## If we use the phrase "precision medicine" what do you think of?


For many, perhaps most people, genomic tests for targeted cancer drugs and precise diagnosis of rare, inherited disease will be some of the applications that spring first to mind. Tremendous advances, certainly. The ability to distinguish between tumour types at a molecular level and design the cocktail of therapies most likely to combat it is one of the wonders of the last decade. And, in inherited disease, the ability to cut short the long diagnostic odyssey – the journey from one specialist to another in the hope that the symptoms are recognised – is a boon for many families who have access to whole exome or genome sequencing.

The benefits are clear and the technology is ready but is precision medicine actually changing lives as it promised? To many patients and families around the world, access is the issue, since the tests are often not widely available and often quite expensive, as are many of the drugs that precision medicine requires. So it is in the interest of pharmaceutical companies to help establish the diagnostic infrastructure needed to properly direct the medicines involved to create a wider market for their products, a task too few of them appreciate. It is also in the interests of companies like Illumina, ThermoFisher and BGI to develop and advocate the clinical and economic case for the routine use of precision medicine, not just in highly developed health systems but also in middle income countries. For there are few countries that do not wish to participate to the extent they can afford in the precision medicine revolution.

But, as the science and technology of personalisation proceeds, a new vista is opening up: precision health. Here we look not at the personalisation of the treatment of challenging

diseases but at the challenge of keeping most people healthy and active for as long as possible – "healthy longevity". This has been the focus of a recent official effort in the UK in which Professor Richard Barker and Tina Woods have been involved: the All-Party Parliamentary Group on Healthy Longevity. Or, as some prefer to call it, "healthspan".

Of course, there are many national or community level initiatives that can be taken to improve the prospects of the whole population, such as legislation of the level of sugar in processed foods, or the price of alcohol. However, one of the most exciting areas for progress is personalised prediction and precision interventions in normal life to maximise the probability of a long and healthy life.

Personalised prediction can come at two stages: the identification of the likelihood of future disease and the early detection of pre-symptomatic conditions. It is emerging that genomic test early in life can quantify the risk of later heart disease, among others, and the UK is initiating a polygenic testing programme to cover 5 million people with this as the goal. In certain cases the tests will reveal a potential for sudden cardiac death, as sometimes encountered in otherwise fit athletes. In others it will identify predisposition to high lipids, causing later heart stacks and strokes, as in familial hypercholesterolaemia.

A fast-developing second front in this war on future disease comes from liquid biopsy tests for circulating tumour DNA. This has been shown by companies such as GRAIL to spot cancer patients months or even years before the tumour becomes apparent symptomatically.

An alternative, or perhaps complementary, approach is to use artificial intelligence programmes to interrogate routine medical records to identify high risk individuals that should be tested more thoroughly and to determine epidemiological patterns. That approach obviously applies not only to cancers that might make their presence felt in symptoms such as anaemia, abdominal pain or frequent headaches, but also many other diseases including the most widespread cardiovascular diseases, liver diseases, and depression. In cardiometabolic conditions in particular, it seems that each of us is on a personalised journey, where blood pressure, lipid level and emergent insulin resistance – and perhaps even mental health – interact to determine the probability of future disease, as is being investigated by companies such as Metadvice and many research centres from Harvard Medical School to Amsterdam UMC. The application of artificial intelligence algorithms to medical data allows us to analyse vast data silos with a promise of predicting the future life course of a patient and determine the best intervention points and strategies.

This new era of personalised prediction poses some important questions if these technologies are to move from intriguing research tool to widespread use. Firstly, how to build a convincing clinical and economic case for system-wide adoption? Screening tests have always faced their

version of the "number needed to treat" – the number of patients needed to be tested to reveal one actionable case. (This has been an ongoing debate in breast and PSA screening, for example.) Secondly, how to overcome the "silo budgeting" issue: how to ensure there is enough in the diagnostic budget to undertake tests that will save costly late stage interventions with poorer outcomes? This is a policy issue for many systems, but one that the diagnostic manufacturers will have a strong interest in being effectively tackled. Thirdly, how to develop and pay for AI tools that bridge between the vast amounts of genomic and phenotypic data coming available and actionable insights? Such tools would be beneficial to both health systems and the insurance industry.

But, if history is to be our guide, these questions should not be left to hard-pressed health system managers, whose priority is always and understandably how to grapple with the demand from today's obviously sick patients. Now, at a time of global pandemic, especially. The life science and insurance industries need to be active participants in tackling these questions.

Finally, precision health is extending to the application of digital health tools to the personalised management of the lives of healthy citizens, as well as patients. The wealth of apps – or broader digital solutions linked to our personal health data – point to a future in which each of us can more actively manage our health lives. Here we see the power of incentives, prompts or gamification to change our behaviour in areas such as diet, exercise and smoking cessation. These are tools that not only benefit the individual but also the health system in the longer term and the insurer, as demonstrated already by Vitality Health. Should they be a question only for the individual or is there a role for the to promote or even reimburse them?

We witness a dawn of a new era, the era of precision health. It poses questions for health systems: how to evaluate and adopt among a plethora of tools that could change the shape of the curve of future disease? It opens up a new horizon for the diagnostic industry: how to introduce a new generation of advanced genomic tests into routine use? It challenges the digital health world: how to make the case to both individual customers and healthcare providers to weave them into their lives and practices? It provokes the insurance industry to ask: do we need new approaches to health risk assessment and insurance product design? And, for the most powerful economic engine of the life sciences world, the biopharmaceutical industry: how to participate in this new era, with its diagnostic and digital opportunities, and the prospect of business models that are very different from those in the past?

That is why, for advisory firms such as New Medicine Partners, the transition from precision medicine to precision health is intriguing: tough questions, still-emerging answers and enormous opportunities.