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Geographical segregation and IL-6: a marker of chronic inflammation in older adults

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Abstract

Aim—To examine environmental sociodemographic risks of high IL-6, a marker of chronic inflammation in older adults.

Methods—We spatially linked 1990 USA Census tract demographic and economic measures to a prospective cohort study of representative community residents aged 71 years and older, from over 1700 of whom a cytokine protein and biological marker of chronic inflammation, IL-6, was collected. Using generalized interactive mixed models, we modeled 1989–1990 individual and census level risk factors for the dependent variable high IL-6 between 1992–1993 (high IL-6 = upper quartile: >2.96 pg/ml).

Results—After individual health risk adjustment, IL-6 remained elevated in communities with greater densities of poor older adults (odd ratio [OR]: 1.25 per 10% increase in exposure. 95% confidence interval [CI]: 1.05, 1.48) and in racially segregated communities (OR: 1.14 per 10% increase in exposure. 95% CI: 1.04, 1.25).

Conclusions—Socially disadvantaged environments may influence IL-6, a biomarker of age-associated inflammation.

Keywords

elderly; environmental impact; health risk; IL-6; Inflammatory marker; longitudinal study

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

The United States Environmental Protection Agency (EPA) and the National Institute for Environmental Health Sciences (NIEHS) recently outlined the unique health vulnerabilities of older adults and highlighted a need for research on environmental risks to this vulnerable segment of the population [1–3,¹⁰¹]. Gaps identified are especially pressing, given the growing demographic force of the population aged 65 and older and the looming magnitude of potential health risks and economic burden. Challenges highlighted include the observation that few studies are available to identify elders at high and low environmental risk, or to identify biological mechanisms by which environments differentially impact vulnerable elders. Work is also needed to spatially locate environmental exposures that might contribute to, interact with, or enhance existing individual predisposition for adverse environmental effects [1–3,¹⁰¹].

Data sets linking environmental exposures to physiological biomarkers of exposure and health outcome in older adults are also sorely needed, especially data sources that allow control for a wide range of potential confounding influences [1,4]. Such biomarkers have been frequently used for monitoring health in other vulnerable populations. In children, for example, public health standards and surveillance systems exist for evidence-based monitoring of blood-lead levels [5,6]. Given currently projected demographic trends in the population aged 65 years and older, the absence of information about environmental health risks and biological impact on older adults is at a critical juncture, which has led to a number of recent federally supported initiatives to promote work on markers of environmental health in this fast-growing segment of the population [¹⁰¹].

To begin addressing these issues, we spatially linked geographically-based measures of community level socioeconomic and sociodemographic exposures from the 1990 USA Census to a large, federally supported longitudinal cohort study of older adult health – the Duke Established Populations for Epidemiologic Studies of the Elderly (EPESE) [7,8]. Biological markers of age-associated physiological dysregulation were assayed from blood samples taken from over 1700 older persons in the Duke EPESE data set. IL-6, a key age-associated cytokine biomarker of chronic inflammation and health status [9], was assayed and is reported here.

Importance of inflammation in older adult health & senescence

Our research team published some of the earliest work on biomarkers of chronic systemic and vascular inflammation in seniors, showing that blood markers of inflammation, such as plasma D-dimer (fibrin degradation) product. TGF- β and IL-6, are elevated in older adults, associated with impairments and functional limitations, and predictive of future adverse events including death [9–12]. Since the late 1990s. It has been widely recognized in the aging literature that biomarkers of inflammation are good indicators of current and future older adult health and health events [13–22]. In fact, chronic inflammation is now purported to be a key mechanism of senescence, playing a significant causal as well as consequential role in age-associated impairments, chronic conditions and functional decline [19–21]. According to this view, causal inflammatory ‘stress’ can be of any origin (viral, bacterial, chemical, psychosociological and so on), each having signaling pathways and mechanisms that trigger the body’s defensive inflammatory responses. According to one theory of inflammatory senescence, a ‘two-hit’ model explains how the body responds in the short- and long-term to such stressful and antigenic stimuli. In one type of ‘hit’ to the aging physiological system, different individuals may have an increased level of susceptibility and response due to heterogeneity in genetic

¹⁰¹Website

101. US EPA (Environmental Protection Agency); The Aging Initiative. www.epa.gov/aging/Index.htm *Website for the USA EPA’s new Aging Initiative, which summarizes programmatic area of emphasis, lists new requests for proposals and available funding and summarizes recent research.

background [19–21]. In another type of ‘hit’, an additional ‘inflammatory background’ is partly determined by accumulating chronic conditions, injuries, insults and defense mechanisms that deteriorate with age, which together serve to additionally increase physiologic vulnerability to exposure.

Evolving evidence supports the idea that proinflammatory genetic predisposition plays a role in aging [20], and may also vary by race [23–26]. This makes the idea of inflammatory biomarkers of environmental effects doubly interesting given [26–28]:

- The substantial health disparities that exist in the USA
- The fact that minorities are more likely to live in adverse environments and bear greater toxic burden
- There has been little focus on whether and how the environment contributes to these known health disparities

In the current work, we used USA Census-based descriptors of environmental disadvantage to test the hypothesis that the places where senior citizens live may also function as a type of inflammatory ‘hit’ during the aging process. We propose that biomarkers of inflammation such as IL-6 may be excellent indicators of adverse environmental exposure and future health risk, and that exposure risks that segregate to different geographical communities may contribute to age-associated chronic inflammation. We show that a key cytokine biomarker of inflammation and older adult health, IL-6, is differentially elevated in communities with greater densities of poor older adults and in racially segregated communities, effects which are independent of the most important individual level risk factors known to contribute to chronic inflammation in older adults. This work is also important because it demonstrates how existing data sets can easily be merged to meet some of the needs recently highlighted by special panels at the EPA and the NIEHS [1–3, 101].

Materials & methods

Participants

The EPESE at Duke University is a 10-year prospective cohort study of the health and health services use of a representative sample of community residents 65 years of age and over [7, 8]. This population was selected using a four-stage sampling design, which yielded a probability sample of household residents 65 years or older in a five-county urban/rural Piedmont area of North Carolina, USA (Durham, Franklin, Granville, Vance and Warren counties). African-Americans were oversampled to increase statistical precision for this group. Of the 5221 persons selected, 4162 (80%) were successfully interviewed (54% African-American, 45% White, 26 [$<1\%$] of other race/ethnicity, 35% male and 56% urban residents). Participants were evaluated in person at home using structured questionnaires at baseline (1986–1987), 3, 6 and 10 years later (1989–1990, 1992–1993 and 1996–1997), and by telephone, 1, 2, 4 and 5 years after baseline. This study was approved by the institutional Review Board of Duke University Medical Center. Signed informed consent was obtained from all sample members.

Primary outcome: serum IL-6, a biomarker of chronic inflammation

In 1992–1993, 6 years after baseline, blood samples were requested from surviving participants who were able to give consent. These blood samples were used for routine hematologic and blood chemistry determination, and to ascertain levels of coagulation and inflammatory factors, including IL-6. Since baseline, 993 (24%) of the original 4162-person cohort had died and 606 sample members (15%) had refused to continue or were otherwise lost to follow-up, leaving 2553 survivors still enrolled. Of 2207 participants who remained in the target area, blood was

successfully drawn from 1705 participants and partial blood draws were obtained on an additional 52 people, for a total of 79.6% with blood assays. Of the 450 participants who did not provide blood, 221 were unable to personally give consent because of cognitive difficulties, while 229 refused the blood draw, were unavailable or blood could not be drawn for technical reasons.

Standard ELISA methods were used to measure plasma IL-6 levels (pg/ml) for the current study. Details on measurement of IL-6 in this sample have been reported previously [10], with high reliability and reproducibility over a period of 36 days (intraclass correlation coefficient: 0.87) [29]. IL-6 information was available on 1726 of the 1757 participants who gave blood. Of the donors, 65% were female, 53% Black, 54% urban (46% rural), 40% reported fair or poor health and approximately 43% reported one or more functional limitations. Comparison of those from whom blood was drawn with those from whom blood was not drawn (because of inability to give consent), and with refusers, indicated that donors were younger, included a larger proportion of males and Caucasians, had lower levels of impairment in activities of daily living (ADL), and had better self-rated health and cognitive status [10]. There were no significant differences between the three groups, however, in areas of residence or years of education.

Values on IL-6 were skewed, ranging from minimally perceptible (assays <0.6 pg/ml were coded as 0 pg/ml as in previous studies) to 201 pg/ml, with a median value of 1.70 pg/ml. For this analysis we dichotomized IL-6 at the top quartile (>2.96 pg/ml) as has been done in several recent analyses of this outcome. We then modeled the probability of an individual having an IL-6 level in the highest quartile in this geographically representative cohort of older adults.

Census tract information

Data on geographical areas were obtained from the publicly available 1990 USA Decennial Census data [30] and linked to the Duke EPESE data set by home address. Descriptors were obtained for USA-defined census tracts, which are variable in geographic area but have a mean population size of approximately 4000 people. Based on a review of the literature and inspection of crude associations with measures of IL-6, we selected five sociodemographic domains of heterogeneity in census tract built environments that are similar (to those previously identified to be most important at the census tract level, and which have also previously been linked to health outcomes in different population groups [31].

First, we included a measure of population density; that is, number or persons/km². Second, we examined three markets of area diversity (in terms of race, age and gender). Racial segregation was determined by examining the percent nonLatino-Black in each census tract (original sampling showed that White people in the sample and source population were also primarily non-Latino at the time of this study). The effects of age and gender segregation were examined by including the percent of elderly residents within the census tract, and the percent of female-headed households.

Third, following previous work identifying economic variables critical to the study of area-based effects [31], the following census level poverty-related indicators were selected:

- Median family income
- Percent of residents of all ages living in poverty, according to the poverty line established by the USA Census Bureau based on year 1990 data
- Percent of residents aged 65 years and over and in poverty

The fourth domain was occupational class. We examined occupational class effects by characterizing the 'percent of blue-collar workers within a census tract area'. This was a

summary variable, comprised of the sum of the proportion of residents in a census tract whose primary occupation was classified by the USA Census Bureau as 'sales', 'clerical', 'services', 'farming', 'craft', 'operative' or 'laborer'.

Our fifth and final domain of investigation examined aspects of housing quality and/or desirability in census tracts. As measures of housing desirability we evaluated the percent of all housing units that were vacant or owner-occupied and we included median housing value.

With the exception of housing value and income, all census tract variables were recorded in percentage units and were analyzed in units of 10% Increment. The odds ratio (OR) estimates for these variables can be interpreted as the amount of increase in the odds of having high IL-6 for each 10% change in exposure. ORs for median family income and median housing value are reported per US\$1000 increment.

Individual level information

The individual level characteristics selected for study were either known covariates of IL-6, or characteristics hypothesized to be associated in a potentially causal way with systemic inflammation in older adults. For example, older age has repeatedly been found to be associated with increased IL-6 levels, as have selected health conditions, functional limitations and depression; although in uncontrolled cross-sectional analysis race, gender and urban (versus rural) residence have not [9–11]. Low-grade inflammation, and hence a likely association with IL-6, has been associated with cognitive decline, obesity and smoking [32]. While information on these characteristics has been included largely for covariate control, we point out that most of the previous study designs have been cross-sectional; this study is unique in its investigation of these individual level variables as prospective indicators of future inflammation and in its simultaneous adjustment for area-based effects.

We focused on individual health status in 1989–1990, which was coincident with 1990 census data, and prior to determination of IL-6 level (1992–1993). Information was obtained on individual demographic characteristics (age and education), race (Black and non-Black), gender and income (adjusted to year 2006 standards using the most recently published data from the USA Bureau of the Census [33]). Health status measures included the number of prescription drugs taken in the previous 2 weeks, a four-point self-rated assessment of health (excellent: 1. poor: 4) and trichotomized BMI: BMI less than 25 kg/m² (normal: reference group), 25–30 kg/m² (overweight), or greater than 30 kg/m² (obese) [34]. Functional status was measured by the aggregated sum of 13 ADL tasks [35], comprised of five basic ADL tasks [36], five instrumental ADL items [37] and three mobility tasks [38]. Depressive symptomatology was ascertained by a modified Center for Epidemiologic Studies Depression (CES-D) scale with Score dichotomized to indicate severe depressive symptomatology [8, 39], and cognitive status by number of errors on the ten-item Short Portable Mental Status Questionnaire [40]. Health behaviors included current smoking and alcohol intake at baseline, and whether any vitamins, or minerals were being taken (an indicator of preventive health behavior). In addition, the number of self-reported negative life events experienced in the previous year was used as an indicator of recent stress (e.g., occurrence of severe illness or injury to the individual or a close family member, death of a close family member, relocation or financial challenges). Finally, information was obtained from each person on duration of residence at the current address and adequacy of current housing (absence of any one of indoor toilet, electricity, running water or adequate heat indicated inadequacy).

Statistical analysis

For continuous variables, descriptive characteristics of the sample were determined using means, standard deviations and ranges. Frequencies are reported for categorical variables. As

the majority of variables had no more than 4% missing data, the Biomedical Data Processing (BMDP) regression estimation procedure for missing data was the general method of choice used to impute regression-predicted scores for most missing variables [41].

We estimated the association between IL-6 and neighborhood level variables, while accounting for individual level measurements from individuals ‘clustered’ within geographical areas (i.e., census tracts). Special statistical models are needed for this type of analysis because individuals who are ‘clustered’ within the same Census tract will tend to be more alike in their responses and outcomes than individuals in different tracts. This has the potential to induce lack of independence and correlated errors in individual measures of predictor and outcome variables if traditional regression models are used. For this reason, we used the generalized linear interactive mixed modeling procedure (GLIMMIX), specified with a logit link, in order to model our binary outcome while at the same time accounting for spatially clustered effects and correlated errors (SAS Statistical Analysis package version 8.0; SAS Institute, Cary, NC, USA). The GLIMMIX application has previously been shown to be particularly useful for analysis of hierarchically and spatially clustered data. From the GLIMMIX model specified, we report ORs and 95% CIs representing the odds of being in the top quartile of IL-6 per each unit change in the predictor variable (or for each 10% change in census tract variables that were recorded as percentages).

Results

Distribution of individual covariates & serum IL-6 levels in the Duke EPESE area

Descriptive characteristics of the 1989–1990 Duke EPESE sample ($n = 1726$) are shown in Table 1. These data are concurrent with the 1990 USA Census data and were used to adjust for individual level health risks. Figure 1 shows the kurtotic distribution of individual IL-6 values in the Duke EPESE cohort. Assays ranged from 0–201 pg/ml (median: 1.70 pg/ml). As in previous work, high IL-6 was defined as an IL-6 assay value in the upper quartile (>2.96 pg/ml) [9].

Figure 2 presents median plasma IL-6 concentrations for Duke EPESE participants (age 71–105 years) measured in 1992–1993 by quartile of selected census tract characteristics for the year 1990. These data show that median IL-6 increases as person density (per km²), the proportion of blue collar workers and percentage housing vacancy increases, and as median housing value and owner occupied housing decreases. Higher levels of IL-6 were also observed in census tracts with a greater proportion of non-Latino Black people, female-headed households, percentage elderly and overall percentage living in poverty, and in census tracts where median family income was lower. These results are consistent with the hypothesis that poor neighborhood quality may contribute to patterns of chronic inflammation in old age.

Census-based geospatial variables associated with chronic inflammation in the Duke EPESE cohort

Odds ratios for census level and individual level characteristics are shown in Figure 3, reflecting their simultaneously estimated association with elevated levels of IL-6 in the Duke EPESE cohort. After controlling for confounding at the individual and census level, each 10% increase in the proportion of older adults living in poverty was associated with a 25% elevation in the OR for high levels of chronic inflammation (OR: 1.25, 95% CI: 1.05–1.48). Similarly, each 10% increase in the proportion of African–Americans in a census tract was also associated with an increased risk of high IL-6 (OR: 1.14, 95% CI: 1.04–1.25). We could not attenuate these effects despite the most comprehensive adjustment ever conducted for important individual level and census-based risk factors for chronic inflammation. Neither could we attenuate the effect of living in a census tract with a higher proportion of elderly living in

poverty by simultaneous adjustment for percent in poverty (regardless of age) or by controlling for the proportion of elderly people living in a given area (without considering poverty). In fact, neither percent in poverty nor percentage elderly had any effect on IL-6 in the fully adjusted models. Similarly, the census level effect of racial segregation was not eliminated even though we controlled for the substantial individual level effect of African-American race on IL-6 (Figure 3).

Individual level factors contributing to chronic inflammation in older adults

While the focus of our investigation was on census level effects that remained after controlling for individual health risks, the individual level data also yielded interesting and novel results that may be especially important in this study given the prospective design and the simultaneous control for census level exposures. Being older, African-American, taking more prescription drugs, having a BMI greater than 30, consuming greater levels of alcohol and being a current smoker were all strong and important individual level predictors of elevated IL-6. Vitamin/mineral use, a likely indicator of protective health behavior, substantially reduced the odds of elevated IL-6.

Having two or more negative life events and subjective report of problems with housing were also positively associated with high levels of IL-6, but the effects did not attain statistical significance. The length of time lived in place was also not associated with high IL-6. Nevertheless, we retained these individual level covariates in all final analysis models to maintain optimal control over potential confounding by these characteristics.

Where are the high-risk communities?

County and census tract boundaries for the Study area in North Carolina, USA, as well as locations of major interstates are shown in Figure 4 (top map). Figure 4 also shows gradations in exposure distributions for the two primary Variable of interest (non-Latino Black and age-associated poverty), and for median census tract IL-6. Gradients in levels of census tract exposure and outcome are determined here using Jenks natural breaks [42]. These crude descriptive data spatially complement the more fully adjusted statistical analyses. For the three census tract maps showing percentage non-Latino Black, percentage elderly in poverty and median IL-6, simultaneous overlap in darker-shaded areas are observed in portions of Granville, Franklin, Nash and Halifax counties. In addition, dual elevations in the elderly in poverty and IL-6 are noted in portions of Granville and Orange counties (since first interviewed, some residents had moved to neighboring counties). Interestingly, for some counties, exposure and outcome are elevated only for percentage elderly in poverty, while for other counties percentage non-Latino Black (and not percentage elderly in poverty) appears to be the more relevant exposure. This qualitative finding is consistent with the objective statistical finding that percentage elderly in poverty and percentage non-Latino Black both have independent effects in the fully adjusted models. In combination with the statistical results, these figures illustrate qualitatively how mapping of exposures and biomarkers such as IL-6 might highlight geographic areas for more detailed study.

Discussion

Generating biological & health data to study environmental impacts on seniors

Our group and others have previously reported individual level associations between IL-6 and mortality and morbidity [9–13]. This paper reports the first ever identified associations between a biologically relevant blood biomarker of inflammation in older adults and spatially based descriptors of the environments in which older people live, particularly environments with substantial segregation according to race and old-age poverty. While provocative, these findings are not conclusive but suggest a need to further explore the types of inflammatory

exposures older adults experience in different types of geographical areas, interactions between personal and environmental risks and ongoing evaluation of spatially referenced environmental stressors contributing to chronic inflammation in older adults.

Another highly important outcome of this study is its demonstration that merging existing geographical and health-related databases can create unique opportunities to evaluate the health impacts of environments on vulnerable individuals, fast-growing senior segments of the population. Comparable analysis in similar merged data sets might quickly address several major gaps in our knowledge of older vulnerable populations that have recently been highlighted by both the EPA and NIEHS. Our group has further plans to use a similar methodological approach to the one used in this study to investigate census level effects on mortality and morbidity, as well as health utilization and access.

Environmental contributions to health disparities?

We found that racial differences in IL-6 were present both for the individual level race variable and for census tract measures of racial segregation. These results were somewhat unanticipated given our previous report in the EPESE cohort that race was not associated with IL-6 [9]. However, in contrast with the previously reported findings, which were only minimally adjusted for statistical confounding, the present study is comprehensively adjusted for a number of known social and biological risk factors for inflammation. Most notably novel compared with the previous report, in this study we were able to control for confounding factors by a wide range of census-based (including racial segregation) effects on inflammation, which was not possible in the previous investigation of this cohort (geocoding and linkage to census information had not yet been completed at the time of the previous report). Importantly, we find that the individual level effects of race do not attain statistical significance without the additional control of census level effects, even with extensive individual level control of confounding factors.

The finding of enhanced inflammation in African-Americans and in areas with a greater proportion of African-American resident is consistent with previous work on health disparities in minority communities, and highlights the possibility of environmental contributions to those health disparities via inflammatory mechanisms. We note that racial differences in allele frequencies for proinflammatory cytokine genes such as IL-6 have been identified [23] and documented in samples of North Carolina residents [24], and speculate whether such differences may put African-Americans at greater risk if they are also preferentially exposed to environments with higher levels of social stressors or greater pathogenic burden. Ongoing work in this area could help to determine whether this type of gene-environment interaction may be important in a number of health outcomes known to differ among Caucasians and African-Americans in North Carolina, including cardiovascular disease, cancer, HIV, stroke, diabetes and preterm birth [43].

The combination of environmental risk & individual age-associated vulnerability

We would expect older adults living in environments with large antigen burden to be at greater risk than those living in healthier environments. In addition to a genetic predisposition to increased inflammation that may be present for some individuals [21], increased age additionally predisposes individuals to more total (i.e., life cumulative) antigenic burden, hence greater immune challenge and potential compromise in the body's normal defenses, with consequent enhanced inflammation. We examined whether the effects of age-specific poverty that we identified in census tracts represent straightforward compositional effects of individuals within areas rather than environmental effects of census tract areas as hypothesized. For example, we wondered whether IL-6 might be elevated within tracts simply because of the presence of more old individuals (who are known to have higher IL-6) or to more global poverty

(irrespective of age). Our results show that this is not the case. Merely living in areas with large numbers of older adults or in areas with higher global levels of poverty are not the key age-associated area-based risks for older adults (Figure 3). Rather, the greatest census level risk came from higher proportions of people who were vulnerable owing to both age and poverty – a type of ‘double jeopardy’.

This finding is novel and relevant to current discussions of the interaction between environmental risk and individual vulnerability. We note that the longest-lived older adults in recent studies of longevity have been shown to have genetic predisposition to ‘damping down’ inflammatory responses to environmental anti-genic stimuli [19], which might confer additional advantages if such individuals live in safer environments. Future work should continue to investigate whether the converse may also be true: living in adverse environments may confer the greatest harm to the most vulnerable segments of the older adult population (i.e., poor elders and certain minority groups), who are already at higher risks for chronic inflammation and poor health.

Limitations

One of the principal limitations of this study is a lack of repeated measures of IL-6. IL-6 has been criticized by some as unstable because of its relatively short half-life (~2 h) compared with other biomarkers of inflammation such as C-reactive protein [44]. However, a recently published extensive review of the literature and meta-analysis of the effects of IL-6 on coronary disease outcomes accounted for within-person variability owing to fluctuations over time, and showed that after accounting for this variance, associations with IL-6 were actually greater than previously reported in the literature [43]. This finding is of special concern with respect to the current report if our findings similarly underestimate the potential magnitude of associations with IL-6. Ongoing investigations of environmental associations with chronic inflammation are needed in which repeated measurements of both IL-6 and the environment are available.

An additional concern in any observational study is the possibility of residual confounding. In response to one reviewer, we conducted sensitivity analysis of potential confounding by seasonality effects and diabetes on the estimates of association with IL-6 reported here. No differences in the results were obtained and we were unable to attenuate the results reported. Overall, while we acknowledge that unmeasured confounding is always a threat to the validity of observational studies, the control of measured potential confounders in this study was more extensive than in previous investigations of IL-6.

Conclusion

Our findings that both racial and age-specific segregation are associated with an objective biological marker of chronic inflammation suggest a need to further investigate high-risk areas and determine whether these findings are generalizable to other nationally and internationally representative geographical areas and to other types of age-associated health outcomes. More detailed analyses also are needed to identify specific types of environmental and gene–environmental risks that might contribute to inflammation and subsequent poor health in minority groups and in vulnerable seniors.

Future perspective

While previous studies have explored the association of environmental and census tract characteristics with population level health conditions and health service use, this is the first longitudinal study to examine the effect of census tract characteristics (the environment in which people live) on a biomarker of health status (IL-6), which may be an indicator of future

coronary heart disease [43]. We anticipate that there will increasingly be attempts to link longitudinal environmental and census track data to longitudinal person level data in order to better ascertain the long-term effects of the residential environment on health, and thus identify potential areas of intervention that could result in broad improvements in health at the population level.

Executive summary

- The USA Environmental Protection Agency and the National Institute for Environmental Health Sciences have highlighted a critical need for research on environmental risks to older adults and on physiological biomarkers of those effects.
- Currently, few studies identify elders at high and low environmental risk or identify biological mechanisms by which environments differentially impact vulnerable elders.
- Work is needed to spatially locate environmental exposures that might contribute to, interact with or enhance existing individual predisposition to adverse environmental effects.
- The present study shows that it is possible to link geographically based measures of community level socioeconomic and sociodemographic exposures from the USA Census to a longitudinal cohort study of older adult health that includes biological markers of age-associated physiological dysregulation.
- Although geospatial coding of persons with protected health information requires careful privacy-protection procedures, it is feasible nevertheless. Given the increasing interest in and feasibility of obtaining biomarkers, and the availability of longitudinal studies of representative samples of the population, increasing use of geospatial linkage should be anticipated.
- Typically, interventions to improve health status have focused on individuals, and occasionally population-affecting intervention has been used (e.g., fluoridation of water, supplementation of milk and flour). The present study demonstrates that an alternative approach – identification of socially adverse geographic areas – may provide an additional indicator of the likelihood of poorer health, and thus indicate an alternative source of intervention.

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Figure 1. Distribution of IL-6 values in the Duke EPESE cohort

Median = 1.70 pg/ml; 25th percentile = 0.95 pg/ml; 50th percentile = 1.69 pg/ml; 75th percentile = 2.95 pg/ml

Figure 2. Median plasma IL-6 concentrations for Duke EPESE participants

Age 71-105 years in 1992-1993 by quartile of selected census tract characteristics for the year 1990.

Figure 3. Census-based geospatial factors associated with chronic inflammation in older adult residents

Statistically significant associations are shown in light blue. Housing value and family income are reported per US\$1000. Odds ratios for all other census variables are reported per 10% elevation in exposure. For age, elevation in the odds ratio is shown per each 1-year increment in age.

Figure 4. County and census tract boundaries for the study area in NC, USA

Gradations in exposure distributions for the two primary variables of interest (non-Latino Black and age-associated poverty), and for median census tract IL-6. Graphical maps of descriptive data for census tract variables, census tract boundaries and interstate highway locations were created using ARCGIS software (version 9.1, Environmental Systems Research Institute, Inc., CA, USA).

Table 1
Descriptive characteristics of the Duke EPESE sample in 1989–1990.

Individual level covariates	Mean (SD) or %
<i>Demographic characteristics</i>	
Age	74.6 years (5.4)
Sex (% female)	65.0%
Race (% Black)	52.8%
Education	9.0 (4.1)
Income [*]	
• ≤US\$8414	35.5%
• US\$8415–15,894	27.9%
• >US\$15,894	36.6%
<i>Health status</i>	
Number of prescription drugs	2.3 (2.2)
Self-rated health	
• Excellent	17.4%
• Good	44.4%
• Fair	32.4%
• Poor	7.8%
BMI	
• <25	42.5%
• 25–30	37.7%
• >30	19.7%
Depression	7.8%
Short Portable Mental Status Questionnaire (mean number of errors [SD])	1.2 (1.5)
Functional limitations on 13-item scale (mean [SD])	1.4 (2.3)
• 0 problems	52.2%
• 1–2 problems	29.2%
• 3+ problems	18.6%
<i>Health behaviors</i>	
Current smoker	13.1%
Alcohol drunk/month (ounces absolute alcohol)	0.6 (8.1)
• Any	22.8%
• None	77.2%
Current vitamin/mineral use (any)	17.4%
<i>Negative life events (including potential housing exposure) in past year</i>	
No negative life events	53.1%
One negative life event	26.6%
Two or more negative life events	21.3%
Years at current address	23.8 (17.3)
Missing indoor toilet, electricity, hot/cold water or enough heat	8.0%
<i>Census tract variables[‡]</i>	
Population density (persons per sq. kilometer)	575 (688)

Individual level covariates	Mean (SD) or %
% Non-Latino Black	49.17 (25.94)
% Female-headed household	27.22 (14.89)
Median housing value	US\$61.956 (22.357)
% Blue collar	62.39 (11.77)
% aged 65 years and over	14.71 (4.73)
Median income	US\$34.444 (11.641)
% Occupied housing	54.87 (19.11)
% Persons in poverty	17.85 (10.67)
% Elderly in poverty	22.87 (11.37)

* Income adjusted to year 2006 using the most recent data from US Census Bureau [34].

‡ Weighted means reported for Census tract variables represent 1726 individuals in 84 Census tracts.

EPESE: Established Populations for Epidemiologic Studies of the Elderly; SD: Standard deviation.