Yes we can treat cancer – even in the poorest countries

So says Ian Magrath and his INCTR partners, and they have the evidence to prove it

➜ Simon Crompton

Ian Magrath has spent more than a decade helping develop strategies and build capacity for treating cancer and researching new protocols in low- and middle-income countries, including in areas that had no facilities at all. The foundations built over these years, and the experience gained, will be crucial to the success of current efforts to stem the rising tide of cancer in the developing world.

Upstairs in the Brussels offices of the International Network for Cancer Treatment and Research (INCTR) are shelves packed with colour-coded box files. They contain data from clinical trials conducted all over the world, and each has a story to tell. Ian Magrath, president of the network, points to the navy blue, sky blue, green and red files containing data about INCTR research on breast cancer.

The story he tells about the blue file from a cancer institute in India is that 40% of women diagnosed with breast cancer never get treatment – it's either too advanced, or the women simply can't afford the time away from family responsibilities. In Pakistan, many of the information forms were chewed by rats. In Egypt, many records weren't available because some departments were reluctant to share information.

This is a world of cancer that few of us in higher-income countries encounter. But it's a world with which Magrath, at the helm of the network for 10 years, is intimately familiar. He's at pains to point out the statistics that should make the rest of us sit up and think. "85% of the world's population lives in low- and middle-income countries, but there are far fewer cancer facilities in these countries than in the rich world," he says. "Around 80% of all childhood cancers are in developing countries, and 70% of cancer deaths are in low- and middle-income countries because access to care, for the most part, is extremely poor and expertise of all kinds is very limited."

"We in the rich world are actually losing out by paying so little attention to cancer in developing countries. Not only is there the humanitarian issue, but we're missing research opportunities to learn more about cancer that would benefit everyone."

It's a strength of conviction borne of a working lifetime spent challenging the assumption that cancer is the same whether it's in the USA or Africa; that cancer knowledge is easily transferable from country to country; that the best treatments devised for the developed world are also best for the developing world. But he's also proved it is possible to research and implement effective treatments and care structures that suit resource-poor environments – if only you work closely with doctors and care-givers there.

INCTR

The Burkitt lymphoma ward, St Mary's Hospital, Lacor. The low-cost, low-tech, less-toxic protocol used to treat these patients has proved its worth in other African centres, and was recently introduced at this highly respected hospital in northern Uganda after it joined the INCTR Burkitt's lymphoma programme

People assume that tackling cancer in a country like Africa is too complex, too expensive, and not a high priority compared to infectious disease, says Magrath, but they're wrong. With life expectancy increasing, cancer is overtaking infectious diseases, and, indeed, all other causes as the leading cause of global death, and there are more deaths from cancer in the developing world than from AIDS, tuberculosis and malaria combined, he argues. Only in the low-income countries do deaths from all infectious diseases combined outweigh those from cancer.

Furthermore, it is possible to achieve big cuts in cancer mortality in low- and middle-income countries. But this can't be done by sending over CT scanners, linear accelerators or expensive targeted therapies, as the main problem is that most patients are diagnosed too late. What is needed are simple and unglamourous interventions: introducing tobacco control, improving healthcare structures, ensuring prompt diagnosis, using locally appropriate protocols that best utilise surgery, radiation therapy and cheap and well-established chemotherapy drugs.

A spectacular success

The most spectacular example of how successful this approach can be is a protocol devised by Magrath many years ago for the treatment of Burkitt's lymphoma – a fast-growing cancer that has been the focal point of Magrath's career. Rare in the western world, Burkitt's lymphoma is the commonest of childhood cancers in equatorial Africa, causing 3000 deaths every year. Low-tech treatment protocols pioneered by Magrath and colleagues in the 1970s and adapted since then have resulted in survival rates in countries like Egypt and India rising from 45% to 70%–80%. They form the basis of ongoing attempts to improve survival rates in equatorial Africa.

His work has won him acclaim – he's received numerous awards, including the Princess Adela Bint Abdullah Recognition Award in Childhood Cancer, earlier this year. But Magrath is not the type to sell his achievements. Talking at the INCTR offices, housed

in the concrete block of the former Institut Pasteur, in Brussels, he recounts a career where he has written more than 340 articles centred on the pathogenesis and treatment of malignant lymphomas and leukaemias, as well as cancer in developing countries. He has also headed research on paediatric lymphoma at the US National Cancer Institute (NCI).

But as he chats, he consistently focuses on what he feels is important or interesting rather than dwelling on what has been achieved. Sometimes this involves a detour into evolutionary theory, philosophy or Chinese wisdom, but Magrath always remembers where he left off and returns to a starting point. He calls it his 'grasshopper' mind – "I go through phases where I'm interested in languages, then music, then quantum physics or mathematics."

He's always been a bit of an independent thinker, he reflects. Perhaps it had something to do with coming from what he describes as a "relatively humble background". He was brought up in a post-war London he can only remember as black, the buildings smothered in soot, food still rationed. "I suppose part of what drove me was a desire to get beyond the world in which I found myself and so I pushed hard to go to medical school. To be a doctor was something that as a child I couldn't conceive of being within the realms of reality."

After his basic medical training at the University of London, he developed an interest in cancer while a senior house officer at Charing Cross Hospital under Ken Bagshawe, a world expert in the treatment of choriocarcinoma – a cancer found to be curable by chemotherapy alone by pioneering chemotherapists. This led to an early interest in the lymphoma discovered in the 1950s by British surgeon Dennis Burkitt – another cancer highly responsive to chemotherapy.

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Building capacity. This group of data managers from centres across India are on an INCTR training course on monitoring outcomes in acute lymphoblastic leukaemia. The ALL protocol used in India was developed more than 30 years ago by Magrath (pictured standing in the doorway), in conjunction with staff at cancer centres in India

A taste of Africa

Magrath wasn't convinced he wanted to follow the conventional medical career course. He yearned for colour beyond monochrome London and was intrigued about how a condition such as Burkitt's lymphoma should be so rare in the UK whilst apparently so devastating in equatorial Africa. So in 1971 he started work at the Lymphoma Treatment Centre in Kampala, Uganda, run jointly by the American NCI and Makerere University.

His tenure there was to have a lasting effect. "It obviously made me want to continue in the field of oncology, because one could see some patients with massively disfiguring Burkitt's lymphoma of the jaw being cured by even one or two doses of chemotherapy alone," says Magrath. "It was also clear to me that patterns of cancer were very different in Uganda from in the UK." Along with Burkitt's lymphoma, hepatocellular carcinoma and Kaposi's sarcoma were very common (even prior to the AIDS epidemic). Here were some interesting research opportunities, thought Magrath.

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The potential to follow them up in a fully equipped laboratory increased when the American NCI contingent left the centre – mainly, says Magrath, because of the difficult situation being created by Uganda's notorious President, Idi Amin. It was not unusual at that time to hear gunshots coming from the nearby university campus. But in 1974, he was invited by the NCI to become a senior investigator at the new paediatric cancer branch being established at their headquarters in Maryland, USA. He was asked if he'd like to work there for a couple of years. It turned into a stay of 26 years, with Magrath eventually becoming chief of the lymphoma biology section.

His research over those years followed up the leads he found in Uganda, examining the treatment and molecular pathogenesis of B-cell lymphomas, particularly Burkitt's lymphoma, and the causative role of Epstein-Barr virus. This was no research sideroad, emphasises Magrath.

"Burkitt's lymphoma is so interesting not just because it is curable by chemotherapy, but because it led to the discovery of Epstein Barr virus," he says. The virus infects 95% of people – up to 100% of people in parts of the developing world – causes infectious mononucleosis and is associated with cancers such as nasopharyngeal cancer, types of T-cell lymphoma and Hodgkin disease. It was discovered from a cultured cell line derived from Burkitt's lymphoma cells in 1964. "It's also important because there's a specific chromosomal translocation associated with Burkitt's lymphoma which provided a model for understanding related cancers."

The potential practical applications for his research became clear when hospitals around the world began to ask him for help. In 1976, the director of a cancer institute in Chennai, India (then internationally known as Madras), visited the NCI seeking help because all the children she was treating for acute lymphoblastic leukaemia were dying. "All my colleagues were off doing examinations for their boards, so she spoke to me. I became interested in the problem, and asked her to send me some slides of blood and bone marrow, as well as information about the treatment they were using." Later, he visited the Indian centre himself and convinced the doctors that, though they wanted to set up a bone marrow transplant unit, a better option was to first make sure they were treating patients properly with standard therapy, adapted to the local circumstances. "We worked with them, and other hospitals that became interested in Bombay [Mumbai] and Delhi,

A fighting chance. This mother got her child to Tanzania's Ocean Road Cancer Institute, which has been using the INCTR protocol for Burkitt's lymphoma with great success for more than five years – most mothers in Africa will have no such facility to turn to

TRISH SCALAN

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and developed a treatment protocol specifying the use of particular drugs at particular stages of treatment, which led quite rapidly to a doubling of the survival rate. This, or closely related protocols, are still in use in India, and the survival rate has continued to improve over the years. The knowledge is now metastasising across the whole of India as young trainees at the cancer centres go off and use it elsewhere."

The survival rates are now around 60%–70% – lower than in the US and Europe, because of lower levels of supportive care, more high-risk patients and later diagnosis, but it is a similar rate to high-income countries 10 years ago and to high-risk patients today. "It may be that they're getting as good results as they realistically can, given the patient population and available resources," says Magrath.

Later on, the same protocols were successfully used in another project, in Egypt, funded by the United States Agency for International Development. Magrath started to travel the world researching leukaemias and lymphomas and their treatment, discovering, with his colleagues, differences in the molecular abnormalities behind these cancers in different parts of the world.

Serving the greatest need

"In the 1990s, I became more and more interested in the tremendous need of these countries, where often there wasn't just bad treatment but no treatment at all. In countries like India and Brazil there were some centres able to provide high levels of treatment, but in the rural regions of many low- and middle-income countries it was like going back to the Stone Ages. I wanted to dedicate all my time to cancer in developing countries, and I started to look for ways to accomplish that."

The opportunity came in 1999, when he was appointed president and medical director of the INCTR. It had been founded a year earlier by the Belgian Institut Pasteur and the International Union Against Cancer (UICC), to help build capacity for cancer treatment and research in less economically developed countries. The executive committee of the NCI agreed to provide support.

Magrath, who still holds an NCI position and is adjunct professor of pediatrics at the University of the Uniformed Services in the Health Sciences, has concentrated INCTR efforts on children's and women's cancers – in part because paediatric cancers

INCTR

A strategy for the coming decade. To mark its 10th anniversary this year, INCTR invited representatives from the WHO, the IAEA, the UICC and the American NCI to a gathering in Brussels to review the successes and failures of past initiatives and discuss strategies for taking cancer control forward in developing countries

are his own field of interest, but also because of the vast numbers of children and young people in developing countries. Women are also more vulnerable in these countries, which generally remain patriarchal, yet much can be done for patients with, for example, early breast or cervical cancer. At the core of the organisation has been a mission to help health services find what works best in the here and now.

Before the establishment of the INCTR, which is still funded largely – though not exclusively – by the NCI, this wasn't happening to any significant extent, says Magrath. "You need to understand the local resource limitations and do research that's regionally appropriate. You have to be prepared to train and educate the professional staff – select a disease or discipline, and one or more centres, and try to develop those into centres of excellence or reference centres, with whom we can work on a long-term basis so that you develop a standardised, evidence-based approach to treatment, agreed with colleagues." Such centres also become resources in their own countries, where they serve as training centres and help improve access in other regions to better diagnosis, treatment and palliative care, which is sadly lacking in low- and middle-income countries in spite of enormous need."

These standardised approaches are then assessed in clinical studies – which examine the effectiveness of the treatment, and how it may be affected by the context in which it is given. "At the same time, because people have to collect data, they learn about evidence-based medicine – it's a concept that doesn't exist in much of the developing world, and it's important that we help train them in this." Currently, treatment protocols developed in the UK or USA are often modified in developing countries to cut costs, without follow-up to determine outcomes.

Tailored solutions

The obstacles to good cancer care in poorer countries are completely different to those in richer ones, says Magrath. There's the lack of human resources: in Tanzania, 16 histopathologists serve a population of 40 million while in Switzerland there are 400 histopathologists for 7 million people. There's the lack of physical resources – blood supplies are often very limited, for example. There are organisational problems that mean that chemotherapy drugs often don't arrive where they're needed. And there's a crucial lack of supportive care, which changes the whole nature of cancer management.

"If we took the treatments presently used for Burkitt's lymphoma in Europe and the United States, and applied them, unmodified, in equatorial Africa, we would probably kill more people than we cured," says Magrath. "Such treatments are very intensive, and many of the patients would die of toxicity, given the limitations in supportive care, poor hygiene and the higher incidence of underlying infections and infestations."

Which raises questions, says Magrath, about what international organisations mean when they call for the 'best' cancer treatments to be made available in every research setting. The World Medical Association's Declaration of Helsinki says that, in medical research, a new intervention must be tested against the 'best current proven intervention'. But 'best' where? "If you say 'best available in the world', then research in most developing countries would not be possible, because such treatment may either be unavailable, unaffordable and/or inappropriate given the local circumstances. We need to develop research designs that are appropriate for disease profiles, affected populations, and existing healthcare and support systems for cancer patients in developing countries."

That is not to say that Declarations of this kind do not play an important role, he is quick to add. "They focus attention on a specific problem and can often bring people to the realisation that one size does not necessarily fit all." Initiatives such as the UICC's World Cancer Declaration can also be important in helping bring problems to the attention of governments and civil society, and mobilising political will. "But expectations must be tempered in terms of their short-term benefits. For example,

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INCTR
International Network
for Cancer Treatment and Research

Founded in 1998 by the International Union Against Cancer (UICC) and the Brussels-based Institute Pasteur, and largely funded by the American NCI, the International Network for Cancer Treatment and Research:

- is dedicated to reducing the suffering and the number of lives lost to cancer in developing countries;
- aims to promote evidence-based practice through long-term research projects investigating the most effective approaches to cancer care in specific settings, and supporting the growth of centres of excellence and training networks;
- has programmes in clinical research, pathology, palliative care and paediatric oncology, as well as programmes building capacity in clinical research, primary healthcare (for early detection), and gathering data to support evidence-based cancer control;
- has branches in Brazil, Cameroon, Canada, Egypt, France, Nepal, Tanzania, UK and USA;
- is creating, with other organisations, an open access resource of cancer educational materials, to aid the education of health staff and students in developing countries.

For further information see: www.inctr.org

they cannot be expected to have a rapid beneficial effect on incidence or survival rates in developing countries – only appropriate and sufficiently extensive actions in such countries can accomplish that, and signing declarations doesn't necessarily lead to action, especially when resources are so sadly lacking." Sensitising people to cancer, he emphasises is only half the battle. "You've got to have adequately trained healthcare professionals to diagnose and treat the people who have been sensitised and have symptoms that could be caused by cancer."

Magrath continually returns to the importance of the nuts and bolts of how you actually make people better. He avoids the exciting but often impractical aspirations for change that most of us get swept up by. So although the use of new technology – mobile phones, videoconferencing, e-learning, and web-based clinical information sharing – is very much on the INCTR agenda, he is wary of seeing it as a panacea (as some seem to) for the developing world's problems.

Such is his realism, that each time I ask Magrath what achievements he is proudest of, the conversation somehow strays into issues to be dealt with, or scientific discoveries awaiting a clinical response. One or two areas of satisfaction seep through: that this year the INCTR became one of only two cancer non-governmental organisations to enter into official relations with the World Health Organization; that by creating INCTR branches around the world he has helped create an international community of cancer professionals; that more people have access to palliative care in, for example, Hyderabad in India, or a poor region in São Paolo, Brazil or Katmandu, Nepal; that INCTR's project on Burkitt's lymphoma has now treated more than 360 children in four African countries. "Since that's the area where my international interest began, it represents a full circle in my journey," he says.

But then the hard demographics kick in again, and leave only a sense of the daunting task ahead. "Cancer is increasing, and if governments don't start doing something now, it's going to be more and more of a problem in the developing world as population structures change. If we miss the boat now, millions of people are going to die as a consequence."

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