A chasm of misunderstanding

The widening gap between public perception and scientific consensus

Philip Hunter

The gulf between public perception and scientific consensus seems to be widening in a number of key areas with significant consequences for policy, funding and research. The science of climate change has featured prominently in this context, but profound gaps are also evident in some areas of the life sciences, including genetically modified organisms (GMOs) and risk assessment in medicine.

Public acceptance and trust in science has not been helped by several high-profile cases of fraud, deliberate falsification and the withholding of clinical trial data, some cases of which have had significant public health consequences. These have happened at a time when science is reaching ever more deeply into the lives of citizens with the rapid rise of 'omics' technologies, which are changing not only the life sciences, but also public health through personal DNA tests.

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The basis for these scientific and societal developments was laid in the 1990s with the Human Genome Project (HGP), which laid the scientific groundwork for the omics revolution that came in the next decades. The HGP improved sequencing technology, computational biology and other technologies used to generate and analyse large amounts of biological data. Socially, the publication of the sequence of the human genome in the year 2000 was accompanied by a flurry of articles, speeches and public commentary that highlighted the enormous value of the 'blueprint of life' and how it

would enhance and revolutionize medicine. Today, sequencing an individual's genome costs just \$1,000 compared with the cost of \$28.8 million in 2004.

The technological progress being made in sequencing and analysis and society's interest in the life science's contribution to health eventually converged a few years ago when the first companies began to market DNA sequencing technology to individual consumers. These companies sought either to provide genetic information related to ethnicity or ancestry and/or to offer DNA testing services that would predict the risk of developing certain diseases. The latter application in particular continues to provoke controversy and has divided medical practitioners, researchers and regulators over whether such tests should be restricted or even banned.

The US company 23andMe was among the pioneers and, perhaps partly as a result, now bears the brunt of regulatory scrutiny. Its *Saliva Collection Kit* and *Personal Genome Service*, most recently available for US\$99, have become mired in controversy: in December 2013, the US Food and Drug Administration (FDA) ordered the company to stop selling its DNA analysis kits. The FDA argued that 23andMe had not demonstrated that they have “analytically or clinically validated the *Personal Genome Service* for its intended uses” and expressed its concern over the public health consequences of inaccurate results.

The product is now in a state of abeyance: 23andMe offers the basic data, but without any insight into what it means. The company declined to comment while negotiations with the FDA over resumption of the full service are ongoing. Nevertheless, 23andMe has received some support from the research community, largely on the basis that suppression of data will ultimately prove

counterproductive and that the public must learn to engage with genetic information, even if it is often ambiguous and inconclusive. “Websites like 23andMe do an excellent job of teaching uninitiated lay people about risk, since most consumers are not grounded in probabilistic statistics”, explained Eric Topol, Director of the Scripps Translational Science Institute at the Scripps Research Institute in California, USA. “These tests will be increasingly affordable and widely available, and will go well beyond a starter kit like 23andMe to whole genome sequencing in the future”. According to Topol, such enhanced services will be unlikely to trigger immediate life style changes in consumers [1], but should generate a great deal of useful information for research: “[...] there is considerable value for the pharmacogenomic information and some of the disease susceptibility data,” he said. “Overall, there is great potential for net benefit”. His argument is that the results of genetic tests in the short term will yield valuable data that add to that collected from research and organized trials, but will not, for the time being, bring profound benefits for the consumers taking them.

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Misha Angrist, Assistant Professor at the Institute for Genome Sciences & Policy at Duke University, North Carolina, US, argues that scientists have been guilty of overstating our ability to make predictions from

genetic risk factors. Angrist thinks that data from 23andMe have poor predictive value and, as a result, that 23andMe has been the architect of its own recent problems with the FDA. His argument is that the value of the tests and their ability to predict future events has been exaggerated, even if not deliberately. Nevertheless, he acknowledges that the direct to consumer (DTC) genetic testing genie is now out of the bottle with positive affects overall. “It has undoubtedly raised public awareness of genetics”, he said. “It seems to me that banning access to information—even uncertain, largely inscrutable, tenuous information interpreted at

\$99 a pop for those who want to spend that money—is rarely a good idea”.

Angrist contends that the medical profession is also prone to giving tenuous information based on its tendency to place too much emphasis on single individual risk factors, rather than looking at wider interactions between genes and external influences in various pathways and networks. “Our understanding of the genome and its complex interactions with the environment is still in its infancy. But we—and by ‘we’ I mean not only 23andMe, but most people and institutions involved in human genomics—pretend otherwise”.

The problem of communicating complex issues extends beyond genetic testing to other medical topics, such as the risks and benefits associated with clinical drugs, especially those that are relatively new. This is highlighted by the case of statins, which lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase that plays a central role in its production. About 70% of total body cholesterol is produced in the liver, and increased levels are associated with cardiovascular disease (CVD). Statins reduce the incidence of cardiovascular disease not only for secondary prevention among those who

already have early-stage CVD, but also in primary prevention for those who might be at risk.

But two recent articles in the *British Medical Journal* have argued that the benefits of statins are outweighed by their risks and that cholesterol is not the main issue [2,3]. These papers have in turn been attacked by cardiologist Rory Collins at Imperial College, London, UK, who was reported in *The Guardian* newspaper (London, UK) to have argued that the articles overstate the risks and that they are probably “killing more people than had been harmed as a result of the paper on the MMR vaccine by Andrew Wakefield. ‘I would think the papers on statins are far worse in terms of the harm they have done’” (<http://www.theguardian.com/society/2014/mar/21/sp-doctors-fears-over-statins-may-cost-lives-says-top-medical-researcher>).

At this stage, it is not possible to determine whether statins pose a health risk to people deemed at lower risk for CVD. The question in those cases is whether the side effects of statins are a greater threat to health than the relatively lower risks posed by CVD. The main point, though, is that the public are receiving mixed and confusing messages on statins, just as they received mixed messages on the safety of the MMR vaccine in the light of the Wakefield paper, which claimed a link between the vaccine and autism. Even though the paper was finally withdrawn in 2010, after Wakefield was found guilty by the UK General Medical Council of dishonesty and flouting ethics protocols—following numerous studies that failed to repeat the findings—the public’s confusion persists.

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The lesson is that the medical and research professions need to come up with ways to better counter claims about the safety or dangers of new treatments that are based on only a few publications, or even anecdotal evidence. Elizabeth Wager, Chair

of the Committee on Publication Ethics, an international organization that promotes ethical practice among scientific journals, commented that “It will always be easier to scare people than to ‘unscare’ them, hence the perpetuation of urban myths. [...] This relates to a broader issue that human interest stories, however unscientific, tend to trump solid evidence, so a single case study may carry more weight in the public’s mind than a dozen well-conducted but dry studies”.

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The tragedy of the Wakefield case is that its impact on public attitudes to vaccination has still not worn off, more than a decade after the paper was almost unanimously rejected by the medical community at its publication and four years since its retraction. “There is still lower uptake of vaccination in both the UK and North America than there was beforehand”, Wager said. But one positive outcome, she thinks, is that the medical profession has learnt that it needs to combat anecdotes with anecdotes, rather than just dry evidence. “I think we need to be sensationalist ourselves, but with a solid evidence base behind us. I think people do respond to that”. Wager cited the positive impact of cases where celebrities have raised the profile of a particular disease or medical issue, even though such cases are not quite the same situation as countering negative publicity about a treatment. “In the UK, the case of Jade Goody raised awareness for cervical screening, especially among younger women, and, a few years ago in the US, General Norman Schwarzkopf’s prostate cancer also raised the profile of the disease”, she noted.

Some publishers are beginning to help researchers and others reach out to the public directly by introducing features that communicate findings more simply for laypersons. Among them is the Cochrane Collaboration, a global indepen-

dent network of health practitioners, researchers, patient advocates and others, that is making progress through its public communication initiative called Evidence Aid. “In the past, Cochrane reviews were very worthy and useful, but awfully dull, and there was no attempt to make them user friendly”, Wager said. “Now they have realized that people apart from doctors and specialists use them and they have had plain language summaries for some time. With things like Evidence Aid, they have been tweeting and using social media, and realizing people need information at the right time in bite-size chunks”.

Evidence Aid emerged as an international initiative to improve non-specialist access to review articles and was initially set up to communicate the impact of interventions and actions relevant to natural disasters in response to the 2004 Tsunami in the Indian Ocean. However, its scope quickly expanded to include health-related outcomes, and its first conference in 2011 was attended by the World Health Organization (WHO) and the US Center for Diseases Control and Prevention (CDC). Wager also noted that the Cochrane Organization is collaborating with Wikipedia to disseminate research information. The aim is to extend the work of Evidence Aid by providing public access to emerging research findings and presenting them in a manner suitable for a non-scientific audience. But as Wager noted, such findings need to be representative of current research, rather than just focused on positive results.

Wager also supports the AllTrials campaign (<http://www.alltrials.net/>), which was launched in January 2013 by Bad Science, the *British Medical Journal* (BMJ), the Centre for Evidence-based Medicine, the Cochrane Collaboration, the James Lind Initiative, PLOS, Sense About Science, Dartmouth’s Geisel School of Medicine and the Dartmouth Institute for Health Policy & Clinical Practice. The initiative campaigns to register all past, present and future clinical trials in order to report their results, with the aim to reduce reporting bias and to make it harder for both fraud and major errors to occur, thereby avoiding adverse consequences for public health.

Scientists and public health experts have long feared that high-profile fraud cases in biomedical research might not only impact public health policies,

but could also damage public trust in scientific advice in general if the public lose faith in scientists. However, some specialists in research ethics believe that a constant drip feed of minor transgressions, such as ignoring inconvenient outlying data, is much more damaging to the scientific enterprise than the occasional major fraud. “Viewed from the perspective of the reliability of the research record, minor misbehaviour or what have been called ‘questionable research practices’, are more important than the misbehaviours defined as misconduct”, said Nicholas Steneck, Director of the Research Ethics Program at the University of Michigan’s Institute for Clinical and Health Research. “There is currently too much emphasis on misconduct and not enough on the more subtle misbehaviours that have serious impacts on the reliability of the research record and therefore on the public”.

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A similar factor that can skew the public’s perception of scientific expertise is the suspicion that research is driven by vested interests, which has been a major issue in the debate about GM crops, especially in Europe. To some extent, the situation can be likened to the Wakefield case, as the public opposition to GM crops continues, despite the lack of evidence of environmental harm, even in places where GM plants have been grown extensively. A big difference though is the consistent lobbying of government and the public by environmental groups opposed to the

research, whose claims are aided by the attitude and approach of the GM industry. David Baulcombe, Regius Professor of Botany at the University of Cambridge, UK, commented that “The anti-GM movement has operated on a wide front and it has been successful, in part, because it attacked a series of legitimate targets based on industrial agriculture. [...] They have targeted industrial agriculture because they see that it has unfortunate side effects—loss of biodiversity, degradation of other ecosystem services and pollution, reduced employment and prosperity in rural communities. Many of these side effects are real, but GM has failed to present itself as a solution, even though it could be. In the eyes of the anti-GM people, the new technology reinforces the problems”.

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The anti-GM movement has therefore supported what Baulcombe calls the dysfunctional regulatory process, because it is very effective at suppressing the introduction of new crops. “This strategy has a feedback component because the only organizations able to bear the regulatory cost are the large multinational companies that practise the current model of industrial agriculture”, Baulcombe explained. He went on to note that “They [agricultural policymakers] have failed to find a strategy for diversity in agricultural economy in which there is managed coexistence of ecological and industrial agricultural

systems that exploits the best of both”. Nevertheless, Baulcombe remains optimistic that the argument in favour of GM crops will gradually win out, simply because of the benefits. “I am optimistic because emerging traits are so useful—disease-resistant potato for example. I suspect that GM rice in China is the threshold—it has been developed and tested and will influence global perception when it is introduced”.

There is hope, then, that some of the problems that lead to the perception gap between scientists and the public have been recognized and are being addressed. Scientists need to understand their role in communicating research to the public and the consequences of their behaviour, and the public need to be helped to understand that scientific evidence is rarely one hundred per cent conclusive and that policy judgements have to be made on the basis of probabilities, rather than irrefutable facts. In that sense, DTC genetic testing might have another role to play: even if it does not have a significant and immediate impact on public health, it might still be used to teach consumers about risk and statistics, which might go a long way to reducing the perception gap.

Conflict of interest

The author declares that he has no conflict of interest.

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