

Original Research Article

Oncology patient preferences in reporting on symptoms

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ABSTRACT

Background: Collecting patient reported outcomes (PROs) in oncology clinical trials is becoming increasingly important. However, there is limited consensus on the most appropriate frequency of PRO administration in oncology trials. The aim of this preliminary study is to examine the perspective of participants with a cancer diagnosis on the importance of completing PROs and to identify at what frequency participants prefer to report on their cancer-related symptoms.

Methods: 166 participants with a self-reported cancer diagnosis completed a multiple-choice online survey regarding perceptions of symptom importance and reporting preferences.

Results: When asked about the benefit of reporting oncology-related symptoms daily, 44% of participants indicated there would be “very much” a benefit, 29% indicated there would be “quite a bit” of benefit, and 17% indicated there would be “somewhat” of a benefit. When asked about how frequently they would prefer to report symptoms, 41% of participants preferred “as they occur,” 36% preferred “once a day,” 18% preferred “once a week,” 4% preferred “twice a day,” and 1% preferred “every 4 hours”.

Conclusions: PROs in oncology clinical research are most often collected at weekly, monthly, or longer intervals; however, meaningful fluctuations in cancer-related symptoms can occur more frequently. While concerns regarding patient burden are often raised to support infrequent reporting, these data suggest that participants would like to report symptoms with greater frequency, as episodic and daily reporting options were most popular. Based on these data, more frequent PRO data capture is not only feasible but perceived as important by individuals with cancer.

Keywords: Patient reported outcomes, Oncology, Frequency, Symptoms

INTRODUCTION

In 2018, the Food and Drug Administration (FDA) issued 63 new approvals and safety notifications for cancer products.¹ While overall survival and tumor response rate remain the preeminent primary outcome measures in oncology clinical trials, there has recently been a marked shift in the regulatory landscape toward including patient reported outcomes (PROs) in the risk-benefit evaluation for cancer therapeutics.² In fact, the most recent FDA guidance released in 2018 indicates that, “PRO measures demonstrating improvement in a patient’s quality of life,

improved physical functioning, or improved tumor-related symptoms can represent direct measures of treatment benefit,” and states that cancer drug approval should be based on such evidence.³ The European Medicines Agency (EMA) guidance on evaluating anticancer medicinal products agrees, stating that symptom control is a valid measure of therapeutic activity and may serve as a primary endpoint in late therapy studies.⁴ Despite the endorsement of PRO measures for the evaluation of oncology symptom data, the FDA acknowledges that missing data and infrequent assessments can complicate analyses.³ The objective of the current survey study is to explore oncology patients’

motivations for completing PROs, as well as identify at what frequency patients prefer to report on their cancer-related symptoms.

The benefit of including PROs in clinical trials extends beyond regulatory acceptance and into clinical care, as simply completing self-report measures has been associated with increased physician communication about symptom changes and lower symptoms of depression.⁵⁻⁸ Capturing PROs ‘electronically’ (ePRO), has the opportunity to extend these benefits even further. Utilizing an electronic device allows for changes in symptoms to be flagged to physicians well before patient contact would have otherwise occurred, ultimately resulting in reduced symptom severity and even increased survival.⁹⁻¹⁰ Patients appear to recognize the benefits of ePRO as well. When given the chance to provide symptom information regularly in the form of ePROs, 87% of patients felt that it was important to do so, with 79% indicating that they felt their responses were included in treatment decisions.¹¹ These data suggest that patients are not only willing, but eager to provide information via electronic device and that doing so may have measurable positive impact on treatment outcomes.

Currently, there is limited consensus on the most appropriate frequency of PRO administration in oncology trials. Often, PROs are administered once every couple of weeks, once a month, or less at in-clinic visits. However, there is evidence to suggest that cancer-related symptoms, particularly those associated with chemotherapy, show daily and even intra-day variability.¹²⁻¹⁴ Thus, reporting symptoms more frequently and via electronic devices may provide important information for both drug development and clinical care. As the field has shifted to incorporate more PROs, concerns have been raised regarding balancing patient response burden with need for data.¹⁵ While preliminary evidence suggests that a relatively lengthy battery of PROs was not perceived by patients as significantly burdensome, it is unclear if patients would be willing to complete PRO measures with more frequency.¹⁶ A first step toward clarifying optimal frequency of PRO reporting in oncology is to examine patient preference in reporting. To that end, the current study aimed to gain a better understanding of oncology patients’ reporting preferences. Individuals with a lifetime cancer diagnosis were asked to complete an online survey comprised of several questions regarding reporting oncology symptoms in a clinical trial, including preferred reporting frequency and method, as well as perceptions of the importance and benefit of symptom report.

METHODS

Survey design

A panel of experts in assessment design, patient reported outcomes, and data collection in oncology clinical trials

compiled questions for this survey, with the goal of better understanding oncology patient preferences regarding symptom reporting. The questions were reviewed and edited by an independent expert before submission to the IRB.

Participants and procedure

One hundred and sixty-six participants who self-reported a diagnosis of cancer (age 18-87, 56.6% female) completed the anonymous online survey from February to March 2019. Participants were recruited via email from Clinical Connection (clinicalconnection.com), a website designed to connect prospective participants with clinical trials. As the survey was anonymous, consent was inferred via opting to complete the survey. Participants were not required to complete the entire survey and were allowed to skip questions. After survey completion, participants could choose to provide an email for entry into a drawing for a \$100 gift card. All procedures were reviewed and approved by the Western Institutional Review Board.

Statistical analyses

Prior to any data analysis, survey data were cleaned. Responses were removed if individuals completed the survey more than one time, indicated that they did not have a cancer diagnosis, or completed the survey in less than 50% of the median time. The nature of this study is observational as response options were categorical or ordinal. As such, one-way chi-square tests were used to confirm that response distributions were non-random and represented true participant preference.

RESULTS

Data cleaning

Two hundred and three participants filled out the survey prior to data cleaning. Ten duplicate response sets were removed, 8 response sets were removed because the participant indicated they did not have a diagnosis of cancer, and 2 response sets were removed due to very short time of completion. Seven response sets were removed because participants only completed the demographics questions. No participants elected to skip questions, although 27 discontinued before completing the entire survey.

Demographics

One hundred and sixty-six participants (57% female) were involved in the final, observational analyses. Participants ranged in age from 18-87 (mean=61.28, SD=12.24). Table 1 shows complete demographics information.

Table 1: Participant demographics.

Variable	Total (n=166)	Breast cancer (n=54)	Prostate cancer (n=32)	Lung cancer (n=9)	Skin cancer (n=15)	Other cancer (n=56)
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Age (years)						
Range	18-87	34-79	51-87	53-77	32-82	18-86
Mean (SD)	61.28 (12.24)	57.67 (10.27)	66.56 (7.83)	65.78 (6.97)	61.27 (12.46)	61.02 (15.04)
Sex						
Female	94 (57)	52 (96)	0 (0)	6 (67)	6 (40)	30 (54)
Male	70 (42)	1 (2)	32 (100)	3 (33)	9 (60)	25 (45)
Prefer not to answer	2 (1)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)
Education						
Advanced degree (MA, MD, PhD, MD)	27 (16)	9 (17)	10 (31)	0 (0)	0 (0)	8 (14)
College Degree (BA/BS)	41 (25)	16 (30)	8 (25)	2 (22)	5 (33)	10 (18)
Some college/technical degree/AA/AS	63 (38)	25 (46)	9 (28)	1 (11)	7 (47)	21 (38)
High school graduate/GED	29 (17)	4 (7)	4 (13)	5 (56)	3 (20)	13 (23)
Some high school	5 (3)	0 (0)	1 (3)	1 (11)	0 (0)	3 (5)
8th grade or less	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)

Survey responses

When asked, “If you were participating in a clinical trial for oncology, would you feel there is a benefit to reporting changes in your oncology-related symptoms, such as pain, nausea, etc. to the study doctor on a daily basis?”, 44% of participants indicated there would be “Very much” benefit, 29% indicated there would be “Quite a bit” of benefit, and 17% indicated there would be “Somewhat” of a benefit (one-way chi-square; $n=164$; $\chi^2(4)=92.098$, $p<0.0001$; Figure 1). Only 10% of participants indicated there would be “A little bit” or “None at all”. Participants’ attitudes toward symptom reporting benefit appeared similar across cancer types, as participants most frequently chose that there was “Very much” benefit to reporting symptoms. When examining responses within each type of cancer diagnosis individually, 87%-97% of patients reported that there was “Somewhat”, “Quite a bit”, or “Very much” benefit to reporting changes in oncology related symptoms.

To examine preference of frequency of reporting, participants were asked, “If you were participating in a clinical trial for oncology, how frequently do you feel you would need to report your symptoms?” Participants showed relative preference for the options “As they occur” (41%) and “Once a day” (36%) as compared to “Once a week” (18%), “Twice a day” (4%) and “Every 4 hours” (1%; one-way chi-square; $n=165$; $\chi^2(4)=105.394$, $p<0.0001$; Figure 2). When examining responses by

cancer diagnosis, the most frequently chosen options remained “As they occur” (27%-45%) or “Once a day” (30%-53%) for all diagnoses. “Once a week” was the third most frequently selected reporting option among breast cancer (23%), prostate cancer (19%), and other cancer (17%) diagnoses. However, individuals with skin cancer chose a reporting frequency of “Twice a day” third most often (13%).

Responses to the question “If you were participating in a clinical trial for oncology, how would you prefer to report your daily changes in symptoms?” revealed that the majority (63%) of participants would prefer to report symptoms in a daily eDiary that would be reviewed by study doctors. In addition, 17% preferred to report symptoms directly to doctors at study visits, 14% preferred to report symptoms on a paper diary, and 5% did not want to report symptoms (one-way chi-square; $n=166$; $\chi^2(3)=134.627$, $p<0.0001$; Figure 3). When examining the response pattern across cancer diagnoses, eDiary report was the most preferred option within prostate cancer (78%), breast cancer (61%), skin cancer (60%), and other cancers (58%).

When asked, “If you were participating in a clinical trial for cancer and were asked to complete several questionnaires about your health status on an electronic device such as a smartphone, tablet or iPad, do you believe that the doctor reviews the answers that you provide?” 87% of participants indicated “Yes” (one-way,

chi-square; $n=159$; $\chi^2(1)=89.063$, $p<0.001$). Importantly, 96% of patients indicated it is “Very Important” (71%) or “Important” (25%) to them that study doctors review

information provided about their health status (one-way chi-square; $n=139$; $\chi^2(3)=173.374$, $p<0.0001$).

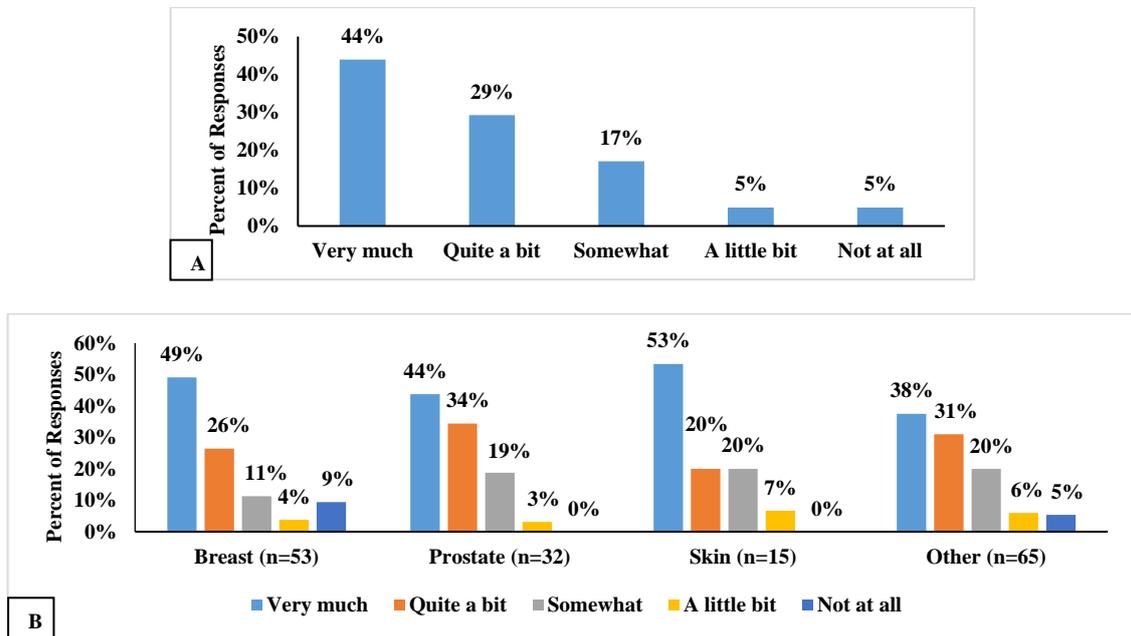


Figure 1: Perceived benefit of reporting oncology related symptoms. (A) All participant responses to “If you were participating in a clinical trial for oncology, would you feel there is a benefit to reporting changes in your oncology-related symptoms, such as pain, nausea, etc. to the study doctor on a daily basis?” (B) Participant responses to “If you were participating in a clinical trial for oncology, would you feel there is a benefit to reporting changes in your oncology-related symptoms, such as pain, nausea, etc. to the study doctor on a daily basis?” by self-reported cancer-diagnosis.

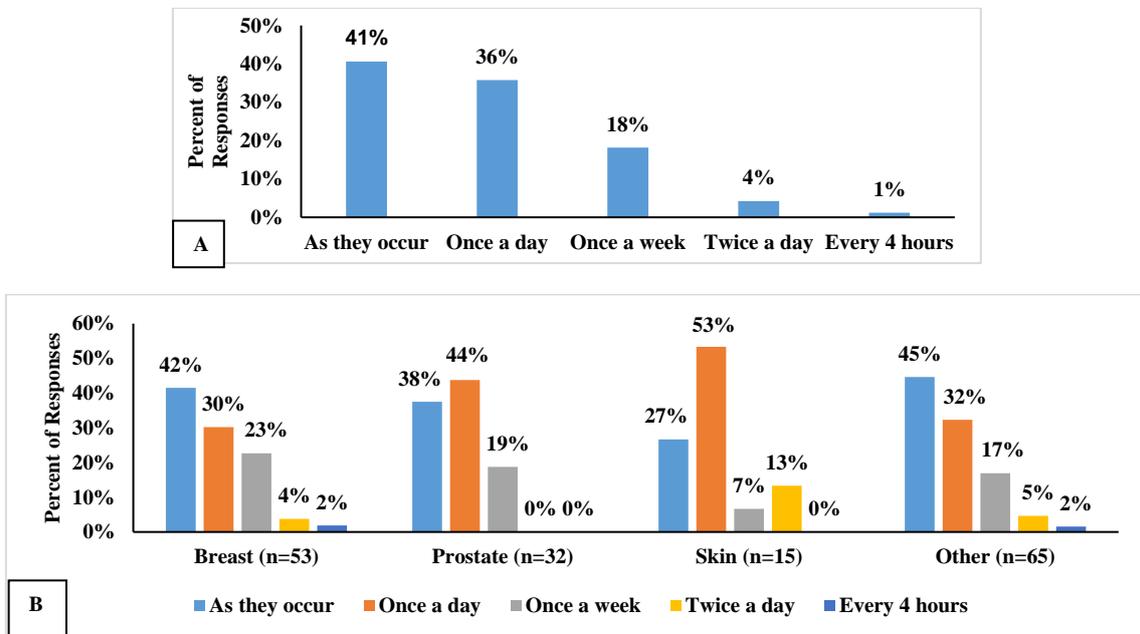


Figure 2: Preferred cancer-related symptom reporting frequency. (A) All participant responses to “If you were participating in a clinical trial for oncology, how frequently do you feel you would need to report your symptoms?” (B) Participant responses to “If you were participating in a clinical trial for oncology, how frequently do you feel you would need to report your symptoms?” by self-reported cancer-diagnosis.

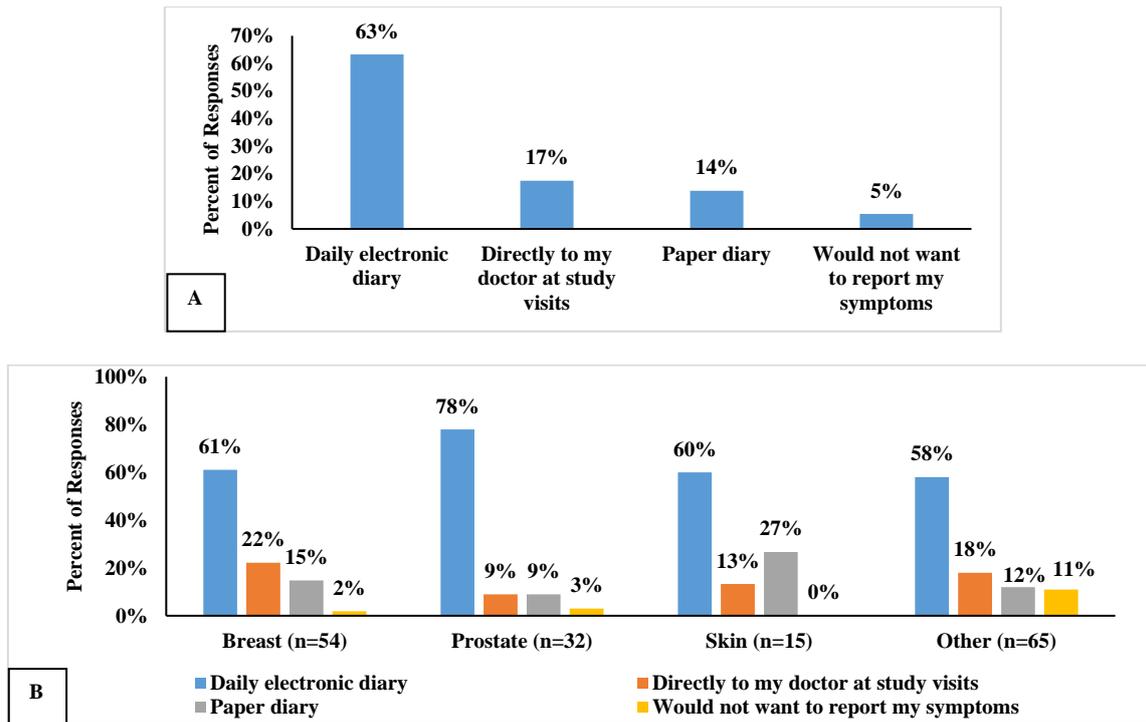


Figure 3: Preferred cancer-related symptom reporting method. (A) All participant responses to “If you were participating in a clinical trial for oncology, how would you prefer to report your daily changes in symptoms?” (B) Participant responses to “If you were participating in a clinical trial for oncology, how would you prefer to report your daily changes in symptoms?” by self-reported cancer-diagnosis.

DISCUSSION

Collecting PROs in oncology clinical research is becoming increasingly important, as regulatory agencies recognize PROs as measures of clinical benefit and applied research highlights their role in improving clinical care.³⁻¹⁰ In oncology clinical trials, PROs are regularly collected at weekly, monthly, or longer intervals; however, potentially meaningful fluctuations in cancer-related symptoms can occur more frequently.¹²⁻¹⁴ Thus, capturing symptoms at weekly or longer intervals may be missing vital information. In this survey, participants indicated that they would find it beneficial to report oncology-related symptoms more frequently, as episodic (41%) and daily (36%) reporting options were most popular. In fact, only 18% of participants chose weekly reporting as their preferred option. This pattern was consistent across cancer diagnosis groups, suggesting that the perceived benefit of reporting symptoms with increased frequency is likely not driven by cancer-specific symptoms - such as urinary problems that are most commonly seen in prostate cancer - but by symptoms that are common across cancer types such as poor sleep or fatigue.

Patient burden is often raised as a concern regarding the inclusion of PRO instruments in oncology trials, however, in a study conducted by Atkinson et al patients who completed a lengthy battery of PRO assessments reported minimal response burden.¹⁶ In fact, in that study

32% of participants indicated that they would have liked to report additional information. While the current data cannot directly address response burden of increased reporting, patient preference for episodic or daily reporting suggests that patients do not expect to be overwhelmed by such demands. At the very least, it appears that patients would like the opportunity to have more autonomy in reporting.

It is possible that the observed preference for reporting symptoms episodically or daily is related to perceived importance of providing such information. Consistent with prior work, nearly half (44%) of our sample indicated that there would be significant benefit to reporting symptoms on a daily basis and almost all (90%) reported that there would be at least some benefit.¹¹ Perceived benefit of reporting oncology-related symptom changes daily via eDiary was high across diagnosis groups, with 87-97% of patients across breast, prostate, and, skin, cancers reporting that there was at least some benefit to doing so. Indeed, patients in the current sample overwhelmingly (96%) reported that it is important that trial doctors review the information that they provide electronically and 87% endorsed believing their doctors do. Although not evaluated here, Seow et al have shown that patients believe symptom information from eDiaries is used to make decisions about their care and treatment, revealing potential motivations driving willingness to report.¹¹

It is important to note that the current results specifically target reporting utilizing an electronic diary. In line with other indications, electronic clinical outcomes assessment in oncology continues to be the most reliable way to gather symptom and quality of life data.¹⁷⁻¹⁹ Not only is compliance higher when using electronic capture than with paper, prior work shows that oncology patients consistently prefer reporting electronically.¹⁷⁻¹⁹ In one study, 94% of patients went so far as to say that they would recommend an electronic diary to other patients.¹⁸ The current survey results bolster the extant literature, as the majority of participants indicated they would prefer to report symptoms in a daily eDiary rather than reporting on paper, directly to their physicians, or not at all.

There are several limitations to this study that merit discussion. The observational survey nature of the study limits our ability to make strong conclusions regarding patient motivations or conduct statistics to that effect. However these observations provide robust foundation for further exploration into frequency of PRO reporting in oncology studies. Furthermore, diagnosis of cancer is self-reported and not clinically verified and we are only able to acknowledge patterns among specific cancer diagnoses that appeared with regularity in our data. While this provides depth for our current observations, further exploration is needed to understand reporting preference in specific cancer diagnoses. Finally, the online nature of the study may have limited access to individuals who do not regularly use the internet, however our recruitment strategy specifically targeted individuals who are seeking clinical trial participation via an online resource.

CONCLUSION

As PRO collection in oncology clinical research becomes increasingly important, the field has the obligation to better understand the impact of PROs from a patient perspective. These preliminary data suggest that, among a group of individuals with self-reported history of cancer, most respondents would prefer to report symptoms via eDiary on a daily or episodic basis, feel that there is benefit to reporting their cancer-related symptoms, and overwhelmingly preferred to report them via an electronic device. These preliminary findings provide a strong foundation to inform further patient-centered research on how to best implement PROs in clinical trials in oncology.

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Conflict of interest: Current and past employees of ERT (ALP, MG, JL, and SMD) played a role in study design, data collection, data analysis, writing and submission of the paper

Ethical approval: All procedures were reviewed and approved by the Western Institutional Review Board

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