Peter Boyle: the man behind the statistics

Marc Beishon

As a young epidemiologist, Peter Boyle once had to give a talk on trends in smoking-related cancer, having lost his father to the disease that same morning. Now head of the IARC, his great strength is an ability to inject a sense of the reality behind the statistics his staff work on every day, and a sense of outrage at the inequalities they reveal.

Peter Boyle can't quite believe he's heading one of the world's foremost cancer research organisations. As he says, for a career epidemiologist and statistician, there are few more prestigious posts than director of the World Health Organization's cancer body, the International Agency for Research on Cancer (IARC).

It's all a far cry from his formative years in one of Glasgow's infamous inner-city areas. However, Boyle's credentials fit the bill, from earlier research work at the IARC itself in the 1980s to a long spell at the European Institute of Oncology in Milan, where he rose to international prominence with work that included reassessments of the European Code against Cancer and developing a cancer atlas for the European Union.

What stands out is an empathy with the plight of millions facing cancer in the developing world, and a determination to help improve their lot. As he took control of the IARC last year, the World Health Assembly (the supreme body of the WHO) drew up its first ever resolution on cancer prevention and control, which was adopted this year. It has also introduced the Framework Convention on Tobacco Control. Both are in line with Boyle's aims for the IARC and with his long-standing interest in addressing health inequalities (as well as building on his considerable track record in tobacco research).

"The issue today for cancer is the developing world," he says. "When the IARC was formed 40 years ago, cancer was a disease of Western Europe, North America and Australia – now the majority of new cancer cases are occurring in low- and medium-resource countries. These countries are facing a triple whammy – chronic disease is increasing, there is a high background of communicable disease and they don't have the resources to cope with the rising tide of the cancer burden."

With the growing world population – 6.5 billion now, rising to 9 billion by 2040 – the percentage of older people will grow and cancer rates are set to explode. On his computer at the IARC's headquarters in Lyon, France, Boyle has a programme that shows how the population is

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"All my career I've tried to grasp the clinical side rather than just the numbers"

With the prime minister of India, Manmohan Singh, earlier this year. IARC is working with partner organisations in Mumbai, Trivandrum, Hyderabad and Jaipur on a range of screening trials in cervix, breast and oral cancer

growing and ageing in China. As he brings up each year in the decades to come, the ageing effect is quite dramatic.

The figures have huge implications, yet presented in this neat digital form, they look somewhat spooky and divorced from reality. This a perception that Boyle is very keen to break through. "I still miss Milan because the European Institute of Oncology was based in a hospital and there are always patients and their families milling about – the reality was there. When I came to the IARC I reminded the staff here that cancer is affecting humans and not just laboratory mice – a few said 'hooray' and some said, 'Goodness what's this?'"

Since assuming the director's post – an elected position voted for by the IARC's Participating States – Boyle has worked quickly to sort out several other more pragmatic issues. One was to address criticisms that the procedures to resolve conflicts of interest in its famed Monographs series, which evaluate the carcinogenic risks of various agents, were not transparent enough. Another was to simplify and improve the structure of the IARC – out has gone some 25 team reports on the agency's work at director level; in has come five scientific 'clusters' linking, for example, epidemiology with biology, and pathogenesis with prevention.

The key role of the IARC, says Boyle, is to develop unique work programmes that cannot be conducted at national level. "Our descriptive epidemiology, very influential in the developed countries, is now having a huge impact in the developing world, and the Monographs programme that evaluates carcinogenic hazards is essential and frequently the basis of environmental health legislation at country level." Other highlights are EPIC (European Prospective Investigation into Cancer and Nutrition – a large multi-centre cancer study), the TP53 mutation database, and a major project on cervix cancer screening in rural India. And a common thread now, he adds, is "integrating epidemiology with a laboratory component – mainly genetic".

With some 300 staff, IARC is a sizeable concern, and in Boyle it has a director with long experience of applying such analysis to real world problems from an early stage of his career.

Boyle was one of the first students to read for a brand new statistics degree at the University of Glasgow, and initially his ambition was to be a schoolteacher. It was by chance that a project he selected – a study on the risk factors for post-operative pain – got him involved with healthcare and he moved to Glasgow's Western Infirmary as a doctorate student. After various statistical analyses and consulting work he got the chance to help organise the West of Scotland's cancer registry and projects around it, such as clinical trials, with a particular focus on epidemiology.

"I was hooked – I liked the work very much, but all my career I've tried to understand what the clinical side of the problem is, rather than just looking at the numbers. It would have been a waste for me as a statistician to just sit in a room and wait for someone to give me data to analyse – although such pure academic research is fine for some people. I've never been involved in actual patient care but I have constantly been exposed to clinicians and they accept you if you understand what they are talking about and can help them."

He recalls a time in the cancer registry, laboriously writing down age-specific cancer rates – 0–4, 5–10, up to 85+ – on forms in the days before desktop computers. "There was a uniformity. You knew that say at age 50–54, if you had 50 cases in one year you wouldn't get 3,000 the next, as you might with an epidemic infectious

disease. It meant we could investigate underlying mathematical structures and see what was going to happen – and make the big jump, to why it was happening."

This drive was to propel him on a journey that would lead him to work among the elite names of epidemiology – Richard Doll, Richard and Julian Peto, Brian MacMahon – names he recites with almost as much reverence as those of Glasgow Celtic's European Cup winning team of 1967.

Laying his hands on Scottish cancer mortality data from 1911, he updated the registry information, demonstrating the huge and predictable changes in tobacco-related cancer over time. "I submitted a paper to a big epidemiological association meeting in Edinburgh and got on the programme," he says. "On the morning of the day I was due to speak, my father died from lung cancer – he was a smoker most of his life – and in the afternoon I gave a talk on the trends of smoking-related cancers in Scotland. That was tough – but it was reality."

Boyle was then to leave Scotland, so far for good, with his wife Helena and his first child. In a roundabout way, via a training fellowship at the IARC, he found himself as an assistant professor at the departments of biostatistics and epidemiology at both the Harvard School of Public Health and the Dana-Farber Cancer Institute. "After an hour I realised that the cleaners knew more about epidemiology than I did – I didn't have a clue about the fundamentals."

And the biostatistics group, he says, "had written the book about how you do clinical trials – and may well have been the best group of biostatisticians ever assembled. It was the attention to detail – data quality, model selection, examination of interactions and ensuring the randomisation worked before coming up with answers. Looking back it seems obvious, but it wasn't then."

The challenge is not just to conduct rigorous randomised controlled trials, which for so long were considered the gold standard in medicine. As Boyle points out, in public health work evidence may need to come from a variety of both 'hard' and 'soft' sources. "One of the first things I did here was create a tobacco unit – there had never been one at the IARC – and we want to now write a series of handbooks on the scientific evaluations of tobacco control recommendations.

"If we were looking at say a substance such as formaldehyde, which we do in our Monographs, we have a choice of maybe a hundred peer-reviewed papers in the literature – but a lot of work on tobacco interventions that, say, try to stop children smoking are not published in the same way – or not published at all. The level of information you can use to make decisions is weaker and is more sociology and psychology than hard-nosed science."

Developing methods of sufficient scientific rigour that consider 'softer' evidence is certainly needed, particularly to identify interventions that target health inequalities. As Boyle mentions, measures for getting people to quit smoking have often been more successful with well-off people with more motivation and better access to resources – potentially widening the health gap (his home country of Scotland being a prime example).

The need to focus on the real issues was brought home to Boyle in the US by John Cairns, "a father figure of biology". "He said that from time to time you have to look at issues, not just uniquely focused scientific questions," says Boyle. "John got me to look at a paper in *Science* that said that since the introduction of the cancer chemotherapy programme in the 1950s, it was saving 150,000 deaths a year in the US. I looked at the data and put it together with what we knew about outcomes and found that the number of deaths saved a year was 15,000 – maximum. We did get a reply in *Science* – but

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they left off the tag that 10,000 medical oncologists were preventing only 1.5 deaths each a year."

Boyle managed to escape intact from the US after this, and faced with a choice between working in Glasgow or the IARC at Lyon, chose the latter. He directed a programme called Search – Surveillance of Environmental Factors Related to Cancer in Humans – a series of case-control studies across several centres on subjects such as children's brain tumours.

Then in 1991 he was invited to head up the department of epidemiology and biostatistics at the European Institute of Oncology in Milan – in fact he was the first employee at the then fledgling outfit, one of the many brainchilds of famous cancer surgeon Umberto Veronesi.

Boyle mentions several highlights of his long tenure at the institute. One was being able to continue research interests such as the link between pancreatitis and pancreatic cancer – with various collaborations he helped the work through all the way to identifying a gene from an initial case control study.

"Veronesi was also very generous in allowing staff to be involved in bigger projects – and I got a lot of exposure in the European Cancer Experts Group." One of Boyle's inputs to this group – which is a European Union meeting of experts – was a document informing a consensus meeting on tobacco. Approved by the then European health commissioner, Padraig Flynn, and after a good deal of reworking, it led to the European tobacco directive on the content of cigarettes. "I was invited to the European Parliament for the final approval vote – that was public health in action," says Boyle.

He pays particular tribute to subsequent health commissioner David Byrne, who saw both the EU tobacco content and advertising directives through. "I was very close to David – he was magnificent despite having to contend with major dramas such as BSE ['mad cow disease'] and other food scares. He wasn't a public health man by training but could see what a huge impact tobacco control could have in Europe and he put his career on the line."

Tobacco is a big preoccupation for Boyle. He is lead author of the book *Tobacco: science, policy and public health* (OUP, 2004) – and he is naturally worried that this century will turn out to be even more grim "There are currently about 1.2 million cases of lung cancer around the world – if nothing changes this will rise to the same number in China alone by 2030. We will be swamped by smoking-related disease." He has high hopes for the WHO tobacco framework, although time is clearly short even for a global organisation to make an impact.

As he adds, public health professionals will only see results through the often brave action of politicians, such as David Byrne and others on the tobacco front in places like Ireland, Italy and New York. Boyle's engagement with movers and shakers at European – and now world – level have certainly given him insight into the art of the possible and the politics of running organisations.

That insight was quickly tested at the IARC, when EU funding streams for several cancer projects such as EPIC were cut off, and he's had to provide bridging monies while alternative sources were sought.

He also inherited an attack on the integrity of the IARC over possible conflicts of interest on regrading the status of certain carcinogens. "We couldn't put our finger on an instance where a meeting was deliberately hijacked by undeclared vested interests," says Boyle. "Classifications can go up and down as more evidence becomes available." To silence the critics, however, the IARC has now created a new category of 'invited specialists,' where any with conflicts are not allowed to write drafts, vote or

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chair working groups, and all names are published on its website.

Inevitably he is well plugged into the politics of the European cancer community – a particular concern is that there are rather too many obstacles at present to achieve the kind of unity that would maximise European resources. "Things are still too national – there are huge barriers to mobility within Europe," he says. "It's not so much at the administrative level, but cultural – it's very difficult to recruit a 45- to 50-year-old professional who may be at his or her most productive, when they are tied down with children's education and other factors. It means that, for example, if the head of the National Cancer Institute in the US wants to set up a national proteomics centre he'll get the cream of 280 million people to work in it – in Europe with 500 million people, the UK, Germany, France and so on will all set up their own."

Further thoughts will no doubt arise from a major grant from the European Commission that Boyle has been awarded – for a feasibility study on co-ordination of national cancer research activities.

On the vexed question of a European wide cancer society, Boyle feels that FECS (the Federation of European Cancer Societies) was a great idea at the time – but it now suffers from being an organisation whose members are other membership bodies. If it can evolve into a society with more individual representation it would probably assume a higher international profile, he feels.

And while recognising that the recent European breast cancer resolution has raised the profile of this disease, he is concerned that the fight against cancer should not be fragmented too much – "We have to find ways of unifying interest groups," he comments.

Integration across a broad range of cancer research issues is certainly Boyle's aim with the IARC's cluster structure. "One of the great advantages we have is that we have all groups here – genetics, epidemiology, biostatistics and so on – which you don't have in most other institutes." As an example he cites the genetics and epidemiology cluster, which has researchers with a spectrum of strengths in the two disciplines, plus laboratory expertise. "That cluster works together very closely – we collect the data and the correct biological material in well-designed epidemiological studies, and it is analysed in the lab in a state of the art way to be interpretable in terms of what's happening in the population."

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Boyle's 300 staff, at the IARC headquarters in Lyon, cover a wide range of cancer-related expertise, including epidemiology, pathology, genetics and biostatistics

Boyle's focus is now of course on the world cancer stage, which is guiding where this expertise is targeted. "If we want to make an impact we have to focus more on the low- and medium-resource countries – while not neglecting the developed countries, where we can still help.

"For example, there is an epidemic of oral cancer in Central and Eastern Europe – the mortality rate has gone up 10 fold in Hungary in the last 30 years. We have got to compare risk factors there with Western Europe, where the mortality rate has not gone up, and we're not only interested in alcohol and tobacco as risk factors – is there a genetic cause too? These are the sort of big studies we organise."

But it's clear too, he adds, "that in the poorer countries effective prevention is going to be much cheaper than treatment and we need to develop appropriate strategies." As such, screening work is assuming a higher profile. "For example, we now have results from ten years' follow-up of a screening study of oral cancer in Kerala, India, which shows mortality reduced by one-third among those at high risk. We also have a randomised trial of 120,000

Getting results can depend on brave action by politicians such as David Byrne on the tobacco front

women in rural India for cervix cancer. It's a huge and extremely important study and we have finished the first round of screening – and again, while no results are yet available we are extremely pleased that we managed to treat over 80% of women who we thought were positive. That's so different from what goes on in poor rural settings at present."

The cervix screening work is backed by the Bill and Melinda Gates Foundation, which Boyle says is one of the major funding sources for projects of this nature. He adds that such work also needs to take account of local conditions – "We in the West may have been guilty of identifying what we perceive as the priorities and applying a Western solution. That may not be the way to go."

In the cervix cancer programme in India, for example, a 'low-tech' visual inspection is also carried out to 'see and treat' immediately – as many women would simply have been lost to further clinic follow-up. As part of a consortium of public health agencies, the IARC has also launched a toolkit for implementing cervix cancer screening, while Boyle, on a recent trip to India, was invited to meet prime minister Manmohan Singh – "He is aware of health and poverty issues."

While the low- and medium-resource countries have pressing priorities, Boyle is also struck by just how much disparity is present in the developed world. In the IARC's cancer mortality atlas of Europe, which covers the expanded European Union, some of the worst figures for lung cancer do come from the poorer member states. "But the highest rate of all is in Glasgow, where 70–80% of the population are in deprivation categories six and seven."

He mentions a study on breast cancer outcomes in Scotland that found a big gap in survival rates between well-off and poor people after adjusting for prognostic and treatment factors. "We have to find out what's driving that – there's something inherently unfair in a poor person having a poorer survival outlook compared to a more well-off person with identical disease. It's the sort of inequality that leaves you really cold." He's also acutely aware that in some advanced countries – the US, for example – women from some sections of the community are also still presenting with advanced disease.

As he adds, it's only been in recent years that these differences have been visible through population indexing techniques. It all adds to the complex jigsaw that makes up the risk factors and risk determinants for cancer, and Boyle feels that deprivation is a critical factor that is not receiving enough attention.

Boyle's broad understanding of the cancer research spectrum has put him well up journalists' contact lists for comment on topics such as risk factors, screening and treatment that tend to flood the media. As he notes, there are some hundreds of risk factors for breast cancer alone, and there are many institutes sending out press releases – a recent one from the IARC itself concerns a study showing that vegetables and fruit are not protective against breast cancer. And a current IARC study on mobile phone use is bound to generate great interest.

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While he professes exasperation at some of the more absurd media reports, he points out that sometimes the cancer community has itself to blame. "A particular bee in my bonnet is at meetings where papers are press released to get media attention, but often have many holes in their findings, being suitable only for a poster or short presentation.

"A while back at the ASCO [American Society for Clinical Oncology] annual conference plenary session there was a paper that claimed that PSA testing reduced the mortality rate of prostate cancer – it got huge publicity. I'd seen the paper a month before – and I said at the meeting that using an 'intent to treat' analysis showed there was absolutely no evidence of a protective effect." This publicity machine "is wrong and a disservice" to the cancer community, adds Boyle.

On a personal note, Boyle has certainly proved that it is possible to develop a career away from his roots. His three daughters were educated in Lyon and Milan and are all now pursuing medical careers – the "stream of strange foreign medical people arriving for dinner" over the years being a clear risk factor in their choice, as he puts it. However, his wife Helena did have to give up her career as a maths teacher to look after the family and help the children with their studies.

His great passion is football – he used to play himself and has always been a fanatical Celtic supporter. But Scotland in general is a great reference point. In talks he's spoken of the 'good, bad and ugly' of cancer work in the country, from outstanding progress with a national cancer plan down to the continuing impact of deprivation. He's quoted Voltaire saying, "We look to Scotland for all our ideas about civilisation" – as its model of cancer control is eminently exportable (and there also seems to be quite a lot of Scots making waves in world cancer work). At home in Lyon, he always logs on to the Internet to see the latest news from Scotland.

Looking ahead to achievements for the initial five years of his post at the IARC – and a second term could be on the cards – Boyle says he was first encouraged to set targets, which he has resisted. "In 1985 when Europe Against Cancer was set up, the cancer experts met for the first meeting in Milan and, against a huge rise in cancer rates, they set a target to reduce the number of deaths in Europe by 15% by the year 2000. I saw this published at the time and colleagues and I laughed.

"But through a series of actions on screening, primary prevention and tobacco control there was a 9% reduction in the number of cancer deaths expected." Boyle was in fact lead evaluator for the target by this point. To achieve more than half of that ambitious target was tremendous, he says, and there is plenty of merit in having such goals even if they are not met (and since then the EU has set a new target of a 20% decline in cancer mortality for 2015).

For someone so well versed in number crunching, though, his preference is for a more qualitative approach for the IARC. "If I can increase the quality and relevance of the research we do here, increase prospects for cancer prevention and help improve the situation in the poorer societies, I'll be quite happy."

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With David Byrne, then European Commissioner for Health, who Boyle says "put his career on the line" to get through the European directives on tobacco content and tobacco advertising