Patients First: Pioneering Partnerships

Report of the joint AMRC / ABPI conference held on 20 March 2018

Introduction

This meeting, organised by the Association of Medical Research Charities (AMRC) and the Association of the British Pharmaceutical Industry (ABPI), was convened to discuss how the industry and medical charities can work together to put the beneficiaries of research efforts – patients – first. It was the second meeting of its kind, building on one held in 2016.

Both chief executives of the sponsoring organisations gave short addresses to open the meeting. **Mike Thompson**, CEO of the ABPI, described the uniquely challenging environment in which his industry, one of the UK's most successful, finds itself in 2018. He was the only speaker to mention 'the B-word' (Brexit) from the main stage. He emphasised that the UK Government has made it clear it wishes to maintain the close cooperation the industry has with all stakeholders across supply of medicines, research programmes to find new breakthrough innovation, pharmacovigilance to maximise patient safety and on a single infectious disease monitoring system to protect all citizens in the EU and UK. He noted that it is industry's desire to work closely with patients too to impress upon the Commission and all EU Member States that this is the right outcome for EU patients too.

Aisling Burnand is CEO of the AMRC, which represents over 140 charities that together raise about £1.6 billion annually for medical research. She compared the movement to involve patients and the public in that research with the suffragette movement. Patients, like nineteenth-century women, are too often patronised but should be trusted with enough information to make informed choices. She quoted Baroness Tessa Jowell, best-known as 'Minister for the Olympics' and now a brain tumour patient, calling for greater access to experimental clinical trials, and suggested that disparate organisations should work in partnership to achieve significant and lasting change.

Opening Plenary: From Patient to Patient Entrepreneur

Michael Seres, 11 / Health

Appropriately enough, the opening plenary lecture was given by a patient. **Michael Seres** has lived with Crohn's disease, an inflammatory bowel condition, for about 35 years, having been diagnosed at the age of 12. He has had over 25 operations; he was the first patient in Oxford and only the eleventh patient in the UK to receive an intestinal transplant. Despite advances in surgical techniques and medical care, he has seen disappointingly little change during his 'patient journey' in the key relationships between healthcare professionals and patients. The key qualities of trust, respect and empathy that are key to these relationships are all too often disrupted or missing.

Seres proposed that the collaborative, respectful patient-professional relationships that he – and, indeed, all 'Patients First' speakers – would like to see can be mediated through digital technology. The idea that computer power 'can [now] be harnessed effectively to relieve the burden on clinicians and leave them more time for patient care' has been proposed from time to time since the 1980s but is still far from being realised. However, patients are increasingly happy to submit

information about their conditions to their healthcare providers digitally and in 'real time'. Well over half of all patients surveyed are comfortable with using email, text and online chat for this, with only social media lagging behind. Seres has been sharing his own data digitally for years. He described a time when his doctor accidentally tweeted his blood results to the public timeline and a clinician in another country responded by recommending that he check his potassium levels.

Patients are in a unique position to spot problems with their care and sometimes to propose solutions. Seres, like many with his condition, has to collect his stools in a colostomy pouch. It is sometimes difficult for users to tell when these need emptying, which is unpleasant and embarrassing. He developed a wearable electronic device to sense a bag's changing shape and send a signal to the user's device when it is full. He founded his company, 11/Health, which is the only healthcare company known to include a Chief Patient Officer on its board of directors to develop and market these and other wearable devices.

Seres ended his presentation by highlighting the advantages that the healthcare industry can gain from thinking outside the box, from learning from other industries – in the case of 11/Health, the gaming industry – and, in a phrase that was to come up again and again in the meeting, from taking courage.

Morning Keynote: Partnering with Patients, for Patients

Helena Chung, Astra Zeneca in conversation with **Michael Seres**

But how can 'patient centricity' be defined? **Helena Chung**, who runs a patient engagement program in oncology within Astra Zeneca's Global Medical Affairs department, worked with Seres and others in the industry to define the needs and values of cancer patients and how these should impact the industry. She began her presentation with a one-sentence summary of their results, published in detail in *BMJ Innovations*: "*Putting the patient first is an open and sustained engagement of the patient to respectfully and compassionately achieve the best possible experience and outcome for that person and their family*". Therefore, pharma companies should 'bring patients to the table' as equal partners as early as possible within the drug development pathway, involving them in all aspects of the process, from setting research questions and defining unmet needs to monitoring products in clinical use.

She then described a 'patient centricity [research] framework' (PaCe) that has been established at Astra Zeneca to implement these ideas, dividing it into three phases: before, during and after the clinical study:

- Patient advisory boards and questionnaires provide input into **study planning**, and they run protocol simulations to optimise the patient experience
- During **study delivery**, consent forms have been made clearer and simpler to encourage patient participation and patients can choose a range of support methods, including an app.
- **After the study**, patients are thanked for their involvement; they also help to produce lay summaries of the results that are made freely accessible online.

Astra Zeneca's oncology division has also developed a methodology, termed Patient Reported Outcomes, for discovering and measuring 'the things that matter most to patients' in balancing the efficacy of a medicine against its side effects. Small groups of patients, carers and survivors are invited to share their perspectives of different diseases in a Patient Partnership Program, and this now extends beyond oncology to include, for example, severe asthma. And patient involvement has been incorporated into the company's code of ethics, which aims to maintain 'respect, compassion and empathy' towards patients in all these activities.

Panel Discussion: Partnerships that put Patients First

Chair: **Faisal Mehmud**, Bristol Myers Squibb

Panel: **Steve Ford**, Parkinson's UK

Emma Law, NHS Research Scotland

Leonor Stjepic, RAFT

Many research initiatives that involve patients as partners are themselves partnerships between other stakeholders: companies, charities and healthcare providers. The first panel discussion, chaired by BMS' medical director for the UK and Ireland, **Faisal Mehmud**, examined this issue from the perspective of large and small charities, small enterprise and the NHS.

As a small medical research charity focusing on a single indication – acute trauma - RAFT sees partnerships with industry, academia, clinicians and, of course, patients as its lifeblood**.** Its CEO, **Leonor Stjepic**, described a case study: Smart Matrix®, a 'scaffold' developed within the company to promote acute wound healing. This product was ready for clinical trials in 2010-11, when little investment funds were available, and the charity's board decided that the product could go forward most effectively as a commercial venture. The result was the creation of a separate company, Smart Matrix Ltd. A steep learning curve followed for RAFT's directors, particularly Stjepic, who was legally required to act as CEO of both the charity and the company, but they have learned important lessons: not least, how manage relationships with a much wider range of stakeholders, including bankers, regulators and patent attorneys. And, most importantly, the product reached clinical trials far faster than it would had its development stayed within RAFT.

The work of Parkinson's UK is driven by the voices of people living with Parkinson's disease. The charity's chief executive, **Steve Ford**, described asking as many Parkinson's patients as possible what would improve their lives most. Not surprisingly, the commonest answer was 'Better treatments and a cure – but faster!". It is fifty years since the discovery of Levodopa, which is still the most effective drug for the disease. Yet the gap in funding between early stage research into neurodegeneration and late clinical trials is still wide. Working in partnership with patients, the charity has now developed a new framework for funding late pre-clinical and early clinical research. Its 'Virtual Biotech' funding stream acts like a venture capital fund, investing millions in setting up single-asset 'virtual companies' to develop novel therapies. The first of these, Keapstone Therapeutics Ltd., is exploiting novel research at the University of Sheffield. Parkinson's UK also funds the Critical Path for Parkinson's, linking industry, academia and patient advocacy groups to improve patient experience of clinical trials.

In the UK, most patients' experience of healthcare begins and ends with the NHS**. Emma Law** of NHS Research Scotland (NRS) described the NRS Neuroprogressive and Dementia Network, which she manages. The philosophy that underpins this network is that everyone should have the opportunity to participate in their research. It set up a patient and public involvement group in 2010 to help people overcome their fears of research by giving them choices. Now, patients and the wider public are involved in study oversight groups, in reviewing the website, patient information leaflets and research proposals, and in app testing, focus groups and even talking to the Press. Law described case studies of patients who found that involvement in the network improved their lives, largely by letting them take back control of their disease. This initiative in taking back control also helps carers like Tommy Whitelaw, whose award-winning blog on caring for his mother with dementia has had millions of hits.

Workshop: New standards for patient involvement

Simon Denegri & Philippa Yeeles, NIHR INVOLVE

Involving the public in research means it is carried out with or by members of the public, rather than 'to', 'about' or 'for' them. This also includes how research is designed, undertaken, evaluated and reported. New gold standards for how to do this kind of Patient and Public Involvement (PPI) was the focus of the workshop delivered by NIHR's INVOLVE. The workshop began with a clear indication from attendees, by way of traffic light voting cards, that such standards would be helpful for those new to, as well as those more experienced in, PPI.

As Simon explained, PPI is incredibly important but until now it has been unclear what 'good' public involvement looked like. That's why the standards were developed for members of the public and community groups – allowing them to scrutinise what good looks like and compare with their own experiences. The standards are also to help guide researchers and research organisations in their PPI work too.

Work developing the standards started in 2013, with substantial effort to establish and maintain buy-in from the PPI community, by making the standards practical and engaging. NIHR identified key partners to engage with, including community groups, throughout the development of the standards and created a website and network with over 450 members. Stakeholders gave a clear message, they did not want iterative rounds of consultation and refinement – instead preferring the NIHR to develop standards from what currently exists.

In 2016, the standards were drafted, ready for consultation in 2017. Throughout the remaining part of 2017 and into 2018, the standards were re-drafted following feedback from the consultation, including refining the standards and changing the language so that it emphasised that standards should be a self-reflection and learning tool. The output of that work was the set of standards launched at Patients First: Pioneering Partnerships.

The standards are now being launched and piloted in 'test beds', the shared learning of which will be useful for their subsequent development throughout the rest of 2018 and into 2019. The NIHR is still looking for help outside of the test beds, from organisations wanting to undertake 'freestyle' projects in which the principles will be applied and the evaluation shared with NIHR. To take part, participants need to consider what they want to achieve from their project, the difference they want to see from using the standards, how it will be evaluated, and what will be learned. Additionally, participants will be asked to score how well they think the NIHR is meeting the standards. This will be a useful reflective tool for the NIHR itself to improve its own PPI efforts.

The workshop concluded with participants discussing how their organisations might meet, implement, and communicate the standards. While it was clear from the group discussions that some challenges may lie ahead, there was a clear sense of excitement for implementing the standards in the immediate future.

Lunchtime Seminar: Introduction to patient involvement for industry and charities

Speakers: Chris Macdonald, Arthritis Research UK

Claire Nolan, Parkinson's UK

Frances Borrer, Patient Insight Partner, Arthritis Research UK

A well-attended seminar was held during the lunch break offering a practical introduction to Patient and Public Involvement for companies and medical research charities. The seminar addressed questions such as what should patient involvement look like, and what are the benefits for organisations?

The seminar began with a discussion around the value of patient centricity and involvement, which made it clear that this type of approach changes attitudes to collaboration. Claire described the strategic importance of collaboration for Parkinson's UK, emphasising that this was a two-way conversation. The term 'involvement' (as opposed to, for example, 'participation') implies a two-way connection in all stages of drug discovery, not just with patients as subjects in clinical trials.

Patients can be involved throughout the research lifecycle – from setting research priorities (broadening understanding), through planning (development of attitudes to risk, end points, inclusion and exclusion criteria, public involvement plans, involvement on trial steering committees, recruitment strategies), at regulatory discussions, and at adoption and delivery of effective research.

Chris also stressed that times are changing – patients want charities to engage with industry. From a recent Arthritis Research UK survey, only 6% of patients said they did not want the charity to engage with industry. There is a clear appetite for these kinds of partnerships.

Chris then introduced Frances, an Arthritis Research UK Patient Insight Partner. Frances was diagnosed with rheumatoid arthritis at the age of 23, and at her current age of 63, she has a self-confessed lifetime of experience.

Frances explained that rheumatoid arthritis was not her career – but that no-one understands a condition better than someone living with it. Seemingly small details to a company, such as asking participants in a study to fill in multiple questionnaires during a study, would be nearly impossible feats for many arthritis patients who struggle to hold a pen or type. Frances made the point that patients can also provide solutions too, pointing out that many patients keep a diary of their symptoms and pain scores. A company could use this to gather feedback from patients on these issues, rather than asking them to complete an additional questionnaire.

Frances also spoke openly about the importance of language – especially around clinical trial inclusion criteria, where it often says, "the patient has failed on previous drugs". Frances said the patient hasn't failed anything – it's the drug that failed the patient. Language is important in creating a balanced relationship between the researcher and the patient.

Frances asked the audience to make a brave first step and try patient involvement activities. She stressed it doesn't have to be perfect. She also asked pharmaceutical companies to be brave – reminding everyone in the room that involving patients also makes good business sense.

Panel Discussion: Frameworks Supporting Partnerships

Chair: **Mark Duman,** Patient Advocate

Panel: **Luke Cowie,** NICE

Alessandra Gaeta, Medicines Discovery Catapult

Eric Low, Amyloidosis Research Consortium UK

Paul Robinson, MSD

Heather Simmonds, PMCPA

The afternoon panel discussion featured four short case studies on partnerships for drug development: both partnerships with patients and partnerships between organisations. These were followed by an extensive discussion, ably chaired by clinician and patient advocate Mark Duman.

The first talk was given jointly by **Eric Low**, who chairs the Amyloidosis Research Consortium UK, and **Luke Cowie**, a scientific advisor at NICE. It focused on the collaborative role of medical charities and patient advocacy groups in clinical research, at a time when it seems increasingly difficult to translate our fast-growing knowledge of human biology into tangible patient outcomes. Only the patients will know to what extent they are willing to trade risk for benefit, and this will vary from patient to patient. In myeloma treatment, for example, some patients will prefer the convenience of an oral treatment while others would rather take an intravenous treatment with a probability of more significant clinical improvement. In this and other indications, NICE is collaborating with charities in researching patient preferences to feed into clinical trial design.

Despite decades of scientific innovation, the process of drug discovery is still 'too slow, too expensive and inefficient'. **Alessandra Gaeta**, Syndicate Programme Director at the Medicines Discovery Catapult, explained how her organisation is re-thinking the traditional, linear model of drug discovery with the first half of the pathway a 'patient-free zone' to put patients and their associated data at the centre. Involving patients as research partners in drug target selection and validation, for example, should allow companies to select outcomes that are most important to them and, to some extent at least, 'de-risk' the discovery process.

The 'Big Pharma' sector has been thought of as the most conservative part of the industry, but collaboration is becoming the norm even there. **Paul Robinson**, the Executive Director of Patient Perspectives at MSD, described a European consortium with no fewer than 34 mainly industrial partners that his company and ABPI are involved in. PARADIGM (or 'Patients Active in Research and Dialogues for an Improved Generation of Medicines') has been funded by the EU's Innovative Medicines Initiative to develop tools for involving patients in all stages of drug development, from priority setting through trial design to dialogue with the regulators. Patient engagement is already happening and it is up to companies and advocacy groups to develop ways of working together to maximise its benefits.

The ABPI set up its Prescription Medicines Code of Practice Authority (PMCPA) to administer its code of practice throughout the UK pharmaceutical industry. This sets standards for medicine promotion including the prohibition of advertising prescription medicines directly to the public. The final speaker in this session, PMCPA director **Heather Simmonds**, plotted a path through the legislation, standards and self-regulation so companies that set out to involve patients and the wider public in pharmaceutical development could continue to do so, whilst adhering to the industry's widely respected ABPI Code of Practice.

These short presentations were followed by a wide-ranging discussion that raised questions about the role of contract research organisations in patient involvement; the extent to which patient preferences can be encouraged at all points in the drug discovery pathway; the value of the QALY concept and the need for the ABPI's Code of Practice to adapt as practice itself changes.

Afternoon Plenary: Talking about Patient Data

Nicola Perrin, Wellcome Trust and **Emily Travis,** Patient Advocate

Data, including patient data, is increasingly important in healthcare, but the use of data from individual patients can still be problematical. The issues underlying the use of patient data were discussed in the afternoon plenary session, in a fascinating conversation between **Nicola Perrin**, head of the Understanding Patient Data initiative at the Wellcome Trust, and **Emily Travis**, a scientist, Stage IV cancer patient and self-confessed 'data nerd'.

Perrin and Travis began by showing a short, accessible video produced by the Wellcome Trust that described the importance of patient data in diagnosis, treatment planning and medical research, and how the privacy of individual patients can be safeguarded. Perrin explained that most people still know little about how data is used in medicine and newly diagnosed patients will have many concerns about this issue, but they generally become more comfortable with sharing their data the more they know about it. She and her colleagues are developing resources to help patients and the wider public understand what data can be collected from them and when, and how it will be used.

Travis illustrated this with a moving story of her own experiences as a cancer patient. She was diagnosed with leiomyosarcoma in September 2014 and went into remission following surgery; bone and liver metastases were discovered in late 2017 and she is now stable and feeling relatively well on a clinical trial. She described two points on her 'cancer journey' where she could have been helped by better use of data: the month preceding her accurate diagnosis, when she was shunted backwards and forwards between five hospital departments, and the four months between the scan that revealed spots on her liver and surgery for metastatic disease. But if data is to be widely available, it must be shared; the public supports data sharing if it is done responsibly, so there is an urgent need to champion the responsible use of patient data.

Closing Keynote: Lessons from a Mighty Boy

Sarah Pullen, Author of *A Mighty Boy: A Mother's Journey Through Grief*

The final lecture of the conference was a tour de force: a personal story that underlined all the reasons why patient engagement matters. **Sarah Pullen** is a full-time mother of 'a bundle of boys' who has endured what must be every parent's nightmare: the death of a child. Silas, the 'mighty boy' of her title, was ten when he was diagnosed with glioblastoma multiforme and eleven when he died. She described being told he had a few months to live (with treatment it turned out to be 17) and sent away with no information, not even a leaflet. Although patient leaflets for this cancer are (and probably have to be) 'terrifying', she would rather have known the worst. Even now, cancer information on the Internet is patchy and can be misleading. During those 17 months she and her family rapidly became 'experts by experience' in Silas' tumour.

Since her son's death, Pullen has channelled her grief into writing – specifically, her profoundly moving book *A Mighty Boy*, published by Unbound in August 2017 – and into activism. The family set up the Silas Pullen Fund under the auspices of the Brain Tumour Charity to raise funds for research into brain tumours in children, and the website http://www.itisanobrainer.com/ to raise awareness of this devastating disease. The Brain Tumour Charity is also establishing BRIAN, a global databank of medical records submitted by patients themselves with the aim of enabling their successors to make more informed decisions about their treatment.

Pullen ended her talk with two quotes which, taken together, could sum up the purpose of the day. One is from Dame Tessa Jowell: "*So many cancer patients collaborate and support each other. All we now ask is that doctors and health systems learn to do the same and for us all to work together and learn from each other."* More broadly still, she quoted the neurosurgeon and cancer patient Paul

Kalanithi: *"Human knowledge is never contained in one person. It grows from the relationships we create between each other and the world, and still, it is never complete."*

Final Remarks

In closing the conference, Thompson for the ABPI and Burnand for the AMRC both thanked all the speakers, and particularly those 'experts by experience': the patients and carers who had shared their stories with delegates. They both stressed the need for significant change in the industry. Burnand picked up on a phrase that Chung had used in her opening keynote: the 'Trojan mouse' that makes small changes that become significant. We can all aspire to be Trojan mice. Thompson is intending to commit some of the ABPI's resources to helping companies become more patient-centric, and to investigating whether there need to be changes to its code.