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### Abstract

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 filings 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 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.