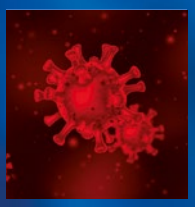
WORLD POLICY CONFERENCE



FIRST WPC HEALTH

DECEMBER 2, 2020
ONLINE MEETING

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WORLD POLICY CONFERENCE

WPC – HEALTH

DECEMBER 2, 2020

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Contents

Background

Created in 2008, and building on the success of twelve yearly editions, the World Policy Conference (WPC) has become a not-to-be-missed event on the global agenda. The annual meeting of the WPC brings together major figures from all five continents – politicians and business leaders, academics and media people – in a spirit of tolerance that is key to promoting the common good.

As Sino-American competition takes an aggressive turn and the rise of populist or nationalist forces, with disturbing ideological rivalries in the background, can be witnessed just about everywhere, the WPC's approach seems more relevant and necessary than ever. The excesses of liberal globalization are largely to blame for those trends. The WPC seeks to contribute to the improvement of global governance with an eye to ensuring the viability of a reasonably open world. That means striking the right balance between the dominant late 20th century ideology of a "flat world" open to all the winds of capitalism; and the temptation, despite the Internet and social media, to return to an inter-State system ruled by the idea of the balance of power, where the collective approach to security would be reduced to the bare minimum, including in the economic order in the broad sense. A good approach to global governance must start with understanding the existence of States as the fundamental reality of the international system as a whole despite the Internet. This system must aim for a method of organizing collective security that is effective in dealing with the wide-ranging challenges brought about by interdependence. It must be such that no State has an interest in breaking free from it without incurring great risk to itself. The quest for such a method of organization is a real challenge but it must be met: as 2020 draws to a close, the odds of the international system breaking down and drifting towards a form of World War III, although still low, are rising.

The main fact of globalization in 2020 is obviously the COVID-19 pandemic, which has spared no country. It took all the planet's leaders by surprise, not because public health experts had not issued warnings about the possibility, but because, since nobody in living memory had ever experienced such a cataclysm (except to some extent in certain Asian countries), no government was seriously prepared for it. Consequently, a shock is resounding around the whole world, continuing to accelerate and dramatize pre-existing trends, including helter-skelter deglobalization. And yet, because of its low

mortality, COVID-19 is not the worst pandemic that could have happened.

It is time, then, to introduce health as one of the WPC's major themes, on an equal footing with more traditional ones such as geopolitics or geo-economics, which sometimes overlap with it. We obviously do not claim to create a new professional international conference on health. There are many of them. Our purpose is to raise awareness of the key political, social, technological, economic and ethical dimensions of this subject, for an audience whose major concerns are the policy aspects of interdependence among nation-states.

To that end, we want to hold an annual one-day forum, called WPC – Health, that brings together a few dozen figures, mostly from academia, public organizations, business, politics and civil society, before the next plenary WPC in Abu Dhabi. The participants will be expected to have a significant background and interest in promoting health-related policy issues for the benefit of non-expert but influential circles. It is our intention to follow up on this one-day meeting. A printed report will be widely disseminated, and a digital version will be available on the WPC website. Last but not least, a plenary session and/or a workshop of each plenary edition of the WPC will be dedicated to the main issues discussed during the previous WPC – Health meeting.

After careful consideration, due to COVID-19, we have decided this year to focus our efforts on substance, and therefore to hold the first WPC – Health meeting as a video-conference, mainly although not exclusively between the speakers on the originally scheduled program. The idea is to have a truly interactive format. However, the day's proceedings will be fully recorded and available immediately afterwards on the WPC website, where the above-mentioned report will be posted.

Now here are some words on the four parts of the first meeting that are currently planned. All the talks will revolve around the idea of global governance. Therein lies not just the originality but also the legitimacy of our project. During the opening session, I will introduce the project in its entirety, placing it more specifically in the present international context. And then we will ask to the Director-General of the WHO to develop his vision based on his strategic position, awaited all the more eagerly since the United States has called his management of the crisis into question. He will also set the tone of our work.

The following session will be called The Lessons of COVID-19. The key question, we think, is whether the WHO's present statutes allow it to adequately meet the global health governance challenge. This is a thorny issue, comparable to arms control in that it entitles the international community to look into the domestic affairs of States. The many lessons of COVID-19 will be examined from four complementary points of view: that of recognized public health experts at the global level; one specialist at the regional level (Africa); industry at large (pharmaceuticals, insurance, etc.); and the UN as a whole. In passing, it should be noted that as a matter of principle the WPC associates all global governance stakeholders, i.e. obviously public players (States, international organizations, etc.) but also economic ones, without whose participation effective governance is inconceivable, in its approach to global governance. It will be necessary to gradually bring in other stakeholders, such as NGOs and the media, as well.

The running thread of the second session, Technology, Economics, Health Ethics, starts with technology, whose breathtakingly swift developments are critical in all governance issues. The issues of information in the broadest sense (including fake news) and access to, control and processing of big data are at the heart of technology. This raises major economic and ethical concerns. The more traditional aspects of the conditions of access to technology, such as machinery in the broad sense, is also a key factor in access to healthcare, especially in developing countries. Neither technology nor the economy should be reduced to the digital dimension. For example, the COVID-19 pandemic has raised awareness of the extreme delocalization, during decades of liberal globalization, of the manufacturing of even the most common medicines. Today this raises serious geopolitical and even geostrategic issues that must be thoroughly analyzed. The introduction of ethics in this session is necessary because no global health strategy is conceivable if it is not socially acceptable. Tracing is an obvious example. But this already huge challenge is complicated by cultural differences from one country to another. If we stick to the COVID-19 pandemic, ethical questions have arisen around more or less implicit trade-offs between the economy in the medium term and health in the short term, between the lives of the young and the old, etc. All the issues discussed in this section are therefore effectively interrelated.

Lastly, we wish to introduce topics that more or less straddle geopolitics or classic geo-economics and the issue of global health governance, such as trafficking in drugs or other substances and their links with wider forms of criminality (trafficking in humans, weapons, etc.), which are already episodically discussed at the WPC. That is why at the first edition of WPC – Health we want to introduce a third session on a theme that we conceive of as being potentially vast, Mental Health and Addiction. The general public is unaware that the WHO has recognized addiction to images as a full-fledged illness—and this illness is a global phenomenon. The WPC has a duty to integrate, i.e. to link together issues with important although not immediately obvious connections between them, and a duty to foresee. Its task, then, is also to address certain governance problems before circumstances make people aware of them later.

I would like to end this presentation note by thanking the people who, for months and under unusual conditions, have encouraged us on the path presented here and allowed us to better formulate our project: putting health at the heart of global governance. We are aware that we will not succeed in one day. But our motivation is strong because this is a key to the future of peace.

Thierry de Montbrial
Founder and Chairman of the WPC
Founder and Executive Chairman of Ifri

Agenda

Opening: Global Governance and Public Health

09:00 – 09:30

Thierry de Montbrial, Founder and Chairman of Ifri and the WPC

Keynote Speech

Tedros Adhanom Ghebreyesus, Director-General of the WHO

Session 1: The lessons of COVID-19

09:30 – 11:30

Chair: **Michel Kazatchkine,** Special Advisor to the Joint United Nations Program on AIDS in Eastern Europe and Central Asia, Senior Fellow at the Global Health Centre of the Graduate Institute of International and Development Studies

Speakers:

Antoine Flahault, Director of the Institute of Global Health at the University of Geneva

Alexandre de Germay, Senior Vice President Global Head of Cardiovascular and Established Products at Sanofi

Jean Kramarz, Head of Business Line Health at AXA Partners

Elhadj As Sy, Co-chair of the WHO/World Bank Global Pandemic Preparedness Monitoring Board, Chair of the Kofi Annan Foundation Board

Juliette Tuakli, Medical Director, Chief Executive Officer of Family, Child & Associates, Chair of the Board of Trustees of United Way Worldwide

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Session 2: Technology, Economics, Health Ethics

11:30 – 13:30

Chair: **Patrick Nicolet,** Capgemini's Group Chief Technology Officer

Speakers:

Daniel Andler, Emeritus Professor at Sorbonne University, Member of the French Academy of Moral and Political Sciences

Jacques Biot, Board Member and Advisor to companies in the field of digital transformation and artificial intelligence, former President of the Ecole Polytechnique in Paris

Carlos Moreira, Founder and Chief Executive Officer of WISeKey, former United Nations Expert on Cybersecurity and Trust Models

Alexandra Prieux, President of Alcediag, Founder of SkillCell

Arthur Stril, Chief Business Officer and member of the Executive Committee of Cellectis

The running thread of the second session, Technology, Economics, Health Ethics, starts with technology, whose breathtakingly swift developments are critical in all governance issues. The issues of information in the broadest sense (including fake news) and access to, control and processing of big data are at the heart of technology. This raises major economic and ethical concerns. The more traditional aspects of the conditions of access to technology, such as machinery in the broad sense, is also a key factor in access to healthcare, especially in developing countries. Neither technology nor the economy should be reduced to the digital dimension. For example, the COVID-19 pandemic has raised awareness of the extreme delocalization, during decades of liberal globalization, of the manufacturing of even the most common medicines. Today this raises serious geopolitical and even geostrategic issues that must be thoroughly analyzed. The introduction of ethics in this session is necessary because no global health strategy is conceivable if it is not socially acceptable. Tracing is an obvious example. But this already huge challenge is complicated by cultural differences from one country to another. If we stick to the COVID-19 pandemic, ethical questions have arisen around more or less implicit trade-offs between the economy in the medium term and health in the short term, between the lives of the young and the old, etc. All the issues discussed in this section are therefore effectively interrelated.

Session 3: Mental Health and Addiction

14:30 – 16:00

Chair: **Thierry de Montbrial,** Founder and Chairman of Ifri and the WPC

Speakers:

Michael van den Berg, Health Economist and Policy Analyst at the OECD

Roberto Burioni, Professor of Microbiology and Virology at the Vita-Salute San Raffaele University, Milan

Jean-Pierre Lablanchy, Medical Doctor and Psychiatrist, member of the Supervisory Board of Edeis

Mental health conditions constitute a major group of NCDs, with ties to cancer, diabetes, cardiovascular and respiratory illnesses. Yet throughout the last few decades, programs addressing a range of mental illnesses have been woefully under-supported and under-funded, often due to stigmatization and a lack of trained mental health workers in many countries. The number of people suffering from some form of mental illness, including depression, is in the hundreds of millions globally. Moreover, the double-edge sword of mental illness and substance abuse contributes to the rising number of suicides globally, especially among young people. The number of people living with one or more chronic conditions increases in most developed countries and will continue to do so in the coming decades. People with such conditions, particularly those with multiple conditions, have significantly raised rates of depression, anxiety and other mental health problems. More in general, chronic conditions can have a major impact on people's ability to live a meaningful life and on their overall wellbeing. Many developed counties are spending around 10% of their GDP on health. Health systems collect massive amounts of data on inputs, spending and activities. However, we know extremely little about whether health systems are truly delivering what people need and help improving their quality of life. In a shared effort, OECD countries have started to move toward a next generation of health reforms, supported by an international data collection on patient-reported outcomes. This session will explore the urgent need to raise as an international priority the interlinked threats of poor mental health, rising substance abuse and addiction.

16:00 Closing

Opening

Global Governance and Public Health

Global Governance and Public Health[1]

Thierry de Montbrial

Founder and Chairman of Ifri and the WPC

Good morning, everyone. It is my great pleasure to open the first edition of the World Policy Conference – Health. I will start by reminding you of the context of the World Policy Conference. Since its inception in 2008, the World Policy Conference has aimed to improve global governance. This means that since the world is increasingly interdependent and, compared to the past, there is a qualitative at least as much as a quantitative change, it is absolutely essential to strengthen regulatory mechanisms. In physics you would probably use the term 'control mechanism'. That way, whenever there is a shock the system is not totally destabilized and subject to butterfly effects. In fact, since 2008, when the WPC began, we have had many such shocks and a number of serious butterfly effects. The first one was the financial subprime crisis during the first WPC in Evian in October 2008. Then, in 2011, we had the so-called Arab Spring, which had a terrible butterfly effect. We are still living with its consequences. We have had a number of such jolts within the European Union: the financial crisis, Brexit, migration/refugee shocks, to name but a few. Now, of course, we are living through the greatest of all shocks since the beginning of the WPC, COVID-19, which probably belongs to the highest category of conceivable shocks. As a result, we will have to introduce health as a fundamental subject in all the discussions and reflections about the future of global governance.

Let me remind you of a few aspects of global governance. Usually, everyone talks about multilateralism and rescuing it after Trump, etc. In fact, multilateralism is not a very clearly defined concept. When we think of multilateralism, the first thing that springs to mind is the UN system. That system is legitimate in theory but relatively inefficient. I say "in theory" because in fact it is less and less legitimate since the UN system as it exists today was formed after World War II and the balance of power has changed considerably since 1945. This is why there are more and more questions about the legitimacy of the P5 for instance, the permanent members of the Security Council. You have a number of institutions within the multilateral system, of which the WHO is a part, but there are also questions about the legitimacy and efficiency of all these institutions. I think this was particularly the case with the WHO in relation to the COVID-19 crisis.

However, multilateralism as defined is only one aspect of governance. Political scientists also speak about plurilateralism, which means something like cooperation not with all the members of the UN system but with some of them. For example, the G20 is a plurilateralist institution. We have weak plurilateralism and strong plurilateralism. For example, the OSCE, the Organization for Security and Cooperation in Europe, is a weak plurilateralist organization. The European Union itself can be interpreted as a very strong plurilateralist organization. In fact, in my view, the European Union is the best model for multilateralism in the future. When a set of countries is increasingly integrated, institutionalized cooperation becomes increasingly efficient, even if it has to go through painful stages in the process, as we can see in the construction of the European Union.

Then there is a third category, minilateralism, which in the extreme is bilateralism. The best example I can give is arms control during the Cold War, which is/was a minilateralist concept that, by the end of that period, was starting to work very well between the United States and the Soviet Union. In fact, it spawned a number of very interesting developments. For example, it created a common language between the two competitors and gave each a droit de regard, an efficient, legal framework to look carefully at what was happening in the other country. Of course, you also had systems like the so called hotline, which allowed easy communication in times of crisis. If I emphasize the minilateral or bilateral aspect of multilateralism, it is because I really think that something like that might be necessary in the field of health. That is, a system that would allow major countries to seriously look inside other countries to understand what is happening at a very early stage, particularly when a major crisis such as a pandemic occurs. This does not exist at all today.

As I said, the WPC – Health is a new concept within the WPC organization. We thought of it very early on and actually had the idea before the pandemic started, but with the pandemic it has become a real obligation. Let me now tell you about a few key aspects I see in the global governance issue within the health framework, which we will have to develop not just today for the first edition of the WPC – Health, but also for the future. I will make four brief points.

I will start with the economic aspects of the issue because nothing can be done if we do not have a clear understanding of the economic stakes of this problem. The first point, and this should be very easy for anyone who has been trained in economics to understand, is that of course, human life has no price, but it has a cost. That is the difficulty. When you say human life has a cost you immediately raise the ethical problem. At this point, I would like to make some remarks about the concept of public goods. As a former mathematical economist, I dare say that the global public good is a tricky concept. A public good is first and foremost non-private. For instance, if I drink a glass of water, someone else cannot drink the same glass of water at the same time; it is impossible. If I take a drug, a pill, nobody can swallow the same pill at the same time. It is very private in that sense. The case of vaccines is more subtle since the vaccination of any particular person contributes to the protection of the community. That is, it carries positive external effects. In that sense, it contributes to the public good. You can even argue, like Professor Kazatchkine, that in the case of COVID-19, vaccinating the world population is a relevant example of a "global public good" independently from any specific nation-state. The other side of the definition of a public good is non-exclusiveness. This means, for example, that if I am walking in a public garden, I cannot prevent other people from walking in and enjoying the same public garden at the same time. In the field of medicine, drugs, pharmaceutical products, etc., it is usually possible to exclude others from consuming the same goods. For sure, public health like defense, as institutional concepts, are public goods, a priori inseparable from nation-states or of international organizations. It follows from this brief discussion that vaccines are both private and public goods. But on the public good side, we say little as long as we do not specify the institutional mechanisms that make the subject operational.

We could develop that at length. The global public good is a rich concept. In practice, what we are really talking about is how to cooperate at a global level, for example to make medicine more accessible. However, you then immediately come back to the issue of cost and, therefore, to the issue of how to share costs and who should pay for what and for whom. This in turn is related to ethics. Therefore, our approach to the economic dimension of healthcare should not be too naïve.

My second remark is that there are various kinds of dependencies. For instance, if you look at the Fukushima tragedy in 2011, one of the first consequences involved value chains and the location of industries. In 2011, many people had already identified this problem as a weak spot of globalization, which was related to the localization issue. Of course, we had exactly the same problem this year with the pandemic; everyone identified the problem of localization or delocalization of the pharmaceutical industry, among others. This is partially an economic problem and partially a security problem. Should I remind everyone that when one speaks of multilateralism one speaks first and foremost about security issues? We have a huge and serious security problem that is now clearly identified.

1. Introductory remarks, revised

The third dimension I want to stress is the technological one. The technological revolution is the most fundamental aspect of globalization. It is not only continuing, but also accelerating. Therefore, exploring all the healthcare and global health facets of the technological revolution should certainly be one of the most important missions of the WPC – Health endeavor. Here too, we find the interdependence problem and related vulnerabilities, typically 5G; whoever controls 5G controls some of the most significant aspects of the world.

The fourth aspect is one I have already mentioned several times, but I want to put it into a special category: ethics. Ethics are extremely important in every decision-making process where complexity is involved, that is to say in any situation where it is not easy to decide what is good and what is not. You have to exercise judgement, which is partially philosophical and at the same time extremely human, because we all face hard choices in our private lives and collectively. Again, as far as health is concerned, as far as matters of life and death are concerned, these ethical issues are and should be at the forefront of any discussion.

Let me conclude by reminding you of the global context of global governance, including health, in the coming years. The global context is clearly the rivalry between the United States and China. That is going to be the most fundamental aspect of international relations in the foreseeable future. It is not an easy issue because the two 21st century superpowers are bound to cooperate on a number of issues since they have much closer relations with each other than, for instance, the United States and the Soviet Union did during the Cold War. At the same time, the competition is very tough because the stakes are who will be the number one power in the world sometime in the next two decades or so.

I cannot imagine that the United States will easily relinquish its first-power status by 2049, for example. Why 2049? That will be the hundredth anniversary of the victory of Mao Zedong in China. My friend and a friend of the WPC, Professor Joe Nye, now likes to talk about "cooperative rivalry", which is a nice concept that could perhaps work for the next few years for a number of reasons but in my judgement, certainly not in the longer term. The issue is how to develop and strengthen global governance mechanisms in a context where you have both a major rivalry between two major powers and increasing interdependence at the same time. That is the big challenge and I think that the contradiction between the two aspects will make everything extremely difficult, including the health issue.

I would like to ask all of you today and all the WPC friends at the forthcoming WPC in Abu Dhabi and later sessions to speak about these issues in a non-naïve way. It is too easy to be naïve, which is why I challenge the concept of the global public good. In a minute, Dr. Tedros, will also mention this concept. So let us pay more serious, careful attention to such concepts.

Moving on to the organization of this WPC session, in a minute we will hear from Dr. Tedros, Director-General of the WHO, whom I thank very much for agreeing to speak to us at the beginning of the first edition of WPC – Health. Then we will have the first session, which is called, 'The Lessons of COVID-19', as we see them today. This will be followed by a second session that takes the issues of technology, economics and ethics as a coherent framework to analyze global health issues. This afternoon, after sharing a very virtual lunch, we will have a shorter session on a more specific subject, 'Mental Health and Addiction', which I think will have to receive increasing attention in the future. When we first thought about introducing this subject it seemed relatively marginal compared to COVID-19, etc., but, with COVID-19 we are realizing that the issue of mental health lies in fact at the core of the pandemic's consequences.

That will be it for today's first edition. It is now my pleasure and honor to give the floor to the Director General of the World Health Organization.

Tedros Adhanom Ghebreyesus

Director-General of the World Health Organization

Excellencies, dear colleagues, and friends,

I would like to thank Mr Thierry de Montbrial for inviting me to address you today. WHO welcomes your initiative to make health a core theme of next year's World Policy Conference. The COVID-19 pandemic is a health crisis unlike anything any of us have seen in our lifetimes. But it is more than that – it has also shaken the foundations of social, economic and political stability, and put the multilateral system to the test. The pandemic has demonstrated the need for strengthening in several key areas.

First, stronger multilateralism. The pandemic has shown us that international cooperation is the only solution to an international crisis. Working together might not always be easy, but it is essential. We must rethink and strengthen multilateralism to address the pressing challenges of our world in a coordinated and coherent way. I am heartened by the commitment made by heads of state at the UN General Assembly, the recent G20 summit and other fora to strengthen multilateralism and elevate health to the top of the political agenda. I am also encouraged by initiatives such as the Alliance for Multilateralism, led by France and Germany, and the policy discussions putting forward new solutions for multilateral cooperation. Many countries have already emerged as leaders of this global reset, and I trust that the new US administration will soon joint this effort.

Second, stronger global health governance. This means three things: reinforcing core institutions, more effective policy tools, and greater accountability at country level. Many leaders and institutions have already called for an expansion of political and financial support for WHO so we can deliver on our constitutional mandate and meet the high expectations of our Member States. I especially appreciate the leadership and support of France and the European Union in this regard. At the same time, we need to strengthen both the International Health Regulations and national capacities. The IHR is a powerful legal tool, but the pandemic has shown it needs to be sharpened and modernized. A review committee is now evaluating the functioning of the IHR during the pandemic and is expected to deliver its recommendations by May.

Third, stronger solidarity. Unparalleled financial resources have been mobilized to support the Access to COVID-19 Tools Accelerator to develop vaccines, diagnostics and therapeutics fast, and allocate them fairly, as global public goods. The ACT Accelerator sets a strong precedent for a solidarity-based global response to health threats. Almost 190 countries and economies have now joined the COVAX facility, which facilitates an equitable global sharing of COVID-19 vaccines. Forty countries and many organizations have signed up for the COVID-19 Technology Access Pool to share knowledge and rights to research and technologies. The values that underpin all these innovative platforms and tools are the same: solidarity, equity and inclusion. Their aim is to create more equal opportunities for everyone and ensure that all COVID-19 tools are treated as global public goods. I hope that these values will stay with us in the future and remain defining values of global health governance.

Finally, let me say that the pandemic has shown us that health and the economy are inter-dependent. We need a new narrative that sees health not as a cost, but an investment that is the foundation of productive, resilient and stable economies.

I wish you a productive meeting. I thank you.

Session 1

The Lessons of COVID-19

Introduction

Michel Kazatchkine

Special Advisor to the Joint United Nations Program on AIDS in Eastern Europe and Central Asia, Senior Fellow at the Global Health Centre of the Graduate Institute of International and Development Studies

With COVID-19, the health and well-being of millions of people were abruptly put in danger and half of the world's population forced into confinement. Our economies and the very structure of our societies have been shaken and put the multilateralism at a test.

And the crisis has yet not finished unwinding its negative impact. Here in Europe where only 7% of people have been infected with the coronavirus so far, the Institute of Health Metrics at the University of Washington, predicted a few days ago that daily deaths from COVID-19 will continue to rise in the coming weeks, reaching a peak only around mid-January, with hospitals being stretched to breaking point from December to the end of February.

Against a certain lack of interest in health issues that has been prevailing in recent years, the world is realizing how much, among all global issues, it is health that, in the short term, has the greatest potential of disruption in our globalized world.

I find it encouraging to see, on this occasion, a near-consensus forging on the importance of science as a basis of health policies and on the priority given to the safety of people over economic considerations, even at high cost. Public health is a political choice that most countries have made in this crisis against competing priorities and interests. To say that the virus affects us all does not mean, however, that it affects us all equally. We have seen countries competing for resources, whether for masks, as we saw in the first wave of the pandemic here in Europe, diagnostic tests or now, vaccines. It is not difficult to guess who will emerge a winner in such a competition in the absence of global regulation, global governance, and of common resources for common goods.

The unprecedented crisis we are facing requires unprecedented global solidarity. In his wake-up call last July, UN Secretary General Antonio Guterres, called on the global community to move from international chaos to the construction of an international global community capable of meeting and solving tomorrow's challenges. Clearly, a pandemic response rooted in global cooperation makes everyone safer. Of course, it demands an emergency response. But it must also encourage us, beyond the emergency, to lay the foundations for a world that is more united and more resilient in the face of challenges, which will have to go beyond the current geopolitical equilibria to involve more the major emerging players, China obviously, but also India, Russia, Latin America and Africa.

The crisis Europe and the world are facing is not only about health, it is about politics too. This why today, for the first time the WPC is dedicating a side-conference to health.

Updates and first lessons on COVID-19

Antoine Flahault

Director of the Institute of Global Health at the University of Geneva

Our purpose is to provide an update on the epidemiology of the COVID-19 pandemic and a general overview on its evolution in the world. Most parts of the Northern hemisphere temperate zone are facing a huge surge in cases whereas in most Asian countries, the COVID-19 wave is very well-controlled. On the other hand, Africa is a grey zone because we do not have sufficient tests to analyze the trends in many countries, but it seems to have been less affected by the virus. It is important to understand the basic reproductive rate is a variable. We must focus on the 10% of the cases who contaminate more than one person because they are the only ones who contribute to the pandemic. There are two tracing approaches in the world: forward tracing and backward tracing which is more efficient. Regarding the three main routes of transmission of COVID-19, small droplets are probably the major route. Besides, preventive measures, lockdown measures, seasonal force/environment and immunity are the four available brakes that can slow down the spread of the pandemic. Of course, the aim is also to explore some pharmaceutical and non-pharmaceutical treatments, as well as the different vaccines under development, and, apart from medical solutions, to identify digital solutions like tracing applications. We will eventually imagine different scenarios for the coming months.

In a collaboration between the University of Geneva and the two engineering schools of Zürich and Lausanne (ETHZ and EPFL), we provide on a dashboard (https://renkulab.shinyapps.io/COVID-19-Epidemic-Forecasting/) with daily updates of COVID-19 forecasts for 209 countries and territories. We can see at this time of the year that most parts of the Northern Hemisphere temperate zone are facing a huge surge in cases. However, in Asia, where the surge continues in Japan and South Korea, but not China, it is very well-controlled and at a safety level that is far below the incidence we are seeing in Europe, the USA or Canada. Neither the USA nor Canada have yet

got their wave under control, while for the moment, Europe is trying to take control of the second wave of the epidemic.

In some parts of Sub-Saharan Africa, we do not have sufficient data on tests to analyze the trends in many countries, but we can say that there are three different profiles in the continent. The northern part of Africa has a very similar trend to Europe, with a recent winter COVID season second wave, as in Morocco, Libya, or Tunisia. For the countries where we do have data in Sub-Saharan Africa, such as Senegal, Ivory Coast, Ghana, Togo, Nigeria, Ethiopia, Kenya, and others, they report very little activity up to now and it seems that these countries are not facing such a dynamic wave. The reasons are not clear, though of course there is the shortage of testing as reminded above, but a burden of infection would have been detected and it has not. Is it the role of the climate since of course there is no winter season? It is not clear, but we see other respiratory viruses such as influenza in all parts of inter-tropical zones and there were high levels of coronavirus activity in Latin America and Singapore in the recent months, so this hypothesis is not very convincing. The role of demography could be more convincing because the median age is much younger in Sub-Saharan Africa (18 years) than Europe (42 years). It is true that there are still some elderly people in Sub-Saharan Africa but fortunately, we do not see them massively in hospitals. Cross-immunity has been suggested as playing a role against the coronavirus, which would be the immunity provided by other viruses that could block the propagation of this virus, but so far none has been documented. A protective genetic susceptibility among black people is also not convincing because black people in South Africa, North and South America have been hit very hard by the virus. Since there is no clear explanation, we should explore it more and keep vigilant, it may be a question of time. The relative lower connectivity of the continent with the rest of the world may have only delayed the progression of the pandemic in Africa. The third profile is South Africa, which behaved like Australia, Pacific islands, and South America with their strong winter wave between June and September, which was successfully controlled. However, there are worrying signals of a new surge in South Africa, as well as South America (Brazil, Argentina, Chile and even Uruguay), which may be a cause of concern in the coming weeks.

We do not make long-term predictions, we only provide daily seven-day predictions for the 209 countries and territories worldwide. We restrain ourselves when it comes to mid- or long-term predictions. We remember the US CDC forecasts for Ebola in 2015, when they predicted one million plus cases for Liberia alone, but fortunately there were less than 30 000 cases all over the world. Of course, it was far too many but not of the same order of magnitude. Wrong three-month predictions have been released for COVID-19 too, so let us avoid long-term and even mid-term predictions because with the current models available in the world today, we cannot really know what will happen with this pandemic in the coming months.

It is important to understand the basic reproductive rate because it is not a constant, it is a variable. When we say it is two to three, it is an average. We have to realize that maybe almost 70% of cases will not contaminate anyone and maybe 20% will contaminate just one person and will not contribute to the pandemic at all. We have therefore to focus on the 10% who contaminate more than one person because they are only ones who contribute to the pandemic dynamic. As a consequence, there are two tracing approaches in the world. The Western style of forward tracing, searching for contacts of reported cases, is not very efficient because 90% of the reported cases will not contaminate anyone. Backward tracing is a lesson we can learn from the Japanese and other democratic Asian countries, where they look for the person who has contaminated the reported case. Because of this so-called "over-dispersion", the asymmetry between the 90/10 described above, they do not waste their limited time and resources in tracing all contacts, they prioritize the contacts of potential superspreaders (i.e., those 10% who contaminate more than one person). If someone has already contaminated one person, i.e., the reported case, of course, the probability that he or she contaminates another person is much higher.

The main rules of transmission for Sars-Cov-2 are still being debated and even hotly debated. Of course, there are a number of potential routes, but let's focus on the following three major routes:

- Large droplets – This is the ballistic route when you cough, sneeze or sometimes even speak and may expel some large droplets more than 100 micrometers. These may just hit someone in the nostrils, eyes or mouth and contaminate them. It is probably not very frequent when you respect physical distance which may not be easy in homecare facilities, childcare and of course, sometimes in hospital settings.
- Small droplets – These are the droplets below 100 micrometers you expel when you breathe or 10 times more when you speak, and 50 times more when you sing or yell. Small droplets are aerosolized and can float in the air for a couple of minutes of even hours in poorly ventilated, closed settings, these aerosols may contain some coronavirus.
- When these droplets fall on top of surfaces, these small droplets contaminate fomites, which make a route of transmission.

It is not clear that virus attribute a part of each route and it depends on the settings. Outdoors the aerosols most probably do not play any role, but they seem to play a leading role indoors. Intensive handwashing programs have been assessed through randomized clinical trials for other respiratory viruses and they show a risk reduction of 16%, which is substantial but not dominant. Small droplets are probably the major route indoors.

There is not one COVID-19 disease, there are at least three different type of diseases according to its prognosis. A Danish series of more than 10,000 cases of confirmed COVID-19 show that cases under 50 do not have a high risk of having severe complications or dying from COVID-19; at the most, they were as safe as for many viral, respiratory diseases. Between 50 and 70 it becomes a very severe disease and with comorbidities (50% of the population at this age have comorbidities such as hypertension, diabetes or are overweight), having a risk of dying that is close to that of SARS in 2003, around 10%. It is a very severe disease. Above 70 it becomes a highly dangerous disease, like Ebola in West Africa, with mortality rates sometimes close to 50% or above. There are four available brakes that can slow the spread of this pandemic.

- Preventive measures – handwashing, wearing masks, physical distancing, ventilation of closed rooms.
- Lockdown measures – homeworking, closure of schools, universities, bars and restaurants, non-essential businesses, restrictions on mass gatherings, limitations of movements. More personalized lockdown measures are in fact the testing/tracing/isolating process because you lockdown those you find are infected or at risk.
- Seasonal force/Environment – We have seen the seasonal force in the Southern Hemisphere during their winter and we are now observing it in the cold seasons in the Northern Hemisphere. The seasonal force in summertime in temperate zones is not a blockage it is a brake, and it may happen that it slows the process. I will come back to the environment component below.
- Immunity – Of course, the more the disease progresses without any substantial mutation gives an acquired immunity. Today, in Paris, London, and Geneva we have probably reached almost 20% of the population being immunized. It is not enough to block, but it is a brake that slows down the process. Of course, vaccines and treatments will help a lot completing it.

We have recently published a work showing four different weather conditions all linked with accumulation of fine particles in the air. In Tenerife in the Canaries, we found that sandstorms led to fine particles in the atmosphere and were followed by an outbreak of COVID. In London, Paris, and Ticino in Switzerland, we have seen that the atmospheric conditions led to fine particles in the air and were associated with a spike in outbreaks of COVID-19 concomitantly of soon after. We have seen that for the first wave, and it seems to have also been reproduced in the second, so climate and seasonal conditions may play a role, as well as the environment. When we cannot act against weather conditions, we certainly can contribute to avoid air pollution in these specific atmospheric conditions.

Like all other European countries, Ireland has experienced a second wave during the Autumn and on October 21 the government decided to lockdown again. On October 25, four days later, we saw a break in the exponential trend. It is quite exceptional to see the effectiveness of a political intervention on this pandemic in just four days. In fact, we can say that there was a citizen participation anticipating this policymaking. The Google mobility data show a 40% reduction in mobility using public transportation from October 4th, i.e., a couple of weeks before the second official lockdown. It is interesting to see the self-lockdown that people in Ireland used to anticipate the political decision, which has also been shown in France. In democracies, governments often follow and endorse their people's own decision and perception of the risks.

When it comes to treatments, we have not got very far, we have only confirmed the efficacity of Dexamethasone, an old and cheap corticosteroid. We are on the verge of seeing some interesting results from monoclonal antibodies, which were administered to President Trump when he had COVID. There have also been some non-pharmaceutical treatments such as appropriate timing of assisted ventilation and oxygen, and the prone position when ventilated. However, some others may be promising and are still being assessed in clinical trials, so for the moment, we do not know if other products will significantly contribute to the treatment. More optimistically, we can say that the survival rates in hospitals have dramatically

improved over the previous six months, with survival rates being 30% to 50% higher, just using Dexamethasone and better care with non-pharmaceutical treatments.

We are much more advanced with vaccines with some very promising results. We have not seen any publications for the moment, but the dossiers are being evaluated by regulatory agencies and the UK agency already approved the BioNtech-Pfizer mRNA vaccine. The Moderna vaccine is following soon and AstraZeneca, which is a vector borne vaccine, will probably also follow very soon, but could be delayed a bit by some difficulty in accessing some data. BioNtech-Pfizer and Moderna produced two very promising vaccines, but there are many others, about 150 in development and 50 of them currently in clinical trials, some may come to the market soon.

We do not know exactly how long immunity will last. We can hope that it will last for a couple of weeks or months, but of course we do not have enough experience of that.

When it comes to the scenarios for the coming months as we are waiting for the effect of these vaccines. First, we have to land towards our safety zone before easing and lifting the lockdown measures. After that, we will have to change and adjust our testing strategy towards a backward tracing strategy, prioritizing while not giving up on the other one if we have enough resources and time. We will also have to improve the isolation of contagious people in dedicated hotels, as the Asians and Australians did. We also need to use more and better apps and digital traces because they are very useful partners for catching cases and contacts. Afterwards, we will have to conduct seroprevalence studies to know exactly what the acquired immunity is. If we have still low immunity levels, i.e. below 10%, in some areas, the risk of resurgence would be very high, and it will be very difficult to ease the restrictions. If we have higher prevalence, maybe above 25% or 30%, that will represent a beneficial brake and a sufficiently low risk to open bars and restaurants and other non-essential businesses, with some caution and maintaining some preventive measures. In between, we have moderate risk, and we will have to be cautious. Wintertime, the cold season in the Northern Hemisphere, will remain a dangerous period and we keep most of the existing preventive measures.

In conclusion to avoid COVID-19, please remember to:

- Avoid crowding indoors,
- Avoid poorly ventilated areas,
- Avoid going unmasked,
- Keep your distance even when wearing masks, since aerosols close proximity is a risk factor,
- Avoid long periods of exposure in these rooms, which is why we are not all in the same theatre with Thierry de Montbrial today,
- Avoid singing and yelling. In Japanese railways, passengers are not allowed even to speak!

And hopefully, with the vaccine, we will be free of all these measures and constraints in a coming future.

Three ways to strengthen our health systems: lessons from COVID-19

Alexandre de Germay

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Improving health systems is a constant challenge. Today, the global pandemic highlights this as a challenge of the utmost importance that the public and private sectors must take on together. The slow progress in the modernization and strengthening of health systems hampers the fight against COVID-19 which continues to spread at high speed. It is now a matter of demonstrating our resolve for greater efficiency to guarantee better public health. Solutions exist to strengthen our health systems: reinforce focus on prevention and more effective management of chronic diseases, make greater use of digital technologies and data, and encourage multi-sector collaboration to seek innovative approaches and secure the needed investment and resources. A new age in global health is achievable. When all stakeholders actively work together behind a common goal, we can find solutions to even the most difficult challenges.

There is global consensus the COVID-19 crisis has been a wake-up call for all of us in public health: modernizing and strengthening our healthcare systems can no longer take the form of a long, winding road, bordered by good intentions. Rather, it is an urgent requisite and change must happen faster to avoid the full brunt of future catastrophic events like pandemics.

Of course, overhauling healthcare systems is an onerous undertaking – and requires many actors engaging in concert behind common or complementary objectives. But the COVID-19 crisis has shown us that it is possible to effect wide and large-scale change when certain hurdles are overcome through innovation and concerted coordination from all actors. I believe similar shifts in the post-pandemic world must come in the form of incentivizing and rewarding effective prevention. In other words, we can do more to prevent and better manage our health issues in life before costly and sometimes irreversible damage occurs. That is good for individuals, systems, and entire societies. Here are three ways we can do this: (1)

doubling down on prevention and more effective management of diseases (2) accelerating the adoption of digital technologies and data integration and (3) building a cross-sector approach to encourage investment and resourcing behind innovation.

1. Doubling down on prevention and more effective management of diseases

Despite the recognized benefits of preventive health measures – take vaccination as an example – more can be done to ensure our healthcare systems are set up to encourage healthier lifestyles and reward better health outcomes. Most healthcare systems are set up as "sick-care" systems where interventions happen only when a person gets sick. This continues despite demonstrated improved value for healthcare investments with prevention.

Take chronic diseases for example, even before COVID-19 brought our hospitals to the brink, the burden of chronic conditions weighed heavily already: Diabetes affects 463 million adults worldwide and accounts for $760 billion. Left alone, these figures are expected to increase to 700 million people living with diabetes by 2045 and a cost of $845 billion.

These are largely evitable burdens of disease if we take a population health approach targeting effective prevention amongst those most at risk. These costs I have outlined are disproportionately weighted among people whose predispositions, characteristics and behaviors otherwise lead them down this difficult and costly road of chronic disease. Clearly, when well-controlled, these diseases will not take such a heavy toll as they do today. We know that when patients reach and maintain goals established through medical guidelines, they live healthier lives and encounter far fewer burdensome and costly complications. But from real-world experience, we also know those goals are not often met and patients and HCPs continue to struggle to effectively manage disease.

We need to tailor health interventions to this segment of the population before they progress into irreversible disease. And we need to do so with holistic lifestyle applications and engagement that can fill the gaps in the months between clinical check-ins. That is where digital comes in.

2. Accelerating the adoption of digital technologies and data integration

Digital has already begun to make good inroads in helping the public health community better understand and implement optimal preventive health solutions. We can see applications thrive in the pandemic context when people need to find faster and more efficient ways to manage care. There are now smoothly working user-facing virtual apps like those for making and managing medical appointments. There are also sophisticated new digital diagnostic technologies using powerful computing and machine learning to pre-empt problems, like Google's retina scanner that can spot people at risk for cardiovascular disease just by "looking them straight in the eye," albeit very deeply![1]

We may be witnessing finally the beginning of a true integration of digital into health and wellness. But to fully reap the benefits smart technologies can offer both patients and the system, we'll need more. The World Heart Federation has raised several points in their recent white paper on how to accelerate digital's power in improving health for those suffering from chronic circulatory diseases, of which I believe one is of special importance and urgency.[2]

Large-scale upgrades to digital ecosystems in healthcare will make them more interoperable and secure. This is truly foundational as it may be the largest single inhibitor of optimal digital health today. As patients at one time or another, we have all seen how specialties of care work in silos and don't always exchange well. Interoperable digital health records between patients and their sometimes-multiple caregivers and wellness support systems could help health systems effectively identify the most at-risk populations and facilitate physicians' abilities to seamlessly connect and understand the unique case of each patient to provide truly optimal care.

If we can collectively continue to push for wider adoption and use of digital technologies, it could propel healthcare systems to a new model, centered around real-world data, evidence-based medicine, and better patient outcomes.

3. Building a cross-sector approach to encourage investment and resourcing behind innovation

Increased partnerships will be essential to making this much-needed shift to prevention. This transformation can only happen if all parts of the system work together towards the same goal. We must build global, cross-sector collaborations if we seek to make change sustainable.

In the pandemic response, we saw exceptional partnerships rising up and bringing together expertise and resources from all stakeholders in public health. Take Sanofi's collaboration with GSK and the U.S. Biomedical Advanced Research and Development Authority (BARDA) for the development of a recombinant protein-based COVID-19 vaccine: rarely do two competitors come together to create a new vaccine, and in concert with a government agency, no less.

Another example is the COVAX Facility co-led by Gavi (The Vaccine Alliance), the Coalition for Epidemic Preparedness Innovations (CEPI) and the World Health Organization. In this Facility, any country can join with others to pool resources and reserve COVID-19 vaccine doses for their populations. And finally, we have seen a clear reinforcement of Europe's critical geopolitical collaborations in health with the recent announcement of a Health Emergency Response Authority (HERA), also referred to as a "European BARDA" (European Agency for Bio Preparedness).

Across these and other examples, we can see that policy makers, academia, civil society and industry colleagues are clearly now coming together, taking the learnings from COVID-19, and ensuring we are not caught off-guard by the next pandemic.

4. Questions we must answer together

As we rethink our healthcare systems in a post-pandemic world then, we must ensure that we can also apply learnings to other domains of systemic health care improvements. Most importantly perhaps, we must create the right governance that will allow us to earn the public's trust and unlock rapid and concrete change. Whether it is in prevention, digital health or innovation writ large, we need to create a better designed and governed healthcare ecosystem.

With this in mind, there are two key areas for us to consider in the immediate:

- Continue to explore and find more ways to facilitate coordination amongst all the players of healthcare systems, especially between public and private sectors;
- Forge greater alignment and coordination across countries and across the local, regional, and global dimensions of public health.

No one can do this alone, but if we undertake a concerted effort to work together, I believe a new age in global health is achievable. We have already seen how this kind of coordination can work in the pandemic response: when all stakeholders in public health actively work together behind a single critical goal, we can find solutions to even the most difficult challenges.

Notes

1. https://www.newsweek.com/google-retinal-scans-predict-heart-attack-812098

2. https://www.world-heart-federation.org/wp-content/uploads/WHF-The-case-for-the-digital-transformation-of-circulatory-health-WEB-.pdf

Health is strategic

Jean Kramarz

Head of Business
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The COVID crisis has put in evidence that in many countries, Health was not treated as an essential strategic asset and more like a commodity. Priority was in costs saving, with a belief that free trade would cover for the essential needs of a Nation at a better cost. The economic and politic impact of this lack of anticipation is so huge that we can expect major changes in the future.

1. **Relocalization of the production of essential medical goods (protective garments, drugs, vaccine…). Health will not be treated as a commodity abiding by the economic rules of free trade anymore. And this will have a cost.**
2. **Change of rules for data management. The small shop management, which is still usual, every team, every hospital keeping its own data practice will be challenged by the urge for big data strategy. And therefore, strategy towards GAFAM will be revisited. From ignorance to cooperation or conflict.**
3. **Investment in social media strategy is necessary to repair trust. Public health strategies need obviously to be supported by massive acceptance of general population. This implies in depth modernization of public communication, entering the social networks area to build long term, stable trust towards public health policies.**

The purpose of Insurance is to cover for unexpected events in a predictable, measurable environment. COVID-19 taught us in a hard way that the Health environment was less predictable and measurable than we all thought. The impact on global economy of this crisis is of the same magnitude than a large bank bankruptcy and we discover that we are in fact less prepared than we expected. COVID-19 was a "black swan", something possible in theory but so rare that you do not really plan for it.

In other words, COVID-19 reminded us that Health is Strategic. Health is critical. Poor management of Health, insufficient anticipation, wrong decisions can turn into a disaster for individuals, for the global economy, for governments.

What everybody has understood is that Health must be managed like a strategic asset, not like a commodity. With an insurance point of view, when we think of strategic crisis with high impact and low frequency, we think "prevention". COVID-19 means that we need better prevention. And for better prevention, I would insist on three factors where we can expect changes in the future. One is preparedness: how robust is the system that we have built, is it fit to face a massive Health crisis? And what does preparedness imply in terms of international cooperation? More or less? The second is Data: how can we use data better: to understand what is going on, to implement better treatments, to predict better what is coming next. The last one is behaviors: how will individual behaviors influence, ease or make difficult bounce back after the shock. Three dimensions where Nations can decide to play stand-alone or cooperation.

1. **Prevention: Vulnerabilities in the supply chain will be mitigated, at a cost**

As everybody knows there has been a lot of disputes in France about the stock of protective masks. There should have been a strategic stock, like there is one for oil for instance and in fact for various reasons the stock was empty. One of the reasons why the stock was empty was that there was a belief that medical goods, especially when they were inexpensive and manufactured in low-cost countries, would be always easy to procure. If you had money, there would be always someone to sell. Shortage could be temporary, due to logistic issue, but never critical enough to endanger a Nation. Another reason was building stocks was considered as expensive and not really necessary.

But in fact, it was not true. What we have discovered with Masks is that accepting delocalization of production implies a certain level of risks. And what applies to masks was also visible for some critical drugs, cortisone, curare and so on … And it was also true for medical respirators. And true also for medical professions themselves. When doctors and nurses are poorly paid, it is difficult to hire them in public hospitals and especially not in a snap of fingers when a crisis occurs.

Basically, a choice was made for Health in France and in many other countries, to do with less money, less stocks, less people, less margins to maneuver in case of crisis. Because it was not understood that Health was strategic, which means that a failure on Health could endanger a whole nation.

Now that vulnerability and the political cost of it is understood, one of the first questions now arising is: is it safe for a country to rely on critical drugs or vaccines manufactured abroad. What is a place safe enough to offshore production of a critical good? India? China? Eastern Europe? Turkey? What about the UK after Brexit? And what about the USA? Who in case of crisis will not keep these goods for themselves? Who will not use them as a lever for a political quid pro quo?

Uneasy answers, but my guess is that public opinions will not take anymore as granted that free trade will guarantee easy supply. As a result, the balance between "national production" and "free trade" will be more in favor of "national production" which means that Health in general and especially drugs could be more expensive in the future. Good news for the Pharma industry for instance, not necessarily for social security systems. Securing production on your own territory has a cost which many countries are probably ready to pay now.

2. **Second lesson, data are essential but still managed in a very primitive way. This will change.**

A short history of COVID-19 is also a history of transparency on data, collecting the right data, analyzing the data, publishing the data, working in a modern and industrial way on data.

When did the first cases really occur in China? Where do we get infected? Was hydroxychloroquine efficient or not and for which type of patients? And Remdesivir? Are masks efficient? Does the virus disappear in summer? Are some people genetically protected or vulnerable? The distrust in public health decisions which was seen in many countries comes also from a lack of homogenous analysis of the millions of people sick or treated or saved from COVID-19.

When vaccines have been developed and made available with incredible velocity, treatments are lagging behind. Dozens of protocols have been tested in hospitals. We only start having some indications; It is still based on a relatively small number of cases when you consider that globally dozens of million people have been infected and millions have been hospitalized. It is not only a question about Hydroxychloroquine or Remdesivir. It is about applying the best protocols and saving lives. Many doctors take their decision based on what they see by themselves or based on what they read. Governments do the same. They sign contracts or give authorization based on very partial set of data,

sometimes biased.

And what is frustrating is that there are millions of patients, so potentially a huge amount of data, but we all know that these data are not collected, or not in the right way. By design, each study is in the hands of a small number of doctors, focusing on one aspect of the topic and leaves an area of doubt. Is it a dream to imagine that one day, like meteorologists, doctors will collect and share critical data through the same protocols and in the same data bases? That trust will be enough that one treatment validated in Milano or Seoul is immediately shared to the medical community in a way that they can understand how much it works, for whom, at which stage of the disease?

On top of that, a critical set of data is left apart: genomic data. Do we know why people under 40 with no preexisting conditions die? Is it satisfying to leave it on bad luck? As long as this specific set of data is left unattended, genomic data and personalized medicine will not reach COVID-19.

So definitely, our data asset is still very immature. Fit for a time when data are of interest for scientists who have time, not for governments fighting pandemics in a hurry. So what can we imagine for the future? Can we expect an acceleration of National Health Data hubs? And what is the best approach? Are National Data hubs the most efficient? Is there room for intergovernmental data hubs, at least at European level? Which governance should be put in place? And which level of collaboration is optimal with GAFAMs? Is keeping them apart the only possible approach for Governments, in the name of sovereignty? Or can we imagine GAFAM collecting billions of real-life data and accelerating victory over the virus? Detecting where infected people live, what is their social network, whom they have met in the metro, or at the super-market? They are very logical candidates to collect, store and analyze an incredible amount of data. Apple, Google have started Health Studies and of course COVID-19 is good topic for their ambition to collect and aggregate trends from thousands of devices. Typically, this will be much quicker and efficient to analyze "post COVID-19 syndromes" than the present status where individuals rely only on expertise of isolated medical teams, treating a small number of patients scattered in multiple hospitals.

My guess is that data analysis will not be left as an experimental toy for long and more structured strategic initiatives will be taken. There again, different paths can structure our future. Some countries will play a nationalist game, keeping expertise for themselves, sharing what they want of it. "Medical intelligence" could be another field of competition between nations. Cooperative approach is more efficient on the paper, unless you think you can have a competitive approach or you fear to expose your weaknesses, inefficiencies, vulnerabilities. And the role of GAFAM will change. Nations will have to choose if they want to forbid, control, team with these entities for Health. "Ignore" will be soon an impossible option.

3. **Behaviors: major attention to soft power battles will be necessary**

Governments have used a lot of coercive measures to tame the COVID-19. Lockdowns, curfews, quarantines, administrative closures, administrative permissions, closures of borders … Police officers controlling your whereabouts. Neighbors reporting uncivil behaviors. Very similar to war times to be honest.

But it is now widely understood that these coercive measures work better when there is a strong public acceptance. And this popular support has been mined in numerous countries by social networks. This is an area where it is easier to destroy confidence than to build confidence, with devasting consequences, when you think of immunization or masks for instance. When doctors officially criticize other doctors, when government officials at the highest level criticize doctors and doctors criticize governments, how could the ordinary citizens be fully confident of anything and follow the instructions they are given?

Governments must reinvent communication and build or rebuild trust in the long term. They must envisage the social networks as a major battlefield, also for Health. A place where you can be under attack by your own public opinion but also by external enemies manipulating this opinion. When governments will have a good view of what should be done to fight a pandemic, they will still need to convince each and every citizen to do the right thing. In democracies where consensus is fragile and temporary, public support will not come without a massive and long-term effort to create public opinion medical leaders able to influence citizens. How do you keep doctors immune from the suspicion to be sold to Pharma companies? How do you create an iconic public "brand" in the medical field? Which medical institute or medical university deserves this respect? How long does it take? The failure of The Lancet shows how fragile can be a brand image nowadays.

This is for me the final lesson from COVID-19. The best public health policies can fail if the social network weapon is not mastered and there is here a massive potential for progress for governments.

COVID-19 Lessons learned in Africa

Juliette Tuakli

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A misguided preoccupation on our continent at the expense of a closer assessment of European and North American Public Health resources and preparedness led to an unexpectedly chaotic, inefficient set of responses in North America and Europe rather than in Africa. Prior experiences with Ebola and the presence of a newly minted well-resourced and well-prepared African CDC went a long way to encourage an effective use of Data, Pharma-Medical, Human and Financial resources throughout Africa. Coordinated innovation, strategic regional and national partnerships and transfers of knowledge led to successful co-opting of the population in an effective containment, prevention, and social protection. Digitalization of education, communications, and medical care as elsewhere, became the norm. Agile coherent leadership was noted in the most COVID-19 resilient African nations. Whilst there was some politicization of COVID-19 management, as in other parts of the world, Africa fared much better than feared. As Africa's economies regroup and redress the socio-economic vulnerabilities and challenges the pandemic highlighted, it is clear that a re-constellation of effective governance internationally, regionally, nationally and locally around health, environment, and data are now the challenges for us all. Particularly in Africa where a young and dynamic population most needs to become part of the political/economic/human resource solution.

COVID-19 pandemic created a global twin crisis of Health and Politics. Public Health in most countries of the world was particularly adversely impacted. Trends common to many of such countries included a notable increase in use and broader applications of technology, a long overdue and increased recognition of importance of health workers as well as a reduction in discretionary/elective healthcare. Conversations at the local, regional, and global level on increased financing and innovation of healthcare provision,

commodities and improved governance have been a particularly significant outcome.

It is important to note that most of what comprises Health, either good or bad, occurs outside of clinics and hospitals!

Specifically in Africa, there included a focus on and support for increased institutional funding for healthcare; increased demands for improvement of the health infrastructure, commodities and equipment; a re-assessment and full evaluation of current supply chains and the viability of local pharmaceutical production.

The relatively low numbers of COVID-19 deaths and cases were also notable; not the least because of a distinct variability within the continent. For example, of 2,120,967 cases and 50,924 deaths (as of November 27, 2020), in Africa, the Republic of South Africa, which has the strongest public health system and one of the highest continental GDPs, has had approximately one third of all cases and forty two percent of all deaths.

African countries that fared the best, demonstrated, in general, specific attributes. First and most important in my opinion, a strong political will to be involved in the national management of COVID-19. This, backed up with consistent, informed leadership. Next, an early and consistent engagement of reliable, data informed Public Health officials who worked closely with official regulatory and governance sources. Regular Presidential communications to the population using all forms of social media, and traditional oral routes (middle level health staff and traditional leaders as communication agents) in conjunction with the implementation of wide-ranging protective measures especially mask use and social distancing. In many instances, masks were available freely or at less than the cost of a bottle of Coca Cola. Reminder Posters in vernacular were posted in all public spaces encouraging masks and social distance. A full and early closure of all institutions and markets was mandatory. The early use of data both locally and regionally determined the need to close all national borders very early. Active stakeholders included all levels of the society from fishermen to teachers to politicians. In Ghana, it was market women who essentially gave the signal to politicians of the need to re-open certain facilities with COVID-19 preventive measures ensured and in place in order to ensure social order and livelihoods. I shall return to the importance of data collection, use and sharing further on.

Along with effective leadership of some countries, Africa also demonstrated agile and innovative responses at global, regional and local levels. Globally, engagement with COVAX, WHO, Bill & Melinda Gates etc. remained a constant where required. Triangular regional partnerships (Government-Private and Public Health) as well as significant bilateral (South-South) support, and notable (Diaspora African-Continental African) partnerships vis a vis effective commodity manufacture and distribution and therapies were important and highly effective. Notably Madagascar reminded the continent of symptomatic but effective local plant and herbal remedies; Ghana engaged in mass post contact tracing and testing that proved both effective and resource efficient. There was also a redeployment of public facilities for quarantining and the use of many informal workers in contractual mask and PPE manufacture supervised for quality by the high performing African CDC. Senegal created effective low-cost respirators and COVID-19 test kits. Rwanda strengthened health access and COVID testing by strengthening its already impressive universal health system and Uganda manifested an extraordinary capacity for effective data collection, management and application in its effective COVID-19 containment.

As many of the urban population (especially) live in crowded dwellings, social isolation and restriction of movements became a challenge. Both Gender Based and Domestic violence increased notably during the lockdown period as in many other parts of the world. Africa was not spared the Strategic weaponization of social media and the political application of misinformation unfortunately. The African CDC did initiate early systems to identify and expose such which has helped lessen the degree of authoritarianism certain countries became subject to.

Certain epidemiological and demographic factors have played into Africa's favor; most notably a younger, resourceful, underemployed population than in the western hemisphere. But one cannot underestimate the impact of effective leadership, innovation, and agility on COVID-19 containment. Local factors such as lifestyle (smoking), air pollution (Harmattan) still require assessment of their impact on the variable incidence between Morocco, Algeria, Egypt, South Africa etc.

An increased use and dependence on technology necessitated by COVID-19 highlighted significant socio-economic disparities in national populations. Virtual education, virtual health and virtual case management have become essential for many families. Three population groups, rural, younger and female members of the society have been at a significant deficit for all virtual engagements. Handheld telephones abound amongst the continent's 1.3 billion people; but the quality and capacity of the telephones is significantly disparate and lower in these three groups. I-pads and computers have been gadgets mostly accessed and accessible to the well to do. Millions of children, particularly young girls and women have significantly lagged in their access to health and education as a result. This will impact already high national dependency ratios and access to sustainable livelihoods for many!

Whilst not immune to social media issues such as fake news, we in Africa were spared the incalculable damage apparent in other hemispheres as a result of our prior dire experiences and/or exposures to severe medical outbreaks such as Ebola. Complacency has been present but not as problematic.

The nexus of Social Protection and Public Health with Governance during and following the COVID-19 crisis was evident. Clearly local solutions must continue to be developed as national health issues are considered and effectively managed. Communicable diseases such as malaria, TB, HIV remain rampant even as a looming epidemic of Non-Communicable Diseases looms over the African continent. Mental health issues were very common; few facilities were available however. The role of accurate local data collated, integrated and applied effectively at the local and regional level cannot be underestimated. A well-functioning regulatory/governance body such as the Africa CDC has been invaluable. Apps created for COVID-19 containment can be adapted to support middle level public health training and application (so long as interoperability and connectivity issues are addressed) in the management also of malaria, TB, Sickle Cell and HIV. Africa has historically always been found (if not placed) at the middle of geopolitical issues. As the Global Order shakes itself out, it behooves African countries to strengthen regional governance and regulatory systems, effectively. Data will remain critical in this. We health professionals and leaders in Africa must pay closer attention to data collection, review and management that underpins our support and regulation in the health sector. We have to ensure we no longer continue to be managed as a monolithic entity i.e. with a single story by either Global and/or Regional Health Leaders. Indeed, there are many other lessons that can be learnt in a bidirectional manner between established global health leaders such as GAVI, PAHO Bill & Melinda Gates Foundation and others such as emergent regional and local health leaders on the African continent. A most important lesson however has been that Health must be viewed and managed as strategic national/international asset vulnerable to the quality of our national/international data and social networks as much as the quality of our populations.

Human behavior in the time of a global pandemic

Elhadj As Sy

Co-Chair of the WHO/World Bank Global Pandemic Preparedness Monitoring Board and Chair of the Kofi Annan Foundation Board

We are in the middle of an unprecedented pandemic and the response lies in politics, responsible leadership but also science, at a local and global level. In this situation, we tend to panic and when it subsides, perhaps we should not go back to what we consider to be normality and we should shape the future we really want. COVID-19 has exacerbated some of the dysfunctionalities in our national and international institutions and has shown the breakdown in and the need for global leadership. We also suffer from a great lack of trust in the global system, and the global order risks turning into a global disorder. Human behavior is central to the pandemic and the way the virus is spread or stopped. That is why global citizenship and responsibility as well as solidarity are key to slow down the pandemic.
We also need multilateralism that goes far beyond the UN system, in order to reach a true global response to the health crisis. If COVID-19 is a "global public bad", then we need a global public good as a response. Finally, we need to be somewhat naïve and to believe in human solidarity.

We will always be confronted by political shocks, climate shocks and health shocks. The question is whether those shocks will necessarily become crises or will lead to catastrophic situations or to an unprecedented pandemic, like the one we are in the middle of. I believe that the answer lies in either preparedness in responsible leadership or lack of it. It lies in active citizenship that must go hand in hand with responsible leadership, in science which should be guiding our analysis, as well as our response in politics, in action and activism or lack of response – we are seeing children on the street reminding us of the importance of the climate. We are seeing people living with HIV/AIDS now telling us that they are experts because they host the virus in their own bodies. It lies in partnership or lack of it, in solidarity, in local action and global action. I would also say it lies in trust, but there will be no trust without accountability.It is against that context that we see how we respond or react. We ultimately react rather than respond honestly because we find ourselves in what we find the cycle of panic and neglect. When we are confronted by an unprecedented shock, we all panic, and we focus all our attention and resources on one. When it subsides, we seem to go back to whatever we consider to be normal. This time, we are being reminded that perhaps we should not go back to normal because normal has not worked. We now have to move forward and then shape the future that we would really like to see.

COVID-19 has revealed all of that and it has also exacerbated some of the dysfunctionalities that we have seen in our national and international institutions. It has shown that, in the real breakdown in leadership, the world is crying for leadership and we do not have a critical mass of leaders, political or otherwise, at a global level, that could track the way forward. What is dysfunctional in our national and international institutions is mainly caused not by the institutions or bureaucrats themselves but the very members that should be funding, supporting, guiding and, giving the authority to those institutions to do the work they are supposed to be doing. I would like to be naive. The United Nations had a Charter that started with real people and not with governments. Perhaps then we would put the people back at the center of what we do to make sure that leadership is about delivering on promises we make to people and their wellbeing. If we do not, we should not deliver on those promises. We do not have the trust required and unfortunately, we currently have a deficit in the level of trust in the global system.

The generation I belong to is the one that started studying international relations with the first chapter called "The World Order". It is about the global order, but we are seeing today or risk seeing the global order turning into global disorder. Why? The member states, partners and members of the institutions that make it work turn out to be the ones who are weakening it. The World Health Organization (WHO) is a good example. Among the biggest funders of the WHO are the non-member states and a private foundation, and those were maybe supposed to lead. We have seen examples of people withdrawing their funding and questioning their membership in the WHO. At the same time, we expect an authority and a guidance from this organization and that will not happen in these conditions.

Human behavior is central, not only the behavior to prevent disease, but also our behaviors and attitudes when we face shocks and hazards and how we respond to those. We can change our behaviors, but what is most difficult is to sustain them. We can compare this to quitting smoking and it is often said ironically: "Quitting smoking is very easy, I did it 10 times". That is what we are facing now in the time of COVID-19. We are talking about a second wave, but I believe we are still in the same wave because nothing has changed in the overall situation, or in the way the virus is transmitted or stopped. What has changed dramatically is our behavior and when we relapse, it will relapse. We are seeing that happening increasingly in the different situations we are facing.

I also want to be naive to believe that there will be a growing critical global citizenship beyond borders, that it will challenge leadership and then that it will take in that network of solidarity that is required to put the pressure on all decision-making levels: local communities, private sector, government, international institutions. Therefore, equity and inclusion are not just a wish but at least something we apply to make sure that we are all safe. I think there will be no winners at all in this "competition" because we fail to remember that in a pandemic, none of us is safe. Multilateralism is far beyond the UN. Of course, we need the UN and international fellowship discussions. We need multinationals that are even becoming subjects of international law and very important factors in international relations. We need pharma and economies too, so that it becomes a true global response. We also have to believe that a national response prevails over a government response. We need communities at the center. We will have to heal the trust that is broken between leaders at national levels and their citizens. Additionally, we always continue to try to strike the balance that we need science, and we should definitely not take it for granted. Science has been challenged by so many naysayers, anti-vax campaigners and social media amplifying all kinds of fake news. We need politics that are part of the solution, not part of the problem, and we need activism that holds us all accountable. Maybe Utopia, naivety and solidarity I completely believe in will be required to guide us, so that it will lead to local action and a global response. Finally, if COVID-19 is really a "global public bad", we may need a response that is called a global public good. It does not matter how we define it, if it is in the spirit of solidarity, equity, or the spirit of just making sure we are all safe. And we use this way of making sure that the investment we are making within our geographic borders will not be challenged by the lack of investment in action somewhere else in the world. Again, none of us is safe and can ignore that.

Session 2

Technology, Economics, Health Ethics

Managing healthcare: the need for, and the difficulty of, a strategic approach

Jacques Biot

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The World Health Organization defines Health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. This discrete, binary, demanding formulation (to be, or not to be, in good health) leaves way to a very detailed, universally recognized segmentation of diseases, ICD-11, listing about 55'000 different pathological situations. Five priorities are listed by the institution but pertain to transverse issues.
Economists and policy-makers, for their part, look at health almost exclusively as an expenditure, whether collectively or privately funded. These expenditures are comprised of an extremely diverse basket of goods and services, the profitability of which is extremely heterogeneous, and which are only rarely mentioned as contributing positively to GDP formation. Few recognized KPIs exist to measure and compare the performance of various healthcare systems.
Industry players, whether care providers or suppliers of healthcare goods, receive little guidance from buyers and payers as to the possible or desirable type of services or goods that should be made available to serve the public in the future, except for a generalized, and mostly blind, request for overall cost-cutting. Hence, with a few exceptions, no consensual planning exists to orientate research, development and capacity-building investment. Hence innovation in the field is still mostly science and technology driven, a favorable feature to provide disruptive remedies to some major health issues, but which allows for no reasonable marketplace to reconcile demand with supply and rationalize economic flows.
The present paper calls for the emergence of a strategic body which would provide the public with a rationale analysis of health needs, sort out priorities in lien with the public's preferences, and provide guidance to industry players as to the expectations of healthcare systems, so that investment in R&D and in manufacturing could be progressively tailored to the expectations of the general population in a way that is financially sustainable for society.

1. Background

The World Health Organization (WHO) defines Health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'[1]. This comprehensive, and demanding, definition has not been amended since 1948. This discrete, binary formulation (to be, or not to be, in good health) leaves way to a very detailed, universally recognized segmentation of diseases, ICD 10[2], to be updated by the 11th version[3] as of Jan 1, 2022, listing about 55'000 different pathological situations. WHO on its website communicates about 177 different 'topics', ranging from the very general, e.g. 'cancer', to the very focused, e.g. 'Buruli ulcer' or 'Crimean-Congo hemorrhagic fever', with no rating of relative importance. Five priorities are listed by the institution but pertain to transverse issues.

Economists and policy-makers, for their part, look at health almost exclusively as an expenditure, whether collectively or privately funded. These expenditures are comprised of an extremely heterogeneous basket of goods and services, and are only rarely mentioned as contributing positively to GDP formation[5 6], contrary to the vast majority of other value-creating human activities. Few recognized KPIs exist to measure and compare the performance of various healthcare systems. In purely financial terms, the difference in profitability between various contributors in the chain is abyssal.

Industry players, whether care providers or suppliers of healthcare goods, receive little guidance from buyers and payers as to the possible or desirable type of services or goods that should be made available to serve the public in the future, except for a generalized, and mostly blind, request for overall cost-cutting. Hence, with a few exceptions such as the US cancer plan or the Bill & Melinda Gates Foundation's plea for vaccination, no planning exists to orientate research, development and capacity- building investment. Hence innovation in the field is still mostly science and technology driven, a favorable feature to provide disruptive remedies to some major health issues, but which allows for no reasonable marketplace to reconcile demand with supply and rationalize economic flows.The present paper calls for the emergence of a strategic body which would provide the public with a rationale analysis of health needs, sort out priorities in lien with the public's preferences, and provide guidance to industry players as to the expectations of healthcare systems, so that investment in R&D and in manufacturing could be progressively tailored to the expectations of the general population in a way that is financially sustainable for society.

2. Management of healthcare: where do we start from?

Healthcare provision and health-product supply are currently scattered amongst innumerable players. Leading players in healthcare provision, whether expressed in number of beds, number of stays, or monetary units, are in majority public (governmental) systems such as the National Health System (NHS) in the UK, or its equivalents in other countries. By contrast the world-leader in for-profit health provision, HCA Healthcare[7], operates less than 200 hospitals among the 5500 facilities active in the US. In 2017, the top 10 US provider systems were responsible for only 18 % of all inpatient days in the country, with an additional 3,000+ operators accounting for the remaining 152 million inpatient days[8].

In the pharmaceutical industry, the current leader in ever-changing League tables, Pfizer[9], owns about 5% of the total prescription drug market[10]. In the medical technology industry, the top ten companies own only 40% global market share.

This comes in strong contrast to other similarly technology-intensive industries, such as the aerospace industry, or information and communication technology (ITC) industries, which over the years have become highly concentrated with two or three world leaders commanding most of the market. The same concentration is observed in more recent data-based activities, with the GAFAMs controlling quasi-monopolies in their respective fields, according to the now classical saying "the winner takes all".

On the buy side, the split of the customer function between the patient (consumer), the prescriber (decision maker) and the payer/insurer, makes it difficult to rationalize buying patterns as the three parties often display conflicting interests in front of care-suppliers. As a consequence, inefficiencies abound:

- Most patients get no benefit from the drugs they take – the number-needed-to-treat (NNT) is, for most drugs, extremely high[11 12], (Note: which does not mean patients should stop taking their prescription medicines)

- Iatrogenesis exerts a considerable toll[13]. For illustrations, WHO estimates that the occurrence of adverse events due to unsafe care is likely one of the 10 leading causes of death and disability in the world, that in high-income countries, one in every 10 patients is harmed while receiving hospital care, or that in OECD countries, 15% of total hospital activity and expenditure is a direct result of adverse events
- Productivity is low. As an illustration, in the US between 2001 and 2016, healthcare delivery contributed 9 % of the growth in the economy in constant $ terms—but 29 % of new jobs[14]. McKinsey estimates that over this period, multifactor productivity in healthcare decreased by 420 basepoints per annum and had a negative contribution (13%) to the growth of the sector, which was mostly driven by job creations. To tackle these inefficiencies, the market regulation is driven mostly by payers and/or insurers, mostly at a macro-level. While pricing and reimbursement regulations vary widely from one market to another in terms of bureaucratic refinement, the general trend leads to overall cost-cutting in old developed countries, with belated reallocation of resources[15] between diseases and types of care, taking place at a much slower pace than the pace of changes in the epidemiology or in health technology. The pattern may be different in emerging countries[16], such as Eastern Africa (e.g. Rwanda) or China, where the Gross Domestic Product (GDP) growth, combined with a strong political will, has allowed a proactive switch from traditional medicine, i.e. almost from scratch, towards a 'rationale' health system.

Finally, the health industry is left without much clue, and with even less economic incentive, as to which domains should be prioritized to satisfy the future expectations of healthcare systems. The uncertainty as to what the social demand will be a few years down the road, combined with the considerable time and risk it takes to move a discovery from the bench to the market, pose a formidable challenge to those in charge of planning investments. The next sections aim to identify more in detail the hurdles that should be overcome to allow for better management of healthcare.

3. Which metrics for health?

As was hinted in the introduction, enjoying 'good health' according to the WHO definition is almost unachievable. The major issue for decision makers at all levels is hence to define the optimal health status that can be achievable with available resources. This in turn can only rest on the existence of a consensual continuous metric allowing to measure and compare health status for individuals and for populations, keeping in mind that the health status is not an additive value. Another issue that will be discussed in further sections is the considerable hysteresis in resource allocation, which reduces the ability of decision makers to allocate resources in an optimized way at a micro economical level in accordance with the recommendations of health intervention assessment. What should be reminded is that there are about 55'000 different diseases according to the ICD (International Classification of Diseases)[17]. Within each of these diseases, a gradation of severity is most often likely to occur. The evolution of any given pathology over time, even at the same grade of severity, is often different from one individual to the other. For a given disease, the pattern of symptoms may also vary from one patient to the other, leading to a perception of disability which is very subjective. Actually, only mortality is a readily quantifiable data – and even so, the age at which death happens is not indifferent and there is no equivalence between a death at birth, during childhood or adolescence, young adulthood, or old age. Epidemiologists, whose task is to reckon the number of patients in various boxes of similar disease and severity, clinical investigators, whose task is to assess and quantify the efficacy and safety of health interventions, especially innovative ones, and health economists, whose task is to assess in a comparative way the amount of resources needed for such interventions and to establish cost- efficiency comparisons between different interventions, are thus left with extremely heterogeneous data to deal with. In order to be able to compare the burden of diseases[18] on populations and on individuals, health economists have developed the concepts of aggregate indicators such as Disability Adjusted Lifeyears (DALYs) lost, and Quality Adjusted LifeYears (QALYs). However, these indicators are potentially flawed because they are based on human preferences, assessed by samples of patients, and there is ample literature[19] pointing to the ethical, methodological and contextual limitations of such ratings.

4. Which metrics for the value of interventions?

The gold standard to demonstrate that a novel health intervention is safe and efficacious is the so-called RCT (Randomized Clinical Trial)[20], in which two samples of patient population, carefully selected to be standardized and absolutely identical to each other at entry, are exposed in a double-blinded way[21] to two (or more) different treatments (typically placebo vs. active, or active A vs. active B if a reference treatment is already available). Typically, major determinants of a RCT are the size and homogeneous definition of the study population, the designation of the primary endpoint considered as the marker for success, and the expected size of effect on this particular outcome. While the choice of primary endpoints for a given, well studied disease is usually fairly consensual within the relevant clinicians' community, many debates arise down the road, especially as investigators are led, in many chronic, slowly evolving diseases, to rely on so-called surrogate endpoints[22], because it would not make sense to wait for a difference in clinically material endpoints (typically overall survival) which may take many years to emerge with statistical significance. Health technology assessment agencies, which have to rate the utility of a novel intervention in order to guide government and insurance reimbursement and pricing decisions, are thus confronted to a major dilemma:

- On the one hand, they are amongst the staunchest defenders of the RCT concept, because they view this as the only statistically valid method of comparing interventions
- On another hand, they express a number of reservations[23] [24] once they are presented with the outcomes of a study:
  - o They – rightly – claim that the study population is not identical to the real-world target population and hence study outcomes may not be extrapolated to a use in the general population
  - o They often challenge the clinical relevance of clinical endpoints chosen to demonstrate efficacy, and tend to devalue the 'size of effect' even when the analysis does carry statistical significance.

As a consequence, the very constraints that innovative investigators have to follow to expedite conclusive clinical trials and to secure a fast registration process, backfire once submitted to health technology assessment agencies.

Independently of these methodological considerations, any lay person looking at global market access procedures, however refined regulations may be to try to ensure some consistency in the assessment of novel interventions, will recognize that the process of clinical trials, while totally unavoidable and scientifically undisputable, does not provide any clue, nor intends to provide any, on the preferability of addressing disease A rather than disease B, if resources are restricted and do not allow to treat both. This is why health economists in some countries resort to QALYs, in order to turn highly heterogeneous clinical endpoints into a universal metric which, in their view, would allow to compare the efficacy and the efficiency of health interventions across the board. However, as mentioned and referenced in section 3, the consistency of QALYs is subject to caution. Finally, the number of clinical trials has to be taken into consideration. As of end-2019, more than 350,000 trials were on course in the world[25] (Figure 1), of which (Table 1) more than 280,000 are interventional i.e. aim to measure the effect of a given intervention, of which more than 150'000 pertain to drugs or biologics and 60,000 to medical technologies. This number has grown from hardly more than 2,000 studies back in 2000.

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Figure 1: Number of registered studies

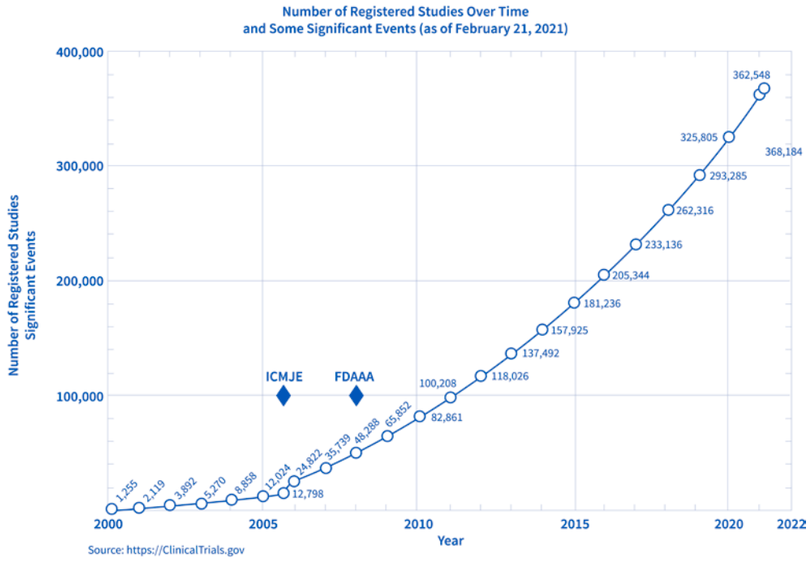


Table 1: Type of studies

Study and Intervention Type (as of November 23, 2020)		Number of Registered Studies and Percentage of Total	Number of Studies With Posted Results and Percentage of Total***
Total		358,767	46,119
Interventional		280,551 (78 %)	43,337 (94 %)
Type of Intervention*	**Drug or biologic**	154,481	33,247
	Behavioral	92,233	8,462
	Surgical procedure	29,373	2,341
	Device**	36,410	5,987
Observational		76,663 (21 %)	2,782 (6 %)
Expanded Access		704	N/A

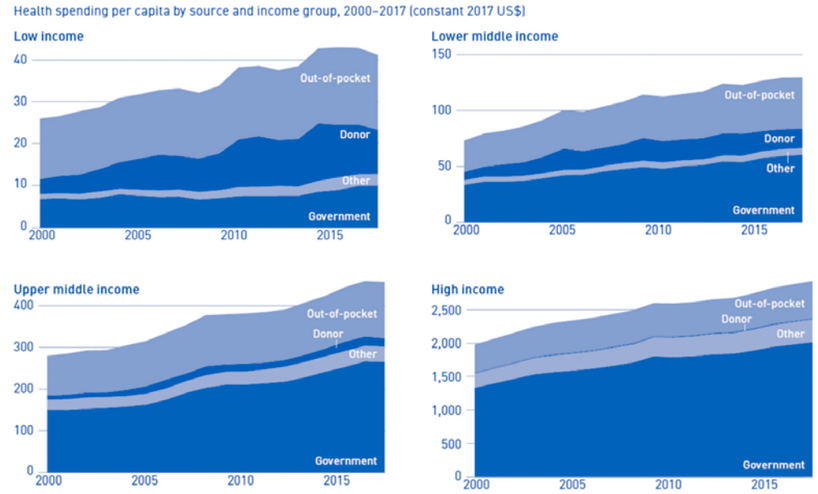
Actually, just a proportion of all clinical studies end up with the publication of their outcomes, namely 46,000 as of 2019. However, this still generates a wealth of micro-information which is obviously essential to guide individual care but is in no way aimed at guiding an overall health strategy.

5. Which preference for governments?

The French President's recent stance on COVID-19, stating that France would fight the virus 'whatever the price', echoes the common wisdom in the French opinion that *"La santé n'a pas de prix"* which, rather than qualifying health as 'priceless', which could be ambiguous, would better be translated by 'health is invaluable'. This dogma is of course contradicted daily by public decisions which, in many domains not limited to health management[26], have a bearing on citizens' health, have a cost and as such carry an underlying valuation of human life and disability.

In contradiction with the idealistic French view, all governments are bound to recognize, and try to control, the cost of health care, albeit at varying levels and with varying success. Relative growth of healthcare budgets is a universal feature[27], with global healthcare spending growing at a compounded pace of 3.9% p.a. from 2000 to 2017 while GDP grew 3.0% p.a. Overall the public contribution to health expenditures reaches 60%, ranging from only 24% in low-income countries up to 69% in high income countries, although the pace of growth was higher in low- and middle-low-income countries (Figure 2). Focusing on OECD countries[28], 71% of health spending is from public sources, with one outlier country, Switzerland, where coverage by private insurance is mandatory. The weight of healthcare expenses within total government expenditure is in average 15%, ranging from 9% to 23%. In absolute terms, spending for health from all sources amounts to about $4000 per capita in average in OECD countries, varying from hardly more than $1,000 in Mexico to more than $10,000 in the US.

Figure 2: Global spending on healthcare



In contrast to ever-growing health expenditures, health outcomes, as measured on existing indicators[29], are stalling in many developed countries. The crudest indicator of all, life expectancy, has declined in 2015 in 19 countries. Detailed indicators vary widely from one country to the other, even within the relatively homogeneous group of OECD countries – a mirror of widely varying approaches to healthcare management[30].

Governments, and private health-insurance organizations, where relevant, have long struggled to curb the growth of health expenses, and in some cases to make them more efficient for a given amount of spending. To this purpose, potential levers are not many, and payers face a number of constraints to exert control. Foremost, considerable hysteresis exists in terms of human resources. It takes about 12 years to train a medical doctor, hence the doctors' demography of today is driven by Medical School recruitment of more than one decade ago. Inside this population, the break-down between respective disciplines is inherited from cumulative interns' choices years and decades ago. Hospitals carry huge tangible assets, which heavy technology tends to inflate, thus weighing on future amortizations. Closing beds or restructuring care provision is a social, political and financial conundrum. Actually, the only short-term variable on which payers have an immediate say are healthcare goods, whether drugs or disposable medical equipment.

To face this challenge, payers oscillate between various schemes [31] [32] resorting to global budgets, activity-based payments, or payments by result. In many cases, funds are still allocated within silos, thus limiting the ability to funnel savings from one

branch to another. Prevention is often underprioritized because its expected benefits are harvested on the long term, not in line with political horizons.

As regards the procurement of healthcare goods, the British have long taken a position which restrains the coverage of drugs or medical technologies only to those which, based on QALYs gained according to clinical study outcomes, stay within a range of 20'000-30'000£/QALY gained. In consequence this leads to coverage denial for a number of expensive interventions aimed at small populations suffering from specific cancers or rare diseases, leading to vocal patient dissatisfaction within the ranks of related families [33] [34]. Although devoid of a similar rationale threshold, the French authorities temporarily or definitively disallow the reimbursement of many innovative drugs in the field of cancer (e.g. immunotherapy in dermatological cancers), or transplantation, or in some orphan diseases.

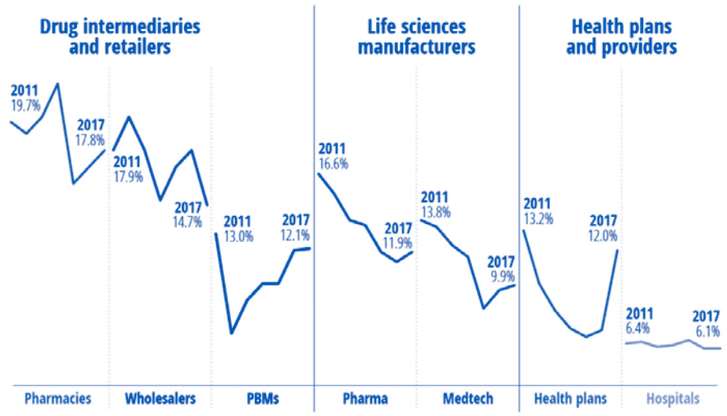
With 5'000 to 8'000 rare diseases identified [35] [36] [37] and high patient expectations within the related families, and with the growing segmentation of therapeutic areas such as oncology in the wake of precision medicine made possible by genetic research, governments will increasingly be faced with social demand for allowing access to costly, highly innovative interventions targeted at small or ultra- small patient populations. The sustainable business model for the dispensation of care to these groups remains still to be invented.

In summary, at a time where science-driven solutions flourish to address a growing number of rare conditions, and where at the same time global performance indicators tend to stall in most developed countries, governments and payers remain impeded, in their effort to streamline health provision, by the existence of silos and by the global hysteresis of health systems.

6. Which economics for providers and suppliers?

On the supply side, all players have seen their profitability decline over years, with an important gap between healthcare provision and healthcare product manufacturers – with some strong disparities within each category[38].

Figure 3: Return on capital in life sciences and health
Return on capital performance in life and health care nosedivided between 2011 and 2017



Sources: Teresa Leste, Yakir Siegal, and Maulesh Shukla, *Return on capital performance in life sciences and health care: How have organizations performed and where are best bets going forward?*, Deloitte, April 30, 2019.

In the provider universe, profitability is typically in the low one-figure percentage in most countries: according to Deloitte[39] 12 % of German hospitals are in financial distress, the average profit margin in 2017 for top hospitals in the Netherlands was 1.8 %, and a typical major US hospital with a current 3 % margin will show a negative margin of (3.5 %) in 2023. Similar estimations are provided by McKinsey [40] for stand-alone hospitals, with a ROIC in the 3-5 % range in the US, although some

innovative care dispensation schemes are described as providing significantly higher returns, e.g. 10-15 % for ambulatory care. In other geographical settings, high profit niches can also prosper, such as dialysis clinics in France which yield an average 15 % return on revenues[41]. In general, a trend towards specialized care addressing targeted therapeutic areas (e.g. dermatology, gynecology, ophthalmology, oncology, etc.) can be observed, as a way for agile players to gain attractivity and improve productivity and profitability.

The fundamentals for widespread low profitability of health provision are to be found on both ends of P&L accounts. In terms of production factors, this activity remains mostly a workforce-intensive service industry, although more heavy medical equipment, such as robots or radiotherapy devices, is involved in care delivery. Flexibility in case of evolving demand is limited by the dedication of the staff and of the facilities, so that fixed costs are weighing heavily on the expense side. Delocalization can most often not be considered – until the progress of communications in the wake of 5G deployment allows the transfer of image interpretation and telesurgery to cheaper environments. On the revenue side, tariffs are set by payers who have a stronger bargaining power and manage to keep providers close to break-even.

Major trends in the provider industry are expected from increased technology adoption, including AI, with an impact on care organization, resource utilization, quality of care, patient and medical staff satisfaction. It remains to be seen if quality and productivity improvement will benefit providers or whether increased productivity will be confiscated by payers as efficiencies are rolled out.

By contrast, the health product industry (biopharma and medical technology) enjoys traditionally lofty profits. The traditional 'moral' motive for this lies in the intensity of R&D and in the high level of risk attached to drug discovery and development.

However, here again, the market tends to become segmented between different categories. Broad-portfolio generic companies, facing heavy competition and devoid of measurable differentiation, operate in a commodity universe: a recent BCG study[42] estimates that about half of their products have a negative ROI. Only agile generic companies focusing on being First-to-File or First-to-Market may temporarily enjoy significant returns.

In innovative biopharma and health technology, traditionally yielding high returns[43], R&D remains the driver of growth and the strategic backbone of business. However, the way in which it is conducted has changed dramatically over years.

In the biopharmaceutical industry, after massively outsourcing development in the 1990s[44] to large, specialized contractors (Clinical Research Organizations or CROs), manufacturers have gone one step further and rely now in majority on external sources to discover new biologicals or new chemical entities. These external sources are more or less mature companies, funded by Venture Capital, which have been formed to develop potential applications of disruptive discoveries stemming from the academic research – or sometimes from large companies which did not dare carry the risk[45].

This change in the conduct of new product targeting and development has led to the fact that in 2018 63% of all new drugs originated from small companies. This led to a sizable increase in new drug registration, which almost trebled compared to a decade ago, with an all-time record number of new drug registrations in 2018 (59) of which 33 (58 %) aimed at rare diseases. During that year 50 % of NDAs originated from small structures and less than 50 % stemmed from in-house R&D efforts[46]. A study by Deloitte[47] shows that the Internal Return Rate (IRR) of biopharma R&D in a sample of 12 top pharma companies has declined from 10.1 % to only 1.9 % from 2010 to 2018. In terms of risk, this means that a large share of the risk has been transferred on Venture Capitalists, but the counterpart is to be found in the extremely expensive price that acquirors have to pay to source-in new products once their risk profile has been reduced.

Finally, the business model for the medical technology industry is even more fragmented, as this definition includes products reaching from very unexpensive disposables such as surgical gloves, up to extremely costly imaging, surgical or radiotherapeutic equipment and all the sterile environment which may accompany these tools. Globally, Bain[48] qualifies the medical technology as extremely profitable, with margins in the range of 22%. Compared to the pharmaceutical industry, medical technology carries less risk of development failure, shorter development times, and enjoys an immediate proximity with users. Actually, most innovations stem from a need identified by a surgeon and turned into a product by an engineer, following highly entrepreneurial opportunistic models.

7. The need for a strategy

The sections above have listed the raison d'être and the financial drivers behind each of the players in the healthcare system. The question now arising is:

where is the system heading, operations-wise and financially? And which invisible hand drives it? Let's summarize respective interests. Governments and payers at large are confronted with the fantasy of Nature, which has provided, as per the ICD-11, for about 55,000 different pathological situations to curse mankind, without reckoning with the advent of unexpected pandemics from time-to-time. The burden of each of these diseases varies over time, geography and location. There is no universally accepted metric to gauge the said burden and provide comparisons or cost evaluations. Epidemiologists have developed good models and can reasonably calculate how the burden of disease will or may evolve over time (excluding pandemics) based on currently available interventions. But they have no legitimacy to suggest priorities if resources are not infinite – which they are not.

To tackle these woes, governments and payers can allocate funds levied on the rest of the economy via diverse means, which come in competition with other public or private needs. Part of this money can relatively easily be reallocated (drugs and or medical disposable procurement), notwithstanding the long-term effect of such savings on employment and on future R&D investment, and the rest of expenses is pretty much fixed in amount (heavy equipment amortization and wages) and disciplinary repartition (duration of medical training and equipment specialization). On the (fast-growing) edges of the system, public deciders are left with the option to reimburse, or not, innovative therapies which emerge at an ever-faster pace from clinical research (with its 350,000+ trials under course), on which in the majority of cases they had no initiative as payers, but which meet some kind of social demand irrespective of the level of the burden.

Health providers, on their end, compete locally for market share, for skilled physician and skilled nurse recruitment, and in some places for trained caregiver recruitment. Their revenues are driven by volume (i.e. epidemiology) and payment schemes. As already underlined, their costs are pretty much fixed and their leverage on tariffs is fairly low, as their industry is not consolidated and faces powerful, often public monopolistic, payers. Investment in additional capacity may be subject to prior clearance from the health authorities. In other words, strategic drive is limited, highly dependent on governments and payers' decisions – which we have seen are not necessarily driven by an explicit strategy, and the only leeway to improve profitability resides in better care organization, potentially in delocalizing of some work-intensive tasks in the wake of AI and communication progress, and in opportunistically developing disciplinary focused offers in therapeutic areas where pricing pressure is lower or out-of-pocket expenses more common.

Finally, for manufacturers in the fields of innovative biopharma and medical technology, the current strategic guidance is based on the crossing of several sources of data:

- epidemiological data, to prospectively assess the respective burden of diseases in terms of number of patients, severity of disease, unmet needs, ease of demonstration of potential effect
- consumers' and/or payers' willingness-to-pay
- availability, and affordability (via a licensing or an M&A agreement) of potential drug targets in the burgeoning universe of biopharma R&D start-ups.

As this process is mostly based on a mix of academic serendipity and commercial greed, the resulting port-folio, on the promises of which the value of companies is assessed, has little reason to match the expectations of governments in terms of public health – should governments have such expectations.

Globally, at the end of this process, the system ends up with more proposed new interventions (drugs or devices or equipment), targeting ever smaller populations, for an ever higher individual price per patient – with manufacturers claiming that the cost and time to develop an orphan drug are not different by an order of magnitude of what is needed for a blockbuster targeting hundreds of millions of patients. If this reasoning is applied to 55'000 pathologies, or even just to 6000 rare diseases at several hundreds of millions of dollars revenues each, it is clear that the whole economy is not sustainable.

This is a reason why more and more voices call for a more rationale, data-based, socially acceptable strategy to be concerted [49] [50] [51] amongst healthcare stakeholders, including patients.

8. Conclusion

One central player in this whole construction has been little mentioned in this paper: the patient – current or future[52]. Spontaneously he of she feels that remedies should be proposed for every ill he or she suffers, or may suffer, from. Yet as an insured individual, or as a tax-payer, no patient is ready to contribute without limits to the ever-growing costs of the system. The arbitration between supply of goods and services, and solvent demand, usually performed even unconsciously by consumers, is here delegated to outside players, the prescriber, and the payer. At a micro-level, even though mechanisms exist to try and prioritize the reimbursement of care, many contradictory decisions persist when it comes to funding interventions. At the macro-level, no institution is vested with the role to define, and the power to enforce, a strategic distribution of limited resources to the innumerable health interventions that patients request individually.

The time has come to reinforce research and education in epidemiology and health economics. The fast improvement of data collection and management, using high performance communication and augmented intelligence gear, should allow for a more informed, consensus-seeking, definition of public preferences in terms of health-policy, which would serve as a basis for the allocation of public resources to all healthcare players.

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Where has technology brought us today?

Alexandra Prieux

President of Alcediag,
Founder of SkillCell

Since the invention of the stethoscope in 1816 and the discovery of penicillin in 1928, technology has completely transformed the medical world. Patients' management and treatment dramatically improved while technology increasingly became a central factor of medicine. Immunotherapy, fetal surgery, new generations of drugs, etc. saved many lives and gave hope in the most desperate situations.

With the yearly number of patents fillings having more than doubled between 2000 and 2019 for healthcare, the trend is clearly accelerating. It is driven by the nearly systematic use in the healthcare industry of technologies initially developed for other domains, leading to the use of robotics for surgery, radioactive molecules for medical imaging, advanced materials for prostheses, artificial intelligence for diagnostics, etc.

The use of these new technologies mostly aims at one of two seemingly opposite objectives. The first one is an increased efficiency for medical treatments which are often available at first to a small portion of the population. The second is a wider financial or geographical accessibility (i.e., telemedicine). In both cases, the extensive use of technologies permanently changes medical practice as well as the role of the doctor who becomes more and more a technology user.

Alongside with the progresses carried by technologies come new challenges that will need to be overcome. They include the necessity:

1. to test and validate the efficiency of a large number of new products and solutions, often on human beings,

2. to control the costs of these new technologies,

3. to master the challenge of resistance to change which is proportional to the level of innovation.

Where has technology brought us today? To assess this, let us go back to the year 1850. At that time, life expectancy was 40 years old. If it was still the case today a large majority of the population would already be dead. As a woman, I would also have a higher risk of dying in childbirth. Newborns would also be at great risk, as at the time, about 25% of deaths were children under the age of five. In 1850, the three main causes of death were pneumonia, tuberculosis, and diarrhea. Faced with these diseases, medicine was then mostly helpless. Medicine was developing – the smallpox vaccine, for instance, was invented in the 18th century – but many diseases were still considered incurable.

Where do we stand today? Life expectancy in the Western world has doubled reaching about 80 years old. Infant and childbirth deaths are now very rare. The three leading causes of death are heart disease, cancer, and stroke. We managed to virtually eradicate the three former causes of death in the 19th century. This change has been made possible by better hygiene and more advanced medicine, but science and technology also played a prominent role.

Since 1850, countless innovations have been introduced, including antibiotics, radiotherapy, immunotherapy, and advanced surgery. Progress is not going to stop there: future innovations are likely to change our lives in the years to come. Examples include artificial organs and CRISPR-Cas9, a technology that can be used to edit genes within organisms. Such progress involves great challenges and raises many questions. There are three challenges to address these innovations: the process of their validation, the role of doctors, and their cost.

First, the challenge of validating innovations and, more specifically, regulatory validation. Validating an innovation requires clinical trials, patients, clinicians, and regulators. However, the system in place today is extremely risk-averse and it continuously demands more proof of efficacy, more details and essentially expects that there are no side effects. This means that more preclinical studies and clinical trials are being conducted, in more centers and on more patients, and with more money.

This draws very clearly the limitations of such a system. Already today, people wanting to launch an innovation face tremendous competition for access to well characterized patients for clinical trials. That is why we are experiencing such a significant development of biotechnologies. Excluding COVID because it does not reflect the usual process, the result of such a validation process today is that it can take more than 10 years to put a new drug on the market and it can cost around USD 1 billion. The issue of adverse side effects is problematic because a drug will never have exactly the same effect on seven billion people. Therefore, it is very difficult to guarantee no side effects. Genetic manipulation is a perfect example of this limitation. The direct result of that is that in some therapeutic areas only about 2% or 3% of drugs reach the market in the end. There is a real limitation on what we are going to be able to do just in the innovation validation step. The upside is that it does protect the patients, the downside is that it certainly hampers development at the same time.

Second, the role of doctors. Given the speed of technological and scientific progress, the level of required expertise for doctors increases dramatically, even for general practitioners. This will no longer be possible once a certain level is reached. In France, the studies to become a general practitioner last about ten years, but during this training, very little time is spent on the theory of mood disorders, including depression, which affects 19% of the population during their lifetimes. Most patients with depression only consult a general practitioner first. This is a problem; something needs to change. Progress implies that doctors must be experts, but there is also another way of looking at it. Progress in technology threatens to turn doctors into highly skilled technicians who operate sophisticated machines and computers, only to prescribe paracetamol. Artificial intelligence is already sometimes more efficient than trained doctors in detecting cancers on X rays. As technology advances and has such a big impact on healthcare, there should be in-depth reflection on the role of doctors and how it should evolve and adapt to the progress of science and technology.

Third, the cost in healthcare and innovation. Today, the United States spends around 17% of its GDP on health and this figure is increasing. Yet the quality of care in the United States is often criticized. Where does the problem lie? Are we not spending enough, or are we not spending well? It is hard to say, but there is obviously a limit to the amount of money that can be spent, even on health. Two questions arise: what do we expect from innovation and which innovations should we defend? More precisely, there are two categories of innovations. The first category consists of innovations that increase efficiency, i.e., those that can do at least as well as what is already available on the market but at a lower cost. This kind of innovation is adopted in blind faith - the cheaper the better.

The second category is more complex. It is essentially innovations that bring something new, that cure new diseases or something similar. How do we assess such an innovation? We make a ratio between the price of human life and the cost of research. We try to assess the value of one year of a patient's life, according to the country and the age of the patient. If an innovation is intended to extend a patient's life by one year, and if the cost of that innovation is lower than the value of this one additional year, then it is economically viable. Otherwise, the adoption of that innovation will be compromised or impossible. A very good example is that the cost of one dose to try to save infants with spinal muscular atrophy is over USD 2 million. This figure already gives an idea of how much a baby is worth.

This is one way of assessing the problem of cost, but it can be assessed in terms of of R&D and investment; when and where should we invest? The problem is that money is not enough. R&D is about searching and not necessarily about finding. Many people find it normal that the vaccine for COVID-19 was found so quickly because governments invested so much money. However, it is not that simple. For example, the Bill and Melinda Gates Foundation has made massive investments in malaria, for a rather underwhelming outcome. Their research has concluded that the best prevention should be the use of mosquito nets impregnated with insecticide, which is not a revolutionary treatment. When it comes to technology and cost, the key takeaway is that, in the end, there is no choice. Technology will have to allow for a global reduction in costs, because only then the system will be sustainable.

Where will progress lead us? Progress has always been faster and more spectacular, and we tend to think it will never stop. Thinking that progress is limitless affects our position as a society with regards to death. Many people rely on technology to find a cure for everything: AIDS, cancer, Alzheimer's. The consequence is that most deaths today have become unacceptable. Dying during surgery for any disease is considered unacceptable. Deaths in childbirth are even less acceptable. Even dying from COVID-19 at the age of 90 years old is not acceptable. People may die in a car crash, cancer, or old age, but everything else is not acceptable. However, the use of technology in healthcare will one day reach its limits. The question is whether we will realize when we reach that point, and if so, how will we then react.

Another question we may ask at this point: is innovation a synonym with progress? The answer is not that obvious. Innovation gives rise to new issues, which may even question the notion of progress. Human cloning, genetic manipulation and human embryos are undisputed examples of major innovations, yet most countries agree that they are also highly unethical. The immediate question is where is the red line? Where should science and technology start? When should we decide to stop trying to cure and save? Answering these questions will be a huge challenge for anyone who finds themselves in the driver's seat.

Ethics in health in our technological age: Why, what, when, where, how?

Daniel Andler

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Ethics is a major concern in healthcare, and biomedical ethics, over the last six decades, has shown how to systematically integrate ethics in the decision-making processes at all levels, from policy to individual care. The coming technological revolution, powered by AI, robotics, genetics and other areas of biology, raises new problems. One is that there is no well-established way of developing and deploying technology while holding on to an ethical line. Another problem, in the case of present-day massive technologies, is that they are part and parcel of globalization, so that effective governance must transcend national borders.

Ethics is not just a matter of enforcing agreed upon norms. It is also, and mainly, a common search for norms, a never-ending process. Ethics is produced on the fly, as new possibilities arise, new values emerge, new expectations crystallize in various social groups. Over the last three decades health technologies have produced a steady flux of revolutionary inventions, disrupting established practices and common understandings of some basic ethical and anthropological notions. Hence the need for guidelines, which provide a legible representation of the ethical and legal issues which allows agents in the field to navigate the situations they encounter daily. But guidelines depend on the ethical reflection conducted by society at large, they are not the beginning nor the end of the process of ethics.

Many obstacles stand in the way: technological fatalism, the concentration of power and knowledge in the hands of a few, and above all the rush for dominance, whether by corporations, nations or individuals. What is needed above all is the time for "the new forms of the good to take a definite shape" (Joseph Raz): slowing down may be the most urgent need in our epoch of technological revolution.

Ethics is important. But why is it especially important in healthcare? Because, on the receiving end are people who, singly and collectively, have a lot at stake, are a captive market, and are vulnerable; because, on the providing end, in both public and private arenas, the budgets are enormous as are the opportunities for enrichment; and because research and clinic are intermingled yet pursue different agendas, raising serious conflict of interest issues. That much is fairly obvious, while somewhat vague at first. It has taken the emergence in the 1960s and 70s of the field of bioethics, together with medical and clinical ethics, and its subsequent considerable development, to give substance to our intuitions in this regard, to reveal unsuspected complexities, and to show that bringing ethics to the fore can be productive.

The question before us today is whether the advent of hugely powerful, disruptive technologies alters the problem situation and in what ways. Part of the problem is globalization, which both amplifies these technologies and is largely enabled by them. Their governance must accommodate interdependence between nations, on pain of remaining ineffectual, and intergovernmental ethics is no simple matter. But first we must ask a more basic question.

1. What is ethics?

We know an ethical issue when we see one. When we hear about handicapped children having been injected cancerous cells to further research programs in oncology, our 'ethical bell' gives out a loud ring. When we find out that Boeing let the 737 Max fly after the first crash although they knew what caused it, our bell sounds again. These are cases of what we think of as clear violations of ethical norms. A different sort of case is exemplified by end-of-life decisions in intensive care units: ethics is involved, we clearly sense, but in the form of dilemmas rather than violations. Examples abound, and our daily and professional lives, however callous or forgetful some of us may be, some or all of the time, are strewn with ethical issues.

Being familiar with the phenomenon doesn't entail being clear about it. Institutions with the term 'ethics' in their title or mission struggle with spelling out what it refers to— they tend to fall back on examples, as I've just done. The best definition I can suggest is that of philosopher Joseph Raz: Ethics is the endeavor to give substance to the abstract category of the good.

To 'give substance' can be understood in two ways. If we allow ourselves to look back in time, we can imagine a moment where oncological experimentation on handicapped children was seen as a dilemma, not a violation: physicians looking for a cure were laboring for the long-term benefit of humanity, and pondered about whether this noble end justified the means. Going back just a little further, it perhaps did not occur to physicians that it might raise any ethical issue at all. It is precisely that sort of case which gave birth to the field of bioethics. And what these examples show is that ethics isn't just about making sure that ethical norms are followed; it is also, in fact for the most part, about creating and discussing the norms to be established. These are two different ways of giving substance to the abstract category of the good.

Moral codes connect the two: they provide a temporary conclusion to the search for norms, and they make precise what is it to violate them. The Ten Commandments specify what it is to honor the good in a number of generic, familiar situations. It may be thought that such a code of conduct, suitably amended and completed, should suffice. It is important to recognize that it does not. First, because no code can come close to covering all the types of situations that people, organizations and societies run into. Second, because when new possibilities arise and new practices emerge, they often require a fresh ethical treatment. The existing 'ethical blanket', so to speak, cannot be stretched to cover the new territory.

2. The impact of technology on ethics

This is precisely what technology brings about: new possibilities and new practices. The more powerful the technology, the more areas it can penetrate, the more numerous the possibilities, the more outlandish and possibly transgressive the practices. The potential for disruption is even greater when cutting-edge innovations converge, creating synergies that defy extrapolations—this is what has been unfolding in the last couple of decades, as aptly described at the beginning of the millennium under the label 'NBIC' (nano-bio-info-cogno)[1]. Data science and AI boost genetics and drug research, nanomaterials boost robotics, AI and nanomaterials conspire to deliver brain-machine interfaces, smartphones boost the internet, which enables data collection, which feeds deep learning models, which empower AI, etc.

Examples in the health sector abound. We are about to hear about genetic engineering and the ethical 'red line' of germline modification, and in the next session about enhancement and the goals of transhumanism. The commodification of DNA sequencing raises a series of ethical conundrums bearing on privacy violations and incidental findings (unwanted revelations about exposure to incurable diseases or kinship relations). Patient's consent for therapeutic or palliative use of sensors, cameras, tracking devices, robots, raise issues for non- or partially competent patients. e-health can lead to the accumulation of untoward amounts of personal information on some or all members of a population, with the attendant risks of surveillance and control, or unequal protection and coverage. Generalization of systems of e-health can cause increased inequalities, either because the underprivileged lack access or the minimum skills to navigate the system, or because only the more opulent sectors of the health system can afford the best, up-to-date information and apps; or again because personal, face-to-face care might increasingly become a privilege. Progress in intensive care technologies lead to insoluble end-of-life problems. Progress in neuroimaging lead to intractable problems with comatose patients. The health sector is particularly vulnerable to misinformation, and thus concerned with the ethics of free expression. Relatedly, the anti-vaccine movement raises the typical ethical question of individual liberty vs. the protection of society, which may not seem to arise from technology, yet has a global dimension brought about by the infosphere. A whole other set of concerns arise from the enormous costs involved in the deployment of digital systems, medical equipment such as surgical robots, discovery of drugs for rare diseases or of vaccines against new viruses—conflicts of interest, political interference, share of costs and risks pose ethical challenges, as we are witnessing right now. This a just a sample of the ethical issues arising specifically from technological interventions in the health sector.

3. When does ethics come in?

It is often said that intractable ethical issues arise when technology has been given free rein to release new tools before due consideration is given to what situations their release might lead to. "Think first", the age-old motto of practical wisdom, is offered as key to avoid finding oneself in a situation where it is too late to backtrack, and where the best one can hope for is to limit the ethical damage. Familiar examples are provided by artificial intelligence, which is now scrambling to turn into a force for the betterment of the human condition; by the internet, which is due for a 'reset' according to critics, including its founding father Tim Berners-Lee and our speaker in the next session, Carlos Moreira; and by digital social networks, whose destructive effects are well known— all three of which are mutual enablers.

Think last seems therefore a bad idea, but think first doesn't work either. One reason is that before the technology is at least somewhat developed and deployed, debating about its potential risks remains abstract and general: on that level, experience shows, no consensus can be reached, no decisive argument can be made in favor of pursuing or dropping the idea. Another reason is that even when one can begin to discern the shape and likely effects of the proposed device or set-up, it is impossible to foresee how, once deployed, it will interact with other novel systems emerging at the same time. Yet more importantly, it is impossible to guess what scenarios will play out as society at large and communities take hold of the new technology. One example from the distant past and a distant country is that of the French telephone operator's Minitel, an ancestor of today's tablets: the device was distributed for free to all telephone subscribers in order to replace the costly and wasteful paper directories; but it soon got to be used as the 'Minitel rose', the ancestor of on-line dating and prostitution, with the attendant ethical and legal problems. An example from the future is the self-driving car, whose full deployment, if it ever happens, is sure to generate countless ethical puzzles, far beyond the notorious trolley problem: a self-driving car, a fleet of self-driving cars lend themselves to uses that we cannot imagine ahead of time, as they would satisfy longings and honor values that will come into being only once (and if) these vehicles populate our streets. Finally, an example from our time and age, in the health sector, is resuscitation technology: thinking first could not possibly have led to give up on the idea, nor could it have helped avoiding the distressing situation brought about by the discovery of forms of near-eternal, irreversible coma, coupled with the emergence of entirely novel religious and legal norms.

The right time for ethics is neither after nor before: it is now. Ethics is a permanent feature of human action, it is guided by action as much as it guides it. It is an ongoing task that proceeds by spurts, on the fly, as fresh challenges are brought about by new types of situations arising, new practices crystallizing, new expectations being expressed, new understandings emerging.

4. Where is ethics produced?

It may be thought that ethics is primarily produced by dedicated boards, councils, committees that establish guidelines, charters, codes of conduct, recommendations. These however are pragmatic tools that help agents on the ground, at all levels, to act in accordance with ethical principles that have

been agreed upon, or tacitly endorsed as the case may be, without having to reflect on the principles and on how to apply them, a time-consuming and difficult task. What the committees achieve is to turn a complex web of ethical and closely related legal issues into a set of feasible guidelines, prima facie compatible with economic, social and practical constraints. These mid-level principles must be expressed in a pared-down vocabulary ensuring shared understanding and fostering clarity in communication. Agents can then effortlessly take them on board, memorize them, tune them to local circumstances and transmit them further down the line.

The task of these dedicated committees is by no means easy, and it does involve its members in ethical reflection. But it is limited in scope, for several reasons. Membership is limited to professionals and does not extend to the variety of stakeholders and end-users whose life is impacted by the technologies. The presence of industry representatives, though necessary, comes with the risk of less than full disclosure of interests and information. More importantly perhaps, the decision process is constrained by a predetermined set of terms and by rules that are thought to be necessary to achieve a consensus among the representatives of various legal, political and religious creeds. Not much room is left for questioning the basic assumptions driving the industry.

In the case of technology-enhanced healthcare, there exists an entire field, Health Technological Assessment (HTA), devoted to answering questions of the form: Do the ends—the presumed benefit in terms of health— justify the means—the cost of the proposed technology, together with the systemic changes and collateral effects it would bring? But although the field explicitly includes the ethical perspective in its official charter, by its own lights it has so far been at pains to do it, probably because deliberation in HTA is even more constrained than in guideline-producing bodies.

Ethics is produced to a large extent outside of these bodies, in two kinds of settings. In the first kind, practitioners, philosophers, social scientists debate about what general shape the good assumes in the field at hand (in our case, technology-enhanced healthcare). They aim at identifying principles that should be upheld come what may and be systematically called upon when various feasible options are considered, in the light of their conception of the kind of future they want. Nor are these principles set in stone: the path that has led to them continues, as they are constantly reinterpreted, refined and occasionally updated. Such settings need not be restricted to formal structures. In fact, they should not be: however carefully balanced a committee might be, in the end it includes a few people, generally picked among those who are most eager and prepared to intervene in that setting, and it leaves out most people, including those who may well have a deeper understanding and the willingness to take a step sideways. Moreover, no time limit can be set on the process, no protocol can be imposed on the flux of ideas. The conversation must be allowed to unfold in many venues, on different time scales, and assume many forms, including books and scholarly papers as well as debates of all kinds. Bioethics, an area closely related to, and largely overlapping with today's topic, provides an illuminating example. It settled some decades back on four major principles: autonomy, beneficence, non-maleficence, justice. These were not the result of any single committee's work, but rather the temporary conclusion of an extended discussion in many venues, drawn by the two authors of a celebrated treatise, first published in 1979 and now in its 8th edition[2]. These principles are understood as useful conceptual guideposts, organizing a complex and evolving process of collective intelligence that not only pursues ways of applying these principles but can go as far as questioning their value.

The other kind of settings in which ethics is generated or pursued are local ethics committees and other non-formalized venues, where decisions are made regarding singular cases — how to treat this particular patient in these particular circumstances; whether to adopt this particular piece of software in this particular healthcare system to deal with this particular population of patients, etc. Many of these decisions can be made by way of routine application of existing guidelines and codes of best practices, and/or by reference to closely resembling cases. But not all decisions can be disposed of in this way, because different principles back incompatible recommendations, or because no principle seems to apply, or because the values of the people concerned clash between themselves or with some principles normally honored in the time and place where the case has arisen. The 'labor of ethics', in Marta Spranzi's (full disclosure: my wife) felicitous phrase[3], deployed in such cases serves a dual purpose: deliver an acceptable decision, and further the understanding of the underlying ethical issues, often suggesting ways to expand and refine it.

5. How can ethics find its place in today's technological surge?

How ethics is produced in the area of bioethics and clinical ethics is fairly well understood. The process consists in a collective effort in which principles and practices are considered in alternation and side by side. The quest for general principles or rules follows a cycle of iterations, starting from a preliminary understanding of the actual and possible practices, and proceeding to formulate some principles, rules and recommendations on the basis of a first assessment of what is right and what is wrong in the set of practices used as a starting point. These principles and rules then redraw the boundaries of the set of theoretically acceptable or preferred practices. Tested in the field, however, these reveal new issues, calling for a reconsideration of the principles and rules. Meanwhile, scientific, technological and clinical novelties occur, which also call for a revision of principles and rules. And so the cycle goes on. When it comes to making particular decisions, principles and practices are simultaneously enlisted, and in some cases clash, leading to a call for reform. Whatever the exact details, which vary as one moves from one issue to another or one area of applied ethics to another, the responsibilities are fairly clearly apportioned, no stakeholders are systematically excluded from the collective reflection, and the policy decisions can be revised in the light of experience within a reasonable timescale.

So much cannot be said when it comes to the new technologies, making an integration of the ethical dimension particularly problematic. As is being extensively discussed, the responsibility for developing new technologies rests on a minuscule group of people with exclusive access to knowledge, power and money and who answer to virtually no-one. Deployment involves governments, and thus to some limited extent, via democratic representation, a larger set of people; in practice however, the decisions rest essentially on the technocratic structure; the social gap remains immense. Just as wide is the temporal gap: by the time a technology which has been selected for development and deployment hits the world, it has gone from emerging to entrenched, and previous ways of doing things or inhabiting one's surroundings have been foreclosed. One further problem is that the technologies most transformative for health are generally (though not exclusively) global in nature, so that national policies are mutually dependent and must be coordinated in order to have any lasting effect.

These problems are well known, and humanity is not at a complete loss before them. In fact, in the last several years we have been witnessing a rich set of initiatives aiming at turning around the direction of compliance, from humanity complying to the demands of technology to the reverse. One of these in fact is this very conference, WPC – Health, and we will hear this call voiced by Carlos Moreira in the next session. But calling and hoping do not amount to achieving. There are many obstacles standing in our way. Technological determinism, together with pessimism arising from historical evidence, may discourage too many people, leaving the rest too weak to change the status quo. Conflicting interests, mediated by politics, will continue to be an essential driver of technological evolution; in fact, the battle cry of putting humanity first founders on the issue of who do we take humanity to be: values, situations and priorities differ. Finally, we know, again from experience, that when push comes to shove ethics tends to be an afterthought.

In the face of these obstacles, we need to be imaginative and tenacious, but there is no reason to despair: we are witnessing a vigorous pushback against fatalism. I do have a worry, though. We also need to be patient. For as Joseph Raz puts it, "The new forms of the good take time, and require the density of repeated actions and interactions to crystallize and take a definite shape, one that is specific enough to allow people to intentionally realize it in their life or in or through their actions[4]". Where Raz says "people", we should read, for our purposes, "society", but the point remains. What we are witnessing in AI, robotics, and above all biotechnology is the mere beginning of a revolution, or so we are told. The rush to dominance, by nations, corporations, scientists, is underway. In such a moment in history, how on earth can we be collectively persuaded to slow down so as to leave time for the new forms of the good to take shape? This is the question with which I leave you.

Notes

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The rise of biological engineering: does the end justify the means?

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The views and opinions expressed in this article are solely my own.

The 21st century will be the century of biology and medicine, fueled by the rapid accumulation of biological engineering breakthroughs such as viral vectors, gene editing, and reproductive medicine, which are drastically reshaping human healthcare. But does the end justify such technological means?
First, the R&D and manufacturing costs of these complex technologies lead to hefty price tags: how can governments and payers ensure that patients in need access those treatments, while keeping healthy incentive systems for innovation? Second, as science offers increasingly practical challenges to fundamental societal frameworks such as genetic transmission and family structures, how can we ensure they are being regularly revisited and debated? Third, how can we collectively address breakthrough events such as the first genome-edited human embryos engineered by Chinese scientist He Jiankui in 2018? Fourth, with the advent of direct-to-consumer solutions such as genetic tests, how can we ensure citizens are not left to themselves?
The recipe for success will neither be to hand over societal and ethical choices to technologists, nor to shy away from the multiplication of such use cases. Far from trying to gauge whether the end justifies the means, the overarching question becomes instead: can we put in place appropriate global governance structures to promote a healthy dialogue between scientific progress and ethical guidance, so that societies can truly choose the medical and biological future they want to live in?

If the 20th century has been the century of chemistry and physics, the 21st century will be the century of biology and medicine, with the promise of a flurry of medical innovation stemming from a better and deeper understanding of fundamental biological mechanisms underpinning the human body and mind. In order to understand how such technological progress provides challenging use cases for ethicists and policymakers today, we can come back to the very birth of the century, in 2003, with the completion of the Human Genome Project and mapping of the entire human genome[1]. This was actually a product of successful global scientific governance, with genome sequencing being performed over the span of several years across the US, Europe, Japan, and China, and the resulting work being immediately published and accessible to all. But did that mean it was truly a public good? Such answer came a decade later, in particular through the landmark US Supreme Court case - *Association for Molecular Pathology v. Myriad Genetics Incorporated*, in 2013[2]. Myriad Genetics discovered the precise location and sequence of the *BRCA1* and *BRCA2* genes, whose mutations are now known to dramatically increase the risk of breast cancer, and sought to patent *BRCA1* and *BRCA2* for their relevance to the market of breast cancer genetic tests. However, the US Supreme Court unanimously ruled that human genes could not be patented because "a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated", and further added that "Myriad did not create anything (…) it found an important and useful gene, but separating that gene from its surrounding genetic material is not an act of invention[3]". This landmark case provided an answer to one of the most pressing ethical questions: in one of the rare cases of the history of biotechnology, the global scientific effort of unlocking the code to the human genome was deemed a public good.

In parallel, the rapid accumulation of technological breakthroughs in biological engineering further accelerated the field of cell and gene therapy:

1. Viral vector technologies allowed to genetically alter cells of patients suffering from genetic disorders by making them express healthy versions of the mutated genes. The concept relies on leveraging viruses' ability to infect host cells and integrate their genetic material into the host cells' DNA. By reprogramming a virus to add in its DNA a healthy copy of a mutated gene, it is possible to integrate such DNA in the patients' cells and restore normal genetic function. These approaches have already led to approved therapeutic products to treat certain monogenic disorders (AveXis' Zolgensma® is relying on an adeno-associated virus to deliver a healthy copy of the *SMN1* gene to treat spinal muscular atrophy[4], Spark Therapeutics' Luxturna® is also relying on an adeno-associated virus to deliver a healthy copy of the *RPE65* gene to treat inherited retinal disease[5]), or in cancer immunotherapy (in particular with autologous CAR-T cells such as Novartis' Kymriah® or Kite Pharma's Yescarta® and Tecartus® for blood cancers[6]).
2. Gene editing technologies such as meganucleases, zinc finger nucleases, transcription activator-like effector nucleases (TALEN®), and most recently and crowned by a 2020 Nobel Prize, clustered regularly interspaced short palindromic repeats (CRISPR), allowed any research center or biotechnology company to seamlessly copy, cut and paste human genes[7]. These tools can be engineered at will to recognize a chosen location of the human genome, and coupled with an enzyme that makes a break in DNA at that specific location. This break triggers a cellular repair mechanism (known as non-homologous end-joining), where the cell tries to repair such break but generally fails, leading to a complete knock-out (inactivation) of the gene. With such tools, it is therefore possible to edit out virtually any gene in the human genome, as well as knock-in (insert) other genes at their place (for instance, in a monogenic disorder, knocking-out the mutated version of the gene to knock-in its healthy version). These approaches have already shown clinical promise to treat additional monogenic disorders such as sickle cell anemia, or in cancer immunotherapy (in particular with allogeneic, or off-the-shelf, CAR-T cells)[8].
3. Reproductive medicine technologies drastically opened up the toolbox available to humans to address their fertility. A range of pharmaceuticals and surgical procedures are now routinely used, as well as assisted conception (through intrauterine insemination or *in vitro* fertilization, including with egg or sperm donation). In 2017, 2% of all infants born in the United States were conceived with the use of assisted reproductive technology (defined as fertility treatments in which either eggs or embryos are handled, i.e. excluding intrauterine insemination for instance)[9]. By allowing the possibility for fertilization to occur in a laboratory ex vivo (outside of the human body), and combined with the abovementioned technologies, these approaches are opening up the way for mankind to operate on its own germline.

It should be noted that the COVID-19 pandemic provides a fantastic use case of such acceleration, with a recent and innovative technology, synthetic messenger RNA (mRNA)-based vaccines, being at the cornerstone of the first two FDA-approved vaccine from Pfizer/BioNTech and Moderna. Such

vaccines are made of mRNA coding for the spike protein, one the key proteins of SARS-CoV-2. Upon injection, such mRNA will make the recipient's cells express the spike protein, thereby triggering an immune response that will protect them against a potential subsequent SARS-CoV-2 infection[10].

The ethical questions raised by these technological evolutions are certainly not new, but the practical applications are. First, while the initial use cases of cell and gene therapy are hardly debatable (treating certain forms of cancer or inborn genetic disorders), the R&D and manufacturing costs of these extremely complex technologies lead to hefty price tags. The first gene therapy, Novartis' *tisagenlecleucel* (commercially known as Kymriah®), was approved by the US FDA in 2017. It is made of autologous CAR-T cells, a customized cancer treatment created using an individual patient's own white blood cells, which are genetically modified to target and kill leukemia and lymphoma cells, and carried a $475,000 list price[11]. Just two years later, in 2019, the US FDA approved AveXis' *onasemnogene abeparvovec-xioi* commercially known as Zolgensma®, another gene therapy to treat spinal muscular atrophy, a rare neuromuscular disorder, in small children. With a list price of $2.125 million[12], this became the world's most expensive drug, and explained AveXis' acquisition by Novartis for $8.7 billion[13]. What are currently isolated pricing cases are bound to become the norm in the coming years, with close to 400 cell and gene therapies being in development in the US alone. In many cases, such treatments also require highly complex manufacturing and supply chains in order to be customized for each patient and delivered in a timely manner. Therefore, the questions of access that are being particularly acutely felt for COVID-19 vaccines and treatments will continue to rise together with the tide of cell & gene therapy. Since most of these developments initially come from academic institutions and biotechnology companies, and are generally taken at a later stage by pharmaceutical companies, how can governments and payers better coordinate and negotiate to ensure that patients in need access those treatments, while keeping healthy incentive systems for biotechnology innovation? From a manufacturing perspective, how can efficient technology platforms and supply chains be built across the globe to further industrialize and make these highly complex technologies truly accessible, off-the-shelf, to those in need? Second, profound societal changes are to be expected from the rise of these technologies. The evolution of the concept of family and parenthood has been partly driven by technology, starting with the first in vitro fertilization baby in 1978. Indeed, in vitro fertilization is a highly complex set of medical procedures which require in particular medication for ovulation induction, surgery for egg retrieval, sperm retrieval, conventional insemination *in vitro* (in the laboratory), and finally surgery for embryo transfer. With the possibility to rely on donors for both egg and sperm, the traditional concept of the family unit was severely undermined. Yet today, the questions are infinitely more complex. In 2016, the first "three-parent baby" was born from mitochondrial transfer. This intervention involved a prospective mother with diseased mitochondria, the structures that provide energy to cells, which were exchanged by mitochondria of a healthy, unrelated donor. The new-born thereby carried genetic information from three "parents": the sperm donor, the egg donor and the mitochondria donor. This came from a very ethically acceptable principle: offering mothers the ability to avoid passing on metabolic diseases caused by faulty mitochondria to their offspring[14]. Yet, this technological prowess triggered the need to rethink once again our preconceived notions of parenthood, genetic transmission, and family structures. Today, countries across the world battle with the place to give to culturally complex situations rendered possible by modern reproductive technology, such as IVF or surrogate pregnancies. How can we ensure that such core cultural concepts are being regularly revisited and debated at a local and global level, as scientific innovation offers increasingly practical challenges to fundamental societal frameworks?

Third, more debatable use cases are coming to life, such as the first genome-edited human embryos by Chinese scientist He Jiankui in 2018. Interestingly, this has led to a rapid Chinese and international outcry, but one must remember that the original purpose of such intervention, at least on paper, was as much a medical one as the others previously highlighted. Indeed, the purpose was to offer an HIV-positive father and an HIV-negative mother the possibility to have children that would be free of infection. To do so, the embryos were edited by the CRISPR gene editing technology to inactivate the *CCR5 gene*, which encodes a protein that HIV uses to enter and infect human cells[15]. The purpose of this was to reproduce a naturally occurring rare phenomenon seen on the so-called Berlin patient and London patient, where a mutation on *CCR5* conferred innate resistance to HIV[16]. Here, the world quickly asked the difficult question: did this commendable end justify the means of human germline editing? Thankfully, this led to a rapid global response through the creation of the International Commission on the Clinical Use of Human Germline Genome Editing which provided guidance at a global level this September 2020. Their key conclusion was that "no attempt to establish a pregnancy with a human embryo that has undergone genome editing should proceed unless and until it has been clearly established that it is possible to efficiently and reliably make precise genomic changes without undesired changes in human embryos. These criteria have not yet been met and further research will be necessary to meet them." Some of the key concerns included the specificity of gene editing, that is the ability to avoid off-target, undesired gene edits; mosaicism, which is a situation where not all cells continue to carry the genetic mutation during embryo development; as well as chromosomal abnormalities, which can lead to severe genetic defects[17]. The evolution of gene editing tools is very likely to reduce or eliminate these issues. But importantly, this review did not wish to conclude on whether these interventions should be permitted once the technology matures. It called to continue ongoing national and international conversations on ethical, moral, and religious views for potential long-term societal implications, without forgetting issues of cost and access as highlighted previously. It essentially aimed to provide a sound scientific foundation for ethics to be "guided by action", "confronted with cases" and "produced on the fly" in the words of Professor Daniel Andler, in order to aim for global, science-driven consensus, while avoiding the dramatic pitfall of ethics dumping.

Fourth, it is important to remember that all our previous case studies, even the most controversial, fell under the supervision of physicians and medical practitioners. At least in our modern societies, each patient is being guaranteed *informed* consent, that is their right to choose a given medical intervention with the appropriate knowledge on its benefits and risks provided to them by experts. But what happens when complex biological information is being directly provided to individuals, without clear guidance on the underlying medical significance of such data? The advent of direct-to-consumer genetic testing, pioneered by companies such as Ancestry, 23andMe, FamilyTreeDNA or MyHeritage, provides an interesting use case to such question. Such companies offer a paid service accessible to everyone, without prescription or medical supervision, where the customer is expected to provide a personal saliva sample which forms the basis of a process of DNA extraction and sequencing. The company is then able to analyze individual variations in the DNA sequence called single-nucleotide polymorphisms (SNPs) which can be more or less powerful predictors of the customer's ancestry and predispositions to certain health conditions[18]. While the former offering already raises a number of ethical questions (by revealing to a given customer genetic links to other customers – or lack thereof), the latter is of particular interest as it provides access to raw genetic knowledge without any medical interpretation. Indeed, the understanding of the significance of SNPs is still being the object of numerous studies, with certain SNPs (such as the ones on the apolipoprotein E, tightly linked to heart disease or Alzheimer's disease[19]) being more relevant to predictive medicine than others. Is it ethically acceptable to provide unrestricted access to such knowledge, knowing that most customers will not have the relevant scientific background to assess the relevance of the data provided to them? Is it medically relevant to exploit genetic data to provide an individual with precise risk factors of contracting currently incurable diseases such as Alzheimer's, if there are no actionable solutions to offer? Certain countries clearly answered no to both questions, with restrictive legislations on recreative genetic testing. In France for instance, direct-to-consumer genetic testing for health purposes is banned[20]. In the US, pioneer companies like 23andMe had a difficult start with the regulators (in 2013, the FDA's suspended 23andMe's tests over concerns "about the public health consequences of inaccurate results[21]", with such tests being resumed only in 2015). Additional concerns around privacy and the importance of personal genetic data followed suit when companies like 23andMe announced partnerships with pharmaceutical companies centered around drug discovery and development[22]. More generally, many countries are still debating about the consequences of affordable, direct-to-consumer genetic testing, and the impact this will have on the relationship of citizens to their genetic makeup.

It is evident that, with the rapid progress of technology and absence of international consensus on ethics, such dilemmas will flourish in the future and our societies will need to understand and address them. The risk otherwise is to fuel a rising tide of scientific defiance and misinformation, as we have seen for instance with anti-vaccine movements, which would be extremely damageable to healthcare systems across the world. Instead, the recipe for success will neither be to hand over societal and ethical choices to scientists and technologists, nor to shy away from the multiplication of such technological use cases. The middle ground will require to keep building bridges between scientific, medical, technological expertise and political systems. It will require strong and trustworthy fora where biotechnologists, the 21st century's technologists, will keep a constant and healthy dialogue with politicians and lawmakers to ensure that each have a say in shaping the path of tomorrow's medicine. Far from trying to

gauge whether the end justifies the means, the overarching question becomes instead: can we ensure that appropriate global governance structures are in place to promote a healthy dialogue between scientific progress and ethical guidance, so that societies can truly choose the medical and biological future they want to live in?

Notes

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Data, Security, and Standards: a New Geopolitical Battleground

Patrick Nicolet

Capgemini's Group Chief Technology Officer

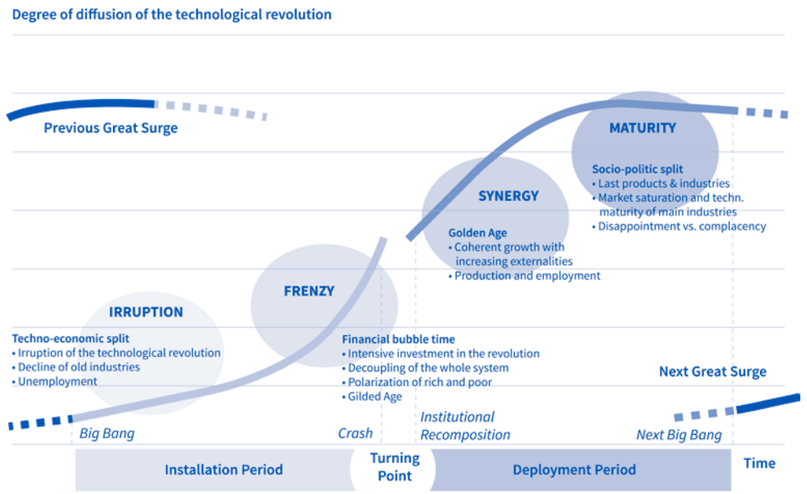
Information and Communication Technologies (ICT) form the backbone of our societies, but their usage so far has been centered on short-term convenience slowly taking a toll on the Earth finite resources. In this context, what if the most pressing healthcare challenge for mankind is not COVID-19 itself but a deeper transformation of our individual and collective practices and behaviors through planet-centric design. After all, mankind is only as healthy as its ecosystem. And since any technology is a solution in search of a problem, ICT can easily be repurposed to support this new sustainable and healthy world.
However, our ability to design and run such planet-centric models supported by information technology depends on our capacity to harness the potential of different technology domains such as artificial intelligence or cloud which are all supported by three technology principles: data, security and standards. In this article, we show how the ability to shape these principles have become a new geopolitical battleground.

1. Planet-centric design

It is any technology expert's natural tendency to focus on the way a technology works – the 'how?', when their audience is oftentimes more interested in the reason why this technology should work – the 'so what?'. Technology is, after all, a solution in search of a problem. What is therefore the problem(s) we are looking to solve through the massive deployment of Information and Communication Technologies (ICT) which form the cornerstone of our modern societies since the 1970's? As often, history is the best teacher.

Neo-Schumpeterian economist Carlota Perez's seminal work on techno-economic paradigm shifts and the theory of great surges[1] offers a retrospective view of previous technology revolutions starting with the industrial revolution and followed by the age of steam and railways, the age of steel, electricity and heavy

engineering and the age of oil, automobiles, and mass production. For Perez, these 50-60 year-long ages are all characterized by a first phase of massive technological disruption where the value is captured by the few before a turning point leads to a phase of stabilization in which society takes back control and decides on the best applications for the technology.



Recurring phases of each great surge in the core countries[2]

We find ourselves in the middle of the age of information and telecommunication which started with the mass production of processors, led by Intel at the end of the 20th century. This paved the way for other technology companies to emerge such as Google, Amazon, Facebook or Apple whose excesses are now well documented and often make the headlines, especially when it comes to the near to monopolistic situation some of them are experiencing on the market. Recent and increasingly pressing calls for dismantling these companies echo back to past examples such as Rockefeller's Standard Oil which controlled up to 90% of the U.S. oil refining and distribution before the Supreme Court ruled to end its monopoly in 1911 by breaking it up and forcing it to sell its affiliates. According to Perez's model, we are approaching this turning point where society takes back control and aligns on shared goals for what to do with technology. The 'so what?' question.

In France, despite social turmoil and a tense political climate, a recent study by think tank Destin Commun shows that 68% of the French population believes that the environment is an issue that can bring people together across lines of division[3].

Although counterintuitive, this demonstrates increasing awareness on the fragility of a system based on finite resources as we commemorate Earth Day sooner and sooner each year. It is now clear that business models centered on mere consumer satisfaction have taken us to the brink of collapse to the point that some scientists now consider we have entered a new geological era that they call Anthropocene as a reference to the impact of human activities on the planet.

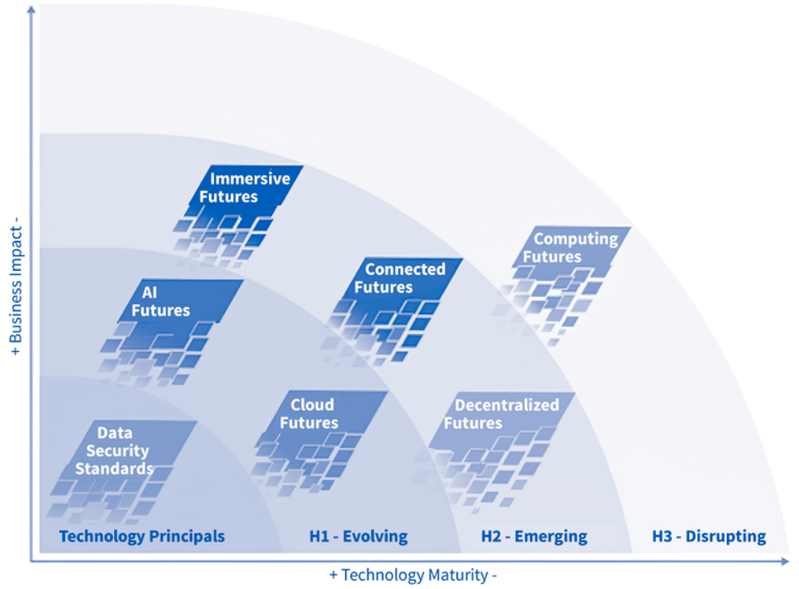
In this context, what if the most pressing healthcare challenge for mankind isn't COVID-19 itself but a deeper transformation of our individual and collective practices and behaviors through planet-centric design. After all, mankind is only as healthy as its ecosystem. Organizations had long been focused on the improvement of the product or service they were providing when a user-centric model emerged offering to shift the mindset to the experience of the consumer, leveraging ICT to improve the understanding of their customers. Social listening for instance allowed brands to send targeted adds for goods or services which you can now literally receive on your doorstep.

From product and user to planet focus[4]

A similar shift is now required to find the right balance between societal needs and their impact on the resources of our planet ; connect these needs to the societal and local reality to ensure maximum added value for the users, the enterprises and the planet ; account for the short, middle and long term benefits ; and adopt a systemic approach to apprehend all stakeholders, their interconnections and the societal needs[5]. Awareness around global warming and the need to protect our ecosystems has spread in recent years beyond activists' circles and many companies now include sustainability, not only as part of their corporate social responsibility agenda but as a core element of their long-term strategies. These efforts from both the public and private sectors as well as the end-users need to be uplifted if we want to build a sustainable and healthy environment for our generation and the ones to come. ICT can become the infrastructure for this new sustainable world with concrete examples already in place for instance the French platform Agrilocal[6] which connects local producers with public buyers or startup Elzeard[7] which brings the power of technology to small farmers.

2. Technology Principles and Geopolitics

Our ability to design and run planet-centric models supported by information technology depends on our capacity to harness the potential of different technology domains who are in different state of maturity. Artificial intelligence and cloud computing are already in wide enterprise adoption but still evolving significantly while augmented and virtual reality or 5G are in limited enterprise adoption but emerging strongly. Others like quantum may not yet be enterprise viable yet but definitely have a big disruptive potential.



Technology Principals and Horizons[8]

All of these domains are supported by three technology principals namely data, security and standards. The French Institute for International Relations (Ifri) has joined forces with consulting and IT services provider Capgemini to study the geopolitical dynamics surrounding the definition and control of these technology principles and published several reports on the topic. In November 2020, they have launched a dedicated research program co-founded with Dassault Systèmes, Crédit Mutuel Equity, Orange and the French Institute for Research in Computer Science and Automation (INRIA)[9].

3. Data

Getting, storing, making the most of, and communicating data is the object of information technology. In July 2018, our report warned: "Data no longer should be understood as a sole commercial or regulatory issue, but rather as an actual stake of international politics. Mastering data is an issue involving different set of actors, with diverging motivations: it is a sovereignty and national security stake for states, a democratic stake for people (personal data), and a fundamental source of value creation for companies."[10] Back then, we invited the European Union to not only settle for its General Data Protection Regulation but develop an industrial strategy which includes data relocalization to protect our digital sovereignty against the USA and China. The battle for healthcare data rages on. According to our most recent study with Ifri on the GovTech market, the GAFAM represent 73,3% of global investments in artificial intelligence for Healthcare[11]. During the COVID-19 sanitary crisis, 23 European countries chose to use an interface developed by Apple or Google for their tracing application, France being a notable exception for sovereignty reason according to Cedric O, Secretary of State for the Digital Economy. So far it has been downloaded by 10 million people[12]. On October 14th, 2020, the French Conseil d'Etat validated the launch of the Health Data Hub, a platform designed to share health data for research purposes. However, Microsoft which was the original pick to host the data on its cloud platform may be evicted from the project due to data protection regulation.

Battles around date localization however will not absolve western countries' leaders from their shared blatant inability to exploit publicly available data to mitigate the spread of the COVID-19 pandemic through cluster tracking while some were able to organize election or re-election campaigns for which the use of citizen's publicly available personal data allowed to design effective targeted campaigns.

4. Security

Security is equally important to keep an organization alive. However, it was never part of the information technology's initial design which focused solely on performance and cost. The transfer of value online, through data, generated growing interest from government agencies and organized crime alike. In another note from November 2019, we showed how digital power was now fully integrated in the portfolio of coercive measures used by states against each other. "Being powerful in the digital world requires the ability to create a favorable ecosystem, to control data, to control networks' competitive edges and to coordinate its digital capabilities with other forms of power."[13]

As for data, security concerns around healthcare are on the rise. In a recent blog post, Tom Burt, Corporate Vice President, Customer Security & Trust at Microsoft wrote "In recent months, we've detected cyberattacks from three nation-state actors targeting seven prominent companies directly involved in researching vaccines and treatments for COVID-19. The targets include leading pharmaceutical companies and vaccine researchers in Canada, France, India, South Korea and the United States. The attacks came from Strontium, an actor originating from Russia, and two actors originating from North Korea that we call Zinc and Cerium."[15]

5. Standards

Information technologies are built in silos and require standards for technology portability – preserving your independence from one vendor – and for technology interoperability – enabling you to work with others. The ability to create standards is an attribute of the digital power of a state. In December 2019, our study on China's smart city model presented how Chinese technology companies teamed up to propose an "in a box" smart city solution for urban areas located in emerging countries especially in Africa. Not only was it designed to opened new market for Chinas' technology champions, but it was also a core instrument of the Chinese government's expansion strategy (Belt & Road) through its active proselytism of the concept of safe city, rather than smart. "Trade tensions have already led to technological tensions, and the US-China rivalry will shape the way that smart cities develop globally. It is unlikely that smart cities will be able to smoothly combine Chinese and US/Western technologies in the future."

Standards in healthcare are critical to any democratic society. Recent examples in countries like Japan and South Korea have shown that distributed systems which respect the individual's right to privacy while offering the possibility to collaborate in times of crises. Their response to the COVID-19 sanitary crisis helped debunk the Chinese narrative tying up use of technology and limitation of individual rights in a centrally managed system deployed in smart cities such as Wuhan, which was the epicenter of the pandemic.

Notes

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The human is and will always be the greatest and most advanced technology the world has ever known

Carlos Moreira

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We must rethink the way the internet is built in order to unleash the potential of technology for healthcare as this sector is still mainly an analogue sector waiting to be digitally transformed. By bringing human at the center of gravity and allowing it to freely consent to the use of its personal data, we can provide three immediate benefits: Consent, Traceability, Protection. The main question that the *TransHumanCode* book asks is "Are we building a better future for humanity with the help of magnificent technology or are we instead building a better future of better technology at the expense of humanity?" We must learn to put humanity first instead of getting caught up in the promise of technological advancement. Humans have been able to adapt, morph, and compromise in every situation we have faced over the centuries and have been able to maintain dominance. We must approach the promises of technology with the same adaptability. The Health sector transformation is going to be revolutionize by Artificial Intelligence of Things "AIoT" acting as the brain that will power the nervous system of the network of IoT health related identities and objects. With the introduction of 5G, the ecosystem will continue to grow at a much faster rate as 5G will enable the connection of every object, person, and machine. AIoT will embed AI into the core health system infrastructure components including Root of Trust, semiconductors, and edge computing. Specialized APIs are then used to provide interoperability between health applications at the device, software and platform level to optimize system and network operations. Data processed through AIoT is then collected and made accessible to extract value and enhance health intelligence and knowledge for the ecosystem. AIoT also enables secure automation of actions and business decisions based on real time data and enables IoT to work independently with minimal human support, unlike the current state of the market which requires that all actions be coded in advance based on pre-defined scenarios. With the use of AI algorithms and predictive maintenance implemented through AIoT, health IoT devices will have the capability to dynamically determine actions to take decisions and self-program based on analytics and customer defined knowledge, resulting in lower operating and maintenance costs for health providers.

The most complex information-processing system in existence is the human body. If we take all human information processes together, i.e. conscious ones and unconscious ones, this involves the processing of 1024 bits daily. This astronomically high figure is a million times greater than the total human knowledge of 1018 bits stored in all the world's libraries. The human is and will always be the greatest and most advanced technology the world has ever known. Doesn't it then make the most sense to place the understanding, improvement, and utilization of humanity as today's highest priority?

Unfortunately, it is easy to lose sight of our preeminence in the grand ecosystem—especially during an era in which it is tempting to lean on technology to lead us into the future we desire. Do we really believe that technology—technology that we created mind you—can become more complex and necessary than we are? Can the created ever really supersede their creator?

It is a question you have to answer for yourself. We all do. And together we must collectively decide if we are building a better future for humanity with the help of magnificent technology… or building a future of better technology at the expense of humanity. There is really no simpler way to put it. The future is still in our hands. But a future is possible in which we are not in control. There would be no one to blame but ourselves.

Humanity is once again faced with playing its own protagonist or antagonist, and the conclusion has not yet been written. The wave of advances preceding our current technological brink is just as noteworthy as it was during the turn of the twentieth century—from Robert Metcalfe's first Ethernet in 1973 and Cerf and Kahn's first Internet in 1975 to Jobs and Wozniak's first personal computer in 1976 and Berners-Lee's World Wide Web in 1990. These thrilling advancements spawned the first browser, the first search engine, the first social network, the first smartphone, and the first app. Technology is now accelerating further with developments like virtual reality, Blockchain, digital currency, Artificial Intelligence, and robots.

Today's technological world was built, and is governed, by the minds and resources of a few hundred thousand people. As a result, we are living in a society in which the richest 1%—most of whom made their fortune in technology—have now accumulated more wealth than the rest of the world put together. Through our concession to technology, we have unknowingly authorized an economy for the 1% instead of creating an economy that works for the prosperity of all, for future generations, and for the planet. This imbalance will be accelerated if we do not collectively remember the value inherent in humanity at large and begin to put the rights of people ahead of the rush to profits.

We-the-global-community have the opportunity to tap the minds and resources of 7.5 billion people interconnected by more than 50 billion devices through the rapid growth of the Internet of Things (IoT)—the aggregation of all connected devices around the world. Consider the implications of this. Consider what this means for humanity's ability to create, innovate, and problem-solve in a swift manner on a massive scale. If we can use technology to access the processing capability of the entire population—the original vision of World Wide Web creator Sir Tim Berners-Lee—we can ignite the equivalent power of more than a billion Summit supercomputers. It is no stretch to assert that the best future we can imagine for the most people is more available than we think. We just must seek it more than short-term convenience.

These solutions and improvements we desire are within our grasp, many of them within our lifetimes, if we take the necessary steps to cement ourselves in the seat of authority and accountability, one technological advancement at a time, those already created and those still to come.

We must constantly ask ourselves: what is prevailing – humanity or technology? And we must do what is necessary to ensure our answer is humanity, and always humanity, the world over.

Some believe we should unconditionally render control of our future to the machines. They base their beliefs on something called technological singularity, which hypothesizes that the artificial intelligence already present will eventually cause an intellectual explosion resulting in a powerful computer super-intelligence that would, qualitatively, far surpass all human capabilities. The great fault in this hypothesis is that is does not account for the spiritual and moral mores of humanity that

set us apart from every species on the planet—characteristics like intuition, empathy, vision, conviction, and ingenuity that stems from a constant desire for better. Computer programs will never match human complexity, its range of emotions and tribal characteristics.

What if the information being compiled on you does not tell the full story? What if what you are looking for, aiming for, is deeper than a dozen digital imprints a day? Most critically, what *else* can be done with the information these companies have on you? In a world where we are increasingly influenced by the technology we use, the more we use the more we lose our freedom to be human.

The pot of gold for modern technology is compiling, translating, and selling your identity, personal data, and behavior to marketers of other companies who need this information to sell you their products. This algorithm, called behavioral targeting, effectively uses technology's translation of your behavior to influence your future decisions. It sounds harmless at face value; seems little more than astute marketing in the modern age. The easy conclusion is that we do not have to let it affect us. Perhaps you don't believe it does? Unfortunately, this prevalent path for monetizing technology does more than improve corporate marketing efforts. It changes what we think about ourselves, which directly influences how we act and who we become.

A 2016 *Harvard Business Review (HBR)* study showed that behaviorally targeted advertisements imply social labels on us that we embrace because we believe our technology's conclusions are accurate, perhaps even more so than our own. In the study, 188 undergraduate students were exposed to an ad for a high-end watch that they believed was either targeted to them or not targeted at all. The test administrators then asked the students to rate how sophisticated they perceived themselves to be (the subjects had also been asked the same question before the test). The results show that "participants evaluated themselves as more sophisticated after receiving an ad that they thought was individually targeted to them, compared to when they thought the ad was not targeted."

"In other words, participants saw the targeted ad as reflective of their own characteristics. They accepted this information, saw themselves as more sophisticated consumers, and this shift in how they saw themselves increased their interest in the sophisticated product."

HBR took these results a step further. They administered another study to determine if the changes in self-perception from the ads would extend to behaviors beyond purchases. In short, they did. This time a group received a behaviorally targeted ad for an environmentally friendly product and, like before, subsequently rated themselves as "greener" than they had before the study. They were then asked to donate to a pro-environmental charity. Most were more willing to give money after receiving the targeted ad than before receiving it. In other words, the targeted ad telling them they were green swayed them to act more greenly.

While this is a small sampling, it demonstrates that the permissions we have given to technology to date are more than harmless, and the outcomes are not benign. Today's technology can mold who we are, what we do, and who we become—for commercial purposes, not humanitarian ones. If we are to become a better world, we each must flip that script.

While you might not mind the timely product and service suggestions dotting your inbox and flanking your screens, the implication of your daily concession to technology is much more than accepting commercial governance for greater convenience. At the heart of it all, behind a veiled reality few can see, you are outsourcing your humanity to a shortlist of companies who, while possibly well-meaning, can never fully protect you, never wholly represent you, and never facilitate the realization of your hopes and dreams. In most cases, they are doing the precisely opposite – undermining your basic human will and rights.

This is much bigger than an economic concern. We are talking about a real and present threat to humanity's livelihood in the universal ecosystem. We are the pinnacle of existence, the crown of creation. For this to remain true is no longer a forgone conclusion. We have unknowingly created our greatest nemesis in the global story—our modern-day Frankenstein. But we still have control over the story's ultimate outcome. We must wield that control willingly and wisely.

When Sir Tim launched the World Wide Web nearly thirty years ago, the purpose was not monetary. His vision was for it to foster collaboration between universities and scientists in an open, uncontrolled, and accessible manner. It quickly grew into a tool that expanded all of humanity's ability to learn from one another, help one another, and collaborate to improve the world. This was a beautiful thing. Today, however, Berners-Lee's profound humanitarian invention has evolved into an estimated $2 trillion industry with a handful of platform companies vying for control. This has led Berners-Lee to confess that the Web has lost its original egalitarian spirit. At the 2017 World Economic Forum, he plainly said, "It has not yet become what it was intended to be." More recently, in an article for *Vanity Fair*, Berners-Lee was more to the point, admitting that the Web has "failed instead of served humanity, as it was supposed to have done."

While it is commendable that many tech titans, with Facebook at the forefront, have made it clear that they aim to ensure that 7.5 billion people can access the Web and connect to over 50 billion devices by 2020, a conflict of global proportions has arisen since these corporations are subject to shareholders and market cap obligations. In other words, they must monetize the Web by converting it into their own private network in which their users become their products. The shareholders and board members of these companies are far less interested in helping you make more friends than in how to best capitalize on your social data graph. The reason why many of their services are free or very cheap is because you pay them with the traits of your humanity which are sold to advertisers for everyone's profit but yours. While we are finally wising up to this reality, there is much work still to be done to untangle the influential web we have wrapped ourselves in. The book in your hands is an important beginning.

Over the previous three industrial revolutions, humanity employed water and steam to mechanize production, then electric power to create mass production, and finally electronics and information technology to automate production. The Fourth Industrial Revolution has been growing from the Third for the last half century and it is characterized, according to renowned German economist Klaus Schwab, "by a fusion of technologies that is blurring the lines between the physical, digital, and biological spheres."

This blurring is a highly promising prospect if deployed properly. Global problems like clean water and cancer that have remained for decades, are now solvable in the present. Global mandates like education that have seemed unattainable for decades, are now a reality in our lifetime. But as it stands, the blurring of spheres that Schwab describes has largely led to the abuse of humanity's resources and the loss of our grip on the future.

The essence of the human spirit and the hope of humanity is freedom: the freedom to be ourselves, to express our personal convictions, and to become the best version we can become. In truth, we are more than human beings; we are human "becomings". What we collectively become writes the script for our world's future. Are we becoming the best version of us?

Session 3

Mental Health and Addiction

The Patient-reported Indicator Surveys: measuring what matters to patients

Michael van den Berg

Health Economist and Policy Analyst at the OECD

Although health systems across the OECD spend around 9% of their GDP on health, we still do not know to what extent health systems are truly delivering what people need. Until the returns on investments in health can be stated more clearly in terms of outcomes, policymakers will be flying with little guidance to direct decisions on the mobilization and use of resources. Slowly but surely, a paradigm shift is taking place in the way we think about healthcare, with a focus on the people who use it. Policymakers, academics, healthcare providers and patients are joining forces to make health systems more people-centered. The use of Patient-Reported Outcome Measures (PROMs) has become common in the past years, particularly in clinical settings. There is a rich variety of tools and initiatives, but opportunities for international learning are limited because of this variety withing and across countries. Moreover, PROMS are mainly used in hospital settings, and for specific conditions, whereas a growing group of healthcare users lives with multiple conditions and is mainly treated in primary care settings.
During their Health Ministerial meeting in 2017, health ministers called on the OECD to lead the development of a new generation of health performance measures and to support countries in implementing them. This was the start of the Patient-Reported Indicator Surveys (PaRIS) initiative. Country officials, academics, patient organizations and providers have joined forces in this first-ever international survey on patient-reported measures of this scale. This international collection of patient-reported measures is a necessary step to take on our shared journey towards more people-centered healthcare systems.

What are health systems delivering to people using them?

Health systems collect massive amounts of data on inputs, spending and activities. There are international standards for the recording and calculation for healthcare costs, diagnoses, hospital admissions, prescriptions, mortality and many others. Such information is essential intelligence for policymakers, funders, and providers of care. However, as comprehensive as they are, none of these data touches on the very essence of healthcare: does it make patients' lives better?

Although health systems across the OECD spend around 9% of their GDP on health, it is shocking how little we know about whether health systems are truly delivering what people need [1,2]. This puts emphasis on one question: what exactly are health systems delivering to people using them? In the past two decades, the body of literature on health systems performance, the number of performance indicators and the amount of benchmarking exercises has grown in most OECD countries. Despite the useful insights that these approaches generate, the perspective of the patient is painfully absent. Does healthcare improve what really matters to patients? How do patients experience the care they receive? Do they feel ready and empowered to manage their conditions and take good care of their health?

The inability to answer such vital questions is problematic: until the returns on investments in health can be stated more clearly, policymakers will be flying with little guidance to direct decisions on the mobilization and use of resources. In addition to massive human suffering and loss of lives, the COVID-19 pandemic has laid bare many vulnerabilities of health systems. Older people and people living with chronic conditions are impacted most, but their health systems know very little whether they have what they need to better manage their health needs.

Slowly but surely, a paradigm shift is taking place in the way we think about healthcare, with a focus on the people who use it. Policymakers, academics, healthcare providers and patients are joining forces to make health systems more people-centered. The willingness is there, now it is time to walk the talk, and the COVID-19 pandemic has only made this effort even more urgent. Making this a shared effort is the only way forward.

Populations are changing

The populations in most countries have changed dramatically: we all have aging populations, and this goes hand in hand with a continuous increase of chronic conditions. In the age group above 65, 6 out of 10 people live with two or more chronic conditions. In the overall population, this share concerns 1 out of 3 people. They are not going to be cured, but they rely on healthcare to manage their conditions, to provide regular care, prescribe medication, provide lifestyle counselling, etc. The purpose of health systems is not only to cure diseases, and to lengthen life, it is about the quality of life, supporting people in what matters to them.

This cannot be measured in clinical outcome measures, You can only get this information by asking patients about the outcomes and experiences with care. Next to physical health, mental health plays an important role. And here we should not just think about disorders or mental diseases, but also about the quality of life in general. Are people able to do their work, can they engage in social activates, or are they hampered by pain, concerns, fatigue, limitations in mobility, sleeping problems, etc.?

Measuring outcomes and experiences

The use of Patient-Reported Outcome Measures (PROMs) has become common in clinical settings. There is an abundance of available instruments to measure PROMs, and their use has become increasingly common. Healthcare providers are intrinsically interested in how their patients are doing. PROMs tools can help fostering a constructive dialogue between patient and provider, and help tailoring care to their needs. Moreover, providers can learn from each other by comparing results. Examples of patient-reported outcomes that hugely impact people's lives are levels of pain, mobility, the ability to participate in social activities, and anxiety. However, the ability for policymakers to capitalize on existing data collections has been limited so far, for several reasons.

First, there is a large variety of tools and initiatives across and even within countries. Opportunities for international comparing and learning are therefore limited.Second, PROMs are mostly used in hospital settings and typically apply to curative, episodic situations with a clear 'before and after' the intervention. However, there is a large, and growing, group of healthcare users who live with chronic conditions and receive healthcare in primary care settings for years or even decades. In such cases, there is no 'before and after'; their healthcare is a continuous process.

International effort

Policymakers, patients, healthcare providers across the globe agree that health systems need to change; from health systems that are centered on

supply and 'curing illness' to health systems that are centered on people's individual needs and well-being. The question is not so much 'if' but how this should materialize. This fundamental change has important implications for how we measure health system performance.

During their Health Ministerial meeting in 2017, health ministers called on the OECD to lead the development of a new generation of health performance measures and to support countries in implementing them[3]. Today, countries inside and outside the OECD have joined forces in this international effort called the Patient-Reported Indicator Surveys initiative (PaRIS), and first data collection will commence in 2021[4].

In the past years, the OECD has had intensive dialogues with leading experts across the globe to make a feasible plan for this ambitious undertaking. Together with an international expert Taskforce seven key principles were formulate that are leading in the PaRIS initiative.

Seven key principles of the PaRIS initiative

1. **Inclusive development:** Stakeholders and countries are developing the PaRIS survey together. By making this a shared undertaking, policy makers, patients and health care providers are involved to ensure that instruments and indicators are relevant for them. PaRIS has an international Patient Panel of patient organizations and a Technical Advisory Community. The work is overseen by an international Working Party in which all participating countries are represented.
2. **Supporting people-centered health systems:** Data collection is only a means to a goal. The survey will provide 'actionable' information that helps policy makers improve care.
3. **Alignment with national directions and initiatives:** The survey will create synergy with initiatives already going on in countries. Where possible, PaRIS should be implemented in a way that it strengthens national strategies. Based on the international standards, a country-specific plan is developed to ensure a smooth implementation.
4. **Multi-level approach:** The survey will combine information on the levels of patients, health care providers and health care systems to get the full picture. The different layers of information will help policy makers identify priorities on the right level.
5. **Phased approach:** The development of PaRIS will go through three phases: a development phase, a field trial and the implementation of the main survey. Countries commit to the project phase by phase.
6. **Future-proof data collection:** The survey will use state-of-the-art innovative methods for data collection and data sharing that are safe, privacy-respectful, and user-friendly.
7. **Protection of data privacy and security:** The survey design and the practices of data processors fully protect the privacy of survey participants, both patients and health care providers.

At the time of writing, a majority of the OECD member states has joined the PaRIS initiative. The development and implementation are supported by an international consortium of academics and one of the industry leads in international survey research. This will be the first-ever international survey on patient-reported measures of this scale.

In 2021, the field trial phase of PaRIS commences. This phase will take 1.5 years and during this period, questionnaires will be translated and tested. The survey will be implemented on a small scale. After evaluation of the results, the main survey will be implemented in the second half of 2022.

Next Steps Towards More People-Centered Health Systems

If you cannot measure it, you cannot improve it. The international collection of patient-reported measures is a necessary step to take on our shared journey towards more people-centered healthcare systems; health systems that are organized to support people in those aspects that matter most to them. There is no other purpose of health systems than serving patients. Patient-reported measures are no 'soft data'; they must be measured in a valid, rigorous way and developed together with all stakeholders at the table. It is not about fees, it is not about bar charts and league tables, it is about the lives and well-being of patients.

Notes

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Fake news and trust issues in times of pandemics

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Together with a pandemic caused by the new coronavirus, we must face a second pandemic, made of fake news that is widely circulated and believed by the general population. While COVID-19 is stressing our health systems and endangering public health, fake news is on one hand eroding the general trust in public health institution, on the other is bringing many to personal decision and conducts that are endangering public safety. A vaccine for stopping both pandemics is a major medical and social need.

We are at an unprecedented moment where all disciplines are converging and crossing each other in the face of this pandemic emergency and the consequences in many different fields.
As a medical doctor and a virologist, I am not formally involved in mental health and addiction but in the last few years in Italy I have had the opportunity to fight misinformation about vaccination. This also gave me good experience and ideas on how to deal with fake news when this pandemic started in January.
We are facing two kinds of pandemics. One is a virus that is spreading very easily and very fast, the other is made up of false information. This can be very dangerous because firstly, false information can be very attractive. People want to know that everything fine, going well and not dangerous and we have known this from ancient times and the works of Julius Caesar. He wrote that people are very likely to believe what they want and what people want to hear in these difficult times is that masks are not necessary, the virus is not dangerous and does not even exist. Unfortunately, this kind of false information provides the grounds for very dangerous behavior by individuals. We must remember that fighting a pandemic is something that we have to do as individuals, and everybody is really equal in the face of the virus and everybody can be important for the spread or the containment of the virus.
The second thing that was very bad at a certain point was an idea that was also spread by some very important politicians, that some drugs were effective without there being any proof. Once again this was dangerous with people trying to buy these drugs and taking them from people who really needed them. It also generated a kind of frenzy for the idea that was pushed just in my own country and also

by some politicians, that an effective treatment had been withdrawn from the population for some reason, because of an extremely powerful international plot.
One of the most dangerous issues is that fake news can really orient public opinions in a very dangerous way. When you tell your citizens that the virus is a Chinese virus or even that it was constructed and synthesized in a Chinese laboratory and spread deliberately, you are really preparing the ground for people to hate each other and this is once again extremely dangerous. We have past experience of how bad this can be, and it could be a huge problem for scientific collaboration from the international point of view, which is absolutely vital for making the rapid scientific advances that are the only thing that can save us in this sort of situation.
Another major problem that depends on the spread of this false news is the erosion of trust. That is trust in the WHO, seen by some people as a political entity, which it is not. That is trust in institutions like governments, ministers of health, as well as doctors. In Italy we had people saying that everything had been invented and that doctors were just killing people in the hospitals and creating this emergency, which is really incredible. This is very dangerous because you must rely on trust. We must trust the FDA to authorize a new vaccine, new drugs or the EMA in Europe. It is very bad when these very reputable institutions are being pushed politically, as happened in the US for example with President Trump pushing for an immediate greenlight for some treatments or even a vaccine. If important institutions lose trust, then it is very difficult to regain it.
These are the problems, but I also think it is very important to point out a few solutions. First, we need crystal clear scientific data about safety and efficiency, but this is not enough. My experience of vaccines shows clearly that good, clear scientific data is not enough. We are no longer in an age where people just follow what the doctors say without any discussion. Now, people try to inform themselves through the Internet and social media and the information is very often incorrect.
One very clear example demonstrates how inadequate very good scientific data is. We have one vaccine against the human papillomavirus, which actually protects against cancer which is not a negligible clinical entity. This vaccine is safe, extremely effective and is wiping out cancer where it is widely used, such as Australia and in many countries, Italy for example, it is provided to patients for free. In Italy, almost 40% of parents actively refuse this vaccine for their children, in Holland close to 50%, more than 50% in Germany and even higher in France. People refuse a vaccine that protects against cancer, which is safe and effective. Considering this, it is clear that data is not enough.We must realize that times are changing, and we have to go out from our universities and speak to people. Talking to people is very different from talking to patients who come to our offices and who trust us, students in our universities who want to learn, or colleagues who basically speak our own language and understand the process of scientific debate. We are basically talking to people who are not interested in what we are talking about or confident about what we say, thus requiring to be extremely convincing.
Another problem arises from the fact that many doctors and scientists with opposing views talk to the public. That is absolutely normal because in the initial phase of a pandemic caused by a new virus that we had never seen before January 2020 there is not a lot of knowledge and there is room for scientific opinion. However, this is very bad for the general public because if this legitimate scientific discussion happens outside scientific conferences, universities, or journals and instead on TV shows in front of public audiences it will generate a lot of confusion.
The last point I want to highlight is the need for a strong institutional voice. These often contradictory voices are all heard because there is an empty space left by the institutions. I think that at this moment we realize how important it is to have an institution that is trusted and convincing. That not only requires strong and clear scientific data but also with the skill to present them in a way and with a storytelling that will convince people who believe them and act accordingly. In this case, the form really becomes the substance. The way you talk to people is very important, not only what you tell them, which obviously must be true and must be a correct scientific information.
There are many things we can learn from this very bad experience and there are useful things we can use over the next months, when hopefully we will have a vaccine that could end this whole terrible story of the pandemic which really had a bad impact on everyone's lives. I would like to give people something to believe in, not just good data or optimistic forecasts but really to convince them that they can trust authorities. They must trust the FDA when it approves the vaccine. They must trust the government when it tells them to stay home, or when they say children can go to school. One thing that what we can learn from this terrible experience is that we must build this trust in "peace time" because it is something that will be very useful during the war. Certainly, from the virological point of view, I do not know when, but I am sure we will have to face some other pandemics. I hope we will be ready with the diagnostic tools, vaccines, isolation, quarantine, and personal equipment for protection, but we also need to be ready from the crucial point of view and able to face worried and scared people with the voice authority and trust from the institutions.

Mental Health and Addiction issues in the context of COVID-19

Jean Pierre Lablanchy

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In the middle of the pandemic, the French Minister of Health Olivier Véran declared that a third wave would be that of "mental health". In saying this, he recognized that the effects of COVID-19 on the mental condition of the population can be as harmful as that of the virus itself, and that there had been a lack of attention paid to this issue so far.
Mental health is unfortunately a field that is still often neglected and absent from the public debate, insofar as its effects are difficult to measure and not always clearly visible. However, its consequences can be dramatic, as shown by the COVID-19 crisis we are now facing. Lockdowns and isolation measures have exacerbated pre-existing pathologies in several population groups, such as drug addiction or depression, which caused the death of many people who had not even been infected by the virus.
It is fundamental to understand that mental issues are real medical conditions which require attention and dedicated care, otherwise they can cause significant damage to the economy and the society.

This specific topic was important to us since Mental Health is such a key issue, and yet – as M. de Montbrial highlighted so well – "the subject of Mental Health and Addiction is usually not brought at the center stage when people talk about Healthcare and global Health".

With a bit of retrospective, this subject had an even greater importance due to the unprecedented COVID-19's context which impelled to isolate everyone from one another with the ramifications that this sort of decision implies. In this regard, I would like to highlight the ins and outs of addictions and issues people face – which applies in our context – as well as the challenge it represents at many levels. Finally, I shall give some possible solutions to respond to such a challenge.

1. The real threats lying behind the COVID-19

The first question to ask is: are we facing a global/international problem? Of course, the answer is "yes" simply because in many ways, it is linked to what is called the "human condition".

Mental health issues that have emerged for some time in the public debate are not new, but COVID-19 contributed to exacerbate some of them.

First, we have noticed a regression among people because of the fear they experience in our current situation: they are getting weaker on a mental level, as they are less likely to resist to dogma and deceitful speeches.

Second, we must deal with a huge and silent enemy: depression. On one hand, what we understood with the pandemic is that some people are inherently more likely at-risk: the elderlies and the people presenting co-morbidities. On the other hand, what we do not seem to understand is the mental health issues caused by the COVID-19. Here are a few key facts and figures:

- Suicide is the second cause of death among young people.
- 16% deaths are caused by suicide among 15-24 year olds.
- 20% deaths are cause by suicide among 25-34 year olds.

The virus kills some people; depression kills many.

Moreover, it has been showed by some studies that 39% of people in recovery from an addiction prior to lockdown have experienced a relapse of their addictive behavior since lockdown. If we can trust that percentage, it means that more than a million people are concerned on a national scale. Of course, many reasons can explain it: financial issues, isolation, fear for the future, etc.

2.Mental health diseases are somatic diseases

It is important to point out that a mental disease is also a somatic disease, meaning that the body is physically affected as well. For example, as we can observe, addiction to psychoactive substances is expressed in a dependence syndrome, resulting in physical and visible effects. Addictions are caused by a combination of psychological, environmental but also biochemical and genetical factors. As a result, studies show that substance dependents suffer from dysfunctions in the central nervous system, preventing them from a well-balanced ability to process sensory information.

We can count four main problematic personality traits placing people at-risk for substance use:

- Hopelessness
- Anxiety
- Impulsivity
- Sensation seeking

We call them *"Sensory processing disorders"* (SPD); they characterize over or under responsiveness to environmental stimuli. People with those previous traits are often described as moody, irritable, and lacking social skills.

Because of an altered brain neurotransmitter, having SPDs includes a decrease in dopamine uptake, an altered dopamine synthesis and deficits in serotonin reuptake sites.

As a result, substance dependents were seeking for a compensatory mechanism for their unmodulated arousal level or for a relief of a particular affective state.

And this is where I would like to emphasize the importance of hypersensitivity. As a matter of fact, individuals with sensory hypersensitivity are particularly at risk with addictions. Hypersensitivity and toxic abuse often go as a pair: people with hypersensitivity are at high risk of being addicted. If you help people deal with hypersensitivity, you help them fight addiction.

Also, we have to understand that the same event does not have the same impact from a person to another; some people are not shook up by bombings, but are traumatized by the death of their pet. It is not about the event you live; it is about the way you receive it, the way your brain interprets it. This is where we ought to talk about Post Traumatic Stress Disorder (PTSD).

3. PTSD

Rachel Yehuda (Psychiatrist), who worked with firemen after 9/11, proved that huge stress producing PTSD affects the cortisol receptors which implies that you cannot behave the way you did before. When it happens, some genes are hampered, sometimes even destroyed. She also states that those traumas can be transmitted to the next generations. Patients concerned by this tend to be self-destructive, mentally ill and substance dependent. What is PTSD? This is a psychiatric disorder, which affects the patient over a long period of time, generally more than a month, with the following symptoms:

- Reexperiencing the traumatic event repeatedly (flashbacks, nightmares, physical sensations, negative thoughts, etc.).
- Avoidance and emotional numbing.
- Trying to avoid being reminded of the traumatic event.
- Choosing isolation and withdrawnness.

How to treat it? Mostly with Psychological therapies and meditation such as CBT (Cognitive Behavioral Therapy) and EMDR (Eye Movement Desensitization and Reprocessing).

You can also use medication, antidepressants and especially beta blockers (to help patients not re-express the trauma and the pain it involves).

An interesting fact about some of those medications (pointed out by the professor and psychiatrist Marion Leboyer) is that, in the context of the COVID-19, we observe a "protective effect" against the virus (antidepressants, anxiolytics and antihistamines). During confinements, psychotropic drugs were persistently increased. for instance, the anxiolytics use increased by 18,6% in the first 2 weeks of the first wave.

4. Existing psychiatric tests

When we talk about addiction and mental health issues, there are three major tests that are worth mentioning given data they produce.

With somatic diseases, the first one you can make is checking cortisol in the urines.

The second one is to do a blood test (called Dexamethasone Suppression Test) in which the level of Dexamethasone is checked. If it is low, it means that it is killing your cortisol's production, i.e. you are under PTSD.

The third one is MMPI-2.

The MMPI-2 Test appeared in the 1940's. It is the most published psychological test, because: it is accurate, especially to gauge psychological stability for persons at high-risk.

It is very easy to implement it. All you must do is answer 330 questions linked to 10 clinical subscales: hypochondria, depression, hysteria, psychopathic deviate, masculinity/femininity, paranoia, psychasthenia, schizophrenia, hypomania and social introversion.

If you want to go further, you can also go for a brain SPECT imaging: more expensive but very accurate as well. It also shows and proves once again that psychological diseases are somatic diseases; you can see on the images some very concrete and physical changes. With the PET and an MRI, you can see the metabolism of neurological cells and how the brain works basically. This is where you can compare and observe on the scans the huge differences between sane cells and addicted cells.

5. The importance of Genetic

Genetic tests to check emotional instability have been conducted for 10 years. Thanks to them, we were able to observe whether your genes are functional, or not.

This test should be run on patients showing moodiness, anxiety, sleep disorders, suspicion of depression, hyperactivity and so on.

On this test which checks the state of 9 genes, any mutation is a problem. Some people have 2 or 3, some people have 5, and some even have 8 or 9 (out of 9) mutated genes. It makes catastrophic lives.

This test is very important for the psychiatrist to be able to explain his/her patient that he/she should take a treatment. For example, before the test, that one person with 9 mutated genes refused to take any kind of drugs. With the help of the test, I was able to explain to that patient that I could not do anything using psychotherapy as my only tool and convince him to take the treatment.

The important fact to understand here is that those patients were born this way and they must deal with this condition all their life. It is not their parents' fault, neither education nor environment: it is all about mutated genes that were either normal at first or transmitted from a generation to another (due to traumas and epigenetic modifications).

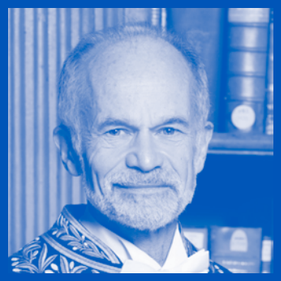
6. Conclusion

Facing this difficult human condition, this huge suffering with a high risk of disease killing people, we do have tools. However, we need to explain a few things to patients:

- Dark thoughts are never normal
- Consult a clinician
- Do not hesitate to go for a psychological assessment
- Genetic is key and there are genetic tests
- You can also go for a medical imaging which is accurate

Speakers

Andler, Daniel. Emeritus Professor at Sorbonne Université and a member of the Académie des sciences morales et politiques. He began his academic career as a mathematician, specializing in logic and teaching at Paris 7 and other universities, He then was appointed as Professor of philosophy of science at the universities of Lille, Nanterre and finally Paris IV. He is chiefly interested in cognitive science and artificial intelligence, and in their import for education, collective decision and public policy. He was the Founder and first Director of the department of cognitive studies at the Ecole normale supérieure in Paris. His book on the significance of the present surge of artificial intelligence is forthcoming.



Berg (van den), Michael. Health Economist and Policy Analyst at the OECD. Michael is specialized in health systems performance assessment, quality of care, performance indicators and primary care. His current work is driven by the ambition to move towards a new generation of indicators that will enhance international learning on the value of healthcare as reported by patients themselves. He is passionate about international collaboration and as a member of the OECD Health Division, he helps countries achieve high-performing health systems. He studied sociology, wrote a PhD thesis in the area of primary care and has been working on health services research and policy advice for more than eighteen years.

Biot, Jacques. Board-member and advisor to companies in the field of digital transformation and artificial intelligence, and a Trustee to several scientific academic institutions. First Executive President of Ecole polytechnique, he has international professional experience in higher education and research, life sciences (Roussel-Uclaf, Pasteur-Mérieux Serums and Vaccines, JNBD, Guerbet, GBT, Euronext), industry and technology financing, and public administration (French Prime Minister's office). The motto of his career has been about how to turn scientific innovation into societal and economic value. He is a graduate of Ecole polytechnique (X71) and a member of the Corps des Mines.

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Flahault, Antoine. MD, PhD in biomathematics. Professor of public health at the Faculty of Medicine, University of Geneva where he is the Founding Director of the Institute of Global Health. In 2019, he was elected as Deputy Director of the Swiss School of Public Health. He previously served as Founding Director of the French School of Public Health, Co-Director of the European Academic Global Health Alliance, and President of the Agency for Public Health Education Accreditation. He has conducted his research in mathematical modelling of communicable diseases and he has chaired the WHO collaborative centre for electronic disease surveillance. He is a corresponding member at the Académie Nationale de Médecine.

Germay (de), Alexandre. Global Head of the Cardiovascular and Established Products Franchise at Sanofi. With more than 20 years of experience in the healthcare field, he is a trusted and strategic executive possessing a proven track record of enabling innovative and winning strategies to achieve significant and sustainable results across markets. Before joining Sanofi in 2016, he held several positions with Pfizer as Global Established Pharma Regional President for Japan-Asia-Pacific, Director Worldwide Marketing Group, General Manager. Alexandre de Germay earned two master's degrees in business administration and finance from Paris XIII University in France.

Ghebreyesus, Tedros Adhanom. Director-General of the World Health Organization since 2017. Prior to his election, he served as Ethiopia's Minister of Foreign Affairs from 2012 to 2016 and as Minister of Health from 2005 to 2012. He holds a PhD in Community Health from the University of Nottingham and a MSc in Immunology of Infectious Diseases from the University of London. He is globally recognized as a health scholar, researcher, and diplomat with first-hand experience in research, operations, and leadership in emergency responses to epidemics. Throughout his career Dr Tedros has published numerous articles in prominent scientific journals, and received awards and recognition from across the globe.

Kazatchkine, Michel. Special Advisor to the Joint UN Programme on HIV/AIDS (UNAIDS) for Eastern Europe and Central Asia, he has over 35 years of experience in global health as a leading physician, researcher, administrator, advocate, policymaker, and diplomat. He is Emeritus Professor of Immunology at Paris Descartes University, Senior Fellow with the Global Health Centre of the Graduate Institute for International and Development Studies in Geneva, and a member of the Global Commission on Drug Policy. He was Executive Director of the Global Fund to fight AIDS, Tuberculosis and Malaria, Director of the French Agency for Research on AIDS, and UN SG's Special Envoy on HIV/AIDS in Eastern Europe and Central Asia.

Kramarz, Jean. Director of the Healthcare activities of the AXA Partners Group. He is a specialist in the development of healthcare services in France and around the world. Before joining the AXA Group, where he launched medical teleconsultation for the general population in France, he was Director of New Services at Malakoff-Médéric Group, Director of Development at Europ Assistance, Director of International Health Subsidiaries at Gras Savoye Group. He also worked in the French public sector, including in the Oil & Gas and Automotive Departments of the Ministry of Industry and in the Treasury Department of the Ministry of Finance. Jean Kramarz is an alumnus of Sciences Po Paris and ENA.

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Montbrial (de), Thierry. Executive Chairman of the French Institute of International Relations (Ifri), which he founded in 1979. He is Professor Emeritus at the Conservatoire National des Arts et Métiers. In 2008, he launched the World Policy Conference. He has been a member of the Académie des sciences morales et politiques of the Institut de France since 1992, and is a member of a number of foreign academies. He serves on the board or advisory board of a number of international companies and institutions. Thierry de Montbrial chaired the Department of Economics at the Ecole Polytechnique from 1974 to 1992. He was the first Chairman of the Foundation for Strategic Research (1993- 2001). Entrusted with the creation of the Policy Planning Staff (Centre d'analyse et de prévision) at the French Ministry of Foreign Affairs, he was its first Director (1973-1979). He has authored more than twenty books, several of them translated in various languages, including *Action and Reaction in the World System - The Dynamics of Economic and Political Power* (UBC Press, Vancouver, Toronto, 2013) and *Living in Troubled Times, A New Political Era* (World Scientific, 2018). He is a Grand Officer of the Légion d'honneur, Grand Officer of the Ordre National du Mérite. He has been awarded the Order of the Rising Sun – Gold and Silver Star, Japan (2009), Commander of the Order of Merit of the Federal Republic of Germany (2016) and other state honors by the French and several foreign governments. Thierry de Montbrial is a graduate of the Ecole Polytechnique and the Ecole des Mines, and received a Ph.D. in Mathematical Economics from the University of California at Berkeley.

Organization

The French Institute of International Relations

Founded in 1979 by Thierry de Montbrial, Ifri (Institut français des relations internationales) is the leading independent research and debate institution in France dedicated to the analysis of international issues and global governance.

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