Is tree loss associated with cardiovascular-disease risk in the Women's Health Initiative? A natural experiment

Geoffrey H. Donovan a,*, Yvonne L. Michael b, Demetrios Gatzios a, Jeffrey P. Prestemon c, Eric A. Whitsel d

a USDA Forest Service, Pacific Northwest Research Station, Portland, OR, USA
b Drexel University, Department of Epidemiology and Biostatistics, Philadelphia, PA, USA
c USDA Forest Service, Southern Research Station, Research Triangle Park, NC, USA
d University of North Carolina, Gillings School of Global Public Health, Chapel Hill, NC, USA

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Data from the Women's Health Initiative were used to quantify the relationship between the loss of trees to an invasive forest pest—the emerald ash borer—and cardiovascular disease. We estimated a semiparametric Cox proportional hazards model of time to cardiovascular disease, adjusting for confounders. We defined the incidence of cardiovascular disease as acute myocardial infarction requiring overnight hospitalization, silent MI determined from serial electrocardiograms, ischemic or hemorrhagic stroke, or death from coronary heart disease. Women living in a county infested with emerald ash borer had an increased risk of cardiovascular disease (HR = 1.25, 95% CI: 1.20–1.31).

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1. Introduction

A growing body of research supports a health-promoting role for the natural environment. However, two related methodological issues can make it challenging to interpret the results of this research. First, when studying the health effects of residential exposure to green space, it can be costly and time consuming to experimentally manipulate the natural environment. Therefore, many studies are cross-sectional (Astell-Burt et al., 2013; Bell et al., 2008; Coombes et al., 2010a; Dadvand et al., 2012; Donovan et al., 2011; Groenewegen et al., 2006; Hu et al., 2008; Kuo and Sullivan, 2001; Lovasi et al., 2011; Maas et al., 2006; Nutsford et al., 2013; Stigsdotter et al., 2010; Witten et al., 2008). Second, the association between the natural environment and health outcomes is prone to confounding by unmeasured factors (Frumkin, 2013). For example, long-term cigarette smokers are less likely to live in areas with green space (Villeneuve et al., 2012), and the probability of living in areas with fewer trees can vary significantly by race (Jesdale et al., 2013).

In a previous study (Donovan et al., 2013), we addressed these two challenges by quantifying the relationship between the spread of an invasive tree pest—the emerald ash borer (EAB)—and county-level cardiovascular and lower-respiratory mortality. The emerald ash borer has killed over 100 million ash trees since it was first detected in Detroit, Michigan in 2002. This significant, and rapid, loss of trees is a unique natural experiment in which observed and unobserved characteristics of participants at the individual or aggregate level are independent of exposure. In addition, although tree cover in urban areas is correlated with socio-economic status (Heynen et al., 2006; Jesdale et al., 2013), the loss of trees in far less likely to be correlated with demographic changes because of the speed and pattern of EAB’s spread (Fig. 1). Crucially, the spread of EAB allowed us to study the relationship between public health and tree loss longitudinally rather than the relationship between trees and public health at one point in time. We found that counties infested with EAB had increased rates of cardiovascular and lower-respiratory mortality, and the magnitude of this relationship increased as an infestation progressed. From 2002 to 2007, EAB infestation was associated with an additional 15,000 deaths from cardiovascular disease and an additional 6000 deaths from lower-respiratory disease across 15 states in the Midwest and East.

Although our approach avoided some of the challenges of past cross-sectional studies, it did have other limitations. In particular, we focused on county-level mortality, so our results may be subject to

* Correspondence to: PNW Research Station, 620 SW Main, Suite 400, Portland, OR 97205, USA. Fax: +1 503 808 2033.
E-mail address: gdonovan@fs.fed.us (G.H. Donovan).
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ecological bias. To address this limitation, we make use of individual-level outcome data from one of the largest studies of women's health undertaken in the U.S—the Women's Health Initiative (WHI)—to determine whether loss of trees from EAB is a risk factor for cardiovascular disease.

Several other recent studies have quantified the relationship between the natural environment and cardiovascular disease. Pereira et al. (2012) focused on the link between coronary heart disease, stroke, and the natural environment in Perth, Australia. In common with many large-scale studies, they measured greenness using the normalized difference vegetation index (NDVI), which is derived from satellite imagery. After controlling for confounders, they found that adults living in neighborhoods with highly variable greenness had a 37% lower rate of coronary heart disease and stroke. Interestingly, total greenness was not significantly related to incidence of either disease. Paquet et al. (2014) examined the relationship between access to public open space and cardio-metabolic risk factors. They found that proximity to open space was associated with lower levels of diabetes and pre-diabetes. In Taiwan, Tsao et al. (2014) measured subclinical cardiovascular disease in 104 volunteers who worked in a forest environment versus 114 who worked in an urban environment. After adjustment for confounders, urban workers had higher total cholesterol, LDL cholesterol, and fasting glucose. Mitchell and Popham (2008) analyzed the health records of over 40 million people in England. They found lower rates of circulatory-disease mortality in greener areas. They also found that health disparities were lower in greener areas. Not all studies found a significant relationship between greenness and cardiovascular disease. Richardson et al. (2012) used a land-use model to quantify the relationship between greenness and city-level mortality in the 49 largest cities in the US. They found no relationship between greenness and cardiovascular mortality demonstrating that green-health relationships observed at the individual level are not always seen at the population scale.

To our knowledge, there have been no longitudinal studies of the relationship between the natural environment and cardiovascular disease. Indeed, there have been few green longitudinal studies of any kind. One notable exception is Alcock et al. (2014), who, found that moving to a greener area was associated with a sustained improvement in mental health.

A number of recent review articles have summarized the literature on the health benefits of nature. For example see James et al. (2015) or Lee and Maheswaran (2011).

1.1. Mechanisms linking the natural environment and cardiovascular disease

In a recent paper, Hystad et al. (2014) outlined four possible mechanisms linking the natural environment and public-health outcomes: (1) Reducing environmental risks factors such as air pollution; (2) Encouraging exercise; (3) Increasing social contacts; (4) Reducing stress. We begin by summarizing the evidence that the natural environment can influence health outcome via these four mechanisms. We then focus on the importance of these four mechanisms for cardiovascular disease.

1.1.1. Air pollution

There is strong evidence that the natural environment can reduce air pollution. For example, research has found that increased greenness is associated with reduced nitrogen dioxide (Rao et al., 2014; Yin et al., 2011), ozone (Alonso et al., 2011), and particulate matter (Nowak et al., 2006). In turn, multiple studies have found that air pollution is associated with increased incidence of cardiovascular disease (Feng and Yang, 2012; Metzger et al., 2004).

1.1.2. Exercise

Several studies have identified a positive relationship between exercise and distance to parks. For example, Coombes et al. (2010b) found that adult exercise frequency was negatively correlated with distance to green space. Roemmich et al. (2006) showed that young children with greater park area in their neighborhood exercised more. However, not all studies found a significant relationship between exercise and access to the natural environment. For example, Foster et al. (2009) failed to find a correlation between access to green space and self-reported recreational walking in adults. Similarly, Witten et al. (2008) found no relationship between exercise and distance to parks. The relationship between the natural environment and exercise may not be clear; however, the relationship between exercise and the risk of cardiovascular disease is well established (Kohl III, 2001; Li and Siegrist, 2012).

1.1.3. Social connections

A relatively small body of research has shown a positive correlation between the natural environment and social support. Maas et al. (2009) found that adults with less green space within 3 km of their homes were more likely to self-report loneliness and low levels of social support. Kim and Kaplan (2004) found that higher amounts of open space within a residential development was associated with increased sense of community. In turn, numerous studies have found that a low level of social support is a risk factor for cardiovascular disease (Barth et al., 2010; Heffner et al., 2011).

1.1.4. Stress

A number of experimental studies have shown that exposure to the natural environment can reduce short-term markers of stress. For example, Park et al. (2008) exposed 12 male students to a forested and an urban environment. Subjects in the forest had significantly lower blood pressure, salivary cortisol, and heart-rate variability. Ulrich et al. (1991) exposed 120 volunteers to a stressful video followed by six different videos of urban and natural scenes. Stress recovery was quicker and more complete, when subjects watched a video of a natural scene. Wichrowski et al. (2005) studied stress reduction in 107 people participating in an inpatient cardiopulmonary rehabilitation program. Post intervention, the horticultural-therapy group had lower heart rate and lower total-mood disturbance. Further, elevated cortisol (Fraser et al., 1999), increased heart-rate variability (Tsuij et al., 1994), and high blood pressure (Staessen et al., 2000) are risk factors for cardiovascular disease.
EAB kills virtually all untreated trees. In contrast, some tree pests—pine beetles, for example—preferentially attack stressed trees (Negrón et al., 2009). This is problematic, from a statistical perspective, as tree stressors—heat and drought, for example—can also impact public health (Patz et al., 2005).

The spread and pattern of EAB’s spread (Fig. 1) make it unlikely that tree loss is confounded by an unmeasured cause or marker of cardiovascular disease. In particular, EAB spread has a random component: satellite populations that appear far from the nearest infestation. These satellite populations are a result of accidental transport often in firewood (Muirhead et al., 2006).

Past research has established a link between the natural environment and cardiovascular disease. In addition, there are several, plausible mechanisms linking tree loss and cardiovascular disease. Finally, the loss of trees to EAB is unlikely to be confounded by other drivers of cardiovascular disease. Therefore, we hypothesize that the loss of trees to EAB will be associated with an increased risk of cardiovascular disease in women enrolled in WHI.

2. Methods

2.1. Study population

The WHI began in 1991 to study the three leading causes of death and impaired quality of life in post-menopausal women: cardiovascular disease, cancer, and osteoporosis. The WHI consists of a clinical trial (68,132 participants) and an observational study (93,676 participants). Women in the clinical trial were randomized to three sub-trials: hormone therapy, dietary modification, or calcium and vitamin D supplementation. Women were recruited at 40 clinical centers and were 50–79 at recruitment. Data were collected at baseline and updated by mailed questionnaires throughout the follow-up period (September 30, 2010). For more details on design, eligibility, and recruitment in WHI see Hays et al. (2003). We included all participants in the observational study and clinical trials (Table 1). Of the 161,808 women recruited into the study, 5662 had a history of stroke or MI at baseline and were excluded.

2.2. Outcome assessment

We defined the incidence of cardiovascular disease as acute myocardial infarction requiring overnight hospitalization, silent MI determined from serial electrocardiograms, ischemic or hemorrhagic stroke, or death from coronary heart disease. Outcomes of interest were self-reported by the study participants and confirmed locally or centrally through medical record review (During the study period, 14,518 women experienced an episode of cardiovascular disease). We did not include revascularization procedures in our definition of cardiovascular disease, because the probability of undergoing a revascularization procedure is positively correlated with socioeconomic status (Rose et al., 2012).

2.3. Exposure assessment

The presence of EAB in a county is officially determined by the USDA Animal and Plant Health Inspection Service. Once the agency has positively identified EAB, quarantine is imposed—ash firewood cannot be transported out of an infested county. Identifying EAB during the early stages of an infestation can be problematic, as exit holes are typically high on a tree. The first signs of infestation are dieback of peripheral limbs (damage to a tree’s phloem disrupts water transport). For our purposes, uncertainty about the precise start date of an infestation is not a major concern, as we are

For a more thorough review of the mechanisms linking the natural environment and health, see (Shanahan et al., 2015) or (Hartig et al., 2014).

1.2. The spread of emerald ash borer as a natural experiment

The emerald ash borer is a phloem-feeding beetle native to eastern Russia and Northern China. It was first confirmed in North America in 2002 in Detroit, Michigan and Windsor, Ontario (Poland and McCullough, 2006). None of the 22 species of North American ash have any significant resistance to EAB. Infested trees die in 3–7 years depending on the severity of an infestation (Fig. 2). Insecticides can be used to control EAB (Grimalt et al., 2011). However, treatment is costly, the most effective must be administered by an arborist, and treatment must be continued for the life of the tree. Therefore, insecticide treatment is unlikely to significantly impact the spread of EAB. In addition, biological control, using predatory insects from EAB’s native range, has not had a significant impact on EAB’s spread (Ulyshen et al., 2011).

The spread of EAB is uniquely well suited to studying the relationship between the trees and cardiovascular health for a number of reasons. Ash is a common urban tree, so killing ash trees has a major impact on the urban natural environment. Comprehensive data on ash abundance in urban areas are not available, but inventories have been done for several cities impacted by EAB. For example, 10.9% of trees in Chicago are ash as are 17.4% of trees in Milwaukee (unpublished data on file with author).
interested in tree loss not the beetle itself. Using established geocodes (Whitsel et al., 2006), we created a variable denoting the number of years since EAB was first detected in a county and linked exposure status with the WHI data. By the end of the WHI follow-up period in 2010, 245 counties had been infested with EAB.

2.4. Missing data

This data merging process created missing values for time-varying covariates due to the different follow-up schedules in the CT and OS. Some baseline variables also had a significant number of missing values. Of particular concern were income (7148 missing) and smoking status (2804 missing). To address these two sources of missing values, we used Bayesian multiple imputation. The imputation models included all dependent and independent variables as well as time. We estimated a 20-iteration imputation model, which took 22 h to solve using a Stata’s MI IMPUTE and STCOX commands on a quad-core 2.4 GHz processor.

2.5. Statistical analysis

Using these imputed data, we estimated a Bayesian semi-parametric Cox proportional hazards model of time to cardiovascular disease, adjusting for confounders. The Cox proportional hazards model is a member of a larger group of time-to-event models, in which the dependent variable is time to some specified event (cardiovascular disease in our case). Time-to-event models can be single or multiple failure. In a multiple-failure model, a participant remains in the analysis even if the specified event occurs. In a single-failure model—which we estimate in this paper—a participant no longer remains in the analysis, after the event occurs for the first time (Rothman et al., 2008). A participant may exit the analysis for other reasons—dying of a cause death other than cardiovascular disease or being lost to follow up, for example. These events are called right censoring and are treated as exits from the analysis rather than an occurrence of the event under study.

In a Cox model, a hazard function describes the risk of the event per unit of time. In contrast to other types of regression models in which covariates are additively associated with the dependent variable (ordinary least–least squares regression, for example), covariates in a Cox model are multiplicatively associated with hazard. In a semi-parametric Cox model, it is not necessary to specify the form of the hazard function (Cleves et al., 2010).

We selected potential confounders based on past research on cardiovascular disease in the WHI (Howard et al., 2006; Manson et al., 2003; Rossouw et al., 2007). We used a variance-covariance matrix to avoid including highly co-linear combinations of variables in the model (variables describing education and income, for example). We refined this initial group of variables using iterative backwards selection using progressively lower p-value thresholds (final threshold of \( p < 0.05 \)). Once we had a final model, we systematically reintroduced dropped variables and retained them, if the coefficients of interest changed by 10 percent or more (Rothman et al., 2008).

Table 1 shows that there are significant demographic differences between women living in counties infested with EAB and those living in counties that were never infested. It is also possible that EAB and non-EAB counties differ in unobservable ways. To evaluate this issue, we estimated two additional models. First, we estimated a model including only women living in counties that were infested with EAB in 2010 (the end of the study period). Excluding women living in non-EAB counties reduced the sample size by 89 percent but ensured that our results were not an artifact of unobserved differences between the two types of counties. Second, we estimated a model with an index of neighborhood-level SES that was significant in previous WHI studies (Dubowitz et al., 2012). The index was only available for women living in metropolitan statistical areas, which reduced the sample size by 56 percent.

3. Results

Women in the WHI were diverse with respect to race/ethnicity, income and education; 17.5% were racial minorities, the majority reported an income of $20,000–$30,000 per year, and a quarter attended at least some college (Table 1).

Living in a county infested with EAB was associated with a 41% increased risk of CVD (Table 2, full model). Effect estimates for other covariates were in the expected direction with the exception of race. Non-white women had a reduced risk of cardiovascular disease compared to white women, which is different from national estimates but consistent with other studies using WHI data (Manson et al., 2003).

Among the sub-set of the women living in metropolitan statistical areas (44%), after adjustment for neighborhood SES, the effect of years of EAB infestation on CVD risk was virtually unchanged and remained highly significant (HR = 1.42, 95% CI: 1.36–1.50).
When we re-estimated our model including only counties that were ever infested with EAB, the hazard ratio was reduced but remained highly significant (HR = 1.25, 95% CI: 1.20–1.31) (Table 2, EAB counties only). This suggests that the hazard ratio from the full model may have been influenced by uncontrolled differences between EAB and non-EAB counties. Therefore, the hazard ratio estimated from only counties that were ever infested with EAB is the most defensible estimate of the impact of EAB on cardiovascular disease.

4. Discussion

In this prospective study, loss of trees from EAB was associated with an increased risk of CVD, which is consistent with our previous ecological study (Donovan et al., 2013) and other studies demonstrating an association between the natural environment and cardiovascular disease (Pereira et al., 2012; Tsao et al., 2014; Villeneuve et al., 2012; Wilker et al., 2014). It is important to note that our study, in isolation, does not provide direct evidence that trees offer a protective effect for cardiovascular disease, as we studied the health impacts of the loss of trees not the presence of trees. Our results are consistent with past studies than have identified negative health impacts of ecological degradation (Sieswerda et al., 2001; Speldewinde et al., 2009). If tree loss has negative health consequences, then, intuitively, it would seem reasonable to conclude that planting or retaining trees would have a positive impact on public health. Indeed, it is difficult to imagine a scenario in which tree loss has a negative effect on public health, but the presence of trees has no public-health benefits. However, little is known about the mechanisms linking trees and cardiovascular disease, so our results should be interpreted with caution. We believe our results suggest that the loss of trees is a risk factor for cardio-vascular disease in post-menopausal women. We also believe that our results suggest that trees offer a protective effect for cardiovascular disease, but the strength of evidence for this conclusion is lower. However, demonstrating that the loss of trees is a risk factor for cardiovascular disease strengthens the overall evidence that exposure to greenness may offer a protective effect for cardiovascular disease.

Our results do not provide direct insight into the mechanisms linking trees and cardiovascular health. However, the coefficient on EAB infestation was significant even after controlling for recreational energy expenditure, which suggests that, at least in post-menopausal women, the relationship between trees and cardiovascular disease is not solely mediated by exercise.

The EAB hazard ratio was attenuated, when we confined our analysis to counties that were infested with EAB by the end of the study period. This suggests that EAB infestation may have been somewhat confounded by unobserved differences between women living in counties infested with EAB and those living in non-infested counties. Therefore, we believe the hazard ratio for EAB-only counties (HR = 1.25, 95% CI: 1.20–1.31) is the most defensible estimate of the impact of EAB on cardiovascular-disease risk.

Our results may reflect survivor bias. Women were 50–79 at recruitment, so a disproportionate number of high-risk minority women may have died before they could be recruited into the study or were excluded on recruitment (83% of women included in
the analysis were white, compared to 77% of excluded women). Survivor bias may also explain the unexpected association between race and CVD in our models.

Our study has several limitations. Although we used individual-level health data, our measure of EAB exposure is county level. We don't know whether a particular woman lived in an area with many or few ash trees. Similarly, we don't know a woman's exposure to a given amount of tree loss. For example, one woman may spend several hours a day outside, whereas another may rarely go outside. Therefore, our results should be interpreted as the aggregate effect of tree loss on cardiovascular-disease risk.

Our natural-experimental study design has some limitations. We make use of individual-level outcome data, but our exposure variable is county level. We do not know an individual's exposure to tree loss. However, the scale of our exposure variable does match the scale of possible policy remedies. For example, if tree loss is a risk factor for cardiovascular disease, then a public-health intervention—a tree-planting program, for example—would likely occur at the city or county level.

5. Conclusion

Studying the health benefits of the natural environment can be problematic, as experimentally manipulating the natural environment is often costly or impractical, and the association between the natural environment and public-health outcomes is prone to confounding. We address these issues by making use of a natural experiment—the spread of the emerald ash borer—to study the relationship between tree loss and cardiovascular disease in the Women’s Health Initiative. Future studies could fruitfully take advantage of other natural experiments to study the relationship between nature and health. At the national or international scale, invasive species and climate change will cause major changes in the natural environment. Coincidentally, for example, ash trees in Europe are being killed by a fungus (Hymenophyphus fraxineus). At a smaller scale, green-infrastructure projects—for storm-water management, for example—may present opportunities to quantify the impact of improvements to the natural environment on public health. Conversely, residential and industrial development may provide opportunities to study the effect of loss of natural amenities.

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