Introduction

Exploring personalised cancer medicine

Personalised medicine for cancer is at the forefront of the new bioeconomy and visions for the future of healthcare. It promises treatments tailored to individuals' genomes and those of their cancers, as well as more precise diagnosis, prognosis and prevention. Widely celebrated as revolutionary and transformational, the risks and ethical conundrums of personalised medicine are confronted every day by patients, clinicians and researchers, but are consistently underplayed in the mainstream media (Marcon et al. 2018). Cancer research has a long history of optimism: the hope of living well with and beyond cancer permeates much of contemporary life. But not everyone is set to benefit from these advances in cancer medicine, and concerns about hype and over-optimism can be found across practitioner, academic and patient communities. Cancer patients, their families, policymakers, practitioners and researchers are entwined in novel practices as they navigate the promises and pitfalls of personalised medicine. In this book we investigate these practices, focusing on what is involved in promoting, receiving and delivering personalised molecular predictions, diagnoses and treatments for cancer. How is the work of crafting the optimistic or more modest and contested futures of personalised cancer medicine distributed and to what end? What kinds of value – personal, social as well as economic – are created through these practices, and for whom (Dussauge et al. 2015; Birch 2017)? How might things be organised differently to produce different kinds of values and futures for cancer patients, healthcare providers and society more generally?

Our book is based on a five-year UK-based multi-sited qualitative study of a diversity of patient, carer, practitioner, researcher, manager and policymaker experiences and accounts of genomic medicine in

cancer, funded by a joint Senior Investigator Award in Society and Ethics from the Wellcome Trust.¹ We draw on a rich diversity of interviews, observations in clinics, laboratories and public events as well as textual analysis of public, policy and professional literatures and media discourses.² The focus of our study has been on genomics, the branch of molecular medicine concerned with mapping genomic profiles, and how this is reshaping cancer medicine and the experience of cancer. This has included diagnostic and predictive tests for cancer based on molecular profiling (shifting from single genes to panels of genes to whole genome and next generation sequencing); treatments targeted at cancers with particular molecular signatures (sometimes called tailored treatments or precision oncology); clinical trials of these new diagnostics and treatments, including new kinds of trials which offer combinations of treatments and/or adapt treatments over the course of the trial; and other research studies which gather molecular information about patients and their cancers to try to identify subtypes of cancer that are more responsive to particular treatments. We have also explored patient and public involvement in personalised cancer medicine, not just as service users or research participants, but as representatives on patient panels and other forms of involvement and engagement. Together, these activities and agendas are key parts of so-called P4 medicine, characterised as predictive, personalised, preventive and participatory (Hood and Friend 2011).

In a culture marked by enormous anticipation that biomedical innovations such as genomics may cure feared diseases such as cancer, it is hard to sound a note of caution without appearing to dash those very hopes. Maybe this can come across as a lack of compassion or even a disregard for those experiencing the disease and for those involved in their care. Our intentions could not be further from this – we want to put such experiences at the centre of our analysis because they are at the centre of personalised medicine. Yet we also want to address some of the wider, more distant processes of biomedical innovation, their drivers and their consequences. This involves unpicking how the cultural imperative to be hopeful and positive about the potential to overcome cancer, an imperative amplified by the promises offered by powerful molecular technologies, is enacted and experienced by people affected by cancer. Patients and their supporters frequently voice these hopes and obligations

not only for their own, but for other patients' futures, invoking the need to extend these hopes to others. As one patient in our study commented: 'I think it's hugely exciting and I don't know if the message has entirely got across to the public out there but it's just so exciting.' Together with their clinicians, patients try out new diagnostics and drugs, take part in research, trials, fundraising and campaigns to bring this future into being. These hopes peppered our encounters with practitioners too – in the words of one oncologist: 'My hope is that by continuing to dissect the genomics [of cancer] we will come up with better treatments for specific subgroups of cancers which are genomically driven.' Being hopeful is not just an activity for the cancer clinic or clinical trial, it is part of everyday life too, marking encounters with friends and family, charitable fundraising and popular culture, where stories of the triumphs and losses of cancer are ever present. Governments, institutions, organisations and companies together with scientists, healthcare practitioners, politicians, business people and regulators also actively anticipate future benefits, including service improvements and cures as they seek to encourage participation and raise support and investment for genomic research, healthcare and bioscience infrastructure, including new molecular diagnostics and therapies for cancer. Policy discourses are replete with the language of hope and anticipation, asking us to 'welcome the genomic era and deliver the genomic dream!' (Davies 2017: 1).

These kinds of promissory discourses can be problematic for patients and professionals alike. Concerns have been raised about over-inflated expectations and harsh disappointments when test results are poor, or treatment options diminish, including when experimental and cutting-edge drugs cannot be accessed. One of the clinicians in our study clearly articulated this caution when noting, for all of the anticipation about exceptional responses, in the trial in which they are involved: 'I think that's fair to say, I mean I don't think any of the patients I've seen has had a dramatic response to date.' Frustrations with the sense of obligation always to be positive are also well documented, exemplified in feminist challenges to the 'good patient' and 'pink washed' cultures of breast cancer in particular (Ehrenreich 2001; Jain 2013; Steinberg 2015). As one patient in our study, reflecting on her experiences of being positive for family and friends fundraising on her behalf, said: 'I'm a very

strong person ... but it did get to the point where I just felt like I cannot cope with this' (Stacey, see Chapter 6). Living in a culture of hope takes work and involves an emotional toll, no matter your orientation towards the promises of personalised, genomic medicine for cancer.

Traversing people's experiences and personal accounts of living with the risks and realities of cancer developing, mutating, resisting, progressing and returning and the professional work to identify, prevent and mitigate the effects of cancer in busy laboratories and clinics, we look at the kinds of futures being crafted by the actors involved, and how they interact, inflect and at other times coexist in parallel planes as genomic medicine unfolds. Our key focus is on how cancer patienthood is developing in the genomic era, including how patient identities and collectives are evolving in the context of molecular information and interventions (Clark et al. 2003; Landzelius 2006; Sulik 2009). Our exploration of performing and living 'patienthood' brings such experience into dialogue with the wider drivers of personalised medicine. This covers questions of what counts as being a 'good' or 'deserving' patient living with cancer, its risks, mutations and remissions, and how patients construct hopeful futures of cure and prevention for themselves and others, as well as the more contingent futures where foreshortened lives with cancer can be made liveable. We also explore how crafting these futures takes time, resources and care from affected individuals, families and practitioners, teasing out the strategies of maintenance, the silences, engagements and even the avoidance that this involves. This work is, at times, intense and difficult; we consider how it takes place in the context of personhood more broadly, including other kinds of life strategies, working practices and political agendas which co-produce as well sometimes overshadow or interfere with crafting personal and collective futures. The futures of patient collectives (including families and former patients), institutions and workplaces also have to be hewn alongside the work of cancer management and control, including mutations in cancer patienthood as the types and risks of cancer are stratified along molecular lines. We consider how the accounts and practices we uncover trouble narrow understandings of individual responsibility and biomedical innovation as the engine of prosperity, linking this to wider struggles around futures, democracy and value in late capitalist societies.

Future-crafting: great expectations and questions of value

More than a decade after the financial crisis, the slow growth of damaged economies and the politics of austerity in countries such as the UK have widened health inequalities and hollowed out public services. Cancer can be seen as a bellwether for late capitalist societies. Although survival rates for some cancers have improved in recent years (Arnold et al. 2019; Harrison et al. 2019), people's chances of surviving cancer vary not only according to which cancer they have but also their socio-economic circumstances. In the UK, stubborn inequalities persist and improvements in outcomes are not evenly experienced. Cancer remains a major cause of death, while estimates suggest that in the UK, 38 per cent of cancers are preventable and almost half of cancer patients are diagnosed at a late stage.³ Incidence is on the increase, nationally and globally, due to ageing populations, with the most common cancers worldwide being lung, female breast, bowel and prostate cancer. Cancers with poor outcomes (e.g. liver, stomach) are more common in richer countries, but researchers have found that people living in poorer countries are experiencing increasing rates of cancer (Merletti et al. 2011), and there are significant differences in survival (although not incidence) depending on race and ethnicity (Ward et al. 2004). With the exception of breast cancer and melanoma, cancer is more common among deprived groups in countries such as the UK. Research in England has found that people from the most deprived areas have the highest rates of lung and cervical cancer, whereas people from more affluent areas have higher rates of breast and skin cancer (Shack et al. 2008).⁴ Despite success stories due to improved treatments and prevention programmes, some cancers remain stubbornly incurable and some are less visible in research, fundraising and the media. Fear of cancer and of a lack of timely intervention are compounded by problems with health service provision, including in publicly funded systems such as the National Health Service (NHS) across the UK, which is currently experiencing severe staffing problems.⁵ Improved screening and prevention programmes, earlier diagnosis, and better, more effective treatments have improved cancer mortality rates for some cancers, but services are stretched, patient experiences are diverse, and access to expensive treatments including some chemotherapy may not be available to all. Charitable fundraising for individual treatments,

living costs and hospice treatment is on the increase, with patients and their families turning their leisure time and private lives over to public displays of worthiness in an effort to raise resources for targeted treatments not currently provided by the state.

The hope of personalised treatments for this most feared disease has long been part of a wider set of expectations and investments in scientific capacity and biomedical expertise in nations that have nurtured world-leading universities and hospitals as part of their global economic positioning. As countries such as the UK struggle to carve out a new economy in the face of nationalism, predatory capital and political upheaval, the bioeconomy has grown in importance. Harnessing the scientific and biomedical expertise and infrastructures of the country, particularly in the golden triangle of the south-east of England, together with the data and biological assets of the NHS, the UK has invested heavily in the genomic life sciences, with cancer a key site of collection, analysis and intervention. Working in close alliance with private capital, through a range of spin-out companies and multinationals, the UK national and devolved governments, together with major charitable funders and the expertise of the university sector, have developed an ambitious set of projects, trials, studies and initiatives to expand the new economy of personalised medicine. Patient data, tissue and other kinds of engagement and participation (for example, to improve genomic literacy), and involvement in research and uptake of services are key to the success of this new economy.

A new social contract with cancer patients is therefore emerging where their participation in research is becoming routinised as part of a drive to develop biomedical research and innovation and to improve health systems, services and patient outcomes. The vision is that patients' participation will grow the economy and secure the longer-term future of the NHS, including via special licensing and profit-sharing agreements with industry. As a result, services will become more agile and efficient, avoiding unnecessary and ineffective treatments through a more personalised approach. A focus on preventing disease rather than having to spend money on treatment will generate further savings, with the rest of the profit realised by industry contributing to national economic growth more generally. Meanwhile, individual patients are supported in their quest for tailored therapies and diagnosis through a range of experimental and cutting-edge

treatments and trials. The industry, charities, advocates and carers encourage and enable patients to source new treatments, find new trials and even challenge bureaucratic decisions to extend their compromised futures. But not all patients or professionals are convinced of the logic of these investments or promised benefits, especially those who are too ill or those for whom new therapies remain beyond the horizon, only accessible for future patients, not patients in the here and now. As one patient advocate, Toni, commented about precision medicine: 'It's got everything going for it in terms of making the gap even greater between the richer and the poorer countries because these drugs, by definition, are much more expensive but they have a huge difference in their ... potential impact.' Yet opportunities and capacities to voice this kind of concern or critique are constrained by the dual promise of innovation and hope that surrounds personalised cancer medicine.

How, then, can we understand and, more importantly, intervene in these possibilities, inequalities and silences around personalised cancer medicine to craft better futures for patients, healthcare workers, services and economies? To answer this question, we need to begin with what people are currently doing – to make personalised cancer medicine work in practice – to explore what future-crafting involves and what kinds of futures are being anticipated and pursued. We need to consider how futures overlap and impinge upon each other and widen our focus from the normative vision of these biomedical developments to consider what kinds of alternative futures people carve out through their encounters with personalised cancer medicine. And we need to attend to how value circulates through these approaches and agendas – what kinds of value are being sought or achieved, and how might this be otherwise?

There are many rich and varied traditions of social scientific and philosophical literatures on which we have drawn to guide our inquiry, detailed throughout the chapters that follow. We can, however, summarise some of our key influences here, by way of introduction.

First, we are influenced by feminist and science and technology studies (STS) scholarship which seeks to change, as well as describe, the social world. This means that we aim to build on the rich description of what we have encountered in the course of our work, drawing from our findings to imagine different futures and

future-crafting activities that might be cultivated as a response to our inquiry. This is not only a matter of ‘putting ourselves in our story’ as a reflexive ethnographic project, but of actively grappling with our own version of future-crafting. We do not do this, first and foremost, as cancer patients, or relatives of current cancer patients, but as engaged scholars with a stake in our collective futures whatever role cancer might play. As part of this engaged scholarship we have also tried to remain sensitive to the gaps, silences and omissions in our research (Haraway 1988; Puig de la Bellacasa 2011; Murphy 2012; Jain 2013), particularly the limitations in the range of voices and experiences that we have been able to document here, something we discuss further in Chapter 7. We also endeavour to reflect on our own practices of narrative as a craft – cutting, sewing, sticking, fitting, tinkering, patching data and analysis. In so doing we try to be mindful of the contingencies and relationalities, the messiness and stop-start nature of storytelling as future-crafting. This allows for the possibility of it being, at times, a relatively solitary individual practice and, at other times, a collective practice, enacted with others in one place, or across different localities and timescapes.

Second, and relatedly, we are putting patient and practitioner experiences of genomic medicine centre-stage, trying to pull together an analysis from a wide array of accounts and observations of how patients think and feel about their cancer and its treatment in the genomic era, and how practitioners keep patients in mind as they try to develop research and provide a service. We combine an interest in professional accounts and practices as well as policy approaches and agendas in an effort to understand how professional jurisdictions, epistemologies and organisations are changing in relation to personalised medicine (much of which is discussed in Chapter 1), with an interest in the complexities, tensions and contradictions of the lived experiences of patients. We are influenced by scholarship which prioritises attention to articulation work, care and emotional labour (Star 1985; James 1992; Twigg et al. 2011; Murphy 2015), work that is traditionally associated with women’s devalued contribution but that is also a key part of being a patient, a provider of healthcare and a worker in the service sector. This draws our attention to the routine, mundane, everyday work of genomic medicine for cancer as a form of craft, including the intricate and skilful work of patients or practitioners that may be invisible and undervalued but is crucial

to the test, treatment or research being conducted, and thereby closely linked to the work of crafting a future for ourselves and others. It also invites us to think critically about how care and other kinds of work can be experienced as neglect or inattention by others (Murphy 2015). We attend to how patient and carer identities and relationships are changing as they do some of the work of cancer research and treatment, not just as providers of data or care but as champions of new kinds of services and research, whether as representatives, campaigners or supporters of fellow patients, engaging in new kinds of ‘evidence-based activism’ (Rabeharisoa et al. 2014) and biosociality which forms a crucial part of the landscape of contemporary biomedicine (Rose 2001).

Third, and finally, we are focusing on futures, both imagined and made, as crafting projects rooted in practice (Adam and Groves 2007). There is a long and fascinating tradition of scholarship which investigates imaginaries and expectations as meta-discourses that perform the sociotechnical economy, establishing new markets and innovation (Hedgecoe and Martin 2003; Selin 2008; Tutton 2012; Jasanoff 2015; Brown and Rappert 2017). Medical humanities and the sociology of health and illness both have a rich seam of research on survivorship and identity-work where crafting ‘culturally plausible narratives’ (Frank 2003) involves embodied work in the lives of cancer survivors and the communities they come to feel responsibilities towards (see also Kaiser 2008; Kerr et al. 2019). But we know less about how contemporary cancer patients or prospective cancer patients engage with, take up or repudiate dominant expectations of prediction, personalisation, prevention and participation in this genomics era. As Michael (2017a) argues in his analysis of the enactment of ‘big’ and ‘little’ technoscience futures in which we are embroiled, there is a need to attend to how lived experiences and larger cultural and economic narratives interact. For us, these engagements, or indeed disengagements, need to be properly understood if we are really to appreciate how innovation works in practice and how it can be improved or repurposed for social good. Questions of value (Dussauge et al. 2015) are key, and here we draw on the area of valuation studies which has focused attention on the kinds of value and processes of making value that characterise all facets of contemporary working and intimate lives. In addition to understanding how economic value is produced, we want to know what

other kinds of value are being made and come to light when we attend to the lived experience of innovations in the making, for recipients and subjects of research as well as professionals. This includes the value of being together with others, of feeling cared for and of worth, the value of an imagined community of other and future patients and of individual and collective meanings.

Our approach

We have tried to follow through on our commitment to lived experience, imagining other ways of generating and sharing value and attending to the craft work of future making through our own scholarship and ways of working. As a large team of researchers, we have taken on different roles and relationships to the project, the field and the writing of this book. We have also worked with others not represented as authors in this work, but whose contributions we have nevertheless sought to recognise as we write. It has been particularly important to us to write as a collective and to recognise the work of researchers who have done the bulk of data generation in the attribution of authorship for this work. At the same time, we note that we have not chosen to produce an edited collection or to attribute authorship of particular chapters as a way of delineating our contributions. Instead, we recognise that some of our team have had more of an input to specific chapters, and we have worked collectively to review and refine the analysis and writing as part of our wider collaborative efforts.

We conducted around 250 interviews with clinical and laboratory staff, patient advocates, people affected by cancer and some family members across a few UK cities between 2016 and 2019. The bulk of this fieldwork was performed by the researchers on the project (Tineke Broer, Choon Key Chekar, Sue Chowdhry, Emily Ross and Julia Swallow). This included interviews with patients and family members across five main case studies of genomic tests, studies, trials and treatments in NHS settings and private healthcare. We also carried out over sixty observations in clinics, laboratories and at public events, and a further set of digital observations across online platforms including cancer charity forums, Twitter, blogs and Facebook pages. Working with these groups and in these settings

has been difficult and complex, not least because patients are often very unwell. Many of the patients we interviewed as part of our work have died, sometimes shortly after the observations or interviews took place. This brings with it a strong obligation to respectfully analyse their accounts, in all of their complexity. Cancer experiences are highly personal and emotional, and capturing the details of these experiences without intruding or causing distress is a finely balanced undertaking. Not only does it involve empathising, sensing feelings and capacities to contribute, especially knowing when to stop interactions, but it encompasses navigation of the complex institutional arrangements and representatives involved in cancer research and care. This spans the formal structures of ethical review and risk management as well as the organisational and logistical aspects of research studies, laboratories, clinics and patient pathways. It also involves working beyond physical institutions across virtual networks, to find people to engage with as part of the research, secure agreement for observations and analysis and ensure that patients and interested publics are able to shape our research agendas rather than simply act as research subjects or audiences. We had to work closely with, indeed rely upon, staff and patient advocates who acted as key gatekeepers for our study, and in so doing navigate the burdens we placed on their own time and resources, which were often stretched or in demand from numerous quarters. This included working with two Patient and Public Involvement groups we set up at the start of our research, who guided us throughout on the appropriate ways of involving and approaching patients regarding participation and in relation to the dissemination of our findings.

Our research took place at a time of crisis and worry about the future of the National Health Service after a prolonged period of low investment following the financial crisis of 2008 and an ongoing process of marketisation. It was also shaped by the cultural politics of Brexit in the UK and a growing discomfort about the politics and identities surrounding immigration, inequality and nationhood. Although this makes it a somewhat British story, it is also international in its implications and scope. We can trace the ways in which patient communities, promissory rhetoric, drugs, tissue, novel medicines and diagnostics traverse nations through our own case studies. Yet we also see many of the stories of genomics and data as national resources, and access to tests and treatments as patients' rights and

responsibilities, in other national agendas and stories from patients in other countries. The complex and, at times, troubled context of the NHS clinics and laboratories made us particularly attentive to the activities and dedication of clinical and laboratory staff involved in making genomic medicine work for patients in the present and for the future.

We also became acutely aware of the gaps or absences in our inquiry as we made our way through the episodic encounters in the hospital or the community. We carried with us a strong sense of the more marginalised patients and social groups who we did not manage to speak with and include in our work, and the ever present danger that we would slip into the amplification of more articulate and insistent repertoires or ‘culturally plausible narratives’ (Frank 2003) as we conducted our research, as well as the difficulties of not sufficiently attending to or not being able to attend to silences, rejection and non-participation. We reflect more fully on this across each chapter and in particular in Chapter 7.

Below we detail the case studies and primary focus of each chapter, drawing out the main themes of our analysis, which we reflect upon in the concluding chapter. We briefly consider these recurrent themes here to provide a scaffold for the detailed analyses that follow and to highlight some of the implications of our work for scholarship about personalised medicine and other innovative health technologies.

First, understanding how hope operates involves grounding STS and other sociological analyses of promissory tropes in the everyday, tangled practices of personalised cancer medicine. A critical appreciation of the technoscientific promise of personalisation and attention to failures and disappointments in practice is vital, but we must also acknowledge the limits of critique, given the ways in which hopefulness around personalisation is a resource which can be taken up and reworked by embodied beings to craft liveable presents and futures. The value of critical engagement with tropes, discourses, templates and rhetoric is blunted and complicated by the messy realities of living with cancer or trying to care for those it affects. Attending to caring practices (including their limits), work, and the measurable and more diffuse kinds of care this generates has helped us to reorient our critical impulse to an appreciation of expectations as contingent, contradictory and in the making. We

ask our readers and other researchers to take this complexity to the heart of their engagements with the cancer encounters we capture here and to their scholarly inquiries with patients and practitioners more generally.

Second, our research has heightened our sense of discomfort with the experiential, identity-focused work of the sociology of health and illness where documenting individual narratives and lived experience takes precedence over engagement with the institutional, political or economic processes through which experiences are lived out. Working across our case studies has made us acutely aware of the institutional structures that determine who can access or remain on these novel treatments and tests, taking us well beyond questions of survivorship as identity-work to survivorship as part of a wider political economy of material and financial resources. Medical sociological approaches to cancer crafting that are primarily concerned with identities and experiences, focusing on studies of particular types of cancer patient or community, can all too easily miss this wider terrain of patient, practitioner, carer and post- or even pre-cancer patienthood across which initiatives such as personalised medicine operate. Writing this back into their stories is a laborious and difficult process, but it is key to understanding how these technologies make their way through the world to impact patients and their carers.

Third, although we draw huge inspiration from theories and ideas of biosociality and citizenship where structures of feeling, responsibility and identity are interwoven with politics and economics, we find ourselves concerned that, once again, the focus on how experiences are organised into communities with particular subtypes or conditions does not readily fit with what we have encountered across our research, which is much more fluid and multi-layered than a focus on the molecular details of diagnostics might suggest. Patients are sometimes joined in shared agendas and pursuits in relation to their particular type of cancer, but they are often working with a diversity of other patients and allies, forming networks and collectives across molecular and bodily categories as well as across other social categories, including class and gender. We need to attend to these relationalities and the possibilities they bring for new kinds of cancer politics of solidarity in the era of personalisation, just as we must remain mindful of those patients, or groups of patients,

who are excluded or marginalised from these new collective and community formations.

Fourth, welding together the different layers of engagement with personalised medicine, traversing big and little futures, also involves thinking about the work of patients, carers and researchers together, crossing laboratory, corridor and clinical spaces and moving between physical and virtual worlds where patients and their allies form networks and agendas. This process of ‘moving across’ settings and subjects is not a research technique that is readily accommodated by disciplinary or institutional traditions, especially ethical review or risk management, but it is vital to gathering a nuanced understanding of how personalised medicine operates at a range of levels, and, crucially, changes over time for individuals and collectives. We hope to have captured this despite the limitations of our work, and to advocate for a bolder form of interdisciplinary, ethnographic inquiry that co-researches with practitioners and patients to explore these new biomedical territories. These collaborative ways of working are vital to understanding and seeking to improve the benefits personalised medicine might bring to patients and practitioners alike.

Fifth, and finally, this study of genomics is part of a suite of social scientific and medical humanities research into innovative health technologies that have seen significant investment and interest from scientific institutions and policy actors. We have benefited from this interest and we are grateful for this support. But our study of genomics has, at times, felt like chasing a rainbow, as we switch between reading scientific and policy texts to the daily realities of the clinic, the laboratory or life with cancer. Researching with and caring for cancer patients, as well as living as best one can with cancer, certainly encompasses technological forms of personalisation and precision, but also involves navigating organisational and environmental infrastructures and barriers to care and science, work which can be relentless and at times overwhelming. We fail to capture this when we maintain a blinkered focus on the small numbers of patients – the unicorns, as one of the clinical trials assistants in our study described them – who benefit hugely from genomic personalisation. Even when we manage to capture the complexities of being part of genomic research or being on targeted treatment, we risk erasing the experiences of patients and practitioners for whom these new technologies are not available, are maybe largely irrelevant or are just one part

of a wider picture of research and care. Researching genomics and other forms of personalised medicine needs to attend to all of these forms of non-participation to fully capture what these technologies mean for patients, practitioners and communities.

Book outline

Personalised medicine for cancer has many technologies, research initiatives and forms of care, including those in current practice, those in development and those anticipated. It has a variety of different meanings, interpretations and antecedents. In this book we will focus on a range of case studies of genomics and cancer that give insights into the main approaches and agendas in personalised medicine. Throughout these case studies we explore the different agendas, experiences and work involved in making the test, treatment or research trial/study work, and what kinds of value are derived in the process. We attend to the way responsibilities are distributed as futures are envisaged and enacted, how work is recognised and rewarded, what kinds of voices or experiences are discounted or absent from view, and how particular kinds of value are generated in the process. Here we add a further double P to our study of the P4 medicine agenda of which genomic medicine for cancer forms a part – *practices of promise* – alongside prediction, personalisation, prevention and participation. Throughout we highlight the constructed and contingent nature of these transformative agendas while also drawing attention to and at times querying their normative attributes.

Chapter 1 sets the scene for these case studies, drawing on STS and related literatures to trace the development of molecular understandings of cancer, tests and treatments and their place in the cancer clinic. The chapter covers the evolution of clinical trials and biobank research, including the rise of adaptive, basket and umbrella trials. We also explore the development of new molecular taxonomies of cancer and the implications of this fragmentation for research and treatment. The drive for personalisation is associated with new understandings of cancer as evolutionary and adaptive, and we explore how professionals make sense of this dynamism when developing treatment and understanding its effects, expressing both optimism and caution about their impact and potential. We

consider the new technologies and infrastructures that genomic medicine in cancer involves, particularly in relation to tissue, data and eligibility, as well as new professional arrangements, including multidisciplinary team working, national and international consortia and public-private collaborations. We explore expert disputes, for example about the effectiveness and value of new genomic approaches, particularly in relation to the development of flexible or adaptive trials. Throughout we reflect on what these developments mean for making personalised cancer medicine work in practice, key themes in the chapters to follow.

The next three chapters form a set; they look across a range of tests, treatments and research agendas in personalised cancer medicine in NHS patient care at the time of our study. We explore personalised medicine as healthcare practice and as clinical research, beginning, in Chapter 2, with a test that is now part of standard care, moving on to consider another test that was being utilised in a small feasibility study in Chapter 3, and then to a much larger national trial of targeted treatments discussed in Chapter 4.

Chapter 2 explores the promise of prediction and prevention of recurrence in personalised medicine for some kinds of breast cancer through the case of a genomic technique already widely adopted within the UK NHS: gene-expression profiling. Although breast cancer has seen rapid advances in diagnosis and treatment, and is often cited as one of the highest-profile cancers supported by well-resourced research initiatives, it remains the most common cancer in the UK and represents 7 per cent of all cancer deaths.⁶ We consider a genomic test, Oncotype DX, which seeks to identify among early breast cancer patients those who would or would not benefit from chemotherapy to prevent future recurrence. The aim here is to limit exposure to chemotherapy, which can be toxic and debilitating. The test was made valuable to the health service, practitioners and patients as a means of prediction and prevention, including via practitioners' and patients' contributions to processes of regulatory and clinical decision making surrounding the test. Considering how the test was envisaged as a benefit to the NHS and to patients in policy, practitioner and patient accounts of their experiences of decision making regarding chemotherapy, we explore how it fitted in with already complex cancer experiences and hopes for a cancer-free future. We look at

how the narrative that the test offers reassurance and prediction came to dominate policy, but also consider situations where prediction and prevention were more contingent and provisional, particularly in the context of clinical encounters.

Chapter 3 explores another technique that offers personalised predictions of responses to treatments for cancer based on molecular profiling, this time for later stage gynaecological cancer patients seeking to prolong foreshortened futures in a non-curative context. Gynaecological cancers encompass cancer of the womb, ovaries, cervix, vagina and vulva and mainly affect post-menopausal women. Awareness of these cancers is low compared with other cancers such as breast cancer (in women); diagnosis and treatments and a range of campaigns and research agendas have been developed to address this. We consider a commercial test developed by a company for which we have adopted the pseudonym *Virtue*, not yet in routine use, that was embedded in a feasibility study in one hospital. We looked at how the feasibility study was part of building a network of collaborations and evidence to extend molecular tumour profiling in gynaecological and other cancers, and how expectations of precision and actionability were fashioned yet not always realised in practice; we focus in particular on the kinds of work this involved for practitioners and patients in the process.

In Chapter 4 we explore another route by which advanced cancer patients are offered the promise of tailored treatments that may prolong their lives, focusing on an adaptive multi-centre trial for lung cancer that aims to optimise treatments through a process of ongoing adaptation. Lung cancer has a lower public profile than some other cancers and it remains highly stigmatised because of its associations with smoking and higher prevalence among disadvantaged socio-economic groups. Concerted efforts are underway to enhance understanding of the disease and to develop new treatments. We show how the promise of the trial and targeted approaches offered a glimmer of hope for patients and practitioners coping with a bleak prognosis, exploring how the trial, treatments and patient and institutional futures were optimised in these very challenging circumstances (Montgomery 2017b). We look at how disappointments, failures and anxieties were navigated by patients and practitioners through containing scepticism backstage, calibrating expectations,

including lowering (personal) expectations of extended futures (Gardner et al. 2015), and cultivating expectations that other patients will benefit in the future instead.

The next two chapters explore personalised medicine approaches that are more novel and to some extent remote from standard NHS care, but nevertheless rooted in the institutional, political and economic dynamics of UK healthcare. Chapter 5 looks at a research study of great importance to the national project of building the bioeconomy, where patients involved in cancer treatment are being recruited, but where results are unlikely to impact directly on their care. Chapter 6 looks beyond the NHS to people who are not able to get treatments that they want as part of standard care because of the regulatory and approvals process, and so are involved in raising funds or self-funding these treatments privately. These kinds of personalised medicine are therefore more innovative and speculative than the cases discussed in the previous three chapters, and as such they involve a range of pioneers and vanguards. Both chapters are set within the context of considerable inequalities in access to care and research and in the burden of cancer across different socio-economic groups (and indeed areas) in the UK, despite the public provision of a national health service which is free at the point of use. The ways the technologies are developing and are made available are shaped by the context of both austerity and marketisation of the NHS.

Chapter 5 is about large-scale national studies, recruiting patients with a range of cancers to collect extensive molecular information about cancer and ultimately inform routine patient care via precision medicine, focusing on Genomics England's 100,000 Genomes Project. After discussing the rise of these mass-participation initiatives and their strong national imaginaries of economic development and cutting-edge healthcare, we explore how practitioners, patients and families made sense of their participation, and how this related to their investment in particular institutions and futures. We explore the participatory logic of these initiatives, and the ways in which informed consent processes and genomic literacy agendas were developed and enacted to increase participation. We contrast efforts to improve genomic literacy and informed consent by clearly demarcating personal benefits in terms of improved care from the research dividend to the NHS with blurred boundaries in practice. Patients and family members

were seeking care through participation and reworking efforts to improve their understanding to establish their worth as a patient and ensure optimal, personalised care into the future. We explore how this was managed by professionals to meet the aims of the programme despite their reservations about its value and implications.

While many cancer patients experience molecular diagnostics and targeted therapies as part of standard treatment or through clinical trials provided free-of-charge within the NHS, others turn to private providers to craft their own care pathways, utilising private health insurance, spending savings, taking out loans or raising money via crowdfunding online. In Chapter 6, we explore how practitioners, patients and their relatives seek to tailor their care and treatment pathways via these kinds of engagement with private healthcare. We examine the ambivalence about access to expensive experimental treatments as part of NHS or private care, and draw associations between optimisation, actionability and adaptability via personalised diagnosis and therapies and patient entrepreneurship and the intensified responsibilities for health and healthcare therein. Through this exploration we situate personalisation in relation to transformations in citizenship and consumption via social media platforms, and argue that this brings another layer of care, biosociality and identity work for patients and their relatives as they navigate the hopes and social obligations of personalised cancer therapies.

The final two chapters range across the material in the earlier chapters and bring in additional reflections about what is missing from the focus on personalisation, prediction and especially participation across our research, and in the wider public and personal narratives about personalised medicine we have been able to document. Chapter 7 considers non-participation and exclusions as well as reservation, consternation and rejections around genomic medicine in our research and in the public sphere more generally. We investigate the particular social and cultural contexts in which disengagement and resistance are generated. Exploring negative views and experiences or simply a lack of response to genomic medicine, we consider when these kinds of personalised medicine are ‘not relevant to us’ and why some people just do not have the capacity or resources to engage with them. Rejecting or refusing opportunities to engage with genomic medicine also results from the awareness of contested priorities such as health equality or preventive healthcare as well

as a commitment to other forms of care. Not every patient can or wants to craft their own treatment pathway, or looks to the future with a sense of agency and control, and we reflect on what it means to opt out, be excluded or feel left behind by these kinds of research and care. We also discuss the ways in which different agencies and actors strive to tackle disengagement by reaching out to different communities to appeal to their sense of responsibility towards contributing to the prospects of better care for individuals and the community now and in the future. We argue that these practices present an important counterpoint to the dominant, inclusive vision of P4 medicine, particularly with regard to personalisation and participation.

In the Conclusion we draw together some broad conclusions from our case studies, reflecting on how future-crafting operates across the different groups, technologies, experiences, accounts and settings that we have explored and the kinds of work and value involved therein. We consider what rethinking and revaluing the kinds of work and futures we have encountered would mean for future research and practice.

Notes

- 1 Award number 104831/z/14/2 (2015–20). Ethics approval NHS REC 1 and 2 and AREA Ethics Committee University of Leeds and University of Edinburgh Usher Research Ethics Group.
- 2 We have anonymised interview and observational data, using pseudonyms where we draw extensively on quotes and fieldnotes involving participants, and general designations when we use quotes or fieldnotes illustratively (e.g. ‘patient’ or ‘oncologist’).
- 3 www.cancerresearchUK.org/health-professional/cancer-statistics-for-the-UK (accessed 22 October 2019).
- 4 In England cancers with the lowest five-year survival estimates are mesothelioma (6.6%), pancreatic cancer (6.9%) and brain cancer (11.5%). Testicular cancer (96.8%), melanoma of skin (91.7%) and thyroid cancer (88.5%) have the highest five-year survival estimates (Nuffield Trust five-year cancer survival rates for adults in England between 2011 and 2015, followed up to 2016). Breast cancer is the most common cancer in women worldwide. Survival has improved due to advances in treatment,

better screening programmes and awareness. Five-year survival rates for breast cancer in UK have improved, reaching 85.6% in 2010–14.

- 5 The UK has good screening arrangements but when compared to other similarly wealthy countries (e.g. Japan, Australia) (see www.nuffieldtrust.org.uk/resource/cancer-survival-rates (accessed 2 October 2019)), Cancer Research UK estimates that more than 1 in 10 NHS diagnostic posts are unfilled and thousands more NHS staff will be needed in the future (see www.cancerresearchuk.org/get-involved/campaign-for-us/shoulder-to-shoulder#Shoulder_to_shoulder_across_the_UK (accessed 2 October 2019)).
- 6 www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Two (accessed 28 October 2019).