ASSOCIATIONS BETWEEN EXPOSURE TO AIR POLLUTION AFTER A DUST EVENT AND HOSPITALIZATIONS.

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Dedication

Dedicated to my wonderful and deeply missed Mother Luz Maria Cuellar Ayala (1936-2017) and my Father Donato Molina Razo (1934-2017), may they rest in peace. My wonderful parents taught me that with God's direction, love, hard work and perseverance, we can succeed in life. My dad had Alzheimer's disease and knowing the pain of what families go through and the terrible feeling the patient must have, I also dedicate this work to those patients, families and caregivers who wish a cure is nearby.

Love you and miss you so much!

ASSOCIATIONS BETWEEN EXPOSURE TO AIR POLLUTION AFTER A DUST EVENT AND HOSPITALIZATIONS.

by

ESTRELLA DE JESUS HERRERA-MOLINA, MS.

DISSERTATION

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Abstract

The Southwestern region has been identified as one of the most persistent dust producing regions of North America. Exposure to inhalable particulate matter (PM_{10}) originating from desertic landscape during dust events / dust exposures (DEs) can reach hazardous levels. El Paso, Texas's ambient air has reached hazardous levels of PM_{10} above 4000 $\mu g/m^3$ with near zero visibility due to these natural events. There are very few prior studies in the southwestern United States pertaining to the associations between exposure to atmospheric aerosol after DEs and hospitalizations, nor are there many epidemiological studies globally in dusty environments where most of the atmospheric aerosol is soil derived. Therefore, the relationship between dust exposure and hospital admissions due to neurodegenerative diseases (ND), mental illness (MI), Valley fever (VF), Asthma, Coronary Atherosclerosis, Associated Diseases (AD), and ICD-9 category and the modifying effect of the demographic factors (age, income and education attainment) was assessed at the County of El Paso, TX.

A conceptual model with all predictive and response variables with model equations was performed to analyze most factors influencing hospitalizations during DE in El Paso. The predictive model was able to describe factors related to hospitalization during blowing dust events and to predict future hospitalization rates based on dust events. This model analysis may be applied using data mining in other arid locations. Descriptive data results showed that from 2010-2014 there were more hospitalizations in a DE (62%) than in a regular day (RD) (38%). During DE there was a factor of 11.38% more hospitalizations due to acute conditions; 11.81% more from chronic conditions and 1.53% more from mental health than in a regular day.

An intelligent tool was developed using Case-based Algorithm based on Ant Colony Algorithm and the programming language Java (J2SE). Proposed algorithm helps to improve the

ambulance routing demand by 35% of cases during and after a DE in El Paso County. Using Bluetooth, it is possible to use our proposed model of ambulances in an emergency related to a severe dust storm. In addition, a Kriging Model of incidence with birth cases (single liveborn, delivered by cesarean section) was performed, and shows that in the predicted future of increasing dust storms there will be a necessity of more ambulances to transport more patients during a dust event.

Using a Poisson regression, it was found that the relative risk of hospitalizations due to VF, coronary atherosclerosis, genitourinary diseases, ND, injury and poisoning, circulatory system conditions, respiratory system diseases, births, septicemia, AD and all ICD-9 admissions were significantly positively associated with DE (through increases of at least 100 micrograms per cubic meter of daily maximum hourly PM_{10}, and/or increases of at least 10 mph in daily hourly average wind speed in El Paso, Texas between 2010 and 2014, at different lag periods after exposure, indicated from higher to lower significant risk. Patients with medium and low socio-economic status showed a significant need to pay for their chemotherapy services; circulatory system conditions; aftercare services; and injury and poisoning associated with a DE. As age decreases, the chances of a patient being hospitalized due to AD after a DE increases.

Recommendations for reduction of outdoor and indoor exposures to DE should be generated for El Paso County. Public policies and individual actions are essential to reduce the human health effects of DE. Due to forecasts that suggest DE will continue to rise an additional urgency of public policies to reduce DEs need to be taken, such as physical wind erosion control measures such as paving roads and reforestation. Individual actions need to be taken e.g., avoiding outdoor activities, wearing a mask and eye coverings during a DE, improving household insulation, and raising an environmental conscience.

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THE UNIVERSITY OF TEXAS AT EL PASO
Office of the Vice President for Research and Sponsored Projects
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El Paso, Texas 79968-0587
phone: 915 747-8841 fax: 915 747-5931

FWA No: 00001224

DATE:	August 8, 2016
TO:	Estrella Herrera, M.S.
FROM:	University of Texas at El Paso IRB
STUDY TITLE:	[939896-1] Associations between exposure to air pollution, and the incidence of cardiovascular and respiratory diseases in El Paso Metropolitan area.
IRB REFERENCE #:	College of Engineering
SUBMISSION TYPE:	New Project
ACTION:	DETERMINATION OF EXEMPT STATUS
DECISION DATE:	August 8, 2016
REVIEW CATEGORY:	45 CFR 46.101(b)(4)

Thank you for your submission of New Project materials for this research study. University of Texas at El Paso IRB has determined this project is EXEMPT FROM IRB REVIEW according to federal regulations.

Your study has received approval at UTEP but may require further review and approval from the institutions listed in your application. Please verify with their IRB prior to engaging in research. Please ensure to forward a copy of all IRB approval letters to the UTEP IRB office.

Exempt protocols do not need to be renewed. Please note that it is the Principal Investigator's responsibility to resubmit the proposal for review if there are any modifications made to the originally submitted proposal. This review is required in order to determine if "Exemption" status remains.

We will put a copy of this correspondence on file in our office.

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Chapter 1: Introduction

Dust Storms and Particulate Matter

In southwest North America, dust storm frequency is increasing (Tong et al., 2017) and the seasonality of dust events is changing (Hand et al., 2016). Hand et al. (2016), based on their springtime trend analyses at southwestern USA, indicate that regional mean $PM_{2.5}$ (particulate matter with mean aerodynamic diameter smaller than 2.5 micrometers) dust concentrations have increased 5.4% per year ($p<0.01$) from 1995 to 2014, especially in March, reflecting in an earlier onset of the spring dust season by 1 to 2 weeks over the 20-year time period from 1995 to 2014. In addition, Tong et al. (2017), report a "direct evidence of rapid intensification of dust storm activity over American deserts in the past decades (1988–2011)". They estimate that the frequency of windblown dust storms has increased 240% from 1990s to 2000s and with it the infection rate of Valley fever, a dust-related disease, increased 800% from 2000 to 2011.

My study focuses on El Paso, Texas, the largest city in the U.S. portion of the Chihuahuan Desert. The northern Chihuahuan Desert is the one of the most significant sources of dust in the Western Hemisphere (Lee et al., 2009; Novlan et al. 2007; Prospero et al., 2002). The high frequency of dust events (DE) in these regions are associated with large-scale dry climate (climate type -according to the Köppen climate classification system- hot desert (BWh) (Lee et al., 2012). In this region, agricultural lands, ephemeral lakes, and dry riverbeds have been identified as the main sources of the dust from this desert that is blown into El Paso, Texas (Lee et al., 2009 & Rivera Rivera et al., 2010). In El Paso, dust events have been identified as important environmental hazards (Lee et al., 2009 & Novlan et al., 2007). Based on data collected at the El Paso International Airport from 1932 through 2005, dust events in El Paso occur on average 15 times a year and last an average of 2 hours each (Novlan et al., 2007). In this region, dust events occur most commonly

during the months of December through May when ambient air is dry and winds can reach high speeds (>25 mph), blowing primarily from the westerly and southwesterly directions (Novlan et al., 2007). At wind speeds greater than 25 mph, dust can be raised into the atmosphere and/or transported for long distances by synoptic-scale weather systems (horizontal length scale of the order of 1000 kilometers or more), which results in widespread exposure to ambient air particle mixtures (Lee et al., 2009). High wind speed indicates the predominance of coarse particles and can be used as a surrogate variable for the PM_{10} (particulate matter with mean aerodynamic diameter smaller than 10 micrometers) dust in El Paso (Staniswalis et al., 2005).

Poor visibility is a side effect of dust events. Visibility can easily be reduced from 0 to 3 miles with PM_{10} >140 $\mu g/m^3$ and wind speed >10 mph. For example, on January 16th of 2012, the visibility was reduced to 1.3 miles with a wind speed of 14.8 mph, and PM_{10} of 141.1 $\mu g/m^3$. Flight delays, closed roads and difficulty to recognize distant objects by unaided eye beyond 0-3 miles (depending on the severeness of low visibility) such as distant buildings, trees, hills, incoming traffic are some effects of low visibility. During such conditions the sky looks brownish (Horvath, 1998).

Health Effects

The major sources of inorganic particulate matter (PM) in the dry region of Texas even on non-dusty days are fugitive dust from unprotected surfaces, including geologic materials from the surrounding desert and unpaved roads, and include trace elements from re-suspension of deposited metals previously emitted from several regional point sources (Gill et al., 2009 & Van Pelt & Zobeck, 2007). An example of point sources of anthropogenic aerosols in the region are petroleum refineries within this study area. Petroleum refineries are documented in many cases as having serious adverse effects to the land and population's health (Oil Change International, 2018). Air

toxins emitted from petroleum refining (La, Na, K, V, Ni, Co, Cu, Zn, Ga, As, Se, Mo, Cd, Sn, Sb, Ba, W, and Pb) (Bozlaker et al., 2017) can cause cancer, birth defects, chronic conditions like asthma (EPA, 2018) and damages in learning and memory to populations exposed to these elements (Bozlaker et al., 2017). Furthermore, Khan and Strand (2018) showed that road dust elements most frequently referenced in articles are Pb, platinum-group elements (Pt, Rh, and Pd), Al, Zn, V, and polycyclic aromatic hydrocarbons which have harmful effects.

Much less is known about the overall health effects of atmospheric aerosol particles during a DE compared to the thousands of studies of urban, industrial, and traffic-derived PM health effects (Morman & Plumlee, 2014). In recent years, an increasing trend has been observed in the number of studies investigating the associations of blowing dust events on human health, specifically the inorganic aerosol particles that are of desert origin which have in common an inflammatory response pathway from the body. One of the associations is the relationship of hospital admissions during dust storms to cardiovascular disease (Al et al., 2018; Behzad et al., 2018; Ebrahimi et al., 2014; Khaniabadi et al., 2017; Morman et al., 2013), respiratory diseases (Schweitzer at el., 2018; Yu et al., 2012) and diabetes (Chan et al., 2018), but fewer on mental health and other diseases. Studies on this subject are being mostly done in Asia and Middle East (Al et al., 2018; Behzad et al., 2018; Chan et al., 2018; Ebrahimi et al., 2014; Khaniabadi et al., 2017; Morman et al., 2013; Schweitzer at el., 2018; Yu et al., 2012) which have reported significant associations.

Al et al. (2018) investigated the effects of desert dust storms and climatological factors on mortality and morbidity of cardiovascular diseases in patients admitted to emergency department in Gaziantep, Turkey. They concluded that acute coronary syndrome (ACS) was increased by the presence of dust storms, PM_{10} elevation, and maximum temperature. Ebrahimi et al. (2014)'s

findings showed a significant increase in emergency admissions for cardiovascular and respiratory diseases during dust storms in Sanandaj, Iran. Khaniabadi et al. (2017) studied hospital admissions in Iran for cardiovascular and respiratory diseases attributed to dust storms and demonstrated a significant impact of air pollution on people. Kanatani et al. (2010) found that desert dust exposure is associated with increased risk of asthma hospitalization in children in Toyama, Japan. Chan et al. (2018)'s study showed that Asian dust storms were positively associated with diabetes hospital admissions for women. Studies by Keil et al. (2016 a & b) reviewed the health effects from exposure to atmospheric mineral dust near Las Vegas, NV, USA. They found that brain CD3+ T cells and natural killer cell activity were significantly reduced and suggested that dust from this area may present a potential health risk.

The main mineral component of dust is silica or Silicon Dioxide (SiO_2). Liu et al. (2017) showed that exposure to silica as respirable dust has potential adverse effects on the blood-brain barrier (BBB) -which serves as a barrier between the central nervous system (CNS) and the peripheral circulation. The brain tissue has very limited regenerative capacity which is a reason why it is protected by the BBB. The BBB serves as a natural barrier between the central nervous system (CNS) and the peripheral circulation and maintains the brain homoeostasis and neuronal microenvironment. It consists of a vascular structure of brain micro vessel endothelial cells (BMECs) coupled with astrocytes and pericytes in the brain (Disdier et al., 2015). It is demonstrated that SiO_2 passes through the BBB structure and induces inflammation by reactive oxygen species (ROS) and Rho-kinase (ROCK) pathways (Schreibelt et al., 2007). Silica also activates IL-1B secretion in human macrophages analyzed in media supernatants (SN) and in cell extracts (Cell) (Figure 1.1) (Dostert et al., 2008).

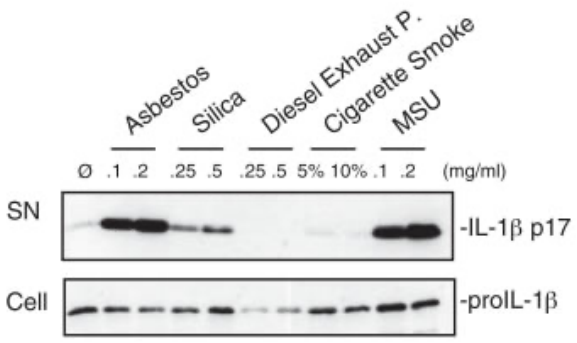

Figure 1. 1 Silica activates IL-1B secretion in human macrophages. Analyzed in media supernatants (SN) and in cell extracts (Cell). From Dostert et al. (2008)

This systemic inflammation could explain why silica dust (mostly present in dust events) shows effect on brain function (Sharma et al., 2009); decreases the number of brain CD3+ T cells after dust exposure with silica and heavy metals present in the southwest USA soil (Keil et al., 2016); reduces the immune response with PM of 4.6, 3.1, and 4.4 μm at the southwest USA (Keil et al., 2018); passes across the placental barrier and enters fetal liver and brain (Yamashita et al., 2011); had adverse mental health outcomes in retired factory workers (Jiang et al., 2014); incremented epithelial permeability in patients with silicosis who smoke (Nery et al., 1993); was associated with diabetes in women after exposed to Asian Dust Storms (ADS) (Chan et al., 2018); and increased hospitalizations during DEs for expected causes such as respiratory and cardiovascular disorders (Khaniabadi et al., 2017; Yu et al., 2012). In addition, a combination of SiO_2 exposure with several adverse factors such as hypertension, stress, and environmental toxicants could aggravate brain pathology and induce cerebrovascular toxicity by increasing pro-inflammatory responses and disturbing the BBB integrity (Sharma et al., 2013; Zhang et al., 2012).

In summary, Zhang et al. (2016) did a systematic review of global desert dust and associated human health effects (Figure 1.2), stating that “many study results suggest that the

allergic inflammation aggravated by desert mineral dust may be due to mineral elements (mainly SiO_2)" and that "it is widely accepted that desert dust has the capacity to (1) cause damage to the alveolar walls and bronchial epithelial cells through a direct physical effect; (2) influence oxidative stress and release of pro-inflammatory cytokines in respiratory epithelial cells; (3) damage DNA (the organic compounds and the insoluble particle-core might be the main contributors to DNA damage); and (4) cause a deterioration in pulmonary function".

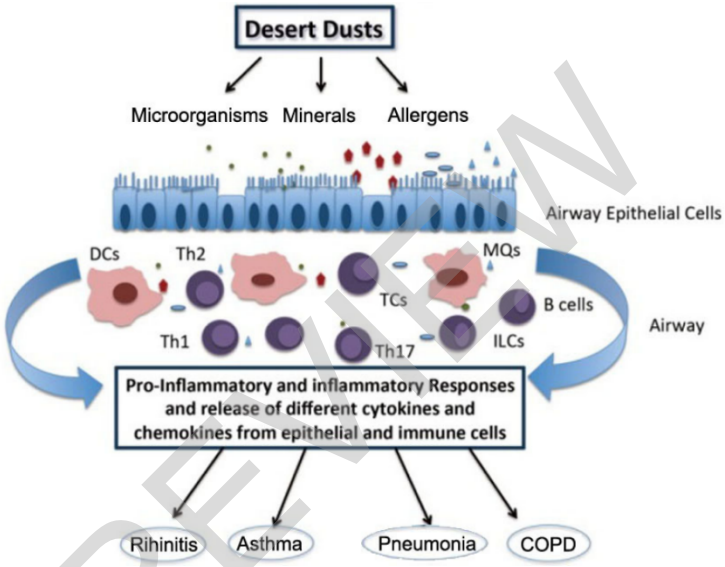

Figure 1. 2 Systemic inflammation mechanism due to desert dust. Diagram shows how desert dusts affect the respiratory and immune systems by causing a direct effect to the alveolar walls and epithelial cells; by influencing the oxidative stress; and release of pro-inflammatory cytokines. From Zhang et al., 2016.

Studies on DE health effects completed in the Chihuahuan Desert are very limited in number despite the abundance of dust storms in this geographical location. Rodopoulou et al. (2014) studied the associations of ambient particulate matter and ozone with hospital emergency room and admissions for respiratory and cardiovascular visits in adults in Dona Ana, NM. However, they did not specifically study the associations of natural PM during blowing dust events and the effects of PM on other diseases. Another analysis by Grineski et al. (2011) studied the

hospital admissions for asthma and acute bronchitis and if age, sex, and insurance status modified the effects of dust and low wind events in El Paso, Texas. They found that dust and low wind events were associated with increased chances of hospitalization for asthma and bronchitis amongst all ages and adults. Adults covered by Medicaid and without health insurance had higher risks of hospitalization for asthma and acute bronchitis.

Optimization of Ambulances Via Algorithms

Understanding if individuals are vulnerable to the effects of extremely high exposure to desert-originated PM during DEs is relevant for the communities living in the southwestern U.S., as well as for other similar areas where dust storms are common, and the need of efficient ambulance routes is essential (Mohammad et al., 2017). It is imperative that we understand this dynamic so that the proper regulations and planning can be implemented.

During disasters it is expected to have a large number of injured/sick people requiring medical aid at the same time; the response scenario is of the greatest importance. The ambulance usage can be improved by a smart routing (Talarico et al., 2014). Nowadays, digital maps are increasingly common to greatly improve the optimization of evacuations performed by emergency vehicles such as ambulances or fire trucks. With the progress that has been made in technology, these maps are becoming more sophisticated, in the way that they are able to find specific locations, draw routes and so forth. The objective of this part of the work is to develop a system to help create routes based on the emergencies given in El Paso, Texas using a system of neighborhoods of ants that allows them to create routes to take care of patients affected by a dust event or other types of emergencies in a quick way. The bio-inspired algorithms are a technique of artificial intelligence

focused on the solution of different problems, especially optimization problems (Kolavali & Bhatnagar, 2009).

Methodology and Aims

To fill these gaps in the literature,

- I analyze the health associations of dust events in El Paso County, Texas, an area with Köppen climate classification type BW [arid; Chihuahuan Desert of Texas (CDT)] using data from the Texas Hospital Inpatient Research Data files (RDF) at the Texas Department of State Health Services (TDSHS) from 2010-2014. This set of data classifies hospital admissions based on the Principal Diagnostic Code.
- I develop a bio-inspired algorithm system to help create ambulance routes based on the emergencies given in El Paso, Texas using a system of neighborhoods of ants that allows them to create routes to take care of patients affected by a dust event or other types of emergencies in a quick way.
- I study the association (day of and 7 days after) in El Paso, Texas, between elevated exposure of 100μg/m^3 increments in daily maximum of hourly PM_{10} and/or 10mph daily maximum wind speed increase (day of and 7 days after), representing dust exposure, and hospital admissions due to neurodegenerative disease (ND; Parkinson's, Alzheimer's, and Huntington's), mental illness (MI -depression and anxiety), Valley Fever (VF), Asthma, Coronary Atherosclerosis, other associated diseases which is the aggregated effect of the most frequent hospitalizations associated with at least 5% of hospitalizations and independently (AD; Respiratory Diseases, Circulatory System Diseases, Digestive Diseases, Genitourinary Diseases, Births, Encounter for antineoplastic Chemotherapy, Unspecified Septicemia, Other Chest Pain, Dehydration, Cellulitis and Abscess of Leg,

Osteoarthrosis, Diabetes Mellitus And Mental Disorders) and all ICD-9 categories by hospital admissions by Codes from the International Classification of Diseases, Ninth Revision (ICD-9) category and assess the mediating or moderating role of demographic factors (age, and SES -income, and educational attainment).

This research project is conducted by exploring the following three specific aims:

Specific Aim 1. Characterization of a preliminary predictive model to analyze the effects of dust events in a society with Köppen climate classification type BW and its long-term health effects.

Hypothesis: It is hypothesized that the proposed predictive model will be able to analyze involving factors related to hospitalization during DEs in a society with Köppen climate classification type BW in order to predict future hospitalization rates based on dust events. Several hospitalizations will increase due to DE.

Specific Aim 2. Creation of an efficient route of ambulances using an intelligent tool for decision making, via a bio-inspired algorithm at El Paso County during DEs from 2010-2014.

Hypothesis: It is hypothesized that the proposed algorithm will provide time effective routes during the expected high demand of ambulances on a DE day.

Specific Aim 3. Determine via a Poisson regression modeling if increasing increments of PM_{10} and/or wind speed during DEs is associated with an increase in hospital admissions due to acute or accelerated disease progression of ND, MI, VF, Asthma, Coronary Atherosclerosis, AD

(independently and in aggregation), and all ICD-9 categories and determine the mediating/moderating role of the demographic factors, in the County of El Paso, TX.

Hypothesis: It is hypothesized that the exposure to elevated PM_{10} and/or wind speed during DEs will be positively associated with hospital admissions due to ND, MI, VF, Asthma, Coronary Atherosclerosis, AD and all ICD-9 categories at different lag days, being the highest effect during the actual day of DE. SES will moderate the association with some hospital admissions due to elevated PM and/or Wind speed exposure during DE, with admissions being higher among individuals living in areas of lower SES. In addition, age will mediate the association between overall hospital admissions and air pollution exposure during DE.

Significance

My study is notable for both having been planned to include inpatient hospitalization and also being a more comprehensive study in that it investigates the associations of ambient particulate matter and maximum wind speed during DE due to acute or accelerated disease progression of ND, MI, VF, Asthma, Coronary Atherosclerosis, AD, and all-ICD-9-category diagnosis and the mediating/moderating role of age, gender, and health disparities by the SES in the desertic region of CDT. In addition, identifying the algorithm necessary to optimize the ambulance routes during the high demand in DEs at El Paso County. Few studies have been explicitly conducted to analyze the critical relationship between air quality and human health in the regions of CDT. This study's results will help to reduce not only the risks of the associated diagnosis but also mortality, morbidity, medical costs, health disparities and social and economic inequalities.

Therefore, it is important to study DEs health associations, because these events are expected to rise globally due to climate changes and the rise in desertification caused by natural and anthropogenic events. This could lead to a substantial increase in transport of foreign, invasive,