Feasibility of oncology clinical trial-embedded evaluation of social determinants of health

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April 12, 2022

Abstract

Social determinants of health (SDoH) are associated with stark disparities in cancer outcomes, but systematic SDoH data collection is currently absent from oncology clinical trials. Trial-based SDoH data are essential to ensure representation of marginalized populations, contextualize outcomes, and identify health-equity intervention opportunities. We report the feasibility of the first pediatric oncology multicenter trial-embedded SDoH investigation. Among 448 trial participants, 392 (87.5%) opted-in to the embedded SDoH study; 375 (95.7%) completed baseline surveys, with high longitudinal response rates (87.2-92.8%) over 24-months of therapy. Trial-embedded SDoH data collection is feasible and acceptable, and must be consistently included within future oncology trials.

Introduction

Social determinants of health (SDoH) are associated with stark disparities in adult and pediatric cancer outcomes.[1-3]Adverse SDoH—including poverty, unmet material needs, and unsafe environmental conditions—drive higher cancer incidence, limited clinical trial access, and lower overall survival for individuals from low socioeconomic status or historically marginalized backgrounds.[3-8] Despite robust evidence that SDoH are independent risk factors for cancer outcomes[9], US cancer trials have historically failed to collect these data. Only 63% of US oncology drug trials in the last decade even reported race, a proxy for SDoH exposure due to longstanding structural racism.[10]

The majority of pediatric oncology care nationwide is delivered via multi-institutional clinical trials—thus, trial-integrated SDoH data collection is critical to assess equitable access to cutting-edge therapeutic options,

evaluate generalizability of trial findings to a real-world context, and identify opportunities for health-equity interventions in the trial setting.[11] We have previously demonstrated the feasibility of systematic, parent-reported SDoH evaluation in a clinical context in a single center.[12] However, there are no existing data on the feasibility of this approach as a standardized component of a first-line therapeutic clinical trial, and SDoH data collection is not routinely conducted as a part of cooperative group trials. We report here the feasibility of the first pediatric oncology multicenter trial-embedded SDoH investigation.

Methods

The Dana-Farber Cancer Institute (DFCI) Acute Lymphoblastic Leukemia (ALL) Consortium phase III randomized clinical trial 16-001 (clinicaltrials.gov ID: NCT03020030) enrolled children with *de novo* ALL aged 1-<22 years at 8 US and Canadian centers from 2016-2021. DFCI 16-001 included an embedded study to prospectively evaluate parent-reported SDoH and outcome disparities, powered to investigate household material hardship (HMH: food, utility, or housing insecurity) as the primary SDoH exposure. At trial consent, parents/guardians of children <18 years of age were eligible to opt-in to the SDoH study. Parents completed a 50-item survey (English, Spanish, French-Canadian, or any language with interpreter) in-person or by telephone or remote video platform with research personnel within 32 days of enrollment (T0), and longitudinally at 6, 12 and 24 months of therapy (T1-T3). Surveys were preferentially read aloud to participants to overcome health literacy barriers, though self-completion of paper surveys was allowed. Parent-reported SDoH data included parent language, health literacy, and education; household income; and HMH; as well as parent-reported child race and ethnicity.[13] SDoH were collected as confidential research data, and neither evaluated in real-time nor shared with treating oncology teams. DFCI 16-001 was approved by the DFCI Institutional Review Board (IRB) and site IRBs.

Among the SDoH study-eligible cohort, we compared baseline demographic and disease-related data between participants (defined as those who completed T0 survey) and non-participants (those who declined opt-in consent, or provided consent but did not complete T0) using Wilcoxon rank-sum test for continuous variables and Fisher exact test for categorical variables. Statistical analysis was performed using SAS version 9.4.

Results

As of December 2021, among 448 eligible DFCI 16-001 participants, 392 (87.5%) opted-in to the SDoH study (Figure 1), of whom 375 (95.7%) completed T0 surveys a median of 19 days (range, 1-35 days) from trial registration. Longitudinal response rates were 90.9% (T1), 92.8% (T2), and 87.2% (T3). Complete HMH data (98.2-99.3%, T0-T3) and complete income data (89.6%-91.6%, T0-T3) were provided in nearly all surveys. Patient and leukemia characteristics did not differ between SDoH study participants and non-participants (Table 1).

Discussion

Trial-embedded evaluation of patient-reported SDoH is feasible and acceptable as evidenced by high participation and response rates, low data missingness, and minimal attrition in the first pediatric oncology trial-embedded SDoH study. Baseline SDoH surveys were completed during ALL induction therapy—frequently a time of high clinical acuity and family stress—with a response rate of nearly 96%, demonstrating both the feasibility of early data collection and the salience families place on sharing these data with researchers. We identified no significant differences in baseline characteristics between the overall trial cohort and SDoH cohort study participants, indicating acceptability of this trial-embedded study approach to a representative population of families. Finally, this study successfully collected SDoH survey data from families regardless of language (including English, Spanish, French, Russian, and Portuguese) utilizing an equity-based approach that allowed survey administration with an appropriate interpreter.

Adverse SDoH are highly prevalent within the US population, with poverty as a key example. Nearly one in six US children live in households that meet the federal definition of income poverty,[14] and poverty is associated with higher rates of relapse, lower overall survival, and inferior patient- and parent-reported outcomes.[2,8,15,16] Given that the financial toxicity of cancer therapy—including economic bur-

dens of travel to and lodging near treating institutions, out-of-pocket medical expenses, and foregone parental income due to treatment-related work disruptions—can cause or exacerbate financial hardship for families,[13,17,18]longitudinal assessment of SDoH over the course of cancer therapy is critical, and feasible as demonstrated by low attrition rates in our study.

These feasibility data directly challenge the narratives that patients are hesitant to share sensitive sociodemographic/socioeconomic information in a clinical-trial context, and that patient-reported SDoH data collection is overly burdensome to sites or participants. Pediatric oncology has embraced the systematic collection of identified biological risk factors for outcome even absent effective drug interventions, in order to inform future interventional research. Vital next steps include integration of SDoH data collection in cooperative group trials alongside collection of biological risk factors, and development and evaluation of trial-embedded health-equity interventions.[19] This effort will require institutional and payor-level commitment to funding scalable social-needs care delivery models.

Limitations of this study include demonstration of feasibility within a small (8-center) consortium with sites limited to the US East Coast and Canada. Evaluation of similar trial-embedded SDoH collection is ongoing in Children's Oncology Group trials across >180 sites. As detailed sociodemographic data are not routinely collected in trial case-report forms, we are unable to determine whether SDoH study non-participants differ from participants on the basis of family income, insurance status, or other SDoH. Finally, this study design utilized an opt-in approach at time of trial consent given lack of feasibility data regarding collection of SDoH in a trial setting. While we observed no differences between participants and non-participants in our study, this methodological approach reinforces the preconception that these data are not important to families and may lead to bias in data collection. Future studies must integrate SDoH data collection as a required component of clinical trials based on evidence of salience to child outcomes and feasibility of collection.

Achieving health equity in disease outcomes is paramount and cannot be accomplished in the absence of SDoH data to guide design and evaluation of interventions. SDoH data collection must become standard practice within oncology clinical trials, alongside trial-embedded health equity interventions to ameliorate outcome disparities.

Conflict of Interest Statement

The authors declare no conflicts of interest relevant to the subject matter discussed in this manuscript.

Acknowledgements

Preliminary feasibility data were presented at the 2019 American Society of Pediatric Hematology/Oncology Conference in New Orleans, LA. Dr. Zheng was supported by an American Society of Hematology HONORS Award. Dr. Bona is supported by the National Cancer Institute at the National Institutes of Health grant number K07CA211847.

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Figure Title and Legend

FIGURE 1 Flow diagram for SDoH study. Flow diagram showing participant flow through each stage of the opt-in embedded SDoH study (eligibility, consent, completion of baseline survey, longitudinal survey completion, evaluable data). For reported percentages, the denominator represents those who are eligible for survey completion and have passed the window for that timepoint of survey administration.

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FIGURE 1 SDoH Study Flow Diagram