GeneWatch UK response to the BIS Consultation on Proposals for Long-Term Capital Investment in Science & Research

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GeneWatch UK is a not-for-profit organisation which aims to ensure that genetic science and technologies are used in the public interest.

In 2010, GeneWatch UK published the report 'Bioscience for Life?' which examines investments in the biosciences since the 1980s.[1] We found that research funding decisions are strongly influenced by a small coterie of advisors within the 'scientific establishment' who are not accountable to taxpayers but dominate the decision-making for R&D investments. Major investment decisions lack 'scientific diligence' and are often based on hype and unrealistic claims about what can be delivered. Investments follow vested interests, not the public interest, and the costs and risks of public-private partnerships are largely borne by taxpayers, who are excluded from decision-making. There are likely to be significant opportunity costs as a result of poor R&D investments.

One major investment we studied in 'Bioscience for Life' was the New Labour Government's proposal to build a vast database of electronic medical records (the Spine). The objective was to combine information from medical records stored in the NHS with genomic data from sequencing DNA, utilising the vast amount of information available within the NHS to create individual risk assessments allowing the "prediction and prevention" of disease. We documented this proposal in detail in an appendix to our report.[2]

The same project (with some changes) has now been revived as the "care.data" scheme for electronic medical records, combined with a plan to include people's genomes as attachments to their records later on. Care.data involves creating a database of medical and social care records in the Health and Social Care Information Centre (HSCIC) and sharing this data with commercial companies without individuals' consent. Health Secretary Jeremy Hunt has stated that he wishes the whole genome of every baby in NHS England to be sequenced in the future[3], and the 100,000 Genomes Project is seen as a pilot project for sequencing the whole population.[4] Data will be shared with private companies (e.g. Google), who will use computer algorithms to calculate the risk assessments. GeneWatch has again raised extensive concerns about these plans in relation to their implications for privacy, human rights and the future of the NHS.[5]

We are concerned that the consultation document identifies "Bridging the genotype to phenotype gap" as the largest area of funding, with a proposed allocation of £1.1bn, supported by other investments such as those in e-infrastructure, data services (including a bio-social data service), high-throughput genome sequencing and longitudinal studies that are also likely to include genomics. Although it does contain some other potentially useful elements, this proposed funding appears to be focused on the Wellcome Trust and Human Genomics Strategy Group's proposal to create a DNA database of the entire population within the National Health Service (NHS). [6] This proposal has little scientific merit and risks wasting large sums of taxpayers' money on poor research priorities, whilst also posing a major threat to privacy and the future of the National Health Service (NHS). The proposal to spend such a large sum of taxpayers' money on the infrastructure for this project (collecting and interpreting the genomes would cost many more billions) should be the subject of much broader public consultation, not hidden away in a document that is directed largely at researchers and research funders.

GeneWatch UK believes that fundamental reform of the R&D funding system is needed to make investments more accountable. We therefore welcome the opportunity to input to this consultation. Objectives of reform should include:

- More democratic decisions about research funding priorities and a more diverse research agenda;
- Greater accountability and scrutiny of major research investment decisions: including economic assessments and appraisals, scrutiny of scientific and technical assumptions, and active steps to prevent political 'entrapment' in research agendas based on false assumptions and misleading claims;
- A role for public engagement in setting research questions and priorities: including consideration of a variety of alternative approaches to addressing problems, and greater democratic accountability for science policy decisions;
- More public engagement in research itself, involving closer co-operation between universities, communities and civil society organisations;
- More funding for research which does not necessarily benefit large corporations but may deliver other benefits: including economic ones (for example, public health research, and research into improving agro-ecological farming methods);
- Funding for 'counter-expertise' and multi-disciplinary research which can identify long-term scientific uncertainties and regulatory gaps;
- Ensuring a thriving scientific culture that can analyse, critique and develop the theoretical concepts that often underlie decision-making, and which are key to developing new understandings;
- A commitment to take public opinions into account in decisions about science and innovation, including methods to ensure full consideration of the broader social, environmental and economic issues associated with adopting particular approaches and technologies.

Q1: What balance should we strike between meeting capital requirements at the individual research project and institution level, relative to the need for large-scale investments at national and international levels?

The main situation to be avoided is 'lock in' to major capital investments which suck all future research money in a particular direction. This is because capital investments tie in major operational costs far into the future and lead to a focus on the development of particular skills and ways of working. For example, it is already well known (see below) that human genomes have little predictive value for common diseases in most people or for most adverse drug reactions. Thus a commitment to sequence large numbers of healthy people and data mine this information in an attempt to predict their risks would be largely wasted money. There would be massive opportunity costs in diverting money away from more fruitful approaches, including focusing genomic research on the most useful areas (genetic disorders and perhaps cancer tumours, plus sequencing pathogens) and developing public health approaches to tackling more important risk factors for the big killer diseases, such as unhealthy eating, lack of exercise, smoking, poverty and pollution. To make progress in public health, more diverse approaches are likely to be needed.

Q2: What should be the UK's priorities for large scale capital investments in the national interest, including where appropriate collaborating in international projects?

The proposed infrastructure spend for "Bridging the genotype to phenotype gap" and associated infrastructure (at least for human genomes) should be significantly cut back so that it focuses on areas that are likely to be of most benefit. The ideas that everyone should have their genome sequenced (including all babies at birth), and that a vast DNA database should be built within the NHS, should be abandoned.

The 1995 Foresight Report on health and life sciences includes *"genetics in risk evaluation and management*" for common multi-factorial diseases, such as heart disease, as a key area for greater investment. The report states (Section 4.2) that: "*It is too early to predict how difficult it might be to dissect out the complex interplay of factors at different stages in life that lead to disease, or how effective individualised risk might be as a public health measure*". Annex 2 also notes: "*It might become possible to use individuals' genetic makeup, lifestyle and environment to individualise risk and target interventions,* ***but it is questionable how widespread and useful this would be at a population level****. The effectiveness of public health interventions is strongly influenced by education, culture, affluence and other variables. Identifying risk without changes on other areas might have little impact*" [emphasis added]. Nevertheless, the report concludes (Section 4.2): "*Despite the uncertainty, the genetic element in common disease is potentially so important that the UK should begin building a leading-edge position in research in the area. Consumer demand will certainly be strong, and the export potential is high*".

This mentality - that investments should be directed at trying to create markets, regardless of the evidence of benefit - has continued as this idea has been incessantly promoted by a small circle of advisors (including current Life Sciences advisor and Chair of the Human Genomics Strategy Group, Professor Sir John Bell, and the Government Chief Scientist Sir Mark Walport). Over time it has become even clearer that sequencing the whole genomes of the population would not be useful for improving the health of the population. For example:

- many studies show that adding information from multiple genetic variants to risk-prediction models, provide no or little additional discrimination to current risk-prediction models (i.e. genomics contributes little to predictions of who will become ill or stay healthy) [7];
- this inherently limits the clinical usefulness of such tests[8,9]
- it is possible to demonstrate that adding more genetic information will not improve this situation[10,11,12,13,14];
- most genetic tests which aim to predict drug response (pharmacogenetic tests) also have limited clinical use:[15] for example, genetic testing for warfarin response does not improve clinical outcomes, although this has long been regarded as the 'poster child' for this approach.[16]

Further, there is in reality very limited consumer demand for genetic testing in the absence of medical need. Hence the latest version of this idea is that taxpayers, not consumers, will pay up front for sequencing and individuals will have no say in the matter until their individual genetic risk assessments are fed back to them. This means that the spending on this project by taxpayers will not be tested in the market place: it is expected to be subsidised via a top-down decision by ministers without any public say.

The idea of creating a DNA database of the whole population persists only because:

1. A few very influential people refuse to admit they are wrong (such as Bell[17, 18])
2. Most scientists will not speak out for fear of losing funding (due to not wishing to "bite the hand that feeds them" [19,20])
3. Policy makers have been kept in (perhaps wilful) ignorance.
4. There is no mechanism to conduct 'scientific diligence' on this or any other R&D investment.
5. Powerful corporate and other vested interests still expect to profit (provided the infrastructure is heavily subsidised and promoted by the Government): mainly by using the risk assessments for personalised marketing;
6. There are significant potential secondary uses in terms of surveillance of the population (because every individual and their relatives can be tracked using their DNA).

Relevant vested interests include: genome sequencing companies, IT firms, Google (who wants to develop the algorithms to make the risk assessments), firms that want to sell 'personalised' health products to healthy people (drugs, foods, supplements etc.), private healthcare (extra tests and treatments), harmful or polluting industries (fast food, tobacco, chemical and nuclear) who want people to blame their genes for health risks, rather than their products.

The main means to monetise genetic risk assessments is through personalised marketing i.e. through the "marketing of fear" by telling people they are at high genetic risk and selling them supplements, drugs or other products. For example, lobbyists are beginning to call for the breast cancer drug tamoxifen to be used in this way. This will significantly expand the drug market and cause a lot of over-treatment and unnecessary side effects (because most of the 'at risk' group will be treated unnecessarily as they would never have developed the disease).

It is not difficult to see that subsidising the creation of a DNA database of the whole population in the NHS is an enormous waste of public money, which will undermine rather than benefiting public health. It is also going to be extremely controversial, as the Government (like the previous one) actively seeks to undermine data protection, erode privacy and remove requirements for informed consent, in order to implement the plan.

This of course does not mean that genomics research should be abandoned altogether. Whilst the 100,000 Genomes Project is problematic because it is seen as a pilot project for sequencing the whole population, it is actually focused on the areas most likely to be of clinical use, i.e. undiagnosed genetic disorders (in children with symptoms) and cancer genomes (i.e. the genetic mutations that arise in cancer cells), as well as sequencing pathogens. However, because the aim is to establish rules for sharing data widely with commercial companies, and to create a market for Oxford Nanopore (despite the poor performance of this company's technology), there are serious question marks about the consent forms used and also about whether sequencing can deliver reliable enough information for diagnosis of diseases. Further, the approach of collecting yet more cancer genome data may not be effective.[21]

Sub-questions:

How can we maximise collaboration, equipment sharing, and access to industry to ensure we make the most of this investment?

This question fails to acknowledge that data-sharing can cause problems as well as (in some cases) providing benefits. This is particularly the case with proposals to allow commercial access to personal data, including medical records and genomes.[22] It is extremely problematic to give people the impression that their e-health records will be shared mainly within the NHS and imply that "approved researchers" means some hazy idea of academic scientists, when in reality the aim is to hand all the data over to Google and others (as "authorised researchers") without people's knowledge or consent. As Google is first and foremost an advertising company it will be immediately obvious to most people that the risk assessments it wants to calculate will be used for personalised marketing and that this is likely to have the opposite effect to the claimed benefit of improving health. If public trust is to maintained there actually need to be tight restrictions on who is allowed to store and access genomes and what they can be used for, giving due to consideration to how genetic data might be commercially exploited or misused by governments, police, security services, insurers, employers, advertisers, journalists and criminals etc.

What factors should we consider when determining the research capital requirement of the HE estate?

There is an important gap in the failure to conduct 'scientific diligence' to assess the extent to which claims of future benefit are realistic. All kinds of false claims are made when scientists want to get research funding or companies want to create markets. Currently, no one is responsible for assessing claims, conducting due diligence on behalf of taxpayers, or avoiding 'optimism bias' (which is recognised when building bridges etc. but not when undertaking the far more risky enterprise of turning the whole NHS into a database, for example).

One example is the proposed "Bio-social Data Service" which would combine genomics data with social science data. The whole area of behavioural genomics science has delivered exactly zero (no confirmed genetic associations with any behavioural trait) so why this area of research (which is based on out-dated eugenic theory and bad statistics) is thought to be worth pursuing is a total mystery.

Taking a "Big Data" approach to social science will change the nature of this work in ways that are not necessarily beneficial[23], just as abandoning hypothesis-driven science in favour of Big Data is also a mistake.

Should – subject to state aids and other considerations - science & research capital should be extended to Research and Technology Organisations (RTOs) and Independent Research Organisations (IROs) organisations when there are wider benefits for doing so?

A major problem with the current system is that too much public money is wasted attempting to de-risk corporate investment strategies, instead of addressing market failures (such as the lack of new antibiotics). There is a tendency for taxpayers to pay for stupid decisions because neither corporate interests (which are not risking their own money), nor the democratic system (which claims to take a 'hands off' approach to science) takes any responsibility for failure to deliver. Funding decisions which create jobs for scientists and technicians are also often promoted as successful regardless of whether promises of better health or new products are actually met. It does not make sense to make this situation worse by subsidising yet more private entities.

What should the criteria for prioritising projects look like?

There are some problems with the criteria in annex B2 (affordability, excellence, impact, skills efficiency and leverage): mainly with how they will be assessed. The most problematic criterion is leverage because it implies that taxpayers' money is best spent where others would like it to be spent. Google, the Wellcome Trust, Oxford Nanopore, the security services, IT companies etc. would all love taxpayers' money to be spent on building a vast DNA database within the NHS, but this doesn't mean that this would be a wise investment (see above). The other criteria are not unreasonable but are very vulnerable to misleading claims being made about them by the same vested interests that expect to profit from the investment (but whose risks will be limited by the substantial spend expected by the taxpayer).

Are there new potential high priority projects which are not identified in this document?

The main problem with the list is not that projects are missing but that too much money is allocated to the "genotype to phenotype" project (and associated spend on related projects), meaning that other projects would have to be stopped or scaled-back. A better response to this problem would be to considerably scale back the expected spend on sequencing human DNA so it focuses on the most useful or potentially useful areas. This means dropping the idea of working towards screening the whole genome of the whole population.

Should we maintain a proportion of unallocated capital funding to respond to emerging priorities in the second half of this decade?

Yes. There are bound to be some new priorities which emerge over time. Delivering the best value-for-money for the public does not mean paying out large sums of money for untried and untested technologies for dubious applications (such as screening healthy people's genomes using Oxford Nanopore's technology). There is no point trying to create markets for things that don't work or that won't deliver on the ultimate outcomes (e.g. improved health). It is important to avoid "lock in" to outdated technologies or theories. For example, technologies may become more accurate, less energy intensive and cheaper over time. Theories may change so that, for example, it is recognised that factors other than genomes are more important in complex disease and therefore the whole direction of research (what needs to be measured and why) needs to change.

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