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Stratified, precision or personalised medicine? Cancer services in the ‘real world’ of a London hospital

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Abstract We conducted ethnographic research in collaboration with a large, research-intensive London breast cancer service in 2013–2014 so as to understand the practices and potential effects of stratified medicine. Stratified medicine is often seen as a synonym for both personalised and precision medicine but these three terms, we found, also related to distinct facets of treatment and care. Personalised medicine is the term adopted for the developing 2016 NHS England Strategy, in which breast cancer care is considered a prime example of improved biological precision and better patient outcomes. We asked how this biologically stratified medicine affected wider relations of care and treatment. We interviewed formally 33 patients and 23 of their carers, including healthcare workers; attended meetings associated with service improvements, medical decision-making, public engagement, and scientific developments as well as following patients through waiting rooms, clinical consultations and other settings. We found that the translation of new protocols based on biological research introduced further complications into an already-complex patient pathway. Combinations of new and historic forms of stratification had an impact on almost all patients, carers and staff, resulting in care that often felt less rather than more personal.

Keywords: UK, personalised medicine, breast cancer, ethnography, stratification, healthcare markets

Introduction

Stratified medicine is a term that has been widely used since the 1990s in relation to genomics and subsequently other fields of biology. It is a form of medicine that sorts a population into the most biologically appropriate groupings to determine the optimal therapeutic response. However, this approach can also be described both as personalised and as precision medicine. The former term has been adopted by NHS England for their forthcoming Strategy (2016) and the latter in the USA in President Obama’s Precision Medicine Initiative (2015). Both these government initiatives stress how such developments will replace the previous ‘one size fits all’ or ‘trial and error’ approach to medicine and health care in the same way as proponents of

stratified medicine. Precision medicine builds on the finer sub-classification of disease to add repeated monitoring of disease markers to enable recursive tailoring of treatment to individual response. Personalised medicine can be used to incorporate both the more precise biological stratification and a holistic approach, which accords a role to patient participation and preference (Cribb and Owens 2010). As Tutton (2012, 2014) has emphasised, consideration of the dual biological and social aspects of health care has a long history in the UK, which may explain why the term ‘personalised medicine’ is most commonly used. In this article, we use stratified medicine as a cover term as it is more inclusive of other forms of biological differentiation which pre-date the newer terms; we use the terms precision and personalised medicine only when they are specifically intended.

Stratified medicine is strongly supported by the UK government through funding for the life sciences and drug development as well as the National Health Service (NHS). Thus, the UK Medical Research Council’s 2014–2019 research strategy emphasises the possibilities of stratified, personalised and precision medicine and the Secretary of State for Health announced Genomics England in 2013, explaining:

The UK will become the first ever country to introduce this technology in its mainstream health system – leading the global race for better tests, better drugs and above all better, more personalised care to save lives. (Genomics England 2013)

In order to explore the translation of stratified medicine into existing systems and the possibilities of a more personalised care, we focused on cancer services where some diseases are now subdivided into several biological groupings. For example, 10 or more types of breast cancer were described in 2012 (Curtis *et al.* 2012), confirming that breast cancer is a heterogeneous disease at the genetic level. These types respond to different treatments, and experimental and translational cancer research are woven together with standard cancer care in ways that have become more complex since the ‘-omics revolution’. (Keating and Cambrosio 2007, 2011, 2012a, 2012b)

Breast tumours are staged according to their size and anatomical spread, and graded by histological appearance; molecular typing improves estimates of prognosis and the likely benefits of different therapies. Subtyping includes histological grade, the expression of hormone receptors (oestrogen and progesterone) and the amplification status of the *HER2* gene. Additional molecular tests may be performed to distinguish subtypes that might benefit from different therapies, and combination therapies are used to address the intransigent issues surrounding drug resistance. Yeo *et al.* emphasise the improved survival rates associated with new targeted therapies and conclude, ‘We are on the brink of an era of diverse molecular stratification of breast cancer, and the development of increasingly personalised medicine’ (Yeo *et al.* 2014: 4).

What counts as stratified medicine is contested. Tamoxifen, a hormonal therapy initially licensed in the UK to treat advanced breast cancer in 1972, is not commonly included because it is not based in genomics. It has been used widely since the 1980s for oestrogen receptor positive (ER+) cancers but, as 80% of breast cancers are ER+, further profiling is also required to inform treatment strategies. Similar problems arise with even the best-known examples of a stratified (genomic) approach. About 15% of breast cancers have amplification of the *HER2* gene (Yeo *et al.* 2014) and trastuzumab (brand name Herceptin), a monoclonal antibody, is routinely given to improve disease-free survival. The use of *HER2* as a biomarker has become a key stratifying diagnostic, which is intrinsic to decisions about therapy. This biomarker reflects somatic change in the tumour and is targeted by trastuzumab, but it is not inherited by transmission of a germ-line mutation, as is the case with *BRCA1* and *BRCA2* and so its status in the new stratified medicine has also been disputed (Hedgecoe 2005).

Since the draft sequence of the Human Genome Project, scholars and commentators have explored the hope, promise and anticipation as well as the scepticism surrounding personalised genomics and its institutionalisation in health care. Social research has explored the role of speculation and of expectations that might bring the future into the present along with the necessary collaborations, resources and infrastructure to deliver this new medicine. Some have explored this in relation to increasing the markets for treatments (Gabe *et al.* 2012), introducing the notion of surplus health (Dumit 2012), including the promise of modern genomics in relation to the increasing prominence of bio-sociality and labour market opportunities in outsourced clinical trials (Fortun 2008, Sunder Rajan 2006). Others have looked at health care in relation to the move from 'bench to bedside', observing that knowledge and practice travel in more than one direction, enrol companions along the way and produce, at least from the perspective of researchers and industry, unanticipated results (Hedgecoe 2006, 2008). These contributions have illuminated developments in industry and marketing, including the growth of online genetic testing, new companion diagnostics associated with targeted therapies ('theranostics') and shifting medical aetiologies. Less sociological attention has been devoted to the mundane business of integrating new practices of medicine within existing services, although Hedgecoe (2004, 2008) has explored the use of pharmacogenetics in the clinic, including genetic tests.

Some research-intensive units, where stratified medicine is developed and implemented, have below-average ratings in patient experience surveys (see for example Quality Health 2013). We undertook a small pilot evaluation of patients' experience in a large, research-intensive cancer unit. We analysed survey responses from 777 patients and carried out 25 hours of observation in the services, observing and talking to 28 patients, 14 companions and 10 staff. We were struck by the complexity of patients' journeys, involving multiple and repeated visits to different elements of the service for detailed diagnosis, monitoring and treatment. Problems arose when the 'system' did not work in drawing all these elements together and patients were left feeling vulnerable and wondering, 'who is thinking of me when I am not here?'

On the basis of this pilot, we hypothesised that stratified medicine might promote fragmentation and depersonalised care while at the same time delivering more biologically precise treatment. We further hypothesised that this situation resulted from medical practices that amplified concurrent developments intensifying the stratification of the workforce and the market. We therefore designed a study to examine how recent developments were embedded in a large London breast cancer service in the light of sociological attention to the -omics revolution as well as the translation of new medical knowledge and practices.

Methods

We conducted an ethnographic study to explore the translation of stratified medicine to the 'shop floor' of cancer services in a research-intensive London hospital. Following the initial pilot, we researched breast cancer, the largest tumour group, combining observation with interviews from 2013 to 2014. Staff and patients contributed to the study design, and the study included interviews of patients and staff about their experiences. The study had ethical and local regulatory approval (London, City and East Research Ethics Committee 12/LO/0685, Imperial College London Joint Research Office).

The study was advertised through staff meetings, posters and leaflets in the hospital site and two local non-government organisations (NGO). We focused our observations on a large out-patient department (clinic) that acted as a hub, bringing together many specialised staff, patients, carers, researchers and NGO workers such as Macmillan Cancer Support staff. This

clinic also provided the main site for recruiting research participants to interview. Patients were informed about the study by clinical staff and introduced to researchers on site or asked to contact the research team by e-mail or phone. Eligible patients (≥ 18 years of age and receiving treatment or follow-up care for breast cancer) were provided with information about the study by clinical staff and through publicity, and those who volunteered to participate in interviews were asked for their written consent. They were then invited to complete two interviews, 3–6 months apart. Patients who were interviewed were also asked to name people who had been central to their care, ‘key individuals’ (who may have been companions, family, friends or NGO or healthcare staff), and to approach them with invitations to participate in the study. Staff were also recruited through advertising posters and staff meetings. These other participants (key individuals) were asked for their consent in the same way as the patients but to a single interview. We interviewed the patients, carers and staff about their own experiences of the cancer services using minimal structured prompts from a topic guide.

Observations and interviews were carried out by four researchers (SD, LM, CS and HW), who kept extensive field notes of the observations and conversations. The interviews were audio-recorded, transcribed and organised using NVivo. Data were coded and checked for consistency and comprehensiveness by four members of the team, who also cross-referenced interview material to field notes by date and theme so as to construct a single data set.

Key themes were identified and discussed in monthly team meetings before coding, enabling a shared foundation for continuing fieldwork. Where appropriate, material was also discussed and checked with staff in the breast cancer service. The integration of these varied data enabled fuller interpretation: interview material was extended by observations of participants across different settings, while fieldwork notes were elaborated in the light of individual views and explanations. The analytic approach is common to ethnographic studies insofar as it frames what people say they do in relation to what they are observed to do (Bernard 2006), acknowledging the influence that social positions will have on differing perspectives of a wide range of clinical, administrative and other activities.

Results

We observed 75 half-day sessions in the cancer services; most were in a large outpatient department (OPD, clinic) but we also spent time in the chemotherapy unit and in multidisciplinary team meetings. In total 33 patients were recruited and 23 were re-interviewed between February 2013 and April 2014.¹ Re-interviews allowed us to check our original information and to extend our understanding of the patient’s journey in a situation of increasing rapport. We also interviewed 23 key individuals, again with their written consent. Most of these 79 interviews lasted 50–70 minutes and took place in the hospital or offices of a neighbouring NGO; two were conducted at the participant’s home. Patients participating in interviews ranged in age from 38 to 79 years (median: 58.7 years) and most were white ($n = 26$). Most were being treated for the first occurrence of breast cancer ($n = 22$) and had begun treatment fewer than 5 years previously ($n = 23$). Key individuals participating in interviews included eight family/friends; 14 healthcare staff: nurses, doctors and ancillary staff; and one NGO worker.

We found that the terms, stratified, precision and personalised medicine were used rarely. In order to assess the translation of stratified method into routine care, therefore, we begin with the meetings at which these terms were introduced and discussed before turning to understandings of the patient pathway or journey. We use ‘*HER2*’ as an exemplar of the new approach in clinical consultations that we observed.

Stratified medicine: the promise of genomics

There is so much going on, like building cathedrals in the Middle Ages. Molecular science is so exciting. (Oncologist, 2013)

Direct reference to stratified medicine was observed spontaneously only in meetings, some of which included events for patients and the public. In these meetings, developments in biology provided the foundations of a vision that would lead to better treatment and care, indicating how references to biology implicate other matters (Hacking 2007). An oncologist and cancer scientist explained the future for a new centre at one such event, pointing to facilities for genome sequencing and drug testing. He emphasised how critical this multidisciplinary perspective had been to the development of new drugs and methods of detection, as indicated by our paraphrased field notes:

New translational research from genome studies of the code is critical. . . . This is very important because cancer is strictly Darwinian. People die not because they're not sensitive to treatment. . . . 90% of women will respond. Women die however because tiny numbers of cells in any cancer are dislodged into the blood stream, and mutations in DNA overcome the blockage imposed by the drug. Now the drugs exist to kill 99.9% of sensitive cells but the remaining 0.1% cells survive. It's not the drugs that create mutations; they were there from the beginning. Previously, you needed a lump of tissue to sequence a genome. Soon you will have the whole genome sequenced commercially from a single cell.

The speaker described how selective drugs (unlike standard chemotherapy) inhibit specific proteins in the metabolic pathways associated with cancers. However, a small number of pre-existing mutations will be drug resistant and so the therapy will select for their growth. Later on, the speaker provided an illustration from work on *BRCA* proteins, underscoring the importance of heterogeneity in cancers. In answer to a question, he explained that inhibition of the enzyme that helps mend broken bits of DNA should have led the cancer cells to die. However, they grew out with this inhibitor because the sub-clone had been there from the beginning, and so the cancer cell survived. He continued:

Should we add extra drugs to the cocktail? Now, we guess and we use three or four drugs at the outset. It will take another five years, perhaps a total period of 15 years, to develop combination treatments at the outset that are more than guesswork. Cancer is so clever but we will be able to overcome it eventually so that it will become more like diabetes. We'll sequence in a blood test for an emerging clone. [He describes the current situation and continues] If we can, we'll turn cancer from a very frightening and aggressive illness to a chronic illness that we monitor before the lumps ever appear. This is more than a vision. (Oncologist, 2013; paraphrased notes from meeting)

This promissory vision that will turn breast cancer into a more benign condition diagnosed by a blood test and treated before 'lumps' form has been extensively analysed in relation to contemporary developments in biocapital as well as the sociology of speculation (see Dumit 2012, Fortun 2008, Gabe *et al.* 2012, Sunder Rajan 2006: see also Good 2001). It is important to appreciate, too, how this optimism enrolls staff as well as patient participation, and motivates career choices and subsequent practice. We found that many healthcare workers responded to the new science with reflections on their own encounters with illness. Subsequently, some specialised in cancer care or research, while others volunteered to work with patients. Another

inspiring account from an oncologist, again for non-specialists, indicates the attraction of this atmosphere; here speaking of the earlier introduction of tamoxifen in the way that oncologists speak of trastuzumab or similar drugs today:

I became interested in endocrine therapy when I qualified. . . . [A] patient, who had been there for 6 months with mental health issues, was physically sick. This turned out to be breast cancer but no-one had examined her. In those days, there were no physician oncologists and oncology was a Cinderella specialty. . . . And so I became interested in oncology and especially in breast cancer where there was a new drug on the block called tamoxifen. This we gave to her and she got better. The breast cancer melted away and she recovered mentally too because the hormone that the cancer cells were producing was gone. And she returned home and to a normal life. . . . There is so much going on, like building cathedrals in the Middle Ages. Molecular science is so exciting. (Oncologist, 2013; paraphrased notes from meeting)

The presentation of a new biology that promised a better future was typical of a wide range of meetings we attended, and this vision is congruent with the developing NHS England Strategy for Personalised Medicine.

Stratified medicine: oncology out-patients

Stratified medicine was rarely mentioned in the clinic although individuals commonly spoke of genetics and, with probing, patients referred vaguely to improved outcomes. Some spoke with relief about an initial *HER2* positive diagnosis since they had confidence that trastuzumab would help, even though the prognosis is intrinsically worse than for other types of breast cancer. A senior nurse appeared equally nonplussed and said during a discussion of stratified medicine:

I didn't know what you were talking about until your colleague explained the emphasis on genomics. Medicine here and nursing just as much have always been stratified. This is nothing new. (Field notes 2014)

On being questioned, the oncologists explained how stratified medicine was embedded in everyday practice and as ordinary as previous efforts to classify patients (Hedgecoe 2004). In this context, newly stratifying diagnostics joined older forms, linking trastuzumab and tamoxifen within the same routines. It was hard therefore to identify the specific forms of stratified medicine that derived from -omics and we selected *HER2* as an exemplar of the new approach.

Patients spoke less of their particular type of cancer than of waiting. At least 2 days a week, the large OPD had three oncology clinics in breast cancer running simultaneously, involving approximately 10 doctors, five outpatient nurses, a specialist lymphoedema nurse with her own clinic, clinical nurse specialists (CNS), two phlebotomists, three reception staff and a volunteer greeting patients. Throughout our fieldwork, up to a hundred patients congregated for long periods in this OPD and interacted with these as well as other hospital and university employees, and NGO workers such as Macmillan Cancer Support staff. Patients receiving treatment might spend most of the day at the hospital, waiting to have their bloods taken, waiting to see an oncologist, waiting for their script to be made up in the pharmacy and waiting for a chair in the chemotherapy suite. They might also do all this work and leave without receiving the planned treatment but with a further appointment on the horizon. In such circumstances, some patients asked whether the delay would affect the course of a cancer that would not wait. In the context of a busy urban NHS service, waiting has many inflections: inefficiencies and

bureaucratic inflexibility; triage; and also a form of care among those waiting and working together. Occupying physically the OPD, patients commented both on their appreciation of an NHS that belonged to them and also on their humiliation as they were defined, contained and put on hold by the system (Day 2015, Livingston 2012). Patients contrasted the inefficiencies of the system almost universally with what they considered the uncommon kindness, admirable skills and excellent care on the part of individual members of staff, especially with reference to their clinical expertise.

In clinical consultations, patients' perspectives on their type of cancer occasionally surfaced during interactions with doctors; we therefore provide examples from clinical consultations. A doctor told a patient who was positive for *HER2* that she had metastases on her lungs: 'yours is an unusual case; your cancer has spread while having Herceptin. That was very unlucky'. This patient was not eligible for the new treatment trial because it would probably give her too many side effects and the consultation concentrated on resolving what might be an effect of the cancer and what might be a side effect of treatment or perhaps yet another issue. Another woman learned that she had not responded to treatment. She was taken off trastuzumab after five cycles as 'she' (that is, her cancer) was progressing and she had a tumour in her chest. The specialist registrar said that this was very unusual: 'Most people respond', to which her patient replied that she wanted to be told that she'd got 20 years' remission. An elderly woman with metastatic cancer asked this same doctor if trastuzumab could be causing her rhinitis. She explained first that she could not leave the house without tissues and then asked if the doctor could please check the tumour. It had been aching and she had been coughing. She had various side effects and, in her words, saw a spine doctor, a diarrhoea doctor and a kidney doctor, between them managing cancer in her spine, lung, spleen and kidney. She attended this OPD every 3 weeks although, she said, 'I have never been ill'. Having lived with cancer and its treatments for many years, this woman declined further chemotherapy as, she said, 'it only has 26–28% success anyway'. She explained to the doctor that her sister had 'nursed her husband to death through his cancer and the chemo had only made things worse'. After some discussion, doctor and patient decided to wait for results of tumour markers before doing anything further.

These brief examples show that cancers, therapies and people do not always behave as expected, and failures caused surprise. Regular monitoring enabled interventions to be tailored recursively to a changing mix of cancer, treatment, side effects and other issues, and the new biomarkers and treatments were subject to a process of testing through trial and error just like the old. Misunderstandings were common, as the following example on the importance of monitoring indicates.

An oncologist explained the close attention given to repeated test results in the clinic one day, perhaps for my (SD) benefit and perhaps, too, for the benefit of a patient's granddaughter. During the consultation, the granddaughter, a healthcare professional, asked pointed questions to which the doctor responded; 'first are the blood markers, second the scanning and in her case she'd had an X-ray and a spinal CT [computed tomography] scan, third the breast examination'. The marker was CA15–3, which half the patients had and which was also the best possible marker. Hers was stable: 'if you have more of them, you've got more cell division'. The doctor said of the X-ray:

[W] ell, perhaps it's a bit misleading as it was done 6 weeks before we began treatment and so it [the shadow] would have grown before the treatment [could have] worked.

Bone scans could also mislead as they flared up when they were healing; 'it's not a great test to order, especially if you see a junior doctor next time and they don't know this'. On

examination, the doctor concluded that her tumour was softer and much less defined than it had been. He looked back over the scans and wondered if she even had a shadow in her breastbone; there was no confirmation from the CT scan, no cancer in her spine or rib, and so he was not at all convinced by this shadow in the sternum.

Did she [the patient] want to look at the scans? ‘The scans are so accurate nowadays and [of] such good resolution that they pick up everything. . . [The older woman asked her granddaughter to look instead.] You can see how small this possible shadow is in relation to the rest here’. The patient was confused by the quantity of information but she heard her doctor conclude, ‘no, the lump isn’t growing and all is under control’. She was not interested in the results and concluded, when she was told that she would most likely be on that treatment for the standard 2 years, ‘well, at least that means I’ll be living for another 2 years’. (Field notes 2013)

Monitoring often led to more tests in the effort to achieve greater precision, informing decisions about the next step. The sequence of steps describes a patient pathway and existing procedures have become more complex with the introduction of new practices of stratified medicine.

Stratified medicine in the clinical pathway: implications for the division of labour

The epistemic, political, and economic status of the cancer patient within protocols and the protocol-production process has been a recurring theme for both patients and practitioners, especially when the time comes to choose which road to take – which path to follow or decision to make – in that embedded series of protocols commonly referred to as the therapeutic process. (Keating and Cambrosio 2007: 215)

Continued monitoring can modify treatment: cancers resist or adapt and so treatment must evolve to stratify and calibrate disease differently over time. The new medicine is embedded in trials that span the world and have introduced protocols that dictate procedures seen as pathways (Berg 1998, Timmermans and Berg 1997). Reciprocally, as Keating and Cambrosio (2007: 215) assert, ‘All patient pathways converge sooner or later on a protocol’. They continue:

Presently, even though few adult cancer patients actually participate in clinical trials, virtually all of them are diagnosed, treated, and advised according to a protocol, be it a routine or an experimental protocol.

The concept of pathways arose in the 1980s. Pathways not only plot the steps to caring for and treating patients but also a range of other requirements: they guide costing and rationing, workflow and performance management as well as clinical practice (Rotter *et al.* 2010). From a service perspective, the pathway is a standard built from evidence-based practice which is addressed to groups of patients, conditions or molecular activities (strata) that are both more and less than individuals (Zuiderent-Jerak *et al.* 2012). For most staff, pathways were peopled with abstract as well as particular patients, along with their most predictable variations, who figured in a host of requirements that were glossed simply as standards. Some of these standards referred to clinical protocols and others to government requirements that set a clock ticking to a prescribed timeline and provided the basis for calculating costs and payments. For example, a ‘14-day target’ specified the approved limit for referral from a primary care

physician with suspicions of cancer to an appointment in a specialist clinic; and service providers would be sanctioned if they missed this target. For patients, by contrast, the pathway represented their own journey through treatment and, in interview, few appeared to know what would or should happen next. For example, one woman spoke of the period after surgery:

This test, next test, and I had to go under that machine... For a while, I was coming in nearly every other day... When you come back, you have to go to here. You need to go and have a scan. Then they phone you: 'Oh, you have got to go and have this'. I spent every other day here... Every day, someone's, 'Go here, go there'.

The distance between views of the pathway helps to explain why no-one we interviewed could map the whole pathway in concrete terms onto the particular hospital site.

Staff were aware that the expansion of treatment might provide 'adaptive' or 'tailored' care and improve outcomes but they were also concerned that developments would promote differentiation of the workforce, which could affect patient care negatively. As several staff explained, stratified medicine requires specialist expertise distributed along the pathway. The extended taxonomy of breast cancers understandably lengthens a hospital line: a patient needs more tests and monitoring to find the right treatment; analysis requires more biostatistical expertise and new kinds of trials. You cannot test a stratified medicine on an unstratified population and so fewer patients are eligible for each trial; drugs are tested in combination and biological targets constantly move. At the same time, they explained, elements of the pathway can be delegated to non-specialists. The new biological medicine's protocols outline fixed steps to follow according to the best evidence and so they allow less qualified staff to simply follow instructions where processes are not yet automated, freeing experienced clinical labour to deal with problems that arise.

These observations suggest that the new biological stratification is one important factor promoting the increasing stratification of the workforce. Moreover, we observed that specialist clinical labour was directed increasingly towards the complex technical requirements of management. Services supporting the breast cancer pathway, which ideally run alongside clinical care, were provided more often by autonomous NGOs such as Macmillan Cancer Support, by volunteers and by family members.² In practice, the increasingly elaborate division of labour can make it very difficult for patients to receive and staff to deliver the appropriate care, and any common standard (Bowker and Star 1999) for the patient pathway is in danger of unravelling. The separation between some support and medical services indicates the importance of a third form of stratification that might address the problems of integrating an increasingly fragmented pathway, at least in the view of service leads who were responsible for improving services.

Stratified or personalised care?

The doctors do not seem to understand that it is not answers but assistance that we seek.
(Patient, 2014)

In the UK at least, stratified medicine is seen as a step along the way to a fully personalised approach although, during fieldwork, references to the latter became scarce in response to the difficulties that we have described. Nonetheless, personalisation is the best known of the three terms for the new biology, as well as for other practices in health and social care. Personal budgets in social and some health care, for example, present the service user as a customer who can shop around the emerging market to choose the best package of care.³

Patients expressed frustration when they were 'lost' or 'missed' because of a lack of integration along their complex pathway. A patient might need to see a surgeon, radiologist, clinical

oncologist, plastic surgeon, chemotherapy nurse and radiographer, and some complained that they rarely saw the same person twice. Although the UK NHS has long contained markets in care, it is only recently (2012–2013) that the UK Health and Social Care Act opened them to all willing providers. As a consequence, cancer services in some regions were put out for tender. The UK's main cancer charity that supports patients orchestrated one such bidding process. According to *The Guardian* newspaper, Macmillan Cancer Support's advisory role was grounded in the desire

to overhaul cancer care in the county to make it more *joined-up* after some patients complained that they were “*getting lost* in the system, having to repeat themselves all the time, and that care [was] not always factoring in their *personal circumstances*.” (Campbell 2014, our italics.)

The charity was criticised for its possibly unwitting ideological support of privatisation when a number of firms attended their briefings. Macmillan's chief executive responded with the claim that the new programme would offer ‘an integrated approach’ and ‘[b]y appointing one organisation to take responsibility for managing the whole cancer care journey, we can demand truly seamless care’ (Devane 2014).

The problem of navigating complex systems has been made more acute by the requirements of stratified medicine with its increasing specialisation and monitoring. Support along the patient pathway has traditionally been delivered by a CNS, who meets patients at the diagnosis and offers them support during treatment. However, the increasing complexity of the pathway and a growing caseload had made this role more challenging. Survey results show that having a CNS correlates with a better patient experience (Quality Health 2013). Our research participants valued supportive relationships with CNS but some patients were not sure who this person was or whether they had a named CNS at all. One, for example, could not identify a specific CNS, referring instead to a ‘cast of thousands’ involved in her care. Another, with metastatic disease, looked blank when asked but her husband wondered if one of three particular nurses might be a CNS. All three were ‘very good most of the time’, ‘anything that's wonky, they sort it out’, but when one of them went on holiday, the couple found they were unable to reach the named alternative support. This particular couple also explained that they had been happy to liaise with the consultant's secretary, who could resolve problems when the system did not function well, but her job had disappeared during restructuring (Ward and Day 2013).

The allocation (or subcontracting) of navigation and some supportive care to non-clinical staff and external bodies such as charities constitutes a further form of stratification, leaving clinical care with the more technical and protocol-driven elements. Research participants, staff and patients alike, expressed disquiet at the impersonal nature of many clinical interactions in the same way as Macmillan and many bemoaned the lack of ‘generalist’ expertise that could hold the pathway together. Clearly, these problems have not been caused directly by the translation of biological developments into health care; complaints about the impersonal nature of bureaucracies are pervasive. However, the practices of stratified medicine have an elective affinity with both the outsourcing of particular support services and occupational specialisation, suggesting that an indirect relationship exists between developments in these different forms of stratification. As far as clinicians and patients were concerned, the spaces for holistic care have become more and more restricted.

In this context, it is worth noting a paradox recognised by a range of participants: the most personalised medicine in the sense of both experimental biology and holistic care (Tutton 2012, 2014) was found at the limits of protocol-governed treatment where there was simply no biological evidence and only minimal market demand. We encountered patients with

advanced disease who were receiving palliative treatment to control their symptoms or slow down disease progression. Chang⁴ fell in this group and her views changed over the course of our year's fieldwork. Initially, she explained that her chances of recovery were slim because there were no treatments for her 'triple negative' status. An ex-nurse, she was clear that she would refuse treatment if it made her feel worse but, after some time, agreed to chemotherapy for secondary tumours. As she explained, 'first they burnt my brain and now, there are just a few strands [of hair] here and there'. Her double vision had returned. 'Never mind', she said, 'this hat keeps me warm and with the scarf too'. Now, she thought, she would stop treatment only if tests showed that the tumours were growing: there would be 'nothing left to do'. She spoke of a referral to a hospice and for morphine syrup but said it was too early; she was not ready. Discussing the all-important results, Chang agreed that she, not the doctors, would decide:

[D]octors hope; they want to carry on treatment but they are very good... and yes, I will not have treatment unless it is working. What is the point?

Chang was on the last cycle of the treatment when we [SD] met again and then, she said, 'it is currently a full stop'. A few days later, she joked about which doctor she would see with a fellow patient, Yuna, in the OPD. Yuna said her doctor had told her there was no answer. Chang retorted, 'the doctors do not seem to understand that it is not answers but assistance that we seek'. Was Chang asking when the interventions to track and respond to biological pathways would cease and when someone would offer her the help she needed? If dying and living are experienced together (Das 2015), at what point should the biologically defined pathway end and how?

Although we were focusing on breast cancer, elements of the cancer pathway were shared and we met Chris during our pilot study receiving treatment for a different tumour. A few months later when we met again by chance, I [SD] asked about the treatment and Chris shrugged. It was not clear, he said, and added, 'I'm on the last shot. Anything from now on is experimental'. Noting that '10 years ago, I wouldn't have had a chance', he acknowledged that there was no clear evidence but a number of drugs to try. Chris was positive about his experimental treatment. To be treated as a unique 'case' meant that there were no validated biomarkers or therapies but only personalised care. This personalisation was attuned to a stratum of one but Chris, unlike Chang, considered experimentation a form of responsiveness that might encompass the biological, the financial, the bureaucratic or any other facet of what was always also his singular position. If Chang saw the biological 'personal' in opposition to a more holistic or social care, Chris considered them to be closely connected. He might have said, as Kit did in Iain Banks's (2013: 159) *The Quarry*, 'I know Guy's cancer is not contagious; you can't catch it off him... That's the thing about cancer; it's all yours – it's entirely, perfectly personalised'. Paradoxically, it is only when a stratum of $n = 1$ is defined that the biologically personalised joins the socially personalised medicine.

Discussion

We have described how stratified medicine is experienced as it is introduced in a large research-intensive cancer unit. While it is not possible to isolate the impact of translational medicine from other developments in breast cancer care through an ethnographic approach, we have identified a number of key findings. Firstly, we observed how clinicians and scientists embrace the new molecular medicine with great optimism, anticipating the successful transformation of cancer

management using precise diagnosis, monitoring and therapy. Secondly, stratified medicine was seen to have placed additional strains on the service through its requirement for a highly skilled workforce and a meticulously integrated patient pathway that, in the context of budget constraints, were difficult to deliver. Highly skilled staff have moved increasingly to back office functions such as laboratory analysis, the research and testing of algorithms and the continuing development of protocols and they have been replaced in frontline functions by less qualified staff following the protocols of the new medicine. This leads into the third point; this recalibration of staff roles has enabled hospitals to trim budgets and carry on, but staff and patients alike reported increasing fragmentation and particular difficulties in coordinating the steps along a pathway. Finally, we show how measures to improve coordination and navigation, with the introduction of new roles and some external providers, do not always work, with the result that some patients describe care that is far from personalised.

If the requirements of the new medicine were not sufficiently exacting in the UK today, its realisation is complicated still further by largely contingent developments that may amplify the processes that we have observed. Elements of government, industry and research are intent on bringing a 'better' medicine to the patient. Personalised medicine has been considered variously in relation to New Labour, neoliberal reforms and the new austerity (Cribb and Owens 2010, European Alliance for Personalised Medicine 2013, Savard 2013) but, with its many associations, it can coincide with a wide range of regimes. New legislation mandating the tendering of services to 'all willing providers' enables the outsourcing of parts of the pathway. These developments, in turn, mean that services will be able to sustain the technical and biological work required by the new medicine. Stratified medicine may promise to create a person-centred hub in place of the Fordist line that patients described, but interventions towards this end already threaten to bring the pathway to a stop. Future outsourcing might resolve problems in the pathway and initiate alternative directions but it could equally intensify the direction of current developments so that staff and patients alike find themselves in pieces, scattered along the pathway and struggling to put the parts together.

Stratified medicine is contrasted favourably with a previous and less desirable 'all-comer' medicine. All-comer medicine fails to treat effectively because it treats uniformly and 'one size' is intended to 'fit all'. The modernist notion of health care for all, cradle to grave, seems inappropriate to new biologies, burgeoning expertise and consumer preferences. In the UK, this all-comer, also known as 'empirical' (Hingorani *et al.* 2013), medicine has been practiced in a national service that met needs through centralised planning associated with bureaucratic inflexibilities and relatively effective price control. Having evolved over the last 60 years to include all manner of quasi-public and quasi-private service providers, the NHS is considered by some commentators to be too unwieldy to deliver personalised medicine, that is, a set of practices that holds patients at the centre of a pathway receiving treatment that will work on their type of cancer.

Participants in this particular cancer service were unclear about the contours of a better medicine that might integrate care with treatment and improved outcomes. Many spoke of elements from a pre-genomic, as well as the genomic, era and emphasised the importance of a form of care that delivered an inclusive service. Even though the traditional NHS form of stratification was compromised by its association with a callous bureaucracy and a one-size-fits-all form of cancer care, patients strongly supported the admission of all-comers and they emphasised how thrilled they were to be welcomed and treated themselves. However, the relations between an inclusive service on the one hand and improved outcomes on the other remained hazy. The 'better' market form on offer was equally tainted by association with an inappropriate or unethical profit motive and, at times, a similarly vague association between market efficiency, on the one hand, and better outcomes, on the other, was implied.

Even though participants were unclear about the path to a better medicine, several expressed concern about future lines of exclusion that would replace valued public realms, in which the NHS continues to occupy a central place, with thoroughgoing market principles (Day 2015). In the 21st century, valuation creates biological markets through inevitably evaluative processes of sorting that are currently bundled under the rubric of an -omics revolution. This revolution points to a seemingly impossible leap in cancer care where the individuation of biologies and customer preferences will coincide with numerous other, potentially divergent measures tracking costs, governance requirements, safety, participation on the part of both staff and patients, and, of course, health outcomes in a single pathway. How can value become equally an outcome and an experience, a notion of inclusion or equity and a price that government, insurers or others will pay?

Conclusion

Stratified, precision and personalised medicine constitute a field of overlapping and shifting meanings that appeal to notions of evidence, new expertise and person-centred care as well as subgroup medicine. Personalised medicine, conceived in terms of a welcome attention to the person of the patient, which is exquisitely attuned to individual genetic and – by extension – social factors, is perhaps the best known of these three terms and it is also the most fluid and contested. It remains an aspiration and, in the meantime, stratified medicine refers to and produces new forms of disease that inevitably combine with previous ones.

In one research-intensive, large, urban centre from 2013 to 2014, the translation of stratified medicine into routine care led to a combination of practices that promoted less rather than more integrated, personalised and seamless care. This result may describe a temporary phase of health-care delivery and it cannot be attributed solely to the new biology. Nonetheless, the empirical consequences of new medical practices and the elective affinities that we have outlined between developing forms of stratification in medicine, the market and workforce suggest that the translation of -omics into standard care will have similar, unanticipated effects in other UK settings.

Expectations and the promise of biological developments are an important theme in the sociological literature. However, the focus of previous studies has tended to be on the big players – in science, industry and government, or on particular perspectives within the translational pathway. By observing and integrating the perspectives of the many different players involved with stratified medicine in health care we have shown that high expectations of the new stratified medicine are widely shared by participants who are often considered to have distinct views and interests, with health care staff on the one side and patients with their families and friends on the other. Furthermore, speculation about a better future is embedded in everyday interactions within the service. In this context, the mundane challenges we have discovered to the introduction of stratified medicine may prove difficult to reconcile with widespread optimism.

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Notes

- 1 Of the original sample, four were either too unwell or had died, one could not be reached and five declined a second interview.
- 2 Research participants alluded to support services closely associated with the hospital journey such as volunteers in the OPD and chemotherapy suite, carers who accompanied patients and three particular NGO, one that operated within as well as outside the hospital and two local services. These support services had independent sources of funding. When interviewed about their journey more generally, patients spoke of a much wider range of support.
- 3 For example, one provider describes their plans for personal care budgets, 'This is a completely different approach to an historic 'one size fits all' system of individuals having to access, and fit into, care and support services that already exist which have been designed and commissioned on their behalf by Local Authorities for example. Individuals will receive their own budget and can decide how, who with and where they wish to spend that budget in order to meet their needs and achieve their desired outcomes. Whilst there is initial focus on social care and support services, the principles of personalisation are being embedded into a range of other public service areas such as health and education.' (Skills for Care 2016).
- 4 Names (pseudonyms) are used in examples where it helps the reader to follow the narrative.

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