The Avatar Acceptability Study: Survivor, Parent and Community Willingness to Use Patient-Derived Xenografts to Personalize Cancer Care

Wakefield C.E. a,b,* , Doolan E.L. a,b, Fardell J.E. a,b, Signorelli C. a,b, Quinn V.F. a,b, Tucker K.M. c,d, Patenaude A.F. e, Marshall G.M. a,b,f, Lock R.B. b,f, Georgiou G. a,b, Cohn R.J. a,b

a Kids Cancer Centre, Sydney Children's Hospital, Randwick, NSW, Australia
b School of Women's and Children's Health, UNSW, Sydney, NSW, Australia
c Hereditary Cancer Clinic, Department of Medical Oncology, Prince of Wales Hospital, NSW, Australia
d Prince of Wales Clinical School, Faculty of Medicine, Prince of Wales Hospital, NSW, Australia
e Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Department of Psychiatry, Harvard Medical School, Boston, MA, USA.
f Children's Cancer Institute, Lowy Cancer Research Centre, UNSW, Sydney, NSW, Australia.

Abstract

Background: Using patient-derived xenografts (PDXs) to assess chemosensitivity to anti-cancer agents in real-time may improve cancer care by enabling individualized clinical decision-making. However, it is unknown whether this new approach will be met with acceptance by patients, family and community.

Methods: We used a cross-sectional structured survey to investigate PDX acceptability with 1550 individuals across Australia and New Zealand (648 survivors of adult and childhood cancer, versus 650 community comparisons; and 48 parents of childhood cancer survivors versus 204 community parents). We identified factors influencing willingness-to-use PDXs, willingness-to-pay, maximum acceptable wait-time, and maximum acceptable number of mice used per patient.

Findings: PDXs were highly acceptable: >80% of those affected by cancer felt the potential advantages of PDXs outweighed the disadvantages (community participants: 68%). Survivors' and survivors' parents' most highly endorsed advantage was 'increased chance of survival'. 'Harm to animals' was the least endorsed disadvantage for all groups. Cancer survivors were more willing to use PDXs than community comparisons [p < .001]. Survivors and survivors' parents were willing to pay more [p < .004 respectively], wait longer for results [p = .03; p = .01], and use more mice [p = .01; p < .001] than community comparisons. Male survivors found PDXs more acceptable [p = .01] and were willing to pay more [p < .001] than female survivors. Survivors with higher incomes found PDXs more acceptable [p = .002] and were willing to pay more [p < .001] than survivors with lower incomes. Mothers found PDXs more acceptable [p = .04] but were less willing to wait [p = .02] than fathers.

Interpretation: We found significant attitudinal support for PDX-guided cancer care. Willingness-to-pay and maximum acceptable number of mice align well with likely future usage. Maximum acceptable wait-times were lower than is currently achievable, highlighting an important area for future patient education until technology has caught up.

1. Introduction

Patient-derived xenografts (PDXs) can be created by engrafting an individual patient’s tumor into immune-deficient mice [1,2]. Once the tumor has engrafted, the tumor is extracted and implanted into secondary recipient mice, creating further cohorts of mice with tumors which closely mirror the patient’s original tumor. These PDXs (or ‘mouse avatars’) can then be used for drug efficacy studies by randomly assigning...
Research in context

Evidence before this study

Using patient-derived xenografts (PDXs) to guide treatment decision-making within personalized medicine programs may represent a significant advance in cancer care. However, patient and community preferences can shape the success of newly developed technologies. PDX models are nearing implementation into personalized medicine programs worldwide, warranting this timely evaluation of their acceptability and likely future uptake in personalized cancer care.

Added value of this study

This is the first study to evaluate the acceptability of PDXs to guide treatment decision-making in cancer care. This study of 1,550 individuals affected by cancer and community comparisons comprehensively assesses: perceived advantages/disadvantages of PDXs, willingness to use PDXs if diagnosed with cancer, maximum acceptable out-of-pocket costs/patient, maximum acceptable time to receive PDX results and treatment recommendations, and maximum acceptable number of mice used per patient. Our study compares the perspectives of cancer survivors with community comparisons (who may face a future cancer diagnosis), strengthening the study’s generalizability. It also investigates the perspectives of parents considering PDXs for their child.

Implications of all the available evidence

Our results show high willingness-to-use PDXs, indicating a likely high uptake of PDXs in future practice, particularly for children with cancer. Participants’ willingness-to-pay and maximum acceptable number of mice align well with planned PDX models. However, current wait times appear too long for participants, who preferred potentially unachievable maximum wait times in current models. This emphasizes the need to educate potential patients appropriately upon enrolment into PDX-guided personalized medicine programs to manage their expectations. Our results will inform the successful implementation of PDX models, and similar technologies, and guide the future of patient involvement in cancer treatment decision-making.

groups of mice to receive different therapies [1,3]. Therapies demonstrating efficacy in the mice can then be prioritized as potential targeted therapies for the patient [1,4]. In some instances, drug efficacy studies can be carried out using mice directly engrafted with the original patient biopsy material, without the necessity for engraftment into secondary recipient mice [5].

PDXs represent a new advance in the use of murine models for personalized cancer care [2]. Until now, mice carrying human cancer tissue have largely been used pre-clinically to understand oncogenesis, develop new therapies, and evaluate drug sensitivity for future patients [2,3,6]. While traditional models remain invaluable, they cannot address inter-patient variability in drug response [2,3]. PDXs used in ‘real-time’ personalized medicine platforms may better predict the likely effectiveness of an anticancer therapy for an individual patient, potentially identifying therapies that might not normally be used in the conventional treatment of a particular cancer type.

Early data on the drug response concordance between the original and the engrafted tumor are promising [5,7,8], suggesting that adding a personalized in-vivo approach may increase the predictive value of in-vitro testing in personalized medicine trials [1,4,9]. PDXs have been trialled in childhood [6,10] and adult [7,8] cancer. PDXs may offer a means of selecting the best therapy for cancer patients in personalized medicine programs worldwide, potentially increasing survival rates [2], avoiding toxic and costly side-effects of ineffective therapies [3], and, ideally, yielding a faster recovery [3]. Additional benefits may include new discoveries that benefit future patients [11] and, if nothing else, reassurance that the healthcare team ‘tried everything’.

Despite their exciting potential, PDXs have limitations. Engraftment success rates vary widely, affected by tumor type and transplantation site [1]. While engrafted tumors are often faithful to the original tumor (up to approximately 80% of cases) [2,10,12], they may not perfectly mirror it [3,11]. The kinetics of engraftment also vary, with some engraftments taking months [1,12], creating substantial delays before recommendations can be made. For some, recommendations will not be possible because of technical challenges, including lack of engraftment of the original patient’s tumor [2,11].

Patients will usually receive standard care while they await their PDX-derived treatment recommendations. Some will need to decide whether to change treatment after receiving recommendations. Others will receive the recommendation too late to be of clinical use [2,11]. PDXs also use varying numbers of mice per patient (often determined by multiple factors, including the patient’s tumor type, the number of possibly useful anti-cancer therapies identified for the patient, the amount of tissue available, and the availability of laboratory resources). PDXs are also expensive, raising questions about ‘who should pay and the acceptable cost [13].

PDX-guided personalized medicine has the potential to revolutionize future cancer treatment [2]. Yet, neither individuals affected by cancer, nor the general community, have been consulted regarding PDXs. Given that successful implementation of new technologies into clinical care relies on patients’ acceptance and possibly on their willingness-to-pay [14], it is important to assess acceptability before new technologies are widely adopted. PDXs are on the cusp of implementation into personalized medicine programs worldwide, with the US BEAUTY study [15], the Canadian Cancer Avatar Study [16], and the Australian Zero Childhood Cancer program [17].

We collected data from individuals who have been affected by cancer (including, survivors of adult cancer, survivors of childhood cancer, and parents of childhood cancer survivors) and those who have not been affected by cancer (community comparisons). We used five research questions to index the acceptability of PDXs:

1. What are the perceived advantages and disadvantages of PDXs?
2. How willing would participants be to consent to using PDXs if offered to them (or their child) after a cancer diagnosis? (willingness-to-use)
3. What is the maximum acceptable out-of-pocket cost per patient? (willingness-to-pay)
4. What is the maximum acceptable turnaround time to receive PDX results/recommendations? (willingness-to-wait)
5. What is the maximum acceptable number of mice used per patient?

For each question, we investigated differences between cancer survivors and community adults and between survivors’ parents and community parents. We also aimed to identify sociodemographic factors which influenced PDX acceptability. In the cancer groups only, we also investigated the impact of cancer type.

2. Materials and methods

2.1. Design and procedure

We followed the STROBE statement in reporting this study [18]. We used a cross-sectional observational design. Due to the paucity of relevant research, we began with a pilot, conducting 24 semi-structured
telephone interviews with 16 cancer survivors (9 female) and 8 parents of survivors (5 mothers). We used these interviews to identify participants’ seven most commonly endorsed advantages and seven most endorsed disadvantages of PDXs (Supplementary Table 1). The main study used the themes arising from the pilot for a comprehensive quantitative assessment. The Institutional Review Boards of 11 Australian and New Zealand hospitals and UNSW Sydney provided ethical approval. We recruited participants from January 2016–April 2018.

2.2. Participants (Table 1)

2.2.1. Individuals affected by cancer

1) Cancer survivors: Eligible survivors included survivors of childhood and adult cancer, diagnosed at least 6 months prior to study participation who had completed cancer treatment and were aged 16 or older.

2) Parents of childhood cancer survivors ("survivors' parents"): Parents of childhood cancer survivors who were aged <16 years.

2.2.2. Individuals not affected by cancer (community comparisons)

3) ‘Community adults’: Community members with no history of cancer, no children with cancer and currently aged 16 or older.

4) ‘Community parents’: Parents with no history of cancer, no children with cancer and at least one child aged under 16.

2.2.3. Exclusions

We excluded individuals with insufficient English and those considered unsuitable by their medical team (e.g. severe cognitive impairment).

2.3. Recruitment

Aligning with the protocol [19], we aimed to recruit a minimum of 323 individuals affected by cancer and 323 community comparisons. We matched the community comparison groups to the groups affected by cancer (by age and sex). We recruited survivors of adult cancers and community comparisons through three voluntary online research panels (Register4 and PathFinder for adult cancer survivors, PureProfile for community comparisons). The panels have national coverage and reach a demographically diverse participant group. We emailed panel members an invitation to complete screening questions before directing eligible participants to an online survey. Community comparisons received ~AUD$5. We prevented responses from duplicate IP addresses.

There is no similar online panel for childhood cancer survivors and pediatric hospitals do not routinely collect email addresses, so we posted study invitations to childhood cancer survivors and childhood survivors’ parents. Childhood cancer survivors/survivors’ parents provided demographic data via a paper questionnaire and then completed a structured telephone interview with trained interviewers with no previous relationship with participants. We digitally recorded and transcribed interviews verbatim.

2.4. Measures

Participants self-reported their: sex, education, postcode, parental status and income. Individuals affected by cancer reported their (or their child’s): cancer diagnosis and time since diagnosis (in years).

We briefly described PDXs to all participants (Supplementary Table 2) and then asked participants to indicate how well they understood the description [1 = ‘not at all’, to 5 = ‘completely’].

We then assessed participants’ willingness-to-use a PDX if facing a cancer diagnosis in themselves (survivors, community adults), or in their child (survivors’ parents, community parents) [1 = ‘not at all willing’, to 7 = ‘very willing’].

We asked participants to rate the seven advantages and seven disadvantages identified in the pilot study [1 = ‘not at all important’, to 7 = ‘very important’], and then re-assessed willingness-to-use.

We assessed willingness-to-pay by gradually increasing a suggested out-of-pocket cost until participants indicated that they were not willing to pay that amount [from AUD$100 to AUD$50,000; NZD$110 to NZD$55,000; equivalent to approximately USD$75 to USD$38,000].

We assessed maximum acceptable wait-time to receive results/recommendations by increasing wait-time from two weeks to one year.

We assessed maximum acceptable number of mice/patient by first asking participants whether the number of mice would influence their decision. If participants answered yes, then they indicated how many mice would be acceptable, with response options increasing from 10 to 1000 mice until participants indicated that they would be unwilling to use that number.

2.5. Statistical analysis

The primary outcome was decisional balance score. Similar to Tercyak et al. [20], we created a decisional balance score for each participant by calculating the individual’s mean advantages ratings divided by their mean disadvantages ratings. Values above one indicated a leaning towards the advantages, suggesting that PDXs were considered “acceptable”. Values below one indicated a leaning towards the disadvantages, and that PDXs were “not acceptable”. A value of one represented decisional equivalence, that is, neither the advantages nor the disadvantages outweighed the other. For this study we categorized a decisional balance score of one as “not acceptable”.

We excluded a random selection of 135 community adults under the age of 43, and a further 95 male community adults under the age of 43 to match the cancer and community groups. We used independent and paired samples t-tests and a 2 × 2 repeated measures analysis of variance (ANOVA) to examine between and within group differences in the cancer and community groups. We computed exploratory regressions to explore sociodemographic factors (sex, income, education and rurality) influencing four outcomes: decisional balance, willingness-to-pay, maximum acceptable wait-time, and maximum acceptable number of mice. We produced bivariate correlations between outcome variables and influencing factors first, and then included correlations with p ≤ .02 in the final regression models. We performed bootstrapping on all final regression models. Given the differences in timing and type of treatment patients typically receive across cancer diagnoses (e.g., chemotherapy for hematological cancers, surgery for solid tumors), we also conducted a secondary analysis investigating differences between hematological and solid cancers for the four main

Table 1
Participant groups included in the study and comparisons made.

| Individuals affected by cancer | Community comparisons |
|-------------------------------|-----------------------|
| Adults considering PDX for self | Survivors of adult and childhood cancer versus Community adults |
| Parents considering PDX for their child | Parents of childhood cancer survivors ['survivors' parents'] versus Community parents |

Abbreviations: PDX: patient-derived xenografts.
outcome variables. Significant differences were determined using Welch’s t-test, given the large difference in sample size across these two diagnosis groups [21]. We planned a priori to analyze data from participants who indicated that they did not understand PDXs separately [19]. Regressions that included income as a variable excluded participants who chose not to report their income (Table 2). We have provided a denominator (i.e., the number of participants who provided a response) for each reported statistic, to highlight any missing data. We used SPSS25.0 and considered results significant at p < .05, with no adjustment for multiple comparisons.

### 3. Results

1550 individuals participated [1298 in the adult groups (648 survivors versus 650 community comparisons) and 252 in the parent groups (48 parents of childhood cancer survivors versus 204 community parents)]. See Table 2 for demographic/clinical characteristics.

The groups were well matched: there were no significant sex, age, income, or rurality differences between survivors and community comparisons. A higher percentage of survivors had post-school qualifications compared with community participants, so we included education in all regression models. There were no significant sociodemographic differences between survivors’ parents and community parents. One adult survivor, eight community adults, and one community parent indicated that they did not understand PDXs. The groups were too small to conduct separate analyses, so we excluded these participants from final analyses.

#### RQ1. Perceived advantages and disadvantages of PDXs and decisional balance

Survivors and community comparisons rated the potential advantages of PDXs (cancer: M = 6.37, SD = 0.95; community: M = 5.91, SD = 1.39) significantly higher than potential disadvantages (cancer: M = 4.81, SD = 1.34; community: M = 4.96, SD = 1.29; F = 839-66, p < .001), however, the magnitude of this difference was significantly larger for survivors (F = 50-41, p < .001).

Eighty-three percent of survivors (535 out of 648) and 68% of community adults (444/650) had a decisional balance greater than one (Fig. 1). Decisional balance was significantly higher in survivors

### Table 2

Demographic characteristics of the four participant groups (N = 1550).\(^d\)

| Characteristic                  | Adults (n = 1298) n (%) | χ²  | p  | Parents (n = 252) n (%) | χ²  | p  |
|---------------------------------|------------------------|-----|---|------------------------|-----|---|
| Sex                             |                        |     |   |                        |     |   |
| Male                            | 98 (15.1)              | 0.92| 34| 4 (8.3)                | 0.92| 34|
| Female                          | 550 (84.9)             |     |   | 44 (91.7)              |     |   |
| Age: Mean (SD)\(^c\)            | 59.57 (12.4)           | 1.74| 0.08| 14.83 (3.3)            | 1.74| 0.08|
| Range                           | 17–83                  |     |   | 9–31–00                |     |   |
| Income\(^e\)                    | Nil income             | 2.00| 0.02| 2 (4.2)                | 0.02| 0.02|
|                                 | Less than $29,999      | 3.78| 0.07| 2 (4.2)                | 0.07| 0.07|
|                                 | $30,000–$39,999        | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | $40,000–$89,999        | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | $90,000 or more        | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
| Income\(^e\)                    | Prefer not to answer\(^f\) | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
| Education                       | No post-school qualifications | 2.00| 0.02| 2 (4.2)                | 0.02| 0.02|
|                                 | Post-school qualifications | 3.78| 0.07| 2 (4.2)                | 0.07| 0.07|
| Rurality\(^g\)                  | Major city             | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Other                  | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Multiple area codes    | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
| Diagnosis of survivor\(^h\)     | Breast cancer          | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Prostate cancer        | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Other solid tumors     | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Leukemia               | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Lymphoma               | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Time since diagnosis in years: Mean (SD) | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|
|                                 | Range                  | 0.00| 1.00| 2 (4.2)                | 1.00| 1.00|

\(^a\) Between-group difference analyzed using independent t-test.

\(^b\) Multiple area codes’ and ‘Other’ were combined for analyses, as cell counts were <5.

\(^c\) We excluded one adult survivor, 8 community adults, and one community parent who did not understand PDXs after receiving the brief description. 34 adult survivors and 48 cancer parents were not asked this question.

\(^d\) Age refers to age of the target patient for whom PDX was considered; for survivors and community adults, it was themselves. For parents, age represents the age of the child with cancer (survivors’ parents) or the average age of all their children (community parents), therefore group difference was not statistically compared. NB: After matching for age and sex, 54 participants remained who incorrectly entered their age in the questionnaire (e.g., entered their birth year as the current year). We were able to estimate ages for 25 community and 16 adult participants based on their responses to a categorical age question (e.g. if the participant indicated that they were between 30 and 40 years of age but they also entered today’s date as their date of birth, we allocated their age as 35 years old). We excluded 13 adult participants who entered their age incorrectly and we were unable to estimate their age.

\(^e\) Missing data for 2 community adults and 1 survivor parent.

\(^f\) Participants who preferred not to answer were excluded from analyses that included income as a variable. Male survivors and male community adults were more likely to report their income than female survivors (p = .03) and female community adults (p = .02). Survivors from rural/regional areas were more likely to report their income than survivors from major cities (p = .02). Younger survivors were more likely to report their income than older survivors (M = 58.14, SD = 12.78 versus M = 60.91, SD = 11.00, p = .01). Community parents and survivors’ parents who did not report income were not significantly different to those who did on sex, education or rurality.

\(^g\) We classified participants’ rurality using the Accessibility/Remoteness Index of Australia, which categorizes regions according to accessibility of services. We grouped regions into ‘major city’, ‘inner regional’ and ‘outer regional’. We manually categorized New Zealand postcodes according to the Statistics New Zealand Urban/Rural Profile Classifications. We had missing data for 3 survivors, 5 community adults, 2 survivors’ parents, and 3 community parents.

\(^h\) Missing data for 36 adult survivors.

---

\(^d\) N = 1550.
Given the unequal sample sizes between parent groups, we conducted separate paired t-tests to compare within group differences in perceived advantages and disadvantages for the parent samples separately. Survivors’ parents and community parents rated the potential advantages of PDXs significantly higher than potential disadvantages (cancer: MD = 2.57, t(46), p < .001; community: MD = 0.76, t(203) = 8.07, p < .001).

Eighty-nine percent of survivors’ parents (42/47) and 68% of community parents (138/204) had a decisional balance greater than one (Fig. 1). Decisional balance was significantly higher in survivors’ parents than in community participants [MD = 0.96, 95%CI [0.53, 1.40], t(50.30) = 4.45, p < .001] (Supplementary Fig. 1). Survivors’ parents, mothers, and those with higher income were more likely to indicate a higher decisional balance score.

When considering the seven listed advantages/disadvantages of PDXs, the most important perceived advantage varied across groups (survivors and survivors’ parents: ‘improving survival chances’, community adults: ‘faster recovery’, community parents: ‘avoiding other drugs’) (Supplementary Table 1). Survivors, community adults and community parents endorsed ‘recommended treatments being unavailable/too expensive’ as the most important disadvantage. The least endorsed advantage across all groups was ‘reassurance doctors tried everything’ and the least endorsed disadvantage was ‘PDXs harm animals’.

**RQ2. Willingness-to-use PDXs, before and after consideration of advantages/disadvantages**

Cancer survivors indicated a higher willingness-to-use PDXs than community comparisons, when averaged across before (cancer: M = 6.03, SD = 1.46; community: M = 5.47, SD = 1.77) and after (cancer: M = 5.85, SD = 1.36, community: M = 5.31, SD = 1.69; F = 43.21, p < .001) consideration of the advantages and disadvantages of PDXs. A main effect of time-point (i.e., comparing before and after scores, averaged across group) suggested that participants’ willingness-to-use PDXs decreased after consideration of the advantages and disadvantages (F = 38.07, p < .001), with the magnitude of this decrease similar for survivor and community participants (F = 0.38, p = .54).

In the parent groups, community parents’ willingness-to-use decreased after consideration of the advantages and disadvantages of PDXs (MD = 0.25, t(203) = 4.76, p < .001), whereas, survivors’ parents ratings did not significantly change (MD = 0.11, t(46) = 1.22, p = .23).

**RQ3. Willingness-to-pay for PDXs**

Seven percent of survivors (36/542) reported being willing to pay the maximum proposed amount (AUD$50,000/NZD$55,000), while 2% of community adults (11/520) were willing to pay the maximum (Fig. 2). Survivors were willing to pay more than community participants (t(1060) = 9.04, p < .001). Survivors, men, and participants with higher incomes, were more likely to indicate a higher willingness-to-pay (Table 3).

Thirty-eight percent of survivors’ parents (14/37) reported being willing to pay the maximum, while 15% of community participants (t(156) = 3.41, p = .004). Survivors’ parents with higher incomes were more likely to indicate a higher willingness-to-pay (Table 3).

**RQ4. Maximum acceptable wait-time for results/recommendations from PDXs**

Two percent of survivors (11/603) reported being willing to wait the maximum time (one year), while 0.5% of community adults (3/584) reported being willing to wait that long. Survivors reported a willingness to wait longer than community participants (t(1185) = 2.43, p = .02).
education were more likely to indicate a higher maximum wait-time (Table 3).

Among survivors' parents, 16% (7/43) were willing to wait the maximum time (one year), compared with 2% (3/180) of community parents. Survivors' parents were willing to wait longer than community parents ($t(51.36) = 2.94, p = .01$), Fig. 3. Survivors' parents, fathers, and those with post-school education were more likely to indicate a higher maximum wait-time (Table 3).

**RQ5. Maximum acceptable number of mice/patient.**

Nine percent of survivors (19/217) endorsed a willingness-to-use up to 1000 mice, while 5% (11/219) of community participants (who indicated the number of mice would influence their decision) were willing to use up to 1000 mice. Survivors' parents were willing to use many more mice per patient than community parents ($t(37.59) = 4.12, p < .001$), Fig. 4. Survivors' parents, and those with post-school qualifications, accepted a higher number of mice, Table 3.

**3.1. Secondary research question: Acceptability of PDX by cancer type**

In the survivor group, average decisional balance, maximum acceptable wait-time, and maximum acceptable number of mice did not differ between those diagnosed with hematological cancer versus solid tumors ($MD = 0.22, -0.01, 1.08; p = .19, 0.96, 0.21$ respectively). Survivors diagnosed with hematological cancers were willing to pay more for PDXs compared with survivors diagnosed with solid tumors ($[MD = 0.15], 95\% CI [0.44, 2.63], t(28.45) = 2.86, p = .01$). There were no significant differences in decisional balance, willingness to pay, acceptable wait-time, or acceptable number of mice across children's cancer diagnoses among survivors' parents ($MD = 0.34, -0.35, -0.58, 0.20; p = .43, 0.73, 0.15, 0.77$ respectively).
4. Discussion

Most cancer survivors, parents of childhood cancer survivors, and the general community favor the use of PDXs in future cancer therapeutic strategies. Participants reported a high willingness-to-use and a perception that PDX advantages outweighed disadvantages, suggesting high consent rates when PDXs are implemented into personalized cancer care. Reflecting the salience of the cancer experience, those affected by cancer were more willing to use PDXs and were willing to pay more, wait longer, and use more mice, than community participants. Reflecting the notion that the ‘stakes are higher’ when considering cancer in a child, parents reported being willing to pay large sums and use many mice, for their child. Other sociodemographic factors appeared important too. Males found PDXs more acceptable, and were willing to pay more than females, while mothers found PDXs more acceptable but were willing to wait less time, than fathers. Participants with higher incomes found PDXs more acceptable and were willing to pay more. Willingness-to-pay and maximum acceptable number of mice appeared largely in line with the likely PDX services of the future [2,11], although many participants’ maximum acceptable wait-times were lower than is currently achievable [11].

PDX efficacy data, while promising, is not yet robust [2,11]. Our description of PDXs did not state that PDXs were effective, yet many participants endorsed ‘potential improved survival’ as their most important perceived advantage (particularly survivors and survivors’ parents). Potential health benefit is a key motivator for many patients and parents considering enrolling in research [22]. While willingness-to-use did decline somewhat after consideration of the advantages and disadvantages of PDXs, willingness-to-use remained high, especially in those affected by cancer. It seems that disclosure of PDX limitations will be unlikely to dissuade families. Ensuring fully informed consent will be challenging, given the complexity of the PDX process [2], differences in PDX models across institutions [2], the often overwhelming availability of cancer information [23], and low pre-existing health literacy in some patients [24]. PDX information should follow patient education guidelines [25] to ensure that materials are easy-to-understand, while consent consultations should carefully gauge patient/parent understanding, and encourage question-asking.

Fig. 3. Panels showing the cumulative frequency of willingness to wait for PDX results, presented separately for adult and parent groups, with the 50th percentile highlighted.
of likelihood of adoption [14,28]. Fear of cancer recurrence, which remains prevalent even decades after treatment completion [29], may have driven survivors’ and survivors’ parents’ willingness-to-use and pay. This powerful fear likely represents a vulnerability for families desperate for a cure [13]. Given that commercial laboratories are already offering costly direct-to-consumer PDX services [3,30], this raises concerns about how PDXs will be marketed to vulnerable families, and highlights the need for careful PDX regulation [3].

The role of animals in society appears to be transforming. Animal advocacy groups often fight for a reduction in the use of research animals, yet PDXs will involve dozens of mice per patient. Despite these numbers, and the fact that PDXs form a more direct link between animals and individual patients, our finding that ‘harm to animals’ was the least endorsed disadvantage reflects an acceptance of the use of animals for potentially lifesaving purposes. Like other studies [31], we showed that acceptability dropped with the use of more animals. However, individuals affected by cancer clearly accepted the largest numbers of mice (especially survivors’ parents, most of whom indicated a willingness to use up to 1000 mice per child). This research question revealed the strongest discrepancy in views between individuals affected by cancer and community participants, which might create some discordance in future PDX implementation and funding models. It remains unclear how PDX acceptability might be shaped if increasing the number of mice used would also increase PDX efficacy.

4.1. Limitations

We recruited a large sample across two countries, plus a well-matched comparison group. However, anticipated uptake of new technologies does not always mirror actual uptake [14]. Participants’ attitudes might change to reflect a higher acceptability if individuals are currently faced with cancer. It was not possible to calculate study response rates given the different recruitment methods used for each group. Our data may not generalize to other contexts, (e.g. non-English speaking communities, non-universal healthcare systems). Breast cancer survivors and women were over-represented, which is common [32]. Recruiting survivors introduced a survival bias, creating an underrepresentation of aggressive cancers (e.g. lung cancer). A small amount of variance in our regressions was captured by our predictors, suggesting there are likely to be unmeasured variables influencing acceptability. Our different data collection methods (questionnaire versus interview) were necessary to ensure the representation of different cohorts. However, the data may have been influenced by the different data collection approaches.

4.2. Future directions

Prospective studies assessing the impact of using PDXs to guide treatment decisions in personalized medicine programs are needed. There are several technical developments in PDXs which warrant additional acceptability studies, including the use of zebrafish and tumor organoids [11]. Patient/parent willingness to undergo additional procedures to enable PDX creation (e.g. biopsies) also remains unexplored, as does the acceptability of the term ‘avatar’ to describe PDXs. Healthcare systems need to consider the cost-benefits of PDXs as they move into clinical care [2,3]. PDXs will likely improve with time, potentially warranting ongoing research of the acceptability of the more sophisticated technology.

5. Conclusions

PDXs are likely to play a key role in translational cancer care of the future, yielding personalized treatment information to guide clinical decision-making [1]. Despite being expensive and using animals to guide treatment decision-making [1,11], individuals affected by cancer, and the general community, find PDXs highly acceptable.
Declaration of interests

Kathy M. Tucker has received Honoria from AstraZeneca Australia with respect to mainstreaming BRCA genetic testing in adults. No other authors have conflicts of interest to declare.

Author’s contributions

CEW conceived and coordinated the project. She developed the protocol and wrote the manuscript. ELD contributed to data analysis and final manuscript. KFT, AFP, GMM and RBL helped to design the study and contributed to the manuscript development. GG assisted with participant recruitment and data collection and reviewed manuscript drafts. RJC helped to conceive the project, develop the study protocol and contributed to the manuscript. All authors provided feedback on drafts of this article and read and approved the final manuscript.

Funding

Claire Wakefield is supported by a Career Development Fellowship from the National Health and Medical Research Council of Australia (APP1143767). Christina Signorelli and Joanna Fardell are supported by The Kids’ Cancer Project. Richard Lock is supported by a Fellowship from the National Health and Medical Research Council of Australia (APP1059804). Glenn Marshall is supported by NHMRC, CNISW, and CCNSW. This study was supported by the Kids Cancer Alliance, funded by the Cancer Institute NSW. The Behavioural Sciences Unit (BSU) is proudly supported by the Kids with Cancer Foundation. The BSU’s survivorship research program is funded by The Kids’ Cancer Project and a Cancer Council NSW Program Grant PG16–02 with the support of the Estate of the Late Harry McPaul. No funders had any role in the study design, data collection, data analysis, interpretation, or writing of this manuscript.

Acknowledgements

We would like to acknowledge the contributions of Ms. Brittany McGill, Dr. Janine Vetsch, Dr. Kate Hetherington and Ms. Rebecca Hill who conducted interviews and Lucy Hanlon who analyzed the pilot data. We would also like to thank the cancer survivors, parents and members of the community who participated. We would like to thank each of the recruiting sites including Register 4, PathFinder, Pure Pro and the community who participated. We would like to thank each of the volunteers who participated in the study, including Gill, Dr. Janine Vetsch, Dr. Kate Hetherington and Ms. Rebecca Hill who contributed to data analysis.

References

[1] Garralda E, Paz K, López-Casas PP, et al. Integrated next-generation sequencing and avatar mouse models for personalized cancer treatment. Clin Cancer Res 2014;20: 2476–84.

[2] Hidalgo M, Amant F, Blankin AV, et al. Patient-derived xenograft models: an emerging platform for translational cancer research. Cancer Discov 2014;4:998–1013.

[3] Maloney P, Nicolaia SV, Davé V, One mouse, one patient paradigm: New avatars of personalized cancer therapy. Cancer Lett 2013;441:1–5.

[4] Morelli MP, Calvo E, Ordoñez E, et al. Prioritizing phase I treatment options through preclinical testing on personalized tumours. J Clin Oncol 2012;30:e45–8.

[5] Tjahra T, Lock R, Sutton R, et al. Xenograft-directed personalized therapy for a patient with post-transplant relapse of ALL. Bone Marrow Transplant 2016;51(9): 1279.

[6] Jones L, Carol H, Evans K, et al. A review of new agents evaluated against pediatric acute lymphoblastic leukemia by the Pediatric Preclinical Testing Program. Leukemia 2016;30:2133.

[7] Zayed AA, Mandrekar SJ, Haluska P. Molecular and clinical implementations of ovarian cancer mouse avatar models. Chin Clin Oncol 2015;4:30.

[8] Stebbing J, Paz K, Schwartz GK, et al. Patient-derived xenografts for individualized care in advanced sarcoma. Cancer 2014;120:2066–15.

[9] Cheon D-J, Orsulic S. Mouse models of cancer; 2011.

[10] Braekenfeldt N, Vigerup C, Tadeo I, et al. Neuroblastoma patient-derived orthotopic xenografts reflect the microenvironmental hallmarks of aggressive patient tumours. Cancer Lett 2016;375:384–9.

[11] Aparicio S, Hidalgo M, Kung AL. Examining the utility of patient-derived xenograft mouse models. Nat Rev Cancer 2015;15:311–6.

[12] Garrido-Laguna I, Ueno M, Rajeshkumar N, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[13] Krueger GM. Hope and Suffering: Children, Cancer, and the Paradox of Experimental Medicine. Baltimore: Johns Hopkins University Press; 2008.

[14] Cuffe S, Hon H, Qiu X, et al. Cancer patients’ acceptance, understanding, and willingness-to-pay for pharmacogenomic testing. Pharmacogenet Genomics 2014; 24:348–55.

[15] Adli M. Breast Cancer Genome Guided Therapy Study (BEAUTY) USA: Department of Health and Human Services National Center for Biotechnology Information; 2017.

[16] California Pacific Medical Center Research Institute. CPMCR’s Cancer Avatar Project, USA; 2017.

[17] Lau L, Byrne J, Eckert PG, et al. Pilot study of a comprehensive precision medicine platform for children with high-risk cancer. Am Soc Clin Oncol 2017:10539.

[18] Vandenbroucke JP, Vos T, Flaxman SR, et al. Cause of deathcauses of death: Global, regional, and national oncolgi of death for all ages in 188 countries during 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;386:1775–84.

[19] Lu X, Zhang S, Chen J, et al. Prognostic accuracy of tumour engraftment rates for patient-derived xenografts in predicting clinical outcome of ovarian cancer. Br J Cancer 2016;115: 1645–52.

[20] Schepis T, Liu Y, Kuppusamy R, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[21] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[22] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[23] Cheon D-J, Orsulic S. Mouse models of cancer; 2011.

[24] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[25] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[26] Amiram G. Willingness-to-pay as a measure of benefit in the health care industry. J Med Econ 2012;15:679–85.

[27] Cuffe S, Hon H, Qiu X, et al. Cancer patients’ acceptance, understanding, and willingness-to-pay for pharmacogenomic testing. Pharmacogenet Genomics 2014; 24:348–55.

[28] Teeters KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[29] Schepis T, Liu Y, Kuppusamy R, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[30] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[31] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[32] Cheon D-J, Orsulic S. Mouse models of cancer; 2011.

[33] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[34] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[35] Schepis T, Liu Y, Kuppusamy R, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[36] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[37] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[38] Schepis T, Liu Y, Kuppusamy R, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[39] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[40] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.

[41] Schepis T, Liu Y, Kuppusamy R, et al. Tumor engraftment in nude mice and enrichment in stroma-related gene pathways predict poor survival and resistance to gemcitabine in patients with pancreatic cancer. Clin Cancer Res 2011;17: 5793–800.

[42] Delacole M, Lakens D, Leys C. Why psychologists should by default use Welch’s t-test instead of Student’s t-test. Int J Psychol Sci 2017:16.

[43] Tercyak KP, Alford SH, Emmons KM, Lipkus IM, Bs Wilfond, McBride CM. Parents’ attitudes toward pediatric genetic testing for common disease risk. Pediatrics 2011: e1288–95.