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Commentary

Personal protective equipment research and innovation in the context of the World Health Organization COVID-19 R&D Blueprint program

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In February 2020, in response to the coronavirus disease 2019 (COVID-19) pandemic, the World Health Organization (WHO) organized a Global Forum on Research and Innovation for COVID-19 (ie, Global Research Forum), which highlighted the importance of fostering research and innovation in the area of infection prevention and control (IPC), including rational and appropriate use of well-designed personal protective equipment (PPE). Despite its utmost importance for global health, PPE had not been prioritized in the research and innovation agendas of funding agencies and research institutions. Thus, at the start of the pandemic, knowledge gaps existed about PPE use by health workers outside the normative use during single encounters as part of infection transmission precautions. This was the case for extended use, to ration availability, and mask use in community settings as a supplementary emergency measure where epidemic containment strategies (testing, isolation, contact tracing, and quarantine) were unable to effectively identify and manage widespread community transmission of severe acute respiratory syndrome coronovirus-2 (SARS-CoV-2).

The goals of the Global Research Forum were to accelerate research for containing the spread of SARSCoV-2 and help those affected to receive optimal care.[1] This required: identifying and supporting research priorities; creating a global research platform; and strengthening preparedness for prompt information-sharing to bridge gaps in COVID-19 response knowledge and prevent another unforeseen epidemic. This forum was pivotal to encouraging accelerated development of diagnostics, therapeutics and vaccines and ensuring equitable access based on public health needs.

One output of the Global Research Forum was the publication of the coordinated global research roadmap.[1] This roadmap identified nine priority research priorities, one of which was IPC, including health workers' protection.

This commentary provides an overview of WHO's activities on IPC/PPE in the context of the R&D Blueprint for COVID-19, introduces nine PPE-focused research projects funded through the WHO R&D Blueprint for COVID-19, and reports on the current research priorities on PPE identified in the last WHO Global Research Forum, held in February 2022.[2]

BACKGROUND ON PPE

One of the R&D Blueprint priorities for IPC/PPE was to foster PPE innovations and optimize their cost effectiveness in health care and community settings, and in the context of prolonged and universal use. Although health workers are used to wearing PPE, they are not usually asked to extend their PPE use beyond using infection transmission precautions when caring for a single patient. Moreover, universal masking policies (ie, recommending that patients, visitors and caretakers wear masks in health care settings) as well as community masking policies were unprecedented in many countries. WHO's attention on fostering PPE innovation began before the COVID-19 pandemic. The 2014-2016 West Africa Ebola outbreak caused 10,000 deaths,[3] with more than 800 health workers infected, which triggered global attention on the importance of PPE, especially in resource-limited settings. In 2014, in response to the Ebola outbreak, WHO launched the first survey and technical specifications guidance, which highlighted the lack of disease-specific evidence on PPE efficacy and the need for innovation on PPE.[4] The Ebola outbreak and the subsequent COVID-19 pandemic in 2020, underscored the need for continued and coordinated attention on innovation and quality evidence on PPE, including in contexts beyond outbreaks. Since the 2014 Ebola outbreak, WHO has worked continuously to steer the development of global PPE ecosystems, for the safe delivery of health care interventions to mitigate the risk of infection in health workers

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and patients. During outbreaks where asymptomatic transmission plays an important role, local and global PPE ecosystems are even more challenged by the need to ensure available supplies for universal PPE use. This challenge was exacerbated by the COVID-19 pandemic, which, for the first time since the Second World War, led to short supply of resources, even in high-income settings.[5] This situation, challenged local and global capability to innovate, produce, distribute, and dispose of PPE.

In March 2020, the European Commission deviated from standard procedure for PPE conformity assessment and market surveillance within the context of the COVID-19 threat. In fact, with recommendation EU 2020/403,[6] the European Commission recommended that manufacturers use WHO technical documents and guides beyond ISO standards and UNI norms, for both PPE and medical devices.

In March 2020, WHO created a collaborative multidiscipline secretariat of three WHO Directorates (Health Emergencies, Universal Health Coverage, and Operations Support and Logistics), which supported UN partner agencies and countries to maximize the availability of PPE within health care systems and facilities.

While this work was built on WHO's previous experience with PPE evaluation in outbreaks, in 2020 the challenge was to move beyond a continual response to the emergency caused by COVID-19 or Ebola virus disease, and focus also on strategies for the rational use of PPE in the context of severe shortages and local production of quality-controlled PPE for both health care settings and the community.

R&D BLUEPRINT IPC RESEARCH PRIORITIES

In March 2020, no peer-reviewed publication was available that provided evidence on IPC measures to reduce transmission of SARS-CoV-2, apart from simulations suggesting that quarantine, isolation and travel restriction following contact tracing may significantly lower the peak and reduce the predicted cumulative number of infected individuals.[7] Moreover, preliminary studies had reported the presence of SARS-CoV-2 in nasopharyngeal and oropharyngeal swabs[8] as well as evidence of person-toperson transmission among close contacts.[9] In addition, data from previous coronavirus outbreaks (eg, SARS and Middle East respiratory syndrome [MERS] outbreaks)[10] demonstrated that compliance with hand hygiene, medical masks or filtering facepiece respirators, eye protection, gloves and gowns, as the PPE components of contact, droplet and airborne precautions, would likely also prove effective in preventing SARS-CoV-2 transmission.

However, significant knowledge gaps were identified during the Global Research Forum,[1] which hindered identification of effective IPC measures against SARS-CoV-2 transmission, including: modes of transmission and duration of transmissibility; virus stability in the environment and related methods and tools for minimizing environmental transmission; appropriate, effective and cost-effective PPE for both health care and community settings (ie, universal coverage); optimal health care pathways, isolation and quarantine; the most relevant administrative and engineering controls; behavioral and social factors affecting IPC compliance; and IPC measures for community settings.

Based on the above knowledge gaps, four research priorities for the IPC R&D were identified, namely: understanding the effectiveness of movement control strategies; optimizing the effectiveness of PPE; minimizing environmental transmission; and understanding behavioral and sociocultural factors hindering the efficacy of IPC measures in real-life settings (Table 1).

R&D BLUEPRINT RESEARCH PROJECTS ON PPE

In order to generate evidence on the research priorities identified for IPC, 45 research projects, which included 27 multicenter studies in 45 different states, were funded by the WHO. This included 18 studies focused on PPE, which were aimed at: assessing the efficacy of medical masks versus filtering facepiece respirators in hospital settings; understanding the impact of continuous use of PPE on health workers' mental load and communication; defining new methods to decontaminate or reprocess PPE where resources are limited, and assessing the safety and efficacy of these approaches; improving the design of nonmedical masks and face coverings, making them more effective and safer; disclosing the factors affecting mask and respirator fitting for different users; understanding the role of face shields and improving their design; exploring methods and tools for design and local manufacturing of masks, also considering low-resource settings, and assessing their effectiveness; exploring new approaches to PPE delivery for remote areas; generating high-quality evidence on virus transmission in health care and community settings; performing a systematic literature review on persistent antimicrobial treatments for medical masks, respirators and other PPE. These studies contributed substantially to bridging the knowledge gaps identified in February 2020. Of these studies, nine research projects are published in this issue and are briefly introduced in this commentary.

One of the needs during the COVID-19 pandemic was to support IPC interventions in health care and community settings with effective tools for increasing the effectiveness of training. In this issue, Fadaak et al.[11] report on the use of virtual tabletop simulations which assisted IPC teams as they adapted, implemented and integrated IPC guidance into their specific clinical contexts. This study demonstrated that the use of tools for simulations may provide substantial benefits to IPC and safety improvements in public health settings globally.

Most PPE equipment is disposable. However, in the context of severe shortages, decontamination or reprocessing of eye protection, gowns and respirators has been advised as an option for rationing available supply.[12] Decontamination or reprocessing of PPE requires procedures to inactivate contaminating pathogens beyond SARS-CoV-2, including common pathogens which can cause infections in health care settings. Wielick et al.[13] focused on contaminated surgical masks and respirators, and report on the efficacy of methylene blue photochemical treatment in decontamination of a more resistant, non-enveloped gastrointestinal virus and demonstrate efficient photodynamic inactivation of murine norovirus, a human norovirus surrogate. Vos et al.[14] validated the efficacy of methylene blue in combination with sunlight exposure for decontaminating PPE contaminated with murine hepatitis virus A59 coronavirus as a SARS-CoV-2 surrogate. Scholte et al.[15] used photoactivated methylene blue to decontaminate N95 and KN95 respirators contaminated with three variants of SARS-CoV-2 and four WHO priority pathogens: Ebola virus, MERS coronavirus, Nipah virus, and Lassa virus. The results of this study demonstrated that photoactivated methylene blue inactivated all tested viruses on respirator material, albeit with varying efficiency. Kabra et al.[16] focused on medical masks and Revolution-ZERO environmentally sustainable fabric masks, and showed that methylene blue effectively decontaminated both these types of mask when contaminated with SARS-CoV2 at concentrations above 5 μM and10 μM, respectively. Finally, in order to assess the safety of reusing medical masks and respirators decontaminated with methylene blue, Lendvay et al.[17] undertook a laboratory investigation of the amount of methylene blue inhaled by wearers. They concluded that at 500-times the amount of methylene blue needed to decontaminate N95 respirators and medical masks, there was no residual inhalational risk of methylene blue following treatment, thus providing safety evidence for the use of methylene blue for SARS-CoV-2 decontamination.

During the pandemic, face shields were used as eye protection PPE.[18] To generate high-quality evidence on their efficacy, Brainard et al.[19] tested 13 face shield designs in laboratory conditions. The study concluded that all the tested face shields provided some level of protection of the eyes but carried a risk of external contamination

Table 1
Infection prevention and control (IPC) research priorities, March 2020 (adapted from[1])

Research priority	Goal	Knowledge gap
Movement control	• Prevent SARS-CoV-2 transmission • Increase patient and population safety • Minimize the burden on health care systems	• Limited evidence, mainly fromsimulations or related to SARS/MERS • No specific SARS-CoV-2 evidence • Ethical and population-specific concerns regarding increased public health and social measures • Effectiveness and cost-effectiveness of IPC measure • Behavioral and human factors hindering IPC efficacy in community settings (ie, effectiveness of interventions)
PPE for health workers, patients and the community	• Prevent transmission and infection among health workers and patients • Generate high-quality evidence • Explore the direct role of PPE in transmission and acquisition • Improve PPE design	• Appropriate use of PPE in different health care settings and hospital units • Differences in PPE effectiveness, cost effectiveness and safety in high-, low and middle-income countries • Comparison of the effectiveness and safety of different PPE in large cohort studies
Environmental transmission	• Understand contact (direct and indirect), droplet and airborne transmission • Avoid misuse of agents and environmental toxicity • Understand potential emergence of resistance • Minimize the impact on resource utilization	• Identification of new agents and methods for environmental disinfection • Effectiveness of manual cleaning and disinfection methods and new solutions for environmental disinfection • Understanding of the impact of PPE on risk assessment and navigation of patient care spaces (barriers experienced in navigating furnishings and operating medical equipment while wearing multiple PPE items) • Identify settings and environmental risk factors conducive to aerosol transmission
Compliance with IPC measures during outbreaks	• Minimize widespread overuse/misuse of PPE based on fear and misinterpretation of evidence • Minimize miscommunication • Avoid unintended consequences (eg, shortage of supplies, unnecessary sense of (in)security) • Foster evidence-based communication with media and communication experts	• Understanding and removal of barriers and cultural factors influencing compliance in health care systems and in community • Absence of evidence-based policies on a global scale • Limited best practices and principles for IPC adult learning to translate risk communications and training approaches from health settings to public health/community settings

MERS, Middle East respiratory syndrome; *PPE*, personal protective equipment; *SARS-CoV-2*, severe acute respiratory syndrome coronovirus-2.

during prolonged use. To understand user preferences and perspectives about face shields, the same study surveyed 600 community and health care workers in middle-income countries (Brazil and Nigeria) in March-April 2021. Users reported preference for the use of face shields versus masks based on factors such as good communication, secure fixture, good visibility, comfort and fashion.

Cordeiro et al.[20] conducted a scoping review on barriers to PPE implementation and interventions. They concluded that effective implementation of PPE measures involves multilevel transdisciplinary complexity and relies on context-driven implementation strategies which should make use of collaborative implementing partnerships among local and international health bodies.

In the context of severe shortages of PPE caused by the COVID-19 pandemic, accessing remote areas was crucial. Flemons et al.[21] presented the results of a simulation study, which demonstrated that a scalable fleet of small to large drones could be used to improve accessibility of essential supplies, equipment and remote care.

KEY RESEARCH AND INNOVATION PRIORITIES

Significant advances have been made in critical areas of PPE highlighted during the pandemic; nonetheless, several questions remain.

With the goal of protecting health workers, further studies are needed to generate high-quality evidence comparing medical masks with filtering facepiece respirators for effectiveness and adverse events during extended use, repeated use and in combination with other PPE rather than as standalone items. Additional research is needed to understand practical ways of meeting fit testing requirements for the selection of effective filtering facepiece respirators for individual facial features. In addition, there is an ongoing need for novel respirator technologies designed with fit, filtration, breathability, human behavior, and reuse in mind.

Despite the considerable knowledge generated in the past 2 years on decontamination methods and tools for PPE, several challenges remain, including the need for: comparative studies determining the effectiveness of decontamination methods of medical masks and respirators (including elastomeric and powered air-purifying respirators) as well as other PPE; a framework for post-decontamination quality assurance to ensure all relevant infectious agents have been successfully removed while maintaining the essential parameters of the PPE item; and a monitoring system similar to medical device reprocessing for batch recall and disposal when problems are identified. Moreover, there is still the need to enhance this knowledge in order to provide standardized protocols for implementation of decontamination methods and persistent antimicrobial treatments in real world settings, including low-resource settings.

The critical global shortage of PPE during the COVID-19 pandemic led to unprecedented interest in community masks (also known as nonmedical masks, cloth/fabric masks). Research priorities in this field include the definition of adequate standards for their manufacturing (also local manufacturing), mass production, optimal use, reuse, communication strategies to the public and performance assessment. This last priority should include specific studies aimed at understanding: the efficacy, risks and adverse events associated with the use of community masks in a scenario of universal masking; and the impact and safety considerations of methods to improve key performance parameters such as fit, breathability, filtration efficiency and antimicrobial treatments. Standardized nomenclature to assess the size and qualitative parameters of community masks which are understood by the public would be extremely useful for the community.

This pandemic resulted in prolonged PPE use in health settings beyond manufacturer recommendations and the need to provide sustainable, safe and effective solutions for community use of masks. In extending both the length of use and target population, assessing the human factors that affect the effective and safe use of PPE is crucial, since factors such as discomfort or impact on communication may affect the correct use of PPE, hindering their efficacy, and lead to its removal to facilitate social interactions. Moreover, new methods and tools for monitoring and understanding how PPE is really used outside of recommendations would be useful for improving PPE distribution and understanding compliance with other IPC measures. Questions that could be addressed include, for example: in what situations is PPE used as prescribed in guidance versus reused repeatedly; how long are people using their masks without decontamination or disposal and what are the outcomes of this behavior; how is the structural integrity and other essential parameters of PPE items affected by repeated use; and what microorganisms are present and viable on PPE used for multiple days in both health care and community settings.

In the context of universal use of masks enforced as part of public health and social measures, populations whose specific needs are affected by the use of masks or who have an intolerance of currently available masks require further investigation of relationship to benefits, costs and risks. These populations include children, elderly people, people with hearing impairment or cognitive impairment, people with respiratory impairment, people with autistic spectrum disorders, and people with mental health conditions. Understanding how PPE design can be improved to meet their needs is very important.

In relation to the above priorities, it is crucial to improve international standards and design processes of PPE, and medical and community masks, taking into consideration both the scientific knowledge that has been gained through the course of the pandemic on optimal fit, filtration, and breathability, as well as social science knowledge on physical differences, including differences related to gender (eg, female vs. male) and ethnicity.

The severe shortage of high-quality PPE exposed health care workers to unnecessary risks. Therefore, understanding and overcoming the bottleneck that hindered the mass production and capillary distribution of PPE remains a priority in order to improve the lifecycle of PPE including medical and community masks. This should include optimizing quality control, logistics, management, surveillance, and waste management, thus minimizing the impact on the environment (microplastic leaching) and the need for innovative solutions during severe shortages, including decontamination routes.

After 2 years of the COVID-19 pandemic and the deployment of effective means for mitigating the acute effects of COVID-19 (primarily vaccines), it is time to focus on and scale up an exit strategy for PPE use in the context of current and future emergencies, understanding when and how emergency use of PPE measures should be introduced and when they can be relaxed.

CONCLUSIONS

This commentary outlined WHO's effort to tackle challenges related to PPE during the COVID-19 pandemic, in the context of the IPC priority of the R&D Blueprint and COVID-19 agenda. The pandemic presented multiple challenges and resulted in unprecedented situations on a global scale, such as the need for prolonged PPE use in health care settings and universal masking in community settings.

To tackle the pandemic's complex challenges and respond to the needs of health workers and the people, WHO cooperated with other public health agencies, scientific societies, research institutions, practitioners and scholars with different backgrounds across the world to steer the discussion around research and innovation in the area of PPE, which had been not prioritized for funding in previous research agendas. This effort resulted in significant progress; for example, the creation of a global platform for IPC R&D cooperation which may accelerate research to increase preparedness for future emergencies. One of the challenges of this work was the need to align the visions and terminology that different stakeholders and contributors had related to PPE research and innovation. The need to produce actionable technical guidance required further elaboration of research outputs and the evidence generated by each research project supported through WHO. Over the past 24 months, knowledge gaps and research questions have evolved quickly. Many knowledge gaps were bridged, while new priorities have emerged, as reported in this commentary.

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