PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Hope in the Era of Precision Oncology: A Qualitative Study of Informal Caregivers' Experiences
AUTHORS	Kenny, Katherine; Williams Veazey, Leah; Broom, Alex; Peterie, Michelle; Page, Alexander; Prainsack, Barbara; Wakefield, Claire; Itchins, Malinda; Khasraw, M; Lwin, Zarnie

VERSION 1 – REVIEW

REVIEWER	Haddad Ringborg, Cecilia Karolinska Institutet, Department of Neurobiology, Care sciences and Society
REVIEW RETURNED	19-Aug-2022

GENERAL COMMENTS	Firstly, thank you for the opportunity to review this interesting manuscript exploring informal caregivers' experiences of precision oncology and hope. It is of great importance to highlight the people close to the patients, taking a lot of responsibility of the patients' care. Some major and some minor revisions are needed to improve the manuscript even more and to clarify some information that is missing. 1.Missing a definition of a informal caregiver. 2.The background is very extensive, and the discussion is rather short, there are also no references in the discussion part. It would be interesting to have some discussion regarding the results of the current study and previous/other studies. Did this study reveal something that other studies have not found yet? 3. "The thematic analysis was driven by a framework approach". What does this really mean? It is unclear if the authors have used a framework, like a theory for example? Or What does the method really mean? This must be clearer. 4.There is a short sentence in the results part about a six-month follow-up. It is unclear why this follow-up was conducted? Was there any difference in this interview compared to the previous? Some more explanation would be useful to understand this better. 5. There are some references in the result-part? This is very confusing. Is it not the findings from the analysis? My suggestion is to remove these references. 6.Right now, the discussion is more of a repetition of the results. It would be more interesting to discuss more towards previous research and what is needed in the future. 7. More methodological discussion is needed to strengthen the study and its results. Please add some discussion about the quality criterions of qualitative research (credibility, transferability, dependability, and confirmability).

	8. There are some references missing in the reference list. Number 10 and 19. These need to be added. 9. On page 4 the reference is not correct: “As Corn et al[35 e452] note, hope induces”. Also the references after the sentence seems to be wrongly placed? Difficult to understand what reference said what. Please, have a look at the comments. I look forward to reading the revised version.

REVIEWER	Brophy, Jane The University of Melbourne School of Population and Global Health, Centre for Health Equity
REVIEW RETURNED	16-Sep-2022

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. It's contribution to the field is well-justified and the analysis and discussion convincing and compelling. I have no substantive comment, except to note that I presume the 'Author Xs' in the methods section will be updated upon publication.

VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1:

Thank you for your generous and thoughtful engagement with our paper. We have made the following changes in response to your comments:

1.Missing a definition of an informal caregiver.

Informal caregiver is defined in lines 3-4 of the introduction as “people who provide care that is unremunerated and within the context of an existing relationship, such as a family member or friend).”

2.The background is very extensive, and the discussion is rather short, there are also no references in the discussion part. It would be interesting to have some discussion regarding the results of the current study and previous/other studies. Did this study reveal something that other studies have not found yet?

We have followed the conventions of our field (sociology) in structuring the paper, which is why the background is extensive compared to some other disciplinary traditions. Nevertheless, we have revised the balance between background and discussion sections, including the addition of references throughout the discussion, as per the reviewer’s suggestion.

3. “The thematic analysis was driven by a framework approach”. What does this really mean? It is

unclear if the authors have used a framework, like a theory for example? Or What does the method really mean? This must be clearer.

We have revised the ‘Analysis’ section to give a clearer picture of our process and have included clearer referencing for the framework approach (see reference 45).

4.There is a short sentence in the results part about a six-month follow-up. It is unclear why this follow-up was conducted? Was there any difference in this interview compared to the previous? Some more explanation would be useful to understand this better.

We have added some more explanation on this aspect of the study:

“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.”

Broadly speaking, the second interviews were able to capture reflections across time, including in response to changing prognoses, accessing different treatments and so on, thereby adding richness and nuance to the data.

5. There are some references in the result-part? This is very confusing. Is it not the findings from the analysis? My suggestion is to remove these references.

Our preference would be to keep the references in the results section, in accordance with common practice in the social sciences. The references enable us to point towards the relevance and resonances with previous research, making connections with the scholarly literature and paving the way for the following discussion section.

6.Right now, the discussion is more of a repetition of the results. It would be more interesting to discuss more towards previous research and what is needed in the future.

As above, we have revised the discussion section, incorporating discussion of previous work and pointing to the future, as per the reviewer’s suggestion.

7. More methodological discussion is needed to strengthen the study and its results. Please add some discussion about the quality criterions of qualitative research (credibility, transferability, dependability, and confirmability).

We have added some further methodological discussion to the Methods section (under ‘context’). This is in addition to the revised ‘analysis’ section and the information throughout the methods section, which notes the ethical, logistical, and methodological approach of the research study.

“Following Pope and May’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.”

8. There are some references missing in the reference list. Number 10 and 19. These need to be added.

Thank you for noticing these omissions. They have now been added to the reference list.

9. On page 4 the reference is not correct: “As Corn et al[35 e452] note, hope induces”. Also the references after the sentence seems to be wrongly placed? Difficult to understand what reference said what.

We have adjusted the sentence in question, with particular attention to the placement of the references, to clarify the difference between the specific citation (direct quotation) and further references about what hope *does* during the cancer journey:

“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].”

Response to Reviewer 2: Thank you for your kind comments. We have made the minor changes to authors’ details as suggested.

VERSION 2 – REVIEW

REVIEWER	Haddad Ringborg, Cecilia Karolinska Institutet, Department of Neurobiology, Care sciences and Society
REVIEW RETURNED	30-Nov-2022

GENERAL COMMENTS	Well done. Your revisions have improved the manuscript. Congratulations!

REVIEWER	Ackerman, Sara L. Univ Calif San Francisco, Social and Behavioral Sciences
REVIEW RETURNED	22-Feb-2023

GENERAL COMMENTS	Thank you for the opportunity to review this very well written article examining how new precision medicine cancer therapies are transforming the ways in which informal caregivers experience, negotiate and perform hope. The paper will make a valuable contribution to the literature on patient and caregiver experiences with emerging precision medicine treatments. Some specific comments and suggestions: Sampling and recruitment The inclusion criteria appear to be quite broad in terms of demographics. Did the researchers make any explicit attempt to create a diverse sample in terms of income or cultural/ethnic identity? Why/why not? Analysis I found this section difficult to follow. “Application of themes to text” is described early in the paragraph and coding isn’t mentioned until later, which is confusing because standard qualitative analysis involves developing and applying codes to the data and subsequently developing themes with the coded data. If coding and thematic development are conceived and practiced differently by this team, an explanation and justification would be helpful. I also recommend providing a brief description of the framework approach and explanation of how it was used, in addition to stating how many of the authors were involved in coding. Results The quotes in Table 2 suggest that most of the people receiving care by those in the study were in the pre- or early-treatment stage of their precision medicine cancer care. If this is the case, a discussion of whether/how the treatment stage influenced caregivers’ sense of hope would be a welcome addition to the “precision-induced hope” section. It would also be helpful to indicate treatment stage during the first interview in the “participant characteristics” section. I very much appreciated the authors’ attention to the performative and relational aspects of hope, including in therapeutic encounters. In reading the second and third results sections I was hoping to learn something about how hope was navigated between caregivers and patients themselves. Questions that come to mind include how do caregivers and patients co-manage expectations and to what extent do caregivers feel aligned with patients in their sense of comfort in the expectation of longer-term scientific breakthroughs? Discussion P. 13, lines 48-50: It would help to explain the point about moral labour with a bit more detail. Access to subsidised therapeutics is mentioned in the discussion but not in the results. Was this issue relevant to the caregivers who participated in the study? Re my earlier comment about participant characteristics, it would be helpful to know something about their income level and whether they were likely to encounter barriers when attempting to access novel therapeutics.

	Finally, I appreciate the authors’ literature review and encourage them to engage with some additional sociological and anthropological work examining hope as labour and future thinking in cancer care: Kerr, Anne, Choon Key Chekar, Emily Ross, Julia Swallow, and Sarah Cunningham-Burley. 2021. Personalised Cancer Medicine: Future Crafting in the Genomic Era. Manchester: Manchester University Press. Kerr, Anne, and Sarah Cunningham-Burley. 2015. “Embodied Innovation and Regulation of Medical Technoscience: Transformations in Cancer Patienthood.” Law, Innovation and Technology 7 (2): 187–205. Ackerman, Sara. 2022. Promising precision medicine: how patients, clinicians and caregivers work to realize the potential of genomics-informed cancer care, New Genetics and Society, 41:3, 196-215. Brown, Patrick, and Sabine de Graaf. 2013. “Considering a Future Which May Not Exist: The Construction of Time and Expectations Amidst Advanced-Stage Cancer.” Health, Risk & Society 15 (6–07): 543–560

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Cecilia Haddad Ringborg, Karolinska Institutet

Comments to the Author:

Dear Authors,

Well done. Your revisions have improved the manuscript. Congratulations!

Thank you.

Reviewer: 3

Dr. Sara L. Ackerman, Univ Calif San Francisco

Comments to the Author:

Thank you for the opportunity to review this very well written article examining how new precision medicine cancer therapies are transforming the ways in which informal caregivers experience, negotiate and perform hope. The paper will make a valuable contribution to the literature on patient and caregiver experiences with emerging precision medicine treatments. Some specific comments and suggestions:

Thank you for your kind comments and for your generous engagement with our paper. We have taken account of all your comments, and sought to address them as outlined below.

Sampling and recruitment

The inclusion criteria appear to be quite broad in terms of demographics. Did the researchers make any explicit attempt to create a diverse sample in terms of income or cultural/ethnic identity? Why/why not?

The inclusion criteria reported in this paper are broad because all caregiver-participants were nominated by the patient-participant. That is, they were not recruited independently of the patient-participant. In relation to recruitment of patient-participants, the study was initially designed to recruit through the hospital sites (two large metropolitan hospitals in Sydney and Brisbane), which would have largely determined the demographic mix of the sample. However, as recruitment took place during the first years of the COVID-19 pandemic, our ability to recruit via hospitals was significantly limited and we therefore pivoted to recruitment via cancer support groups and online interviews. In this shift from hospital (in-person) to support group (online) recruitment, we potentially recruited a less diverse sample in terms of income and cultural/ethnic diversity. On the other hand, the new method of recruitment facilitated a far greater diversity of cancer type (neuroendocrine cancer, for example, has rarely been explored in relation to experiences of precision cancer care) and geographical spread across the country and across rural, regional and urban settings.

We have added some discussion in relation to this point in the discussion, in a section about limitations of the study (p.15) and added some details in relation to participant diversity in the participant characteristics section (p7).

Analysis

I found this section difficult to follow. “Application of themes to text” is described early in the paragraph and coding isn’t mentioned until later, which is confusing because standard qualitative analysis involves developing and applying codes to the data and subsequently developing themes with the coded data. If coding and thematic development are conceived and practiced differently by this team, an explanation and justification would be helpful. I also recommend providing a brief description of the framework approach and explanation of how it was used, in addition to stating how many of the authors were involved in coding.

We have re-written the analysis section with this feedback in mind – and also bearing in mind feedback on this section in a previous review – so that it now includes a more detailed explanation of the framework approach and how this was applied in our study (p6).

Results

The quotes in Table 2 suggest that most of the people receiving care by those in the study were in the pre- or early-treatment stage of their precision medicine cancer care. If this is the case, a discussion of whether/how the treatment stage influenced caregivers' sense of hope would be a welcome addition to the "precision-induced hope" section. It would also be helpful to indicate treatment stage during the first interview in the "participant characteristics" section.

The quotes in Table 2 mostly reflect how participants recalled and recounted their experience of learning about precision cancer treatment – whether these were recent experiences or longer ago. We have added some clarification to this section (p8).

In the participant characteristics section, we have added the following clarification (p7):

"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)."

I very much appreciated the authors' attention to the performative and relational aspects of hope, including in therapeutic encounters. In reading the second and third results sections I was hoping to learn something about how hope was navigated between caregivers and patients themselves. Questions that come to mind include how do caregivers and patients co-manage expectations and to what extent do caregivers feel aligned with patients in their sense of comfort in the expectation of longer-term scientific breakthroughs?

The relational aspects of navigating hope between caregivers and patients are indeed central to the concerns of this paper but we have also sought to broaden the relational aspects to include clinicians and the broader social networks in which caregivers and patients are embedded. As this paper draws exclusively on data from interviews with caregivers there are limitations in what can be reported in relation to the co-construction or co-management of expectations. Future dyadic analyses will be better positioned to reflect on this point.

We have added some quotes and discussion in the second findings section about the work caregivers performed in order to shore up the hope of the patient at key points of the precision journey, e.g. when embarking on innovative treatments and when receiving 'disappointing' results:

"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." (p10)

In regards to longer-term scientific breakthroughs, the caregivers tended to emphasise their hope that future innovations would emerge 'in time' to benefit their loved ones, especially if current treatments might become less effective in the future. Part of the caregivers' sense of obligation to sustain hope (including shoring up the patient's hope when it wavered) was linked to the recognition in order to have any hope of benefiting from future (hopefully imminent) scientific innovation, they had to keep going and persevere with current treatments. Awareness of being part of something bigger was held in a complex tension with the hopes for benefits for their personal circumstances, thus granting them more (life-)time together. We have made small changes across the paper, including in the discussion (e.g. end of p14), to clarify this point.

Discussion

P. 13, lines 48-50: It would help to explain the point about moral labour with a bit more detail.

We have added a sentence to expand the point about moral labour, specifically in relation to caregivers, and also to indicate how moral labour also underpins cancer innovation – with reference to the literature you recommended. It also speaks to your previous request for discussion of the way hope was navigated between caregivers and patients:

"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]."

Access to subsidised therapeutics is mentioned in the discussion but not in the results. Was this issue relevant to the caregivers who participated in the study? Re my earlier comment about participant characteristics, it would be helpful to know something about their income level and whether they were likely to encounter barriers when attempting to access novel therapeutics.

We have added to the 'Precision-induced hope' findings section, supported by an additional quote in Table 2, to illustrate the sense from caregivers that their 'precision-induced hope' was underpinned by the subsidised treatment and access to healthcare provided by the Australian healthcare system. Cost was never mentioned as an insurmountable barrier to participating in precision therapies – everybody had found a way to access treatments, mostly via the public health system but also in some cases via trials or compassionate access. Even where one patient had self-funded experimental treatment, the caregiver's perspective was that they were able to access this at much lower cost than elsewhere, for example in the USA, so the overall theme of gratitude for the Australian context persisted. Another had self-funded a genetic test that was not (at the time) available in Australia and was able to do so because it was "the only cost" they incurred in accessing precision treatment (as all other treatment was covered by the public health system, private health insurance and via the trial). Therefore, although cost was a relevant concern for some participants (many noted, for example, that if the treatment had not been subsidised or otherwise made available for a relatively low cost, they would have struggled to afford it) the dominant theme was one of gratitude and relief for the support provided by the Australian healthcare system despite the high costs set by the pharmaceutical companies. In addition to the changes noted above, we have made small additions throughout the paper to highlight the relevance of the Australian healthcare context.

Finally, I appreciate the authors' literature review and encourage them to engage with some additional sociological and anthropological work examining hope as labour and future thinking in cancer care:

Kerr, Anne, Choon Key Chekar, Emily Ross, Julia Swallow, and Sarah Cunningham-Burley. 2021. Personalised Cancer Medicine: Future Crafting in the Genomic Era. Manchester: Manchester University Press.

Kerr, Anne, and Sarah Cunningham-Burley. 2015. “Embodied Innovation and Regulation of Medical Technoscience: Transformations in Cancer Patienthood.” Law, Innovation and Technology 7 (2): 187–205.

Ackerman, Sara. 2022. Promising precision medicine: how patients, clinicians and caregivers work to realize the potential of genomics-informed cancer care, New Genetics and Society, 41:3, 196-215.

Brown, Patrick, and Sabine de Graaf. 2013. “Considering a Future Which May Not Exist: The Construction of Time and Expectations Amidst Advanced-Stage Cancer.” Health, Risk & Society 15 (6–07): 543–560

Thank you for your suggestion of engaging with the above work, which was indeed highly pertinent to the paper. We have incorporated it into the literature review and elsewhere in the paper, where it has strengthened the engagement with the current literature and enriched the paper’s arguments.