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Heather F. de Vries McClintock

Douglas J. Wiebe University of Pennsylvania

Alison J. O'Donnell

Knashawn H. Morales University of Pennsylvania

Dylan S. Small University of Pennsylvania

See next page for additional authors

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#### Abstract

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#### Keywords

Administration, Oral, Community Health Services, Diabetes Mellitus, Type 2, Drug Administration Schedule, Female, Humans, Hypoglycemic Agents, Male, Middle Aged, Patient Compliance, Philadelphia, Residence Characteristics, Self Care, Social Environment

#### Disciplines

Business | Community Health and Preventive Medicine | Environmental Public Health | Health Services Administration | Health Services Research | Medical Humanities | Statistics and Probability

#### Author(s)

Heather F. de Vries McClintock, Douglas J. Wiebe, Alison J. O'Donnell, Knashawn H. Morales, Dylan S. Small, and Hillary R. Bogner



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### Neighborhood Social Environment and Patterns of Adherence to Oral Hypoglycemic Agents among Patients with Type 2 Diabetes Mellitus

Heather F. de Vries McClintock, M.S.P.H.<sup>1,2</sup>, Douglas J. Wiebe, Ph.D.<sup>2</sup>, Alison J. O'Donnell, B.A.<sup>1,2</sup>, Knashawn H. Morales, Sc.D.<sup>2,3</sup>, Dylan S. Small, Ph.D.<sup>4</sup>, and Hillary R. Bogner, M.D., M.S.C.E.<sup>1,2</sup>

<sup>1</sup> Department of Family Medicine and Community Health, University of Pennsylvania, Philadelphia, PA, U.S.A.

<sup>2</sup> Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA, U.S.A.

<sup>3</sup> Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA, U.S.A.

<sup>4</sup> Department of Statistics, The Wharton School, The University of Pennsylvania, Philadelphia, PA, U.S.A.

### Abstract

This study examined whether neighborhood social environment was related to patterns of adherence to oral hypoglycemic agents among primary care patients with type 2 diabetes mellitus. Residents in neighborhoods with high social affluence, high residential stability and high neighborhood advantage compared to residents in neighborhoods with one or no high features present, were significantly more likely to have an adherent pattern compared to a nonadherent pattern. Neighborhood social environment may influence patterns of adherence. Reliance on a multi-level contextual framework, extending beyond the individual, to promote diabetic self-management activities may be essential for notable public health improvements.

#### Keywords

primary health care; type 2 diabetes; neighborhood social environment; medication adherence

#### Introduction

Despite the development of effective pharmacological therapy to prevent both macrovascular and microvascular complications and adverse events<sup>1-4</sup> diabetes control remains sub-optimal.<sup>5-7</sup> Poor adherence to recommended regimens is a factor in preventable

**Corresponding Author** Heather F. de Vries McClintock MSPH, Department of Family Medicine and Community Health, The University of Pennsylvania, 3400 Spruce Street, 2 Gates Building, Philadelphia, PA 19104, U.S.A. Phone: 215-746-4181, Fax: 215-662-3591, heather.devries@uphs.upenn.edu.

Trial Registration: clinicaltrials.gov registration number: NCT01098253

morbidity and mortality in diabetic patients.<sup>8,9</sup> While individual characteristics are important contributors to medication adherence, much of the observed variation in adherence rates remains unexplained by these factors.<sup>10-12</sup> Neighborhood environment may shape medication adherence through many factors such as socioeconomic resources, perceptions, expectations and beliefs. Individuals living in the same neighborhood may be more similar to each other than persons living in other neighborhoods because they share common social, economic, systemic, and lifestyle characteristics. Thus there may be common health behaviors that persist over and above individual variation and relate to living environment.<sup>13,14</sup> The assessment of this collective phenomenon is needed to fully elucidate and understand adherence behaviors. However, little empirical knowledge exists about the nature and size of these collective or contextual neighborhood level effects on health behaviors such as medication adherence.<sup>15</sup>

Neighborhood social environment is an important construct in discerning how neighborhood contextual effects influence health behavior.<sup>16</sup> With a movement to examine neighborhood effects beyond the influence of poverty, a focus on social characteristics, organization and culture in relation to behaviors and outcomes has become essential.<sup>17</sup> The concepts of social affluence, neighborhood advantage and residential stability, derived from the work of Sampson et al.,<sup>18-20</sup> have been the subject of much research and have been established as important explanatory factors in understanding the role of neighborhood social environment in health.<sup>21-23</sup> These measures tap into both the influence of poverty as well as social mechanisms and processes hypothesized to link neighborhood environment to health. We seek to understand whether these constructs are related to medication adherence, a critical predictor of prognostic outcomes particularly for patients with diabetes. Our conceptual framework, shown in Figure 1, depicts the key constructs assessed in this study relating key features of the neighborhood social environment to patterns of adherence over time.

Prior work has found that neighborhood residence is associated with medication adherence<sup>13,24,25</sup> and other self-care behaviors,<sup>26-28</sup> even when controlling for individual characteristics. However, these studies have been limited by their cross-sectional designs, reliance on subjective adherence assessments and/or lack of a representative sampling frame due to regional variations in culture, context and available resources. Few identified studies investigated this relationship among diabetic patients, a population for whom the environment may have a particularly salient role. Our work extends current findings by employing a longitudinal study design to examine adherence with medication regimens as assessed by an objective and time-varying measure of adherence among a diverse sample of primary care patients with diabetes. Demonstrating a relationship between features of neighborhood social environment and patterns of adherence to oral hypoglycemic agents will set the stage for interventions targeting resources for persons and neighborhoods most at risk for poor health.

Within a prospective randomized controlled trial we sought to investigate whether indicators of neighborhood social environment (social affluence, neighborhood advantage and residential stability) would be associated with patterns of adherence to oral hypoglycemic agents. Our aim was to examine whether residents in neighborhoods with high social affluence, high neighborhood advantage, and/or high residential stability would be more

Page 3

likely to have a pattern of adherence or increasing adherence over time. We hypothesized that residents in neighborhoods with two or three features present (high social affluence, high neighborhood advantage and high residential stability) would be more likely to have a pattern of adherence or a pattern of increasing adherence than residents in neighborhoods with one or none of these features present. To our knowledge, this is the first investigation to examine social affluence, neighborhood advantage and residential stability in relation to longitudinal patterns of adherence among primary care patients with diabetes.

#### Methods

#### Recruitment

The randomized controlled trial, A Brief Intervention to Improve Adherence through Integrated Management of Type 2 Diabetes Mellitus and Depression Treatment, was designed to assess whether an integrated care intervention in primary care improved glucose control and depressive symptoms in type 2 diabetes mellitus (type 2 DM).<sup>29</sup> In all, 180 patients were recruited from three primary care practices in Philadelphia, Pennsylvania and were randomly assigned to the intervention or usual care. Patients with a diagnosis of type 2 DM and a prescription for an oral hypoglycemic agent within the past year were identified through electronic medical records from April 2010 to April 2011. Patients with an upcoming appointment were approached for additional screening. Eligibility criteria were: 1) aged 30 years and older; 2) a diagnosis of type 2 DM; and 3) a current prescription for an oral hypoglycemic agent. Exclusion criteria were: 1) inability to give informed consent; 2) significant cognitive impairment at baseline (Mini-Mental State Examination (MMSE) <21;<sup>30</sup> 3) residence in a care facility that provides medications on schedule; and 4) unwillingness or inability to use the Medication Event Monitoring System (MEMS). The study protocol was approved by the University of Pennsylvania, Perelman School of Medicine Institutional Review Board. The intervention is described in detail elsewhere.<sup>29</sup>

#### Study Design

The trial was conducted in two phases: the run-in phase and the randomized controlled trial phase. The first phase of this trial consisted of a 2-week run-in phase to obtain preintervention adherence data for all patients. Baseline demographics and glycated hemoglobin (HbA<sub>1c</sub>) assays to measure glycemic control were also collected at this time. Phase 2 of the study, where patients were randomized to the integrated care intervention or usual care, commenced after the 2-week run-in phase and occurred over 12 weeks.

#### Intervention

Integrated care managers worked with patients individually in the intervention group to offer education, guideline-based treatment recommendations, and monitor adherence and clinical status in collaboration with physicians. The integrated care manager addressed factors involved in adherence to oral hypoglycemic agents. The patient-level factors resulting in nonadherence included depression, chronic medical conditions, function, cognition, social support, cost of medications, side effects, and past experiences with medications. We chose this multi-faceted approach because education alone has not been found to be effective for improving adherence.<sup>31</sup>

The intervention was presented to patients as a supplement to, rather than a replacement for, existing primary care treatment. Over a three month period participants had three 30-minute in person sessions (baseline, 6 weeks and 12 weeks) and two 15-minute telephone monitoring contacts. Integrated care managers were two research coordinators (one Master's level and one bachelor's level) who administered all intervention activities. The integrated care managers received training on pharmacotherapy for type 2 DM management during weekly clinical sessions with the principal investigator prior to trial initiation.

#### **Usual Care**

Patients in the usual care group underwent the same assessments at the same time points (baseline, 6, and 12 weeks) as the patients in the integrated care intervention. Research assistants conducted all assessments in-person and were blinded to patients' randomization status.

#### Measurement Strategy

**Patient Characteristics**—Potential study patients were screened for cognitive impairment using the MMSE, a short standardized mental status examination widely employed for clinical and research purposes.<sup>32</sup> At baseline, sociodemographic characteristics were assessed using standard questions. Address data was obtained for participants at baseline. Electronic monitoring data obtained from the MEMS Caps were used to measure adherence to oral hypoglycemic agents. Adherence was assessed as the proportion of medication MEMS cap openings in a given week relative to the prescribed doses for the week. Blood glycemic control was assessed at baseline and 12 weeks in accordance with American Diabetes Association Guidelines.<sup>33</sup> The in2it A1C Analyzer provides point of care testing and was used to obtain glycated hemoglobin (HbA<sub>1c</sub>) assays. This device has acceptable precision and agreement in comparison with laboratory services <sup>34</sup>.

Neighborhood Social Environment—Individual patient residential data was geo-coded at the tract level and then was merged with 2010 tract-level Census data. Factor analysis was conducted on 13 variables as done in prior work by Sampson et al.<sup>18-20</sup> and others to assess key constructs of the social environment: social affluence, neighborhood advantage and residential stability.<sup>12,18,21-23,35</sup> Factor analysis examines the nature of the relationships between variables by identifying the smallest number of factors explaining composites of the observed variables. To decrease collinearity between resulting factors we required that variables loaded above 0.55 on a single factor. All 13 variables loaded above 0.55 on single factor resulting in three single composite factors/variables. Conventional diagnostics such as scree plots also confirmed these three identified factors. These factors represented constructs of neighborhood social environment: social affluence, neighborhood advantage, and residential stability. Social affluence was derived from five variables: percent of households with resident/room ratio greater than 1 (factor loading = 0.57), percent of female-headed households (0.84), percent unemployed (0.77), percent of people below the poverty line (0.87), and percent of people receiving public assistance (0.73). Neighborhood advantage was derived from three variables: percent of residents with at least a bachelor's degree (0.87), percent of people in professional occupations (0.75), and percent of people with a

household income greater than \$75,000 (0.67). Finally, residential stability was derived from two variables: the percent of house owners (0.86) and the percent of residents living at the same address over 5 years (0.86). Factor scores for neighborhood social environment (social affluence, neighborhood advantage and residential stability) were dichotomized as high or low based on the sample median.

**Analysis**—This analysis was conducted employing classifications of patients into patterns of adherence to oral hypoglycemic agents, as per our prior work.<sup>36</sup> In brief, we employed general growth curve mixture models (GGCMM)<sup>37-43</sup> to generate estimated posterior probabilities of unobserved class membership for each patient. This seminal approach improves precision by accounting for both intervention effects and baseline covariates on adherence over time. Longitudinal patterns of adherence to oral hypoglycemic agents were created by classifying patients based on the largest posterior probability of membership across the classes. The resulting categorical variable, patterns of adherence to oral hypoglycemic agents (adherent, increasing adherence, and nonadherent), was employed as the dependent variable for this analysis.

Multinomial logistic regression related neighborhood social environment (social affluence, neighborhood advantage and residential stability) to patterns of adherence to oral hypoglycemic agents. Results are presented in the form of odds ratios and 95% confidence intervals. Neighborhood social environment was assessed categorically. Consistent with prior work, the model included terms to adjust for age, ethnicity, gender, educational attainment, financial status, employment, frequency of medication administration, number of medical conditions, cognitive status, practice, baseline HbA<sub>1c</sub>, and intervention condition.<sup>44</sup> We set  $\alpha$  at 0.05, recognizing that tests of statistical significance are approximations that serve as aids to inference. The GGCMM was fitted using Mplus version 7 (Muthén & Muthén) <sup>45</sup> and other analyses were conducted in STATA version 12 for Windows (STATA Corporation, College Station, TX).

#### Results

#### Study sample

The CONSORT flow diagram for the Brief Intervention to Improve Adherence through Integrated Management of Type 2 Diabetes Mellitus and Depression Treatment trial has been published elsewhere.<sup>29</sup> In brief, of 715 patients with type 2 DM identified by electronic medical records, 265 were eligible and were approached and 190 were enrolled (71.7% participation rate). Consent was followed by a 2-week run-in phase in which adherence to medications was assessed. At the 2-week visit, 5 physicians had discontinued the antidepressant, 1 physician discontinued the oral hypoglycemic agent, and 2 patients were lost to follow-up. In all, 182 patients were randomized to the integrated care intervention or usual care. After randomization at the 2-week meeting, 2 patients in the integrated care intervention were lost to follow-up leaving 180 patients who completed the final study visit for our study sample.

In all, 179 patients had complete data on residential address and covariates of interest and were included in the present analysis. The mean age of our sample was 57.4 years (standard

deviation (s.d.) 9.5 years). One hundred and twenty-one (67.6%) of the patients were women. The self-identified ethnicity of patients was 65 white (36.3%), 101 African-American (56.4%), 7 Hispanic (3.9%), and 6 (3.4%) who self-identified as 'other.' In all, 69 patients (38.6%) were married, and 29 patients (16.2%) had less than a high school education. The mean number of medical conditions was 7.3 (s.d. 2.4) and the mean MMSE score was 28.2 (s.d. 2.3). Social affluence, residential stability, and neighborhood advantage stratified by median factor score as High and Low are depicted in Table 1.

## Neighborhood social environment (residential stability, social affluence, and neighborhood advantage) and patterns of adherence to oral hypoglycemic agents

We examined the relationship between composite neighborhood characteristics and patterns of adherence to oral hypoglycemic agents (Table 2). The column of Table 2 labeled Adherent vs. Nonadherent provides odds ratios estimating the association of neighborhood social environment with patterns of adherence, comparing the adherent pattern to the nonadherent pattern. Compared to residents in neighborhoods with one or no high features present, residents in neighborhoods with high social affluence, high residential stability, and high neighborhood advantage were more likely to have an adherent pattern compared to a nonadherent pattern (adjusted odd ratio (OR)= 8.48, 95% confidence interval (CI) [1.71, 42.02]). The column of Table 2 labeled Increasing Adherence vs. Nonadherent compares the increasing adherence pattern to the nonadherent pattern. Compared to residents in neighborhoods with one or no high features present, residents in neighborhoods with one or no high features present, residents in neighborhoods with one or no high features present, residents in neighborhoods with one or no high features present, residents in neighborhoods with high social affluence, high residential stability, and high neighborhood advantage were more likely to have an increasing adherence pattern compared to a nonadherent pattern (adjusted OR= 12.91, 95% CI [2.20, 75.80]). There was not a significant relationship between neighborhoods with two features present and patterns of adherence.

#### Discussion

The principal finding of this study is that residents in neighborhoods with high social affluence, high residential stability, and high neighborhood advantage were much more likely to have an adherent pattern compared to a nonadherent pattern. Similarly, residents in neighborhoods with high social affluence, high residential stability, and high neighborhood advantage were much more likely to have an increasing adherence pattern compared to a nonadherent pattern. These results provide evidence that features of neighborhood social environment may be important contributors to patterns of adherence to oral hypoglycemic agents, a critical factor in treatment effectiveness and subsequent outcomes.

Before we discuss our findings, the results must be considered in the context of several potential study limitations. First, data was collected from three primary care sites whose patients may not be representative of other primary care practice settings. However, they were similar to other primary care practices in the region in terms of diversity and size. Second, it is important to note that all methods for assessing adherence have limitations. We utilized MEMS caps as our primary measure because they are an objective measure, have a low failure rate,<sup>46</sup> and are more sensitive than other measures.<sup>47</sup> Both groups (intervention and usual care) would experience any influence of MEMS caps on medication adherence

equally. Third, we solely examined the role of neighborhood social environment on behavioral patterns (medication adherence). Future research could incorporate other measures of neighborhood environment (e.g. physical environment: built environment, local food environment) as well as individual factors (physical health, psychosocial stress, and psychosocial resources) and health outcomes in order to delve deeper into the complex interplay of mediating or moderating pathways linking neighborhoods to health across time. Finally, we are constrained by the utilization of an administrative definition of neighborhoods (census tracts), which may not be the most meaningful level of aggregation. It is possible that assessment within a more respondent-derived neighborhood environment.<sup>48</sup>

Despite these limitations, our results are important to consider given that this study is one of the first examine the relationship between neighborhood social environment, as assessed by social affluence, residential stability, and neighborhood advantage, and patterns of adherence. A growing body of evidence has linked indicators of neighborhood social environment, namely measures of socioeconomic status with morbidity and mortality.<sup>49</sup> However, little research has examined more proximal mechanisms to health, health behaviors, which are critical precedents for understanding disease prognosis in diabetes. In our work, we characterize mechanisms shaping the link between neighborhood social environment and health<sup>21,22</sup> demonstrating that the presence of multiple features (high social affluence, high residential stability, and high neighborhood advantage) may be critical in understanding adherence patterns. Our results support evidence that neighborhoods matter and furthermore help to inform and enhance future research on how neighborhoods matter.

While we found that residents in neighborhoods with three high features present were significantly more likely to have a pattern of adherence or a pattern of increasing adherence, we did not find that residents in neighborhoods with two features present were significantly more likely to have a pattern of adherence or a pattern of increasing adherence. This aligns with work demonstrating that accumulation of exposures to multiple contextual factors may explain the health impact of neighborhoods. While the presence of a few features is somewhat influential, the presence of multiple features for extended periods of time is associated with the greatest health impact.<sup>50</sup> Because fewer neighborhood features may have only a modest effect, our study may not have been large enough to provide an adequate test of our hypothesis that residents in neighborhoods with two features present were significantly more likely to have a pattern of adherence or a pattern of increasing adherence than residents in neighborhoods with one or no features present.

Our findings are consistent with the work of Billmek et al. in which nonadherence to medications was examined in relation to neighborhood deprivation among persons with type 2 DM. Billmek and colleagues examined the cross-sectional relationship of neighborhood deprivation, as assessed by the Neighborhood Socioeconomic Status Index comprised of census tract measures, and self-reported adherence. Their findings suggest that social environment as well as related costs may contribute to nonadherence.<sup>24</sup> In our work we enrolled patients who already had filled prescriptions for oral hypoglycemic agents and we adjusted for individual financial status, thus minimizing the influence of cost on adherence

to medication regimens, and supporting evidence that neighborhood social environment and adherence may be linked by factors other than financial pressure. Our work is further delineated from prior work by a focus on features of neighborhood social environment derived from the work of Sampson et al.<sup>18-20</sup> Our findings provide insight into the social mechanisms and process that link neighborhood environment to health. Furthermore, we used an objective measure of adherence, and our use of general growth curve mixture models allowed us to distinguish distinct patterns of adherence over time instead of assessing adherence through proportions at singular point(s) in time with no assessment of variation over time and group classification. Our findings extend prior work by demonstrating that features of the social environment are associated with longitudinal patterns of adherence as assessed by objective measures of medication adherence among primary care patients with type 2 DM.

Our results highlight the significance of features of the social environment in shaping patterns of adherence to oral hypoglycemic agents over time, over and above of the effects of individual characteristics. A framework through which we can characterize the underlying mechanisms relating neighborhood social environment to adherence has been established.<sup>51,52</sup> Following this framework, a lack of social capital and/or cohesion may exist in neighborhoods with low social affluence, advantage, and stability.<sup>53</sup> Such environments may lack a myriad of health promoting social processes such as social control over deviant health-related behavior and attitudes (e.g. over-eating). These environments may promote unhealthy behaviors through social norms,<sup>54</sup> minimal levels of social trust <sup>55</sup> and a lack of a supportive community environment.<sup>16</sup> Furthermore, the character of daily routines, shaped by neighborhood environment (e.g. disorder), dictates the availability of temporal windows to engage in health promoting activities such as medication taking.<sup>56</sup> Such windows may be limited in more compromised neighborhoods. All these processes may be at work in shaping patterns of health behavior over time, particularly when multiple features are present cumulatively over the life course.<sup>57,58</sup>

This study is among the first to suggest that features of neighborhood social environment may influence medication adherence. While the distinct mechanisms for this association require further examination, this study adds to a growing body of evidence that patient's social environment influences behavioral patterns. While such contextual factors play a critical role in shaping health outcomes, they are seldom addressed or incorporated into treatment plans. As a result, patients who receive guideline concordant care may not achieve treatment targets due to factors related to their daily environmental context. Reliance on a multi-level contextual framework, extending beyond the individual, to promote diabetic self-management activities may be essential for effective intervention deployment and notable public health improvements.<sup>59-61</sup> Ongoing efforts to improve access and quality of care should be accompanied by initiatives to integrate the health care systems within community settings. Collaborative networks between healthcare systems and neighborhood communities are needed to foster effective adherence initiatives.

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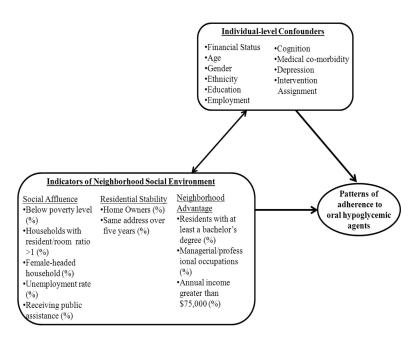
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Note: Patterns of adherence based on Medication Event Monitoring System (MEMS) data.

#### Figure 1.

Proposed conceptual model of indicators of neighborhood social environment and patterns of adherence to oral hypoglycemic agents. This model was adapted from the work of the Translating Research Into Action for Diabetes (TRIAD) study <sup>26</sup> and Carpiano RM <sup>52</sup>

#### Table 1

Social affluence, residential stability, and neighborhood advantage stratified by median factor score (High versus Low).

Neighborhood Indicators	High (n=89)	Low (n=90)
Social Affluence		
Poverty (%), mean (s.d.)	13.52 (1.39)	35.60 (1.22)
Households with resident/room ratio > 1 (%), mean (s.d.)	1.00 (.12)	2.89(.29)
Female-headed households (%), mean (s.d.)	9.87 (.69)	29.71 (.75)
Unemployment rate (%), mean (s.d.)	7.1 (.39)	18.7 (.70)
Receiving public assistance (%), mean (s.d.)	2.22 (.18)	11.03 (.53)
Residential Stability		
House owners (%), mean (s.d.)	60.39 (2.94)	51.77 (1.60)
Same address over 5 years (%), mean (s.d.)	61.49 (1.06)	57.96 (2.06)
Neighborhood Advantage		
Residents with at least a bachelor's degree (%), mean (s.d.)	43.31 (2.21)	11.29 (.79)
Managerial/professional occupations (%), mean (s.d.)	13.85 (.66)	9.2 (.42)
Annual income greater than \$75,000 (%), mean (s.d.)	38.70 (1.95)	12.24 (.81)

Note: s.d=standard deviation. Data obtained from 2010 U.S. Census and all measures are defined in accordance with these guidelines.

#### Table 2

Multinomial logistic regression of neighborhood characteristics and three patterns of adherence (n= 179).

	Adherent vs. Nonadherent OR [95% CI]	Increasing Adherence vs. Non adherence OR [95% CI]
Neighborhood characteristics		
High social affluence, high residential stability, and high neighborhood advantage (n=41)	8.48 <sup>*</sup> [1.71, 42.02]	12.91 <sup>*</sup> [2.20, 75.80]
High social affluence and high neighborhood advantage (n=36)	2.44 [0.67, 8.86]	1.61 [0.35, 7.54]
High residential stability and high neighborhood advantage (n=10)	4.05 [0.28, 57.60]	1.86 [0.12, 28.54]
High social affluence and high residential stability (n=12)	1.78 [0.29, 10.75]	0.50 [0.05, 5.56]
One or fewer high features present: stability, affluence, or advantage $(n=80)$	1.00	1.00

Note: OR = odds ratio; CI = confidence interval

All estimates are adjusted for age, ethnicity, gender, educational attainment, financial status, employment, frequency of medication administration, number of medical conditions, cognitive status, practice, baseline glycated hemoglobin (HbA1c), depression, and intervention condition.

p< .05