Environment International 107 (2017) 147–153

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Do air pollution and neighborhood greenness exposures improve the predicted cardiovascular risk?☆

Maayan Yitshak-Sade[a,c], Itai Kloog[b], Victor Novack[c,*]

[a] Exposure, Epidemiology, and Risk Program, Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[b] Department of Geography and Environmental Development, Faculty of Humanities and Social Sciences, Ben-Gurion University, Beer Sheva, Israel
[c] Clinical Research Center, Soroka University Medical Center, Beer Sheva, Israel

ARTICLE INFO

Keywords:
Air pollution
Neighborhood greenness
Cardiovascular risk
Stroke
Myocardial infarction

ABSTRACT

Background: Numerous studies show associations between exposure to Particulate Matter and Cardiovascular disease (CVD). Current cardiovascular equations incorporate the major risk factors for CVD. The patients' environment, however, is not incorporated in these equations.

Methods: In a retrospective analysis, we assessed the contribution of neighborhood greenness and particulate matter (coarse-PM and PM < 2.5 μm–$PM_{2.5}$) to the development of CVD by analyzing the change in prediction abilities. We included members of the largest health-care provider in Southern-Israel, who had at least one cardiovascular risk factor (dyslipidemia, diabetes, hypertension or smokers). PM exposure and neighborhood greenness (Normalized Difference Vegetation Index-NDVI) were assessed by satellite-based models. We used pooled logistic mixed regressions to obtain the CVD risks including conventional risk factors (i.e. age, gender, blood-pressure, etc.) and measured the model performance with and without PM and NDVI.

Results: We included 23,110 subjects, of whom 12% had CVD. Coarse-PM exposure was associated with stroke and Myocardial-Infarction (MI) (OR 1.02,$p < 0.01$ for both). NDVI was associated with MI: OR 0.72($p < 0.01$) for NDVI 0.1–0.2; and OR 0.52($p = 0.270$) for NDVI > 0.2. The c-statistics slightly improved from 77.30%–77.40% for the prediction of MI ($p = 0.004$) and from 75.60%–75.76% for the prediction of stroke ($p = 0.027$). Calibration was fair in all models. The associations were partially mediated through the patients' comorbidities.

Conclusion: The negligible improvement in the prediction performance, despite significant associations with PM and NDVI, may be due to partial mediation of these associations through the conventional cardiovascular risk factors, suggesting the importance in assessing the environmental effects on more basic physiological pathways when addressing the contribution to the cardiovascular risk.

1. Introduction

Decades ago, the Framingham Heart Study team has published prediction models for the estimation of 10-year risk of developing coronary heart disease (Wilson et al., 1998). Over the years, additional prediction equations and adjustments of the score were developed to improve the models performance in different populations (Conroy et al., 2003; Hippisley-Cox et al., 2007; Ridker et al., 2007).

All risk scores incorporate known predictors proven as risk factors for the development of cardiovascular disease (CVD) (D'Agostino et al., 2008). The most common predictors include age, gender, cholesterol levels, diabetes and smoking status. Yet, beyond these well known clinical factors, there is a plethora of the personal exposures that might influence the CVD risk. Ultimately, the human health is determined by the interaction between the human genome and the environment in its broadest definition (Athersuch and Keun, 2015).

Numerous studies show associations between exposure to Particulate Matter < 10 μm (PM_{10}) and < 2.5 μm in diameter ($PM_{2.5}$) and CVD, usually assessing an increased risk of acute events following the acute increase in exposure (Brook et al., 2004; Mateen and Brook, 2011; Vodonos et al., 2015; Yitshak Sade et al., 2015a, 2015b). Moreover, in recent years, several studies have demonstrated a link between the neighborhood density of the green spaces (e.g. parks) and cardiovascular health (Hu et al., 2008; Pereira et al., 2012). However, the exact pathophysiological pathway question between long term environmental exposure and the development of the disease is not fully

☆ The authors have no competing interests to declare.

* Corresponding author at: Soroka Clinical Research Center, Soroka University Medical Center, Beer Sheva 84101, Israel.
E-mail address: victorno@clalit.org.il (V. Novack).

http://dx.doi.org/10.1016/j.envint.2017.07.011
Received 15 March 2017; Received in revised form 13 July 2017; Accepted 13 July 2017
0160-4120/

elucidated. Two models can be proposed, the detrimental effect can either be mediated through the increase in the conventional risk factors burden or be an independent direct effect. In the former model, we can expect an improvement in the discriminatory ability of the cardiovascular prediction models (already accounting for the conventional risk factors) with the inclusion of air pollution exposure when air pollution is properly assessed across space and time.

In this large population study, we aimed to assess the contribution of green space and PM exposure over 10 years to the development of CVD by analyzing the change in prediction abilities of conventional CVD models.

2. Methods

2.1. Study population

This study was approved by the institutional review board of Soroka University Medical Center before data collection. We included adult members of Clalit Health Services (CHS), residing in Southern Israel between the years 2003–2012, who had at least one of the following cardiovascular risk factors: dyslipidemia, diabetes, hypertension or being known smokers. CHS is the largest health care provider in the area, covering approximately 70% of a population of 730,000 residents. The population in South Israel comprises two main ethnic groups: urban Jews (80%) and Bedouin Arabs (20%). The Bedouin-Arabs are predominantly rural and approximately 40% of them reside in temporary housing.

Subjects with no documented address, subject without documented lab results in the follow up period and children (< 18 years) were excluded from the analysis.

The following patient data was obtained from the computerized database of CHS and Soroka University Medical Center (SUMC): age, gender, ethnicity, hospitalizations diagnoses, chronic comorbidities, smoking status, lab results and medications purchases. Socio-economic status (SES) was assigned based on the subjects' home address and stratified according to the definitions of the Central Bureau of Statistics assigning SES level in a scale of one to ten (Central Bureau of Statistics, 2001).

2.2. Study outcomes and risk factors

The study outcomes were identified using the hospitalization diagnoses: acute stroke (ICD9-CM 432–435) and acute myocardial infarction (MI) (ICD9-CM 410). SUMC is the only medical center providing acute neurological and cardiology care in the area; therefore all the patients with acute stroke or MI are referred to SUMC.

The cardiovascular risk factors considered in the analysis were determined a-priory based on the predictors used in the Framingham score (D'Agostino et al., 2008), the southern European score (Conroy et al., 2003) and the American College of Cardiology, American Heart Association equation (Goff et al., 2014). Similar to the original models, our models included age, gender, systolic-blood-pressure (SBP), smoking, lipids status, and diabetes. We added an adjustment for SES and ethnicity.

Diabetes was established in the presence of one of the following: physician confirmed diagnosis, glucose lowering medication purchase, two or more measurement of fasting glucose ≥ 126 mg/dL or HbA1c > 6.5% (American Diabetes Association, 2014). *Dyslipidemia* was established in the presence of one of the following: physician confirmed diagnosis, lipid modifying medication purchase, two or more measurement of low density lipoprotein ≥ 160 mg/dL or total cholesterol > 200 mg/dL. *Arterial hypertension* was established in the presence of one of the following: physician confirmed diagnosis, documented purchase of calcium blockers among patients who are not treated with Verapamil hydrochloride; beta blockers among patients without ischemic heart disease, congestive heart failure or atrial fibrillation; Verapamil hydrochloride, Angiotensin Converting Enzyme inhibitors, thiazides or Angiotensin II receptor blockers among patients without atrial fibrillation; or alpha blockers among patients without a confirmed diagnosis of benign prostate hypertrophy.

The incidence year for the given risk factor was determined as the year of first documented laboratory results, purchase of the relevant medication or physician diagnosis.

All laboratory results, SBP measurements, and smoking status were obtained from physicians visits in the primary clinics. For laboratory results and SBP, part of the subjects had multiple recordings per year and others did not have records of measurements for each follow-up year. Multiple annual recordings were averaged annually. The majority of the subjects (80%) had at least one measurement in the first, second and third quarters of the 10 year study period, and the median proportion of person years with available measurements per subject was 66%. 38% of the person years did not have records of measurements. In the absence of a measurement in a certain year, imputation was made by applying the subject's measurement from the closest available year.

2.3. Environmental data

Southern Israel (Negev) is a desert area, characterized by high levels of PM and frequently subjected to dust storms (Peters et al., 2001), which can increase daily PM_{10} significantly above the 50 mg/m^3 threshold defined by the World Health Organization (Ganor et al., 2010). PM_{10} concentrations during dust storms can reach levels as high as 4200 mg/m^3 (Stafoggia et al., 2008). Semi-arid lands, such as the Negev desert, are characterized by sparse or absence of vegetation cover. However, the land surface is often covered by biological soil crusts (combination of bacteria, fungi, and green algae) which increase NDVI values (Burgheimer et al., 2006). In the Negev, the biological soil crusts have the highest contribution to the overall NDVI signal. The rest of the variation in the signal is due to trees and vegetation cover that changes depending on the season (Schmidt and Karnieli, 2000). In urban areas, where the majority of the population reside, there are trees and bushes maintained by the municipalities.

2.3.1. Air pollution

Coarse PM and $PM_{2.5}$ daily average concentrations were estimated using a hybrid satellite based model incorporating daily satellite remote sensing data and classic land use regression (LUR) methodologies at 1 × 1 km spatial resolution. In Brief, to estimate PM_{10} and $PM_{2.5}$ concentrations in each grid cell on each day, the AOD-PM relationship was calibrated for each day using data from grid cells with both monitor and AOD values using mixed models with random slopes for day and nested regions in addition to the spatial and temporal predictors such as in a classic LUR. A second model was used to estimate exposures on days when AOD measures were not available (due to cloud coverage, Dust storm days, etc.). The final model was fit with a smooth function of latitude and longitude and a random intercept for each cell (similar to universal kriging) that takes advantage of associations between grid cell AOD values and PM data from monitors located elsewhere, and associations with available AOD values in neighboring grid cells. For more in depth description please refer to Kloog et al., 2015 and Yitshak Sade et al., 2015a, 2015b (Kloog et al., 2015; Yitshak Sade et al., 2015a, 2015b). The model allows us to reliably reconstruct residence levels of air pollution across Israel. Exposure estimates were calculated and assigned for each patient based on their geocoded home address.

2.3.2. Meteorology

Daily data on air temperature and relative humidity for the study period were obtained from the monitoring site located in the center of the largest city in Southern Israel.

2.3.3. Neighborhood greenness

Neighborhood greenness is an ecological exposure that has been