Integrating Social Determinants of Health Into Clinical Trials: Feasibility Assessment and Early Results

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INTRODUCTION

- The design of clinical trials plays a pivotal role in informing the efficacy and safety of healthcare interventions. However, traditional clinical trial design may inadvertently overlook the complex socioeconomic factors, known as social determinants of health (SDOH), that affect health outcomes of real-world patient cohorts.[1]
- Industry-sponsored clinical trials offer an opportunity to conveniently collect and assess SDOH data in a way that is neither burdensome to the patient nor resource intensive for industry sponsors. This can help elucidate important patterns in SDOH and how they relate to health outcomes.
- External stakeholders have also been calling for better collection of SDOH in clinical trials.
  - In 2020, the American Medical Association approved a policy to collect information on genetic ancestry or zip code to better understand the impact of SDOH on health outcomes.[2]
  - NIH also recently launched their SDOH PhenX toolkit (https://nimhd.nih.gov/resources/phenx/)

OBJECTIVE

- To outline the process of developing an SDOH questionnaire to support the integration of SDOH data collection into clinical trials.
- To present an initial assessment of the feasibility of incorporating the SDOH questionnaire into a clinical trial.
- To describe the utility of incorporating the SDOH questionnaire into a clinical trial.

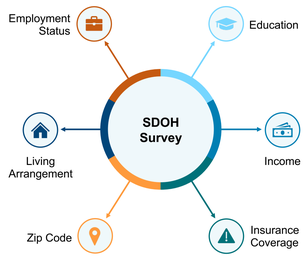
METHODS

Study Design

- This prospective pilot study used a simple questionnaire measuring U.S.-based SDOH to capture important patient and area-level data, such as education, income, employment status, marital status, insurance status, and 5-digit zip code of home residence (**Figure 1**).
  - The questionnaire was only for United States (US)-based enrollees.
  - Data were collected with electronic patient-reported outcome questionnaires.
  - Completion of the questionnaire was optional.
  - Enrollees could choose to skip any questions.
- The 5-digit zip code was linked to trial participant scores on the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry Social Vulnerability Index (SVI), a validated tool that uses 16 US census variables to gather insight on communities that are vulnerable.
  - The SVI is a composite measure of area-level vulnerability based on 16 demographic characteristics collected in the American Community Survey.
  - Respondents are assessed for vulnerability across four themes—household characteristics, socioeconomic status, racial and ethnic minority status, and housing/transportation.
  - The SVI score, ranging from 0 to 1 and indicating greater vulnerability with higher values, ranks areas from least to most vulnerable.
  - Zip code linkage between clinical trial patients and SVI score was performed to provide deeper insights into the socioeconomic factors of where patients who took the SDOH questionnaire are residing.

METHODS (continued)

Figure 1. Patient Factors Comprising the SDOH Questionnaire



SDOH, social determinants of health

- To demonstrate the SDOH questionnaire's utility and provide data analysis guidance, the study authors examined the relationship between collected SDOH variables and patients' health-related quality of life, measured by the EuroQol-5 Dimension (EQ-5D™) at baseline.
  - The EQ-5D assesses quality of life across 5 dimensions.
  - The 5 dimensions on the EQ-5D are mobility, self-care, usual activities, pain and discomfort, and anxiety and depression.
- The SDOH questionnaire was deployed in 3 clinical trials after going through legal and privacy reviews. These trials were:
  - evERA Breast Cancer (breast cancer; (NCT05306340).
  - Kirros (hepatocellular carcinoma; NCT06096779).
  - WeSMA (spinal muscular atrophy; NCT05232929).
- A sample of the evERA Breast Cancer data are presented here.
  - evERA is an ongoing, phase 3, randomized, open-label, multicenter study that will evaluate the efficacy and safety of giredestrant plus everolimus vs physician's choice of endocrine therapy plus everolimus in participants with estrogen receptor–positive, human epidermal growth factor receptor 2–negative locally advanced or metastatic breast cancer.

Development and Launch of the SDOH Questionnaire

- A Work Product Team—comprised of members from Genentech's Medical Network, Evidence for Access team, Clinical Operations, privacy team, Chief Diversity Office, and Legal Department—was gathered to develop the SDOH questionnaire.

STATISTICAL ANALYSES

- Descriptive statistics were used to present the results.

OUTCOMES

- Qualitatively describe the feasibility of incorporating the SDOH questionnaire into the evERA Breast Cancer trial
- evERA Breast Cancer patients' quality of life, as measured by EQ5D at baseline to showcase the utility of incorporating SDOH into clinical trials

RESULTS

Feasibility of Incorporating SDOH Into Clinical Trials

- At the time of this analysis, 100 enrolled evERA Breast Cancer participants completed the SDOH questionnaire. The response rate for the SDOH questionnaire was 83%.
- The complete response for all variables was 100%, except for income (95%) and 5-digit zip code (98%).

Results From Incorporating SDOH Into Clinical Trials

- Characteristics of patients enrolled in evERA Breast Cancer who completed the SDOH questionnaire (N=100) are shown in **Table 1**.
- Compared with the US population, most patients (52%) from the evERA Breast Cancer trial were located in regions that fell within the top 25% of the SVI, indicating very high vulnerability levels. (See QR code for definitions of low, moderate, high, and very high.) This contrasts with only 25% of the general US population residing in similarly vulnerable areas. This trend is mostly driven by more evERA Breast Cancer patients residing in the top 25% areas characterized by representation of racial and ethnic minorities and areas with very high unmet needs in housing and transportation. (See QR code for data.)
- **Tables 2–6** indicate how evERA Breast Cancer patients who completed the SDOH questionnaire scored on each EQ-5D dimension according to income, education level, employment status, marital status, and insurance status (N=99; although 100 participants completed the SDOH, 1 patient had missing EQ-5D data).
  - A greater percentage of patients in the lowest income group reported severe pain than those with higher income. The higher the income, the less likely patients were to report heightened levels of pain or discomfort (**Table 2**).
  - A greater percentage of patients with an education level of high school or less reported severe pain. The higher the education, the less likely patients were to report heightened levels of pain or discomfort (**Table 3**).
  - A greater proportion of retired patients reported mobility issues compared with other employed or unemployed patients (**Table 4**).
  - A greater proportion of patients who were separated or divorced reported physical limitations and higher levels of pain and discomfort than the other marital status groups (**Table 5**).
  - A greater percentage of patients with private/commercial insurance reported physical independence (i.e., mobility, self-care, and usual activities) compared with the other insurance status groups (**Table 6**).

RESULTS (continued)

Table 1. SDOH Variables Among evERA Breast Cancer Trial Participants Who Completed the SDOH Questionnaire

SDOH Variable		N (%)
Education Level (N=100)	High school or less	29 (29.0%)
	Some college	27 (27.0%)
	Graduated from college	24 (24.0%)
	Postgraduate	20 (20.0%)
Income Level (N = 95)	<$35,000	24 (25.3%)
	$35,000–$74,999	28 (29.5%)
	$75,000–$99,999	13 (13.7%)
	$100,000+	30 (31.6%)
Employment Status Before Diagnosis (N = 100)	Full time	41 (41.0%)
	Part time, unemployed, or self-employed	28 (28.0%)
	Retired	31 (31.0%)
Marital Status (N = 100)	Single (never married)	14 (14.0%)
	Married or domestic partner	58 (58.0%)
	Separated or divorced	18 (18.0%)
	Widowed	10 (10.0%)
Health Insurance Status (N = 100)	Uninsured, Medicaid, VA, or other	14 (14.0%)
	Private or commercial	45 (45.0%)
	Medicare	41 (41.0%)

SDOH, social determinants of health; VA, Veterans Affairs.

Table 2. EQ-5D Scores Among Patients Completing the SDOH Questionnaire, by Income

EQ-5D Dimension	<$35,000 (N = 23)	$35,000–$74,999 (N = 28)	$75,000–$99,999 (N = 13)	$100,000+ (N = 30)
M: No problems walking	14 (61%)	19 (68%)	9 (69%)	20 (67%)
M: Slight problems walking	5 (22%)	7 (25%)	2 (15%)	5 (17%)
M: Moderate/severe/unable to walk	4 (17%)	2 (7%)	2 (15%)	5 (17%)
SC: No problems washing or dressing	18 (78%)	25 (89%)	12 (92%)	26 (87%)
SC: Slight/moderate/severe problems washing or dressing	5 (22%)	3 (11%)	1 (8%)	4 (13%)
UA: No problems doing usual activities	13 (57%)	17 (61%)	10 (77%)	18 (60%)
UA: Slight problems doing usual activities	4 (17%)	7 (25%)	1 (8%)	9 (30%)
UA: Moderate/severe/unable to do usual activities	6 (26%)	4 (14%)	2 (15%)	3 (10%)
PD: No pain or discomfort	7 (30%)	8 (29%)	3 (23%)	11 (37%)
PD: Slight pain or discomfort	6 (26%)	10 (36%)	8 (62%)	14 (47%)
PD: Moderate/severe/extreme pain or discomfort	10 (43%)	10 (36%)	2 (15%)	5 (17%)
AD: Not anxious or depressed	11 (48%)	13 (46%)	8 (62%)	9 (30%)
AD: Slightly anxious or depressed	6 (26%)	13 (46%)	2 (15%)	16 (53%)
AD: Moderately/severely/extremely anxious or depressed	6 (26%)	2 (7%)	3 (23%)	5 (17%)

AD, Anxiety and Depression Dimension; EQ-5D, EuroQol-5 Dimension; M, Mobility Dimension; PD, Pain and Discomfort Dimension; SC, Self-Care Dimension; UA, Usual Activities Dimension.

Table 3. EQ-5D Scores Among Patients Completing the SDOH Questionnaire, by Education Level

EQ-5D Dimension	High School or Less (N = 28)	Some College (N = 27)	Graduated From College (N = 24)	Postgraduate (N = 20)
M: No problems walking	17 (61%)	19 (70%)	17 (71%)	11 (55%)
M: Slight problems walking	7 (25%)	3 (11%)	5 (21%)	6 (30%)
M: Moderate/severe/unable to walk	4 (14%)	5 (19%)	2 (8%)	3 (15%)
SC: No problems washing or dressing	22 (79%)	24 (89%)	22 (92%)	17 (85%)
SC: Slight/moderate/severe problems washing or dressing	6 (21%)	3 (11%)	2 (8%)	3 (15%)
UA: No problems doing usual activities	15 (54%)	18 (67%)	16 (67%)	12 (60%)
UA: Slight problems doing usual activities	6 (21%)	4 (15%)	4 (17%)	8 (40%)
UA: Moderate/severe/unable to do usual activities	7 (25%)	5 (19%)	4 (17%)	0 (0%)
PD: No pain or discomfort	11 (39%)	6 (22%)	7 (29%)	7 (35%)
PD: Slight pain or discomfort	5 (18%)	13 (48%)	11 (46%)	11 (55%)
PD: Moderate/severe/extreme pain or discomfort	12 (43%)	8 (30%)	6 (25%)	2 (10%)
AD: Not anxious or depressed	14 (50%)	10 (37%)	10 (42%)	9 (45%)
AD: Slightly anxious or depressed	11 (39%)	11 (41%)	8 (33%)	8 (40%)
AD: Moderately/severely/extremely anxious or depressed	3 (11%)	6 (22%)	6 (25%)	3 (15%)

AD, Anxiety and Depression Dimension; EQ-5D, EuroQol-5 Dimension; M, Mobility Dimension; PD, Pain and Discomfort Dimension; SC, Self-Care Dimension; UA, Usual Activities Dimension.

Table 4. EQ-5D Scores Among Patients Completing the SDOH Questionnaire, by Employment Status

EQ-5D Dimension	Full-time Employed (N = 41)	Part-time Employed, Unemployed, or Self-employed (N = 27)	Retired (N = 31)
M: No problems walking	28 (68.3%)	19 (70.4%)	17 (54.8%)
M: Slight problems walking	8 (19.5%)	6 (22.2%)	7 (22.6%)
M: Moderate/severe/unable to walk	5 (12.2%)	2 (7.4%)	7 (22.6%)
SC: No problems washing or dressing	35 (85.4%)	23 (85.2%)	27 (87.1%)
SC: Slight/moderate/severe problems washing or dressing	6 (14.6%)	4 (14.8%)	4 (12.9%)
UA: No problems doing usual activities	25 (61.0%)	19 (70.4%)	17 (54.8%)
UA: Slight problems doing usual activities	9 (22.0%)	7 (25.9%)	6 (19.4%)
UA: Moderate/severe/unable to do usual activities	7 (17.1%)	1 (3.7%)	8 (25.8%)
PD: No pain or discomfort	14 (34.1%)	9 (33.3%)	8 (25.8%)
PD: Slight pain or discomfort	13 (31.7%)	12 (44.4%)	15 (48.4%)
PD: Moderate/severe/extreme pain or discomfort	14 (34.1%)	6 (22.2%)	8 (25.8%)
AD: Not anxious or depressed	18 (43.9%)	15 (55.6%)	10 (32.3%)
AD: Slightly anxious or depressed	14 (34.1%)	10 (37.0%)	14 (45.2%)
AD: Moderately/severely/extremely anxious or depressed	9 (22.0%)	2 (7.4%)	7 (22.6%)

AD, Anxiety and Depression Dimension; EQ-5D, EuroQol-5 Dimension; M, Mobility Dimension; PD, Pain and Discomfort Dimension; SC, Self-Care Dimension; UA, Usual Activities Dimension.

Table 5. EQ-5D Scores Among Patients Completing the SDOH Questionnaire, by Marital Status

EQ-5D Dimension	Single (Never Married) (N = 13)	Married or Domestic Partner (N = 58)	Separated or Divorced (N = 18)	Widowed (N = 10)
M: No problems walking	9 (69.2%)	39 (67.2%)	9 (50.0%)	7 (70.0%)
M: Slight problems walking	1 (7.7%)	11 (19.0%)	8 (44.4%)	1 (10.0%)
M: Moderate/severe/unable to walk	3 (23.1%)	8 (13.8%)	1 (5.6%)	2 (20.0%)
SC: No problems washing or dressing	10 (76.9%)	51 (87.9%)	14 (77.8%)	10 (100.0%)
SC: Slight/moderate/severe problems washing or dressing	3 (23.1%)	7 (12.1%)	4 (22.2%)	0 (0.0%)
UA: No problems doing usual activities	9 (69.2%)	36 (62.1%)	8 (44.4%)	8 (80.0%)
UA: Slight problems doing usual activities	2 (15.4%)	14 (24.1%)	5 (27.8%)	1 (10.0%)
UA: Moderate/severe/unable to do usual activities	2 (15.4%)	8 (13.8%)	5 (27.8%)	1 (10.0%)
PD: No pain or discomfort	5 (38.5%)	16 (27.6%)	4 (22.2%)	6 (60.0%)
PD: Slight pain or discomfort	5 (38.5%)	30 (51.7%)	4 (22.2%)	1 (10.0%)
PD: Moderate/severe/extreme pain or discomfort	3 (23.1%)	12 (20.7%)	10 (55.6%)	3 (30.0%)
AD: Not anxious or depressed	9 (69.2%)	21 (36.2%)	9 (50.0%)	4 (40.0%)
AD: Slightly anxious or depressed	2 (15.4%)	26 (44.8%)	5 (27.8%)	5 (50.0%)
AD: Moderately/severely/extremely anxious or depressed	2 (15.4%)	11 (19.0%)	4 (22.2%)	1 (10.0%)

AD, Anxiety and Depression Dimension; EQ-5D, EuroQol-5 Dimension; M, Mobility Dimension; PD, Pain and Discomfort Dimension; SC, Self-Care Dimension; UA, Usual Activities Dimension.

Table 6. EQ-5D Scores Among Patients Completing the SDOH Questionnaire, by Insurance Status

EQ-5D Dimension	Uninsured, Medicaid, VA, or Other (N = 13)	Private or Commercial (N = 45)	Medicare (N = 41)
M: No problems walking	6 (46.2%)	35 (77.8%)	23 (56.1%)
M: Slight problems walking	5 (38.5%)	8 (17.8%)	8 (19.5%)
M: Moderate/severe/unable to walk	2 (15.4%)	2 (4.4%)	10 (24.4%)
SC: No problems washing or dressing	9 (69.2%)	42 (93.3%)	34 (82.9%)
SC: Slight/moderate/severe problems washing or dressing	4 (30.8%)	3 (6.7%)	7 (17.1%)
UA: No problems doing usual activities	5 (38.5%)	33 (73.3%)	23 (56.1%)
UA: Slight problems doing usual activities	5 (38.5%)	8 (17.8%)	9 (22.0%)
UA: Moderate/severe/unable to do usual activities	3 (23.1%)	4 (8.9%)	9 (22.0%)
PD: No pain or discomfort	3 (23.1%)	17 (37.8%)	11 (26.8%)
PD: Slight pain or discomfort	4 (30.8%)	20 (44.4%)	16 (39.0%)
PD: Moderate/severe/extreme pain or discomfort	6 (46.2%)	8 (17.8%)	14 (34.1%)
AD: Not anxious or depressed	8 (61.5%)	17 (37.8%)	18 (43.9%)
AD: Slightly anxious or depressed	4 (30.8%)	17 (37.8%)	17 (41.5%)
AD: Moderately/severely/extremely anxious or depressed	1 (7.7%)	11 (24.4%)	6 (14.6%)

AD, Anxiety and Depression Dimension; EQ-5D, EuroQol-5 Dimension; M, Mobility Dimension; PD, Pain and Discomfort Dimension; SC, Self-Care Dimension; UA, Usual Activities Dimension; VA, Veterans Affairs.

LIMITATIONS

This study measured the relationship between SDOH and patients' quality of life at baseline. Further work is needed to investigate if such differences persist over treatment course and/or if there are observable differences in clinical outcomes by SDOH.

CONCLUSIONS

- Collecting SDOH data in clinical trials provides an opportunity to better understand how key SDOH are driving clinical outcomes, which can then inform a more efficient allocation of resources and efforts to address SDOH barriers to improved health outcomes.
- As consistent with the literature, patients' quality of life varied by SDOH, further emphasizing the importance of collecting SDOH in clinical trials.
- By collecting the 5-digit zip code, we gained valuable insights into several key factors:
  - It enabled us to better understand and identify barriers to enrolling a diverse population.
  - It provided us with information on socioeconomic status, enabling us to assess the economic conditions of our patients' communities and how they may relate to clinical outcomes.
- Collecting SDOH data alongside clinical trials is crucial and hopefully will eventually provide a better understanding of key SDOH that drive negative clinical outcomes. This could allow resources/efforts to be better focused towards addressing those populations and SDOH barriers to improved health outcomes.
- Collection of SDOH data will allow us to:
  - Explore the relationship between SDOH and clinical and humanistic outcomes (e.g., progression-free survival, overall survival, health-related quality of life).

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