Precision global health in the digital age

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Summary

Precision global health is an approach similar to precision medicine, which facilitates, through innovation and technology, better targeting of public health interventions on a global scale, for the purpose of maximising their effectiveness and relevance. Illustrative examples include: the use of remote sensing data to fight vector-borne diseases; large databases of genomic sequences of foodborne pathogens helping to identify origins of outbreaks; social networks and internet search engines for tracking communicable diseases; cell phone data in humanitarian actions; drones to deliver healthcare services in remote and secluded areas. Open science and data sharing platforms are proposed for fostering international research programmes under fair, ethical and respectful conditions. Innovative education, such as massive open online courses or serious games, can promote wider access to training in public health and improving health literacy. The world is moving towards learning healthcare systems. Professionals are equipped with data collection and decision support devices. They share information, which are complemented by external sources, and analysed in real time using machine learning techniques. They allow for the early detection of anomalies, and eventually guide appropriate public health interventions. This article shows how information-driven approaches, enabled by digital technologies, can help improving global health with greater equity.

Key words: global health precision medicine; data science machine learning; open science; emerging infectious diseases; noncommunicable diseases; cell phone data; massive open online education; learning health care system

Introduction

In a recent paper, we proposed a definition for global health based on six principles [1]:

1. Global health addresses cross-border and multilevel health issues.
2. It is "trans-disciplinary", i.e., it mobilises all relevant academic disciplines and also nonacademic sectors of society.
3. It studies complex systems in the real world. This complexity requires trans-disciplinary system thinking to help find solutions.
4. It seeks to provide affordable, effective and integrated innovation. This article demonstrates how affordable innovations are key in precision global health.
5. It seeks health for all in a sustainable world. It is no longer possible to develop health care facilities, devices and services without a deep commitment and respect for our planet.
6. Global health is committed to the normative framework of human rights and equity. This is an essential aspect of global health; because health is considered a human right, access to affordable health care matters greatly.

Khoury et al. [2] discussed the *sine qua non* role of public health in the era of precision medicine, extending the discussion to tools beyond genetics, such as health information technology. The authors expressed their concerns about the "disproportionate emphasis on genes, drugs, and disease, while neglecting strategies to address social determinants of health". The authors defined "precision public health" as "providing the right intervention to the right population at the right time", and stressed the need of more accurate methods for measurement. Khoury et al. emphasised the need, in the era of precision medicine, to shift the focus from treatment to prevention. Of note, precision public health would involve improving early detection of pathogens and infectious disease outbreaks (e.g., CDC Advanced Molecular Detection Infectious Disease Initiative). The authors discussed priorities for public health in the era of precision medicine: to make best use of the interconnectivity of digital data, adding molecular markers in registries, and to include and integrate disparate sources of data.

More than 36 million people die annually from noncommunicable diseases (NCDs) (63% of global deaths), including 14 million people who die too young, before the age of 70 years. More than 90% of these premature deaths from NCDs occur in low- and middle-income countries, and are largely preventable. Most premature deaths are linked to common risk factors, namely tobacco use, unhealthy diet, physical inactivity and harmful use of alcohol [3] Preventable deaths could effectively be the target of precision global health. In high-income countries, seven in every ten deaths are of people aged 70 years and older. People predominantly die of chronic diseases: cardiovascular diseases, cancers, dementia, chronic obstructive lung disease or diabetes. Lower respiratory infections remain the only leading infectious cause of death. Only 1 in every 100 deaths involve children under 15 years of age. In low-income countries, nearly four in every ten deaths are of children under 15 years, and only two in every ten deaths are of people aged 70 years and older. People predominantly die of infectious diseases: lower respiratory infections, human immunodeficiency virus / acquired immunodeficiency syndrome (HIV/AIDS), diarrhoeal diseases, malaria and tuberculosis collectively account for almost one third of all deaths in these countries. Complications of childbirth due to prematurity, birth

asphyxia and birth trauma are among the leading causes of death, claiming the lives of many newborns and infants.

Precision medicine, part of the larger movement of personalised medicine, aims to target healthcare better with new technologies, often the so-called "-omics", in order to be more effective. Personalised medicine is not romantic nostalgia for past medicine, when family physicians knew and provided care to each generation with an individual and human approach. Personalised medicine is closer to a mass customisation approach, as pioneered by companies like IKEA. It is not handicraft medical practice, but rather a mass customisation delivery of health care. Knowledge of the genomic sequence of a tumour may inform selection of a drug or treatment with much higher probability of success than a treatment chosen without taking advantage of this information.

In analogy to precision medicine, precision global health aims to propose appropriate, targeted interventions in global public health, thanks to innovation, in order to greatly improve efficacy. Innovations can be technological, providing they comply with the definition of global health in term of ethics, affordability and sustainability. Nontechnological "soft" innovation is also crucial to driving global health intervention with greater precision.

Below, we describe a few examples drawn from the literature, without being exhaustive.

Using remote sensing data to better fight vector-borne diseases

Satellites gather large amounts of data each day and with differing types of measurement. These can be combined and used for developing predictive models for the spread of vector-borne diseases. For example, correlations have been shown between the risk of West Nile virus transmission and changes in the timing of the spring bloom, temperature variability and moisture availability, all observed by satellites over the Great Plains of the US [4]. Various kinds of indicators can be obtained through remote sensing and inform on habitats and transmission risks of mosquitoes, ticks, black flies, tsetse flies, and sand-flies [5]. Improving spatial resolution enables the assessment of risks at the neighbourhood level, for example for Chikungunya transmission in Buenos Aires [6]. In countries where disease surveillance is scarce or failing, the use of remote sensing data to predict a high risk of emerging vector-borne diseases allows preventive measures, such as vector control in affected areas, to be fostered and targeted. By avoiding sprinkling and dispersion of resources, precision global health contributes to better targeting of development aid to where it is needed. It also helps to prioritise prevention of outbreaks of emerging infectious diseases, which are much harder to control after they have started.

Genomics to help targeting public health surveillance

The "Spanish cucumber crisis" was an outbreak of foodborne illness due to a novel strain of *Escherichia coli* O104:H4, which occurred in Germany in May and June 2011. It was severe enough to cause 53 deaths, with 800 patients suffering from haemolytic uraemic syndrome, and affected about 4000 people [7]. Standard methods of investigation misled health authorities, which wrongly linked the bacteria to cucumbers imported from Spain. Later, at the end of June, the European Centre for Disease Control eventually established the link between the bacteria and contaminated seeds of soy bean sprouts imported from Egypt. Had the recently created 100K Foodborne Pathogen Genome Project [8] existed at that time, it would have been possible to quickly compare the genome of the culprit bacteria and existing sequences stored in the database. This would have saved precious time and lives. It would also have saved money, since the outbreak cost innocent Spanish exporters an estimated US$ 200 million/week. Precision global health not only helps saving lives, but has also an important economic impact.

Data sharing platforms

Health information systems everywhere, but especially in low income countries (LICs), are often disconnected from systems which require the data to inform policies on disease treatment and interventions. The data might exist, and this deficit does not usually derive from a lack of research or even published clinical trials. But the data are siloed or not interoperable. Precision medicine, personal or global, requires large datasets to be effective. It is crucial to be able to federate databases in order to provide a body of evidence sufficiently consistent to guide policy. Individual patient data from many trials have been curated to enable interoperability and merged to allow consistent meta-analyses of this much-larger data set. In this way, assembling valuable research data from multiple studies could produce evidence that sparse data in single studies cannot achieve. For LICs notably, the WorldWide Antimalarial Resistance Network (WWARN) [9] is a partnership comprised of more than 260 collaborating institutes around the world. WWARN currently securely hosts more than 350 clinical trial data sets, comprising over 135 000 patient records which have been harmonised. For instance, pooled analyses of artesunate-amodiaquine data (a recommended treatment for uncomplicated *Plasmodium falciparum* malaria) show that providing the artemisinin and amodiaquine as a fixed combination preparation was more effective than treating people with two separate pills with slightly different dosage [10]. Children treated with another antimalarial treatment, dihydroartemisinin-piperaquine, were receiving a lower amount of the drug than expected by the drug developers, and these children were much more likely to fail treatment [11]; this evidence supported changes to the WHO's Guidelines for the treatment of malaria [12].

Merging data from many separate studies would require changes to the traditional path that has been followed for many decades. In addition to publishing each study separately in scientific journals, data sets would need to be shared and analysed collaboratively. This new approach will require the development of fair and responsible data sharing platforms. These platforms would need to assure that patients' information is securely stored and their privacy protected. The Global Alliance for Genomics and Health (GA4GH) is such an initiative [13].

Overall, sharing data from many different trials and producing analyses relevant for common regional actions will be a fundamental requirement for precision public health.

Without this approach, simple accretion of individual studies will not move LICs forward to conquer neglected tropical diseases (NTDs) or emerging infections; collaborative analysis of data from multiple sources or studies can.

Cell phone data to better target humanitarian action

In many LICs the use of the cell phone for health interventions is far more developed and creative than in other parts of the world. This is particularly true for sub-Saharan Africa, which leapfrogged from a stage of no telephone or road networks to an increasingly digital economy based on smartphones. When Ebola hit West Africa in 2014, Médecins Sans Frontières (MSF) and other nongovernmental organisations (NGOs) and health authorities took advantage of cell phone data to better foresee the extension of the epidemic, and also to better target needs of the affected populations [14]. Similarly, outbreaks of cholera have been identified in rural Kenya by identifying abnormally slow movements of customers equipped with cell phones, which could be due either to sickness of people or to flooding (which usually occur two weeks before such outbreaks) [15]. Relationships between travellers and spread of malaria has been studied extensively in Senegal from call record metadata, and provided recommendations to health authorities [16].

Influenza: can Google search terms be used as early warning signals?

Seasonal influenza represents a huge burden each year, both in terms of health consequences, with excess hospitalisation and mortality observed in the elderly, and in terms of economic impact, with sick leaves and increased use of the healthcare system. Although accurate prediction of influenza epidemics would be useful for better planning and controlling these seasonal outbreaks and their impact, this exercise is highly difficult, because of the complexity of the phenomenon and chaotic nature of the signal. Predictions of up to 3 weeks have proved reliable [17], but classic public health surveillance often reports data with a delay of a few weeks, limiting the potential for early intervention. An appropriate selection of Google, Twitter or Wikipedia could be a proxy for real-time measures for influenza epidemics [18–22]. Google Flu Trends, based on Google search terms, was highly promising. It provided an early warning signal for seasonal influenza, specifying when

it started and thus allowing latecomers into the vaccination scheme. At every seasonal outbreak, and particularly when influenza activity is intense, general practices, hospital emergency services, and pharmacies are congested during the period of peak incidence. Better planning and forecasting may help with managing these resources. However, in January 2013, Google Flu Trends wrongly predicted a large outbreak of influenza in New York City, prompting Mayor Bloomberg to declare a state of emergency for the City. Pharmacies and emergency departments were stormed, the general panic was further amplified by the media, which in a vicious circle led to ever more searches on the Internet. Google Flu Trends signal was more and more worrying. A couple of weeks later, the US CDC reported no particular alarming epidemiological situation in New York, which was similar to the rest of the country, and displayed the normal and expected pattern of a seasonal influenza outbreak. Google Flu Trends was then taunted and discredited by the press and the public health community [23]. Google decided to close its open access website, and now provides its controversial data only to a selection of universities for research purposes. We can see this story as teething problems linked to the rather small time series. It further highlights the fact that algorithms on a nontraditional data source used for epidemiological assessment need to be constantly updated. With time and the accumulation of longer and deeper experience, these troubles could be solved. Additional sources of information, such as Twitter [24] or Wikipedia [19, 25], or data from shopping (supermarket loyalty cards, pharmacy sales) should prove able to forecast influenza activity also, and could overcome the lack of accuracy provided by a single source. Health authorities will probably not give up traditional public health surveillance for these new practices, but could use them both.

Drones to improve healthcare in developing countries

Drones are an interesting example of synergies in technological sectors within and outside the health system. As smartphones are solving the communication needs in low-and middle-income countries, drone deliveries might solve transportation needs in countries where the road networks are wanting. Drones could deliver essential medicines, blood products, vaccines and diagnostic tests to remote parts, where traditional land-based transportation is not available or reliable. Many obstacles to drone use exist: regulatory issues about the use of drones to deliver goods; skills and infrastructures needed to maintain and operate such equipment; appropriate and effective coordination between those shipping and those receiving services and products; appropriate packing to maintain product quality. There are, however, currently a few experiments where drones are being tested for medical supply delivery in various areas of the globe [26, 27], and it may be that drones will prove cost-effective.

Massive open online scale for training health professionals

The digital revolution allows for innovative methods in domains where global health diplomacy is struggling. The International Health Regulations (IHR) is an international agreement, which was signed in 2005, between all the members of the WHO, binding 196 countries. It has been acknowledged that IHR is a powerful instrument for preventing diseases from becoming major threats at an international level, but the WHO and other key stakeholders failed to respond appropriately and in due time for many crises, namely the 2009 influenza H1N1 pandemic, the Ebola outbreak in West Africa, or Zika in Latin America. The IHR has has not been accused of this failure, but its implementation seemed inadequate. In many countries, national focal points (i.e., the teams in charge of implementing IHR) are not trained or evaluated, and local capacities in term of diagnostic or healthcare supplies are often lacking. To train these teams, a consortium of European universities led by the University of Geneva (Flahault A, personal communication) has proposed as a pilot project to the WHO, an internet-based platform which simulates health crises through serious games. Serious games had not been used in global health until then. Participants "play" various roles involved in such a crisis (e.g., representatives from various ministries, and various countries, representatives from the WHO), and they are immersed into a health crisis which is fictive but looks highly realistic. They have to take rapid decisions, in an atmosphere which mimics the

one met in such outbreaks. These decisions may influence the course of the outbreak or the health crisis, and the system assesses in real time if answers, reactions and decisions are timely and if they fit IHR. Through better training of officials in charge, we improve readiness and raise the level of coordination.

Towards a learning healthcare system

A learning healthcare system applies the best known evidence, encourages continuous learning, and allows for knowledge generation as a natural by-product of patient care delivery. It aims at creating a virtuous cycle of research and practice, using methods such as systems thinking, translation and patient empowerment [28].

Health informatics is the enabler of such a system, connecting personal, provider and population health information and providing feedback loops at many levels, thus creating computer-supported mechanisms for learning and for improving the quality of the overall health system.

Think of a scenario where care professionals are equipped with data collection and decision-support devices used during patient care. These devices can share some information with public health information systems, which are then complemented by external sources (satellite imaging, air quality measurements, news feeds, disease models, etc.), in order to identify and locate abnormal situations that would necessitate a specific public health intervention. And imagine that these systems are also connected to personal mobile devices that can forward personalised messages to their owners, and can also inform the system with user-generated data and observations. This data ecosystem can be further enriched by social media, internet-based sources, genome sequencing, sensors, etc., thus providing additional context, dimensions, and granularity to be exploited by big-data analytical engines and artificial intelligence algorithms. This could lead to new ways to forecast, simulate, recommend, deploy, and evaluate individual or population-wide precision health interventions.

Most of the building blocks of this scenario do exist, but are insufficiently connected, because of many weak links:

– *Integration* requires unprecedented levels of semantic interoperability and standardization
– *Implementation* faces many technical and organizational challenges, and raises unsolved ethical, legal and societal issues
– *Impact* on health outcomes is difficult to measure, and has been poorly addressed so far

Further research should aim at strengthening these links through the development of robust health information science tools, through the advancement of integration and implementation sciences, and through the elaboration of innovative evaluation methods to demonstrate impact on the health of populations.

Machine learning: making sense of big data

Many of the future innovations in health care and public health will be rooted in our ability to collect very large data sets at unparalleled levels, both in scale and in scope. But data alone has no value *per se* – it needs to be mined, analysed, and interpreted correctly to unlock its innovative potential. Thankfully, our capability of analysing large datasets has kept pace with the capabilities of collecting the data. Advances in machine learning, and in deep learning in particular, allow us to analyse big data in efficient ways. Deep learning is now at a stage where it allows for pattern recognition close to, or at, human accuracy, something deemed impossible just a decade ago. Importantly, deep learning is a form of end-to-end machine learning, and does not require the extreme levels of domain expertise that made traditional attempts at pattern recognition very challenging [29].

We think that such deep learning models will be quite important for precision global health. Two domains with many applications for health are image recognition and text interpretation, which are relevant in a number of settings from correctly interpreting text documents such as health records or social media messages to interpreting medical images. These two areas have seen tremendous advances in the past few years (with error rates on benchmark classifications such as ImageNet dropping from mid-two-digit levels to low one-digit levels in less than five years [30]. Deep learning algorithms will not only help us make sense of large datasets, but can then also easily be implemented on

smartphones, with the potential to create a virtuous cycle of increased data collection and improved algorithms.

Conclusion

Timely and accurate health-related data are a critical resource to monitor, assess and guide public health interventions. The potential of "big data" to transform medicine and raise expectations for precision medicine has driven substantial investments that have improved data collection and analyses. Major progress has been made in recent decades: tools to improve health information systems, including electronic medical records, capacity for transmission of standardised surveillance data, and sophisticated data sharing platforms for genomic information. Yet, the benefits of this progress have accrued almost exclusively to well-resourced regions.

In LICs, the weakness of the health information systems, in terms of accuracy, data quality and access to real time information has slowed down progress in public health. As a result, data sharing between data collectors and policy makers has been minimal, seriously diminishing the utility of the data that are collected. In 2015, the World Health Organization, the United States Agency for International Development, and the World Bank published "The Roadmap for Measurement and Accountability" [31]. The roadmap was a call for action to improve data collection, analysis, access and use. The objectives are very ambitious and will require multiple levels of coordination, resources and political will; all of these will take time to assemble.

Medical interventions and policies have also been adapted and improved in the last decades with a focus on LICs. Despite these improvements, there is limited evidence for interventions focused on particularly vulnerable subpopulations such as malnourished children, pregnant women and patients affected by neglected tropical diseases. Thus, many segments of society in LICs still have the poorest health outcomes. While the demand in rich countries has focused on individual medical interventions, the needs of LICs require broader public health responses; in other words, a precision public health response is needed, prior to individual precision medicine.

Lessons learned and tools developed by well-resourced countries can surely benefit LICs. But how? Resource-poor countries can develop adapted innovative tools to improve their health information systems, including data collection tools, data transmission systems and use of international data standards. These adaptations must also address data security issues and fair systems and governance policy for data sharing and use. In rural LICs, high-speed internet access is still the exception and, in many areas, even mobile telephone technology will not support these modern systems in the near future. Improving and adapting health information system tools and solving these technical constraints are both urgent needs, and these cannot depend solely on commercially driven technology. Precision global health approaches could guide and mobilise the optimal use of resources, for both preventive and therapeutic interventions.

Taking advantage of affordable and sustainable innovations to foster progress and improvement in global health is something we can name "precision global health". We need to provide better access to those innovations that bring better and longer health to populations. We need to propose solutions for global health issues such as outbreaks of emerging infectious diseases, or mental health problems, or noncommunicable diseases, or smoking tobacco, or climate-change related health troubles. For all these complex and cross-border issues, there are examples, mostly success stories, where affordable and sustainable innovations help to bring solutions. Precision global health will contribute to greater effectiveness of intervention measures in global public health, by relying on cutting-edge innovations.

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