Social Determinants of Health in U.S. Counties Where Guideline-Influencing Diabetes Studies Were Conducted

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Social determinants of health (SDOH) strongly influence the development and progression of diabetes (1). As SDOH are infrequently measured in diabetes clinical trials, little is known about how these measures, on both county and individual levels, influence the findings of clinical trials. We sought to compare SDOH in U.S. counties used versus not used for clinical trial sites in guideline-changing studies evaluating pharmacologic treatment for glycemic control.

We screened all studies cited in the "Pharmacologic Approaches to Glycemic Treatment" section of the *Standards of Medical Care in Diabetes—2021* guideline published by the American Diabetes Association (2). Studies had to meet the following criteria to be included in the analysis: *1*) be a randomized controlled trial, *2*) include one or more study sites in the U.S., *3*) evaluate a pharmacologic intervention for glycemic treatment of type 1 or type 2 diabetes, and *4*) report study site location information on ClinicalTrials.gov. Original articles included in systematic reviews or meta-analyses cited by the guideline were also screened, and individual studies were included if they met the screening criteria. Data on the location of U.S. clinical trial sites for each study were ascertained from the study's ClinicalTrials.gov site. The most recent data (which included data collected between 2015 and 2019) on county-level SDOH for all U.S. counties were obtained from the Centers for Disease Control and Prevention data sets (3).

One hundred fifty-two clinical trials evaluating pharmacologic treatments for glycemic control were identified for inclusion. Included studies had clinical trial sites in 612 unique U.S. counties. The median number of sites per study was 43. Over one-half (n = 91, 59%) of the studies were published in 2015 or later, with 38 (25%) published between 2005 and 2010. Twenty-four (16%) were published prior to 2005. Approximately 82% of included studies were multinational. The median number of individuals per study was 529. Most trials included patients with type 2 diabetes (86%) and evaluated first- or second-line therapies for type 2 diabetes (66%).

SDOH in U.S. counties used versus not used for clinical trial sites are shown in Table 1. The proportion of households falling below the federal poverty line was lower in counties that were used by included studies for clinical trial sites compared with counties not used by these studies (9% vs. 10%; $P < 0.001$). When counties were stratified into quartiles according to the proportion of households falling below the federal poverty line, counties used for clinical trial sites were less likely to fall into the highest quartile (17% vs. 27%; $P < 0.001$). Similar trends were observed for markers of education, health insurance, and housing.

We evaluated SDOH in 152 guideline-changing studies of pharmacologic treatment for glycemic control. Measures of SDOH evaluated in this study were significantly different in counties that were not used for clinical trial sites compared with those that were used for sites.

County-level SDOH have been shown to impact outcomes in clinical trials (4). A study utilizing data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) divided study sites into income quintiles according to county-level median household income. Compared with participants enrolled at sites in the highest income quintile, participants enrolled at sites in the lowest income quintile were less likely to reach blood pressure goals (odds ratio 0.48; 95% CI 0.37–0.63) and more likely to experience all-cause mortality (hazard ratio 1.25; 95% CI 1.10–1.41). Findings from the analysis of the ALLHAT also suggest that individuals from low-income areas were underrepresented in the trial. Only ∼8% of participants were enrolled at sites that fell into the lowest income quintile, while ∼38% fell into the highest income quintile. Our findings were similar. When counties were stratified according to the percentage of households falling below the poverty line, only ∼17% of counties used by clinical trial sites were in the highest quartile. These findings suggest that county-level SDOH measures should be considered in the planning and execution of clinical trial recruitment.

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Table 1—SDOH in counties used versus not used by clinical trials*†

Parameter	U.S. counties used in clinical trials, *N* = 612	U.S. counties not used in clinical trials, *N* = 2,530	*P*
Below federal poverty line			
Median (IQR) percentage of households	9.0 (6.6–11.9)	10.0 (7.1–13.8)	<0.001
Number (%) of counties in highest quartile	102 (16.7)	689 (27.2)	<0.001
No high school diploma			
Median (IQR) percentage of population	10.4 (7.9–13.8)	12.2 (8.7–17.4)	<0.001
Number (%) of counties in highest quartile	83 (13.6)	704 (27.8)	<0.001
Uninsured			
Median (IQR) percentage of population	8.1 (5.5–10.9)	8.9 (5.9–12.6)	<0.001
Number (%) of counties in highest quartile	103 (16.8)	695 (27.5)	<0.001
Vacant housing units			
Median (IQR) percent	10.4 (7.3–15.4)	18.0 (12.6–25.6)	<0.001
Number (%) of counties in highest quartile	43 (7.0)	746 (29.5)	<0.001

IQR, interquartile range. *Comparisons between U.S. counties used vs. those not used for clinical trial sites were made using χ^2 and Mann-Whitney *U* tests. †The following cutoffs were used for the highest quartile: below federal poverty line, 13.3%; no high school diploma, 16.6%; uninsured, 12.0%; vacant housing units, 24.0%.

A limitation of our analysis is that some people may have been recruited to a study site from outside the county, although this is likely rare. Moreover, we used Centers for Disease Control and Prevention county-level data on SDOH from 2015 to 2019. Some included studies were published prior to 2015, and it is possible that measures of SDOH changed in counties over time.

In summary, measures of SDOH evaluated in this study were significantly different in counties that were not used for diabetes clinical trial sites compared with those that were used for sites. County-level SDOH should be considered in the planning and execution of clinical trial recruitment.

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