshop in the following chapters. Even if the structure of the foresight activity inevitably presents some limitations and bias, participatory methods allowed the researchers to enlarge the scope of the exercise and facilitate discussions among experts that complement published sources.

2.3 Foresight process overview

The foresight exercise followed the initial research (see Section 2.1 and Figure 1) and aimed to bring a futurelooking perspective, coupled with external expertise, to this particular set of technologies. A tailor-made approach based on tried and tested foresight practices was designed for this project, combining a survey and an in-person workshop. The mix of these two methodologies provided quantitative and qualitative insights that are integrated across this report.



Figure 1. Schematic representation of the foresight steps (inside the box) in the overall research project.

2.3.1 Expert selection

Foresight exercises are often dependent on expertise from outside the organisations where they are developed. Criteria are needed to select and engage external experts, so that different perspectives are taken into account, and complement the insights of the in-house research.

The desk research stage identified two clusters of relevant technologies for indoor pathogen transmission - detection and decontamination. Inside the detection cluster, there were two sub-areas: sampling and identification/quantification technologies. Experts invited for the exercise either had a specialisation in one of these domains or brought an overarching perspective.

Additionally, a multi-stakeholder approach was defined. Experts engaged in the exercise came from different types of organisations relevant for this topic, including: academia, research and technology organisations, private companies, business associations, non-governmental organisations, consultancies and public entities.

2.3.2 Survey

A survey was developed and launched to deliver two main objectives:

- complement the desk research (mainly the technology identification and assessment),
- surface topics that should be discussed in more details during the subsequent workshop.

The survey partially adopted the Delphi method, where participants can observe other respondents' answers and engage in discussions. Through different iterations, this process aims to better inform respondents' choices and seek convergence among them. In this particular case, and due to time constraints, only one round of answers was undertaken. Nevertheless, respondents could observe beforehand and in real time the group's results, explain and even change their individual answers throughout the survey's three-week duration. As not all questions required an answer, the survey results below represent around 35-40 answers per question.

The survey was structured in three sections: the first dedicated to detection technologies, the second to decontamination technologies and a third to applying both types of technology to specific scenarios. As mentioned, the results of the survey are integrated in this report. However, from the methodological perspective the following outcomes can be highlighted:

- Additional technologies were proposed in the survey, complementing the list that was established during the desk research,
- Technologies were prioritised according to the assessment of maturity and potential impact
- Pre-defined criteria for identifying promising technologies were ranked. Additional criteria were proposed by participants for further consideration;
- Funding prioritisation for specific technologies was proposed;
- The scenario section identified technologies that were appropriate for a particular scenario, as well as those that could be applied in more than one context.

In order to translate the ranking of the different criteria into comparable numbers, a numerical analysis was done as follows:

1) To have a distribution of criteria centred on zero, each position in the ranking was given a weighting factor between N/2 and -N/2 in steps of 1, where N is the number of positions in the ranking. For example, for a list with 9 positions, the first position was assigned a weighting factor of 4.5, the second position a weighting factor of 3.5 and the ninth position a weighting factor of -4.5.

2) We counted the number of times that each criterion was ranked in each position (first, second, third,...) and multiplied it by the corresponding weighting factor. $K_{i,N}$ = number of times criterion *i* is counted in ranking position *N*.

3) We calculated a "priority indicator", f_i , for each criterion by adding the numbers obtained from multiplying the counts by the weighting factors. $f_i = N/2 * K_{i,1} + ... + -N/2 * K_{i,N}$

4) We then normalised the results to the highest and lowest values of the ranking number.

Using this mathematical calculation to compare the ranked factors, the most important factor has a normalised priority indicator equal to 1, the least important has a normalised priority indicator equal to -1. All the other factors are ranked in the range -1 to 1. If the normalised priority indicator of a factor is close to 0 it means that it is a neutral factor (not very important but also not negligible).

2.3.3 Participatory workshop

2.3.3.1 Overview

An in-person full day workshop took place on 10/11/2023 in the JRC building in Brussels. Around 30 experts participated in the event, assisted by a team of nine facilitators from HERA and the JRC.

After a presentation of the project objectives and the survey results, the workshop was structured in two main blocks:

- identification and assessment of technologies and contextual factors (morning);
- exploring scenarios and factors of uncertainty (afternoon).

For both blocks, participants were organised in groups. In the first block, two groups examined detection and two decontamination technologies. In the second block, new groups were formed and each examined one of the three scenarios developed for this exercise. In the morning, participants were allocated according to their expertise on specific technologies, complemented by participants with an overall perspective (e.g. with expertise on public health policy, building design, etc.). In the afternoon, participants were re-distributed to ensure different perspectives and know-how in both detection and decontamination were present in each group.

After each block (described in more detail in sections 2.3.3.2 and 2.3.3.3) each group debriefed the plenary on the main findings. This allowed all participants to gain an overview of the results and triggered further discussions and conclusions.

2.3.3.2 Identification and assessment of technologies and contextual factors

The identification and assessment of technologies exercise was composed of three steps:

1. Identifying technologies – allowed participants to become familiar with the technologies identified through the desk research, prioritise specific ones and add missing technologies and innovations.

- 2. Assessing technologies All technologies considered in the previous step were assessed in a twodimensional matrix:
 - Readiness/maturity ranging from Research (TRL 1-3) through Development (TRL 4-6) to Deployment (TRL 7-9).
 - Impact ranging from low (incremental) through medium to high (disruptive).
- 3. Technologies were then clustered in four groups: High Impact and High Maturity (top technologies of the present); High Impact and Medium/High Maturity (top technologies of the future); Medium/High Impact and Medium/High Maturity ("runner-up" technologies); and others.

Contextual factors – This exercise adapted the Futures Triangle framework (Inayatullah, 2023), where relevant drivers², enablers³ and barriers⁴ for technology development and uptake were proposed.

2.3.3.3 Exploring scenarios and factors of uncertainty

This block was composed of two steps:

- 1. Assessing technologies through the prism of one of three different scenarios, participants assessed which technologies were the most appropriate to address both detection and decontamination requirements in each context.
- 2. Scenario development this step involved:
 - First identifying the most relevant drivers that could shape those scenarios and assessing generally their impact and uncertainty.
 - Second understanding the impact of a specific critical uncertainty⁵ in the mid to long term development of this scenario.
 - Third and final assessing if the most appropriate technology(-ies) would still be fit to address the future scenario context, or if other technologies would be preferable.

2.3.3.4 Final remarks

To conclude the workshop, participants were invited to propose actions to be considered by the European Commission and other European and non-European institutions, to foster the development and adoption of technologies used in indoor pathogen detection and decontamination. This allowed the collection of additional insights, relevant for both the assessment of technologies, and most of all for further policy initiatives such as regulation, standardisation, communication and funding.

² Topics that pull us into the future or that shape a different future, such as trends or even megatrends (ongoing or foreseen developments that will impact society)

³ Topics that push us in the present, and present themselves as opportunities, such as supporting policies or funding.

 ⁴ Topics that hold us back and that are a challenge for the development of technologies, such as lack of resources or restrictive policies.
 ⁵ In scenario planning, a critical uncertainty is a driver with high impact and high uncertainty. This driver has at least two distinct and

plausible future developments that could influence significantly the transformation of the scenario. Normally two critical uncertainties are combined to create a set of four scenarios. In this exercise, one critical uncertainty was used to simply introduce disruptive transformation in a present world context.

3 Mapping and assessment criteria of technologies for suppressing airborne pathogen transmission

3.1 Clustering of technologies and selection of performance parameters

Availability of technologies to suppress the transmission of airborne pathogens is crucial for reducing the spread of infectious diseases. To mitigate the effects of such transmission in indoor environments, advanced technologies in two domains have to be considered:

- Detection technologies: promising technologies should combine effective approaches for the capture of pathogens, their processing for further analyses and their identification.
- Decontamination technologies: existing and emerging technologies are being developed for effective removal, e.g. by filtration or ventilation, or for the inactivation of pathogens, e.g. by UV or plasma decontamination.

In some cases, one domain is intrinsically linked to the other. Some situations might require intensive decontamination, e.g. during a pandemic or in hospital settings. However, ideally, in the perspective of smart interventions, decontamination would be proportionate to a need evidenced by the detection of pathogens. Except for specific places (for instance operating surgery rooms) the goal should not be achieving an ever-sterile environment. Living in a sterile environment, without being naturally exposed to endemic pathogens, could also be a health threat, as shown by different researchers and hygiene experts for many years (Bloomfield, 2006). Moreover, decontamination measures are generally energy-consuming and so should be deployed wisely on a need basis.

Current detection and decontamination technologies present different readiness levels and a heterogeneous set of strengths and weaknesses. Several performance parameters that may affect their potential impact were identified through the desk research, survey and workshop. They are listed in Figure 2. The perceived importance of those criteria for the further development of the technology domain was assessed by participants in the survey and the workshop.



Figure 2. Performance parameters to be considered for technology development.

Besides parameters intrinsically related to the technical capabilities of the technology, their practical implementation should also consider non-technological factors, such as:

• the location and building type where they would be applied, taking into consideration the existing indoor air management infrastructure when implemented,

- the socio-economic development of the country where a specific technology should be deployed,
- the environmental impact of large-scale implementation of specific decontamination solutions,
- the cost-benefit analysis of long-term footprint versus immediate public health benefits.

The choice to incentivise a particular technological solution will depend on the requirements of specific use-case scenarios.

3.2 Technologies for airborne pathogen detection

The detection of airborne pathogens indoors is based on two distinct but interconnected technology fields: sampling of the aerosol phase to collect airborne particles for further analyses; and identification and quantification of the pathogens present in the collected sample. The compatibility of sampling techniques with the subsequent identification method depends on the capacity to maintain the structural integrity of the infectious agent's biological activity throughout the process (see Figure 3).



Figure 3. Airborne pathogen detection techniques for aerosol sampling and for identification and quantification of pathogens, together with interconnecting lines indicating compatibility between the two fields of detection technologies

In the area of detection, nine main groups of techniques have been identified, as described in Table 1:

- Three groups correspond to air sampling technologies: Filters, cyclonic and impactor aerosol samplers and condensation aerosol samplers;
- five groups of identification and quantification technologies: cell culture, nucleic acid amplification (NAA)-based techniques, direct identification through physico-chemical properties, biosensors and sequencing technologies;
- one group cross-cutting across sampling and quantification: particle counters (they can perform sample collection as well as count the number of particles, though without identifying the type of particle).

More detailed information about each group has been collected in technology fiches, including bibliographic references and an initial assessment of their maturity, performance parameters and potential bottlenecks. The fiches are available in Annex 1.

High throughput, cost effectiveness, short sampling-to-result times, and multiplexing (large spectrum) pathogen detection are mandatory characteristics for devices aiming at monitoring pathogens in air. Air sampling techniques have traditionally been developed for air quality monitoring purposes. Air sampling includes very efficient technologies but can induce in some cases the complete denaturation of the pathogen particles' structure, making the identification and quantification possible only by methods that do not require intact functional pathogens or pathogen fragments. Such methods are usually based on the amplification and recognition of nucleic acids sequences, but they are intrinsically poorly compatible with high-throughput and real-time detection. In this perspective, labelled or label-free detection of pathogens using bio-functionalized chips (using different signal transduction principles) are very promising as they enable real-time detection of pathogens, minimizing sample preparation and enabling multiplexing. They are also compatible with the most advanced air sampling techniques.

| DETECTION TECHNOLOGIES - SAMPLING | | |
|--|---|--|
| Particle counters | Particle counters can be used for sampling purposes but can also provide information about size distribution and number distribution of collected particles. The increase or decrease of pathogen concentration in sampled air could be related to the size distribution of collected particles as an indicator. Nevertheless, the particle counting is non-specific and does not provide information on the pathogen nature. | |
| Filters | Filtration systems are very effective at capturing particles from air samples, including pathogens. Similar to the cyclonic and impactor samplers, filtration systems are relatively destructive and are generally coupled to identification and quantification techniques that can recognise pathogen debris or denatured proteins. | |
| | These sampling technologies enable the collection of aerosol | |
| Cyclonic and impactor aerosol samplers | particles on dry or wet solid surfaces. They are characterized by high speed of collection, large volume sampling and high collection efficiency for particles larger than 500 nm, but are not optimized for detection of single viral particles. They generally alter the structure of the collected biological agents. Thus, the downstream identification and quantification should be performed with techniques able to identify and/or quantify pathogen fragments, such as techniques based on amplification of nucleic acids, or by the very sensitive culture-based pathogen detection technique. | |
| Condensation aerosol samplers | This type of aerosol sampler is based on the condensation of a water droplet around the collected particles, enabling the gentle landing of the particles on a surface or in a liquid phase. Condensation aerosol samplers generally have a slower throughput than other air sampling methods, but have the advantage of keeping the integrity of the collected biological agents and of having a very high collection efficiency for small particles (< 500 nm). In principle these non- destructive methods are compatible with the majority of identification and quantification techniques. | |

Table 1. Main groups of airborne pathogen detection technologies

| DETECTION TECHNOLOGIES - IDENTIFICATION & QUANTIFICATION | | |
|---|--|--|
| Cell cultures | Culturing of pathogens is a well-established technique that provides information about the whole aerosol sample. However, it requires that the pathogens stay viable during the sampling process. This method is also highly time-consuming (up to one week), not all pathogens can be cultured and the risk of sample contamination and oversampling can make counting difficult and thus less reliable. | |
| Nucleic acid amplification (NAA) -based techniques | These techniques are highly sensitive and specific but also rather expensive and require trained personnel. Techniques based on the amplification of nucleic acids, such as PCR or LAMP detection, usually require that the pathogens to detect have previously been identified and their genomic sequences are known. | |
| Direct identification through physico-chemical properties | A series of analytical techniques can provide a direct identification of pathogens through their physico-chemical properties. These techniques include Raman spectroscopy, FT-IR spectroscopy or mass spectrometry. They are able to identify pathogens with high specificity, but require the pooling of a certain number of pathogens to obtain a good signal-to-noise ratio. Other techniques based on light scattering (e.g. based on the measurement of the refractive index of the particles) can also distinguish pathogen particles from other airborne particles with single particle resolution, but they lack specificity. Direct identification methods have been coupled to artificial intelligence to enhance the identification capabilities and distinguish spectra from different pathogen families. | |
| Biosensors | Biosensors include a large group of techniques based on the recognition of a region of the pathogen (which should be intact) through its affinity for a bioreceptor (antibody, cell receptor, aptamer, nucleic acid, peptide, etc). The biorecognition of the pathogen is then transduced in a measurable signal. The possible signals are optical, electrical, electrochemical, etc. The lateral-flow immunoassay, a paper-based test widely used for human diagnostics is one of the most developed examples of this technology. Biosensors can be low cost, specific and sensitive, but compared to NAA-based techniques remain less reliable. Biosensors are compatible with multiplexing and multi-target detection. | |
| Sequencing technologies | Sequencing methods, such as Next Generation Sequencing (NGS) and protein sequencing methods, can provide detailed information about the genetic and proteomic composition of airborne samples. NGS has allowed the rapid sequencing of DNA or RNA from airborne samples and can be used to identify and characterise the presence of different types of pathogens, including bacteria, viruses and fungi. Protein sequencing technologies determine the amino acid sequence of proteins present in airborne samples, for example by using mass spectrometry. Despite the amount of information that NGS techniques deliver, the methods are generally time consuming, costly and difficult to implement in real-time measurements. | |

3.3 Technologies for pathogen air decontamination

Pathogen air decontamination technologies are useful to address infection control interventions based on the physical elimination of pathogens and/or pathogen separation from the potential host. Our study, comprising literature search and direct input by experts, identified nine main groups of existing and emerging techniques, as described in Table 2. As in the case of detection, more detailed information about each group con be found in the technology fiches in Annex 1.

Ventilation and filtration technologies are worth a particular mention given that some kind of ventilation strategy, incorporating filtration or not, is included by-design in practically every building, i.e. most buildings are constructed with a deliberate consideration for the ventilation needs of occupants. It can range from the passive management of airflows through different building parts via openings and room connections to the advanced computer-controlled active ventilation management systems of modern office buildings. Ventilation is one of the most important means to control cross-infection by exchanging indoor with outdoor air and removing virus-laden exhaled aerosols, humidity and heat. Several studies focus on how modifications to ventilation flow rate, direction and pattern can improve the efficiency of decontaminating indoor spaces. Due to the fact that some kind of ventilation system already exists in most buildings, ventilation can be regarded as a "horizontal category" to be considered for potential improvement in parallel with other technologies.

Table 2. Main groups of pathogen air decontamination technologies

| DECONTAMINATION TECHNOLOGIES | | |
|------------------------------|--|--|
| Filtration / Ventilation | Filtration is a commonly used technology to physically separate pathogens from the atmosphere using different filters (e.g. activated carbon fibre, polypropylene fibre filters). The filtration performance depends on filter material properties and airflow characteristics. The particle size collected can be controlled by varying the air velocity, which is typically in the range of hundreds of litres per minute. Filters generally present high collection efficiencies (>95%) for particles > 0.5 μ m in diameter but need to be regularly replaced. Advances in ventilation technologies, such as the use of laminar flows, allow efficient air handling by avoiding issues with secondary contamination due to recirculation of pathogens captured on filters. | |
| UV UV radiation | UV radiation is a well-established method to inactivate pathogens and sterilise objects and surfaces. Recently, UV-based processes are emerging for the degradation of airborne microorganisms. Current research is focused on the effects of different UV radiation ranges (UV-A, UV-B, UV-C) on microorganisms in relation with intensity and exposure time. At a wavelength of 254 nm UV-C radiation shows maximal effectiveness for disrupting cellular replication by damaging microbial DNA/RNA and can also deteriorate membrane proteins. However, it is dangerous to human skin and eyes and should be directed toward the 'upper room' where it can disinfect without harming humans. Far UV at shorter wavelengths, typically 222 nm, seems both effective at killing microorganisms and safe for human exposure, but creates air pollution due to the generation of ozone. | |
| Electrostatic capture | Electrostatic capture technology is primarily used for the collection of bio-aerosols and removal of fine particle emissions. Using electrostatic technology, the airborne microorganisms and particles are electrically charged and subjected to a strong electric field, causing deposition on the collection substrate. This technology has been widely developed for airborne particulate matter removal and then modified as aerosol sampler for bio-aerosol collection. Electrostatic aerosol samplers can be integrated into HVAC filtration systems and can be operated without interrupting building use. | |

| Thermal inactivation | Thermal treatments are currently used in various methods (moist and dry heat) to control microorganisms in air. The moist heat method is operated using steam under pressure, whereas dry heat is operated only under high-temperature exposure. Thermal treatment of indoor air has been considered a safe and effective method. Inactivation performance is very high: > 99% of bio-aerosols can be inactivated in about 0.2 s at 350 °C using high-temperature bursts on airborne microorganisms in a continuous flow environment. |
|--|--|
| Plasma-based inactivation (including ozone) | Plasma discharges at atmospheric pressure or in a vacuum can generate locally reactive chemical species such as electrons, UV photons, ions, neutral molecules (reactive oxygen species, reactive nitrogen oxide species, nitric oxide synthase) and atoms. In cases where bio-aerosols come into contact with plasma bulk in the discharging area, the produced reactive chemical species directly interact with airborne microorganisms, damaging cell membranes, DNA, and proteins. In a similar way, ozone, a strong oxidising gas, has been used to inactivate airborne pathogens. |
| Chemical aerosolisation | Chemical aerosoliation is a common technology already used for the disinfection of different types of indoor environments. Aerosolisation with concentrated NaOCI solution (10%) was used as a precautionary step during COVID-19. During disinfection with NaOCI, several reactive oxidants (such as OH ⁺ , O ₃ and Cl ⁻) are produced, and have biocidal effect on airborne microorganisms. Different chemical agents have been developed, targeting different types of pathogens. Research primarily focuses on determining the optimal dosage of disinfectants during disinfection procedures. An advanced aerosolisation method based on dynamic fog aggregation exploits a fogging system to distribute disinfectant particles evenly. |
| Microwaves radiation | Microwaves radiation is a method of inactivation based on the propagation of electromagnetic waves in the area to be sanitised. It works on the principle that the structure-resonant energy transfer effect from electromagnetic waves to confined acoustic vibrations in viruses could result in the fracture of the viral membrane through opposite core-shell oscillations. |
| Lysozyme-based bactericides | Lysozyme is an enzyme found in different biological fluids and tissues, which can also be produced synthetically. Lysozyme antimicrobial properties can be used airborne or attached to a filtering surface. Lysozymes carry the ability to physically damage cell membranes. Its activity is quite specific for different bacterial species, so a specific lysozyme can affect its target bacteria but not any other species. Moreover, lysozyme activity is influenced by environmental conditions and this affects the efficacy level of the process. |
| Photocatalytic Oxidation | Photocatalytic Oxidation is a photo-electrochemical effect produced when light (e.g. UV photons) interacts with a semiconducting surface (e.g. TiO ₂), often in presence of photocatalyst material (e.g. noble metals) that lowers the chemical reaction energy barrier. Absorption of light leads to the creation of photo-excited charge carriers that migrate towards the surface of the photoactive material and create different reactive oxygen species. Reactive oxygen species have been proven to disrupt cellular membranes and/or inhibit microorganisms' biochemical reactions. |

3.4 Assessment of performance evaluation criteria

Several performance parameters that may affect the potential impact of technologies were ranked according to their perceived importance by respondents to the survey. The analysis of the ranking is detailed in section 2.3.2.

For both decontamination and detection technologies, affordability was ranked as the most important characteristic. Applicability was also identified as highly important to look at the potential of detection techniques, and ranked in second place, very close to affordability. Sensitivity and broad spectrum (the ability to be used for different types of pathogens) were also considered important but to a much lesser extent, while energy consumption was considered as low importance. For decontamination technologies, affordability was followed by efficacy and applicability as important factors affecting their potential, while treatment capacity was considered not important, neither was energy consumption, even if it is closely related to affordability for some technologies, including for ventilation the most mature and most widely implemented. Even if some factors are interconnected, they might be perceived differently. Operational costs related with energy efficiency in some situations are not perceived as important as up-front investment costs. Details of the ranking can be seen in Figure 4.



Figure 4. Perceived importance of performance criteria for the evaluation of promising detection and decontamination technologies. Data obtained from 40 responses submitted to the survey. Normalisation of all responses from -1 to 1, where 1 = important, 0 = neutral and -1 = not important

4 Forward-looking perspective of airborne pathogen transmission suppression technologies

4.1 Assessment of maturity and impact

The survey asked participants to score technologies individually from 1 to 5 in readiness level and potential impact, where 1 meant low maturity or impact, and 5 was high maturity or impact. Figure 5 shows the mean values of the scores of maturity plotted against impact. Individual responses are presented in Annex 2. The survey results showed filters and NAA-based techniques as the most mature and impactful amongst detection techniques, and filtration / ventilation and UV radiation as the highest in both aspects for decontamination technologies. The technologies were also assessed collectively by groups of experts during the workshop and positioned in an Impact vs. Maturity chart. Both exercises evidenced similar positioning of technologies, though some divergence emerged (e.g. different views on the potential of plasma-based inactivation, as seen when comparing survey results in Figure 5 and workshop discussion in Table 3 below). The combined results allowed the technologies to be clustered in four groups according to the intersection between their perceived maturity and perceived impact (Table 3):

- Top technologies of the present, that present a high maturity and a high impact. These are typically already available in the market, and represent a ready-to-use solution to address present challenges,
- Top technologies of the future, that present a high level of impact, but that are not yet available in the market and/or mature enough to be deployed at scale,
- "Runner-**up**" **technologies of the present**, that combine medium to high maturity with medium to high impact,
- Other technologies, that present several levels of maturity but their impact is perceived as low, or with low maturity and medium impact.



Figure 5. Mean value and standard deviation of maturity and impact scores plotted against each other. Data collected from input of experts to a survey.

Table 3. Clustering of technologies according their perceived levels of maturity and impact resulting from the workshop discussion.

| | DETI | | | |
|---|---|--|--|--|
| | air Sampling | identification & Quantification | DECONTAMINATION | |
| top technologies of the present | filters | for nucleic acid amplification | filtration / ventilation UV radiation (upper room UV-C at 254 nm) | |
| top technologies of the future | aerosol samplers (cyclonic, impactor and con- densation) | biosensors direct identification | plasma-based inactivation | |
| "runner-up" technologies of the present | filters, to capture small molecules ~100 nm | sequencing technologies direct identi- fication, Al-assisted nucleic acid amplification, Point-of-care PCR | microwaves radiation UV radiation (far UV-C at 220-230 nm) electrostatic capture | |
| other technologies | • particle counters | cell culture | J / /thermal activationImage: Chemical aerosolizationImage: Chemical aerosolization | |

4.2 Drivers, enablers and barriers for development and adoption: the "triangle of the future"

Several factors that may affect the development and adoption of pathogen transmission suppression technologies were identified, namely:

- market interest,
- availability of raw materials,
- perception of usefulness,
- existence of appropriate education and skilled workforce,
- the existence of patents,
- R&D&I efforts,
- regulatory guidance,

- investment and funding,
- perception of cost/benefit ratio

The importance of those factors was assessed individually by experts through responses to the survey. The ranking was normalised between -1 and 1, where -1 was considered as low importance and 1 as high, as explained in section 2.3.2. The results evidenced Investment and Funding as the most important factor for both detection and decontamination technological fields (see Figure 6). R&D&I efforts and the perception of cost versus benefit were also considered highly relevant in both fields, while regulatory guidance appeared in second position of importance for the development and adoption of decontamination technologies.

The above factors influencing technology development and adoption could act as drivers, enablers or barriers:

- Drivers are factors that may pull technologies into the future,
- Enablers are factors that may represent opportunities to facilitate the use of technologies in the present,
- Barriers are factors that could halt or delay the development and adoption of technologies.

In the workshop, expert group discussions analysed potential drivers, enablers and barriers for the top technologies of the present and of the future. The insights listed in Table 4 were aggregated by each of the "triangle vertices" of the "Futures Triangle" including all groups' contributions. There was an effort to distinguish between general comments and specific comments for either detection or decontamination, to eliminate redundancies and duplications and to separate the insights applicable to most technologies from the ones related to specific technologies.



Figure 6. Perceived importance of development and adoption factors that may influence detection and decontamination technologies (1= important, 0 = neutral and -1 = not important)

Table 4. Drivers, enablers and barriers for the development and adoption of top technologies of the present and the future in the fields of detection of airborne pathogens and air pathogen decontamination.

| ALL TECHNOLOGIES | R&D&I funding Regulatory guidance in terms of air quality standards, air quality policy, ISO standards and harmonisation of methods and measurements Public education about airborne pathogen transmission Building codes and design of spaces (to facilitate ventilation) Creation of a centralised technical body that takes care of recommendations for Member States to follow Health-based metrics of the impact of technologies Tools for in-situ monitoring | | |
|------------------|--|---|--|
| DETECTION | All detection Direct identification with con- densation aerosol sampling | Unified testing protocols Advantage of prevention over spreading screening NGS for surveillance at airports (to pick up emerging pathogens) | |
| DECONTAMINATION | All decontamination Far UV | Existence of harmonised testing methods Public education Adequate electrification Costs of installation and use | |
| | ENABI | _ERS | |
| ALL TECHNOLOGIES | Skilled workforce for use and maintenance of technologies Modelling indoor air quality Existence of protocols on what to do once a pathogen is detected Presence of COVID-19 and seasonal respiratory infections | | |
| DETECTION | All detection | Internet of Things signalling Passive technologies with low maintenance. Make disposable parts small and easy to replace. Acceptance of testing. De-activation of samples before the lab stage. | |
| | Direct identification with con- densation aerosol sampling | Connected devices Affordability by pulling samples Artificial intelligence for automated data processing | |
| DECONTAMINATION | All decontamination | Architecture enhancing natural ventilation Regulation forcing to apply a certain technology Regulation of energy efficiency in new buildings moving from prescriptive to performance regulation | |
| | Far UV | Easiness of implementation, suitable for ex- isting and/or old buildings Immediate decontamination effect | |

| ALL TECHNOLOGIES | Absence of certification of the environmental dimension of medical devices Low public awareness of air quality Multidisciplinarity of the issue to tackle; it requires integration and trade-offs between different actors Lack of predictive models for infection and transmission of pathogens No infrastructure in LMIC to deploy technologies Confusion between the concepts of efficiency and effectiveness Lack of funding | | |
|------------------|--|--|--|
| DETECTION | All detection Direct identification with condensation aerosol sampling | Lack of EU fast track for emergency authorisation Unsafe handling of samples Lack of definition of what is and what is not a diagnostic Device price Automatic integration of sampling and identification Need to link with industry to develop devices. Public information, e.g. no interest due to bad understanding of the problem Availability of quality testing for the whole detection procedure | |
| DECONTAMINATION | All decontamination | Existing infrastructure, e.g. old buildings without ventilation ducts Habits and behavioural biases Indoor Environmental Quality, including noise and thermal comfort | |
| | Far UV | Safety, e.g. by-products generated by far UV radiation systems Public acceptance Difficult to develop | |

4.3 Technologies to be considered for funding

Experts were given the possibility of selecting which technologies would provide most benefits if properly funded. Participants could indicate up to three technologies of all technologies included in the survey. According to the number of participants that mentioned a certain technology as being among the three most worthy of funding (see Figure 7), two priority groups emerged:

Priority 1 - Technologies mentioned by 35 % - 45 % of participants:

- Filtration / ventilation
- UV radiation
- Biosensors
- Direct identification though physico-chemical properties

Priority 2 - Technologies mentioned by 15 % - 20 % of participants:

- NAA-based techniques
- Cyclonic and impactors aerosol samplers

During the workshop, also genomic sequencing technologies, specifically Next Generation Sequencing, were considered as high priority, comparable to the Priority 1 group.



Most worthy of consideration for funding (Nr. of mentions in 1st, 2nd or 3rd position)

Figure 7. Technologies mentioned more often in the survey as most worthy to be considered for funding

5 Technology choices for possible future health crises scenarios

Scenario planning and the use of scenarios are not designed to predict a specific future outcome. Instead, their purpose, as outlined in the definition, is to transform thought processes, refine decision-making abilities, boost human learning, and elevate organisational performance. Although each scenario presents a vision of what might happen, employing a variety of scenarios enables the exploration of numerous possible futures pertinent to the project, with each scenario offering predictions rooted in thorough analysis. The goal is to foster a broad range of thinking about the potential developments in the future (Chermack, 2004).

Scenario-planning activities focus on pinpointing major uncertainties and envisioning various combinations that could lead to outcomes significantly divergent from what simple extrapolation of current trends might indicate (Scoblic and Tetlock, 2020).

Three possible scenarios were proposed to participants to the survey and/or workshop. In each of them, possible technological solutions were assessed for the scenario as outlined (during the survey and workshop), as well as for the scenario evolving within the constraints of critically uncertain drivers of change chosen among relevant drivers that have the potential of transforming the scenario (during the workshop). These scenarios do not represent an expected or desired future but are artificially created to test different extremes to challenge the technologies implemented in these hypothetical scenarios.

5.1 Scenario A: Tuberculosis endemic in low- and middle-income countries suffering from violent conflict/famine

Description:

In this scenario, improved vaccines for tuberculosis are available in high-income countries (HICs) and most middle-income countries. Existing armed conflicts and instability have increased due to the pressures of climate change, leaving millions displaced. In these populations, vaccinations have been interrupted by large migration movements which placed many in refugee camps and in crowded, unsanitary conditions. While resistance to antibiotics has increased locally, medical countermeasures (MCMs) are not readily available, and disinformation causes significant hesitancy against medicinal products supplied by aid workers.

Use cases:

- Travel and transport hubs in all countries.
- Healthcare settings/schools/places of worship in low- and middle-income countries (LMICs) hosting refugees.

Drivers of change:

(Developments with the potential to transform the scenario)

- Technological/resource access,
- Compliance/public trust,
- Availability/ease of MCM R&D,
- Waste disposal possibilities
- Cost of decontamination
- Reusability of filters
- Quality of treatments
- Education and information
- Presence of trust
- Public acceptance, challenged by mis-, dis-information
- European border openness
- Energy use
- Infrastructure & design
- Government policy to fight against tuberculosis
- Supply chain of consumables
- Skills
- Antibiotics availability

Critical uncertainties:

(Drivers that bear high impact and high uncertainty of developments)

1. Workforce availability

Development 1 – Workforce - Health Care Workers – No restrictions Development 2 – Workforce - Health Care Workers – Restrictions

2. Energy cost

Development 1 – High energy cost Development 2 – Low energy cost

Technological solutions:

(Technology more adequate for this scenario and for addressing the impacts of the critical uncertainties)

• Detection

The group did not select any air sampling technology because detection in the air was not considered important by participants. In LMICs, tuberculosis detection in air was seen as not relevant, though it was for decontamination. This was because transmission requires close contact with infected people for long time periods. Therefore, an efficient strategy would be to test only symptomatic people and isolate them, rather than focussing on detecting the pathogen in air. Detection is nonetheless relevant as a diagnostic test. NAA-based techniques were the preferred option, in particular to identify cases of multi-drug-resistant tuberculosis that are more difficult to treat. Other methods such as direct identification and biosensors would be good for real time monitoring, but they are still under development.

Main technology: NAA-based techniques

Other relevant technologies: Direct identification through physico-chemical properties and Biosensors

o Critical uncertainty 1. Workforce availability

Technology still relevant in both developments, whether workforce availability is restricted or not.

• Critical uncertainty 2. Energy costs:

The technology is still relevant for both developments, high and low energy prices. However, there was not 100% consensus among the group regarding the development in the case of high energy costs.

• Decontamination

The basic first line decontamination procedure would be based on ventilation, with or without filtration. Participants suggested that in healthcare settings where having devices might be difficult, the best would be natural ventilation. In transport hubs the group chose filtration. UV radiation was also proposed as alternative, however there were concerns from part of the group about the extent of applicability in that context, given that it is not even fully available yet in high-income countries.

Main technology: Filtration / ventilation

Other relevant decontamination technologies: UV radiation

- Critical uncertainty 1. Workforce availability
 - Development 1 no restrictions
 - Tents with filters, powered by solar panels better arrangement to limit transmission.
 - Good design of devices (easy to use, not requiring high skills to be used effectively).
 - Development 2 restrictions
 - Filters have to do most of the work.
 - Importance of isolation.
 - Not considering design.

- Critical uncertainty 2. Energy costs
 - Development 1 high costs
 - Favour natural and mechanical ventilation over UV radiation.
 - Aerosolisation for decontamination could also be a low energy alternative to ventilation.
 - Development 2 low costs
 - Both technologies are relevant.

5.2 Scenario B: Influenza pandemic threat with novel hemagglutinin

Description:

The pandemic of highly pathogenic avian influenza in birds continues and multiple mammalian clusters are being described across the globe in species which can act as mixing vessels for reassortment. Due to the large number of reservoirs and no cases of human-to-human transmission, active surveillance remains challenging and expensive over the years in which there is no abating of signals from animals. Eventually, several spillover events into humans lead to large-scale epidemics of distinct influenza strains that are highly transmissible and virulent.

Use cases:

- Airports, transport hubs, hotspots for surveillance.
- Public buildings/schools/healthcare settings in areas where human-to-human transmission has been established.

Drivers of change:

(Developments with the potential to transform the scenario)

- Technological/resource access
- Compliance/public trust
- Availability/ease of MCM R&D
- Wealth
- Demographic change
- Building sustainability policy
- Urbanisation and intensive farming
- Semiconductor components availability
- Temperature
- Litigation and insurance
- Power grid capacity
- Increased capacities of digital tools

<u>Critical uncertainty:</u>

(Driver that bear high impact and high uncertainty of developments)

Regulatory Policy

Development 1 – Science-based policy. Strict and clear policy enforcement. Development 2 – Regulatory capture from a single technology. No regulation / de-regulation.

Technological solutions:

(Technology more adequate for this scenario and impacts of the developments of the critical uncertainties)

• Detection

The group selected more than one technology for the scenario. The group decided that there was one sampling technology favoured, namely large volume aerosol samplers, and since this was considered a high R&D and resources scenario, the group agreed to combine NAA and biosensors for identification and quantification.

Sampling technology: Cyclonic and impactor aerosol samplers

Identification & quantification technology: <u>NAA-based techniques</u> and <u>Biosensors</u>

- Development 1: regulatory enforcement
 - Technologies still relevant, favoured by mass production and reduced price.
- Development 2 de-regulation
 - Technologies still relevant, with the caveat of less innovation.
- Decontamination

The group agreed on ventilation as an overall favourable technology but could not find consensus on other lower TRL technologies with promising impact.

Main technology: Filtration/ventilation (localised filtration)

Other relevant technologies: <u>Microwaves radiation</u>, <u>UV radiation</u> (upper room, far-UV), <u>Chemical</u> <u>aerosolisation</u> (dynamic aggregation)

- Development 1 regulatory enforcement
 - Main technology is still relevant, favoured with more data availability and increased efficacy.
- Development 2 de-regulation
 - More fragmentation in the choice and implementation of different decontamination technologies, more limited deployment of decontamination technologies.

5.3 Scenario C: Respiratory disease burden throughout the year

Description:

In 2035, efforts to develop anti-infectives against common and emerging respiratory viruses manage to maintain the functioning of the healthcare system in high-income countries while low- and middle-income countries struggle year-round due to lack of healthcare workers: COVID-19 waves are experienced throughout the year and the tripledemic in winter continues. Vaccine hesitancy in the elderly is high as a generation age that perceived the response to COVID-19 to be motivated by the interests of big pharma. At the same time, innovation to improve the efficacy of vaccines in the elderly did not deliver significant impacts in mortality and morbidity reduction.

Use cases:

- Care homes & hospitals during peak respiratory season in HICs/LMICs.
- Schools & childcare facilities in HICs.

Drivers of change:

(Developments with the potential to transform the scenario)

- Technological/resource access
- Compliance/public trust
- Availability/ease of MCM R&D
- Shortage of components, affecting production
- Energy cost
- Low-cost test
- Regulation guidelines
- R&D funding
- Funding of healthcare system

Critical uncertainty:

(Driver that bear high impact and high uncertainty of developments)

Political stability and mis- and dis-information (with consequences on the use and acceptance of technology and science).

Development 1 – More stability and less mis-, dis-information Development 2 – Less stability and more mis-, dis-information

Technological solutions:

(Technology more adequate for this scenario and impacts of the developments of the critical uncertainties)

• Detection

Sampling technology: Filters

Identification & quantification technology: <u>NAA-based techniques</u>

- Development 1 more stability
 - Filters are still relevant for sampling.
 - Biosensors might be more fit for identification and quantification, but then the sampling technology should be reconsidered as they are not compatible with filters.
- Development 2 less stability
 - Other technologies might be more fit:
 - Air-to-chip challenge. There are no technologies that can detect directly from the air without the steps of aerosol capture and sample preparation.
 - Combination of filters for sampling with lateral flow immunoassay for identification.
- Decontamination

Combination of ventilation and UV radiation

- Development 1 more stability
 - A more advanced technology could be favoured, e.g. photocatalytic oxidation.
- Development 2 less stability
 - More use of ventilation and simple window opening.

6 Recommendations

It is clear that the call for 'clean indoor air' is not sufficient in itself to bring together the many actors and resources necessary to transform this message into action that leads to a significant improvement in public health outcomes and, inherently coupled to this, pandemic prevention, preparedness and response. Based on the inputs gathered through the survey, the workshop and discussions, we concluded on the following recommendations that emerged to define steps to be taken and challenges to overcome so the technologies outlined in this report can be developed and implemented to benefit us all.

6.1 Focusing on Synergies

Achieving the suppression of pathogen transmission within indoor environments is inherently connected to the built environment. With such large-scale and enduring efforts to decarbonize the economy, reducing energy consumption from buildings is a must. Given the drive to increase thermal insulation and install different forms of heating ventilation air conditioning systems (HVACs), these developments need to be taken into consideration when designing use cases for research and for the technical specifications of any systems to be implemented in those spaces. CO_2 meters and natural ventilation are the basis of all interventions. Measures of general air quality, such as CO_2 levels, are a proxy indication of room occupancy and could be used to estimate the infection risk.

Concrete actions to invest in are:

- Dedicated working groups between agencies and public health institutes to integrate building/environmental standards and regulation with those for the mitigation of disease burden from airborne pathogens and classical indoor air quality.
- Innovation funding for research projects and solutions that accommodate holistic measures of indoor air quality, meaning particulate matter, chemical hazards, as well as infectious agents present in the air.
- Leveraging of evidence-based standards with confirmed health benefit of transmission control or surveillance systems integrated into HVAC solutions or similar to increase competitiveness over existing systems without such a benefit.
- Map the ambient/environmental air quality legislative framework to identify outdoor-indoor interplays of use for IAQ guidelines.

6.2 Defining a research agenda for public health

The effective implementation of technologies to detect airborne pathogens requires the generation of empirical evidence to support standardisation and define which health outcomes can effectively be addressed through concrete solutions to detect and/or decontaminate pathogens from indoor air. Here again, it is important to define the context and envisioned goal of an intervention. Based on the work presented, the clear differentiation between actions to prevent disease outbreaks and to manage transmission from endemic pathogens is important.

This research agenda should:

• differentiate clear and exclusive use cases, e.g. surveillance of seasonal respiratory viruses in healthcare settings, detection of novel pathogens in animal agriculture settings or mitigation of transmission in care settings.

Such studies, focusing on genomic surveillance of known pathogens, including antibiotic resistance markers, could inform the susceptibility to existing medical countermeasures and contribute to their adaptation, if necessary. Sampling over long timeframes could be implemented to monitor respiratory pathogens for low vaccine coverage and constitute an early warning system to support public health decision-making. At the human-animal interface and for environmental surveillance of wildlife, sampling of aerosolised pathogens could support the identification of novel pathogens with epidemic potential and support the surveillance of known zoonotic pathogens, notably highly pathogenic avian influenza.

For transmission suppression, decontamination measures are focusing and should continue to focus on establishing efficacy in specific settings, e.g. in care homes, and be coupled with quantification of

which pathogens can be decontaminated to which degree and with which health outcome, both considering the population targeted by the intervention as well as taking into account the effects on community spread.

• define goals and milestones matched to the specific use cases and quantifiable public health outcomes and actions.

From the research conducted now and the near future, interdisciplinary groups of researchers and public health professionals should assess what further research is necessary, especially to gather the empirical evidence needed to support standardisation efforts. Such milestones could be a change of the measurable concentration of a certain pathogen in the air to reduce the transmission of the same pathogen or the effect on disease progression when onwards transmission is measured.

• bring together researchers from architecture, in-vitro diagnostics, engineering with health professionals (medical doctors, nurses), public health decision-makers and end users to generate a roadmap of milestones across the use cases.

It is evident that those professionals involved in the development of technologies and products for the detection and decontamination of airborne pathogens do not regularly get to exchange with biomedical researchers, healthcare workers, public health professionals, architects, and other professions active in the design and management of buildings. It is necessary to engage individuals from these different sectors at the same time to allow engagement of these perspectives to arrive at approaches that are effective and resilient outside of the laboratory – where they are needed. For this purpose, a dedicated series of conferences is suggested to explore and determine use cases, set priorities for investigations, and most importantly, foster cross-sectoral collaborations.

6.3 Addressing technological bottlenecks

Based on experts' selection of technologies that would have most impact if properly funded, two priority levels emerge in the survey:

- Priority 1: Filtration/ventilation, UV radiation, Biosensors, Direct identification though physicochemical properties
- Priority 2: NAA-based techniques, Cyclonic and impactor aerosol samplers

During the workshop, sequencing technologies emerged as crucial and were perceived as high priority, especially in surveillance and discovery use cases, similar to biosensors or direct identification through physico-chemical properties.

Based on the positioning of technologies in an impact versus maturity chart, we could cluster technologies into the most impactful technologies of the present, which are mature enough to be deployed, and the most promising for the future, which have high impact but are not ready yet.

- Top technologies of the present: Filtration/ventilation, UV radiation, Filters, NAA-based techniques
- Top technologies of the future: Aerosol samplers, Biosensors, Direct identification through physicochemical properties, Plasma-based inactivation (the latter selected only by one group during the workshop)

The intersection of technologies selected as high–medium priority for funding with the top technologies of the present and the future gives an indication of good opportunities for funding:

• Potential opportunities for innovation funding - Technologies of the present:

High impact and high mature technologies could benefit from innovation funding to bring optimisation, improve applicability and reduce costs. Several scenarios require different technical specifications. Support to develop fit-for-purpose products would provide ready-to-use solutions in the short term.

Filtration/ventilation: increasing indoor air quality from particulate matter, noxious gases and aerosolised hazards have led to the maturation of filtration and ventilation technologies. However, their energy consumption is high, especially for filtering small virus-size particles. Even though filtration is a traditional technology, some sophisticated solutions with low TRL are starting to appear, e.g. foam-based and catalytic filters. UV radiation: it can inactivate pathogens but a major shortcoming is that, depending on the wavelength, it can generate toxic radicals and can be harmful for humans. Development efforts are put into methods to decrease toxic radicals and allow for operation in the presence of people.

NAA: NAA-based methods that would increase the speed and multiplexing capabilities would represent a breakthrough in the technology. So far, NAA has to be performed off-line and cannot be applied to unknown pathogens.

• Potential opportunities for research funding - Technologies of the future:

These technologies need further research to achieve their full potential:

Biosensors: they can be low-cost, fast and portable. They are also specific, compatible with multi-target detection and amenable to integration and automation. However, pathogens must generally be kept intact, and sensitivity is still an issue.

Direct identification through physico-chemical properties: This technology is based on real-time, label-free bio-detection systems that can be applied to detect unknown pathogens but are currently laboratory intensive. They are still at a research stage and cannot be widely applied yet: only the proof of concept was done on some pathogens. Research efforts are increasing to achieve their automation through Al-based identification of pathogen signatures.

6.4 Opportunities & Risks

The successful development and implementation of systems for detection and suppression of pathogens present in air faces risks and opportunities. Based on the survey and output from the workshop, several issues were identified and should be considered by stakeholders.

Opportunities:

Efforts to regulate indoor air have gained traction since the COVID-19 pandemic. For example, Belgium introduced a regulatory framework for indoor air quality (Loi 2022/34199 du 6 Novembre 2022), mandating the use of air quality measurement systems in public spaces accessible to the public and the certification of those spaces, while the US introduced building standards for the Control of Infectious Aerosols (CIDRAP, 2023). Clearly, these first efforts will be analysed for their effects and benefits in the medium-term. While new regulations are implemented, cross-national collaboration could improve the speed and quality of early learnings. Similarly, the salience of the topic of pathogen transmission through the air remains elevated in the population. The COVID-19 pandemic has created sensitivity to aerosol transmission across national, cultural and socioeconomic divides. This increased sensitivity should be harnessed, and regulatory and technological developments should go hand-in-hand with education on managing air quality, building on educational approaches for hygiene that are commonplace.

End-to-end products, i.e. solutions that combine the detection/monitoring of airborne pathogens with decontamination measures, that are integrated into buildings or HVACs solutions could provide a competitive advantage for early adopters of such technologies.

Risks:

The simple framing of achieving 'clean air' can generate attention but is not sufficient to move major stakeholders and funders to commit to the long-term support that is necessary to create solutions with meaningful outcomes. It would be a mis-step to overpromise on public health outcomes to be achieved by specific technologies and not engage with existing research that could inform such outcomes, e.g. research on transmission mechanisms from close-contacts in respiratory diseases. The existence of technologies to decontaminate indoor air should also not suggest that simple methods to improve indoor air by manual ventilation are obsolete, i.e. opening doors and windows, opting for well-ventilated venues for crowded events.

Without the implementation of systems for detection and mitigation widely applied and in different settings, it is impossible to assess the risks associated with the technologies covered. Malfunctioning of equipment, possibly exacerbated by high maintenance requirements, resulting in false positive and false negative signals, could undermine the utility of the systems deployed. Related to this, a unique focus on highly sophisticated technology associated with high costs and potentially lacking in resilience compared to low-tech solutions will

decrease the market size and limit widespread adoption, if the benefit of implementation is meaningful only when deployed at scale.

Lacking evidence on monitoring indoor air and long-term testing of decontamination methods makes it difficult to predict potential negative externalities on individuals from being exposed or subject to indirect surveillance from airborne pathogen detection and decontamination systems. While the decontamination methods could directly harm persons, negative externalities from air sampling would highly depend on the methods of detection. Considerations around privacy and individual rights should not be neglected when it comes to the assessment of technologies to be developed.

6.5 Way forward

The following considerations are important points for defining policy actions:

- Science leads the way: The definition of a research agenda is of highest priority. This research roadmap should be defined by a diverse set of stakeholders and the recommendations above suggest an approach to address distinct use cases and public health outcomes.
- Standardisation is key: The effectiveness of the interventions needs to be defined for these systems to be generally accepted. Clear evidence supporting claims of efficacy may make private and public investment made in developing commercial products more attractive and facilitate their acceptance by public health agencies as legitimate measures to improve individual and population health.
- Synergies for optimal results: Quality of indoor air should be subject to regulation and disease burden or health effects from pathogens in indoor air should not be thought of as separate from particulate matter and hazardous chemicals present in air. Especially publicly funded efforts to improve thermal insulation and energy use in buildings should also address the health effects of such interventions. Innovation funding would especially benefit from including provisions on air quality.
- Simple is good too: The growing role of technology to address health concerns stemming from pathogens present in air is clear but should not impede the need for education and public health messaging on easy interventions to reduce transmission, especially when these have added health benefits from reducing pollution.

Conclusions

This report sets out to map technologies, established and in early stages of development, that have the potential to improve individual and public health through the detection and decontamination of pathogens present in indoor air. In the process of the work which precedes this report, it became clear that there are significant discrepancies between what individuals from different sectors view as viable and possible applications of the technologies showcased in the report. Detection of pathogens can but does not have to be coupled to decontamination when used for surveillance purposes or the study of new pathogens. Similarly, decontamination activities do not necessarily depend on (timely) identification of the pathogens present at a given time in a specific environment depending on the goal and circumstances in which this intervention takes place. The clear distinction of 1) the public health goal to be achieved and the 2) physical environment in which the intervention is to take place is a pre-requisite for the effective communication between stakeholders from different disciplines and for the optimal use of resources to develop and assess such interventions.

The desk research identified main groups of technologies, their claimed advantages and their possible limitations. However, through the foresight participatory process, namely by fostering discussions between experts, we can conclude that, as there is no single technology that provides an end-to-end solution, the assessment of the potential of each should not be done in isolation, but in combination and considering the breadth of applications. Each application might need a different technology set: for example, early detection systems would benefit from technologies capable of automated monitoring, which is difficult to achieve with the current broadly used nucleic acid detection methods; some of the state-of-the-art filtration systems with air recirculation that are useful in normal situations cannot be used during a pandemic; far UV at 222 nm is less harmful to humans tissues than conventional UV-C 254 nm radiation used for decontamination but can create ozone and has therefore to be combined with a ventilation system; ventilation cannot be used in old/protected buildings that do not have ducts.

Key technologies for airborne pathogen transmission suppression

Decontamination mostly relies on two mature technologies: filtration/ventilation and UV radiation. However, energy consumption of ventilation systems and the generation of toxic species by UV systems are still a problem. Innovation funding could help overcome those shortcomings. Experts were hesitant to name medium mature alternatives that would have a high impact comparable to existing mature technologies. However, some technologies, such as plasma and microwave/electromagnetic inactivation, were perceived as quite promising for specific applications. Plasma inactivation performs well for sterilising objects and small volumes, but upscaling to the decontamination of a room size is challenging and ensuring that they do not affect human health has to be demonstrated. Microwave/electromagnetic radiation is highly portable and could be installed in a mobile phone for individual personal protection.

Detection technologies presented a larger variety of promising options. Currently, pathogen detection relies on the trapping of air particles on filters and analysis by NAA techniques, mostly PCR. However, such a combination is not amenable to the continuous monitoring that real-time alert systems would require. Aerosol sampling technologies combined with biosensors or direct identification methods could allow such real-time responses. They are good candidate technologies to benefit from R&D funding as they were identified as high impact technologies still needing further research. Condensation aerosol samplers present good collection efficiency for small particles (with size < 500 nm) but are quite expensive as compared to the cyclonic and impactor counterparts. Direct identification methods through physico-chemical properties would benefit from developing AI models to assist in the identification of spectral signatures, for which a large spectra database to train the models would be needed.

Horizontal opportunities across technologies

Miniaturisation and automation are key to be able to use the technologies at the Point-of-Detection. Coupling of technologies with machine learning, when possible, would add a competitive advantage to the technology in question in terms of reliability, automation and response time.

The importance of modelling to target interventions was highlighted, in particular for:

collecting representative samples: Closed spaces do not have a homogeneous distribution of airborne
particles. The placement of detection devices is therefore important for the representativeness of the
sample. Modelling spaces and thermodynamic flows would allow smart sampling by distributing
detection devices in a configuration that would provide a good picture of the concentration levels
across the room. In this regard, the creation of digital twins of indoor spaces would increase efficiency.

minimising super-spreader events: Super-spreaders disproportionately contribute to the transmission
of infectious diseases, but the phenomenon is poorly understood. A network of detectors in strategic
locations that could quickly identify pathogen peaks would help in suppressing the main vectors that
spread. Better models of contagiousness and air transmission to identify and deal with super-spreaders
would be useful to better target interventions.

Most relevant contextual factors

European legislation, EU standards and harmonisation and research funding are essential to enable the use of currently mature technologies and drive technological developments.

On the other hand, lack of education and public information can be a barrier for technology adoption. To increase acceptance, a good way of communicating the advantages of technologies would be by providing an estimate of the number of days that confinement could be reduced if the technology were deployed.

Policy recommendations

Indoor air regulations and guidelines, investment in improving our built environment and the adoption of innovative technologies play a key role in decreasing the frequency of respiratory epidemics and reducing the burden of seasonal diseases.

The study highlights the importance of defining a research agenda for public health to effectively develop and implement technologies to control the transmission of airborne pathogens. Scientific evidence must be gathered to support standardization and to identify the health outcomes that these technologies can achieve. It is crucial to define specific use cases, set corresponding goals and milestones, and foster collaboration across disciplines to develop a comprehensive roadmap for implementation. In this regard, a dedicated series of conferences is suggested to discuss those issues in a cross-sectoral collaboration setting.

The study also highlights the necessity of integrating health, technology and environmental considerations into a comprehensive indoor air quality management framework. Policies and standards should be developed to define and regulate indoor air quality, including the suppression of air pathogens, while maintaining environmental quality and comfort. Current standards in building ventilation system management are considered as baseline for all approaches as they are ubiquitous in most scenarios based in western countries. In scenarios where building ventilation system standards are not met their implementation should be considered a priority.

Guidelines, harmonisation and standards across the EU would facilitate a coordinated approach to indoor air quality and pathogen control. Questions to be addressed include:

- in which situations the detection and decontamination systems would be used continuously or, by contrast, only when needed,
- who is responsible for validating the different technologies,
- how sterile the environment should be, what microorganisms should be controlled and whether there
 is a need to set concentration thresholds. When designing decontamination plans, the objective should
 not be the creation of 100 % sterile environments, except for specific cases, such as operating rooms,
 since airborne microbial flora is necessary to keep human microbiome and virome balance, and
 changing them could have negative health outcomes in the future or create too ambitious thresholds
 without real benefit to individual and population health.

Smart interventions should be supported by solid risk assessment and a better understanding of risk drivers. The use of humidity and CO_2 monitors in the risk assessment of airborne pathogen transmission could be exploited as humidity and CO_2 levels are easy to monitor and have been related to airborne pathogen concentration and survival. Based on risk assessments, new legislation would be welcome for the application of technologies in high-risk buildings, e.g. in schools, or residences for the elderly. Policies should encourage actions that protect the weakest, for instance by developing context-dependent solutions for vulnerable populations and in places where super-spreaders are expected.

Policy actions should encourage multi-sectoral and multi-disciplinary interactions, involving policymakers, civil society, researchers, and technology manufacturers from the beginning to define targets and strategies for indoor air quality and look at the best detection and decontamination technologies to implement them. Architects should also be included in the dialogue as they have a role to play in designing buildings with an architecture that facilitates natural ventilation or incorporates detection and decontamination devices.

Education and communication are important for technology acceptance. Actions to increase awareness of indoor air quality and promote the benefits of using advanced technologies for infection control could be effective and feasible to implement in the short term.

Next steps

By the end of the workshop, participants provided input as action suggestions for the EC. A significant set of contributions regarded the need for a policy framework for the broader issue of indoor air quality and the specific development, approval, use and maintenance of technological equipment addressing pathogen detection and decontamination. On this dimension, and compared with outdoor air quality and pollution, water quality and food safety, where the EU has comprehensive and detailed regulations and standards, several interventions highlighted that indoor air quality is still an under-regulated domain. In this sense and for the sake of public health, similar steps to those taken in similar domains should be promoted.

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List of abbreviations and definitions

| AI | Artificial Intelligence |
|-------|--|
| CEN | European Committee for Standardization |
| CoV | Coronavirus |
| COVID | Coronavirus Disease |
| DNA | Deoxyribonucleic Acid |
| EC | European Commission |
| EU | European Union |
| FT-IR | Fourier-Transform Infrared spectroscopy |
| HVAC | Heating Ventilation Air Conditioning |
| HIC | High-Income Countries |
| HVAC | Heating Ventilation Air Conditioning |
| IAQ | Indoor Air Quality |
| ISO | International Organization for Standardization |
| LAMP | Loop-Mediated Isothermal Amplification |
| LIC | Low-Income Countries |
| LMIC | Low- and Middle-Income Countries |
| MCM | Medical Countermeasures |
| NAA | Nucleic Acid Amplification |
| NGS | Next Generation Sequencing |
| NOS | Nitric Oxide Synthase |
| PCR | Polymerase Chain Reaction |
| R&D | Research and Development |
| R&D&I | Research and Development and Innovation |
| RNA | Ribonucleic Acid |
| ROS | Reactive Oxygen Species |
| RNOS | Reactive Nitrated Oxygen Species |
| SARS | Severe Acute Respiratory Syndrome |
| TRL | Technology Readiness Level |
| UV | Ultraviolet |
| WHO | World Health Organization |

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ANNEX 1. Technology fiches

The following considerations have been used in assessing energy consumption, TRL level and type of deployment for detection and decontamination technologies:

Energy consumption:

| kJ/m ³ | Assessment |
|-------------------|------------|
| 1 | Very low |
| 10 | Low |
| 1000 | Medium |
| 1.00E+04 | High |
| 1.00E+05 | Very high |

TRL levels:

| TRL description | TRL number | Assessment |
|---|------------|------------|
| Basic principles observed | 1 | Low |
| Technology concept formulated | 2 | Low |
| Experimental proof of concept | 3 | Low |
| Technology validated in lab | 4 | Low |
| Technology validated in relevant environment | 5 | Medium |
| Technology demonstrated in relevant environment | 6 | Medium |
| System prototype demonstration in operational environment | 7 | Medium |
| System complete and qualified | 8 | High |
| Actual system proven in operational environment | 9 | High |

Type of deployment:

- Limited deployment: suitable only in places with high-transmission potential, e.g. places of worship, concert halls, to reduce effects of 'super-spreader' events by installing permanent air quality solutions or deploying mobile units,
- Widespread deployment: suitable for widespread use, also including private homes and offices, to significantly decrease contamination of indoor air from human pathogens as well as environmental contaminants such as traces of asbestos, pollen, etc. It should be a cheap all-rounder solution, easy to install with minimal maintenance necessary.

AIRBORNE PATHOGEN DETECTION TECHNOLOGIES FICHES

Nr. 1 | PARTICLE COUNTERS

Family of instruments for the counting of submicrometric particles in an aerosol sample. Description

Particles counters (for example Condensation Particle Counters, CPC) are a family of instruments that collect a sample of air and analyse the aerosol composition in terms of particles size. Particles of the aerosol passes through a laser beam, creating interference or diffraction and are counted one by one with a measure of the primary size. These instruments return a size distribution of particles in number and are used in general to measure how clean indoor air is in terms of ultrafine particles. Viral particles are in the size range measurable with a CPC, so a variation of concentration of virus in a room can be measured with this method. The measurement is direct and the result is instantaneous, but it is non-specific. These systems cannot distinguish between biological or non-biological particles.

| Subgroup | Operation (| | Collection time . to-result | / time- | Energy consumption |
|---|--|---------------------------------------|--------------------------------|---|--------------------|
| Collection/separation/ readout | Real time | | 1 min | | Low |
| Verified pathogen | Broad spe | ectrum use | Efficiency | | TRL |
| None | YES It counts all the viral particles | | >80 % | | High |
| Sensitivity | Specificity | | Type of deployment | | |
| 1 particle/Litre of air | Low | | Widespread | | |
| Source | | | · | | |
| Stolzenburg, M. R., & McMurry, P. H. (1991). An ultrafine Science and Technology, 14(1), 48-65. https://doi.org/10 | | e aerosol condensa 0.1080/02786829 | ation nucl 1089594 | <i>eus counter</i> . Aerosol . <u>70</u> | |
| Estim | | nates | | | |
| Affordability | rdability Applicability | | | Bottlene | ecks |
| High Easy to operate, au control | | utomatic, remote | Specificit and path | y of detection of viruses ogenic viruses | |

Nr. 2 | FILTERS

Family of instruments for the collection of sub-micrometric particles in an aerosol sample. Description

Filters collect aerosol particles using an active air sampling on a filter. Particles are collected on the filter media through interception, inertial impaction and diffusion. It can be used with very high active air sampling rates, up to 1000 L/min. The main disadvantage is the denaturation of the viruses due to dehydration and /or extraction from the filter.

| Subgroup | Operation | | Collection time / time- | Energy consumption |
|-------------------------|--------------------|--|-------------------------|--------------------|
| | | | to-result | |
| Collection/separation | Real time | | Several minutes | Low |
| Verified pathogen | Broad spectrum use | | Efficiency | TRL |
| None | YES. But no | | 50 % | High |
| | detection included | | | |
| Sensitivity | Specificity | | Type of deployment | |
| 1 particle/Litre of air | Low | | Widespread | |
| Source | | | · | |

Silva, P. G., Branco, P. T., Soares, R. R., Mesquita, J. R., & Sousa, S. I. (2022). *SARS-CoV-2 air sampling: A systematic review on the methodologies for detection and infectivity.* Indoor air, *32*(8), e13083. https://doi.org/10.1111/ina.13083

| | Estimates | |
|---------------|--|---|
| Affordability | Applicability | Bottlenecks |
| High | Easy to operate, automatic, remote control | Also collect viral particles. Detection not included. High percentage of viruses are denatured after collection. |

Nr. 3 | CYCLONIC AND IMPACTOR AEROSOL SAMPLERS

Family of instruments for the collection of sub-micrometric particles in an aerosol sample. Description

Cyclones are a family of instruments that, using an active air sampling, collect the aerosol particles in a medium. Centrifugal forces deviate the particles in the incoming airstream to impact on the collection walls. Viral particles are in the size range that could be collected using impactors, but they are more efficient for larger particles (size > 500 nm). They can be used with very high active air sampling rates, up to 400 L/min. The main disadvantage is that, due to the high kinetic energy of the particles, deactivation and denaturation of viral particles often occurs. Impactors aerosol samplers use similar principles but with a different geometry.

| Subgroup | Operation | Collection time / time- | Energy consumption |
|-------------------------|--------------------|-------------------------|--|
| | | to-result | |
| Collection/separation | Real time | Several minutes | Low |
| Verified pathogen | Broad spectrum use | e Efficiency | TRL |
| None | YES. But no | 50 % | High |
| | detection included | | |
| Sensitivity | Specificity | Type of deployment | |
| 1 particle/Litre of air | Low | Widespread | |
| Source | · | · · · · · | |

Silva, P. G., Branco, P. T., Soares, R. R., Mesquita, J. R., & Sousa, S. I. (2022). *SARS-CoV-2 air sampling: A systematic review on the methodologies for detection and infectivity*. Indoor air, *32*(8), e13083. https://doi.org/10.1111/ina.13083

| Estimates | | | |
|---------------|--|---|--|
| Affordability | Applicability | Bottlenecks | |
| High | Easy to operate, automatic, remote control | Detection not included. High percentage of viruses or pathogens are denatured after collection. | |

Nr. 4 | CONDENSATION AEROSOL SAMPLERS

Family of instruments for the collection of sub-micrometric particles in an aerosol sample. Description

A laminar flow condensation tube encapsulates airborne particles into liquid droplets and gently deposits the droplets on a liquid or solid surface. It can be used with low active air sampling rates, up to 1.5 L/min. They maintain the biological structure of the viruses and keep their viability. On the other hand, they are bulky and complex to operate and relatively slow. They work well for small particles (< 500nm).

| Subgroup | Operation | Collection time / time- to-result | Energy consumption |
|-------------------------|-----------------------------------|--------------------------------------|--------------------|
| Collection/separation | Real time | Several minutes | Low |
| Verified pathogen | Broad spectrum use | Efficiency | TRL |
| None | YES. But no detection included | >80 % | Medium |
| Sensitivity | Specificity | Type of deployment | |
| 1 particle/Litre of air | Low | Widespread | |

Source

Silva, P. G., Branco, P. T., Soares, R. R., Mesquita, J. R., & Sousa, S. I. (2022). *SARS-CoV-2 air sampling: A systematic review on the methodologies for detection and infectivity*. Indoor air, *32*(8), e13083. https://doi.org/10.1111/ina.13083

| Estimates | | | |
|---------------|--|--|--|
| Affordability | Applicability | Bottlenecks | |
| Medium | complex to operate, not fully automatic | Detection not included. Low air sampling rates | |

Nr. 5 | CELL CULTURES

Technology for pathogen identification and quantification. Description

Current procedures for microbiological air quality evaluation (ISO 14698-1:2003) are based on passive or active air sampling methods. Passive methods involve the exposition of a petri dish (containing a selected solid culture media) to the environment during an established period, while active methods consist of automatic air samplers with a culture medium that is exposed to a forced airflow. In both methods, samples are incubated in favorable conditions for microorganism (bacteria, yeasts or molds), during 24–72 h. These methods are suitable for the risk assessment through microbial quantification in air [colony forming units (CFU) count]. Nevertheless, these time-consuming procedures generate a delay in the surveillance of microbial air quality.

For non-culturable pathogens such as viruses, the principle is inoculation of permissive cell lines or embryo eggs with infectious samples, propagation for a week (up to 10 days), and observation of different parameters. By using this method, it is possible to determine the presence of viral particles and characterize viral properties. The approaches for the identification and study of viruses using cell culture can be divided into two categories. The first category takes advantage of the cytopathic effect of viral infection, which means that cells die due to the viral infection. These methods are laborious and exhibit low sensitivity. The second approach is related to the generation of a reporter cell line, in which specific cells are modified to produce a reporter protein in response to virus infection. The properties of this reporter should be very specific to the virus to allow to identify the virus of interest. In the case of viral infection, the viral protein recognizes the reporter construct as a viral genome. These methods are often time consuming, and it is not always easy to select a cell line that will be sensitive and ideally selective for a specific type of virus.

| Subgroup | Operation (| | Collection time / time- | Energy consumption |
|--------------------------|--------------------|---|-------------------------|--------------------|
| | | | to-result | |
| Identification | Time consuming | | Days | Low |
| Verified pathogen | Broad spectrum use | | Efficiency | TRL |
| Viruses, bacteria, fungi | Yes | | 80 % | High |
| Sensitivity | Specificity | · | Type of deployment | |
| High | Medium to high | | Limited | |
| Source | | | | |

Bhardwaj, S. K., Bhardwaj, N., Kumar, V., Bhatt, D., Azzouz, A., Bhaumik, J., ... & Deep, A. (2021). *Recent progress in nanomaterial-based sensing of airborne viral and bacterial pathogens.* Environment international, *146*, 106183. <u>https://doi.org/10.1016/j.envint.2020.106183</u>

Dolskiy, A. A., Grishchenko, I. V., & Yudkin, D. V. (2020). *Cell cultures for virology: usability, advantages, and prospects*. International journal of molecular sciences, 21(21), 7978. https://doi.org/10.3390/ijms21217978

Vemula, S. V., Zhao, J., Liu, J., Wang, X., Biswas, S., & Hewlett, I. (2016). *Current approaches for diagnosis of influenza virus infections in humans*. Viruses, 8(4), 96. <u>https://doi.org/10.3390/v8040096</u>

| Estimates | | | |
|--|--------------------------------------|---|--|
| Affordability | Applicability | Bottlenecks | |
| Medium/low, highly time-consuming for trained staff | Low, old and poorly efficient method | very time-consuming and depends on the type of pathogen | |

Nr.6 | NUCLEIC ACID AMPLIFICATION-BASED TECHNIQUES

Technology for pathogen identification and quantification. Description

PCR has become one of the most valuable techniques currently used in bioscience, diagnostics and forensic science (1). It is based on the amplification of specific nucleic sequences exponentially through repeated cycles of thermal denaturation and renaturation. Quantitative PCR (qPCR) or real-time PCR (RT-PCR) are considered the gold standard for pathogenic nucleic acid analysis. Its combination with reverse transcription (qRT-PCR) has been adopted as the first-line assay for confirming the infection of RNA viruses including SARS-CoV-2 (2).

<u>Advantages</u>: ultra-high sensitivity and specificity enable to detect very few or even single copies of target nucleic acids in complex samples (3).

<u>Disadvantages</u>: time consuming, expensive devices and specialized operators, insufficient for rapid and on-site diagnosis during pandemics (3).

Many innovative technologies have been inspired by standard PCR. The implementation of microfluidic systems led to the development of a new family of devices, such as flow-through miniaturized and fast PCR systems, which allow saving time for the measurement, reducing sample volume and contamination risks and providing portability (4).

| Subgroup | Operation | | Collection time / time- | Energy consumption |
|---|---|---|--|--------------------|
| | | | to-result | |
| Readout | Real time for very fast PCR methods. Offline for standard PCR methods | | 4-48 hours (2-6 hours through ultra-fast PCR assays) | 0.2-0,5 kWh/run |
| Verified pathogen | Broad spectrum use | | Efficiency | TRL |
| Virus | YES/NO Yes | Viruses, bacteria, fungi and protozoa | > 95 % | High |
| Sensitivity | Specificity | | Type of deployment | |
| SARS-CoV-2: 4-8 copies per litre of air within a 95% confidence interval | High | | / | |
| Source | | | | |

(1) Chang, Y., Wang, Y., Li, W., Wei, Z., Tang, S., & Chen, R. (2023). *Mechanisms, Techniques and Devices of Airborne Virus Detection: A Review.* International Journal of Environmental Research and Public Health, 20(8), 5471. <u>https://doi.org/10.3390/ijerph20085471</u>

(2) Zhai, T., Wei, Y., Wang, L., Li, J., & Fan, C. (2023). Advancing pathogen detection for airborne diseases. Fundamental Research, 3(4), 520-524. <u>https://doi.org/10.1016/j.fmre.2022.10.011</u>

(3) Bhardwaj, S. K., Bhardwaj, N., Kumar, V., Bhatt, D., Azzouz, A., Bhaumik, J., ... & Deep, A. (2021). *Recent progress in nanomaterial-based sensing of airborne viral and bacterial pathogens*. Environment international, *146*, 106183. <u>https://doi.org/10.1016/j.envint.2020.106183</u>

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| Estimates | | |
|---------------|--------------------------------|--|
| Affordability | Applicability | Bottlenecks |
| Medium | Need of a specialized operator | High-throughput screening, high risk of sample contamination |

Nr. 7 | DIRECT IDENTIFICATION THROUGH PHYSICO-CHEMICAL PROPERTIES

Technology for pathogen identification and quantification. Description

These methods are based on measurement techniques that enable the identification of a pathogen by characteristic features.

Spectroscopic and spectrometric techniques (e.g. Raman Spectroscopy, IR Spectroscopy, Scattering spectroscopy, etc.) are able to identify pathogens by their differences in biochemical composition. Often those differences are minimal but advanced analysis algorithms and AI can detect them. Spectroscopy-based detection can be performed in almost all sample matrices: water, air, food, plants, animal and human specimens. This opens a possibility to develop pathogen identification methods that are reliable, automatized, real-time and applicable to unknown threats. In the case of an outbreak, rapid identification and detection is the first essential step for an effective response. Current biorecognition technologies are often too laboratory intensive and incompatible with automation. AI analysis of spectroscopic information can enable a new generation of real-time, label-free biodetection systems. It could be a disruptive technology allowing the deployment of fast early detection systems, which could improve decision-making in the management of public health threats.

| Subgroup | Operation | Collection time / time | Energy consumption |
|-------------------|------------------------|-------------------------------------|--|
| | | to-result | |
| Identification | Real time | Few minutes | Low |
| Verified pathogen | Broad spectrum use | Efficiency | TRL |
| Yes | Yes | >80 % | Low |
| Sensitivity | Specificity | Type of deployment | |
| 1 particle | High | Widespread | |
| Source | · · · | · · · · | |
| Vol Vob V T Vuo V | Wong 7 Thong N Live LL | $^{\circ}$ Hupper S. V. (2022). Acc | urata virua idantification with |

Ye, J., Yeh, Y. T., Xue, Y., Wang, Z., Zhang, N., Liu, H., ... & Huang, S. X. (2022). *Accurate virus identification with interpretable Raman signatures by machine learning.* Proceedings of the National Academy of Sciences, *119*(23), e2118836119. https://doi.org/10.1073/pnas.2118836119

| Estimates | | | |
|--|---|-------------------|--|
| Affordability | Applicability | Bottlenecks | |
| It depends on the spectroscopic technique used | Possibility to have it fully automated | None in principle | |

Nr. 8 | BIOSENSORS

Technology for pathogen identification and quantification. Description

Biosensors include a large group of techniques based on the recognition of a region of the pathogen through its affinity for a bioreceptor. The interaction of the pathogen with the bio-receptor (antibody, cell receptor, aptamer, nucleic acid, etc.) is translated in a measurable signal by a transducer. The resulting signal can be optical, electrical, electrochemical, etc., depending on the type of transducer. For most bioreceptors, the pathogen needs to be kept intact in the sample, which is a constraint for airborne pathogen sampling. One of the most well-known biosensor is the lateral-flow immunoassay, a paper-based test widely used for human diagnostics. A small volume of the sample to analyse is placed on one end of a paper pad. The liquid is adsorbed and run by capillary flow through different reagent-containing areas. If the target protein is present, it will first bind to antibodies conjugated to a tag, and then to a second antibody in a sandwich assay, for visualisation of a positive test line. This is an example of low cost, easy to perform and fast time-to-result biosensor widely available in the market. Paper-based sensors are also developed for pathogen detection.

Many new biosensors for the detection of airborne pathogens are described in scientific articles. Research is very active in this field, thanks to the development of both the bioreceptor and the transducer part. Biosensors can be low cost, specific and sensitive, but compared to NAA-based they remain less performant. They are compatible with multiplexing i.e. with multi-target detection, and can be fast, and portable without requiring specialised training. They could thus provide a valuable alternative to PCR. However, most of them stay at a low technology readiness level.

| 5 | | | | |
|--------------------------|-----------------|----------------|--------------------------|--------------------|
| Subgroup | Operation | | Collection time / time- | Energy consumption |
| | | | to-result | |
| Identification | Real time or of | fline | Real-time to a few hours | Low |
| Verified pathogen | Broad spectr | um use | Efficiency | TRL |
| Viruses, bacteria, fungi | Depends on | Can be | 80 % | Low to high |
| | bioreceptor | multiplexed | | |
| Sensitivity | Specificity | | Type of deployment | |
| Medium to high | Medium to hig | h depending on | Limited to widespread | |
| depending on the | the bioreceptor | r | | |
| transducer | | | | |
| Source | | | | |

Sivakumar, R., & Lee, N. Y. (2022). *Recent advances in airborne pathogen detection using optical and electrochemical biosensors*. Analytica Chimica Acta, 1234, 340297. https://doi.org/10.1016/j.aca.2022.340297

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Agarwal, D. K., Nandwana, V., Henrich, S. E., Josyula, V. P. V., Thaxton, C. S., Qi, C., ... & Dravid, V. P. (2022). *Highly sensitive and ultra-rapid antigen-based detection of SARS-CoV-2 using nanomechanical sensor platform.* Biosensors and Bioelectronics, *195*, 113647. <u>https://doi.org/10.1016/i.bios.2021.113647</u>

Mazur, F., Tjandra, A. D., Zhou, Y., Gao, Y., & Chandrawati, R. (2023). Paper-*based sensors for bacteria detection.* Nature Reviews Bioengineering, 1(3), 180-192 https://doi.org/10.1038/s44222-023-00024-w

| Estimates | | | |
|----------------|-----------------------------------|--|--|
| Affordability | Applicability | Bottlenecks | |
| High to medium | Easy to use, depending on the TRL | Pathogens must generally be kept intact, and sensitivity is usually lower than amplification based techniques | |

Nr. 9 | SEQUENCING TECHNOLOGIES

Technology for pathogen identification and quantification. Description

Sequencing methods, such as Next Generation Sequencing (NGS) and protein sequencing methods, can provide detailed information about the genetic and proteomic composition of airborne samples. NGS has allowed the rapid sequencing of DNA or RNA from airborne samples and can be used to identify and characterize the presence of different types of pathogens, including bacteria, viruses and fungi. Protein sequencing technologies determine the amino acid sequence of proteins present in airborne samples, for example by using mass spectrometry. NGS techniques are generally time consuming and costly, despite the amount of information that it is delivered.

| Subgroup | Operation | | Collection time to-result | / time- | Energy consumption |
|---|---------------------------------|--|---------------------------------------|----------------------|-------------------------------------|
| Identification | Offline | | Days or weeks | | High |
| Verified pathogen | Broad spect | rum use | Efficiency | | TRL |
| Viruses, bacteria, fungi | Depends on bioreceptor | ls multiplexed | > 80 % | | high |
| Sensitivity | Specificity | | Type of deployr | nent | · |
| High | High | | Limited to widesp | oread | |
| Source | | | | | |
| Hu, T., Chitnis, N., Monos, Human Immunology, <i>82</i> (1 | D., & Dinh, A. 11), 801-811. | (2021). Next-gen https://doi.org/10 | eration sequencir .1016/j.humimm.2 | ng techno 2021.02 | ologies: An overview. <u>012</u> |
| | | Estima | tes | | |
| Affordability | A | Applicability | | Bottlen | ecks |
| Low | N S | leed to be done b pecialized compa | y very nies or labs | Time an techniqu | d energy consuming ie |

PATHOGEN AIR DECONTAMINATION TECHNOLOGIES FICHES

Nr. 1 | FILTRATION / VENTILATION

Description

Ventilation systems can be based on natural or mechanical ventilation. Mechanical ventilation requires fans and ducts to circulate air. They are designed to provide continuous flow of fresh air into a closed space while removing indoor air. Ventilation systems can include air filters and/or air purification systems. Filtration is a commonly used technology to physically separate pathogens from the atmosphere using different filters (e.g., activated carbon fibre and polypropylene fibre filter). (1-2) The filtration performance depends on filter material properties and airflow characteristics. Filters with straight through capillary holes, have a higher possibility that particles smaller than the nominal pore size can get through, therefore, these filters have a significantly lower efficiency compared with disordered pores filters. (3) The particle size collected can be controlled by varying the air velocity (which is typically in the range of hundreds of L/min). Filters typically have high collection efficiencies (>95%) for particles > 0.5 µm in diameter but need regular replacement. (4) This air cleaning technology can be integrated into ventilation and HVAC systems that are already present in buildings. However, the accumulation of collected bio-aerosols over the surface of these filters can continue to grow and reproduce with sufficient moisture and nutrients therefore posing the threat of secondary contamination. Filters must be regularly replaced or decontaminated to ensure safe operation.

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--|--------------------|
| Removal | Dynamic | High for ventilation alone; medium with filtration | n.a. |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Bacteria | | n.a. | High |
| Source | | | |

(1) Stephens, B., (2012), HVAC filtration and the well-riley approach to assessing risks of infectious airborne diseases. National Air Filtration Association (NAFA) Foundation Report.

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(5) Ki, Y.Y., Jeong, H.B., Chul, W.P., Hwang, J., 2008. Antimicrobial effect of silver particles on bacterial contamination of activated carbon fibers. Environ. Sci. Technol. 42 (4), 1251– 1255. <u>https://doi.org/10.1021/es0720199</u>

| | Estimates | |
|---------------|-----------------|---|
| Affordability | Applicability | Bottlenecks |
| High | Easy and simple | Filter replacement and decontamination. Filtration capacity. Increased heating and power consumption for ventilation |

Nr. 2 | UV RADIATION

Description

UV radiation is a well-established method to inactivate microorganisms and sterilize items and surfaces.(1) At a wavelength of 254 nm UV-C radiation shows maximal effectiveness disrupting cellular replication by damaging microbial DNA/RNA (2) but can also deteriorate membrane proteins. Recently, UV-based processes are emerging for the degradation of airborne microorganisms, research focused on the effects of UV radiation ranges (UV-A,UV-B, UV-C)) in relation with intensity and exposure time. (3)

Irradiation at high intensities must remain inaccessible to room personnel because of potential skin and eye irritation.(4) UV radiation shows limited efficacy on spores and protozoa. By product of UV irradiation of air are the by-products like ozone and free radicals, which are harmful to humans at high concentrations. UV radiation technology can be integrated into filters.

Far UV at shorter wavelengths, typically 222 nm, seems both effective at killing microorganisms and safe for human exposure, but creates air pollution due to the generation of ozone.

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--------------------|--------------------|
| Inactivation | Static | Medium | Low |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Virus, Bacterials | | 85-95% | High |
| Source | | | |

(1) Dunn, E.F., Akhtar, A., Dunn, A., Lacey, S., Pauley, E., Powers, C., McKee, J., Petereit, D., (2021). *Evaluating an ultraviolet C system for use during SARS-CoV2 pandemic and personal protective equipment shortage*. Adv. Radiat. Oncol. 6, 100636 <u>https://doi.org/10.1016/j.adro.2020.100636</u>.

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(3) Wang, C., Lu, S., Zhang, Z., (2019). *Inactivation of airborne bacteria using different UV sources: performance modeling, energy utilization, and endotoxin degradation.* Sci. Total Environ. 655, 787–795. <u>https://doi.org/10.1016/j.scitotenv.2018.11.266</u>

(4) Luongo, J.C., Miller, S.L., (2016) *Ultraviolet germicidal coil cleaning: decreased surface microbial loading and resuspension of cell clusters*. Build. Environ. 105, 50–55. <u>https://doi.org/10.1016/j.buildenv.2016.05.024</u>.

| Estimates | | | |
|---------------|---------------|--------------------------------|--|
| Affordability | Applicability | Bottlenecks | |
| High | Simple | Exposure, safety, optimization | |

Nr. 3| ELECTROSTATIC CAPTURE

Description

Electrostatic capture technology is primarily used for the collection of bio-aerosols and removal of fine particle emissions. Using electrostatic technology, the airborne microorganisms and particles are electrically charged and subjected to a strong electric field, causing deposition on the collection substrate. (1) This technology has been widely developed for airborne particulate matter removal and then modified as aerosol sampler for bioareosol collection. (4) Electrostatic aerosol samplers can be integrated into HVAC filtration systems and can be operated without interrupting building use. (5)

The main limitations of electrostatic capture technology are the long contamination reduction half-times and the high energy consumption. It is also not effective against gram-positive bacteria.

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--------------------|--------------------|
| Removal | Dynamic | Low | High (3) |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| - | All, but gram+ bac. | 85-95% | Medium |
| 0 | | | |

Sources

(1) Molchanov, O., Krpec, K., Hor´ak, J., Kubo`nov´a, L., Hopan, F., (2020). *Comparison of methods for evaluating particle charges in the electrostatic precipitation of fly-ash from small-scale solid fuel combustion*. Sep. Purif. Technol. 248, 117057. <u>https://doi.org/10.1016/j.seppur.2020.117057</u>

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| Estimates | | | |
|---------------|---------------------|---------------------------------|--|
| Affordability | Applicability | Bottlenecks | |
| Low | Simple and reliable | Process parameters optimization | |

Nr. 4 | THERMAL INACTIVATION

Description

Thermal treatments are currently used in various methods (moist and dry heat) to control microorganisms in air. The moist heat method is operated using steam under pressure (1), whereas dry heat is operated only under high-temperature exposure (2). Thermal treatment of indoor air has been considered a safe, effective, and environment-friendly method; it does not produce ozone or use ion or filter media. Inactivation performance has been quantitatively investigated: > 99 % of bio-aerosols have been inactivated in about 0.2s at 350 °C using high-temperature bursts on airborne microorganisms in a continuous flow environment. Although it can effectively inactivate airborne microorganisms by denaturalizing proteins and deteriorating the cell structure the thermal technology is not widely utilized because of its high energy consumption (3) making it not very practical for large buildings.

| | <u> </u> | | |
|---------------------|---------------------------------------|--------------------|---------------------------------------|
| Type of suppression | Operation | Treatment capacity | Energy consumption |
| Inactivation | Dynamic | low | Very high |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Bacteria, Virus | All | >99% | Very High |
| Source | · · · · · · · · · · · · · · · · · · · | · | · · · · · · · · · · · · · · · · · · · |

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| Estimates | | | |
|---|-----------------|--------------------|--|
| Affordability Applicability Bottlenecks | | | |
| High | Easy and simple | Energy consumption | |

Nr. 5 | PLASMA / OZONE INACTIVATION

Description

Plasma discharges at atmospheric pressure or in vacuum environment can generate locally reactive chemical species such as electrons, UV photons, ions, neutral molecules (ROS, NOS and RNOS), and atoms (1). In cases where bio-aerosols come in contact with plasma bulk in the discharging area, the produced reactive chemical species directly interact with airborne microorganisms, damaging cell membranes, DNA, and proteins. Over the past few years, new plasma-based devices have emerged with several important applications in medicine, including air disinfection (2), where more than 98% of airborne *B. subtilis* inactivation was achieved, caused by cell membrane rupture (3). This technology is compatible with HVAC filtration systems. For high-end commercial application, the decrease in residual reactive ion species concentration with time and the cost of plasma systems must be considered.

Ozone (O3) is known as a strong oxidizing agent and biocide. It is effective against bacteria, viruses, protozoa, fungi, and various spores (4) since ozone can damage the lipids of cell membranes, organelles, DNA, and RNA. Ozone is a gas at room temperature and atmospheric pressure and therefore has been used for years to inactivate airborne microorganisms (5). However, ozone is a powerful irritant to the respiratory tract and lungs. During operation ozone concentration must be frequently monitored and this technology cannot be used in occupied spaces. Moreover, ozone can degrade indoor items via materials oxidation and must be generated locally because it is not stable at room conditions (6).

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--------------------|--------------------|
| Inactivation | Dynamic / Static | low / high | low |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| All | All | >90% | medium / high |
| Source | | | |

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| Estimates | | | |
|---------------|-------------------------------|-------------------------------|--|
| Affordability | Applicability | Bottlenecks | |
| low / medium | Require specialized personnel | Cost , just-in-time-operation | |

Nr. 6 | CHEMICAL AEROSOLIZATION

Description

Chemical aerosolization is a mature and common technology already used for the disinfection of different types of indoor environments (1). Aerosolization with concentrated NaOCI solution (10%) was utilized as a precautionary step during COVID-19 (2). In the disinfection of NaOCI, several reactive oxidants (such as OH-, O₃,and CI-) are produced, and have biocidal effect on airborne microorganisms (3). Different chemical agents have been developed, targeting different types of pathogens. Research primarily focused on determining the optimal dosage of disinfectants during disinfection procedures (4). Dynamic fog aggregation is an advanced aerosolization method that exploits a fogging system to distribute disinfectant particles evenly. Decontamination by this method can cover large areas in short amount of time and can reach areas that might be difficult to access with traditional cleaning methods (5).

However, the limitations of chemical areosolization are many. It utilizes harmful chemicals at high concentration whose by-products are often harmful to humans, therefore rooms must be evacuated before operation. The by-products abatement operations can be time and energy consuming, and also raise environmental concerns. These chemicals are also often corrosive for indoor items and equipment. On the supply chain side, chemical aerosolization operated at large scale implies the storage and transportation of large quantities of dangerous chemicals.

| 0 1 0 | | | |
|---------------------|---------------------|--------------------|--------------------|
| Type of suppression | Operation | Treatment capacity | Energy consumption |
| Inactivation | Static | High | Medium |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Virus | | >95% | High |
| Sources | | · | |

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| Estimates | | | |
|---------------|-------------------------|--------------|--|
| Affordability | Applicability | Bottlenecks | |
| High | Simple and ready to use | Optimization | |

Nr 7 | MICROWAVES RADIATION

Description

Microwaves radiation is a method of pathogen inactivation based on the propagation of electromagnetic waves in the area to be sanitised. The structure-resonant energy transfer effect from electromagnetic waves to confined acoustic vibrations in viruses could result in the fracture of the viral membrane through opposite core-shell oscillations.

Optimised Electromagnetic waves range from 8 to 10 GHz. The exposure time needed to achieve inactivation is about 1 minute. The protected area is about 3 meters for personal protection and 50 m² for room protection.

Some of the advantages include low temperature inactivation, possibility of integration in mobile phones, and compatibility of electromagnetic fields with dynamic exposure.

Microwave radiation systems have been commercialized in different configurations (e.g see <u>https://www.e4shield.com/en/homepage</u>).

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---|---------------------|---------------------|--------------------------|
| Inactivation | Dynamic | See above | low |
| Verified pathogen | Potential pathogens | Efficacy (IQ range) | TRL |
| Tested with aerosolized SARS COV 2 viruses. | Fungi, | 90 % | TRL 7-8 / commercialised |
| Source | | | · |

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International Commission on Non-Ionizing Radiation Protection (2020). *Guidelines for limiting exposure to electromagnetic fields (100 kHz to 300 GHz)*. Health Physics 118, 483–524. https://doi.org/10.1097/HP.000000000001210

| Estimates | | | |
|---|----------------|-------------------------|--|
| Affordability Applicability Bottlenecks | | | |
| low | Plug and play. | R&D, public acceptance. | |

Nr. 8 | LYSOZYME-BASED BACTERICIDES

Description

Lysozyme is a biomolecule (a protein) found in the cell wall of bacteria and also widely available in other living organisms (1). Lysozymes carry the ability to physically damage cell membranes (2). Lysozymes activity are quite specific for different bacterial species, so a specific lysozyme can only affect its target bacteria but not any other species (3). Moreover, lysozyme activity is influenced by environmental conditions and this affects the efficacy level of the process. Some appropriate chemical modifications have been utilized to understand the broad-spectrum and intelligent bactericidal efficacy of lysozymes as an antibacterial agent, and to address the specificity limitation. For example, discrete peptide self-assembly nanotubes with phenylalanine have been tested and demonstrated a broad-spectrum antibacterial effect (4). Ongoing research on antibacterial lysozymes shows potential application in air cleaning technology.

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--------------------|--------------------|
| Inactivation | Dynamic | high | Very low |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Bacterials, | | 85-95 | low |
| Source | | | |

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| Estimates | | | |
|----------------------------------|--------------------------------|----------------------|--|
| Affordability | Applicability | Bottlenecks | |
| Medium (projected at higher TRL) | Required specialized synthesis | Specificity, Iow TRL | |

Nr.9 | PHOTOCATALYTIC OXIDATION

Description

Photocatalytic oxidation is a photo-electrochemical effect produced when light (e.g. UV photons) interacts with a semiconducting surface (e.g. TiO_2), often in presence a photocatalyst material (e.g. noble metals) that lowers the chemical reaction energy barrier (1). Absorption of light leads to the creation of photo-excited charge carriers that migrate towards the surface of the photoactive material and creates different ROS. ROS have been proven to be able to disrupt cellular membranes and/or inhibit microorganisms biochemical reactions (2). Recently, new photocatalytic materials beyond TiO_2 have been developed to improve reactivity (3). For example, inactivation efficiency of airborne *E. coli* as high as 3.4-log was reached using 2D photocatalytic layers (4). The photocatalytic reaction by-products potentially include several harmful organic and inorganic species (such as aromatic hydrocarbons, ketones, and alcohols) (5), whose accumulation may also reduce or block the photocatalytic reactions. The development of various novel photocatalysts for air disinfection is a growing research topic. Several processing parameters need still to be optimized in order to achieve high reactivity and the fundamental mechanics of the process is not yet well understood. Interestingly, photocatalytic oxidation panels can be driven using solar light, even though this further complicates the technological implementation (1). Photocatalytic oxidation is compatible with filtration technology.

| Type of suppression | Operation | Treatment capacity | Energy consumption |
|---------------------|---------------------|--------------------|--------------------|
| Inactivation | Dynamic | Low/Medium | Low |
| Verified pathogen | Potential pathogens | Efficacy | TRL |
| Virus, Bacterials, | Broad spectrum | 75-95% | Low |
| Source | | | |

(1) Yang, L., Zhou, H., Fan, T., Zhang, D., (2014). *Semiconductor photocatalysts for water oxidation: current status and challenges*. Phys. Chem. Chem. Phys. 16 (15), 6810–6826. <u>https://doi.org/10.1039/c4cp00246f.</u>

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| Estimates | | | |
|---------------|---------------|---------------------------|--|
| Affordability | Applicability | Bottlenecks | |
| Low | Medium | Basic research, efficacy. | |



Annex 2. Individual survey responses scoring impact and maturity levels of detection and decontamination technologies.



Cyclonic and impactors aerosol samplers

Potential Future Impact





Figure A2. Maturity level and potential impact of detection and decontamination technologies as perceived individually by experts in their response to a survey (1 = 1 low readiness and impact; 5 = 1 high readiness and impact)

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