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Longevity, Politics and Science – Moving from the Outcomes to Understanding the Process

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The 15th April 2017 saw the final living link to the nineteenth century come to an end. Emma Morano, one of the five longest lived people in recorded history, died at her home in northern Italy aged 117. Emma was born in November 1899 and is believed to have been the last survivor from the nineteenth Century. One of eight children, she was born in Civiasco in the Piedmont region of northern Italy, and lived through two world wars and more than 90 Italian governments. Emma is succeeded by Violet Brown, a 117-year-old Jamaican woman. The second and third oldest people are two Japanese women, Nabi Tajima and Chiyo Miyako, who were born, respectively, in August 1900 and May 1901. Ana Vela, 115, a Spanish women, was born in October 1901, and is currently the oldest European and the fourth oldest person in the world. None have yet to achieve the longest recorded life, which is still held by Jeanne Calment of France, who died in 1997 aged 122 years, 164 days - the longest documented human lifespan.

Yet still we are achieving these very long lives without the radical intervention that science can bring. Emma Morano did not have stem cell therapy nor a 3D printed heart nor, as far as we know, underwent a calorific restricted diet. Of the 4 recognised drivers of long living – healthy living, disease prevention and cure, regenerative medicine and age-retardation – Emma Morano, like Jeanne Calment before her, achieved her long life by the first two.

Indeed to date, beyond the laboratory, the key question asked by geriatricians, bio-gerontologists and bio-demographers alike is how much longevity (maximum life spans) and life expectancy (average life spans) can we expect to gain *without* the intensive application of scientific medicine? There is an additional interest in estimating the impact of delaying the onset of age-related diseases rather than eliminating them altogether.

In particular there is a growing focus on our understanding of the genetic drivers of very long lived people. Fifteen years ago a study of extremely old people in Japan

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(Robine et al. 2003) concluded that the long lived participants were healthier than the controls despite the fact they were on average 10.8 years older. They possessed significantly better biological and physiological risk factor profiles, less age-related disease, and better physical and cognitive function. The study this endorsed the concept of a "healthy aging" phenotype, whereby certain individuals are somehow able to delay or avoid major clinical disease and disability until late in life. Similarly later research (Wilcox et al. 2008; Morris et al. 2015) has discovered that supercentenarians, those surviving 110 years or more, displayed an exceptionally healthy aging phenotype where major chronic diseases and disabilities were markedly delayed, often beyond age 100. Such individuals had little cardiovascular disease and reported no history of cancer or diabetes.

There is, however, now a growing interest in estimating the longevity and life expectancy we can expect to gain *with* the intensive application of scientific medicine. Lets just take one therapy – stem cells. Increases in life expectancy have been accompanied by the rising incidence of chronic and degenerative diseases. Pluripotent cells, have the ability to develop into skin, nerve, muscle or practically any other cell type. Induced pluripotent stem cells (iPSC) may address the challenges arising from such chronic diseases associated with the widespread ageing of populations. Initially the focus in this space was on curing age-related diseases. In 2013, iPS cells were developed from the skin cells of people with age-related macular degeneration, which in one case at least halted the macular degeneration and brightened vision. Subsequently the question of whether such therapy also induces tumour growth has halted such trails. In addition, it is now recognised that most reprogramming techniques are inefficient: only a small fraction of cells end up fully reprogrammed.

More recently iPS cells have now become an important tool whereby with gene-editing technologies they have become valuable in the fields of human development and neurological diseases. For example, iPS cells have been used to create organoids such as mini-guts and mini-livers, and research has generated cells with precise combinations of Alzheimer's-associated mutations in order to study the effects. The European Bank for Induced Pluripotent Stem Cells, currently centred in Cambridge, UK, has launched a catalogue of standardized iPS cells for use in disease modelling. Key advances are also being made in drug-discovery as particular iPS cells provide a plentiful source of patient-derived cells to screen or test experimental drugs. And in the laboratory there have been successes at growing mouse organs in rats, though it seems we are still a long way off growing human organs in larger animals such as pigs as currently the resulting human-animal chimeras don't grow well, and few human cells survive (Vogel Jan 2017). However for many in this science community, it is "the availability of therapeutic cell types for the replacement of diseased or worn out tissues and organs that remains the ultimate goal of regenerative medicine and provides a tantalising glimpse into a future of personalised medicine tailored to an ageing population" (Fairchild 2017).

Yet, importantly, however as a recent commentary in Nature [www.nature.com/news/how-ips-cells-changed-the-world-1.20079] concluded, the greatest challenges going forward in this area are not necessarily scientific. Researchers are going to need strong support from the pharmaceutical industry and governments to move forward with cell therapies and drug discovery. Indeed, it is at the intersection of science and society where scientific advances have the potential to transform daily life, that the greatest challenges lie. With research consistently suggesting that future healthy life expectancy will not keep pace with overall life expectancy per se, that the drivers of longevity are also increasing our disabled years, many are starting to question the wider implications of such longevity related research.

And it is not only longevity challenges, across our lives science is presenting us with new choices to make. Advances in reproductive medicine are confronting young people with moral choices unimagined by their parents; our workplaces are being transformed by new technology, our jobs rebundled into new set of tasks or replaced completely by AI and robotics, already pitting economic arguments against social needs, and questioning the meaning of work.

This, of course, is not new; scientific advances have long impacted upon our lives. From before the upheaval of the Industrial revolution, through the health advances brought by modern medicine to the modern digitalisation of daily activities, our lives have been transformed by science. Yet it is clear that the present changing political and economic contexts have more than ever before, created the need for more open and critical public debate and a wider understanding of the practical, ethical, moral and social implications of science.

While science is key to solving many of the significant challenges the world now faces, it is essential that the wider public are encouraged and supported to participate fully in an informed manner in evidence-based debates and discussions. For example, while science might be able to distinguish the efficacy at both the individual and population level of drug A versus drug B, scientific evidence alone cannot support which drug, if any, should be legalised for medicinal or recreational use. That requires ethical and moral reasoning, social and economic input into the public and policy debate.

On the one hand recent events such as the global *Marches for Science* on Earth Day 2017 might indicate that public support for science is higher than ever before. In the US both the *March for Science* and the *People's Climate March* were branded as strong shows of support for US science. The first was an almost unparalleled collective public gathering by the US science community in protest to the unprecedented attack on science, scientists and evidence-based policy making by the US federal government. The second was a public show of support for the climate science community in the face not only of the proposed dismantling of US climate change policies, but also proposed budget cuts reducing key scientific work in areas across clean energy, sustainable agriculture, environmental pollution and even related health issues.

However, in the UK, where universities, science, and research have enjoyed strong government support for several years, the post-Brexit future recently triggered the *Campaign for Science and Engineering* to suggest that we are heading back to the 1980s when the then government appeared to believe that there was no relationship between research and the health of the economy, the "brain drain" headed abroad and research impetus was lost due to declining budgets. This time, they argue, the UK faces a potential "brain block", as overseas academics and students turn away from the UK in the belief that they are not welcome.

The broad dimensions of the landscape are clear. Science has made considerable advances in public communication of and engagement with research. Yet while many non-scientists now grasp the *outcomes* of research, academics have not been as successful in conveying the *process* of science, leading to lack of understanding or even misunderstanding, of the complexities of data analysis and oft ambiguity and opacity of findings.

Secondly, the interaction between research, policy making and public engagement is now key. There is a recognised need within government and wider policy circles for the use and sharing of evidence in policymaking, and for an increasing recognition of the advantages when the evidence that has been used to justify and shape a policy proposal is transparent. There can be evaluation leading to improvements in outcomes, the public are better able to understand and engage with the reasoning for policy interventions, and further government initiatives and policy evaluation can be built.[1]

The third dimension has a clear social and political dimension – the growing public lack of trust in experts and evidence. As the Director of External Affairs at the London Science Museum recently wrote there is a "concerning trend of active opposition: some have derided experts, others have sought the 'authenticity' of anecdote……There is nothing palatable about the post-truth era, when facts are cherry-picked or invented to make up any narrative you like, when there is 'policy-based evidence making' and a move to curtail any science that challenges policy and dogma with inconvenient truths.[2]

Jeanne, Emma, Violet, Nabi, Chiyo and Ana may all have achieved their extreme long lives through good genes, good health and good luck. How much twenty-first century scientific advances decide the longevity – possibly extreme longevity – of their grandchildren[3] may not just depend on progress in longevity medicine and science, but on the public environment in which future generations understand both the process and implications of these endeavours; on their contribution to the debates enabling evidence-based policy developments; and on their willingness to trust those in power to use the evidence to the best advantage of individuals and their society.

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[1] Sense about Science 2017.

[2] Showing Solidarity with Future Generations Roger Highfield, Director of External Affairs, Science Museum.

[3] Interestingly few had surviving children.