

## Addressing Social Determinants of Health: Now Is the Time

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Social determinants of health (SDOH)—the conditions in the places where people live, learn, work, and play—are associated with profound inequities in cancer incidence, care delivery, and outcomes—including stark disparities in survival (1). In 2021, the National Cancer Policy Forum of the National Academies of Science, Engineering, and Medicine sponsored a webinar series to highlight the associations between SDOH and cancer outcomes. In this issue of the Journal, united commentaries summarize the evidence on 3 adverse SDOH—unmet basic resource needs of food (2), housing (3), and transportation (4)—among individuals with cancer and the associations of these material hardships with cancer outcomes. Together, they paint a distressing portrait of cancer care in the United States. More than 1 in 5 US patients with cancer struggles to meet at least 1 of these basic needs, and estimates are much higher for patients from historically marginalized populations, including those of Black race, those of Hispanic ethnicity, and those living in poverty (2–5). Material hardships are associated with delays in cancer diagnosis and initiation of cancer-directed therapy, greater distress and financial toxicity, and a higher risk of relapse and death (1–3).

The authors of these commentaries (1–3) unite in a call to action to address adverse SDOH as an integrated part of cancer care with a powerful message: food, housing, and transportation insecurity are associated with cancer outcome disparities and they are modifiable. Unmet basic needs are states, not traits, “treatable facets of human health” (2) identifiable with systematic, longitudinal screening across the cancer care continuum and amenable to interventions at the community, health system, and policy levels.

The challenge, however, is that despite clear and consistent evidence of stark disparities in cancer care delivery and outcomes for historically marginalized patients, almost no action has been taken to systematically address inequities. Oncologists care for patients at their most vulnerable and witness the seemingly insurmountable challenges that many patients face, including inflexible work hours, financial burdens of prescription copays, and persistent anxiety of unstable housing or

transportation. They see SDOH affect diagnosis, treatment, and outcomes for the non-English speaking mother who arrives an hour late due to transportation challenges; the father living in a congregate shelter who is unlikely to choose the clinical trial and its 10 additional appointments; the child living in poverty whose parents enroll them on a front-line chemotherapy trial yet who remains more likely to relapse. Oncologists observe and are distressed by inequities but perceive SDOH as immutable drivers of disparities that are beyond their control. Consequently, the field of oncology has not recognized SDOH as fitting into the framework of investigation and intervention that underlies persistent advancement in cancer discovery and outcomes.

Precision medicine, “the tailoring of medical treatment to the individual characteristics of each patient,” (6,7) has driven steady progress in the diagnosis and treatment of cancer. Advances in genomics, proteomics, metabolomics, and bioinformatics underlie a rapidly expanding portfolio of immunotherapies and targeted drugs that are changing oncology treatment and improving outcomes. Absent from this paradigm of discovery has been consideration of nonbiological factors, including SDOH, to identify “subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment” (6). This is at least in part due to historic biases in the conduct of cancer research. Clinical trials, which produce evidence forming the bedrock of standard-of-care cancer therapy, have never systematically measured SDOH. In fact, in the last decade, only 63% of oncology drug trials even reported race, a proxy for exposure to adverse SDOH due to centuries of structural racism (8). Yet clinical trial data are the language oncologists speak. Trial data define risk criteria based on clinical, tumor genomic, and response-based criteria. Trial data define toxicity profiles and risk of adverse events. Trial data define prognostic information—life extension, cure, quality-of-life. Food insecurity, housing insecurity, and transportation insecurity are not covariates in trial data analyses. Thus, SDOH are absent from the oncology conceptual framework of cancer risk and responsiveness to treatment. But they do not have to be. Raber (2), Fan (3),

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Graboyes (4), and colleagues lay out a stepwise process for actively integrating SDOH into the existing framework of cancer discovery and care, including 1) systematic measurement of SDOH, 2) development and evaluation of interventions to directly target SDOH, and 3) concurrent policy reform to sustain SDOH-targeted interventions for longitudinal impact.

Which begs a thought experiment. What if oncologists were to treat SDOH just as they would a novel tumor gene mutation? What if the fierce optimism of oncologists, who believe there is no such thing as “undruggable,” were to be extended to social risk? What if the fact that SDOH are modifiable were internalized; for example, acknowledging that food insecurity can be ameliorated with steady access to food? What if decades of collaborative approaches to cancer research—bench to bedside, cooperative group clinical trials—were extrapolated to incorporate SDOH as novel targets for interventions to improve outcomes? In this experiment, oncologists could apply a well-established recipe that has steadily improved cancer outcomes over the last half-century directly to SDOH. First, prospectively measure the “risk mutation” in future clinical trials to ensure retrospective evidence of risk is recapitulated. Second, investigate the mechanisms by which that “mutation” confers excess risk in the laboratory. Finally, develop “drugs” to treat it—beginning with readily available nonspecific approaches and eventually introducing targeted agents to mitigate the excess risk the mutation confers. This approach is highly successful and one that can be directly applied to SDOH in the cancer context.

One drug will not cure all cancers, and most cancers require multi-modal therapy; SDOH are no different. Reducing cancer disparities will require a portfolio of multi-level health equity interventions—alone and in combination—to address modifiable SDOH, such as food, transportation, and housing insecurity. Just like drugs, these interventions will require the equivalent of an early-phase trial pipeline to evaluate adverse events and determine the proper dose and duration of intervention prior to efficacy evaluation. Unlike drugs, they will require a priori consideration of potential for scale, policy implications, and engagement of payors to sustain long-term impact. The National Cancer Institute has declared a commitment to improving health equity in cancer and supporting the science necessary to do so. Next steps in achieving that goal (1-3) should build directly on the existing successful models of cancer research in 3 ways.

First, systematic SDOH data must be collected across the cancer continuum, leveraging already published SDOH measures. There is no single perfect measure of SDOH, nor is there a validated social risk score in oncology. Perseverating over this methodological shortcoming will not advance health equity intervention in the next 5 years; collecting data will. Oncologists are no strangers to evolving methodologies that change measurement strategies—consider iterative leukemia trials that have evaluated minimal-residual disease first by Polymerase Chain Reaction (PCR) and flow cytometry, now by next generation sequencing. Evaluation of SDOH among patients with cancer is feasible and acceptable to patients utilizing existing measures. This data collection must be immediately integrated into standard clinical practice, clinical trial case report forms, and sociodemographic banking studies to ensure SDOH are universally available for analysis.

Second, health equity interventions should be developed and tested following the model of successful early-phase oncology drug consortia. This approach will facilitate the rapid development of an intervention portfolio for efficacy evaluations across cancer types and phases of the cancer care continuum. Health equity intervention development will benefit from

organized multidisciplinary teams—including oncologists, nurses, social workers, patients, community organizations, economists, and policy makers, among others—generating a pipeline of creative health-care delivery and supportive care interventions. Leveraging a multicenter trial infrastructure, these intervention concepts can first be pretested and refined using mixed methodology in specific patient populations and then evaluated for feasibility prior to large-scale randomized controlled trials of efficacy. This will require commitment by both governmental organizations (National Institutes of Health) and foundations to support a health equity trial infrastructure.

Finally, policy-level advocacy is needed to address root causes of adverse SDOH and sustain novel health-care delivery interventions that prove effective. Unlike drugs, which are covered by health insurance once proven effective, existing policies pose immediate barriers to the development, evaluation, and sustainability of interventions targeting SDOH. As one example, interventions integrating cash or in-kind resources to address basic needs such as food insecurity face barriers of cliff effects and disenrollment of patients from means-tested programs (eg, the Supplemental Nutrition Assistance Program) as well as hospital concerns regarding inducement regulations. Such policy barriers to novel interventions are antithetical to the advancement of cancer treatment. Food, housing, and transportation insecurity are associated with inferior cancer outcomes; therefore, oncologists are exactly the right stakeholders to ensure interventions to address these risk factors are feasible and scalable (9).

Food, housing, and transportation insecurity are highly prevalent, associated with inferior cancer outcomes across diseases, and modifiable. If these unmet needs were tumor mutations, the race to unravel their mechanisms of treatment resistance and drug them would be long since begun. The time is now to investigate and intervene on these drivers of outcome with the same rigor and optimism with which oncology tackles tumor mutations.

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