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Hope in the Era of Precision Oncology: A Qualitative Study of Informal Caregivers' Experiences

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Hope in the Era of Precision Oncology: A Qualitative Study of Informal Caregivers' Experiences

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ABSTRACT

Objectives: To explore informal caregivers' perspectives on precision medicine in cancer care.

Design: Semi-structured interviews with the informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interview transcripts were analysed thematically using a framework approach.

Setting: Recruitment was facilitated by two hospitals and five Australian cancer community groups.

Participants: Informal caregivers (n=28; 16 men, 12 women; aged 18-80) of people living with cancer and receiving targeted/immunotherapies.

Results: Thematic analysis identified three findings, centred largely on the pervasive theme of hope in relation to precision therapies including: (1) precision as a key component of caregivers' hope; (2) hope as a collective practice between patients, caregivers, clinicians, and others, which entailed work and obligation for caregivers; and (3) hope as linked to expectations of further scientific progress, even if there may be no personal, immediate benefit.

Conclusions: Innovation and change in precision oncology are rapidly reconfiguring the parameters of hope for patients and caregivers, creating new and difficult relational moments and experiences in everyday life and in clinical encounters. In the context of a shifting therapeutic landscape, caregivers' experiences illustrate the need to understand hope as collectively produced, as emotional and moral labour, and as entangled in broader cultural expectations of medical advances. Such understandings may help clinicians as they guide patients and caregivers through the complexities of diagnosis, treatment, emerging evidence and possible futures in the precision era. Developing a better understanding of informal caregivers' experiences of caring for patients receiving precision therapies is important for improving support to patients and their caregivers.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our sample included participants involved in caring for people receiving targeted/immunotherapy for a wide range of cancer types.
- Qualitative data are crucial to better understanding informal caregivers' experiences and to improving future services and supports.
- Recruitment was undertaken nationally and interviews were conducted remotely, enabling participation across a range of settings.
- The study design limits what can be claimed to prevail across time in changing oncology treatment contexts, although follow-up interviews with a sub-set of participants enabled some insights over time.
- Recruitment for this study was limited to Australia; further investigations will be needed to explore similarities and differences across national contexts.

INTRODUCTION

The emergence of precision therapies over the past two decades has been accompanied by changed illness and survivorship experiences, most notably for patients, but also for

informal caregivers (people who provide care within the context of an existing relationship, such as a family member or friend). In oncology, ‘precision’ – the molecular profiling of tumours in order to match them with particular treatments – has led to an increased focus on the identification of cancer biomarkers, and treatment with novel targeted or immune therapies. These precision therapies differ considerably from traditional standard of care treatments such as chemotherapy[1]. Although unequally available across contexts, new precision therapies have inspired renewed hope, produced new landscapes of side-effects and survivorship, and have catalysed escalating costs[2-5].

While the impact of precision oncology on *disease* outcomes is relatively well documented[6], its varied and evolving impacts on experiences of *survivorship* and *informal caring* have received limited emphasis[4]. This is despite the fact that targeted/immunotherapies, when viable and accessible, have radically transformed survivorship (e.g., duration of treatment, types of side-effects and symptoms)[7] and informal caring roles. While some attention has been paid to the emergence of ‘precision survivorship’ (surviving with/beyond targeted treatments/immunotherapy)[7-8], including initial studies of patient perspectives[9-10], no research has foregrounded informal caregivers’ experiences and their interpretations of the precision turn in oncology. In this paper, we begin to fill this gap by delving into caregivers’ accounts of the *relational, affective* and *societal* dimensions of hope in the context of precision therapeutics.

BACKGROUND

Informal Caregivers in Cancer Scholarship

The significance of informal caregivers, and the practical and emotional work they perform in supporting people living with cancer, has received increasing attention since the turn of the century[11-12]. Such research has shown the importance of understanding illness experiences and caregiving in relational terms[13-15]. The shift from an intimate partner or parent-child relationship, for example, to one of care-giver and care-recipient involves changes to roles and responsibilities, communication and decision-making dynamics, identities and emotions[12, 15]. Moreover, the processes of coping with cancer diagnosis and treatment and making meaning of the experience happen in relation to others[16]. Thinking about “dyadic coping”[16] and other forms of interdependence includes attending to the connectedness of caregiver experiences to the capacity of cancer patients themselves to cope with intervention (precision or otherwise)[17].

Research conducted prior to the widespread availability of precision therapeutics emphasises that the type of care tasks performed, and the emotional impact on patients and caregivers, varies significantly across the cancer ‘journey’. During treatment aimed at recovery or disease control, patients and caregivers (particularly spousal carers) may construct a sense of cancer as a shared experience[16,18], while a terminal diagnosis may fracture this sense of commonality as patient and caregiver diverge in their experiences of future time[19-21]. With therapeutic shifts and rapidly changing cancer trajectories, these relational dynamics and caregivers’ engagement require specific investigation.

Precision Medicine and Survivorship

The advent of precision oncology has led to a paradigm shift in cancer research, trials and care[6]. For example, in advanced/metastatic non-small cell lung cancer (NSCLC), precision therapies have increased the median overall survival (OS) rate to

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18–36 months (compared to 8-17 months with chemotherapy)[22], and for ALK-positive NSCLC the median OS has reached 6-8 years[23-24]. Similarly in metastatic breast cancer the introduction of trastuzumab in 2000 improved 5-year survival rates for HER2 positive patients from 2 to 31%[25]. New treatments continue to improve survival [26] and precision oncology is now associated with long-term remissions in a substantial proportion of HER2 positive patients[27]. Researchers are hopeful that future innovative trials with molecularly matched tailored therapies will improve survival even further[28]. However, for those *currently* providing or receiving cancer care, these new therapeutic options can complicate decision-making about treatment pathways due to the constant emergence of new data[4].

Beyond considerations of improved survival, patients' experiences of precision cancer treatment may diverge dramatically from the well-trodden paths of surgery, chemotherapy and radiotherapy. Symptoms, side effects, costs, logistics and implications for everyday life may be very different. For example, patients may need to travel long(er) distances for trials or sub-specialist care (especially patients in rural or remote areas), self-fund molecular testing or expensive drugs, and manage family and community expectations about what living with cancer entails. This all has ramifications (financial, logistical, emotional) for families, partners and other supporters. Moreover, patients and caregivers may need to adjust their understanding of success in a therapeutic landscape in which outcomes are no longer limited to binaries of cure or death. For precision oncology patients, 'success' may involve lifelong treatment and living alongside their cancer in an ongoing way[10].

Affective Dimensions of Precision Survivorship: The Dilemmas of Hope

At the frontiers of precision oncology, hope is intrinsic to cancer care for both patients and caregivers. Experiences of cancer have long been tied to notions of scientific progress, treatment breakthroughs and therapeutic innovation[29]. This dynamic is not without complication as time-to-market, and therapeutic pipelines more broadly, take years and sometimes decades to come to fruition – if, indeed, they bear fruit at all[30]. More recent innovations around precision therapeutics have been positioned as offering considerable hope, albeit with an air of precariousness. This can be seen in biomedical research papers and broader commentary alike, with frequent use of phrases such as "hope or hype" or "hope or reality"[31-33]. Experimental precision oncology trials involving human participants who must be matched, clinically and genetically, to the requirements of the trial[3] offer a sense that medical innovation is happening in real time. Here, biographical time competes with clinical time[34] where the pace of innovation may not be fast enough to out-run the progression of disease. This precarious hopefulness suggests that precision therapeutics, as they stand, have mixed effects, the subtleties of which, including factors beyond disease impacts, deserve significant exploration.

As Corn et al[35 e452] note, hope induces "pathways and agency thinking" towards a particular goal, bringing people together around shared objectives and playing a critical role at many points in the cancer journey[12, 36, 37]. More generally, hope is a crystallisation of the individual and collective desire to survive, to overcome and to prevail – desires that have powerful and complex effects in everyday clinical settings[38]. Hope can be harnessed and deployed in the service of positive outcomes for patients with cancer and is important for caregivers' health and wellbeing, which is strongly influenced by the patients' level of hope – powerfully illustrating hope's *relational* character[12, 39]. Thinking about hope as relational means not seeing hope as absent, present, or otherwise quantifiable[40], but rather to think of hope as a

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complex *entanglement* of a wide range of social expectations (e.g., hope for precision miracles, scientific breakthroughs etc)[41]. In this way, hope can unify – binding people (patient, professional, carer, support network) together in pursuit of common purpose – but it can also become a source of disagreement, conflict and disorientation[42-44].

Hope's perceived therapeutic value can place emotional demands on caregivers (and others), who must work to generate, maintain and protect hope as a way of contributing to the patient's care and potential survival[11,45, 46]. Social science researchers such as Arlie Hochschild[47] thus speak about the *performative* dimensions of emotion management, where individuals invest considerable effort shaping their inner emotions – or, at least, moderating their public expression of these emotions – to meet the demands of their situation and the expectations of their family/community/society. In this sense, hoping is (hard) work that is often undertaken *collectively*, as different individuals – patients, carers, healthcare professionals and so on – encourage one another and co-create hope through implicit agreement. Ambiguous prognoses, for example where novel treatments are extending survival in the context of emerging evidence, thus increase the difficulty of the emotion work performed by caregivers[48].

These more nuanced dimensions of hope – as precarious, as relational, as work, – imbue hope not only with positivity but also with painful potential. Offering hope is not always a kindness and might even become toxic in some circumstances[49]. Certainly, hope can be difficult to manage in terms of expectations versus realities and might even be harmful when inaccurately deployed or internalised (i.e., when the hopeful future does not arrive). In essence, hope is not universally or unquestionably positive, it can also be difficult and, unfortunately, cannot inoculate against suffering. In the context of precision oncology, sufficient attention is yet to be paid to informal caregivers' perspectives on the complex interplay between individual prognoses, interpersonal dynamics, institutional pressures, social expectations, and the political and economic dimensions of therapeutic innovation. In this paper, we draw from our analysis of interviews with informal caregivers to untangle some of these dimensions and to provide new insights into how the relationality of hope is being reconfigured through developments in precision oncology.

METHODS

Context

Taking an interpretive approach to research design, data collection and analysis, this article draws on data from in-depth, semi-structured interviews with 28 informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interviews were conducted May 2020-August 2021 in Australia. Ethics approval was gained through a metropolitan hospital on Australia's east coast. Interviews were carried out as part of a broader qualitative study focused on contemporary experiences of cancer care in the era of precision oncology[10]. The study involved a collaboration between health social scientists and clinician-researchers across three institutions and was aided and supported by five cancer-related consumer groups. Patients, caregivers and healthcare professionals were interviewed for the study.

Patient and Public Involvement

Patients were not involved in the study design/conduct.

Sampling and Recruitment

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This paper reports on the caregiver component of the study. Caregivers were recruited via convenience sampling through patients who were participating in the broader study. Using a purposive sampling method, potential patient participants who had sought out, tested for, and/or experienced targeted and/or immunotherapies during their cancer care were approached by a clinician, researcher, and/or consumer group organiser to explain the study. If they expressed interest in participating, participants were contacted via phone to initiate the informed written consent process and to schedule an interview via video or phone call. Patients were asked if they would like to nominate a partner, family member and/or friend who played a role in their care to be invited to participate in an interview. The researchers then contacted the nominated caregivers. Interested caregivers were provided with an information sheet outlining the aims of the study and were contacted to schedule an interview. To be included, carers had to have been nominated by a patient participant, be 18-years-old or older and proficient in English. Participant recruitment continued until there was consensus among research team members that saturation had been reached.

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Data Collection

Interviews were semi-structured and iteratively explored a range of issues around participants' lived experience of caring for someone with cancer in the context of targeted treatments and/or immunotherapies. Caregivers were asked about their experiences of their loved one's diagnosis, treatment and care, and their experiences of supporting them through these events. The caregiver interviews were conducted by Author X; a sociologist with experience in in-depth qualitative interviewing in sensitive contexts. Interviews were conducted remotely, via video-call (due to COVID-19 public health measures), which facilitated geographical diversity across Australian states. Interviews lasted between 22 and 105 minutes (mean: 58 minutes), were audio-recorded, and were transcribed in full. Transcripts were deidentified, and each participant was assigned a code. Interviews did not focus specifically on hope, but this was a key issue raised by participants. The findings are derived inductively from analysis of participants' interviews.

Analysis

NVivo software was used to conduct a thematic analysis of the full interview transcripts. The thematic analysis was driven by a framework approach, involving the following steps: first, transcripts were repeatedly read, and coded in line with emerging ideas and themes. Data were organised around the key themes and ideas (identification of the framework), and through this process, broader themes were developed to build a picture of the data as a whole[50]. Author X led the initial coding of the data. This initial coding was then cross-checked to facilitate the development of themes (authors X, X and X), moving towards an overall interpretation of the data. Codes were discussed among the authors, who looked for emergent patterns and anomalies across interview transcripts to confirm consistency of interpretation of the data. Analytic rigour was enhanced by searching for negative, atypical and conflicting or contradictory items in coding and theme development.

RESULTS

Participant Characteristics

Informed written consent was obtained from 28 caregivers (16 men and 12 women, aged between 18 and 80) who then participated in one-on-one, semi-structured interviews. Nine caregivers also participated in a follow-up interview approximately 6 months after their initial interview. The sample included people caring for those living with neuroendocrine (12), lung (11), breast (2), rare (2), and brain (1) tumours. Caregivers included spouses (15), adult children (6), friends (3), parents (2), other relative (1), and one support worker. Three patients (with rare, neuroendocrine, and lung cancers) nominated two caregivers who were both interviewed, and one patient (neuroendocrine cancer) nominated three caregivers, all of whom were interviewed. Table 1 provides further details about caregivers' characteristics, including age and geographical diversity.

Table 1: Participant Characteristics

Participant characteristic	***n=28 (%)***
Caregiver sex	
Male	*16 (57)*
Female	*12 (43)*
Caregiver relationship to patient	
Spouse	*15 (54)*
Adult child	*6 (21)*
Parent	*2 (7)*
Sibling	*1 (4)*
Friend	*3 (11)*
Support worker	*1 (4)*
Patient cancer type*	
Neuroendocrine	*12 (43)*
Lung	*11 (39)*
Breast	*2 (7)*
Rare	*2 (7)*
Brain	*1 (4)*
Caregiver location	
NSW	*9 (32)*
Queensland	*8 (29)*
Victoria	*5 (18)*
Western Australia	*4 (14)*
South Australia	*1 (4)*
ACT	*1 (4)*
Caregiver age	
30 and under	*4 (14)*
31-50	*6 (21)*
51-70	*12 (43)*
Over 70	*6 (21)*

** Some patients nominated more than one caregiver. Numbers in this table reflect the number of caregivers caring for patients with a particular cancer type.*

Precision-Induced Hope

The sense of hope induced by targeted/immunotherapies was powerfully evident across many of the caregiver interviews. Caregivers routinely described themselves and their loved ones as 'privileged', 'thankful' and 'lucky' to have access to these new therapeutic pathways, often noting how recently precision treatments for the particular tumour in question had been discovered, approved and/or funded. As the quotes in Table 2 illustrate, many of the interviewees saw the rise and availability of precision therapies in oncology as a *hopeful development*. The ability to access these therapies was often articulated in contrast to others who did not have this access, for example people with different cancer types or living in places/times without these options. 'Precision' care was thus seen to open a new door to hope[3].

Until their loved one's cancer diagnosis, many caregivers professed to having had no prior knowledge of precision therapies, how they worked or acted in/on the body, and what that might mean for their and their loved one's shared present and/or future. Yet their early accounts were strongly underpinned by the fear of – and relief at avoiding – chemotherapy and radiation. Often they associated chemotherapy, to some extent, with hopelessness and debilitating side effects, and thus perceived precision therapies as offering greater hope in terms of *both* life extension and quality of life. However, as carers, patients and clinicians navigated the uncertain waters of precision treatment, the hope and gratitude invested in medical innovation was moderated by everyday experiences of scans, side effects, results, costs and ongoing logistical struggles. In the follow-up interviews, several caregivers expressed gratitude for the time (together) that the precision treatments had already provided, irrespective of how long this could continue. This pointed to the importance of considering hope as relational, which we focus on below.

Table 2: Indicative Quotes: Precision-Induced Hope

Participant[1]	Indicative quote
Spouse, M 70+, neuroendocrine cancer	Oh, I think we're very, very privileged. We are. We're very grateful that it is there for us to use, yes. Yeah, so we are. We're very, very grateful and we just pray and hope that it's going to have some positive effect on the tumours.
Daughter, F 51-70, lung cancer	We were very positive yesterday. I couldn't wait to talk to my brother. Yeah, we're feeling really good, and blessed too. Obviously blessed and thankful. I think we're all hoping for the magic bullet for cancer, but this immunotherapy, it's been fantastic. And I hope a lot of families benefit from it. It's great. [later] It was like winning a prize, I recall. It was like, "Oh, we won. Your cancer is eligible for this new immunotherapy thing."
Daughter, F <30, lung cancer	I'm just really happy that we're in this day and age and not even 10, 20 years ago when this [drug] potentially wasn't around.
Spouse, M 51-70, neuroendocrine cancer (a)	Yeah, well I was just elated. I just thought like, "Here we go. Something's happening. We can do something. We can have a fight." [later] It's just exciting to see that all these people are actually putting all this effort into NETs all of a sudden and they're coming up with all these strange ideas.
Sister, F 51-70, brain cancer	Well, I think it was amazing that he had access to it. Extremely, extremely, extremely lucky, like a fluke really. He's the only one in Australia that I know of that is having this, unless there are trials now. I'm not sure if there's trials in Australia. So he's extremely lucky, and I think everyone should have access to it.
Spouse, M 51-70, breast cancer	[I knew] nothing. When I heard that, "Okay, this is this type of cancer and we've got this drug here which is perfect to target you. You're one of the lucky ones." I remember them saying that, that, "You're the lucky ones because this is made for the

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[1] Participants are identified in data tables by their relationship to the patient, sex (M/F), age range, and patient cancer type. Participants with same information are distinguished by the addition of e.g. (a).

	type of cancer you've got.
Spouse, M 51-70, neuroendocrine cancer (b)	I wasn't aware that there was any targeted therapy before, for any sort of cancer. So, it was completely new to me and it was terrific. You couldn't ask for anything more. The cancers were all, most of them were still there, but they'd reduced in size. Some had gone, but a lot of them had stayed. But I'd never heard of that sort of treatment being as effective before.
Spouse, M 51-70, neuroendocrine cancer (b)	If you start doing chemo, well that's the beginning of the end from my perspective. Not that I ever said that to [patient], but that's how I felt. But then, after the oncologist explained everything properly and we understood that it was an injection once a month and this could go on forever, well, you felt much more comfortable about things.
Son, M <30, lung cancer	I know that we may have to go through chemo down the line, because, from what I've been told, it's all a bit hazy, but I think the targeted therapy will reach a point where it won't have the effects, it won't have the success that it does and then she'll have to resort to chemo. But yeah, it really has just allowed us to have valuable time as a family.

Hope as Relational: From Hope as 'Work' to Obligation

As illustrated by caregivers' perspectives presented in Table 2 and in the interviewees' accounts more broadly, precision therapeutics initially offered caregivers relief and comfort through the knowledge that the 'science' of cancer treatment– including treatment options for their loved one's cancer type – was advancing. This provided a sense that new personalised options were emerging that would have seemed unlikely or impossible even a few years earlier. However, caregivers' stories of hope-in-precision also involved new relational complexities, and perceptions of precision often changed over time, as the follow-up interviews showed. One example of this complexity was a dialectical tension between hope and obligation[51]. Specifically, and as illustrated in Table 3, caregivers frequently reflected that hope was *required* for treatment to be successful, it needed to be found or even manufactured. The *work* of generating or projecting hope[47, 52] was consistently discussed within the caregiver interviews.

Some caregivers observed that the social expectation to profess hope induced a sense of alienation, particularly in relation to people not involved in the everyday reality of cancer. The hopes of others, imposed on caregivers via hopeful talk or encouragement to be positive, was described, for example, as deeply "irritating", signifying, for our participants, a fundamental misrecognition of the challenges of living with, and caring within, the precision-cancer milieu (i.e., not as 'easy' or 'liberating' as one might imagine). Perhaps enhanced by the lack of traditional signifiers of cancer (e.g., hair loss/nausea), the precision scene was seen as exacerbating the disorientations between recognition of suffering and performativity of hope, perseverance and determination, as the quotes in Table 3 indicate.

Hope was also a prominent feature of therapeutic encounters. Just as caregivers felt an obligation to enact hope relationally – to express and practice hope – so too did they see it as an obligation of clinicians to cultivate hope in clinical encounters. Several caregivers expressed a belief that maintaining hope should be a higher order priority for clinicians than managing expectation, which has often been a focus of discussion in and around effective clinical communication[53-54]. In several cases, caregivers discussed supporting the patient to find a new healthcare professional in response to "hurtful" statements of hopelessness, illustrating the tightrope clinicians walk in navigating, negotiating and co-constructing hope with patients and caregivers.

As the indicative quotes in Table 3 illustrate, patients, caregivers and clinicians work (and sometimes struggle) to reframe hope in the precision-oncological context. For example, while clinicians may not use terms like “remission” in this context, for patients and caregivers the absence or refusal of this term may be understood as “killing hope”. Evolving and unsettled evidence, and gaps in lay understandings of treatments and potential outcomes, may mean that patients, caregivers, clinicians and other social actors lack the necessary shared language or knowledge to successfully navigate the complexities of hope in the swiftly evolving landscape of precision therapeutics.

Table 3: Indicative Quotes: Hope as Relational: From ‘Hope Work’ to Obligation

Participant	Indicative quote
Sister, F 51-70, brain cancer	You just have to be hopeful that he’ll have this treatment again and he’ll deal with it quick, if that’s what it was. So yeah, hopeful. Otherwise it’s shit. So you’ve got to be hopeful.
Spouse, M 51-70, lung cancer (a)	And one thing I noticed a lot of people saying, and I had to wonder if I’d ever said it myself, but when your friends and acquaintances hear you’ve got cancer, they all tend to say, “Oh look, she’s a strong girl. You’ll get through this. She’s strong. We’re praying for you. You’ll get through this.” And a few people said that, and I didn’t say anything, but I found it really irritating. That really bugged me because what I thought of was, “No, we’re not walking off into the sunset hand in hand to fight the good fight. This is a bloody ugly street fight.” There’s nothing nice about it. There’s nothing noble about it. It’s not Joan of Arc on a horse with a shield and a sword and, “We’re going to slay this cancer dragon.” It’s nothing like that. It is totally devastating.
Spouse, M 51-70, lung cancer (a)	And this one doctor confused a question and she mentioned something about the side-effects and the medication and the doctor just blurted out in front of everybody, the whole family, “Oh no, there’s no [remission]. You will be on medication for the rest of your life.” […] Now, that was not what she needed to hear […]. And it was just blurted out so matter of factly by a doctor.
Spouse, M 51-70, lung cancer (b)	He [oncologist] probably rubbed [her] up the wrong way immediately because he presented a very negative outcome immediately […]. Reading the notes at the time, they obviously hadn’t been pre-prepared and it caught him by surprise. And because it caught him by surprise, he probably spoke in a way that he probably wouldn’t have otherwise done, but that’s where he killed a lot of hope in [her] because that’s when he said, “You have stage four and there’s no such thing as remission.” […] It really took a lot of positivity out of her response to the disease initially. So, yeah, it was quite devastating for us both.
Spouse, M 51-70, lung cancer (b)	They don’t understand how hurtful some of the stuff they can say is, and the effects it has on their patients. Almost like it’s unconscious, I suppose. But anyway, as I said, in a social context he’d be probably very personable, people would like him. But as far as [she] was concerned, she would prefer

	someone to be a little bit more positive.
Mother, F 70+, neuroendocrine cancer	Give them the facts, sure. But in a way that it's not just all death and destruction. That there is maybe some light at the end of the tunnel with some research or something that's going to go on. "We're progressing all the time," and talk like that, I think. It's a better way of talking.

Speculative Hope and Hope for the Common Good

From the caregivers' perspective, hope spanned the individual and collective, the present and future, obligation and aspiration. The very concept of hope implies a goal or object – something that is hoped *for*. In the precision context, this was often oriented towards the prospect of medical innovation. In this dual focus on presently unfolding progress and as-yet-unknown future advances, caregivers articulated a sense of being part of a wider social phenomenon as well as being embedded in a deeply personal experience. Thus, individualised hopes – for survival, for the future life experiences that survival might bring, for minimal symptoms or side effects – were also considered in relation to the common good or the benefit of future patients, caregivers and families.

Deliberation over benefit was far from stable and a source of ongoing renegotiation within families. For instance, some caregivers expressed frustration or fear that progress would not happen fast enough to benefit their relative/friend, but others were more sanguine, accepting that being at the cutting edge of innovation meant being a "guinea pig" (see Table 4), in part to benefit others in the future. While the idea of lifelong treatment implied a lack of hope for some caregivers (for a return to normal life post cancer – see Table 3), it opened up a hopeful vista of continuation for others (see Table 4). For still others, especially older patients and caregivers, quality of life was more important than life-extending scientific breakthrough as they felt they had lived (a good) enough life.

The hope invested in the notion of ongoing scientific progress was often grounded in the fear that even successful treatments would likely stop working in the future. This shadow of fear drove some caregivers to engage in the 'hopeful work' of advocacy, seeking out trials and treatments and/or lobbying for access and funding. When precision treatments failed or side effects proved intolerable, caregivers and families were often forced to re-evaluate their early hopes for continuation of life, asking painful questions about if and where hope might now be found. Initial responses of relief and gratitude (see Table 2) evolved into complex and fluctuating emotions, characterised by the need to provide consistent support in the face of uncertainty, hope and disappointment, compounded by fluctuating side effects and the fatigue of long-term life on treatment.

Hope, in this precision oncology context, spread across bodies, families, experts and fields of science, holding on to both the potential for an individual disease outcome and the altruism of the common good from participation in science and innovation. Hope, in this sense, was speculative both in terms of the outcomes for those they cared for, and the future possibilities the 'stop and start' of science may offer. This reflects the ethics of hope, as about solidarity as well as about the individual prevailing, and in turn, how uncertainty binds to hope. That is, *being on the precipice* – of breakthrough or death – is a key affective relation permeating the precision environment.

Table 4: Indicative Quotes: Speculative Hope and Common Good

Participant	Indicative quote
Spouse, M 51-70, lung cancer (c)	Well, I'm a supreme optimist. I think that they'll come up with a cure, so I'm not too worried. I think that she'll just keep going, and

	we'll keep doing the same thing. I think [oncologist] was actually talking about it, the next type of TKI would be on the horizon soon. So if these two don't work, then there'll be probably something else or another trial or something, and this'll go on for a few more years, and then eventually they'll have a cure and everything will be back to normal.
Spouse, M 31-50, rare cancer	Oh, it [possibility of entering a trial] was pretty exciting actually. I thought, "Okay, great. Maybe there's this magic pill out there." Then [she] was sort of excited and I was – I'm a little bit more reserved and go "Okay, I'll wait and see until it happens."
Spouse, M 70+, neuroendocrine cancer	I mean, if, in the end, it helps somebody. I mean, the only way we can help other people and develop things is to – Somebody's got to be the guinea pig in the end.
Spouse, M 51-70, lung cancer (a)	My biggest fear is if the targeted therapy that she's currently on doesn't keep working, then we're in trouble. But, as they say, they are developing all the time. […] If that stops working, we have to hope the next one comes along, or we have to hope we can get involved with trials. But that's probably my biggest fear that got me to understand a bit more about the targeted therapy. And also, just as they keep saying, the research keeps advancing, so there is always hope that they are constantly advancing and […] down the track there will be the next generation of drugs that will be a back stop if she feels, or they feel, the doctors feel, "Well, let's move onto the next one to keep this in check."
Spouse, M 70+, neuroendocrine cancer	They did mention [a trial], but it would mean that [she] would have to go into hospital, I think it was once a week for eight hours, for this clinical trial […] I mean, we are sort of getting older and […] I think [she] is still looking at this thing about the quality of life, and not the quantity.[…]So we're thinking, "Well…" And at our age, quite frankly, we've sort of had a good life. We're just sort of saying, "Look, we've had a good life. If this is the end of the story, well, that's fine. We've done quite well. We've done very well."
Mother, F 70+, neuroendocrine cancer	I read everything in the newspapers about trials, but they're all in five years' time, 10 years' time, and all this. What's the use of that for Christ's sake? They're dying now.
Spouse, F 51-70, lung cancer	[We thought] you have your chemo treatment and all that and then this would be the icing on the cake. […] Once you've had the immunotherapy, this is going to be the be all and end all of getting rid of the cancer. And once you've had that year, then that's it. That's how it felt. But then when it didn't work, it was like, "Oh shit, we've only had four treatments. Does that mean the end of it?"
Spouse, M 70+, lung cancer	Well, I didn't know much about it. I mean, I just checked, showed on the internet, and it seems to work with her because initially the cancer shrank. It was 22 millimetres and then it shrank. After three months, it shrank to 18 and so we were in good hope that the medication is effective. But then, with the time, the virus itself changed or mutated the virus cells and the first medicine didn't have any effect anymore. […] And so, yeah, I was in shock again somehow. Because this was a treatment the doctor said was 95% it's working and it is a good alternative and all this, and then just like somebody takes the ground off your feet. And so then we were, of course, talking about alternatives, but obviously they don't have much alternatives except chemotherapy, and that's what they put her on.

DISCUSSION

The last decade or so has been transformative for practice and outcomes in oncology. The precision turn, variable as it is across cancer types, has radically reconfigured expectations around the outcomes of malignancy and introduced new vistas of hope and possibility for many (though not all). What has not been adequately explored is laypersons' perspectives on the precision turn in oncology and in particular, accounts of patients and caregivers. Here we focus on caregiver perspectives, with a particular interest in their experiences of hope in and around precision, and its complexities in this swiftly evolving scene.

Interviews with these caregivers provide important insight into the emerging and evolving social world of precision oncology, and how those in supportive roles view and make sense of care and survivorship in this context. Hope, as it emerged, was a binding narrative within the interviews, but in complex and unexpected ways. Moving beyond simple binaries such as optimism/pessimism, realistic/unrealistic, ignorance/understanding, analysis of the caregivers' interviews revealed the importance of relationships, values and commitment to (or faith in) science/innovation in mediating caregivers' experiences of precision oncology and their orientation around hope, therein. What emerged was a picture of the relational nature of (precision-induced) hope and gratitude, the relational 'work' of upholding hope, associated forms of obligation and also the possibility of solidarity with future beneficiaries of experimental therapies. That is, caregivers' experiences of precision treatments contained a mix of the *enabling* features in terms of patient benefits, increased survival and so on, but also the *normative* including the ways in which new treatment trajectories introduce new sets of requirements and expectations across patients, carers and clinicians in everyday life.

The results also introduce some important concepts as to how we think about care in the context of precision oncology, and indeed, resonate with much of the broader literature on both hope and caring relations. First, hope is less a property of the individual (patient or caregiver) and more a collective accomplishment, negotiated across complex social relations and expectations. Second, hope is a form of *work* – it needs to be generated and projected – with caregivers deeply involved in this practice of hope. This work is not straightforward, often involves considerable suffering, and, as one participant articulated, can be "a bloody ugly street fight" despite the optics of optimism. Finally, these caregivers' perspectives accentuate the power of *hope in scientific progress* – in this case genomic – as mobilising, animating, and directing the scene of oncological survivorship. In this context, hope is not only emotional but also *moral labour*, which operates in a dialectic tension between how *I* may benefit now and how the future *we* may benefit, later. The hope-precision nexus is thus an evolving *ethical system*, whereby participation in trials, acceptance of novel drugs with uncertain outcomes, advocacy for access to (subsidised) therapeutics and so on involves a mix of concern for the self and concern for the other (present or future).

This study of caregivers' experiences provides rich insights into the 'social life' of precision oncology. In particular, it underlines the ways that innovation and change in the precision era can rapidly reconfigure the parameters of hope (unclear therapeutic trajectories, uncertain survival chances), creating new and difficult relational moments and experiences in everyday life. How patients, caregivers and clinicians alike navigate between uncertain chances of success and hopeful possibility and potential will likely remain a challenge in years to come.

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Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	p.1
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	p.2

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Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	pp.3-5
Purpose or research question - Purpose of the study and specific objectives or questions	P3 (para 2) and P5 (final para of intro)

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Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	P15

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Hope in the Era of Precision Oncology: A Qualitative Study of Informal Caregivers' Experiences

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ABSTRACT

Objectives: To explore informal caregivers' perspectives on precision medicine in cancer care.

Design: Semi-structured interviews with the informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interview transcripts were analysed thematically using a framework approach.

Setting: Recruitment was facilitated by two hospitals and five Australian cancer community groups.

Participants: Informal caregivers (n=28; 16 men, 12 women; aged 18-80) of people living with cancer and receiving targeted/immunotherapies.

Results: Thematic analysis identified three findings, centred largely on the pervasive theme of hope in relation to precision therapies including: (1) precision as a key component of caregivers' hope; (2) hope as a collective practice between patients, caregivers, clinicians, and others, which entailed work and obligation for caregivers; and (3) hope as linked to expectations of further scientific progress, even if there may be no personal, immediate benefit.

Conclusions: Innovation and change in precision oncology are rapidly reconfiguring the parameters of hope for patients and caregivers, creating new and difficult relational moments and experiences in everyday life and in clinical encounters. In the context of a shifting therapeutic landscape, caregivers' experiences illustrate the need to understand hope as collectively produced, as emotional and moral labour, and as entangled in broader cultural expectations of medical advances. Such understandings may help clinicians as they guide patients and caregivers through the complexities of diagnosis, treatment, emerging evidence and possible futures in the precision era. Developing a better understanding of informal caregivers' experiences of caring for patients receiving precision therapies is important for improving support to patients and their caregivers.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our sample included participants involved in caring for people receiving targeted/immunotherapy for a wide range of cancer types.
- Qualitative data are crucial to better understanding informal caregivers' experiences and to improving future services and supports.
- Recruitment was undertaken nationally and interviews were conducted remotely, enabling participation across a range of settings.
- The study design limits what can be claimed to prevail across time in changing oncology treatment contexts, although follow-up interviews with a sub-set of participants enabled some insights over time.
- Recruitment for this study was limited to Australia; further investigations will be needed to explore similarities and differences across national contexts.

INTRODUCTION

The emergence of precision therapies over the past two decades has been accompanied by changed illness and survivorship experiences, most notably for patients, but also for

informal caregivers (people who provide care that is unremunerated and within the context of an existing relationship, such as a family member or friend). In oncology, 'precision' – the molecular profiling of tumours in order to match them with particular treatments – has led to an increased focus on the identification of cancer biomarkers, and treatment with novel targeted or immune therapies. These precision therapies differ considerably from traditional standard of care treatments such as chemotherapy[1]. Although unequally available across contexts, new precision therapies have inspired renewed hope, catalysed escalating costs and produced new landscapes of side-effects and survivorship [2-5].

While the impact of precision oncology on *disease* outcomes is relatively well documented[6], its varied and evolving impacts on experiences of *survivorship* and *informal caring* have received limited emphasis[4]. This is despite the fact that targeted/immunotherapies, when viable and accessible, have radically transformed survivorship (e.g., duration of treatment, types of side-effects and symptoms)[7] and associated informal caring roles. While some attention has been paid to the emergence of 'precision survivorship' (surviving with/beyond targeted treatments/immunotherapy)[7-8], including initial studies of patient perspectives[9-10], no research has foregrounded informal caregivers' experiences and their interpretations of the precision turn in oncology. In this paper, we begin to fill this gap by delving into caregivers' accounts of the *relational, affective* and *societal* dimensions of hope in the context of precision therapeutics.

BACKGROUND

Informal Caregivers in Cancer Scholarship

The significance of informal caregivers, and the practical and emotional work they perform in supporting people living with cancer, has received increasing attention since the turn of the century[11-12]. Such research has shown the importance of understanding illness experiences and caregiving in relational terms[13-15]. The shift from an intimate partner or parent-child relationship, for example, to one of care-giver and care-recipient involves changes to roles and responsibilities, communication and decision-making dynamics, identities and emotions[12, 15]. Moreover, coping with cancer diagnosis and treatment invariably happens within the context of myriad relationships[16]. Thinking about "dyadic coping"[16] and other forms of interdependence includes attending to the connectedness of caregiver experiences to the capacity of cancer patients themselves to cope with intervention (precision or otherwise)[17].

Research conducted prior to the widespread availability of precision therapeutics emphasises that the type of care tasks performed, and the emotional impact on patients and caregivers, varies significantly across the cancer 'journey'. During treatment aimed at recovery or disease control, patients and caregivers (particularly spousal carers) may construct a sense of cancer as a shared experience[16,18], while a terminal diagnosis may fracture this sense of commonality as patient and caregiver diverge in their experiences of future time[19-22]. With therapeutic shifts and rapidly changing cancer trajectories, these relational dynamics and caregivers' engagement require specific investigation.

Precision Medicine and Survivorship

The advent of precision oncology has led to a paradigm shift in cancer research, trials and care[6]. For example, in advanced/metastatic non-small cell lung cancer (NSCLC), precision therapies have increased the median overall survival (OS) rate to

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18–36 months (compared to 8-17 months with chemotherapy)[23], and for ALK-positive NSCLC the median OS has reached 6-8 years[24-25]. Similarly in metastatic breast cancer the introduction of trastuzumab in 2000 improved 5-year survival rates for HER2 positive patients from 2 to 31%[26]. New treatments continue to improve survival [27] and precision oncology is now associated with long-term remissions in a substantial proportion of HER2 positive patients[28]. Researchers are hopeful that future innovative trials with molecularly matched tailored therapies will improve survival even further[29]. However, for those *currently* providing or receiving cancer care, these new therapeutic options can complicate decision-making about treatment pathways due to the constant emergence of new data[4].

Beyond considerations of improved survival, patients' experiences of precision cancer treatment may diverge dramatically from the well-trodden paths of surgery, chemotherapy and radiotherapy. Symptoms, side effects, costs, logistics and implications for everyday life may be very different. For example, patients may need to travel long(er) distances for trials or sub-specialist care (especially patients in rural or remote areas), self-fund molecular testing or expensive drugs, and manage family and community expectations about what living with cancer entails. This all has ramifications (financial, logistical, emotional) for families, partners and other supporters. Moreover, patients and caregivers may need to adjust their understanding of success in a therapeutic landscape in which outcomes are no longer limited to binaries of cure or death. For precision oncology patients, 'success' may involve lifelong treatment and living alongside their cancer in an ongoing way[10].

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Affective Dimensions of Precision Survivorship: The Dilemmas of Hope

Hope is intrinsic to cancer care and survivorship for both patients and caregivers. As Corn et al. note, hope induces "pathways and agency thinking"[30] towards a particular goal, bringing people together around shared objectives and playing a critical role at many points in the cancer journey[see also 12, 31, 32]. More generally, hope is a crystallisation of the individual and collective desire to survive, to overcome and to prevail – desires that have powerful and complex effects in everyday clinical settings[33]. Hope can be harnessed and deployed in service of positive outcomes for patients with cancer and is important for caregivers' health and wellbeing, which is strongly influenced by the patients' level of hope – powerfully illustrating hope's *relational* character[12, 34]. Thinking about hope as relational means not seeing hope as absent, present, or otherwise quantifiable[35], but rather to think of hope as a complex *entanglement* of a wide range of social expectations (e.g., hope for precision miracles, scientific breakthroughs etc)[36]. In this way, hope can unify – binding people (patient, professional, carer, support network) together in pursuit of common purpose – but it can also become a source of disagreement, conflict and disorientation[37-39].

Hope's perceived therapeutic value can place emotional demands on caregivers (and others), who must work to generate, maintain and protect hope as a way of contributing to the patient's care and potential survival[11,40, 41]. Social science researchers such as Arlie Hochschild[42] thus speak about the *performative* dimensions of emotion management, where individuals invest considerable effort shaping their inner emotions – or, at least, moderating their public expression of these emotions – to meet the demands of their situation and the expectations of their family/community/society. In this sense, hoping is (hard) work that is often undertaken *collectively*, as different individuals – patients, carers, healthcare professionals and so on – encourage one another and co-create hope through implicit agreement. Ambiguous prognoses, for example where novel treatments are extending survival in the context of emerging evidence, thus increase the difficulty of the emotion work performed by caregivers[43].

In this paper, we draw from our analysis of interviews with informal caregivers to untangle some of the dimensions of hope – as collectively produced through both clinical and emotional work – and to provide new insights into how the relationality of hope is being reconfigured through developments in precision oncology.

METHODS

Context

Taking an interpretive approach to research design, data collection and analysis, this article draws on data from in-depth, semi-structured interviews with 28 informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interviews were conducted May 2020-August 2021 in Australia. Ethics approval was gained through a metropolitan hospital on Australia's east coast. Interviews were carried out as part of a broader qualitative study focused on contemporary experiences of cancer care in the era of precision oncology[10]. The study involved a collaboration between health social scientists and clinician-researchers across three institutions and was aided and supported by five cancer-related consumer groups. Patients, caregivers and healthcare professionals were interviewed for the study. Following Mays and Pope's guidance for assessing the validity and relevance of qualitative research [44], we provide below a clear exposition of data collection and analysis methods; each finding is supported by a range of data excerpts, including outliers or contradictory examples; and the research is placed in dialogue with an extensive literature drawn from both social science and clinical traditions (see Background – above).

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Patient and Public Involvement

Patients were not involved in the study design/conduct.

Sampling and Recruitment

This paper reports on the caregiver component of the study. Caregivers were recruited via convenience sampling through patients who were participating in the broader study. Using a purposive sampling method, potential patient participants who had sought out, tested for, and/or experienced targeted and/or immunotherapies during their cancer care were approached by a clinician, researcher, and/or consumer group organiser to explain the study. If they expressed interest in participating, participants were contacted via phone to initiate the informed written consent process and to schedule an interview via video or phone call. Patients were asked if they would like to nominate a partner, family member and/or friend who played a role in their care to be invited to participate in an interview. The researchers then contacted the nominated caregivers. Interested caregivers were provided with an information sheet outlining the aims of the study and were contacted to schedule an interview. To be included, carers had to have been nominated by a patient participant, be 18 years old or older and proficient in English. Participant recruitment continued until there was consensus among research team members that saturation had been reached.

Data Collection

Interviews were semi-structured and iteratively explored a range of issues around participants' lived experience of caring for someone with cancer in the context of targeted treatments and/or immunotherapies. Caregivers were asked about their experiences of their loved one's diagnosis, treatment and care, and their experiences of supporting them through these events. The caregiver interviews were conducted by AP, a sociologist with experience in in-depth qualitative interviewing in sensitive contexts. Interviews were conducted remotely, via video-call (due to COVID-19 public health measures), which facilitated geographical diversity across Australian states. Interviews lasted between 22 and 105 minutes (mean: 58 minutes), were audio-recorded, and were transcribed in full. Transcripts were deidentified, and each participant was assigned a code. Interviews did not focus specifically on hope, but this was a key issue raised by participants. The findings are derived inductively from analysis of participants' interviews.

Analysis

A systematic thematic analysis – driven by the framework approach[45] – was conducted using NVivo 11 software as a data management tool. Analysis involved the following steps: (1) Familiarisation: researchers reviewed the transcripts. (2) Identification of key themes relating to research aims. (3) Application of themes to text: labelling and arranging each text excerpt, word, term, or research note related to each participant, producing lists including data and notes from several participants according to themes. (4) Charting: headings and subheadings were used to build an overall picture of the data. (5) Mapping and interpretation: associations were clarified, and explanations developed. LWV, a sociologist experienced in qualitative data analysis, led the initial coding of the data. This was then cross-checked (by authors KK, AB and MP, all social scientists), to facilitate the development of themes. This included identifying emergent patterns and anomalies across interview transcripts, moving towards an overall interpretation of the data. The analysis was shared and discussed with the wider research team, including clinician-researchers, to confirm consistency and credibility of the interpretation. Analytic rigour was enhanced by searching for negative, atypical and conflicting or contradictory items in coding and theme development.

RESULTS

Participant Characteristics

Informed written consent was obtained from 28 caregivers (16 men and 12 women, aged between 18 and 80) who then participated in one-on-one, semi-structured interviews. As part of the study design, participants were offered a follow-up interview approximately 6 months after their initial interview, with the aim of eliciting longitudinal insights, including reflections on changing prognoses and experiences of treatment. Nine caregivers participated in a follow-up interview. The sample included people caring for those living with neuroendocrine (12), lung (11), breast (2), rare (2), and brain (1) tumours. Caregivers included spouses (15), adult children (6), friends (3), parents (2), other relative (1), and one support worker. Three patients (with rare, neuroendocrine, and lung cancers) nominated two caregivers who were both interviewed, and one patient (neuroendocrine cancer) nominated three caregivers, all of whom were interviewed. Table 1 provides further details about caregivers' characteristics, including age and geographical diversity.

Table 1: Participant Characteristics

Participant characteristic	***n=28 (%)***
Caregiver sex	
Male	*16 (57)*
Female	*12 (43)*

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Caregiver relationship to patient	
Spouse	*15 (54)*
Adult child	*6 (21)*
Parent	*2 (7)*
Sibling	*1 (4)*
Friend	*3 (11)*
Support worker	*1 (4)*
Patient cancer type*	
Neuroendocrine	*12 (43)*
Lung	*11 (39)*
Breast	*2 (7)*
Rare	*2 (7)*
Brain	*1 (4)*
Caregiver location	
NSW	*9 (32)*
Queensland	*8 (29)*
Victoria	*5 (18)*
Western Australia	*4 (14)*
South Australia	*1 (4)*
ACT	*1 (4)*
Caregiver age	
30 and under	*4 (14)*
31-50	*6 (21)*
51-70	*12 (43)*
Over 70	*6 (21)*

* *Some patients nominated more than one caregiver. Numbers in this table reflect the number of caregivers caring for patients with a particular cancer type.*

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Precision-Induced Hope

The sense of hope induced by targeted/immunotherapies was powerfully evident across many of the caregiver interviews. Caregivers routinely described themselves and their loved ones as ‘privileged’, ‘thankful’ and ‘lucky’ to have access to these new therapeutic pathways, often noting how recently precision treatments for the particular tumour in question had been discovered, approved and/or funded. As the quotes in Table 2 illustrate, many of the interviewees saw the rise and availability of precision therapies in oncology as a *hopeful development*. The ability to access these therapies was often articulated in contrast to others who did not have this access, for example people with different cancer types or living in places/times without these options. ‘Precision’ care was thus seen to open a new door to hope[3].

Until their loved one’s cancer diagnosis, many caregivers professed to having had no prior knowledge of precision therapies, how they worked or acted in/on the body, and what that might mean for their and their loved one’s shared present and/or future. Yet their early accounts were strongly underpinned by the fear of – and relief at avoiding – chemotherapy and radiation. Often they associated chemotherapy, to some extent, with hopelessness and debilitating side effects, and thus perceived precision therapies as offering greater hope in terms of *both* life extension and quality of life. However, as carers, patients and clinicians navigated the uncertain waters of precision treatment, the hope and gratitude invested in medical innovation was moderated by everyday experiences of scans, side effects, results, costs and ongoing logistical struggles. In the follow-up interviews, several caregivers expressed gratitude for the time (together) that the precision treatments had already provided, irrespective of how long this could continue. This pointed to the importance of considering hope as relational, which we focus on below.

Table 2: Indicative Quotes: Precision-Induced Hope

Participant[1]	**Indicative quote**
Spouse, M 70+, neuroendocrine cancer	Oh, I think we're very, very privileged. We are. We're very grateful that it is there for us to use, yes. Yeah, so we are. We're very, very grateful and we just pray and hope that it's going to have some positive effect on the tumours.
Daughter, F 51-70, lung cancer	We were very positive yesterday. I couldn't wait to talk to my brother. Yeah, we're feeling really good, and blessed too. Obviously blessed and thankful. I think we're all hoping for the magic bullet for cancer, but this immunotherapy, it's been fantastic. And I hope a lot of families benefit from it. It's great. [later] It was like winning a prize, I recall. It was like, "Oh, we won. Your cancer is eligible for this new immunotherapy thing."
Daughter, F <30, lung cancer	I'm just really happy that we're in this day and age and not even 10, 20 years ago when this [drug] potentially wasn't around.
Spouse, M 51-70, neuroendocrine cancer (a)	Yeah, well I was just elated. I just thought like, "Here we go. Something's happening. We can do something. We can have a fight." [later] It's just exciting to see that all these people are actually putting all this effort into NETs all of a sudden and they're coming up with all these strange ideas.
Sister, F 51-70, brain cancer	Well, I think it was amazing that he had access to it. Extremely, extremely, extremely lucky, like a fluke really. He's the only one in Australia that I know of that is having this, unless there are trials now. I'm not sure if there's trials in Australia. So he's extremely lucky, and I think everyone should have access to it.
Spouse, M 51-70, breast cancer	[I knew] nothing. When I heard that, "Okay, this is this type of cancer and we've got this drug here which is perfect to target you. You're one of the lucky ones." I remember them saying that, that, "You're the lucky ones because this is made for the type of cancer you've got.
Spouse, M 51-70, neuroendocrine cancer (b)	I wasn't aware that there was any targeted therapy before, for any sort of cancer. So, it was completely new to me and it was terrific. You couldn't ask for anything more. The cancers were all, most of them were still there, but they'd reduced in size. Some had gone, but a lot of them had stayed. But I'd never heard of that sort of treatment being as effective before.
Spouse, M 51-70, neuroendocrine cancer (b)	If you start doing chemo, well that's the beginning of the end from my perspective. Not that I ever said that to [patient], but that's how I felt. But then, after the oncologist explained everything properly and we understood that it was an injection once a month and this could go on forever, well, you felt much more comfortable about things.
Son, M <30, lung cancer	I know that we may have to go through chemo down the line, because, from what I've been told, it's all a bit hazy, but I think the targeted therapy will reach a point where it won't have the

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[1] Participants are identified in data tables by their relationship to the patient, sex (M/F), age range, and patient cancer type. Participants with same information are distinguished by the addition of e.g. (a).

	effects, it won't have the success that it does and then she'll have to resort to chemo. But yeah, it really has just allowed us to have valuable time as a family.

Hope as Relational: From Hope as 'Work' to Obligation

As illustrated by caregivers' perspectives presented in Table 2 and in the interviewees' accounts more broadly, precision therapeutics initially offered caregivers relief and comfort through the knowledge that the 'science' of cancer treatment– including treatment options for their loved one's cancer type – was advancing. This provided a sense that new personalised options were emerging that would have seemed unlikely or impossible even a few years earlier. However, caregivers' stories of hope-in-precision also involved new relational complexities, and perceptions of precision often changed over time, as the follow-up interviews showed. One example of this complexity was a dialectical tension between hope and obligation[46]. Specifically, and as illustrated in Table 3, caregivers frequently reflected that hope was *required* for treatment to be successful, it needed to be found or even manufactured. The *work* of generating or projecting hope[42, 47] was consistently discussed within the caregiver interviews.

Some caregivers observed that the social expectation to profess hope induced a sense of alienation, particularly in relation to people not involved in the everyday reality of cancer. The hopes of others, imposed on caregivers via hopeful talk or encouragement to be positive, was described, for example, as deeply "irritating", signifying, for our participants, a fundamental misrecognition of the challenges of living with, and caring within, the precision-cancer milieu (i.e., not as 'easy' or 'liberating' as one might imagine). Perhaps enhanced by the lack of traditional signifiers of cancer (e.g., hair loss/nausea), the precision scene was seen as exacerbating the disorientations between recognition of suffering and performativity of hope, perseverance and determination, as the quotes in Table 3 indicate.

Hope was also a prominent feature of therapeutic encounters. Just as caregivers felt an obligation to enact hope relationally – to express and practice hope – so too did they see it as an obligation of clinicians to cultivate hope in clinical encounters. Several caregivers expressed a belief that maintaining hope should be a higher order priority for clinicians than managing expectation, which has often been a focus of discussion in and around effective clinical communication[48-49]. In several cases, caregivers discussed supporting the patient to find a new healthcare professional in response to "hurtful" statements of hopelessness, illustrating the tightrope clinicians walk in navigating, negotiating and co-constructing hope with patients and caregivers.

As the indicative quotes in Table 3 illustrate, patients, caregivers and clinicians work (and sometimes struggle) to reframe hope in the precision-oncological context. For example, while clinicians may not use terms like "remission" in this context, for patients and caregivers the absence or refusal of this term may be understood as "killing hope". Evolving and unsettled evidence, and gaps in lay understandings of treatments and potential outcomes, may mean that patients, caregivers, clinicians and other social actors lack the necessary shared language or knowledge to successfully navigate the complexities of hope in the swiftly evolving landscape of precision therapeutics.

Table 3: Indicative Quotes: Hope as Relational: From 'Hope Work' to Obligation

Participant	Indicative quote

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Sister, F 51-70, brain cancer	You just have to be hopeful that he'll have this treatment again and he'll deal with it quick, if that's what it was. So yeah, hopeful. Otherwise it's shit. So you've got to be hopeful.
Spouse, M 51-70, lung cancer (a)	And one thing I noticed a lot of people saying, and I had to wonder if I'd ever said it myself, but when your friends and acquaintances hear you've got cancer, they all tend to say, "Oh look, she's a strong girl. You'll get through this. She's strong. We're praying for you. You'll get through this." And a few people said that, and I didn't say anything, but I found it really irritating. That really bugged me because what I thought of was, "No, we're not walking off into the sunset hand in hand to fight the good fight. This is a bloody ugly street fight." There's nothing nice about it. There's nothing noble about it. It's not Joan of Arc on a horse with a shield and a sword and, "We're going to slay this cancer dragon." It's nothing like that. It is totally devastating.
Spouse, M 51-70, lung cancer (a)	And this one doctor confused a question and she mentioned something about the side-effects and the medication and the doctor just blurted out in front of everybody, the whole family, "Oh no, there's no [remission]. You will be on medication for the rest of your life." […] Now, that was not what she needed to hear […]. And it was just blurted out so matter of factly by a doctor.
Spouse, M 51-70, lung cancer (b)	He [oncologist] probably rubbed [her] up the wrong way immediately because he presented a very negative outcome immediately […]. Reading the notes at the time, they obviously hadn't been pre-prepared and it caught him by surprise. And because it caught him by surprise, he probably spoke in a way that he probably wouldn't have otherwise done, but that's where he killed a lot of hope in [her] because that's when he said, "You have stage four and there's no such thing as remission." […] It really took a lot of positivity out of her response to the disease initially. So, yeah, it was quite devastating for us both.
Spouse, M 51-70, lung cancer (b)	They don't understand how hurtful some of the stuff they can say is, and the effects it has on their patients. Almost like it's unconscious, I suppose. But anyway, as I said, in a social context he'd be probably very personable, people would like him. But as far as [she] was concerned, she would prefer someone to be a little bit more positive.
Mother, F 70+, neuroendocrine cancer	Give them the facts, sure. But in a way that it's not just all death and destruction. That there is maybe some light at the end of the tunnel with some research or something that's going to go on. "We're progressing all the time," and talk like that, I think. It's a better way of talking.

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Speculative Hope and Hope for the Common Good

From the caregivers' perspective, hope spanned the individual and collective, the present and future, obligation and aspiration. The very concept of hope implies a goal or object – something that is hoped *for*. In the precision context, this was often oriented towards the prospect of medical innovation. In this dual focus on presently unfolding progress and as-yet-unknown future advances, caregivers articulated a sense of being part of a wider social phenomenon as well as being embedded in a deeply personal experience. Thus, individualised hopes – for survival, for the future life experiences that survival might bring, for minimal symptoms or side effects – were also considered in relation to the common good or the benefit of future patients, caregivers and families.

Deliberation over benefit was far from stable and a source of ongoing renegotiation within families. For instance, some caregivers expressed frustration or fear that progress would not happen fast enough to benefit their relative/friend, but others were more sanguine, accepting that being at the cutting edge of innovation meant being a "guinea pig" (see Table 4), in part to benefit others in the future. While the idea of lifelong treatment implied a lack of hope for some caregivers (for a return to normal life post cancer – see Table 3), it opened up a hopeful vista of continuation for others (see Table 4). For still others, especially older patients and caregivers, quality of life was more important than life-extending scientific breakthrough as they felt they had lived (a good) enough life.

The hope invested in the notion of ongoing scientific progress was often grounded in the fear that even successful treatments would likely stop working in the future. This shadow of fear drove some caregivers to engage in the 'hopeful work' of advocacy, seeking out trials and treatments and/or lobbying for access and funding. When precision treatments failed or side effects proved intolerable, caregivers and families were often forced to re-evaluate their early hopes for continuation of life, asking painful questions about if and where hope might now be found. Initial responses of relief and gratitude (see Table 2) evolved into complex and fluctuating emotions, characterised by the need to provide consistent support in the face of uncertainty, hope and disappointment, compounded by fluctuating side effects and the fatigue of long-term life on treatment.

Hope, in this precision oncology context, spread across bodies, families, experts and fields of science, holding on to both the potential for an individual disease outcome and the altruism of the common good from participation in science and innovation. Hope, in this sense, was speculative both in terms of the outcomes for those they cared for, and the future possibilities the 'stop and start' of science may offer. This reflects the ethics of hope, as about solidarity as well as about the individual prevailing, and in turn, how uncertainty binds to hope. That is, *being on the precipice* – of breakthrough or death – is a key affective relation permeating the precision environment.

Table 4: Indicative Quotes: Speculative Hope and Common Good

Participant	Indicative quote
Spouse, M 51-70, lung cancer (c)	Well, I'm a supreme optimist. I think that they'll come up with a cure, so I'm not too worried. I think that she'll just keep going, and we'll keep doing the same thing. I think [oncologist] was actually talking about it, the next type of TKI would be on the horizon soon. So if these two don't work, then there'll be probably something else or another trial or something, and this'll go on for a few more years, and then eventually they'll have a cure and everything will be back to normal.
Spouse, M 31-50, rare cancer	Oh, it [possibility of entering a trial] was pretty exciting actually. I thought, "Okay, great. Maybe there's this magic pill out there." Then [she] was sort of excited and I was – I'm a little bit more reserved and go "Okay, I'll wait and see until it happens."
Spouse, M 70+, neuroendocrine cancer	I mean, if, in the end, it helps somebody. I mean, the only way we can help other people and develop things is to – Somebody's got to be the guinea pig in the end.
Spouse, M 51-70,	My biggest fear is if the targeted therapy that she's currently on

lung cancer (a)	doesn't keep working, then we're in trouble. But, as they say, they are developing all the time. […] If that stops working, we have to hope the next one comes along, or we have to hope we can get involved with trials. But that's probably my biggest fear that got me to understand a bit more about the targeted therapy. And also, just as they keep saying, the research keeps advancing, so there is always hope that they are constantly advancing and […] down the track there will be the next generation of drugs that will be a back stop if she feels, or they feel, the doctors feel, "Well, let's move onto the next one to keep this in check."
Spouse, M 70+, neuroendocrine cancer	They did mention [a trial], but it would mean that [she] would have to go into hospital, I think it was once a week for eight hours, for this clinical trial […] I mean, we are sort of getting older and […] I think [she] is still looking at this thing about the quality of life, and not the quantity.[…]So we're thinking, "Well…" And at our age, quite frankly, we've sort of had a good life. We're just sort of saying, "Look, we've had a good life. If this is the end of the story, well, that's fine. We've done quite well. We've done very well."
Mother, F 70+, neuroendocrine cancer	I read everything in the newspapers about trials, but they're all in five years' time, 10 years' time, and all this. What's the use of that for Christ's sake? They're dying now.
Spouse, F 51-70, lung cancer	[We thought] you have your chemo treatment and all that and then this would be the icing on the cake. […] Once you've had the immunotherapy, this is going to be the be all and end all of getting rid of the cancer. And once you've had that year, then that's it. That's how it felt. But then when it didn't work, it was like, "Oh shit, we've only had four treatments. Does that mean the end of it?"
Spouse, M 70+, lung cancer	Well, I didn't know much about it. I mean, I just checked, showed on the internet, and it seems to work with her because initially the cancer shrank. It was 22 millimetres and then it shrank. After three months, it shrank to 18 and so we were in good hope that the medication is effective. But then, with the time, the virus itself changed or mutated the virus cells and the first medicine didn't have any effect anymore. […] And so, yeah, I was in shock again somehow. Because this was a treatment the doctor said was 95% it's working and it is a good alternative and all this, and then just like somebody takes the ground off your feet. And so then we were, of course, talking about alternatives, but obviously they don't have much alternatives except chemotherapy, and that's what they put her on.

DISCUSSION

The last decade or so has been transformative for practice and outcomes in oncology. The precision turn, variable as it is across cancer types, has radically reconfigured expectations around the outcomes of malignancy and introduced new vistas of hope and possibility for many (though not all)[6-10]. What had not, until now, been adequately explored are laypersons' perspectives on the precision turn in oncology and in particular, accounts of patients and caregivers. Here we have focused on caregiver perspectives, with a particular interest in their experiences of hope in and around precision, and its complexities in this swiftly evolving scene.

Interviews with these caregivers provide important insight into the emerging and evolving social world of precision oncology, and how those in supportive roles view and make sense of care and survivorship in this context. Hope, as it emerged, was a binding narrative within the interviews, but in complex and unexpected ways. Moving beyond simple binaries such as optimism/pessimism, realistic/unrealistic, ignorance/understanding, analysis of the caregivers' interviews revealed the importance of relationships, values and commitment to (or faith in) science/innovation in mediating caregivers' experiences of precision oncology and their orientation around hope, therein. What emerged was a picture of the relational nature of (precision-induced) hope and gratitude, the relational 'work' of upholding hope[42,47], associated forms of obligation[46] and also the possibility of solidarity with future beneficiaries of experimental therapies[50]. That is, caregivers' experiences of precision treatments contained a mix of the *enabling* features in terms of patient benefits, increased survival and so on, but also the *normative* including the ways in which new treatment trajectories introduce new sets of requirements and expectations across patients, carers and clinicians in everyday life.

The results also introduce some important concepts as to how we think about care in the context of precision oncology, and indeed, resonate with much of the broader literature on both hope and caring relations[11-21]. First, hope is less a property of the individual (patient or caregiver) and more a collective accomplishment, negotiated across complex social relations and expectations. Second, hope is a form of *work* – it needs to be generated and projected – with caregivers deeply involved in this practice of hope. This work is not straightforward, often involves considerable suffering, and, as one participant articulated, can be "a bloody ugly street fight" despite the optics of optimism. Finally, these caregivers' perspectives accentuate the power of *hope in scientific progress* – in this case genomic – as mobilising, animating, and directing the scene of oncological survivorship. Although experiences of cancer have long been tied to notions of scientific progress, treatment breakthroughs and therapeutic innovation[51], hope in the context of precision therapeutics has been positioned as particularly precarious. This can be seen in biomedical research papers and broader commentary alike, with frequent use of phrases such as "hope or hype" or "hope or reality"[52-54]. Time-to-market, and therapeutic pipelines more broadly, take years and sometimes decades to come to fruition – if, indeed, they bear fruit at all[55]. Yet experimental precision oncology trials involving human participants who must be matched, clinically and genetically, to the requirements of the trial[3] offer a sense that medical innovation is happening in real time. Here, biographical time competes with clinical time[56] where the pace of innovation may not be fast enough to out-run the progression of disease. This precarious hopefulness suggests that precision therapeutics, as they stand, have mixed effects, the subtleties of which, including factors beyond disease impacts, deserve significant exploration. In this context, hope is not only emotional but also *moral labour* [57], which operates in a dialectic tension between how *I* may benefit now and how the future *we* may benefit, later. The hope-precision nexus is thus an evolving *ethical system*, whereby participation in trials, acceptance of novel drugs with uncertain outcomes, advocacy for access to (subsidised) therapeutics and so on involves a mix of concern for the self and concern for the other (present or future).

By revealing these more nuanced dimensions of hope – as precarious, as relational, as work – our findings make explicit not only the positivity of hope but also its painful potential. Offering hope is not always a kindness and might even become toxic in some circumstances[58]. Certainly, hope can be difficult to manage in terms of expectations versus realities and might even be harmful when inaccurately deployed or internalised (i.e., when the hopeful future does not arrive). In essence, hope is not universally or unquestionably positive, it can also be difficult and, unfortunately, cannot inoculate against suffering. In the context of precision oncology, this study has highlighted the previously neglected perspectives of informal caregivers on the complex interplay between individual prognoses, interpersonal dynamics, institutional pressures, social expectations, and the political and economic dimensions of therapeutic innovation.

This study of caregivers' experiences provides new insights into the 'social life' of precision oncology. In particular, it underlines the ways that innovation and change in the precision era can rapidly reconfigure the parameters of hope (unclear therapeutic trajectories, uncertain survival chances), creating new and difficult relational moments and experiences in everyday life. How patients, caregivers and clinicians alike navigate between uncertain chances of success and hopeful possibility and potential will likely remain a challenge in years to come.

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Title and abstract

Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	p.1
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Introduction

Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	pp.3-5
Purpose or research question - Purpose of the study and specific objectives or questions	P3 (para 2) and P5 (final para of intro)

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Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	Pp5 "Context" (ethics); p6 "Sampling & recruitment" (consent); p15 Ethics declaration

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Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	P6 "Data collection"
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	P6 "Data collection"
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Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Results section throughout
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Tables of indicative quotes included

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	Pp13-14
Limitations - Trustworthiness and limitations of findings	P2 Article summary

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	n/a
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	P15

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**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

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Hope in the Era of Precision Oncology: A Qualitative Study of Informal Caregivers' Experiences

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ABSTRACT

Objectives: To explore informal caregivers' perspectives on precision medicine in cancer care.

Design: Semi-structured interviews with the informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interview transcripts were analysed thematically using a framework approach.

Setting: Recruitment was facilitated by two hospitals and five Australian cancer community groups.

Participants: Informal caregivers (n=28; 16 men, 12 women; aged 18-80) of people living with cancer and receiving targeted/immunotherapies.

Results: Thematic analysis identified three findings, centred largely on the pervasive theme of hope in relation to precision therapies including: (1) precision as a key component of caregivers' hope; (2) hope as a collective practice between patients, caregivers, clinicians, and others, which entailed work and obligation for caregivers; and (3) hope as linked to expectations of further scientific progress, even if there may be no personal, immediate benefit.

Conclusions: Innovation and change in precision oncology are rapidly reconfiguring the parameters of hope for patients and caregivers, creating new and difficult relational moments and experiences in everyday life and in clinical encounters. In the context of a shifting therapeutic landscape, caregivers' experiences illustrate the need to understand hope as collectively produced, as emotional and moral labour, and as entangled in broader cultural expectations of medical advances. Such understandings may help clinicians as they guide patients and caregivers through the complexities of diagnosis, treatment, emerging evidence and possible futures in the precision era. Developing a better understanding of informal caregivers' experiences of caring for patients receiving precision therapies is important for improving support to patients and their caregivers.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- Our sample included participants involved in caring for people receiving targeted/immunotherapy for a wide range of cancer types.
- Qualitative data are crucial to better understanding informal caregivers' experiences and to improving future services and supports.
- Recruitment was undertaken nationally and interviews were conducted remotely, enabling participation across a range of settings.
- The study design limits what can be claimed to prevail across time in changing oncology treatment contexts, although follow-up interviews with a sub-set of participants enabled some insights over time.
- Recruitment for this study was limited to Australia; further investigations will be needed to explore similarities and differences across national contexts.

INTRODUCTION

The emergence of precision therapies over the past two decades has been accompanied by changed illness and survivorship experiences, most notably for patients, but also for

informal caregivers (people who provide care that is unremunerated and within the context of an existing relationship, such as a family member or friend). In oncology, 'precision' – the molecular profiling of tumours in order to match them with particular treatments – has led to an increased focus on the identification of cancer biomarkers**,** and treatment with novel targeted or immune therapies. These precision therapies differ considerably from traditional standard of care treatments such as chemotherapy[1]. Although unequally available across contexts, new precision therapies have inspired renewed hope, catalysed escalating costs and produced new landscapes of side-effects, patienthood and survivorship [2-6].

While the impact of precision oncology on *disease* outcomes is relatively well documented[7], its varied and evolving impacts on experiences of *survivorship* and *informal caring* have received limited emphasis[4]. This is despite the fact that targeted/immunotherapies, when viable and accessible, have radically transformed survivorship (e.g., duration of treatment, types of side-effects and symptoms)[8] and associated informal caring roles. While some attention has been paid to the emergence of 'precision survivorship' (surviving with/beyond targeted treatments/immunotherapy)[8-9], including initial studies of patient perspectives[5, 10-12], no research has foregrounded informal caregivers' experiences and their interpretations of the precision turn in oncology. In this paper, we begin to fill this gap by delving into caregivers' accounts of the *relational, affective* and *societal* dimensions of hope in the context of precision therapeutics.

BACKGROUND

Informal Caregivers in Cancer Scholarship

The significance of informal caregivers, and the practical and emotional work they perform in supporting people living with cancer, has received increasing attention since the turn of the century[13-14]. Such research has shown the importance of understanding illness experiences and caregiving in relational terms[15-17]. The shift from an intimate partner or parent-child relationship, for example, to one of care-giver and care-recipient involves changes to roles and responsibilities, communication and decision-making dynamics, identities and emotions[14, 17]. Moreover, coping with cancer diagnosis and treatment invariably happens within the context of myriad relationships[18]. Thinking about "dyadic coping"[18] and other forms of interdependence includes attending to the connectedness of caregiver experiences to the capacity of cancer patients themselves to cope with intervention (precision or otherwise)[19].

Research conducted prior to the widespread availability of precision therapeutics emphasises that the type of care tasks performed, and the emotional impact on patients and caregivers, varies significantly across the cancer 'journey'. During treatment aimed at recovery or disease control, patients and caregivers (particularly spousal carers) may construct a sense of cancer as a shared experience[18,20], while a terminal diagnosis may fracture this sense of commonality as patient and caregiver diverge in their experiences of future time[21-24]. With therapeutic shifts and rapidly changing cancer trajectories, these relational dynamics and caregivers' engagement require specific investigation.

Precision Medicine and Survivorship

The advent of precision oncology has led to a paradigm shift in cancer research, trials and care[5,7]. For example, in advanced/metastatic non-small cell lung cancer (NSCLC), precision therapies have increased the median overall survival (OS) rate to

18–36 months (compared to 8-17 months with chemotherapy)[25], and for ALK-positive NSCLC the median OS has reached 6-8 years[26-27]. Similarly in metastatic breast cancer the introduction of trastuzumab in 2000 improved 5-year survival rates for HER2 positive patients from 2 to 31%[28]. New treatments continue to improve survival [29] and precision oncology is now associated with long-term remissions in a substantial proportion of HER2 positive patients[30]. Researchers are hopeful that future innovative trials with molecularly matched tailored therapies will improve survival even further[31]. However, for those *currently* providing or receiving cancer care, these new therapeutic options can complicate decision-making about treatment pathways due to the constant emergence of new data[4].

Beyond considerations of improved survival, patients' experiences of precision cancer treatment may diverge dramatically from the well-trodden paths of surgery, chemotherapy and radiotherapy. Symptoms, side effects, costs, logistics and implications for everyday life may be very different. For example, patients may need to travel long(er) distances for trials or sub-specialist care (especially patients in rural or remote areas), self-fund molecular testing or expensive drugs, and manage family and community expectations about what living with cancer entails. This all has ramifications (financial, logistical, emotional) for families, partners and other supporters. The increasing entanglement of research and care[4] means it is vital to draw attention to the largely unrecognised embodied and emotional work by patients *and* caregivers that underpins cancer innovation[12,32]. In this changing landscape, patients and caregivers may need to adjust their understanding of success beyond binaries of cure or death. For precision oncology patients, 'success' may involve lifelong treatment and living alongside their cancer in an ongoing way[11].

Affective Dimensions of Precision Survivorship: The Dilemmas of Hope

Hope is intrinsic to cancer care and survivorship for both patients and caregivers. As Corn et al. note, hope induces "pathways and agency thinking"[33] towards a particular goal, bringing people together around shared objectives and playing a critical role at many points in the cancer journey[see also 14, 34, 35]. More generally, hope is a crystallisation of the individual and collective desire to survive, to overcome and to prevail – desires that have powerful and complex effects in everyday clinical settings[36]. Hope can be harnessed and deployed in service of positive outcomes for patients with cancer and is important for caregivers' health and wellbeing, which is strongly influenced by the patients' level of hope – powerfully illustrating hope's *relational* character[14, 37]. Thinking about hope as relational means not seeing hope as absent, present, or otherwise quantifiable[38], but rather to think of hope as a complex *entanglement* of a wide range of social expectations (e.g., hope for precision miracles, scientific breakthroughs etc)[39]. Discourses of hope are intrinsic to the clinical trials industry[32] where the relational *work* of generating hope keeps the "promissory bioeconomy" of medical innovation moving forward[5]. In this way, hope can unify – binding people (patient, professional, carer, support network, researcher, regulator) together in pursuit of common purpose – but it can also become a source of disagreement, conflict and disorientation[40-42]. Hope's perceived therapeutic value can place emotional demands on caregivers (and others), who must work to generate, maintain and protect hope as a way of contributing to the patient's care and potential survival[13, 43, 44] as well as to the potential survival of future patients[12, 32].

Social science researchers such as Arlie Hochschild[45] thus speak about the *performative* dimensions of emotion management, where individuals invest considerable effort shaping their inner emotions – or, at least, moderating their public expression of these emotions – to meet the demands of their situation and the expectations of their family/community/society. In this sense, hoping is (hard) work that is often undertaken *collectively*, as different individuals – patients, carers, healthcare professionals and so on – encourage one another and co-create hope through implicit agreement[5,12,32]. Ambiguous prognoses, for example where novel treatments are extending survival in the context of emerging evidence, thus increase the complexity of the emotion work performed by caregivers[46] as they co-construct hopeful "future-time" with patients and professionals[47] and also work alongside patients to navigate the despair, alienation and anguish that cancer treatment (still) often entails[32].

In this paper, we draw from our analysis of interviews with informal caregivers to untangle some of the dimensions of hope – as collectively produced through both clinical and emotional work – and to provide new insights into how the relationality of hope is being reconfigured through developments in precision oncology.

METHODS

Context

Taking an interpretive approach to research design, data collection and analysis, this article draws on data from in-depth, semi-structured interviews with 28 informal caregivers of people living with cancer and receiving targeted/immunotherapies. Interviews were conducted May 2020-August 2021 in Australia. Ethics approval was gained through a metropolitan hospital on Australia's east coast. Interviews were carried out as part of a broader qualitative study focused on contemporary experiences of cancer care in the era of precision oncology[11]. The study involved a collaboration between health social scientists and clinician-researchers across three institutions and was aided and supported by five cancer-related consumer groups. Patients, caregivers and healthcare professionals were interviewed for the study. Following Mays and Pope's guidance for assessing the validity and relevance of qualitative research [48], we provide below a clear exposition of data collection and analysis methods; each finding is supported by a range of data excerpts, including outliers or contradictory examples; and the research is placed in dialogue with an extensive literature drawn from both social science and clinical traditions (see Background – above).

Patient and Public Involvement

Patients were not involved in the study design/conduct.

Sampling and Recruitment

This paper reports on the caregiver component of the study. Caregivers were recruited via convenience sampling through patients who were participating in the broader study. Using a purposive sampling method, potential patient participants who had sought out, tested for, and/or experienced targeted and/or immunotherapies during their cancer care were approached by a clinician, researcher, and/or consumer group organiser to explain the study. If they expressed interest in participating, participants were contacted via phone to initiate the informed written consent process and to schedule an interview via video or phone call. Patients were asked if they would like to nominate a partner, family member and/or friend who played a role in their care to be invited to participate in an interview. The researchers then contacted the nominated caregivers. Interested caregivers were provided with an information sheet outlining the aims of the study and were contacted to schedule an interview. To be included, carers had to have been nominated by a patient participant, be 18 years old or older and proficient in English.

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Participant recruitment continued until there was consensus among research team members that saturation had been reached.

Data Collection

Interviews were semi-structured and iteratively explored a range of issues around participants' lived experience of caring for someone with cancer in the context of targeted treatments and/or immunotherapies. Caregivers were asked about their experiences of their loved one's diagnosis, treatment and care, and their experiences of supporting them through these events. The caregiver interviews were conducted by AP, a sociologist with experience in in-depth qualitative interviewing in sensitive contexts. Interviews were conducted remotely, via video-call (due to COVID-19 public health measures), which facilitated geographical diversity across Australian states. Interviews lasted between 22 and 105 minutes (mean: 58 minutes), were audio-recorded and transcribed in full. Transcripts were deidentified, and each participant was assigned a code. Interviews did not focus specifically on hope, but this was a key issue raised by participants. The findings are derived inductively from analysis of participants' interviews.

Analysis

A systematic thematic analysis – driven by the framework approach[49,50] – was conducted using NVivo 11 software as a data management tool. The framework approach was initially developed in the context of conducting applied qualitative research[50]. It is a grounded, dynamic, systematic and comprehensive approach designed to facilitate retrieval of original data, comparisons between and within cases, and a collaborative approach to data analysis[50]. Analysis involved the following steps: (1) Familiarisation: researchers (KK, LWV, AB) reviewed all caregiver transcripts, observing patterns and contrasts. One researcher (LWV) conducted an initial coding of data at this stage. (2) Identification of thematic framework: From this initial coding, a thematic framework was developed (KK, LWV, AB), shaped by the research aims, emergent issues raised by participants, and analytic themes arising from patterns in the data. (3) Application of themes to text: transcripts were recoded by applying the thematic framework. (4) Charting: Using the codes, key excerpts of data were brought together to facilitate refinement of themes and identification of anomalies and contrasts across transcripts. (5) Mapping and interpretation: using these charts, associations were clarified, and explanations developed, moving towards an overall interpretation of the data (KK, LWV, AB, MP). A sociologist experienced in qualitative data analysis (LWV) led the initial coding and application of thematic framework. Framework development and interpretation were collaborative stages involving a team of social scientists (KK, LWV, AB, MP) with experience in qualitative data analysis in the domain of health and illness. The analysis was shared and discussed with the wider research team, including clinician-researchers, to confirm consistency and credibility of the interpretation. Analytic rigour was enhanced by searching for negative, atypical and conflicting or contradictory items in coding and theme development.

RESULTS

Participant Characteristics

Informed written consent was obtained from 28 caregivers (16 men and 12 women, aged between 18 and 80) who then participated in one-on-one, semi-structured interviews. As part of the study design, participants were offered a follow-up interview

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approximately 6 months after their initial interview, with the aim of eliciting longitudinal insights, including reflections on changing prognoses and experiences of treatment. Nine caregivers participated in a follow-up interview. The sample included people caring for those living with neuroendocrine (12), lung (11), breast (2), rare (2), and brain (1) tumours. Most of the nominating patients had commenced (and in some cases ceased) precision cancer treatment in the two years prior to their first interview, although a few had longer precision journeys (in one case over 10 years). Caregivers included spouses (15), adult children (6), friends (3), parents (2), other relative (1), and one support worker. Three patients (with rare, neuroendocrine, and lung cancers) nominated two caregivers who were both interviewed, and one patient (neuroendocrine cancer) nominated three caregivers, all of whom were interviewed. Most caregivers – and the patients who nominated them – were Australian citizens with Anglo/European heritage. One caregiver and three nominating patients were Australians with South-East Asian heritage, and one nominating patient had Aboriginal and Anglo-Australian heritage. Most caregivers and their nominating patients were employed in (or had retired from) professional or managerial roles (e.g. teachers, nurses, engineers) although the sample also included transport workers, cleaners, farmers and retail workers. Table 1 provides further details about caregivers' characteristics, including age and geographical diversity.

Table 1: Participant Characteristics

Participant characteristic	***n=28 (%)***
Caregiver sex	
Male	*16 (57)*
Female	*12 (43)*
Caregiver relationship to patient	
Spouse	*15 (54)*
Adult child	*6 (21)*
Parent	*2 (7)*
Sibling	*1 (4)*
Friend	*3 (11)*
Support worker	*1 (4)*
Patient cancer type*	
Neuroendocrine	*12 (43)*
Lung	*11 (39)*
Breast	*2 (7)*
Rare	*2 (7)*
Brain	*1 (4)*
Caregiver location	
NSW	*9 (32)*
Queensland	*8 (29)*
Victoria	*5 (18)*
Western Australia	*4 (14)*
South Australia	*1 (4)*
ACT	*1 (4)*
Caregiver age	
30 and under	*4 (14)*
31-50	*6 (21)*
51-70	*12 (43)*

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Over 70	*6 (21)*

* *Some patients nominated more than one caregiver. Numbers in this table reflect the number of caregivers caring for patients with a particular cancer type.*

Precision-Induced Hope

The sense of hope induced by targeted/immunotherapies was powerfully evident across many of the caregiver interviews. Caregivers routinely described themselves and their loved ones as ‘privileged’, ‘thankful’ and ‘lucky’ to have access to these new therapeutic pathways, often noting how recently precision treatments for the particular tumour in question had been discovered, approved and/or funded. As the quotes in Table 2 illustrate, many of the interviewees saw the rise and availability of precision therapies in oncology as a *hopeful development*. The ability to access these therapies was often articulated in contrast to others who did not have this access, for example people with different cancer types or living in places/times without these options. ‘Precision’ care was thus seen to open a new door to hope[3], a door held open by the Australian healthcare system’s investment in and subsidising of “cutting-edge” treatments. In Australia, cancer care is financed through a complex mix of Federal and State funding, private health insurance and out-of-pocket funds, and delivered by both the public and private hospital systems. Caregivers emphasised their gratitude for the Pharmaceutical Benefits Scheme (PBS), through which the government subsidises (some) precision treatments, and without which most said they would have struggled to pay for such therapies.

Until their loved one’s cancer diagnosis, many caregivers professed to having had no prior knowledge of precision therapies, how they worked or acted in/on the body, and what that might mean for their and their loved one’s shared present and/or future. Reflecting on their responses to learning of the existence and potential of precision therapies, caregivers’ accounts were strongly underpinned by the fear of – and relief at avoiding – chemotherapy and radiation. Often they associated chemotherapy, to some extent, with hopelessness and debilitating side effects, and thus perceived precision therapies as offering greater hope in terms of *both* life extension and quality of life. However, as carers, patients and clinicians navigated the uncertain waters of precision treatment, the hope and gratitude invested in medical innovation was moderated by everyday experiences of scans, side effects, results, costs and ongoing logistical struggles. In the follow-up interviews, several caregivers expressed gratitude for the time (together) that the precision treatments had already provided, irrespective of how long this could continue. This pointed to the importance of considering hope as relational, which we focus on below.

Table 2: Indicative Quotes: Precision-Induced Hope

Participant[1]	Indicative quote
Spouse, M 70+, neuroendocrine cancer	Oh, I think we’re very, very privileged. We are. We’re very grateful that it is there for us to use, yes. Yeah, so we are. We’re very, very grateful and we just pray and hope that it’s going to have some positive effect on the tumours.
Daughter, F 51-70, lung cancer	We were very positive yesterday. I couldn’t wait to talk to my brother. Yeah, we’re feeling really good, and blessed too. Obviously blessed and thankful. I think we’re all hoping for the

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[1] Participants are identified in data tables by their relationship to the patient, sex (M/F), age range, and patient cancer type. Participants with same information are distinguished by the addition of e.g. (a).

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	magic bullet for cancer, but this immunotherapy, it's been fantastic. And I hope a lot of families benefit from it. It's great. [later] It was like winning a prize, I recall. It was like, "Oh, we won. Your cancer is eligible for this new immunotherapy thing."
Daughter, F <30, lung cancer	I'm just really happy that we're in this day and age and not even 10, 20 years ago when this [drug] potentially wasn't around.
Spouse, M 51-70, neuroendocrine cancer (a)	Yeah, well I was just elated. I just thought like, "Here we go. Something's happening. We can do something. We can have a fight." [later] It's just exciting to see that all these people are actually putting all this effort into NETs all of a sudden and they're coming up with all these strange ideas.
Spouse, M 51-70, lung cancer	When we first got the Alectinib, the price was on the box. For a month, it was 6,000[AUD]. […] The month that she was diagnosed with cancer, Alectinib went on the PBS [Pharmaceutical Benefits Scheme] that month. So we were getting the Alectinib for $6.50, as opposed to the actual price on the box. […] We thought, "Wow, we timed that well." […] If we had to pay the full price, we probably could have done it, but it'd be a huge strain on our finances. But yeah, so we're lucky. Got lucky that we're in Australia. If she was in the [country of birth], she wouldn't be alive today, probably.
Sister, F 51-70, brain cancer	Well, I think it was amazing that he had access to it. Extremely, extremely, extremely lucky, like a fluke really. He's the only one in Australia that I know of that is having this, unless there are trials now. I'm not sure if there's trials in Australia. So he's extremely lucky, and I think everyone should have access to it.
Spouse, M 51-70, breast cancer	[I knew] nothing. When I heard that, "Okay, this is this type of cancer and we've got this drug here which is perfect to target you. You're one of the lucky ones." I remember them saying that, that, "You're the lucky ones because this is made for the type of cancer you've got.
Spouse, M 51-70, neuroendocrine cancer (b)	I wasn't aware that there was any targeted therapy before, for any sort of cancer. So, it was completely new to me and it was terrific. You couldn't ask for anything more. The cancers were all, most of them were still there, but they'd reduced in size. Some had gone, but a lot of them had stayed. But I'd never heard of that sort of treatment being as effective before.
Spouse, M 51-70, neuroendocrine cancer (b)	If you start doing chemo, well that's the beginning of the end from my perspective. Not that I ever said that to [patient], but that's how I felt. But then, after the oncologist explained everything properly and we understood that it was an injection once a month and this could go on forever, well, you felt much more comfortable about things.
Son, M <30, lung cancer	I know that we may have to go through chemo down the line, because, from what I've been told, it's all a bit hazy, but I think the targeted therapy will reach a point where it won't have the effects, it won't have the success that it does and then she'll have to resort to chemo. But yeah, it really has just allowed us to have valuable time as a family.

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Hope as Relational: From Hope as 'Work' to Obligation

As illustrated by caregivers' perspectives presented in Table 2 and in the interviewees' accounts more broadly, precision therapeutics initially offered caregivers relief and comfort through the knowledge that the ‘science’ of cancer treatment – including treatment options for their loved one’s cancer type – was advancing. This provided a sense that new personalised options were emerging that would have seemed unlikely or impossible even a few years earlier. However, caregivers’ stories of hope-in-precision also involved new relational complexities, and perceptions of precision often changed over time, as the follow-up interviews showed. One example of this complexity was a dialectical tension between hope and obligation[51]. Specifically, and as illustrated in Table 3, caregivers frequently reflected that hope was *required* for treatment to be successful, it needed to be found or even manufactured. The *work* of generating or projecting hope[5, 12, 32, 45, 52] was consistently discussed within the caregiver interviews. In caregiver accounts, this work was positioned as pivotal to the precision journey: when patients professed concerns or disappointment, caregivers sought to engender in the patient the hope necessary for them to start or continue with precision treatment. At the same time, they had to work hard to maintain their own hopefulness in order to avoid becoming a “burden” to the patient.

Some caregivers observed that the social expectation to profess hope induced a sense of alienation, particularly in relation to people not involved in the everyday reality of cancer. The hopes of others, imposed on caregivers via hopeful talk or encouragement to be positive, was described, for example, as deeply “irritating”, signifying, for our participants, a fundamental misrecognition of the challenges of living with, and caring within, the precision-cancer milieu (i.e., not as ‘easy’ or ‘liberating’ as one might imagine). Perhaps enhanced by the lack of traditional signifiers of cancer (e.g., hair loss/nausea), the precision scene was seen as exacerbating the disorientations between recognition of suffering and performativity of hope, perseverance and determination, as the quotes in Table 3 indicate.

Hope was also a prominent feature of therapeutic encounters. Just as caregivers felt an obligation to enact hope relationally – to express and practice hope – so too did they see it as an obligation of clinicians to cultivate hope in clinical encounters. Several caregivers expressed a belief that maintaining hope should be a higher order priority for clinicians than managing expectation, which has often been a focus of discussion in and around effective clinical communication[53-54]. In several cases, caregivers discussed supporting the patient to find a new healthcare professional in response to “hurtful” statements of hopelessness, illustrating the tightrope clinicians walk in navigating, negotiating and co-constructing hope with patients and caregivers.

As the indicative quotes in Table 3 illustrate, patients, caregivers and clinicians work (and sometimes struggle) to reframe hope in the precision-oncological context. For example, while clinicians may not use terms like “remission” in this context, for patients and caregivers the absence or refusal of this term may be understood as “killing hope”. Evolving and unsettled evidence, and gaps in lay understandings of treatments and potential outcomes, may mean that patients, caregivers, clinicians and other social actors lack the necessary shared language or knowledge to successfully navigate the complexities of hope in the swiftly evolving landscape of precision therapeutics.

Table 3: Indicative Quotes: Hope as Relational: From ‘Hope Work’ to Obligation

Participant	Indicative quote
Sister, F 51-70, brain cancer	You just have to be hopeful that he’ll have this treatment again and he’ll deal with it quick, if that’s what it was. So yeah,

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	hopeful. Otherwise it's shit. So you've got to be hopeful.
Spouse, M 51-70, lung cancer (a)	[W]hen your friends and acquaintances hear you've got cancer, they all tend to say, "Oh look, she's a strong girl. You'll get through this. She's strong. We're praying for you. You'll get through this." And a few people said that, and I didn't say anything, but I found it really irritating. That really bugged me because what I thought was, "No, we're not walking off into the sunset hand in hand to fight the good fight. This is a bloody ugly street fight." There's nothing nice about it. There's nothing noble about it. It's not Joan of Arc on a horse with a shield and a sword and, "We're going to slay this cancer dragon." It's nothing like that. It is totally devastating.
Daughter, F 51-70, lung cancer	It was the unknown. We hadn't been down this path before. We hadn't experienced this. So, she wasn't frightened, but she was concerned, and I guess her concern was loss of independence and becoming reliant on ongoing medical care for the rest of her life. So we talked about it and, I said, "Give it a go. Just give it a crack and just see." And I'm glad we did, because she tolerated it really well and hasn't had any problems.
Spouse, M 51-70, lung cancer (a)	The last meeting she was a bit disappointed with because there was no reduction. So she was a little bit down about that. But as I said to her, "It's better than spreading."
Spouse, M 51-70, breast cancer	You have to be realistic about it, but you can't let what might happen overwhelm what is happening. So, projecting to the future and saying, "Well, what if they find more?" Yet again, it's those techniques of being positive, keeping things normal, not changing routine. Changing as little as possible, because you've got to establish family routine. […] I can't see the value in being negative or dwelling on a negative outcome. It will take you back into that depressive state. You become a burden, for want of a better word. And you don't need that when your partner's battling such a serious illness, you don't want to be a burden there.
Spouse, M 51-70, lung cancer (a)	And this one doctor confused a question and she mentioned something about the side-effects and the medication and the doctor just blurted out in front of everybody, the whole family, "Oh no, there's no [remission]. You will be on medication for the rest of your life." […] Now, that was not what she needed to hear […]. And it was just blurted out so matter of factly by a doctor.
Spouse, M 51-70, lung cancer (b)	He [oncologist] probably rubbed [her] up the wrong way immediately because he presented a very negative outcome immediately […]. Reading the notes at the time, they obviously hadn't been pre-prepared and it caught him by surprise. And because it caught him by surprise, he probably spoke in a way that he probably wouldn't have otherwise done, but that's where he killed a lot of hope in [her] because that's when he said, "You have stage four and there's no such thing as remission." […] It really took a lot of positivity out of her response to the disease initially. So, yeah, it was quite devastating for us both.
Spouse, M 51-70, lung cancer (b)	They don't understand how hurtful some of the stuff they can say is, and the effects it has on their patients. Almost like it's unconscious, I suppose. But anyway, as I said, in a social context he'd be probably very personable, people would like

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	him. But as far as [she] was concerned, she would prefer someone to be a little bit more positive.
Mother, F 70+, neuroendocrine cancer	Give them the facts, sure. But in a way that it's not just all death and destruction. That there is maybe some light at the end of the tunnel with some research or something that's going to go on. "We're progressing all the time," and talk like that, I think. It's a better way of talking.

Speculative Hope and Hope for the Common Good

From the caregivers' perspective, hope spanned the individual and collective, the present and future, obligation and aspiration. The very concept of hope implies a goal or object – something that is hoped *for*. In the precision context, this was often oriented towards the prospect of medical innovation. In this dual focus on presently unfolding progress and as-yet-unknown future advances, caregivers articulated a sense of being part of a wider social phenomenon as well as being embedded in a deeply personal experience. Thus, individualised hopes – for survival, for the future life experiences that survival might bring, for minimal symptoms or side effects – were also considered in relation to the common good or the benefit of future patients, caregivers and families.

Deliberation over benefit was far from stable and a source of ongoing renegotiation within families. For instance, some caregivers expressed frustration or fear that progress would not happen fast enough to benefit their relative/friend, but others were more sanguine, accepting that being at the cutting edge of innovation meant being a "guinea pig" (see Table 4), in part to benefit others in the future. While the idea of lifelong treatment implied a lack of hope for some caregivers (for a return to normal life post cancer – see Table 3), it opened up a hopeful vista of continuation for others (see Table 4). For still others, especially older patients and caregivers, quality of life was more important than life-extending scientific breakthrough as they felt they had lived (a good) enough life.

The hope invested in the notion of ongoing scientific progress was often grounded in the fear that even successful treatments would likely stop working in the future. This shadow of fear drove some caregivers to engage in the 'hopeful work' of advocacy, seeking out trials and treatments and/or lobbying for access and funding[12]. When precision treatments failed or side effects proved intolerable, caregivers and families were often forced to re-evaluate their early hopes for continuation of life, asking painful questions about if and where hope might now be found. Initial responses of relief and gratitude (see Table 2) evolved into complex and fluctuating emotions, characterised by the need to provide consistent support in the face of uncertainty, hope and disappointment, compounded by fluctuating side effects and the fatigue of long-term life on treatment.

Hope, in this precision oncology context, spread across bodies, families, experts and fields of science, holding on to both the potential for an individual disease outcome and the altruism of the common good from participation in science and innovation. Hope, in this sense, was speculative both in terms of the outcomes for those they cared for, and the future possibilities the 'stop and start' of science may offer. This reflects the ethics of hope, as about solidarity as well as about the individual prevailing, and in turn, how uncertainty binds to hope. That is, *being on the precipice* – of breakthrough or death – is a key affective relation permeating the precision environment.

Table 4: Indicative Quotes: Speculative Hope and Common Good

Participant	Indicative quote
Spouse, M 51-70,	Well, I'm a supreme optimist. I think that they'll come up with a

lung cancer (c)	cure, so I'm not too worried. I think that she'll just keep going, and we'll keep doing the same thing. I think [oncologist] was actually talking about it, the next type of TKI would be on the horizon soon. So if these two don't work, then there'll be probably something else or another trial or something, and this'll go on for a few more years, and then eventually they'll have a cure and everything will be back to normal.
Spouse, M 31-50, rare cancer	Oh, it [possibility of entering a trial] was pretty exciting actually. I thought, "Okay, great. Maybe there's this magic pill out there." Then [she] was sort of excited and I was – I'm a little bit more reserved and go "Okay, I'll wait and see until it happens."
Spouse, M 70+, neuroendocrine cancer	I mean, if, in the end, it helps somebody. I mean, the only way we can help other people and develop things is to – Somebody's got to be the guinea pig in the end.
Spouse, M 51-70, lung cancer (a)	My biggest fear is if the targeted therapy that she's currently on doesn't keep working, then we're in trouble. But, as they say, they are developing all the time. […] If that stops working, we have to hope the next one comes along, or we have to hope we can get involved with trials. But that's probably my biggest fear that got me to understand a bit more about the targeted therapy. And also, just as they keep saying, the research keeps advancing, so there is always hope that they are constantly advancing and […] down the track there will be the next generation of drugs that will be a back stop if she feels, or they feel, the doctors feel, "Well, let's move onto the next one to keep this in check."
Spouse, M 70+, neuroendocrine cancer	They did mention [a trial], but it would mean that [she] would have to go into hospital, I think it was once a week for eight hours, for this clinical trial […] I mean, we are sort of getting older and […] I think [she] is still looking at this thing about the quality of life, and not the quantity.[…] So we're thinking, "Well…" And at our age, quite frankly, we've sort of had a good life. We're just sort of saying, "Look, we've had a good life. If this is the end of the story, well, that's fine. We've done quite well. We've done very well."
Mother, F 70+, neuroendocrine cancer	I read everything in the newspapers about trials, but they're all in five years' time, 10 years' time, and all this. What's the use of that for Christ's sake? They're dying now.
Spouse, F 51-70, lung cancer	[We thought] you have your chemo treatment and all that and then this would be the icing on the cake. […] Once you've had the immunotherapy, this is going to be the be all and end all of getting rid of the cancer. And once you've had that year, then that's it. That's how it felt. But then when it didn't work, it was like, "Oh shit, we've only had four treatments. Does that mean the end of it?"
Spouse, M 70+, lung cancer	Well, I didn't know much about it. I mean, I just checked, showed on the internet, and it seems to work with her because initially the cancer shrank. It was 22 millimetres and then it shrank. After three months, it shrank to 18 and so we were in good hope that the medication is effective. But then, with the time, the virus itself changed or mutated the virus cells and the first medicine didn't have any effect anymore. […] And so, yeah, I was in shock again somehow. Because this was a treatment the doctor said was 95% it's working and it is a good alternative and all this, and then just like somebody takes the ground off your feet. And so then we were, of course, talking about alternatives, but obviously they don't have much alternatives except chemotherapy, and that's what they put her on.

DISCUSSION

The last decade or so has been transformative for practice and outcomes in oncology. The precision turn, variable as it is across cancer types, has radically reconfigured expectations around the outcomes of malignancy and introduced new vistas of hope and possibility for many (though not all)[7-11]. What had not, until now, been adequately explored are laypersons' perspectives on the precision turn in oncology and in particular, accounts of patients and caregivers. Here we have focused on caregiver perspectives, with a particular interest in their experiences of hope in and around precision, and its complexities in this swiftly evolving scene.

Interviews with these caregivers provide important insight into the emerging and evolving social world of precision oncology, and how those in supportive roles view and make sense of care and survivorship in this context. Hope, as it emerged, was a binding narrative within the interviews, but in complex and unexpected ways. Moving beyond simple binaries such as optimism/pessimism, realistic/unrealistic, ignorance/understanding, analysis of the caregivers' interviews revealed the importance of relationships, values and commitment to (or faith in) science/innovation in mediating caregivers' experiences of precision oncology and their orientation around hope, therein. What emerged was a picture of the relational nature of (precision-induced) hope and gratitude, the relational 'work' of upholding hope[5, 45, 52], associated forms of obligation[49] and also the possibility of solidarity with future beneficiaries of experimental therapies[12, 55]. That is, caregivers' experiences of precision treatments contained a mix of the *enabling* features in terms of patient benefits, increased survival and so on, but also the *normative* including the ways in which new treatment trajectories introduce new sets of requirements and expectations across patients, carers and clinicians in everyday life.

The results also introduce some important concepts as to how we think about care in the context of precision oncology, and indeed, resonate with much of the broader literature on both hope and caring relations[13-23]. First, hope is less a property of the individual (patient or caregiver) and more a collective accomplishment, negotiated across complex social relations and expectations, and underpinned (or undermined) by the political economy of healthcare and innovation. Second, hope is a form of *work* – it needs to be generated and projected – with caregivers deeply involved in this practice of hope. This work is not straightforward, often involves considerable suffering, and, as one participant articulated, can be "a bloody ugly street fight" despite the optics of optimism. Finally, these caregivers' perspectives accentuate the power of *hope in scientific progress* – in this case genomic – as mobilising, animating, and directing the scene of oncological survivorship. Although experiences of cancer have long been tied to notions of scientific progress, treatment breakthroughs and therapeutic innovation[56], hope in the context of precision therapeutics has been positioned as particularly precarious[5]. This can be seen in biomedical research papers and broader commentary alike, with frequent use of phrases such as "hope or hype" or "hope or reality"[57-59]. Time-to-market, and therapeutic pipelines more broadly, take years and sometimes decades to come to fruition – if, indeed, they bear fruit at all[60]. Yet experimental precision oncology trials involving human participants who must be matched, clinically and genetically, to the requirements of the trial[3] offer a sense that medical innovation is happening in real time. In the caregivers' accounts, biographical time competes with clinical time[61], the pace of innovation set against the progression of disease and

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(almost) inevitable failure of currently available treatments[12]. Sustaining hope *with and for* the patient is grounded in the hope that innovation will arrive in time to give them more (life-)time together. This precarious hopefulness suggests that precision therapeutics, as they stand, have mixed effects, the subtleties of which, including factors beyond disease impacts, deserve significant exploration. In this context, hope is not only emotional but also *moral labour*[62], which operates in a dialectic tension between how *I* may benefit now and how the future *we* may benefit, later. For caregivers, the moral labour of mobilising and maintaining another person's hope involves an additional relational dimension, layered on top of the normative (moral) imperative to be a 'good' carer by working to achieve hope in another. This relational, emotional and moral labour underpins the potentiality of cancer innovation [12, 32]. The hope-precision nexus is thus an evolving *ethical system*, whereby participation in trials, acceptance of novel drugs with uncertain outcomes, advocacy for access to (subsidised) therapeutics and so on involves a mix of concern for the self and concern for the other (present or future).

By revealing these more nuanced dimensions of hope – as precarious, as relational, as work – our findings make explicit not only the positivity of hope but also its painful potential. Offering hope is not always a kindness and might even become toxic in some circumstances[63]. Certainly, hope can be difficult to manage in terms of expectations versus realities and might even be harmful when inaccurately deployed or internalised (i.e., when the hopeful future does not arrive). In essence, hope is not universally or unquestionably positive, it can also be difficult and, unfortunately, cannot inoculate against suffering. In the context of precision oncology, this study has highlighted the previously neglected perspectives of informal caregivers on the complex interplay between individual prognoses, interpersonal dynamics, institutional pressures, social expectations, and the political and economic dimensions of therapeutic innovation.

This paper has focused on the perspectives of informal caregivers, using semi-structured in-depth interviews conducted with caregivers as the primary data source. In so doing, we have been able to highlight this previously neglected perspective. We acknowledge, however, that conducting a full dyadic analysis of the patient-participant and caregiver datasets together might yield further insights. The context in which the study was conducted (i.e., the first years of the COVID-19 pandemic) was both a limiting and enabling factor. The pivot from in-person, hospital-based recruitment to online recruitment drawing on cancer support groups, potentially led to a less ethnically and socio-economically diverse sample but facilitated access to a much more diverse sample in terms of cancer type and geographical location. The experiences of people caring for neuroendocrine cancer patients, for example, have rarely been included in studies of precision cancer care. As we have noted elsewhere, the COVID context had a deep impact on patients' and caregivers' experiences of cancer care [64, 65] and may have affected participants' orientations towards the future. The study should, therefore, be viewed in the context of the place (Australia) and time (2020-21) in which it was conducted. Nevertheless, this study of caregivers' experiences provides new insights into the 'social life' of precision oncology. In particular, it underlines the ways that innovation and change in the precision era can rapidly reconfigure the parameters of hope (unclear therapeutic trajectories, uncertain survival chances), creating new and difficult relational moments and experiences in everyday life. How patients, caregivers and clinicians alike navigate between uncertain chances of success and hopeful possibility and potential will likely remain a challenge in years to come.

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Standards for Reporting Qualitative Research (SRQR)*

http://www.equator-network.org/reporting-guidelines/srqr/

Title and abstract

	Page/line no(s).
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	p.1
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	p.2

Introduction

Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	pp.3-5
Purpose or research question - Purpose of the study and specific objectives or questions	P3 (para 2) and P5 (final para of intro)

Methods

Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	P5, (Methods, context)
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	P5, (Methods, context); p6, (Methods, data collection, ll5-7)
Context - Setting/site and salient contextual factors; rationale**	P5, (Methods, context); p6, (Methods, data collection, ll7-9)
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	Pp5-6 "Sampling & recruitment"
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	Pp5 "Context" (ethics); p6 "Sampling & recruitment" (consent); p15 Ethics declaration

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Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	P6 "Data collection"
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	P6 "Data collection"
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	P6-7 Participant characteristics
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	P6 "Data Collection" & "Analysis"
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	P6 "Analysis"
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	P6 "Analysis"

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Results section throughout
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Tables of indicative quotes included

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	Pp13-14
Limitations - Trustworthiness and limitations of findings	P2 Article summary

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	n/a
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	P15

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*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:
O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
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