the Pontifical Academy of Sciences

Final Statement of the Workshop on SARS-COV-2 Health Policies, Vaccination and Long COVID: Achievements and Challenges

Based on the PAS workshop of 19-20 November 2024

Objectives of the Conference

The Pontifical Academy of Sciences (PAS) has actively addressed SARS-COV-2-related science and societal issues through conferences, statements, and publications. Pope Francis has emphasized the critical role of science in combating the pandemic while advocating for greater attention to equity in health policies. The conference was built on previous initiatives on the pandemic by PAS in 2020 and 2021.[1] PAS remains committed to engaging with science, health policy, and ethical considerations to address the pandemic and its consequences. The objectives of this workshop were to:

1. Draw lessons from diverse health, education and science policies implemented during the pandemic.
2. Review experiences with vaccine innovations, testing, implementation programs, side effects, and communication strategies.
3. Share insights into "Long COVID," including its long-term health consequences, underlying causes, and potential mitigation strategies.

Emerging Lessons from Health and Science Policies

A high-level review of lessons learned from health and science policies during the pandemic

precedes the workshop's focus on vaccines and Long COVID. The COVID-19 pandemic, caused by the spread of SARS-COV-2, has resulted in a profound tragedy, with over 645 million confirmed cases and 6.6 million deaths as of December 3, 2022, with estimates of both much higher. Social and economic recovery remains incomplete.

The workshop examined diverse health policy responses at the global and national level, including prevention measures, such as the impact of lockdowns on health, education and human capital, child development, and vaccination.

The workshop also examined international response efforts such as the COVAX initiative following the announcement of a Public Health Emergency of International Concern (PHEIC) by the World Health Organization.

Insights from Vaccine Innovations and Implementation

The pandemic accelerated vaccine development, leveraging extensive prior research on basic coronavirus biology and immunity motivated by the SARS-CoV-1 and MERS-CoV outbreaks. Due in part to longstanding development of the global research enterprise and pre-existing public-private investments, by August 2022, 356 vaccine candidates were in development, with 34 products approved for large-scale use. Technologies used include mRNA, viral-vectored, inactivated whole virus, protein subunit, and plasmid DNA platforms, each with unique attributes and field application considerations.

Government funding played a crucial role in vaccine development but failed to address intellectual property management effectively. High vaccine costs prevented equitable access in poorer nations for some time, forcing reliance on donations or discounted mechanisms like the Global Alliance for Vaccines and Immunizations (GAVI) alliance. The vaccines pillar of the Access to COVID-19 Tools Accelerator (ACT-A), COVAX was created to enable access to COVID-19 vaccines to the most vulnerable everywhere, regardless of income level. To achieve lasting SARS-COV-2 control, next-generation vaccines with potential for broader epitope coverage, reduction of transmission efficiency, durable protection, and simplified storage and delivery logistics are under development. One of the consequences of unequal access to interventions was the emergence of new SARS-CoV-2 variants and ongoing risk to all populations.

Vaccine Safety, Effectiveness, and Barriers to Vaccination

Surveillance data remains essential for evaluating vaccine safety and real-world effectiveness in preventing infections, severe disease, and mortality. The growing availability of routinely collected health administrative data in electronic form has led to a flood of high-quality controlled observational studies that defined the protection against severe and fatal disease provided by COVID-19 vaccines. These studies have guided policies regarding the timing of booster doses.

While hospitalization and mortality rates have dramatically decreased in vaccinated populations, waning immunity and the emergence of variants have led to breakthrough infections, underscoring the need for booster immunizations being worked into routine vaccination schedules, cost-effective delivery logistics, and sustainable supply chains and production. A universal vaccine remains an aspiration to work on.

Controlled observational studies have also confirmed the safety of COVID-19 vaccines. While some cardiovascular and neurological complications have been confirmed, these are rare and occur with much less frequency with vaccines than with COVID-19 illness. While numerous countries have experienced excess all-cause deaths during and after the COVID-19 pandemic no well-controlled study has linked excess deaths to use of vaccines. In fact, all studies have found lower all-cause mortality in vaccinated than in unvaccinated populations.

Problems with vaccine uptake and access became apparent during the COVID-19 response. Vaccine hesitancy and challenges of disinformation and misinformation related to vaccines, fueled by safety concerns, efficacy doubts, risk perception, and mistrust in authorities, continues to challenge public health efforts. Understanding the drivers of hesitancy and targeting misinformation with clear, context-specific, evidence-based communication can improve vaccination rates and reduce severe illness and mortality. Equitable access to vaccines was associated with cost, socioeconomic status, scientific and public health infrastructure, manufacturing capacity, geography, and political will. Low-income countries had the fewest number of deaths averted by COVID-19 vaccination.

Emerging Science on Long COVID

Long COVID, defined by WHO as symptoms persisting or emerging within three months after infection, significantly impacts quality of life, education, and employment. Although widely recognized, Long COVID’s underlying mechanisms and effective treatments remain poorly understood.

Challenges in diagnosing Long COVID include non-specific symptoms, no universally agreed case definition, a lack of specific diagnostic criteria, variability in self-reporting, and difficulties linking symptoms directly to the infection. Persistent symptoms are reported in up to 35% of outpatients and 87% of hospitalized patients, and the current estimated global cumulative incidence is 5%. The most important risk factors are female sex, comorbidities, lack of vaccination, and recurrent COVID. A subgroup of Long COVID patients suffers from the severe and highly disabling disease Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). ME/CFS is also triggered by various other infections and was already a common and neglected disease pre-pandemic.

Vaccination reduces the likelihood of developing Long COVID. The need to optimize the timing and schedule of vaccination to mitigate Long COVID remains.

Long COVID's effects are physical, mental, social, and economic, necessitating multidisciplinary care, which is often unavailable in many settings. Collaborative research and international surveillance are urgently needed to develop effective treatments, preventive strategies and inform policies addressing healthcare, education, employment, and social support.

Key Findings

1. Health and Science Policies During the Pandemic:

- The pandemic exposed strengths and vulnerabilities in global health and science systems. Effective responses were often hindered by upstream science policy failures and downstream implementation challenges.
- The inadequacy or failure of global health governance, together with the source nation's delayed disclosure of the human-to-human infectious nature of the emerging disease, led SARS-CoV-2 to spread throughout the world and became a devastating pandemic.
- This pandemic illustrated the weakness of the existing global bond as a community, challenged by demonstrated actions of pandemic nationalism.
- Control strategies were varied in their approach and stringency. Approaches to managing the COVID-19 pandemic need to take the context into account. What may be effective and acceptable in one context may not be in another. Lockdown policies, while necessary at times, had significant health, education, and social consequences, particularly for children who lost months of schooling, and were isolated from their peers.
- Access to COVID vaccines remain unequitable. Initiatives like COVAX demonstrated the value of global cooperation. These efforts sought to ovrcome inequities in vaccine access for low-income countries, primarily due to cost barriers, lack of logistic infrastructure to support its delivery, and intellectual property constraints.
- Phytotherapy and aromatherapy were used to reduce symptoms of COVID-19 in some countries. The use of medicinal plants in the COVID treatment deserves further investigation.

2. Vaccination Innovations and Challenges:

- The rapid development of SARS-COV-2 vaccines was a testament to decades of public and private investment in research. However, intellectual property management, vaccine hoarding and wastage, and pricing issues restricted equitable access.
- Vaccine hesitancy, fueled by misinformation and real or perceived side effects, remains a critical barrier to achieving optimal vaccination rates.
- The effectiveness of current vaccines in preventing breakthrough infections and severe disease diminishes over time, mandating continued use of booster doses in at-risk groups. A universal vaccine remains an aspiration to work towards.
- It is essential that individual countries develop the capacity to estimate and then monitor vaccine effectiveness using appropriate analysis of routinely collected health data.

3. Emerging Science on Long COVID:

- Long COVID affects a substantial proportion of individuals post-infection, with symptoms ranging from mild to debilitating.
- Its causes are multifactorial and remain incompletely characterized, potentially involving chronic inflammation, viral persistence, organ damage, and immune dysregulation.
- The condition has wide-ranging effects on quality of life, education, employment, and healthcare systems, with vulnerable groups being disproportionately affected.

4. Health Inequities and Social Impacts:

- Low-income and marginalized populations experienced higher mortality rates and reduced vaccine access, exacerbating health inequity at the global level but also within countries.
- Inadequate healthcare infrastructure hinders access to care for Long COVID and vaccination in underserved regions.
- Remote schooling, introduced as a solution to school closures, exacerbated the gap between children who had access to technology and those who lacked it, as well as between those with parental support in terms of time and capacity and those without.

Recommendations

1. Policy and Governance:

- Explore and develop an effective global health governance and collaboration mechanism that can effectively prepare for, respond to and prevent new pandemics from taking place.
- Identify effective mechanisms and strategies to ensure equitable access to prevention, vaccines and treatments. This may include global frameworks including mechanisms to address intellectual property constraints and pricing disparities and leveraging technology to rethink the global manufacturing and supply chains. Nurture the values of sharing and caring that are essential to bond global villages as a global community.
- Develop and fund resilient health systems capable of handling future pandemics, focusing on vulnerable populations and equity.
- Enable education systems to effectively prepare for future pandemics, ensuring that all pupils and students have equitable access to education, whether through remote learning or in-person schooling.
- Ensure that appropriate data systems are established to monitor the distribution effectiveness of new vaccines.

2. Vaccination Strategies:

- Prioritize research and development of generalizable vaccine designs that can be applied to related pathogens. Increase research and manufacturing capacity of LMICs to work on diseases of regional importance. Emphasize vaccine product characteristics that provide broad immunity, longer protection, and reduced logistical demands.
- Strengthen surveillance to rapidly identify emerging threats and to monitor vaccine safety,

effectiveness and coverage, addressing vaccine hesitancy through transparent, tailored communication and community engagement.

3. **Addressing Long COVID:**

- Invest in multidisciplinary research to understand the mechanisms of Long COVID and develop effective mitigation and treatment strategies.
- Implement integrated care models that provide comprehensive physical, mental, and social support for individuals with Long COVID.
- Create international registries and surveillance systems to track Long COVID prevalence, risk factors, and outcomes.
- Invest in multidisciplinary research to understand the mechanisms of Long COVID and develop effective treatments and preventive strategies.

4. **Public Health Communication:**

- Counter misinformation through higher standards in the science community for interpretation and communication of research results to the media and the public.
- Counter false information through evidence-based campaigns and foster trust in scientific and healthcare institutions.
- Address vaccine hesitancy in specific populations, understanding context-specific barriers and enablers to design context-specific communication strategies that fit the socio-cultural setting.

5. **Global Cooperation:**

- Promote international collaborations for research, vaccine distribution, and treatment strategies, ensuring low-income countries have access to essential resources.
- Encourage partnerships between governments, academia, philanthropy, NGOs, and industry to address gaps in pandemic preparedness and response.
- Strengthen reasoning of ethical considerations and calling on religious communities, including the Church and the Vatican, to facilitate ethical discourse in support of science and voice of marginalized communities, to nurture the willingness and capacity to share and a sense of global community, and to promote Christian ethics for the care of the sick, while respecting the lives of all the sick.
- A global pandemic prevention, preparedness and response action plan, with input from all the actors including WHO, other international organizations and stakeholders, such as Gavi, CEPI and civil society organizations, should be developed and agreed upon by the end of 2025.

Conclusions and Next Steps

The SARS-COV-2 pandemic has underscored the need for an integrated approach to health policy, science, and social equity. By addressing lessons learned and investing in innovation, equitable access, and global collaboration, the international community can better prepare for future health crises while mitigating the ongoing impacts of COVID-19, particularly Long COVID, in

LMICs. Immediate and sustained action is required to build resilient systems that prioritize equity, transparency, and scientific advancement.

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1 Workshop 4-5 November 2021. *SARS-CoV-2: New insights into the causes, actions and consequences of the pandemic, and implications for science and health policy*. https://www.pas.va/en/events/2021/newinsights.html

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10.1126/science.abc2255.https://www.pas.va/en/events/2020/sars-cov-2.html