

Michael Stevens: curing the whole child

→ Marc Beishon

When paediatric oncologist Michael Stevens talks ‘grades’ with parents, he is as likely to be discussing their child’s schooling as their cancer. If young patients are to have a future, you must look at their life as a whole, he says. He wants greater support for survivors and more research to predict which patients can safely be spared the most aggressive protocols.

Children with cancer are constantly in the public eye as subjects of intensely emotional documentaries and fund-raising activities. Few other health topics have so consistently been profiled in recent years, not least because of the dramatic breakthroughs in cure rates achieved since the 1970s.

This attention is a paradox for Michael Stevens, professor of paediatric oncology at the University of Bristol in the UK and an authority on childhood soft tissue sarcoma, with a long track record of organising paediatric oncology services.

“We see only about 115 new patients a year in Bristol – about 10% of the country’s workload in childhood cancer – and there are probably no more than 100 children a year in the UK who have my particular specialty, rhabdomyosarcoma,” he says. “I spend my professional life worrying about service provision for a relatively small number of kids and I’m conscious of how many other issues there are that a paediatrician could be addressing with scarce healthcare resources, particularly in the developing world.”

It is perhaps both a modest and accurate assessment, and one informed by his earlier work in

nutrition and sickle cell disease in Jamaica, but Stevens in no way diminishes the achievements made by paediatric oncologists. “We’ve moved from a position where we really couldn’t do much for children with cancer to 90% cure rates for some diagnoses. Today, one in every 800 young adults in the UK is a survivor of childhood cancer.” Yet it remains the leading cause of death from disease among children and teenagers in the developed world, and there are a special set of issues for teenagers and young people that are concerning oncologists.

When it comes to promoting the interests of paediatric oncology in the far larger world of adult services and research in the UK and Europe, Stevens has in recent years also played a major role. In 2000, he became president of the European branch of the International Society of Paediatric Oncology (known as SIOP). This had been formed two years previously, largely to strengthen the role played by paediatricians within the Federation of European Cancer Societies (FECS – where he is the current treasurer), and to integrate the paediatric oncology effort in Europe, which was far less organised than in North America, particularly in research.

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to be seen in the totality of cancer care,” says Stevens. He notes crucial issues that are greatly affecting paediatric oncology, such as the impact of the European Clinical Trials Directive on academic research, and the availability of novel drugs, while the specialty is also at the sharp end of the need for genuine, high-quality multidisciplinary working.

He also points out that paediatric oncology has pioneered, and continues to lead, in major steps such as first use of combination chemotherapy,

the discovery of the first cancer gene (implicated in retinoblastoma), and now modern research such as the use of minimal residual disease technology to guide therapy in children with leukaemia.

Despite these achievements, Stevens believes paediatric oncologists need to make their voice heard much more strongly if the specialty is to build on the great gains already made. “My fear is if we are not visionary enough we will find that improvements in, say, treating breast cancer will

“People didn’t expect children to succeed in school after being treated”

eclipse our achievements.” This is not about competition but about organisation and resources to find answers to key questions, such as why 30% of children are not being cured at present.

In particular, he worries that paediatric oncology may lose its attraction as a career choice, because it is still a relatively small specialty and of less interest to investment by the pharmaceutical industry – and medical students are more commercially minded these days.

That wasn’t an issue for the young Stevens, who is the only one of his family, past and present, to go into medicine, and it was a year out shortly before graduating from medical school that first introduced him to the type of practice he knew he wanted to pursue. “I went to work in a nutrition research unit in Jamaica, which showed me that paediatrics offered a blend of social and personal interaction and scientific discovery – and paediatric oncology is the same. I don’t think I’d have been a good pathologist.”

Working in adult general medicine in the UK, he was asked to see a 14-year-old boy with a brain tumour who had gone blind after radiotherapy. “My task was his endocrine care, but I remember him well. I found him very challenging and it was like a light bulb going on – and I made my move towards paediatrics and oncology.”

Stevens made great use of fellowships – another spell in Jamaica followed, this time to work in a sickle cell project. He was one of the first paediatricians to be involved in the project, which was funded by the UK’s Medical Research Council and run by the “very dynamic” Graham Serjeant at the University of the West Indies. This gained Stevens an MD and his first major taste of clinical research.

He also held two fellowships at Toronto’s Hospital for Sick Children. “There were few systematic training opportunities in paediatric oncology in the UK, and Toronto was a different order of magnitude in size and structure to the hospital in Oxford I was then working at. It was a two-way trade – I offered

my sickle cell disease experience to Toronto’s division of haematology and oncology, but really I was absorbing knowledge like a sponge.”

He worked on staff for a short while at Toronto, but returned to the UK to seek a consultant’s post in paediatric oncology, and after writing to many departments he landed a job at Birmingham Children’s Hospital, where he worked for more than 15 years alongside Jill Mann, a well-known British specialist. “I chose to specialise in solid tumours rather than leukaemia. It was the early days of forming the subspecialties we see now, and momentum for improving cure rates was building.”

Highlights for Stevens were helping to set up a brain tumour service and building a multidisciplinary approach with people such as specialist nurses, dieticians, play leaders and psychologists. “We did a lot of work on changing attitudes to schooling – people then didn’t expect children to succeed in school after being treated. But our view was that if children are to have a future you need to ‘cure’ the totality of their life. You are doing them a disservice if there is no life at the end of their treatment.”

British children’s hospitals such as Birmingham and Bristol have been among the forerunners of family-centred care and multidisciplinary working, and Stevens would like to see this approach promoted more widely across Europe. One way this is happening is through a joint SIOP/EONS (European Oncology Nursing Society) project, funded by FECS, which is helping doctors and nurses to work together better. “There’s no room any more for the old fashioned view of doctors dominating and coordinating care – in my view it is the senior nurse who often has the best skills to work alongside children and their families, as unlike doctors they are always present on wards.”

It is certainly true that some European hospitals have been slow to make special provision for children, with few or no tailored inpatient facilities, and rules restricting personal belongings and barring parents from spending the night with their child. “An Italian doctor who worked with us at Bristol for a few

weeks expressed surprise at the amount of stuff the families bring with them. We want them to feel comfortable but we do have to make sure we have an environment where we can safely nurse a child. I've been to some hospitals on the Continent that seem rather clinical to me – but I'm not sure what the right balance is."

With evidence pointing to less need for measures such as protective clothing in places like bone marrow transplant units, Stevens is happy that there is a good deal more contact on the wards than once was the case, but with the UK's current poor record on infection control he says parents are understandably very concerned.

"You can't be a good paediatrician without listening to parents – not just of individual children but parent groups as well," says Stevens, adding that an achievement he is particularly proud of is helping to set up a national parents' organisation for children with cancer. "We now have parents participating in national policy making as well," he notes.

The parents' group is one of several committee and health leadership roles that Stevens has taken on. He feels strongly that senior doctors need to be engaged with service delivery and policy making. "In Britain we all have a degree of ownership in our health service – I am disquieted by doctors who decide unilaterally what is best for their patients. You can't make all your own decisions, as we work in a resource-limited environment. How can you manage a healthcare system if doctors won't engage with it?"

At Birmingham, Stevens rose up the ranks to become medical director of the children's hospital – a senior executive position in the UK's National Health Service (NHS) – where he found out just how difficult such a job can be. Not only was he responsible for transferring clinical services to a new location at one point, but he also became embroiled in one of the worst ethical storms to hit the NHS, when it was discovered that children's hospitals had retained organs for research without parental consent.



BRISTOL ROYAL HOSPITAL FOR CHILDREN

"I had to deal with parents' support groups and, at times, a very aggressive media. I did a lot of interviews with distressed parents – as a paediatric oncologist you are used to difficult meetings, but some of these were quite the worst I've had. Some parents were very angry, although some had enormous dignity, and for others we were able to offer comfort for years of unconsolated bereavement, so it wasn't all bad." The EU Tissues and Cells Directive, and in the UK, the Human

Child-friendly by design. Bristol Royal Hospital for Children makes great efforts to bring home, family and play into the hospital environment

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Tissues Act, have brought much needed regulation to this fraught topic.

Stevens left Birmingham, where he was primarily an NHS consultant, to take up his academic position at Bristol – an endowed post funded by the CLIC Sargent children’s cancer charity. It was unusual to make such a move at his level. His current position, of course, still carries clinical as well as teaching responsibilities, and he found the clinical side rather less smooth running and more complex than at Birmingham. “We have developed a model we term ‘shared care’, where we spread care out to localities over a wide area of south-west England. I’ve spent a lot of time building up networks and ensuring that the correct policies and procedures are in place, and we have shown it is perfectly feasible to carry out a lot of care in a child’s own locality. It’s a model promoted by our National Institute for Health and Clinical

Excellence [NICE] and I hope it will be taken up more widely in the UK and Europe.”

Stevens has also been chair of the UK Children’s Cancer Study Group (now known as the Children’s Cancer and Leukaemia Group), which is 30 years old – its main remit is organising clinical trials. It was through this group that he also found time to develop his research interest in soft tissue sarcoma. “I had no particular knowledge of this until I was asked to take on the clinical trials portfolio for the subspecialty. There was no real direction then for managing children with soft tissue sarcoma and we were borrowing strategies from the US – but I found there were clear differences in treatments between the US and Europe, particularly France, and after visiting European colleagues we decided to align ourselves with them.”

One of the main differences has been in the use of radiotherapy for children with rhabdomyosar-

Play time. This young patient at the Bristol Royal is about to insert a Hickman line into a sick teddy bear. Play specialist Sam, who is supervising the operation, is funded by the CLIC Sargent children’s cancer charity



CLIC SARGENT

coma. “If you use radiotherapy on sites such as bladder and head and neck, you can damage kids in the long term, and the Americans had a policy of using radiation for almost all cases. Our work in Europe has shown we can predict groups where radiation is not necessary, but the downside may be using more chemotherapy. We are influencing the Americans – but the argument has been going to and fro for some time. It’s an iterative process.”

It is a process common to other fields in oncology, but as Stevens points out, the relatively small numbers of paediatric cancers places extra challenges on obtaining timely results from research. Wide and well-organised collaboration is crucial. In the case of soft tissue sarcoma, Stevens and colleagues had first to “hammer out what seem like simple things but are fundamental – definitions, how you report results, prognostic factors.” But entering enough children in large trials remains a problem in Europe.

As an aside, he notes that paediatric oncologists tend to be very well organised people as a result of pursuing collaboration – and often make good administrators. “I also took time to learn working French to communicate better with colleagues in France – it’s hard enough being seen as the token English person.” He now numbers collaborators such as Odile Oberlin, at the Institut Gustave Roussy in Paris, Modesto Carli at Padova, and José Sanchez de Toledo in Barcelona among his closest colleagues and friends.

Given his organisational background, it was no surprise when Stevens was asked to step in as president of SIOP Europe, where he set about two priorities for the paediatric oncology cause. “The first was elevating SIOP’s position in FECS, where in all honesty we had not been playing a proper role, although we had board representation. A lot of paediatric oncology colleagues have seen FECS as irrelevant – but I didn’t. If there is an organisation for all cancers it is incomplete without us. My position is if you join something you should contribute as well as you can.”

The second aim was establishing a clinical research structure that should, given Europe’s size, at least rival if not surpass the much more organised Americans. “It just does not make sense, for example, that we have three separate collaborative research groups in soft tissue sarcoma in Europe. If we could harness all researchers we could learn so much faster. For example, I’m just now writing up a trial that started as far back as 1995. The main way to speed things up would be to increase the size of population we work with.

“We have to be realistic about the speed at which national groups want to move, and the different resources and legal frameworks among the countries. However, we are getting people to talk about the issues.” Progress has been made, meanwhile, in less contentious areas such as a paediatric oncology training programme and getting more ‘floor time’ for the specialty at events such as ECCO (European Cancer Conference), where there was little exposure before, he comments.

Fostering SIOP’s relations with FECS, says Stevens, has been very beneficial to these ends. With few funds of its own, Stevens negotiated an agreement for FECS to host SIOP’s secretariat, and the two bodies have jointly lobbied the European Parliament on concerns such as the impact of the European Clinical Trials Directive and the overall needs of children and young people with cancer.

In time Stevens is hopeful that SIOP will realise its ambition to unify European research in paediatric oncology in some form, at least by agreeing more common international protocols. As he adds, there is no other moving force – the EORTC (European Organisation for the Research and Treatment of Cancer), an obvious candidate, currently plays only a relatively small role in child cancer studies, through its children’s leukaemia group.

Along with the challenge of increasing the pool for collaborative research, Stevens adds that more attention needs to be paid to the nature of trials. “Most clinical trials are about survival rates – but maybe we can’t drive cure rates any higher in some

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conditions and it is possible that we might be overtreating some kids,” he says. “We need to do more studies that are equivalence trials where we reduce or remove some aspects of treatment.”

It’s a topic that’s entwined with work he is doing on quality of life and long-term effects. “I see young people in the their late teens who may have been treated when they were just two years old – they have no memory of their disease and the angst it caused their parents. They may be facing infertility, risk of heart problems or physical difficulties, and of course there is also the risk of another cancer. They

do need information and support, but there is little structured clinical provision for this growing population of young people.”

As he adds, if you have diabetes as a child you transition into an adult diabetic service, “but you can’t into adult oncology because you don’t have cancer any more. There is some research on care models for this group, but much more needs to be done.” A balance also needs to be struck between the need for collecting data vital to understanding late effects in populations – which can be many years later, and is being done in large cohort studies – and the stress on individuals of follow-up (see also *Cure at what cost?* by Stevens, EJC 41:2701–2703).

At European level, the future of FECS is important to these paediatric oncology issues and, as the current treasurer, Stevens is optimistic. Certainly he recognises the huge upset caused by the withdrawal of ESMO (European Society for Medical Oncology) as a result of a decision by FECS to become a wider membership organisation. He’s also seen a number of ‘big egos’ at work. But he says a plan to rebrand under the ECCO name at this year’s flagship conference should go ahead. “No one knows what a ‘federation’ means – politicians and patients groups have been telling us we have to talk with one voice.” He will not though be staying on the FECS/ECCO board – but admits he might have aspired to take a leadership post if he thought a paediatric oncologist could hold sway with the membership in the current climate. “I do hope others will have formed a better view of the specialty though.”

Stevens is also one of the founders of the controversial Cancer United initiative, and concedes that the early publicity about links with Roche was damaging. “But no one could argue with our aim of promoting cancer plans across Europe. That work programme got delayed, but we now have financial support from other sponsors and have located the secretariat in the FECS office, where I’d like to see it become one of the main political activities of FECS/ECCO, which has been a major weakness.

MORE OFF-LABEL THAN ON

There are relatively few drugs available to treat childhood cancer patients compared to adult patients, and of these many are actually adult drugs still not authorised for paediatric treatment, despite a very long history of clinical use. The proportion of children entered in trials is much higher than in adults, but the Clinical Trials Directive has compounded the difficulties of resourcing research into new therapies. “That’s because much of our research is funded by charities and government,” says Stevens. “Most of the new targeted therapies are being designed to meet the characteristics of adult tumours. There has been no economic case for pharmaceutical companies to research targeted drugs for children for cancers such as rhabdomyosarcoma – but we would dearly love to see new agents.”

There is promise that agents such as bevacizumab (Avastin), currently in adult use, will ‘trickle down’ to paediatric use, but new this year is a paediatric regulation from the European Union that aims to stimulate the development of child therapies by measures such as requiring drug companies to include paediatric data when seeking approvals, and extensions to patent protection. The regulation also aims to ensure medicines are properly tested and administered to children – correct dosage has long been a problem throughout paediatrics. It is too soon to say precisely what the regulation will mean in practice. “I hope we don’t have to gain retrospective approval for drugs we already use routinely, at least not without financial help for the necessary studies,” notes Stevens, who adds, “I’ve spent most of my career prescribing drugs that have not been licensed for children – but I don’t lose any sleep over it. That’s the nature of paediatrics, but this new legislation is good news.”



Children sans frontières. Two years ago Stevens did a sponsored bike ride, to raise money for an orphanage in Karnataka, India. Having started his career working in nutrition and sickle cell disease in Jamaica, Stevens is painfully aware of how much paediatricians in poorer parts of the world could do with the sort of resources he has at his disposal in the UK

I remain committed to doing what I can to help.”

Helping to develop the next generation of senior paediatric oncologists is also part of Stevens' work. Despite the emotional context of working with children, and the possible lack of kudos, he says there is no shortage of doctors wanting to enter the specialty in the UK. “We also had to turn people away from the first ESO [European School of Oncology]/SIOP masterclass in paediatric oncology held in Italy last year,” he adds. “Most don't go into this field unless they are sure it's what they want to do, although I am concerned that in the UK there is less opportunity for young doctors to get a 'taster' of specialised areas in paediatrics with the way training is now organised.” As he currently chairs the university's medical education committee, and is also director of the university's Institute of Child Life and Health, he's well placed to make sure paediatrics gets a fair hearing at Bristol.

Stevens is a parent himself – although his three children are now grown up and he enjoys life in a quiet village near Bristol with his wife Sue, who is a Church of England vicar, and dog Nellie (great for letting off steam). “I don't really have any hobbies –

I am aware that perhaps I identify myself too much through work.”

A forthcoming sabbatical will allow some more time for himself and his family, and after that any thoughts of early retirement have been postponed in favour of new challenges. “I want to develop more academic research at Bristol – not just my own soft tissue work, but establishing new work on the epidemiology of cancers, why some kids contract the disease and why some respond better to treatment than others. I also want to evaluate properly our national care guidance for children to see what difference it is making to service delivery.”

On the European front Stevens is keen also to play a roving role in helping countries to establish and assess their child cancer programmes, especially in eastern Europe, in line with the aims of Cancer United. He's already done that in New Zealand in 1999, and has also been scientific assessor to a large paediatric oncology unit in France.

The number of local childhood cancers may thankfully remain small – but the opportunities to bring care standards to a much bigger stage are growing.