



Lisa Hutchinson: teasing out the signal from the noise

The explosion of new information in the era of personalised medicine has created a headache for busy clinicians. Lisa Hutchinson has spent the past 13 years helping them keep abreast of developments by sifting, sorting and summarising the clinical research findings that matter most. She talked to **Anna Wagstaff** about the joys of her job as Chief Editor of *Nature Reviews Clinical Oncology*.

Every month, Lisa Hutchinson and three colleagues scan more than 3,500 abstracts published in 70–80 medical and cancer journals to keep abreast of the latest advances and discoveries that could be of value and interest to practising oncologists. She attends cancer conferences and talks to her wide network of people who are pursuing interesting research or have new and thought-provoking things to say.

Together with her team, she filters the information and works out how to present it all in 64 pages.

Hutchinson is just reaching the end of an almost 14-year stint as Chief Editor of *Nature Reviews Clinical Oncology* (NRCO). It's a position she has held since the title was launched in November 2004, as part of *Nature's* first foray into the clinical arena and, despite the long hours, as far as she's concerned it's been nothing but a privilege and a pleasure.

"I think I've got the nicest job of anybody in this room," is how she opened a talk to a group of cancer researchers last year. "I don't have to worry about getting funding, or design fancy experiments. I've still got the enormous privilege and

luxury of knowing what's going on in the cancer world from the people who are the main influencers, and are educating me in the process, and I get a publication at the end of it – and there's the kudos that goes with that, particularly as it's *Nature* branded." As she adds, "It doesn't get better than that!"

Do we need yet another journal?

By the time *Nature* launched its monthly review publication for oncologists, the explosion in medical publishing was already well under way. "Do we need yet another journal?" was the question posed in the launch issue by the journal's external Editor-in-Chief – and former head of the US National Cancer Institute – Vincent DeVita, who went on to argue that it was precisely because of the overload of new information that this new monthly clinical oncology review was needed. "This journal has some unique editorial features that will ease your workload and help you interpret and put into practice the enormous amount of published research," he wrote.



A great job. Lisa Hutchinson at *Nature's* London publishing centre, where she has worked as Chief Editor of *Nature Reviews Clinical Oncology* since its launch in 2004

The concept, explains Hutchinson, was “to filter and tease apart the signal from the noise for busy clinicians, so that we can provide a chronology of the medical research applications that are being reported on, and add an interpretation as well as an informed opinion.” The new journal was to carry no primary data, but provide expert commentaries, short articles, and research highlights written in-house, “crossing the breadth of the literature,” and then the more lengthy reviews and perspectives, which are all commissioned and peer reviewed.

The latter, which make up the ‘back half’ of each issue, provide background to a given topic, but then take an original look at the timeline of recent developments, controversies, where progress is being made, and where once promising research is failing to deliver. “We are proactive as well as reactive to the literature,” says Hutchinson.

Thirteen years on, she feels the journal is needed more than ever. At the start it was a question of keeping abreast of 20–30 journals, but that number has now increased almost four-fold. And it isn’t just the number of journals, she adds.

“They are publishing more frequently, so there is more content coming out on a daily basis, especially as we have advance online publication.”

She admits to being “in awe” of the way clinicians keep on top of the ever-accelerating pace of new information. “I struggle and it’s my day job. I don’t have patients to treat and ward rounds to do.”

Loving science, but not the lab work

A biochemist by training, Hutchinson did her PhD at the UK’s Institute of Cancer Research, starting in 1994, as molecular biology techniques were just beginning to take off. “That was studying Wnt signal transduction in mouse fibroblasts relating to breast cancer. Very preclinical. At the time we did not know or understand the biochemical pathways, our knowledge was based on clonal epistasis analysis.”

All the technologies referred to in *Nature* journals now, she says, are way beyond anything she ever did in a lab.

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Microarrays, she remembers, were just being introduced in the last year or so of her PhD, “and were considered a massive thing”. The second *BRCA* gene was cloned at the Institute, and the findings were published in 1995, “I remember the *Nature* paper coming out on that.”

So why leave research, with all this going on? “I probably didn’t have quite the nurturing environment with my first supervisor during the early part of my PhD,” Hutchinson speculates, “and I thought: gosh, this is a treadmill. I could work for another 5–10 years doing a post doc. Do I want to do a team-leader role as a lab researcher, having to get funding to support four or five people in a lab? And after all, even though science is extraordinarily exciting and interesting, it is the 99% perspiration 1% inspiration rule. I remember the times I was stuck in a lab trying to get minipreps to work for months on end. Trying to clone certain things, get antibodies, and I just thought: I’m not sure I’m in this for the long run – but I loved science.”

Having taken the decision to leave research, a career in science publishing seemed an appealing alternative. An opening for an Assistant Editor arose at *Breast Cancer Research*, where Bruce Ponder was Editor-in-Chief. With her newly minted PhD, Hutchinson got the job, and within a year was promoted to a journal Editor role.

She enjoyed the work, but was soon lured away by a medical communications company, which offered her the chance to do something different, on better pay and a varied role. Her new job gave Hutchinson an insight into the world of product life cycles and pharmaceutical company messaging, which she says has proved invaluable in her current position.

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“I got experience in writing and communicating and working as the middle man; the pharmaceutical companies were writing abstracts for conferences, and we would essentially ghostwrite them. We also put together a publication plan for an insulin sensitiser drug. I got to see how you analyse all the key marketing messages in manuscripts, and try to come up with an editorial strategy to publish and get across those marketing messages of certain products, such as how they compare themselves to competitors.”

When *Nature* then advertised for a Chief Editor to launch

a new oncology review journal, Hutchinson believes her experience working within the medical communications industry helped her clinch the position – as ‘poacher turned gamekeeper’, she knew all the tricks.

“If you understand how the process of a formulation of a manuscript works, you can start to tease apart articles that might not be written first hand by the authors, and see influences that have been exerted by pharma companies. When I’m reading papers I do notice things like that.”

How far does she think the hidden hand of industry really threatens the integrity of the academic literature? “I think it is more prevalent in the literature than people realise,” says Hutchinson. She mentions a study presented at the 2017 ECCO, where 300 corresponding authors were randomised to read abstracts of a key trial that had been written either with or without spin, and were then asked to rank whether they felt those treatments made a difference. “The scoring they got at the end with spin was about 6/10 – 10 being that they thought the drug was really great, and 0 being the opposite. And it was around the 2–4 range without spin. Even experts are being influenced, and these were corresponding authors who had written several similar papers.”

She adds, however, that industry is by no means the only culprit here. “A conflict of interest isn’t always financial. There are other pressures to get a positive result on a research paper, because you are more likely to induce people to read it and to cite it, and it might further research funding.”

Hutchinson wonders, too, about why she keeps coming across the same type of phrasing in a lot of abstracts. “I’m seeing a trend of how things are phrased where there is almost a template, and buzzwords have been inserted – almost like you’ve got to have that in there. It’s got to have ‘multidisciplinary’, it’s got to have ‘translational’ or ‘immunotherapy’ for you to have a chance of getting into the top-tier journals. It’s the same for grant tenure and further funding, they also stipulate that people have got to be publishing in these type of areas with these type of outputs.”

She feels research funding is too bound up with publication track records. It’s not wrong to insist that people have to publish, she argues, but the lack of focus on negative trials does raise questions about the reproducibility of published results. She also feels that promising initial scientific findings are too often allowed to advance into clinical publications without enough attention being paid to issues of clinical utility or benefit for those findings to change practice or influence care. “The pathway for assessing preliminary scientific promise to advance to the clinic is not as well created as it should be.”

She worries too about the “disturbing increase” seen in retractions and falsification of data, and about the increasing numbers of papers that include large sections cut and pasted from other articles. *Nature* is one of many academic publishers who have signed up to the Committee on Publication Ethics (COPE) guidelines, “and we as a company are educating our own staff in-house across the board about integrity issues,” she says.

Broadening readers’ horizons

In her 13 years scrutinising every aspect of clinical oncology, and trying to make sense of it for busy practitioners, Hutchinson has seen some big changes.

“We’re all looking much more at health policy, societal challenges, sustainable healthcare models,” she says, and at a clinical level, as oncology has become more complex, care has become much more multidisciplinary, and there are more pressures to super specialise – though some clinicians don’t want to go down that road, says Hutchinson.

“I get the impression that people are trying to not be too siloed because it’s not in their career interests. They want to be broader, and they are finding avenues to do that, even if it means moving to other institutions.”

She notes also a trend towards horizontal linkages between specialties that used to be more distinct. Molecular biology is no longer just the preserve of clinical oncology – it has a role to play in imaging, radiotherapy, and even surgical oncology. Learning more about other specialities can help people deepen their understanding of their own, and she adds that publishing can play a role in that.

She cites as an example a recent article about the career path of a radiation interventional oncologist, which looked at the interfaces between radiotherapy, radiology and clinical oncology, and where education and training could be improved. “That article was more on the educational side than on the hard core business coverage we typically cover, and it came about through anecdotal conversation. I said, ‘If people don’t know this is a problem, but that there are actually ways this can be achieved by different interactions within departments, getting better internships, things like that could really help.’ Even if this article doesn’t attract high citations, we wanted to cover it because there’s a need.”

The rise of the personalised/precision medicine paradigm happened largely during her editorship. Hutchinson is cautious about the benefits, and devoted one of her editorials to the topic. “The reality is that the clinical benefits of precision medicine, as currently practised, are quite limited.



Well connected. *Nature*’s offices are part of the King’s Cross Science Hub, which now includes the Francis Crick Institute – the largest biomedical research facility under a single roof in Europe. King’s Cross St Pancras station, seen on the skyline, gives rail access to Brussels in less than two hours

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“We are trying to look at how you can get data that will inform clinical practice, but the paradox is that evidence-based medicine is the opposite paradigm to precision medicine. So the field is at a bit of a crossroads – heterogeneity of the tumour, clonal evolution, the snapshot of the tumour, liquid biopsies, how that is helping – or not helping in some cases – inform on disease progression. There are uncomfortable truths in terms of health spending pressures, uncertainty of the precision medicine era, and the billions

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being invested in it that we can't just throw away."

Hutchinson's own best guess is that a better overall understanding of the tumour microenvironment and stromal tumour interactions may be among the more fruitful places to look for answers. "For me, understanding how cancer starts, understanding more about the metastatic process, along this continuum, is going to be the really important thing in the next 10 years."

As she points out, cancer is not like any other speciality, in that it has no organ or system base to it. "It's not like cardiology, where you understand the functioning of the heart and the supply structure intricately in and out." Cancer experts are therefore generalists to a degree, she argues. "We still don't have an essential understanding of how, on the molecular level, the disease starts. The stem cell model – sometimes it's in, sometimes out of favour. That for me is quite interesting."

“There are uncomfortable truths in terms of uncertainty of the precision medicine era, and the billions being invested in it”

Also intriguing is how little we know about 'normal' cells, says Hutchinson, who feels this is an area that deserves far more attention – an issue she first raised five years ago in a conversation with Roger Stupp, now President of the European Organisation for Research and Treatment of Cancer. "We'd been assessing the cancer cell in isolation in cancer patients, without considering the mutations or alterations or influences in the surrounding 'normal' cells. The point I made was that we need to consider the so-called 'normal' or non-cancerous tissue changes, otherwise we lack a baseline comparison, which inevitably is influenced by the cancer cells, and vice versa."

And sure enough, says Hutchinson, "It turns out that there are many mutations in 'normal' surrounding tissue, which has been pre-programmed to some extent by the latent dormant cancer cell. Failure to appreciate this has been providing a bit of a red herring when it comes to drug discovery, which is to some extent why we are in the mess we are in."

She is betting on the potential of 'omics technologies and systems biology to reveal more about how cancer starts and spreads, which would then lead to how to apply "what we have in our armamentarium to treat the patients". But her

best guess for the timescale for reaching a 'biological cure' is measured in centuries rather than years or decades.

"Clinical cure is different. We've reduced colorectal cancer mortality by 40% in the past 30 years. But you are never going to get a full cure. If one in two of us is going to get a diagnosis of cancer, which is what the estimate is, this is here to stay. It is an adaptive complex disease that has had millions of years to use its biological circulatory to its advantage.

"The way I see it, in England we have a map of every single road and we know every single registered car on that road, and have high levels of CCTV [traffic monitoring cameras]. Are we able to predict which accidents happen on the A roads and the motorways? No. With cancer we haven't even got the road map done yet, let alone all the cars on it. So in some ways our progress is quite incredible given the lack of all that knowledge."

Hutchinson is clearly not worried that her journal will become redundant anytime soon, but she herself now feels it is time to move on. Having had the privilege of following at close quarters the explosion of new knowledge about cancer, and been part of efforts to translate that into better outcomes for patients, she is leaving NRCO to follow her interest in exploring the biological commonalities between non-communicable diseases, such as metabolism and inflammatory processes.

"I've had conversations with people at conferences, and we are starting to see this appearing in clinical oncology. Even cancer is not as distinct at a molecular level from other diseases that we've studied as completely separate entities. We are starting to see them interacting more. Biology does that. So understanding biology will help us understand disease pathway roadmaps better, not just oncology but other areas."

It's exciting stuff, but after almost 14 years working with and for clinicians, Hutchinson is clear that she does not want to return to basic science. "For me, the molecular era opens up a vista on how we view diseases on a fundamental level. We are starting to see more synergies about how non-communicable diseases develop and evolve to become incurable. I would love to use my oncology background to help find solutions for many of the key global healthcare problems. For instance, diabetes is a ticking time bomb, with more than 415 million people worldwide living with this disease, with millions more undiagnosed.

"We need to provide a sustainable framework for healthcare globally and tackle the top non-communicable diseases. To be part of this endeavour would be extraordinarily rewarding."