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The Gardener and the Walled Garden

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Introduction

This chapter explores the close connections between health care and research in a London hospital through Jayne's—one of the authors¹—experiences. We are an anthropologist (Sophie Day), a patient with breast cancer (Jayne Smith) and a clinical epidemiologist (Helen Ward) with different positions in this research hospital and different perspectives on experimental cancer

¹We use first names in the text when referring to each other.

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care (Day et al. 2021). The first-person plural that we adopt therefore shifts in its referents. The letter from Jayne (below) shows that she wanted to know whether the samples she contributed to several medical research studies were useful and what had come of, and from, them. Strict governance of health data precluded Jayne from finding out herself, but Sophie and Helen had university positions that allowed them to cross garden walls into what are sometimes called Trusted Research Environments.²

Jayne is an absent presence in the ‘detective work’ we describe, marked by a moniker, ‘the gardener’. This figure organised information flows among staff around hospital and research sites, many of whom had never met Jayne and never knew her history. Because of this traffic, it organised our collaboration initially, configuring an inclusive ‘we’ that refers to our explorations of the history and implications of data-intensive health research and care as well as an exclusive ‘we’ that refers to the efforts that Sophie and Helen made to figure out what had happened to Jayne’s samples and data. Combining insights as a patient and as staff, we show how this ‘name’—referring to Jayne’s occupation—fortuitously offered a conduit into a landscape of research and care, and the connections and gaps between areas of work as they changed over a period of six years.³ We then turn to what the gardener was cultivating, namely ‘Grumpa’, Jayne’s name for her tumour. If Jayne considered Grumpa as hers and indeed part of her, she was happy to share her tumour and Grumpa was detached repeatedly from Jayne in the form of ‘golden’ or ‘precious’ tissue samples and data. These ‘cuttings’ or ‘seeds’ elicited further work as clinical and laboratory researchers cultivated different forms of Grumpa in a series of walled gardens. We therefore understood that there were several gardeners in several gardens, all cultivating aspects of Grumpa and sensing the tumour differently through work practices which themselves changed in response to varied developments including efforts to realise the values of health data more effectively. We recognise a

²Walled gardens describe protected data enclaves where information from health services can be accessed by researchers. Platforms such as Facebook and Google popularised the concept of walled gardens as a way of storing and protecting data they collected on people’s browsing histories or preferences (Plantin et al. 2018). Walls were designed to exclude competitors from access to valuable assets. Health regulators also developed practices of walling gardens or Trusted Research Environments to protect patient confidentiality.

³Sophie and Helen have shown the importance of different perspectives on health services through collaborative work among staff, patients and researchers (Ward and Day 1997; Day et al. 2017).

series of figure/ground reversals that shift the relations between gardener, plant and garden. Grumpa too can be figured as a gardener, cultivating us all—the three authors as well as clinical and research staff—insofar as it motivated sustained exploration into its mutable materiality and the conditions in which it diminished or thrived.

A Letter, Jayne Smith (2019)

After Sophie and Helen had conducted interviews and attended relevant meetings, Jayne put her thoughts into a 2019 letter for the three of us.

“After 2 years of living in fear and denial, I was diagnosed with bilateral metastasised breast cancer in early 2013. ... Just by looking at my breasts it was obvious that the disease was advanced, ... but the clinical staff who treated me showed me the utmost kindness.... In fact, I got the impression that they saw me as an extreme case, if not a curiosity, hence the heightened interest in me.

From almost the beginning of my treatment I became involved in some kind of research. That, in itself, gave me some purpose in dealing with my disease, with a hope that my misfortune could eventually be beneficial to other breast cancer sufferers, and it therefore put a positive spin on my condition. I was first involved in some research with Helen about patient experience, which also helped me clarify things in my own mind.

The first two years of my treatment consisted of hormone medication, which seemed to work for about 18 months, but then fungation⁴ set in, and I had to accept surgery. At the same time, I was offered the opportunity to take part in the RADICAL trial, which was testing a drug which would boost my existing hormone medication. The registrar and trial coordinator seemed very keen that I should do it, so I agreed - if it could be beneficial to me and also help others, why not?

A few weeks after the trial started, I had a mastectomy and lumpectomy, and the tissue removed was given to the RADICAL research team. I was on the trial for three and a half years, and it seemed to work by keeping my disease stable without my suffering extreme side effects.

⁴Fungation occurs when a breast tumour involves the local skin causing a wound which can ulcerate and become infected.

Every four weeks blood samples were taken and sent off for research. As time went on the clinicians caring for me became more and more amazed that I was tolerating it so well. When the trial had to end in June 2018 because my cancer had progressed, the tissue from my second mastectomy also went to research.

Up until now, I just thought that all my cancerous boobs and bodily fluids had disappeared anonymously into an abyss of data, together with those of millions of other cancer patients - just a drop in the ocean. However, I did hear unofficially that my 'bits' were viewed as coming from a 'gold' patient, and that there were only 2 other gold patients in this lab. Given the opportunity, I would love to reveal myself as that 'gold' patient and find out how my samples were used and whether they were instrumental, even in a tiny way, in any breakthrough in the treatment of breast cancer. I know patient confidentiality is of paramount importance, but there must be a way round it for consenting patients.

In the 'Garden' analogy, to me my breast cancer is a unique hybrid plant I have grown, which has been taken for propagation into a walled garden to which I have no access. I would like to see what has happened to it. Did it end up on the bonfire? In the compost? Were seeds/cuttings taken? etc.

Is there a shortage of patients willing to allow their tissue etc. to be used in research, and if so, would the ability to know the outcome increase patients' willingness to participate? The fact that I am still involved in some kind of research such as this continues to put a positive spin on my condition.”⁵

“I’d like to know what they’ve done with my stuff” (Jayne, 2018 interview)

We met in 2013 as Jayne became a patient. She presented relatively late with advanced disease and wanted to avoid surgery and chemotherapy. Following her initial diagnosis and treatment preferences, as Jayne writes

⁵We use double quotation marks for verbatim citations and single quotation marks for records from our field notes.

in her letter, she began hormonal treatment—with an aromatase inhibitor called letrozole. Her tumours shrunk and she remained relatively well for more than a year. In 2014, the tumour on her left side started fungating and, in early 2015, she had a mastectomy and lumpectomy. She also joined a clinical trial, the RADICAL drug treatment trial (Seckl et al. 2017), for three and a half years until further symptoms meant she had to stop the trial drug. As far as Jayne was concerned, the treatment ‘which was to boost up the letrozole’ had worked and perhaps saved her life. She subsequently had a second mastectomy and changed her aromatase inhibitor. We had heard about some of these developments from colleagues, for example, when Jayne featured in a newspaper article about a local gardener on a cancer trial (Rivers 2016) and when she gave a talk to an experimental medicine conference. Her ‘case’ interested staff in the service and beyond and was attached to the label of gardener as it was discussed, with her consent, at internal and external clinical meetings.

Jayne has contributed to Imperial College Tissue Bank, RADICAL trial samples and data, and routine health records but she has access only to her own clinical records. Healthcare staff can retrieve material they need for their job, and some staff have research roles giving them access to datasets related to the institutional tissue bank or to clinical trials, which also sit independently. Governance of research data requires that every tissue sample and related data can be tracked in both directions—back to the patient and forward to the analysis—to ensure research integrity. Being trackable does not mean that data remain attached to their source, and indeed materials are de-identified and stripped of personal markers before use. Tracking is achieved through an allocated identifier which circulates inside a research setting without enabling individuals to be identified. However, researchers often want further samples from or information about their donor for which they rely on intermediaries who can re-identify and re-attach patient samples to the identifier. Where relevant, researchers also feed their results back to senior clinicians who will re-identify individuals if they consider findings clinically relevant. This ‘airlock’ process enables only a few people with specific job roles to ‘unlock’ pseudonymisation and transfer data into and out of research environments.

Walled Gardens

Jayne's data and samples reside in three repositories—the Imperial College Tissue Bank, RADICAL trial samples and data, and health records—which are walled gardens, albeit of very different dimensions, and they are insulated from each other by formal techniques of governance and access.

Jayne had little interest in remaining anonymous, protected by walls that also excluded her. Her questions about what happened to her data might provide a way, she said, of “turning my misfortune into a positive”, that is, generating research findings that would help future patients. She wondered about the value of her monthly blood donations and multiple scans during more than three years on the RADICAL trial: “It would be wrong to expect a cure to come out of my samples, but something...” because, in her view, the trial drug had worked. Jayne was most interested in her tumour samples. She described the removal of a fungating tumour in her first operation and explained with pride how the research technicians waited for a blood sample so it could be couriered together with the tumour to the laboratory. In an interview just before we visited that laboratory, Helen asked, “Have you any idea what they’ve done with your tissue?” Jayne replied, “... As I mentioned in my speech to the people at the ECMC⁶ or whatever it was... this fungating monstrosity, we nicknamed it Grumpa-Loompa.⁷ We’ve always referred to it as Grumpa. I said to her (my sister), ‘I’m going to the lab today.’ She said, ‘I hope Grumpa is not there looking at you in his jar.’” It was through Grumpa that Jayne figured herself as a gardener who had cultivated this tumour unwittingly alongside her everyday occupation. After contributing to various walled gardens in the hospital and university, she thought that her cancer and the tissue samples it provided for other gardeners constituted

⁶ECMC: Experimental Cancer Medicine Centre, a network of cancer research centres in the UK. Jayne had given a talk to one of their meetings about her experience.

⁷Based on the Oompa-Loompas from Roald Dahl's *Charlie and the Chocolate Factory*. https://en.wikipedia.org/wiki/List_of_Charlie_and_the_Chocolate_Factory_characters#The_Oompa-Loompas. Jayne and her sister seem to have associated these figures with their small size, incessant factory work, and mutable, mischievous, improvisational qualities rather than the imperial and racist tones that many have perceived. These qualities resonated with their perceptions of embodied breast cancer.

a unique learning opportunity. As she suggested during the lab tour described below, ‘I don’t want to be big-headed about it. I think I was a bit special when I started because it was so advanced when I presented myself... I think there was a lot of interest in my tumours and me I suppose because of that. [My friends with cancer] haven’t had anywhere near as much interest in them as I have, they’ve felt a bit factory, conveyor belt type thing’.

Walled Garden 1: The Tissue Bank

From 2013 to 2018, Jayne provided samples to the Imperial College Tissue Bank, which is licensed by the 2004 Human Tissue Act⁸ to collect samples with permission for research. When patients donate to the tissue bank, they consent to participate in unspecified research rather than particular studies, and today, they generally provide enduring consent for research use of surplus samples from continuing health care investigations. Samples sit within a walled garden and can only move outside the institution through a material transfer agreement or an existing site license for collaborative research with appropriate data sharing agreements. Researchers apply to the tissue bank to use samples in specified studies within a given time frame—usually for the exploration of emerging questions in basic laboratory science but also in research training or for testing equipment. As far as laboratory researchers are concerned, tissue banking governance provides the flexibility to ask and explore preliminary questions.

Research technicians provided integral, albeit informal, support during Jayne’s many hospital appointments from 2013 to 2018. They also constitute an interface between the service and research but, before 2018, it was not considered appropriate to open this conduit to Jayne herself or indeed to Sophie and Helen except in very partial ways. It was after Jayne

⁸ The Human Tissue Act (2004) came into force on 1 September 2006 and legislates on the use of human tissue samples. It established the Human Tissue Authority (HTA) to regulate activities concerning the removal, storage, use and disposal of human tissue samples for defined Scheduled Purposes, including ‘research in connection with disorders, or the functioning of, the human body’.

stopped contributing regular samples that Kelly Gleason, Senior CRUK⁹ Research Nurse at Imperial College London, organised a visit to a laboratory that had worked with Jayne's tissue bank samples; she invited the three of us to join the tour.

The laboratory group were studying the epigenetics of evolution in hormone-positive breast cancer. Their work relied on repeated samples from the same individuals who had received neither surgery nor chemotherapy. As the head of the laboratory confirmed, these series of samples were 'as rare as white flies', and therefore 'golden' or 'precious'. Since Jayne had initially declined surgery and never undergone chemotherapy, hers were among the small number with which this laboratory group obtained the DNA fingerprint of tumours over a period of one to two years—before, during and after endocrine treatment. They tried to establish what counted as the same or different types of tumour by assessing genetic heterogeneity and asked what made some tumours start to grow again.

During our visit, we learned how tumour samples arrived in dry ice by courier. Close liaison between laboratory staff and clinical research technicians was essential because the samples had to be used immediately in the research. We were shown some of their techniques and tools, including live cell lines of breast cancer from Sister Catherine Frances, a Catholic nun who developed metastatic disease in the chest wall and pleura in 1971. Cells from her pleural effusion were the first to be successfully cultured, and her MCF-7 cell line has led to over 25,000 published reports (Lee et al. 2015). Sister Frances' cells were oestrogen-receptor (ER) positive like Jayne's, and subsequent research using this cell line led to major advances in therapy including tamoxifen and aromatase inhibitors.

Material from serial biopsies has improved understanding of the mechanisms of tumour evolution in ER-positive cancers under selective pressure from aromatase inhibitors (Patten et al. 2018; Rosano et al. 2021). Related studies (see Viney and Day, this volume) have explored cell-free circulating tumour DNA in blood samples for biomarkers that may improve prognosis and suggest earlier interventions (Magnani et al. 2017;

⁹Cancer Research UK is the world's largest independent cancer research charity, funded almost entirely by public donations.

Hong et al. 2019; Coombes et al. 2019). Such ‘liquid biopsies’ offer huge advantages over solid tumour biopsies for the monitoring of disease since they are relatively easy to give as well as to receive, process and store (Hastings et al. 2021). At the end of the visit, Jayne was in conversation with the head of the laboratory who said that he ‘did not have green fingers’ and wasn’t a gardener. She replied that the work he had shown us in the laboratory suggested that he had all the skills and could also be a gardener, if he put his mind to it.

Jayne was much more interested in the uses and values of her tumour samples than the 22 blood donations we found that she had also made available for research through the tissue bank. An audit in 2019–2020 showed that Jayne had provided an unusually large number of samples. Four hundred and seven people each provided between one and twenty-six samples with an average of between two and three; only nineteen people provided ten or more samples. The audit showed that these samples were explored in collaborative research with Sweden and the USA, for example, as well as in the UK.

Walled Garden 2: RADICAL Trial

Exploratory studies using tissue bank samples sometimes lead to proposals for clinical trials. Trials require specific approvals and consent from participants since they involve ‘investigational medicinal products’ such as drugs or devices.¹⁰ They require meticulous record-keeping including the validation of all samples and results in protected databases.

Research technicians were responsible for recruitment and follow up to the RADICAL trial under the institution’s Cancer Clinical Trials Unit. Jayne’s monthly blood samples were spun and stored in a RADICAL freezer. The samples were managed thereafter by the Clinical Trials Unit at a site nearby. The technician responsible for RADICAL from 2017 to 2018 explained how she entered results and data onto an *InForm* ITM (Integrated Trial Management) System, which is used widely in the pharmaceutical industry and charity sector. This ‘walled garden’ includes data

¹⁰ Medicines for Human Use (Clinical Trials) Regulations (2004).

imported from several hospital systems. A technician manually extracted material from the hospital service data system to combine with reports from trial participants and results from separate imaging and neurology systems before collecting signatures from clinicians for the site file. These data were audited on conclusion of the study and archived. Only then, in 2018, did Jayne's blood become accessible outside RADICAL and, as far as we could discover, samples stored at the drug company labs¹¹ were returned to the local centre to be either destroyed or repurposed for other studies.

Interviewing the principal investigator (PI) of this study, Sophie learned that cancer prognosis was worse when fibroblast growth factors, particularly FGF2 (fibroblast growth factor number 2), become elevated. His group investigated molecular mechanisms *in vitro*, then in animals and eventually in people affected by a range of cancers who had become resistant to treatment with letrozole or anastrozole. The group developed a blocker to FGF2 called AZD4547, which they hoped would overcome resistance to treatment. After a pilot study, they trialled the compound in combination with letrozole or anastrozole and reported subsequently that about one-third of participants benefited (Seckl et al. 2017). The research programme then stalled because the group were unable to stratify participants ahead of treatment: 'we need to know how to select those patients [who will benefit] and not the ones for whom it doesn't work, and currently we can't do that. There is a test which gives you results before imaging can, within a few weeks of starting treatment, but it would be better to know before you start treatment. That is tough. ... If we could select patients properly, we could do a bigger trial and properly answer whether this inhibitor works or not' (field notes, 2019). This next step of stratifying patients and selecting only those who might benefit from the treatment required either serial biopsies, which they did not have, or appropriate surrogate markers.

Financial issues may also have contributed to the hiatus in this research programme. Interviewing the first research technician responsible for the study, Sophie heard that the trial drug was 'on the shelf' until researchers made different combinations available for trial across a greater range of

¹¹ The RADICAL trial involved the company AstraZeneca <https://tinyurl.com/y54z34gz>

cancers, thus defining a larger potential market for anything that might be licensed. A colleague also suggested that participants suffered too many side effects for the company to adopt the treatment in early (as opposed to late) breast cancer, which was their only financially viable option because it would include a larger number of people.

When Jayne heard this news, she was unsure whether her donations had been useful but remained convinced that she benefited personally from her 46 cycles of treatment. In addition, she felt she had profited from the close monitoring and incidental findings that were shared. At her first diagnostic appointment in 2013, possible signs of cancer were mentioned in Jayne's lungs, liver and pelvis. Eventually, a consensus developed that there were four small cancerous nodules in Jayne's lungs while RADICAL trial monitoring suggested that there was no cancer in her liver, just fatty cysts. A torn retina was also found and repaired 'then and there'; subsequently, an issue about drainage in her eyes was treated in the hospital, which Jayne understood might have caused glaucoma if left untreated. Jayne also felt that she would not have been recommended her second mastectomy in 2018 had her clinicians not been involved in research, since the tumour was so small—only 15 mm—when it was discerned.

Sophie and Helen learned that Jayne would receive formal notification of trial results when they became available if she had requested them in her original consent form. The trials unit told us that the results were still being analysed at the beginning of 2020 and referred us to a key summary on the CRUK website. Here, the investigators report that the trial showed that AZD4547 combined with one of two aromatase inhibitors appeared to be safe and showed anti-tumour activity in some people.¹² Trials are underway to explore whether results can be improved by selecting patients with specific biomarkers who may benefit most from the drug combination (Tarantino et al. 2020). Jayne hopes that the work will continue.

¹² <https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-azd4547-for-breast-cancer-that-is-oestrogen-receptor-positive-got-worse-despite-having-anastrozole-or-letrozole-radical#undefined>

Walled Garden 3: Patient Records

Jayne's patient records contain traces and links to most of the research activity described above. Clinical consultants recorded decisions in her notes after reviewing the results of tests through which her health and response to the RADICAL trial treatment were monitored. Paper patient records have long been used in hospitals and other clinical settings, and, in recent decades, test results that were stored in electronic form were also printed to add to a patient file. Initially, Jayne had a paper record which contained copies of letters, results, procedures, treatments and clinical notes. She said that her file became so large and heavy that staff would have to use a bag to carry it. Although her paper records contained an enormous amount of detailed data, they were not shared outside the hospital and so were largely inaccessible for research, audit or to Jayne herself. In 2016, the hospital introduced an electronic health record (EHR) system hosted on a platform run by the company, Cerner. Clinicians involved in patient care can view these records in the same way as previous paper records. The system links to other local health records (see below), and Jayne now has some access to these through a patient platform called the Care Information Exchange; Jayne can look at her recent results, add comments and upload data from health trackers. She explained, however, when hospital care was radically curtailed in 2020 that she did not want to receive any results by phone or electronically, only in person.

A Changing Landscape: from Walled Gardens to Data Flows

The figures of the gardener and of Grumpa have evolved in relation to their grounds, the walled gardens. Rapid developments in data collection and the increasing interoperability of data systems mean that traces of Jayne in her data and materials are now embedded in much larger warehouses. Both data and samples may appear to have “disappeared anonymously into an abyss of data” but they are also contributing to the creation

of value in the UK's life sciences strategy to build assets from unique NHS data sets. The gardener and Grumpa are valued as “pluripotent” elements for future research with these datasets.

Although Jayne's materials sit in three and no doubt further walled gardens, some people can travel between them, including research technicians. Given appropriate consent, excess samples can also be repurposed for subsequent research, and clinically relevant information shared. Jayne, for example, consented to the collection of ‘archival tissue samples’ in RADICAL for exploratory work via tissue banking to look for markers that might influence the development of breast cancers or help explore patient responses to treatment. From 2013 to 2020, the ways that data are collected, stored and used were transformed in health services and research. EHRs such as Cerner enable easier reporting and sharing of data, and NHS investment in these EHRs “supports our wider interoperability strategy and avoids the ‘walled garden’ legacy of trapping data in institutions” (Swindells and Smart 2017), simultaneously contributing to core UK government strategies aligning health, life science and economic policies (Department for Business, Energy and Industrial Strategy, 2017).

In the local NHS Trust where Jayne is a patient, a Whole Systems Integrated Care (WSIC) database is now extending this infrastructure (Bottle et al. 2020). A researcher who has been closely involved in its development explained: “[it] is currently used for direct patient care, service evaluation, commissioning and for research [through the system known] as ‘Discover’. For direct patient care, the WSIC team developed disease-specific dashboards, which can be accessed by healthcare professionals with a legitimate relationship with WSIC. For other uses, the database is de-identified” (interview, 2020). This single integrated care system in North West London contains data on 2.4 million people and can be used by clinicians to support the provision of care, by managers and auditors to review activity as well as generating statutory reporting, for example on cancer waiting times. A pseudonymised form of the database (Discover) can also be used for research, and patients who have consented to be contacted for further research can be re-identified if they meet a study's inclusion criteria (Fig. 8.1).

Since 2020, developments in the collection, storage and use of health data have further intensified in response to the COVID-19 pandemic.

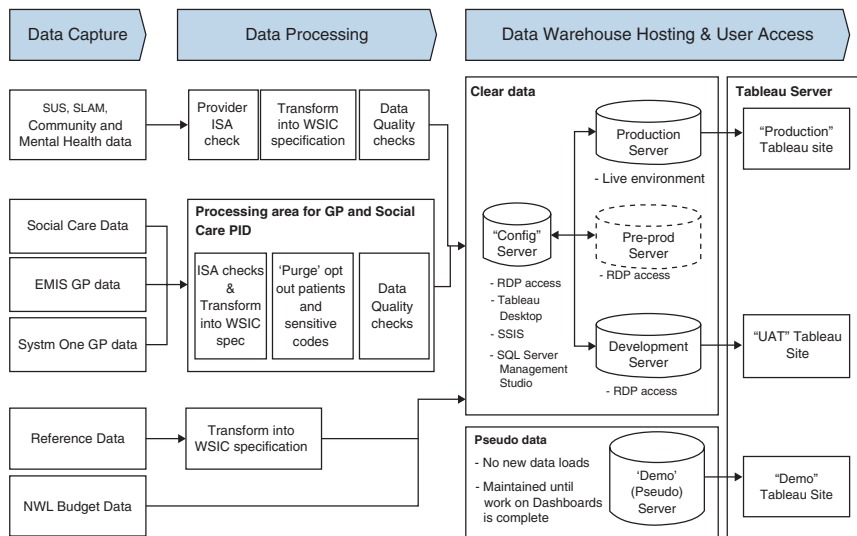


Fig. 8.1 Walled gardens of data: links across the local health sector used to create the Whole Systems Integrated Care database; Figure reproduced from Bottle et al. (2020), under Creative Commons Attribution 4.0 International License

A researcher we interviewed explained how the use of individual and group-level patient data “has been even further facilitated due to COVID, in a way, in that we’ve accelerated development of a virtual platform that our researchers can access, and we’ll have access to anonymised EHR data from Imperial College Healthcare Trust” (interview 2020). The WSIC platform has also been used to track COVID-19: people who use the Care Information Exchange are invited to provide weekly updates on whether they have experienced symptoms, and they can respond to other surveys about their care and preferences, for example, relating to a contact tracing app (Bachtiger et al. 2020). Jayne has participated and found it interesting, indeed unusual, to be invited to provide a written (‘free text’) account of the impact of COVID-19 on her experience of cancer services.

These larger data warehouses are not alternatives to the walled gardens described but rather a larger garden: “The technical solution comprises a ‘walled garden’ approach, which uses secured virtual sessions run from within a secure infrastructure. ... All projects are logically segregated

from each other within the safe haven, and access is controlled and permitted only to those users who have been registered and attended information governance awareness training courses, as well as completed online information governance tests annually for their reaccreditation” (Lea et al. 2016).

Data developments associated with EHR, WSIC and Discover mean that Jayne’s data can be aggregated with millions of other patient records in a way that was not possible five years ago. Data produced from her care—the details and dates of her diagnosis, test results, treatments, visits, etc.—also link the hospital she attends and primary care (UK general practice). A clinical researcher explained how this infrastructure enabled approaches other than traditional clinical trials, “(we) have moved on, beginning to see the utility and using e-health data and electronic health record data, rather than collecting vast amounts of information on patients that we recruit to studies. And how we can really make the best use of that information, to do almost quasi-experimental or natural experimental designs, and improve patient outcomes” (interview 2020). They provided examples showing that this approach can occur in near real time with the introduction of alerts, for example, to a patient who may have sepsis. They can then assess whether alerts led to any improvement in outcomes (Honeyford et al. 2020).

As Jayne cautioned, however, data that is readily available in large quantities is not necessarily any more reliable. She said that letters to her general practitioner (GP) in her medical records had multiple errors including incorrect dates for her scans and her most recent treatment. The very size of these linked data sets “does not eliminate and may even amplify systematic error” (Ehrenstein et al. 2017), which can undermine their usefulness even if the greater scrutiny may also reduce errors.

In sum, our investigations found traces of Jayne’s history of treatment and research participation in clinical records in both identified and de-identified form, in paraffin blocks and serum samples in banks that are kept for 20 years, in DNA sequences and in research results and papers. Sophie and Helen were able to explore three ‘gardens’ in depth and found that Jayne and other patients have provided materials for local research in surgery, a spectroscopy study associated with cell biology and drug delivery systems, other types of cancer including metastatic cancers, a

xenografting study with doubled systems of consent because it involved animal work, PhD projects through specific consents and through the tissue bank. Along with samples from other patients, Jayne's contributions have informed several research papers as well as our own research on the impact of developments in cancer medicine (Day et al. 2017, 2021; McGrath-Lone et al. 2015). We did not find out about derivative uses in further studies such as those repurposing clinical trial bloods.

Grumpa

Jayne thought her involvement in research and care was “all of a piece really” because of the collaborative focus on cultivating Grumpa, whether attached to or detached from its host. As Jayne wrote in her letter (above), “In the 'Garden' analogy, to me my breast cancer is a unique hybrid plant I have grown, which has been taken for propagation into a walled garden to which I have no access. ... Did it end up on the bonfire? In the compost? Were seeds/cuttings taken? etc”.

This figure, Grumpa, was delineated collaboratively over a period of six years by several other gardeners as well as Jayne. Staff in the hospital and university sensed the cancer differently in the clinical trial, the laboratory research programme and during Jayne's continuing care. ‘Cuttings’ were taken for research from Jayne's initial diagnostic biopsy in 2013 and shared. In 2015, Grumpa was distributed again following a lumpectomy and a mastectomy, and once more after another mastectomy in 2018. Relational, comparative and perspectival glimpses (Gal 2016) across at least some of these walled gardens constituted scaling devices which put together a history to Grumpa—and care plans and prognoses for Jayne. But, as the gardener, the one who produced and grew Grumpa and made all the collaborative work across cancer care and research possible, Jayne felt that she had been excluded from the results of this work and their potential relevance for breast cancer care more generally. The history to her ‘cuttings’ was outside Jayne's control and practices of governance also made it very difficult to effect a comparative history across ‘trusted research environments’.

RADICAL trial results from patients with a range of cancers were analysed as a combined set after the trial closed. Jayne was one of many contributors and her Grumpa samples seemed to have “disappeared anonymously into an abyss of data...”. Investigators were also frustrated that they could not differentiate between participants and select only those likely to benefit from the trial drug. Since cancers affecting different individuals respond to treatment and other evolutionary pressures in different ways, it is difficult to conduct clinical trials as though the indexicality of data is uniform and stable. By comparison, the exploratory epigenetic research conducted by another research team was more of a ‘natural’ experiment, rather like the new uses of linked data made possible by the WSIC database. Some materials remained indexed to Jayne over time even though they appeared to have been detached from her continuing care. Sophie and Helen’s detective work showed that information travelled between the clinic and this laboratory group and that developments in one environment were understood in relation to the other—her clinicians were also active research investigators. A natural history of tumour evolution was constructed by integrating the results of clinical observations with laboratory and data research to track the evolution of cancers.

We were all struck by the ‘immortal’ cell line from Sister Frances and Jayne explained how she would love to find that her samples had been similarly important: “Given the opportunity, I would love to reveal myself as that ‘gold’ patient and find out how my samples were used and whether they were instrumental, even in a tiny way, in any breakthrough in the treatment of breast cancer.” This cell line evokes a traceable continuity from donation to discovery that is rare, but recognisable. It reminded Sophie and Helen of research using HeLa cell lines, developed from a sample taken and used without consent or knowledge from Henrietta Lacks. This history is extensively documented as a history of racial and economic abuse that has become well known through the book and film *The Immortal Life of Henrietta Lacks* (Skloot 2010), which depicts the extraction of value without compensation. Jayne considers the (con)figuration of her samples in more positive terms. Her materials have not been used for *in vitro* cell lines (for which specific permission would be required), but the laboratory team clarified that rare, repeated

samples such as hers were of substantial value to research into the evolution of hormone-positive cancers exposed to treatments *in vivo*.

The contrast between the two types of cancer research we have described, a clinical trial and a laboratory programme informed by clinical observations also indicate multiple ways of being cut out of or included in prognoses. Jayne considered that her care benefited directly from research involvement. Like many other people, she hoped to improve the lives of future generations just as previous generations had contributed to her own wellbeing: ‘if I’ve got to have this awful disease, at least it can do somebody else some good. It’s made me feel better about it.’ Benefits of building on historical legacies from generations of people affected by and working with cancer¹³ are commonly indexed to a distant collective future. But Jayne found that her research involvement was continuous with the ongoing care, personal and “near futures”, what Jane Guyer calls a sedimented, cumulative sense and experience (Guyer 2007).

Describing the research uses of Jayne’s samples is “to speak of a distributed, heterogenous thing” (Landecker 2000) which will likely continue to change. It was Grumpa, we suggest, that constituted the key figure driving liaison between Jayne, cancer services and research to explore and respond to its evolution. Staff were aware of what is called clonal evolution, describing distinct subpopulations of cells that emerge.¹⁴ Most models consider that driver mutations and medical therapies represent important triggers in the environment that prompt adaptations. The Grumpa figure from which cuttings were taken enabled inferences to be made about developments in this adaptive landscape and enrolled the labour of clinical and research staff as well as Jayne herself. Preliminary findings raise the possibility that the “metastatic cascade” in hormone-dependent breast cancers is associated with chance epigenetic events rather than the clonal evolution characterising these cancers at an earlier stage before treatment (Rosano et al. 2021).

¹³See Guyer’s (2007) reconsideration of the gifts described by Marcel Mauss that can only be returned indirectly across generations.

¹⁴Davis et al. (2017) note that in a cohort of 104 triple-negative breast-cancer (TNBC) patients, resolving subclones with deep sequencing identified 1 to 19 subclones per patient (Shah et al. 2012). Another study used multi-region sequencing of 50 breast cancers and identified only 1–4 major clonal subpopulations in each patient (Yates et al. 2015).

Conclusion

Classifications, treatments and knowledge change at different rates as they index possible futures in care and research. Jayne's questions about her data and samples led us to ask how her materials shaped several, more or less heterogeneous but interconnected forms of person and cancer, care and research. Jayne saw her stuff '*disappearing anonymously into an abyss of data*' in a study that in her view also saved her life while developing a 'unique profile' in a study of cancer evolution where her *golden samples* might also inform continuing care. Fortuitously, the figure of the gardener, as a moniker for a person whose identity could not be shared across settings, allowed us to begin to 'figure out' processes that were connected in some ways and separated in others. However, it is the second figure of Grumpa, the cancer that lived with Jayne and yielded cuttings and seeds, that elicited collaboration among the authors as well as health-care staff and researchers. Grumpa, distributed to various walled gardens, brings together the experimental and observational, care and research, the personal and impersonal, and the singular and plural as it changes in response to its surroundings, which are also changing.

Helen Verran (2010) describes two forms of generalising, where a one-many relation embeds or abstracts a 'case' such as ours as an example of something in general while a whole-part relation makes the history an emergent entity in a vague whole, whose parts will never add up to a complete picture (Verran 2010; Winthereik and Verran 2012). In Verran's view, there is an irreconcilable tension between these forms of generalising that demands a double vision. Sophie and Helen did not trace clear outcomes from Jayne's participation in research, nor any typical trajectory for those involved in an experimental cancer care combining data-intensive, laboratory and clinical research with health care. We (three) did not find how Jayne's data—stored, sometimes aggregated with others, and analysed—were applied in care settings or further scientific studies. However, describing this collaboration from 2019 to 2020 in terms of figures produces aspects of one-many *and* whole-part generalisations within a constitutionally incomplete picture of many moving parts.

Despite what was in Jayne's view a disappointing lack of closure, that is, the lack of a 'eureka' moment to our investigations, she concluded after discussing a draft of this chapter that her story and our combined figuring might encourage discussion between staff and patients about research that would "turn" what it figured (Haraway 2008:159). The small audit conducted by research technicians was conceived in similar terms: when results were shared, might they promote discussion and engagement with research and tissue banking, as suggested in published studies? (Bryant et al. 2015). Jayne wrote, "The process of contributing to research is a positive incentive, and makes you feel a bit more special and supported. However, don't be under any illusions that your contribution will, on its own, be responsible for any 'Eureka' moment - it is still an unidentifiable drop in the ocean. But without all the drops there would be no ocean".

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