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Short Communication

Health selection into neighborhoods among patients enrolled in a clinical trial

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ABSTRACT

Health selection into neighborhoods may contribute to geographic health disparities. We demonstrate the potential for clinical trial data to help clarify the causal role of health on locational attainment. We used data from the 20-year United Kingdom Prospective Diabetes Study (UKPDS) to explore whether random assignment to intensive blood-glucose control therapy, which improved long-term health outcomes after median 10 years follow-up, subsequently affected what neighborhoods patients lived in. We extracted postcode-level deprivation indices for the 2710 surviving participants of UKPDS living in England at study end in 1996/1997. We observed small neighborhood advantages in the intensive versus conventional therapy group, although these differences were not statistically significant. This analysis failed to show conclusive evidence of health selection into neighborhoods, but data suggest the hypothesis may be worthy of exploration in other clinical trials or in a meta-analysis.

Geographic disparities are among the most glaring type of social inequalities in health that epidemiologists observe. For example, life expectancy at birth differs by up to a decade across neighborhoods within New York City, and by up to 20 years in Richmond, Virginia (The Robert Wood Johnson Foundation, 2015). For context, male life expectancy at age 40 differs by 14 years between the richest 1% and poorest 1% of Americans, after accounting for race (Chetty et al., 2016). On average nationwide, nearly seven years separates the highest (Hispanic) and lowest (Black) racial/ethnic group life expectancies that CDC reports (Arias et al., 2017). Geographic disparities are similarly important in the United Kingdom where life expectancy at birth differs by up to 10 years across Local Authority Districts (Office for National Statistics, 2014a), but only by roughly six years between the healthiest and least healthy occupational classes (Office for National Statistics, 2015).

Explanations for striking differences in health across place fall into three broad categories. The first is compositional; income-based, racial/ethnic, and other forms of residential segregation tend to concentrate non-geographic health risks into neighborhoods. In other words, some degree of the association between health and place reflects confounding by prior common causes of both health and residential outcomes. The other two categories refer to causal processes: a) neighborhood effects on health, and b) reverse causation, or "health selection" into neighborhoods. Epidemiologists still struggle to characterize these causal relationships despite the fact that neighborhood differences in health have been studied extensively over the past 20 years (Arcaya et al., 2016; Oakes et al., 2015). Claims of neighborhood effects on health are supported by ample observational research suggesting that place matters for health (Diez Roux, 2007), and, crucially, by the Moving to Opportunity experiment, which provides casual evidence of neighborhood effects on at least some health outcomes (Ludwig et al., 2011). Health selection into neighborhoods, by contrast, is a poorly understood, but substantively important process, that might reinforce links among poor places, poor people, and poor health (Arcaya et al., 2014). Mechanistically, poor health could sap individuals of the energy required to seek better environments, or it might depress intentions to move among those whose health makes them dependent on place-based resources such as transit systems or local health care facilities. Further, previous work has shown that health status affects future income, educational attainment, employment, and wealth (Case et al., 2005; Smith, 2004), any or all of which could serve as mediators on the causal pathway from health to neighborhood outcomes. While a nascent body of literature suggests that health is predictive of subsequent neighborhood characteristics (Arcaya et al., 2015, 2014; Grafova et al., 2014; Green et al., 2015; Jokela, 2014), understanding the causal role of health as a determinant of neighborhood outcomes will require stronger experimental designs. We are not aware of any efforts to exploit random variation in health to test for health selection into neighborhoods.

In this Short Communication, we demonstrate the potential for clinical trial data to help clarify the causal role of health on locational attainment. We used data from the 20-year United Kingdom Prospective Diabetes Study (UKPDS) to explore whether random assignment to

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intensive blood-glucose control therapy, which improved long-term health outcomes, subsequently affected what neighborhoods patients lived in.

1. Methods

The UKPDS was a randomized, prospective, multicenter trial, that demonstrated for the first time the health benefits of intensive glucose therapy in patients with newly-diagnosed type 2 diabetes mellitus. Between 1977 and 1991, 3867 patients, aged 25–65 years, were randomized to conventional therapy (primarily with diet), or to an intensive glucose control strategy with sulfonylurea or insulin therapy. At baseline, participants in the conventional and intensive treatment groups were well matched with respect to age, sex, ethnicity, and clinical and biochemical profiles (UK Prospective Diabetes Study (UKPDS) Group, 1998). Information on participants' neighborhoods were not available at baseline, nor were data on number of moves during the course of the study. After median 10 years follow-up, which ranged from 5 to 18 years across patients, the intensive therapy group had experienced fewer diabetes related end-points, particularly a 25% risk reduction in microvascular complications, with a borderline non-significant decreased risk of macrovascular disease, and a longer complication-free interval, as measured by time until the development of at least one diabetes-related endpoint (UK Prospective Diabetes Study (UKPDS) Group, 1998). Loss to follow-up was low and non-differential across the conventional and intensive treatment groups, and there was no evidence of differences in all-cause mortality between the two groups at the end of the study (UK Prospective Diabetes Study (UKPDS) Group, 1998). We hypothesized that the health advantage conferred to the intensive therapy group might have translated into a neighborhood quality advantage.

To test this, we used data on English UKPDS patients who had been randomized to conventional or intensive glucose control therapy (n = 3339), and extracted postcode information from addresses for the 2710 surviving participants living in England at study end in 1996/1997. Over the course of the study, 526 patients died (15.8%), 47 moved abroad (1.4%), and 56 were lost to follow-up (1.7%). We assigned each postcode to its corresponding Lower Layer Super Output Area, the smallest geography at which the Office of National Statistics computes English Indices of Deprivation (Office of the Deputy Prime Minister, Neighbourhood Renewal Unit, 2004). Postcodes, which typically contain 15 addresses, identify neighborhoods on a very fine geographic scale, while Lower Layer Super Output Areas contain between 400 and 1200 households (Office for National Statistics, 2014b). We used two indices to compare neighborhood deprivation between the conventional and intensive therapy groups. First, we used the Index of Multiple Deprivation, which is based on measures of income, employment, health and disability, education and skills, crime, housing, and environmental deprivation at the neighborhood level. Secondly, we used the income deprivation index alone, which measures the percent of an area's population that is low-income. Higher scores indicate higher levels of deprivation.

Mean levels of deprivation were computed for both treatment groups and compared using *t*-test statistics.

2. Results

We observed small neighborhood advantages in the intensive therapy group compared to the conventional therapy group, although these differences were not statistically significant. Patients assigned to conventional therapy were, numerically, living in more deprived areas (0.006 ± 0.012, p = 0.30) in terms of income at the end of the study as compared with the intensive therapy group (Fig. 1). Those in the conventional therapy group were also, numerically, living in neighborhoods that faced a higher degree (0.775 ± 1.466, p = 0.29) of multiple forms of deprivation (Fig. 2).

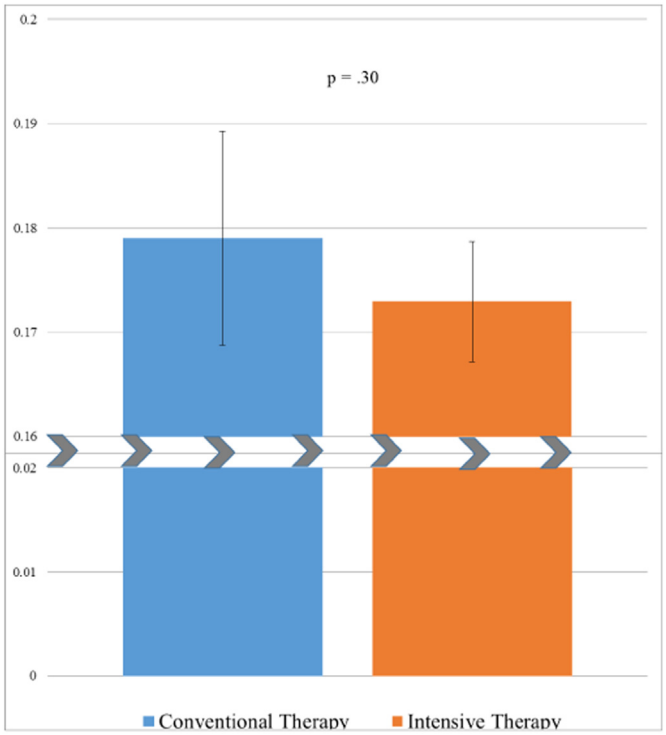

Fig. 1. Neighborhood-level income deprivation in conventional versus intensive therapy patients for the 2710 surviving participants of UKPDS living in England at study end in 1996/1997.

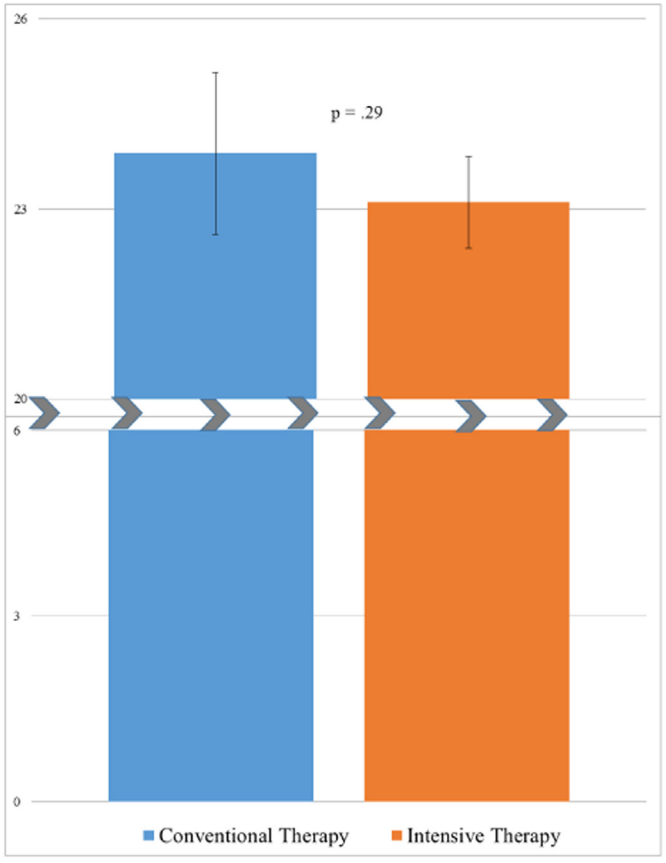

Fig. 2. Multidimensional neighborhood-level deprivation in conventional versus intensive therapy patients for the 2710 surviving participants of UKPDS living in England at study end in 1996/1997.

3. Discussion

Randomized trials have been used to study the causal effect of neighborhood conditions on health (Ludwig et al., 2011), but no clinical trials have explored how randomly distributed health gains affect neighborhood outcomes despite the fact that patient addresses are routinely stored as administrative data. While this study demonstrates the feasibility of using clinical trial data to investigate health selection into neighborhoods, a limitation of the analysis is our inability to test for differences in neighborhood quality between randomization groups at baseline. However, we note that groups were well-balanced at baseline according to correlates of neighborhood deprivation, including ethnicity (Jivraj and Simpson, 2015). Because all-cause mortality and loss to follow-up affected both treatment arms equally at the study's end when neighborhoods were compared, it is unlikely that attrition biased our results.

This exploratory analysis did not show conclusive evidence of health selection into neighborhoods during the trial. In addition to the possibility that improved health confers no neighborhood advantage in general, other explanations for the null finding include an insufficient sample size to detect what may be a weak effect of improved health on neighborhood outcomes. Alternatively, it is possible that more extreme gains in health would be needed to produce differences in neighborhood quality. If health-related neighborhood advantages were to stem from advances in educational levels or occupational categories rather than from incremental costs savings or income growth, for example, there could be important threshold effects in the relationship between health and neighborhood gains. If educational level or occupational class are indeed important mechanisms, a younger cohort may have experienced statistically different neighborhood outcomes across treatment groups when the UKPDS cohort did not. On a related note, these and other individual-level socioeconomic measures should be explored in their own right using clinical trial data where possible.

Another factor that may have limited our ability to detect health selection into neighborhoods was a relative short follow-up period. Larger differences in health emerged in post-trial monitoring than were evident during the course of follow-up, with the protective effect of intensive therapy against risk of myocardial infarction and against all-cause mortality becoming apparent only after the trial ended (Holman et al., 2008). It is possible that statistically detectable differences in neighborhood quality also developed after the trial ended, although we do not have the neighborhood data available at later dates that would be required to test for post-trial differences.

Despite the fact that observed differences are statistically non-significant, neighborhood quality differences do run in the hypothesized direction. A larger sample, which could be obtained by using other clinical outcome trials or a meta-analysis, may be needed to rigorously test the hypothesis that better health predicts subsequent residence in more affluent neighborhoods. Pooling data across trials would also provide more variability in the timing of interventions across the life course and in the types of health endpoints affected, both of which could increase power to detect associations if they truly exist.

Understanding the causal effect of better health on neighborhood outcomes is critical for multiple fields of research, and for designing interventions to promote social and health equity. First, understanding neighborhood selection processes will help researchers better assess the extent to which “reverse causation” may explain observational associations between neighborhood characteristics and health. Second, policymakers must understand the extent to which poor health affects neighborhood outcomes in order to design housing policy and programs that aim to improve the lives of socially vulnerable, and often sicker, populations. Finally, investigating the long-term social impacts of clinical interventions that have been shown to improve health may change the value we place on effective medical treatment. The aim of this Short Communication was to demonstrate that administrative clinical trial data may be an important and untapped resource for exploring health selection into neighborhoods, and to urge additional study of neighborhood outcomes within and across such trials.

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Transparency document

The Transparency document associated with this article can be found, in the online version.

Conflict of interest

No sponsors had any role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

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