

St George's Chapel Lecture: Professor Sir Leszek Borysiewicz on research and impact

Tuesday 23 May 2023

Introduction

Your Royal Highnesses, Ladies and Gentlemen,

Firstly, I would like to say how honoured I am to have been invited to address you tonight. At the same time, that honour is tinged with trepidation especially when I look at the list of past speakers and indeed have been present at their exceptional contributions.

Choosing a topic for this occasion is difficult but I will address the theme of Research and Impact that is fundamental to the UK's position as a globally respected higher education system but more importantly the future wellbeing of the UK depends on the ingenuity and inventive capacity of us as a country. Our major asset is not to be found in re-industrialisation nor the mining of raw materials but in mining the brainpower and talent of future generations. While there are many aspects to this, such as early years education, family support, teaching quality and our schools, I want to focus on the imperative at the higher education end; the delivery of creativity encompassed by research and translating it into societal benefit.

This is a vast topic, and I cannot hope to cover all aspects in this presentation, so I start with two personal biases. The first is that

there is only research and the divide between basic and applied research is artificial. This was summarised by Louis Pasteur:

“There is no such thing as a special category of science called applied science; there is science and its applications, which are related to one another as the fruit is related to the tree that has borne it.”

Or its corollary:

“There is only one type of research - applied research or not yet applied research”.

The second is a philosophical belief that higher education is inextricably linked to the discovery of new knowledge. Proposed by the philosopher Wilhelm von Humboldt in around 1810 it was implemented in the then new University of Berlin. This model requires *‘that universities govern themselves, have academic freedom, and integrate education and research. As a consequence, science is unified, and all academic disciplines are present within a given university. [It] also calls for university-wide interaction and for all university members to communicate such that students become integrated as researching learners and learning researchers through close co-operation with their teachers (Bongaerts, 2022).* This philosophy implies that the student and teacher is actively seeking

new knowledge together and contrasts with the more often cited philosophy underlying higher education espoused in John Henry Newman's widely cited 'Idea of a University'. He holds that the University "*is a place of **teaching universal knowledge***" and "*If its object were scientific and philosophical discovery, I do not see why a university should have students*" (Newman 1852, Preface to University Teaching in Nine Discourses)

But how are Research, and Impact defined? The Cambridge Dictionary defines research as:

a detailed study of a subject, especially in order to discover (new) information or reach a (new) understanding.

And impact as:

a powerful effect that something, especially something new, has on a situation or person.

But these definitions are subjective and do not allow objective evaluation and resource allocation to something so vital for our future. So, the definitions change accordingly. For example, the UK Research Excellence Framework defines Research and Impact as:

Research is defined as a process of investigation leading to new insights, effectively shared. It **includes** work of direct relevance to the needs of commerce, industry, culture, society, and so on to 16 further categories and multiple exclusions.

Impact includes, but is not limited to, an effect on, change or benefit to:

the activity, attitude, awareness, behaviour, and goes on to 17 further domains.

I have used these two examples because they are not wrong in themselves and have a specific and laudable purpose of institutional comparison and equitable resource allocation. However, they are reminiscent of the story of the group of blind men who have never come across an elephant before and who learn and imagine what the elephant is like by touching it. Each blind man feels a different part of the elephant's body, but only one part, such as the side or the tusk and cannot identify the whole!



If we constrain research by these narrow and potentially partial definitions and then reward only by conformation to these criteria in a cyclical time frame, we run a risk in not allowing investigators the freedom to explore, to fail, to collaborate out with their silos and to work to impact in a time scale not predetermined by external pressures. I hold that universities excel in having the interdisciplinary mix and the potential for a variable time frame to achieve impact.

For example, Ludwig Wittgenstein was at Cambridge from the 1920s to 1942 and only published one 72-page book in 1922, yet in a recent survey of US Philosophers he was rated the most important philosopher of the 20th century. An output and a time frame for impact that would certainly not endear him to the Research Excellence Framework!

But this is not to decry research that leads to impact more rapidly. Again, an example from Cambridge: Greg Winter developed the technology of humanised monoclonal antibodies and their expansion to an almost infinite number of targets which has resulted in both a Nobel Prize and a novel class of molecules that now are nearly 20% of all new drugs. This revolution has been rapid over the last 15 years with economic as well as clinical benefit to many. Yet both Wittgenstein and Winter exemplify that their contribution was preceded by long commitment to fundamental research in their

fields. This requirement for long term thinking is essential as if we fail to fill that future pipeline there will be fewer and fewer economic and societal benefits downstream.

So, if these definitions are not inspirational and there are difficulties and uncertainties and often a long-term commitment before impact, what makes any student wish to pursue a research career? There are as many answers as there are established researchers, but mentorship and institutional freedoms are often mentioned.

Returning to Wittgenstein, he was a complex and controversial character with a strong family history of probable depression. He was advised to come to Cambridge from Vienna to study with Bertrand Russell. Three quotes from Russell's writings describe the turbulent nature of the mentorship that developed:

Firstly, having arrived unannounced in Russell's rooms:

"An unknown German appeared, speaking very little English but refusing to speak German. He turned out to be a man who had learned engineering at Charlottenburg, but during this course had acquired, by himself, a passion for the philosophy of mathematics & has now come to Cambridge on purpose to hear me".

Secondly, Russell thought he was a crank and wrote:

"My German friend threatens to be an infliction".

But finally, he decided 3 months later:

“I love him & feel he will solve the problems I am too old to solve”.

But consider whether without the institutional commitment to academic freedom and enquiry, in this instance linking the disciplines of mathematics and philosophy, would this interaction have ever happened?

Personal motivations

I cannot address the motivations of others but can only draw on my experience. Looking back, I can find no single motivation. I was that irritating child who never grew tired of the ‘why question’. Thankfully at university asking questions was seen as positive and opportunities arose to undertake research. I was hooked – whatever I would do in Medicine would always have an element of discovery. Would this have happened without staff with the time and interest to support a student?

But at University, there is also the opportunity to look at the big questions best summarised in my case in three books that have been a lasting influence.

An introduction to Social Medicine (1966)



...first of all the straightforward story of the ineffectiveness of medical therapy historically. The best account is given by McKeown and Lowe (1966). It demonstrates...environmental factors alone were important...and until the second quarter of this century therapy had little effect...

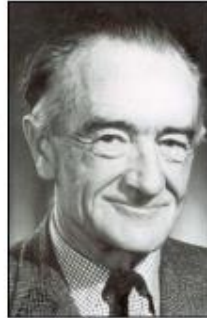
One should, therefore forty years later, be delightfully surprised when any treatment at all is effective, and always assume that a treatment is ineffective unless there is evidence to the contrary.

Cochrane A.L. (1971)

An Introduction to Social Medicine – Charles Lowe and Thomas McKeown

Most of us hold the view that vaccines and antibiotics are the reason that mortality from infectious disease fell. However, examining historical data, this book showed that many common infections were declining before antibiotics and vaccines had been developed. Why? Public health measures such as clean water, alongside improved nutrition, hygiene, and poverty reduction may have affected our resistance to infection? Therefore, do not believe medical intervention is always effective as so succinctly put by Archie Cochrane when citing this book: *“One should be delightfully surprised.... when any treatment is effective, and always assume that a treatment is ineffective unless there is evidence to the contrary.”*

Effectiveness and Efficiency (1971)



"All medical care that is effective should be free to all"

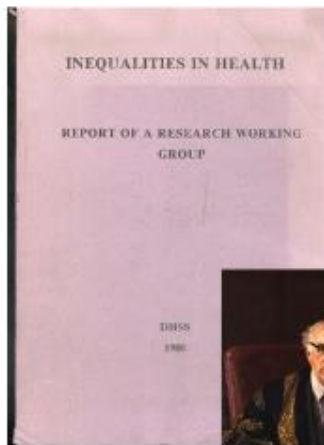
"It is surely a great criticism of our profession that we have not organised a critical summary by specialty or subspecialty, adapted periodically, of all randomised clinical trials"



Effectiveness and efficiency – Archie Cochrane

This theme continued in his seminal work. I was fortunate to be attached to his Epidemiology Unit, when he was writing this small book. That book threw out important propositions: firstly, it was incumbent on investigators to prove objectively that an intervention was effective and secondly that the health care system had to be able to deliver it efficiently if there was to be real benefit.

Inequalities in Health (1980)



Findings:

- Health directly linked to social class
- Ill-health increases down social scale
- Little to do with the NHS
- Linked to social factors:
 - ✓ Income
 - ✓ Unemployment
 - ✓ Poor environment
 - ✓ Poor housing
 - ✓ Education



Inequalities in Health: The Black Report and the Health Divide – Peter Townsend

The Black Report linked social deprivation to disease and clinical outcomes and access to healthcare was not the explanation. Cervical cancer was the one cancer associated with deprivation. Michael Marmot and colleagues, following his book *The Health Gap: the challenge of an unequal world* have refined the relationship of inequality and disease, but we remain a million miles from an effective solution.

Personal motivation to research is one thing but it also requires a supportive environment and mentors. Again opportunity, place, and people. I was fortunate in both: the Hammersmith Hospital was the place and mentors especially Professor Keith Peters, who is here tonight, and the late Professor Patrick Sissons the people.

Patients on the renal transplant unit were dying of cytomegalovirus infection. Yet virtually all of us have been infected asymptotically with this virus as children and consequently carry it with us all our lives without harm. Why and what was the mechanism? We defined the mechanism of immune control of infected cells with this virus, which was by T cells which prevented virus release. When this was diminished by immunosuppressive drugs to prevent rejection, the virus was free to spread. But these observations also identified how all of us keep these viruses at bay and remain well!

That work continued and has been given further momentum by so many others.

However, a third element in defining direction of research is often required – SERENDIPITY.

A chance conversation in the coffee room in an adjacent department changed everything. It was a difficult day in 1989. Experiments had failed and I was drinking coffee with Steve Ingles, a longstanding friend and we talked about what viral vaccine would make the greatest impact on global health. Harking back to the Black report, we thought that human papillomavirus, with its proven association with 99% of cervical cancer, would be an excellent candidate, even though many people were sceptical as the virus was too difficult to work with. Furthermore, we wanted a vaccine that would kill cervical cancer cells as they are infected with HPV that is a

therapeutic as opposed to preventative vaccine. This led to the first therapeutic trial using fragments of HPV and despite the primitive nature of these studies, by today's standards, we were able to elicit a response in patients with advanced disease. This work continues in Cardiff led by Dr Steve Man.

Simultaneously, Dr Ian Frazer in Queensland and a group at the National Cancer Institute were developing a preventative vaccine that has now been utilised in many countries. However, the need for a therapeutic approach alongside prevention is still very much required as the preventative vaccine cannot kill infected cancer cells.

So what factors are important in ensuring candidates for research careers continue to come forward? I surmise this as internal motivation, a supportive environment, and mentors alongside a slice of luck. That means that our national funders must ensure that our universities and their institutes have the required resources to enable this futureproofing to be sustained.

At this stage I had to decide where my future direction lay. Easiest was to continue my clinical and research practice but opportunities in leadership had shown me that a significant impact can be made to address the issues that had inspired me, through supporting and developing research policy and ensuring funding to support investigators and institutions. What would make the greatest impact?

I moved to Imperial College and then to the MRC. The success or otherwise of my ambition is for others to judge but my commitment to the provision of opportunity is best encapsulated with the building of a productive relationship with the NHS, through NIHR, the rebuilding of the Laboratory of Molecular Biology and securing the funding for the Crick Institute in London. These institutes are heavily associated with their universities yet have the autonomy to enable investigators to pursue long-term goals through direct funding.

However, when the opportunity arose to take up the position as VC at the University of Cambridge, it was impossible to resist. This University has the Humboldtian philosophy at its heart with huge academic autonomy and a capacity to embrace academic diversity such that both Wittgenstein and Winter could thrive. This autonomy enables the development of 6000 postgraduate students, in addition to 13,000 undergraduates, alongside 4000 postdoctoral fellows all in a collegiate setting that supports individualised education and mentorship. The ancient splendour of the Colleges is wonderful and has been enhanced by new developments. The biomedical campus is now probably the largest in Europe and new laboratories including the Cavendish Physics Laboratory to the west of the city for engineering and natural sciences have been developed. This is alongside new facilities for the postdoctoral community which has added a new suburb of the city at Eddington.

But ancient though the University is, it thrives at the forefront of impact. Known widely as Silicon Fen, as Europe's largest cluster with 23 science parks all bulging at the seams. It makes a massive national contribution: a 2023 report found that the University contributes £30 billion to the UK economy annually and supports more than 86,000 jobs across the UK, including 52,000 in the East of England. For every £1 the University spends, it creates £11.70 of economic impact, and for every £1 million of publicly funded research income it receives, it generates £12.65 million in economic impact across the UK.

There is impact writ large; yet all this has been achieved without detriment to the academic mission or creation of new knowledge confirming Pasteur's statement that this is indeed the fruit that falls from the academic tree.

Latterly, the opportunity came to Chair Cancer Research UK. This was an opportunity to engage with the funder that has a mission to deal with cancer, approaching it from a fundamental belief that discovery science would lead to major advances that would improve survival and a real reduction in the impact of cancer on patients.

Paradoxically, it combined all the influences and experience alongside my personal interest in cancer as well as the principles that led to my engagements with research in the first place. From my perspective a marriage made in heaven!

Cancer Research UK recently celebrated its 20th anniversary though the history of its parent organisations goes back more than 120 years. Today millions more people worldwide survive cancer and have precious extra months and years with their loved ones thanks to CRUK research.

Progress has been made, but the problem posed by cancer should not be underestimated. The number of cancer cases is rising, in fact 1 in 2 of us will develop cancer in our lifetime and treatments can take a huge toll on patients and too many lives are still lost to this disease. But thanks to research the survival rates are rising such that we can be ambitious and estimate that 3 in 4 patients will survive their diagnosis for more than 10 years. There are recalcitrant cancers where urgent improvements are needed and there are inequalities in cancer outcomes but at no time before could we look with greater optimism to better control of this disease.

The reason behind the optimism is that with each week we better understand cancer and find new ways to beat it both ourselves and in collaboration with others.

One example of global collaboration is Cancer Grand Challenges a joint initiative between Cancer Research UK and the National Cancer Institute in the US. It unites the world's brightest minds against cancer's toughest challenges, empowering them to rise above traditional boundaries and answer research questions that no one

scientist, institution or country would be able to solve alone. To date 11 teams collaborating around the world are tackling issues such as the weight loss associated with some cancers, extrachromosomal DNA, creating complete 3D tumour maps to better target therapy, and solid tumours in children.

Also, I wanted to highlight TRACERx, our flagship lung cancer study. Lung cancer is the biggest cause of cancer mortality both in the UK and across the world. TRACERx has studied 800 people with non-small cell lung cancer, unpicking the complexities of lung cancer such as how the tumour evolves, spreads, and resists treatment aiding the design of new, targeted therapies.

These are just a couple of highlights of the progress that Cancer Research UK has made over the last seven years. I am proud of what we have achieved during my tenure as Chair, and it will continue to go from strength to strength. That is because of all the tireless commitment of everyone across the charity, our Trustees, staff, volunteers, partners, and supporters, and all the patients who participate in the studies.

Cervical cancer

In closing I would like to return to cervical cancer and its global impact. It is the fourth most common cancer in women around the world, still killing more than 300,000 people each year and 9 in 10

deaths are in low- and middle-income countries where there is little access to cervical cancer screening and vaccines.

Those are bald statistics and cannot begin to describe the individual impact of this devastating disease. But the story of Ferdinand Hodler, a Swiss expressionist painter and his partner Valentine Gode-Darel does. They met in 1909.



All was well until 1914 when a year after the birth of their daughter, Pauline, Valentine developed a gynaecological malignancy.

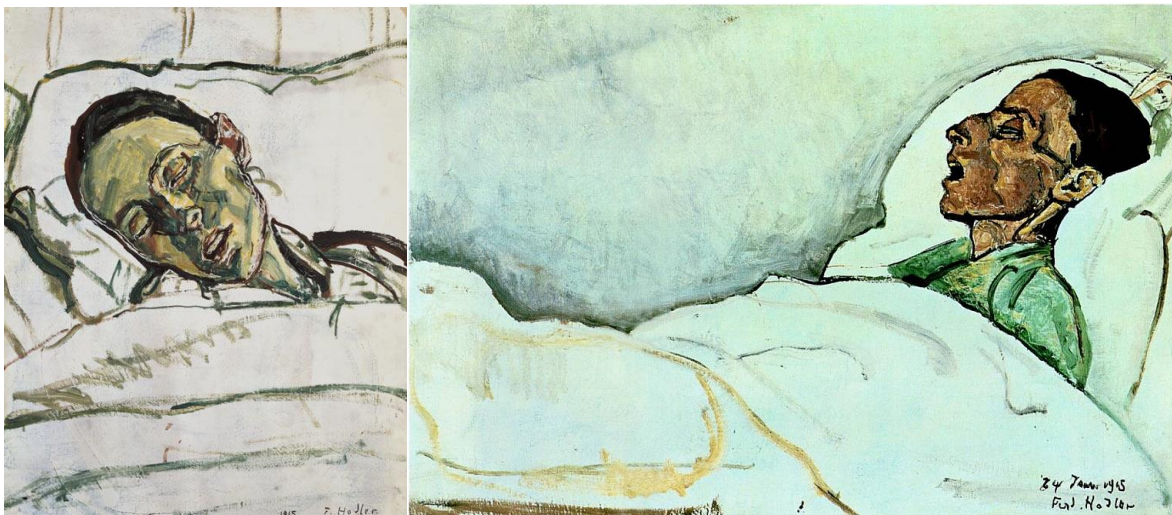
Here she is depicted immediately after surgery, and all was well until 12 months later the cancer returned and again turning to the cycle of over 300 drawings and paintings Hodler made at her bedside...



We see the deterioration in her condition, the weight loss, lethargy, and loss of hope so reminiscent of terminally ill patients. Her decline continued, and we are left with these...



The last two images, the one on your right painted the day before she died.

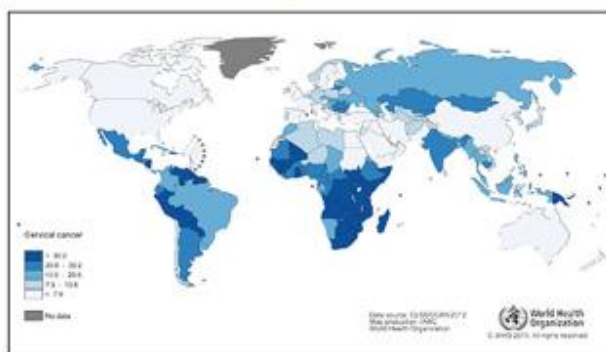


Pictures are worth a thousand words but tragically this story continues to be repeated even though Cancer Research UK's research has shown that the preventative human papillomavirus (HPV) vaccine is cutting cases of cervical cancer by over 90%. Having been personally involved in Europe's first trial of an HPV therapeutic vaccine more than 20 years ago, it truly underlines the power of

research and how far we have come in our understanding of some cancers.

But now something is being done.

Can we consign cervical cancer to history?



Eliminating any cancer would have once seemed an impossible dream, but we now have the cost-effective, evidence-based tools to make that dream a reality.

Tedros Adhanom Ghebreyesus
WHO global initiative to accelerate the elimination of cervical cancer, Nov 17 2020

In 2020, the World Health Organisation (WHO) Director General announced a global call for action to **eradicate, yes eradicate** cervical cancer from the world. In his speech he said, “Eliminating any cancer would have once seemed an impossible dream, but we now have the cost-effective, evidence-based tools to make that dream a reality.”



That will be impact however we chose to define it. To consign this dreadful disease to the archival and historical record is personally and organisationally the ultimate achievement of **real-world impact**. Somehow it feels that it does not need a definition as I first outlined because it is self-evident.

Thank you everyone for your time and I'm now going to hand back to Gary who I think has a few further questions for me.