World Health Organization

Emerging trends and technologies: a horizon scan for global public health

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Preface

This publication presents the findings of a global horizon scan on emerging technologies and trends relevant to global public health conducted in 2020 and 2021. We identified 15 new and emerging technologies and scientific advances that may have a significant impact on global health over the next two decades.

WHO strives to remain “ahead of the curve” in relevant areas of research, science and technology in order to proactively identify, anticipate and shape issues that hold promise for prevention, diagnosis and treatment. The Global Health Foresight function was established in the WHO Science Division for this purpose and to assist Member States in building “futures thinking” into their strategic health planning.

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The horizon scan was conducted by a global expert group that identified and scored the topics and provided invaluable guidance and support throughout the project. WHO expresses its sincere appreciation to all members of this group for their contributions and review. They were (in alphabetical order):

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Declarations of any competing interests were received from all experts who participated in the working group. None of the interests declared were found to be significant. WHO would like to express its sincere appreciation to all members of this group for their contribution, input and review.

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Introduction

Advances in science and technology hold great promise and hope for new and improved ways to address global health and ensure healthier populations worldwide. They could potentially fundamentally transform global health. This horizon scan presents 15 priority topics, including ethical and societal challenges, and risks and opportunities that require closer attention.

Science and technology have undisputed roles in reaching the "triple billion" targets *(1)*, an ambitious WHO initiative to improve the health of billions of people by 2023. They are the foundation of WHO's Thirteenth General Programme of Work, which is "both a measurement and a policy strategy". Shaping the global research agenda and stimulating the generation, translation and dissemination of valuable knowledge is one of WHO's core functions. The 13th General Plan of Work (2019–2023) mandates WHO to "be at the forefront of… new scientific fields and the challenges they pose" and to closely monitor and provide guidance on "developments at the frontier of new scientific disciplines".[1]

The WHO Science Division established the Global Health Foresight function to monitor developments and assist Member States in building "futures-thinking" and "horizon-scanning" into strategic health planning. The aim is to help them to better anticipate and prepare for a changing world, to accelerate and to fully harness the gains offered by new and emerging technologies, while monitoring the risks and challenges that might arise from use of those technologies.

WHO is committed to the highest standards of scientific quality and ethical integrity. Therefore, new and emerging technologies and changes in the scientific landscape must be addressed proactively. Horizon scans have proved useful in identifying emerging opportunities and risks associated with societal and technological change. For this study, the scan was based on structured elicitation of information from experts convened by WHO's Science Division. The experts, drawn from a range of disciplines, undertook a broad analysis of scientific and technological developments that could significantly affect global health during the next two decades and identified 15 priorities. The priorities were then classified by the experts by timeframe, into those that are likely to become prominent in < 5 years to ≥ 10 years. The priorities range from issues of governance to details of new technologies.

[1] The General Programme of Work provides guidance for deciding appropriate measures to impact health. See https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019---2023.

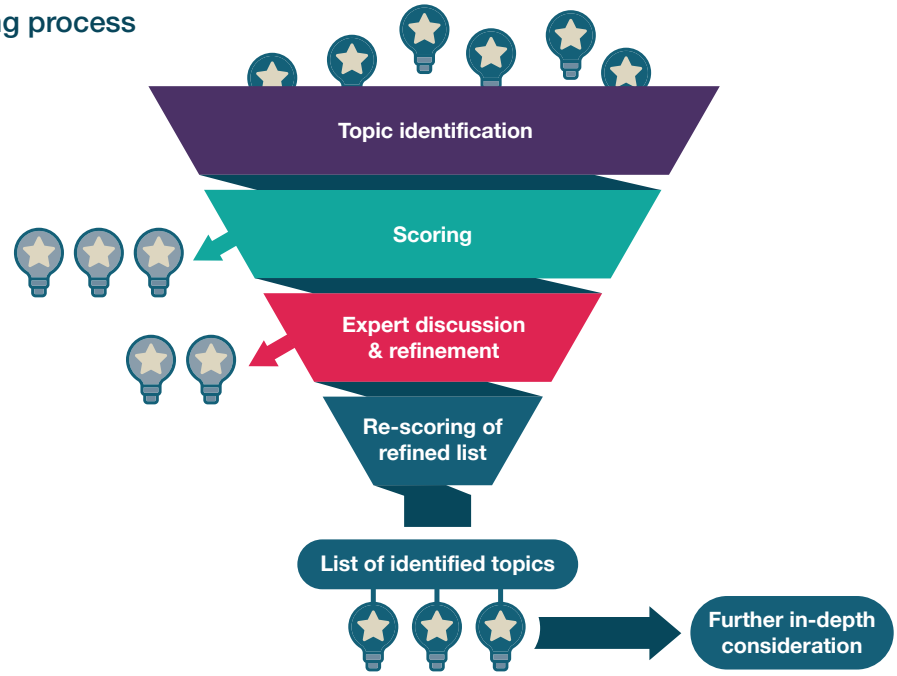
Methods

In the method used for the horizon scan, contributors anonymously proposed issues that they considered would shape the future of global health and were of relevance to WHO. The issues were then anonymously scored, ranked and discussed according to criteria of impact, plausibility and novelty. This shortlist was then debated over a 2 week period, before anonymous rescoring and refinement to draw up the list of priorities (Fig. 1). We used the "investigate, discuss, estimate, aggregate (IDEA)" protocol of structured expert elicitation *(2)*, drawing on 29 experts who proposed the issues and participated in scoring. 16 of whom participated in further consultations (those listed in the acknowledgements). This approach has performed better than other foresight techniques and has been used in diverse areas, such as bioengineering and natural resource management *(3)*. We followed both the general principles in the practical guide to the IDEA protocol *(4)* and previous examples, with minor modifications. We gave the participants summaries of other horizon scanning exercises, briefing notes on judgement and biases, templates for describing issues and instructions for consulting research monitoring platforms (see annex). Global health already has a wealth of foresight initiatives that we sought to build on by providing them to our contributors.

Phase I: Recruitment of contributors and issues

For recruitment, we followed both the practical guide for using the IDEA protocol *(4)* and successful applications. Our aim was to identify a diverse group of experts balanced by discipline, geographical distribution and gender. We explicitly ensured that the participants met these criteria, as discipline, age, cultural background and gender are effective proxies for diverse perspectives, which ensures broad issues and improves the quality of deliberation *(5)*.

Fig. 1 **Steps of the horizon scanning process**



We began by approaching individuals known to the organizers and then used a "snowballing" technique, whereby these diverse individuals with wide networks were asked to recommend other relevant experts. Further candidates were identified in a brief literature review. The combination of sampling from the literature, snowballing and screening according to explicit criteria ensured that the group was diverse. Each individual submitted a declaration of interests as a condition for participation. None of the interests declared was found to be significant.

The exercise yielded a pool of participants with an equal gender balance. Most participants had a background in natural science; six had a background in social science. All six WHO regions were represented in the group of invited participants who identified the initial long list of issues.

Of those identified, 33 experts in various areas were invited to participate, and 29 confirmed their participation. The participants were asked to identify issues "that will shape the future of global health" and were informed that the issues would be evaluated according to their plausibility, impact and novelty (although we noted that previously identified issues could also be proposed). Participants were given several aids to ensure good judgement, including directions to use review platforms such as Meta and the WHO's Global Observatory on Health R&D, a short Foresight training document for practising good judgement, a list of background reading, including previous scans, and a template for proposals.[2] The intention was to ensure that participants had access to the latest foresight exercises and results. The 29 contributors proposed 68 issues, which were combined into a long list of 58 issues, with six created by merging 16 overlapping proposals. The contributors drew on a broad network of experts in proposing topics.[3]

Phase II: Scoring and refining

The contributors were given the long list of identified topics and asked to allocate a score of 1–100 to each issue to reflect its impact and its plausibility. They were also asked to comment on each issue and indicate whether they had already heard of it. Z-scores were calculated by subtracting the mean and dividing by the standard deviation for each issue against the set proposed by each participant to account for different scoring spreads of individual participants, as some scored generously and others more critically. The scores were then ranked by average z-scores, and the first 27 (approximately half) issues were retained. The shortlist, with comments, novelty score and rank of each issue, was then shared with the participants.

Phase III: Deliberation and aggregation

We used an online discussion forum for the deliberation phase.[4] Face-to-face meetings are frequently used for structured expert elicitation, as they are easy to facilitate and ensure participant interaction, engagement and rich discussions through non-verbal cues and body language. They may also result in participants being swayed by face-to-face dynamics. We chose an online forum mainly because of the restrictions imposed by the COVID-19 pandemic. It had the benefit of mitigating biases that may emerge during in-person interaction but had the shortcomings of online interactions.

Before the discussions, each participant was asked to explore at least two issues on the shortlist other than those they had proposed. Thus, every issue was examined by at least three participants who had done background research – the two researchers and the proposer.

The online discussion forum lasted 2 weeks (8–27 February 2021), during which the participants critically discussed the issues and their merits. The forum included two 2 hour "summits", which participants were asked to attend. They were asked to contribute to at least one summit and to provide comments on at least half of the issues. They then scored the shortlist, and the organizers calculated new z-scores and produced final rankings. This list was approximately halved again to the list presented here, with four issues merged into two ("digital health and privacy" and "pandemic preparedness and prevention"). The participants agreed by consensus to limit the list to 15 issues to ensure focus and a proper analysis of each issue.

[2] The foresight training document and a list of background information is annexed to this report.
[3] We estimate that they consulted approximately 270 other experts from the lists of the numbers of people they consulted for each issue they submitted; however, the contributor networks might overlap.
[4] All contributors were asked to submit declarations of interest to WHO. All 16 submissions were cleared, and the 16 experts participated in the final stages of deliberation and re-scoring.

Results

The topics cover a wide range, from emerging areas of science and technology, to novel applications and practices and broader trends. The issues are summarized below, with indications where action is required and where action is already under way. The timeframes are indicative only. Many of the issues are already relevant or are having tangible impacts.

The 15 issues are listed in Table 1, ordered by time to realization: < 5 years, 5–10 years, ≥ 10 years. These three timeframes are estimates arrived at by consensus by the participants.

They are thus judgements and not concrete, calculated timelines. We have not ranked the issues by their final scores to avoid giving an undue sense of certainty and precision.

Table 1 **Global health priorities ordered by probable timeframe**

Timeframe	Issue
< 5 years	Pandemic preparedness and prevention
	Vaccine distribution
	Machine learning for antibiotic discovery
	Apps for disease screening
	Coordinated biobanking
	Addressing misinformation and disinformation
	Using real-world evidence
5–10 years	Biosensor-based point-of-care diagnostic methods
	Artificial intelligence-assisted clinical reasoning support systems
	Pull-through drug development
	Genetically engineered phage therapy
	Digital health and surveillance
≥ 10 years	Telemedicine
	Microbiome-based therapies
	Migrant health

Issues identified to become prominent within 5 years

Pandemic preparedness and prevention

A response to the COVID-19 pandemic requires a significant shift in resources and attention towards pandemic preparedness, particularly for zoonotic infections. Pandemics are likely to become more complex, frequent and difficult to contain for various reasons, including climate change, urbanization and interconnectivity *(6)*.

An area for significant improvement in pandemic preparedness and response is trials of therapeutic interventions. A recent review by the US Food and Drug Administration *(7)* indicates that only about 5% of almost 2900 trial arms for potential COVID-19 therapeutics (involving > 500 000 patients) could be considered both randomized and adequately powered. Most of the studies could not provide useful results for the pandemic. Adaptive platform trials, in which multiple interventions are studied continuously, offer a promising way forward *(8, 9)*.

As finance and policy shift towards infectious disease, efforts must be made to ensure that coordinated multilateral action prevails over national unilateralism. The Seventy-fourth World Health Assembly recommended a timely start to negotiation of an international treaty on pandemic preparedness and response. On 1 September 2021, the WHO Hub for Pandemic and Epidemic Intelligence was inaugurated in Berlin, Germany, and on 1 December 2021 a Special Session of World Health Assembly agreed by consensus to start a global process to draft and negotiate a convention, agreement or other international instrument under the Constitution of the World Health Organization to strengthen pandemic prevention, preparedness and response.

Vaccine distribution

More coordinated, effective systems of vaccine production and global distribution will be necessary both in the coming years, as COVID-19 vaccination programmes unfold, and in the longer term, as countries prepare for future disease outbreaks. During COVID-19, wide inequity in vaccination distribution have become apparent, ranging from "vaccine nationalism", whereby countries prioritize their own populations over the global good, to "vaccine diplomacy", whereby countries strategically provide vaccines to others for geopolitical ends. Targeted, equitable, efficient distribution of vaccines would contain the pandemic sooner, lower global morbidity and mortality rates and reduce the chance of new strains arising *(10)*.

Improving vaccine access will require coordination and significant changes to current approaches, not only extending vaccine production. Vaccines must also be accessible, affordable, trusted and used efficiently *(10)*. Achievement of each of these criteria will require a cooperative global approach.[5]

Machine learning for antibiotic discovery

Machine learning, one layer of artificial intelligence, could become an important tool against the growing threat of antibiotic-resistant microbes. Applications of machine learning in the field of in-silico drug discovery and virtual trials have already resulted in important breakthroughs. For instance, deep-learning algorithms based on chemical libraries have been used to discover structurally distinct, effective antibacterial molecules *(12)*. Similarly, computational tools based on machine learning have predicted the best drug combinations for antibiotic effectiveness in the microenvironments of various pathogen *(13)*. These tools offer means to expedite the identification of candidate antibiotics and simulate their performance in different pathogen environments.

Use of machine learning for antibiotic discovery is not, however, a panacea. As noted elsewhere in this report in relation to drug development incentives, significant market failures have already

[1] The United Nations Secretary General issued "a wake-up call" in his Common Agenda report, which contrasts a world in which vaccines are shared to one that does not *(11)*.

been seen with the current "push-through" model, which has resulted in an undersupply of new antibiotics. Moreover, antibiotic production is a long process, and drug discovery is only one step, followed by intricate, complex, expensive stages of optimizing compounds into drug candidates and conducting clinical trials. While this application of machine learning is not a cure-all, it is nonetheless encouraging and will probably become more widely used. Fundamental research in this area is critical to establish a variety of discovery platforms that can be adapted for antimicrobial resistance, other pandemics and other major diseases.

Apps for disease screening

The wide availability of smartphone apps represents a new source of biomedical data and early disease diagnosis. The advantage of such applications is their accessibility (particularly in remote or rural areas) and low-cost, real-time, point-of-care diagnosis. There are already multiple applications, for example, apps and sensors on a phone can take an electrocardiogram to check for dangerous arrhythmia or improve treatment of hypertension by taking continuous blood pressure readings *(14)*.

These potential benefits are accompanied by challenges, which include exclusion or marginalization of groups with poor access to technology, algorithmic biases, lack of data verification, privacy issues and overdiagnosis through self-diagnosis. It will be important to standardize disease screening apps.

Coordinated biobanking

In a future of greater vulnerability to pandemic threats, biobanking and surveillance systems will become increasingly relevant. Zoonotic pandemics are most likely to emerge in low- and middle-income countries (LMICs), which may be hotspots because of more interactions between humans and wildlife *(15)*. Both urbanization and climate change will probably exacerbate this situation. Emergency responses to pandemics rely on biobanking for monitoring, surveillance, testing and diagnostics, and biobanks were widely used in response to both the Zika virus and the SARS-CoV-2 outbreaks *(16)*. Information provided by biobanks is vital for timely identification and preparation of vaccines and therapies.

Currently, there are few reliable indicators of the quality of samples in biobanks, and standards tend to be from researchers' experience rather than solid research findings. There are no international standards based on peer-reviewed studies *(17)*. In November 2020, WHO and the Swiss Confederation signed a memorandum of understanding and launched the first WHO BioHub Facility as part of the WHO BioHub System[6] to ensure timely sharing of epidemiological and clinical data and biological materials among laboratories and partners globally *(18)*.

Addressing disinformation and misinformation

Disinformation (when false information is knowingly shared to cause harm) and misinformation (when false information is shared, but no harm is intended) are widespread. Misinformation and disinformation distort discussions, misdirect regulation, undermine social cohesion and erode trust in critical institutions. Distorted and false information can be detrimental to global public health initiatives. The effect is magnified by reliance on social media and the Internet as sources of news, fragmentation of the information landscape and coordinated, targeted use of disinformation at unprecedented speed and scale.

Most methods to counteract mis- and disinformation are still in their early stages, and their effectiveness is uncertain. Still, such methods are a critical part of public health policy.

WHO is working to build resilience against misinformation and disinformation. For example, WHO's Information Network for Epidemics (EPI-WIN) was established following the outbreak of COVID-19 to provide essential information about risks, amplify tailored, timely information to specific sectors, convene expert groups and provide

[6] The WHO BioHub System facilitate sharing and access to biological materials with epidemic or pandemic potential for the development of health products including diagnostics, vaccines and therapeutics and to ensure fair and equitable access to such products. For more information, see: https://www.who.int/initiatives/who-biohub

scientific evidence to disprove misinformation and fight "infodemics".

Using real-world evidence

The use of real-world evidence is expected to increase significantly within the next 5 years. "Real-world evidence" refers to observational data in health that are not derived from randomized controlled trials but from sources such as follow-up of trials, longitudinal cohort studies and other structured epidemiological analyses of data from, for example, public health services, insurance companies, electronic medical records and patient registries. This type of evidence is already used in some countries in making regulatory decisions. It offers the prospect of expedited scientific and regulatory decisions and provides a means for studying diseases, including rare diseases, for which randomized controlled trials are not feasible. If used properly, it is an approach in which patients have a greater voice in making decisions, as they report their own outcomes *(19)*. Real-world evidence should not be considered a substitute for clinical trials but, rather, a complement that provides additional information, reduces uncertainties and can also broadly confirm effectiveness and safety in clinical care *(20)*.

A globally harmonized regulatory approach is necessary for collecting, reporting and using real-world evidence. Templates for designing and conducting reproducible real-world evidence research have been suggested *(21)*. Initiatives such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use and the International Coalition of Medicines Regulatory Authorities are starting to coordinate use of real-world evidence.

Issues identified to become prominent within 5-10 years

Biosensor-based point-of-care diagnostic methods

Alternative point-of-care diagnostic platforms will become increasingly important and available. Infectious diseases are the leading cause of death in LMICs, where the majority of mortality is attributable to improper diagnosis and treatment, including lack of access to health-care infrastructure *(22)*. Biosensor-based point-of-care diagnostic platforms with chemical, magnetic, optical or nanotechnological modalities *(22, 23)* are cheaper, more accessible, more effective alternatives to polymerase chain reaction methods. Biosensor-based point-of-care diagnosis allows better, earlier diagnosis, monitoring and management and improves patient outcomes.

New diagnostic platforms themselves will not be sufficient. Patients, particularly in LMICs, already have difficulty in navigating diagnostics systems. This should be accounted for in any new point-of-care method, with new ways to facilitate patients' use of diagnostic services *(24)*.

Artificial intelligence-assisted clinical reasoning support systems

Computerized systems to support medical decisions will increasingly be adopted in the next decade. Such systems have been referred to as "clinical decision support systems" or "clinical reasoning support systems", as a final decision is still taken by a practitioner on the basis of various sources of information. Clinical reasoning support systems can provide statistical reasoning and pattern recognition, but interpretation and application to individual patients still require a clinician *(25)*. Such systems can provide alerts or reminders, recall and facilitate use of clinical guidelines during care, provide advice about possible diagnoses or treatment plans and identify drug–drug interaction. Numerous studies and systematic reviews have been conducted on clinical reasoning support systems. Recent reviews concluded that the impact on clinical care is small to moderate *(26, 27)*, at least so far.

Issues raised about use of these systems include the reproducibility, reliability and quality of data, especially in countries without the appropriate infrastructure. Other concerns are algorithmic biases, workflow disruption, over-reliance and, conversely, "alert fatigue", the cost of introduction and operation and integration into the training of health professionals.

Pull-through drug development

The current system of drug development is a "push-through" model, which mainly reflects commercial interests *(28)*. Global needs are not sufficiently addressed by the current system. These needs include the WHO list of neglected tropical diseases, emerging infectious diseases on the WHO priority pathogen list for research and development, tuberculosis, malaria and specific requirements for treating cancer, hypertension, malnutrition, obesity and diabetes in LMIC.

Numerous market failures and challenges lie behind the current situation. Drug development is a complex, multidisciplinary endeavour. The creation of innovative drugs in particular is prone to failure. During the past decade, only 15 antibiotics have been approved by the US Food and Drug Administration, and 7 of them were supported by companies that have since gone into bankruptcy or have capitalization that represents only a fraction of the funds required for research and development to bring the antibiotic to the market *(29)*.

In a change to a "pull-through" system, drug developers could act as contractors who are instructed to develop drugs with the highest societal interest. One promising initiative for an appropriate pull incentive involves governments purchasing contracts for new drugs on subscription. This system has been adopted by the National Health System in the United Kingdom, which committed up to £10 million per year for 10 years for two new antibiotics *(30)*. The aim is to delink antibiotic revenue from drug use. The largest potential for a pull-through system, greater government involvement and subscription-based models is for antimicrobials, vaccines and diseases that mainly affect LMICs, resulting in a high global disease burden.

Genetically engineered phage therapy

WHO has identified the lack of new antibiotics to overcome antibiotic resistance as a worsening problem. It has been estimated that antimicrobial resistance could result in 10 million additional deaths per year by 2050, with an economic cost of US$ 100 trillion in loss of productivity *(31)*, which will be borne mainly by LMICs. Genetic modification of bacteriophages is the basis for one promising antimicrobial agent. While phage therapy has been in use since 1919, its use has resurged during the past two decades with the availability of more sophisticated genomic editing tools. The first report of successful clinical use of genetically engineered phages was published in 2019 *(32)*.

Phage therapy is a novel, effective treatment for antimicrobial-resistant infections; however, there are persistent barriers to its widespread use. These include the instability of phage therapies, currently high costs and their specificity for a particular infection, rather than a broad-spectrum approach. Affordable, stable, sustainable, "off-the-shelf", mix-and-match, engineered phage collections are necessary, with fast-turnaround and precision diagnostics to guide their rational use. The effectiveness of the therapeutics in combating antimicrobial resistance is closely linked to accurate, rapid diagnostic tools.

WHO has yet to include phage therapy officially in its action plan against antibiotic resistance. Phage therapy would be most beneficial in localized applications, with international sharing of information to facilitate phage matching and global standards to constrain the use of phages. WHO is in a unique position to fulfil the role of local, national and global coordination *(33)*.

Digital health diagnostics and surveillance

Digital health diagnostics are proliferating, bringing an influx of data and benefits and the possibility of more timely surveillance. "Digital health" broadly refers to the use of information and telecommunications in medicine. This includes wearables, genomic databases and health information technology. The amount and range of health data that have been captured and stored have increased during the response to COVID-19. Use of interconnected digital diagnostic tools could ensure faster, more accurate diagnoses, fewer mistakes, better monitoring, lower costs and better access to health care in underserved areas. Interconnected systems with large amounts of health data, however, also pose issues of privacy.

Surveillance through digital health and medical devices is thus an area of increasing concern. "Surveillance capitalism" through profitable commodification of personal data is already a dominant global business model *(34)*. Previous horizon scans have highlighted genomic surveillance by states and law enforcement as an emerging problem that requires coordinated policy *(35)*. Potential surveillance for profit or political purposes is highly likely in a world of widespread digital diagnostics, including wearables. Early studies suggest that users of wearable medical devices are unaware of the risks to their privacy (36). The possible implications include pressing ethical questions as insurance companies impose more targeted premiums based on health data. At the same time, solutions for good governance of health data are emerging, such as health data cooperatives *(37)*.

WHO is aware of the challenges and opportunities of digital health and has issued both the Global strategy on digital health 2020–2025 *(38)* and guidelines on digital interventions *(39)*. While the strategy mentions the importance of robust privacy policies, these vary substantially by region and are often inadequate or lacking.

Issues identified to become prominent within 5-10 years

Telemedicine

"Telemedicine" is a broad term, encompassing tele-consultations (remote clinical care), tele-monitoring (digital systems that transmit biomedical and other data from patients to physicians), tele-collaboration (between on-site and remote physicians) and tele-support for patients (such as electronic reminders of appointments). While we use the broad, encompassing term here, we note that each application has specific problems and opportunities and requires in-depth examination.

The use of telehealth, virtual technology and remote monitoring has surged in recent years and further accelerated during the COVID-19 pandemic *(40)*. Use of telemedicine to maintain patient access to health care and to supplement scarce health-care infrastructure is expanding.

In the long-term, telemedicine could become a dominant method of primary care in many countries. Telemedicine, including the widespread use of mobile phones, simple wearables and electronic exchange of patient data, offers many benefits, including better access for patients in rural and remote areas, lower cost and greater efficiency *(40, 41)*. Håowever, these developments must be accompanied by relevant policies and measures. Potential drawbacks include cross-border regulation, privacy concerns and biometric surveillance *(42)*, misuse of data, exclusion of populations with poor access to technology and monopolization. Widespread adoption of telemedicine is likely to have various limitations as compared with in-person care *(41)*.

Microbiome-based therapies

Recent research suggests that the human microbiome is pivotal to human health. Metagenomic studies on the human microbiome have revealed possible links between the gut microbiome and human diseases such as depression, rheumatoid arthritis and diabetes. Epidemiological studies have established clear relations between factors that disrupt the microbiota in infancy and subsequent immune and metabolic conditions, such as obesity, allergic conditions and bowel diseases *(43)*. Better understanding of the microbiome could pave the way for wide-ranging preventive measures and therapeutic interventions, from changes in diet and exercise to pharmaceutical products, particularly for chronic conditions and also for transmissible diseases. Many such measures and interventions may be low-cost and particularly useful in LMICs.

To date, however, evidence that modulation of the microbiome can have a therapeutic impact in humans is limited. The strongest evidence at present is for recurrent Clostridium difficile infection, for which a positive outcome has been reported in a phase-III trial of a stool-derived gut microbiota capsule *(44)*. There is preliminary clinical evidence that microbiome-based therapies can affect responses to cancer immunotherapy. International collaboration is necessary to integrate and build on initial work to guide clinical and translational studies in the field *(45)*.

There is nevertheless considerable debate about what constitutes a healthy gut microbiome and its role in health and in the etiology of disease *(46, 47)*.

Migrant health

Both intra- and inter-state migration is set to increase further in the future. Much will be due to climate change and its probable effect on disease emergence and dynamics, conflict, politics and food security. By 2070, one third of the future global population could live in areas with a mean annual average temperature of 29°C, a level currently experienced by only 0.8% of the global land surface area (mainly in sparsely inhabited parts of the Sahara desert) *(48)*. Estimates of migrant flows derived by modelling vary, and prediction is inherently difficult; however, there is evidence that environmental change significantly influences mobility and migration, particularly in LMICs *(49)*.

Currently, migrant populations are not always adequately served by existing public health arrangements. In addition, health-care systems are not optimized for migrants in terms of language, access, genomic data and expertise. Noncommunicable disease and mental health problems are particular concerns, whether they be psychological trauma, low vaccination rates or lack of access to antenatal care for pregnant women *(50)*. The problems are compounded in refugee communities, which frequently have poor facilities and hygiene and a high population density.

WHO is actively engaged in the issue and is mapping trends in public health and migration policies and best practices in addressing migrant and refugee health *(51)*.

Discussion

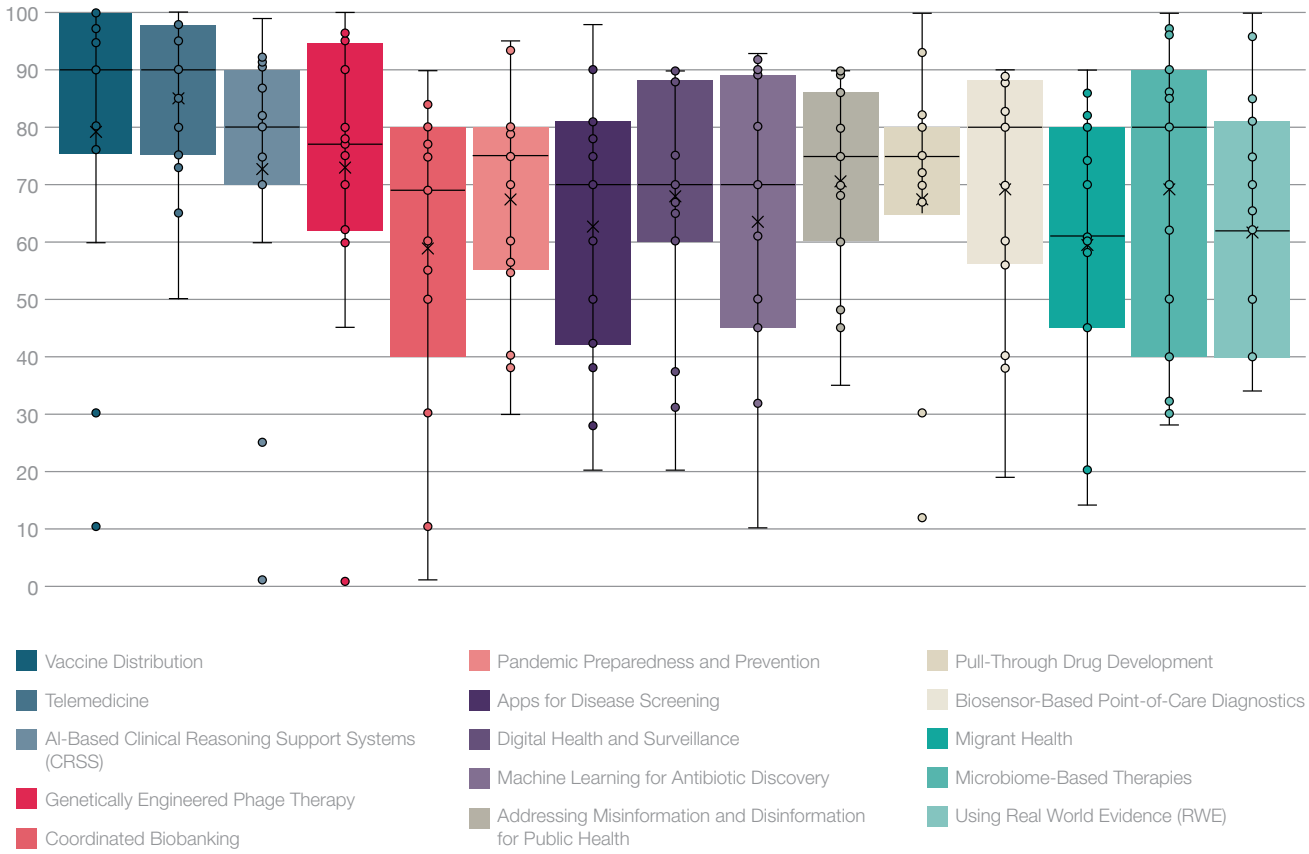
The priorities described above fall broadly into three overlapping areas: changes in science and technology, changes in practices and broader societal and global trends. It must be stressed that these are global trends, and the benefits and risks of the solutions are not equally distributed and differ according to the local context. Issues of access and equity, the distribution of negative and positive impacts and emerging trends in science and technology must be critically assessed.

Many of our priorities are intricately linked. For example, pull-through drug development incentives and the associated market failures were brought up in discussions in relation to vaccine distribution, pandemic preparedness, microbiome-based therapies and genetically engineered phage therapies. In these cases, the political economy of drug development is closely intertwined with emerging therapeutic treatments and also with problems that have arisen during management of the pandemic. Although addressing underlying market failures is likely to have a disproportionate effect on global health, these are likely to be "the most difficult levers to pull".

Fig. 2 provides an overview of the variation in the scoring of the list of priorities. Notably, there was strong convergence on the issues pertinent to the pandemic, during which the exercise was conducted. These are vaccine distribution, pandemic preparedness, telemedicine and, to a lesser extent, pull-through drug development.

Fig. 2 **Variation in scoring the priorities in the second round**

The "box" represents the interquartile range, and the extending lines the minimum and maximum scores. Hence, the issues with the smallest boxes and extending lines indicate the greatest convergence of opinion.

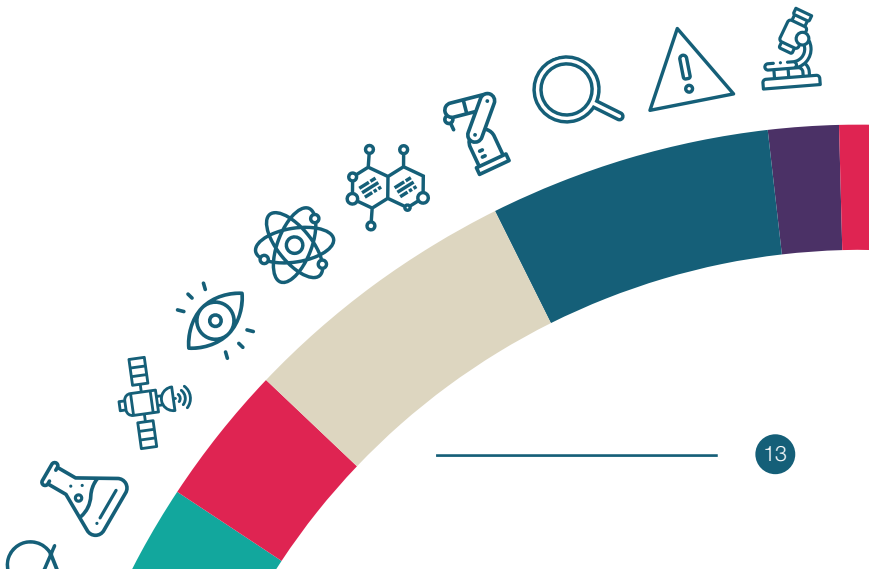


A particularly strong link was found between use of digital technologies and algorithms, including telemedicine, digital health diagnostics, machine learning for antibiotic discovery, apps for disease screening and real-world evidence. The move towards use of machine learning and digital services as enabling tools is accompanied by similar challenges and problems, which include biases in data, the reproducibility of data, the problem of explaining "black box" algorithmic decisions, data privacy and potential vulnerability to cyberattacks. There has already been a wealth of research on the ethics of artificial intelligence, with a corresponding proliferation of ethical guidelines and principles. Guidelines have been mapped globally *(52)*, and the ethical issues of artificial intelligence have been addressed for both, health broadly *(53)*, and the COVID-19 pandemic, in particular *(54)*.

Some of the issues identified by the group were broad, overlapping, poorly defined areas, such as "telemedicine" and "digital health". The group agreed that these areas should be defined more precisely, particularly by WHO. Providing definitions is beyond the scope of this publication; however, as noted for "telemedicine", the general terms often cover more discrete topics (such as tele-monitoring and tele-collaboration), with their particular risks and opportunities. Future foresight might provide a more granular analysis of the more significant issues.

Our scan addressed slightly more technological trends than changes in disease profiles and health. Of our 15 priorities, 7 were mainly policy issues, while 8 were on emerging technologies and therapies. An alternative approach would be to focus on emerging health problems and then identifying solutions; however, demographic changes in health and disease profiles tend to be monitored and assessed better by existing initiatives. This is particularly true for infectious diseases, which are continuously analysed in initiatives such as the Global Public Health Intelligence Network, HealthMap and EpiSPIDER.

Our exercise, like all structured expert elicitations, has limitations. First, it indicates the combined expert judgement of the participants. Secondly, there appeared to be a systematic bias against novel issues, as none of the issues in the initial list that had a novelty score < 60% were carried over to the short list. This reflects a problem of Delphi-like techniques, including the IDEA protocol used here, which frequently do not capture high-impact, low-probability events (55). Thirdly, our sample of experts was limited to 16, which is sufficient but ultimately small for a structured expert elicitation exercise. A larger sample with greater representation from regions such as Africa would be preferable. Fourthly, COVID-19 substantially influenced the study, as our contributors and participants work in fields in high demand during the pandemic; hence, the horizon scan was delayed at all stages and did not include any face-to-face interaction, limiting conversation and in-depth discussions on each topic. Overall, this study should be viewed primarily as a form of forward-looking prioritization of issues pertinent to WHO. The aim is not to predict events or to identify highly novel developments but rather to identify trends and emerging technologies to address opportunities and challenges as early as possible.



Conclusions

In this horizon scan, we identified various technical, societal and economic issues that deserve close attention. WHO is already addressing a number of these areas and is actively engaged, for example, by convening expert groups, issuing guidelines and guidance and setting norms and standards on many of the topics identified.

As WHO extends its foresight mechanism, it will be important to ensure that horizon scans and other foresight approaches are integrated into the Organization's daily work to ensure that new trends and advances in relevant areas are identified early and engaged with proactively. The present horizon scan provides a snapshot of issues identified at a given point in time by a specific group of experts. To understand the complex and dynamic opportunities and challenges facing global health an iterative process with an expanded range of participants, stakeholders and perspectives is required, as well as a deeper engagement with the identified issues.

Moreover, to respond to the dynamic and complex changes in science and technology as well as to wider trends in society that have implications for the future of global health a wider array of tools is required to evaluate and re-evaluate challenges and opportunities over time and to identify and adapt priorities for action.

The toolkit should include deliberative models such as this horizon scan by an expert group, which identified global trends with potential strong impacts on health issues, and also scenario-based explorative approaches to model different strategic approaches. Another aspect is integration of futures thinking into the operational and technical work of the Organization, not to predict the future but rather to identify pertinent trends in specific areas and recognize the steps that must be taken now to open up options and inform strategic planning.

Proactive engagement must include not only critical assessment of the ethical dimensions, such as misuse, but also issues of access and equity. Equally important is building robust capacity and deploying resources to promote benefits and confront challenges arising from advances in science and emerging technologies with relevant skills to assist and inform the work of WHO, its Member States and stakeholders.

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Annex – Background information

This Annex contains information on the two background documents given to participants in the horizon scan exercise. First, the global health signals package, second, the forecasting training document. A shorter summary of the global health signals package is provided below followed by the text of the forecasting training document.

Participants were also encouraged to review a wide range of sources in addition to the information contained in the background documents, including directions to use review platforms such as Meta[7] and the WHO's Global Observatory on Health R&D[8] and a template for proposals.

Global Health Signals Package

Participants in the horizon scan were provided with a document entitled Global Health Signals Package prepared by WHO's Emerging Technologies, Research Prioritization and Support (EPS) Unit, Research for Health, Science Division. The document provided an overview of six horizon scanning activities and was intended to act as a stimulus by providing a brief snapshot of the outcomes of other relevant efforts.

The six horizon scans that were examined in the document were carried out by the European Medicines Agency (EMA), the International Coalition of Medicines Regulatory Authorities (ICMRA), The EU-Innovation Network, Trust CoLab – a collaboration of the United States Pharmacopeia (USP) and the Massachusetts Institute of Technology's Center for Collective Intelligence (MIT CCI), and two horizon scans on bioengineering carried out by the University of Cambridge's Centre for the Study of Existential Risk (CSER).

Each report or study was briefly outlined, with an emphasis on the main findings or the methodology. Below is a list of the projects discussed with key references provided to the participants.

- United States Pharmacopeia (USP) and the Massachusetts Institute of Technology – Trust CoLab study
  - Laubacher, R. and Star, J (2020) Trust or Consequences 2040: Will innovations in health and medicine deliver? US Pharmacopeia, May 2020. https://www.usp.org/sites/default/files/usp/document/200-anniversary/trust-or-consequences-report.pdf
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- International Coalition of Medicines Regulatory Authorities (ICMRA) – Strategic Priority on Innovation – 3D Bio-Printing Case Study
  - International Coalition of Medicines Regulatory Authorities (2019) ICMRA Innovation Project 3D Bio-Printing Case Study: Summary of Discussions and Considerations for the New Informal

[7] Meta is a biomedical research discovery tool of scientific outputs, https://www.meta.org/ (accessed 1 Feb 2022)
[8] WHO's Global Observatory on Health R&D, https://www.who.int/observatories/global-observatory-on-health-research-and-development (accessed 1 Feb 2022)

Innovation Network. Report. 1 October 2019. https://www.icmra.info/drupal/sites/default/files/2019-10/ICMRA_Innovation_WS3_3D_Bio-printing.pdf

  - European Union – EU-Innovation Network
  - Heads of Medicines Agencies – Working group: EU-Innovation Network (EU-IN), https://www.hma.eu/495.html

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Forecasting Training Document

Thinking about the future is difficult. We have numerous biases that can often impede future-focused contemplation, especially for rare events. A shortlist of these is provided below in Table 2, alongside general tips to address them.

There are different ways of mitigating these biases; of making our future thinking more effective. Training in statistics and probabilistic reasoning, or training through games and scenarios have been shown to improve forecasting accuracy (1,2,3). Such training is intensive and lies beyond the scope of this exercise. Moreover, we are not focused on forecasting per se: we aren't concentrating on generating the most accurate quantitative estimates of future events. Instead, we are interested in considering, prioritising and connecting different plausible and impactful developments in global health.

In lieu of this, we have compiled a list of some of the key traits that have been found to be most beneficial for individuals when forecasting future events. These are summarised in Table 3. Keep this broad advice and strategies in mind when investigating, developing and scoring issues.

Table 2 Cognitive Biases and Mitigation Strategies *(4,5)*

Bias/Heuristic	Description	Mitigation Strategy
Anchoring Bias	Relying heavily on the first piece of information acquired on a subject.	• Be aware of your first impressions. • Think critically about the first information you receive on a topic. • Seek more information.
Availability Bias	Overly relying on information that is recent and 'available' in your memory. For example, overestimating the frequency of plane crashes after one is covered on international news.	• Question what recent experiences may be influencing your perspective.
Confirmation Bias	Tendency to seek information and perspectives that reaffirm your existing views and disregard those that challenge it.	• Search for new evidence and consider viewpoints that differ or challenge your initial information. • Consider the case for and against your selected issue. • Be aware of alternatives and consider counterfactuals.

Table 3 The Traits of a Superforecaster *(6)*

Traits	Description
Open-minded	Approaching beliefs as hypotheses to be tested rather than protected.
Reflective	Be introspective and aware of the ideology, biases and worldview that colours your estimates about the future.
Analytical	Capable of considering other perspectives, including those which may clash with your own.
Dragonfly-eyed	Integrate a diversity of viewpoints into your own.
Thoughtful updaters	Change your beliefs and ideas in light of new information.

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