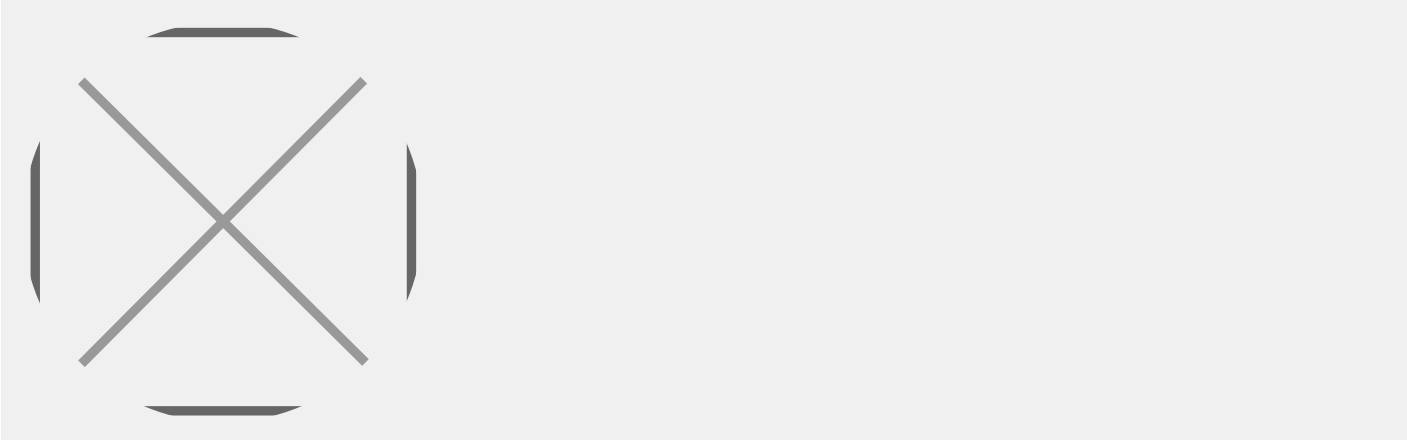
Interview with Vlado Perkovich, Executive Director, The George Institute, Australia



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duction to our international readers of the institute, highlighting recent milestones & achievements and the current focus areas of its research activities?

Broadly speaking, The George Institute for Global Health is an academic research organization that focuses on high impact clinical research. We do this by asking pertinent healthcare and health systems questions and trying to answer these in the most reliable way, with a global and in particular Asia focus, where the greatest burden of disease is looming. Given the Institute's location and links with the Asia-Pacific region, we have an especially important role to play in improving the health of people in the region. . The core of the Institute's work is clinical trial research as it is the most reliable way to identify interventions that work. We also conduct a lot of research on healthcare delivery, trying to understand how to get the treatments that work to the people that need them, an area that has been poorly studied in the past particularly in the Asia Pacific region.

Would you give an example of a research outcome that symbolic for the work of the George Institute?

We recently published the results of the CHEST trial, a 7000-person study that randomized people to hydroxyethal starch to compare the effects of two different fluid replacement solutions in people with critical illness in intensive care. The results showed that there was no advantage in using the starch solution yet there was a high risk of kidney damage from it, despite the fact that it cost 16 times more than the saline solution. As a result of the study, we were able to show that the older,

cheaper drug was equally effective and safer than the new, more expensive treatment, only available to a relatively small group of people by virtue of its cost. This is an example of the crucial findings resulting from the clinical trial research the Institute conduct; where we find a treatment that is not only better but which is more affordable and accessible to more people. You have been appointed earlier this year after heading George Clinical for two years at a relatively young age.

What are the changes that you are looking to implement in such an impressive and successful organization?

The appointment has been a great honor. The Institute has been incredibly successful since its foundation in 1999, and there are a range of world leading experts doing great research. Looking ahead, a key priority is redesigning the clinical trials process and influencing regulatory process in this area. The current process is creaking under its own weight. We need more modern, cheaper, and effective clinical trials that can identify treatments that work. In the delivery of healthcare we need to concentrate on understanding how to increase global access to products and treatments that work. Most people around the world do not have access to the simple proven effective treatments that we take for granted like Aspirin and agents that lower cholesterol or blood pressure. The Institute's priority is to find solutions to this. Many people in Asia and in Australia fall into this category, for example Aboriginal and Torres Strait Islander populations and people who live in socio-economically disadvantaged parts of the country, be they some of the less affluent suburbs of the bigger cities or some of the rural distant areas that suffer by virtue of their location. We are also focusing our work on the broader determinants of health. Healthcare is a much broader issue than treating an illness in hospital, and improving health is more than the pills a person is taking; it is also about their diet and the kind of exercise that they do. The Institute is playing a key role in helping to address some of these issues. An example of this work, is the Institute's work around salt reduction as a way to prevent chronic disease like heart disease and stroke, and reduce the global burden of disease.

How do you determine which parts of the world's global population are most in need of the George Institute's capabilities?

We look at the areas where we can make the biggest difference, for example, by looking where the burden of disease is. If we look, for example, at the causes of death and disability in Asia, the traditional thinking is that it is infectious diseases and child and maternal health. This is far from true. Cardiovascular disease and other chronic diseases are the leading cause of death in every country in Asia. These diseases have been grossly understudied here in the past and are hence an area of focus for the Institute. Not only are they important from an Asia Pacific perspective, but also from a global perspective, because more than half of the patients that are going to develop diabetes or cardiovascular disease over the next decade live in Asia. With the growing burden of disease being in the Asia Pacific region, this is where the Institute's efforts to prevent disease need

to be.

You mentioned delivering more modern, cheaper, and effective clinical trials – what are the biggest flaws in the way clinical trials are conducted today and how is the George Institute looking to change them?

This is a key area of focus for the Institute and it has been for many years. We have a long history of delivering very high quality, rigorously conducted and high impact trials at much lower cost than those conducted through pharmaceutical companies or other Contract Research Organisations. Fundamentally it is about intelligent design, intelligent consideration of the factors that are crucial in clinical trials (in terms of determining their reliability and ensuring that participants are protected). It is also about getting rid of a lot of the additional activities that are routine in clinical trials, but that do not actually provide additional value. We do this by bringing science to the operations side of clinical trials. We evaluate what the impact of site monitoring and other very expensive activities are, and generally we find that they add little value and that there are more modern, technology-based methods of doing the same sort of thing, yielding similar or better results for a much lower cost. If we can reduce the cost of trials by three-quarters or even more, clearly there is an opportunity to do much more research and allow many more people to share the benefits.We have been hearing discontent from some of our interviewees from private sector CROs on the competitive environment.

How do you see the dynamic of government-funded clinical research vs. privately funded clinical research in Australia?

There is a tension between the public sector and private companies, but I am not sure it is an unhealthy tension. Sometimes this sort of tension allows change to occur and allows both sides to evolve. One of the reasons The George Institute has been so successful is that we have been able to work with multiple stakeholders. We run a number of trials that are funded by industry and at the same time funded by the NHMRC. These trials have addressed the needs of both sides of the spectrum: they address public health priorities of the NHMRC while the same as providing a commercial opportunity for a company that seeks the benefits of the trial. Because of the mutual benefit and goals, it is possible to do hugely important research in a very effective way.

Would you outline in a bit more detail what cooperation looks like for the George Institute and could you perhaps give an example?

The CHEST trial that I talked about earlier was a collaboration between the manufacturer of the fluid and The George Institute, as well as the NHMRC and a range of other funding bodies. The company had a requirement to clearly understand what the effects of their product, which was also a addressing a public health issue; and they also wanted to do it in a rigorous way that maximized the reliability of the study and allowed them to be hands-off in the way the trial was conducted. The

company entered in an agreement with the Institute under which they provided funding for the study but the study was run, designed, reported on by an independent academic group. The results were published in the New England Journal of Medicine and have had a huge impact globally, providing important data for the scientific community, for the health community, and for the company. The results of a trial are not always what was hoped, but equally no commercial organization wants to do something that is harmful. This is an example of a case in which there was a need, a value, interest from and benefit for all sides and the resulting study was high-impact.

How important will this type of cooperation become, also as medical research is becoming increasingly expensive?

This is an issue for today and frankly for yesterday – it is something that we should already be doing. We should look for more opportunities for collaboration and where there is a joint need, recognizing the value that both parties can bring to the table and finding ways of working together that maximize these. That has been an area of success for the Institute. Over the past decade we have won over 200 million USD of commercial contracts and have conducted commercial studies in a highly rigorous and transparent fashion. It is also important to be clear about the roles and responsibilities during a trial so that when the results are being interpreted, these factors are taken into account. The pharmaceutical industry cannot develop its products without partnership with health professionals, and health professionals cannot access new treatments and approaches without working with the organizations that have developed them. By partnering in these sorts of studies we can make significant progress in the area of healthcare and healthcare delivery. Although this already happens, it has often been less transparent than it should have ideally been. It is a hugely important goal but it is not sufficient in and of itself. Additional public investment in areas where there is no commercial benefit for industry partners is still needed, and where there is public support, this should be celebrated.

There seems to be a disconnect between Australia's research capabilities and the attention it gets in executive rooms of the global pharmaceutical industry. How do you explain the gap?

There are a number of issues within this question. Australia faces a series of challenges: Firstly, we are a long way from most of the global research and development hubs. This geographical issue does raise the bar in terms of engaging with Australia. We also have a small population relative to other countries, particularly in the Asia Pacific region. For every 100 patients recruited in Australia, India and China should recruit 6.500 patients simply based on the population differences. This is not something that strategy can overcome; it is just a vast difference in scale. In addition, the Australian dollar recently became very expensive, which has made Australia a less competitive place to work. Equally, however, Australia does have some real strength. Our scientific expertise, credibility, and knowledge in health research are very strong and we do outperform most other

countries on a per capita basis in terms of publishing in journals, running big studies or coming up with key insights that change the way health is perceived.

What role do you believe Australia can play in clinical research in the Asian Century?

Although Australia is perceived as a place where it is difficult to recruit large numbers of patients because our population is not so big, there are key examples where people have arranged themselves in a way as to outperform other parts of the world. One of those is in intensive care trials, where we have a very strong and well established network of intensive care researchers who in the past decade have recruited over 20.000 people in Australia and New Zealand alone, far more than anywhere else in the world. It is possible to set up modern or effective systems that are not based on the traditional hospital recruitment system and that allow volumes that are comparable to for example China or other countries. On top of this there are other groups, for instance the Monash Group in Melbourne, who have set up innovative primary care based networks. They are currently recruiting 10-15.000 people to a trial using a novel, highly effective and innovative model of recruitment. These intelligent re-designs of the clinical process are a real opportunity not only for Australia, but for the broader clinical trials community globally. Australia is a leader in this. Furthermore I see the opportunity for Australia not as a bulk producer of clinical trials or a heavy recruiter to clinical trials, although it still is possible, but more as a value-added partner for the broader region. We are in the same time zone which makes communication and partnership much stronger. We understand the culture of the countries around us, and can work very well as a facilitator of clinical research in the region.

How is the George Institute leading the way in establishing Australia as such a facilitator?

The future is not The George Institute bringing our studies into Asia; the future is the George Institute and other organizations like us helping Asia develop its own expertise to be able to run and lead its own studies in partnership.

What enables the country to perform at such a high level on a sustainable basis when it comes to medical research?

It is an interesting question, and I am not sure I know the answer. Definitely Australia and Australians have a number of characteristics that I think lead them to perhaps innovate more than other cultures. We are fortunate to have a very good education system that trains a large number of people to high levels of expertise. We also have a culture that is inquisitive and tends to explore new things, and which is fascinated by novelty to some degree. The Australian culture is also one that does not follow authority blindly. There is a strong tradition of challenging established approaches and of looking for new ways to do things, for different ways to do things and perhaps part of this comes into the approach to clinical research.

And how do you ensure this culture is present at the George Institute? How do you keep the Institute at the cutting edge of medical research in a country that is highly competitive in this regard?

That is an interesting question and I guess in five years we will have to see how successful we have been! The truth is that the Institute is based on its people and we have some of the best and most innovative thinkers in the country, and in the world. We place a lot of effort into making sure we support and help our people to grow as much as possible, and also in training the next generation of key researchers. We try to provide an environment that is facilitative and where people are encouraged to develop new ideas and pursue them; and where they have the platforms they need to implement these. An example of a platform is George Clinical, which is our commercial for-profit subsidiary. It runs contract research for a large number of pharma companies, including registration studies under the highest level of regulatory scrutiny. At the same time it also runs highly efficient academic studies led by researchers within the Institute and elsewhere, that answer fundamental questions of importance to the clinical community, at the lowest possible cost. It has systems that deliver different levels of intensity in terms of study conduct, depending on what is required. This comes back to the idea of intelligent solutions where the requirements of any individual study are carefully defined and a strategy to achieve them is developed that is bespoke for each study. This is really important. The availability of a platform like George Clinical allows researchers in the industry to develop and conduct new trials and learn from the experience of the many people who have come before them, without having to start from scratch each time. These are just some examples of the things that we like to do at the Institute to help support our researchers and that we hope will help us to maintain a cutting edge going forward. The other thing is to constantly be prepared to be forward-looking. We started looking at conducting research and partnering with researchers in India and China in the 1990s, long before other organizations had any thoughts of going there. We see the future now as moving away from the development of new molecules to the more effective, wide-spread and affordable use of established treatments in novel ways. We see this as being a key focus for the future, not only here in Australia where the health system is already struggling under the weight of the burden of an ageing population, and the growing challenge of meeting the demands for the latest expensive new treatments, but also helping to build health systems in countries that do not have them and do not have the funds available to develop them.

How do we do this? How do we for example build a primary care workforce for a country like China that does not have one, from scratch?

One example is a partnership we have developed with the Chinese government and with Chinese universities, where a new study is assessing the value of trained healthcare workers who are not doctors but are trained to provide a very targeted and specific intervention to people in rural China.

We are developing a group of trained healthcare workers who are delivering primary healthcare – preventive healthcare for cardiovascular disease for people in villages in China who do not currently have access to any kind of healthcare along these lines – and, it is going to need quite different models so that the it is affordable. Some of the health systems that we have in Australia have been around for decades and so our work in China provides us with an opportunity to build a 21st century healthcare system rather than one that was based on the type of healthcare provided in the 19th century. There are huge challenges in this but there are also massive and real opportunities to do things much better.

What is your personal mission with the George Institute?

Like most people, my motivation to come and work for the Institute was my strong belief in what it is trying to do and is achieving in a very visible way. We are not focusing on incremental changes to the way things are done, a new version of drug X which is slightly better. We are focusing on big changes to healthcare and the things that are going to make the biggest difference to health globally, and everyone of our team fundamentally believes in this, and are fully committed to improving healthcare. This is an important part of our success.

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