EXPOSITIONS ENVIRONNEMENTALES ET BIOMARQUEURS EN LIEN AVEC LE CANCER : LA PRISE EN COMPTE DES ESPACES D'ACTIVITÉ ET DE LA MOBILITÉ.

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OUTLINE

- The role of individual, contextual and environmental factors on cancer risk
- External exposome and cancer risk
- The importance of moving beyond static exposures
- Introducing the concept of functional exposomics
- Measuring dynamical exposures: introducing Kernel Density Estimation
- A motivating example: The Community of Mine study

THE ROLE OF INDIVIDUAL, CONTEXTUAL AND ENVIRONMENTAL FACTORS ON CANCER RISK

- Increasing evidence demonstrating the etiological role of multiple environmental exposures on cancer risk
- Also critical to improve outcomes among cancer patients (e.g. survival)
- For example, higher ambient air pollution exposure was associated with increased risk for lung cancer incidence and/or mortality.
  - Contributed to the 2013 International Agency for Research on Cancer (IARC) classification of particulate matter (PM) and outdoor air pollution as human carcinogens

Hamra GB, Guha N, Cohen A, Laden F, Raaschou-Nielsen O, Samet JM, et al. Outdoor particulate matter exposure and lung cancer: a systematic review and meta-analysis. Environ Health Perspect 2014;122:906–11.

ENVIRONMENTAL DETERMINANTS OF BREAST CANCER RISK

Air Pollution and Breast Cancer: a Review

Alexandra J. White [1] · Patrick T. Bradshaw [2] · Ghassan B. Hamra [3]

Summary Epidemiologic evidence to date suggests an association between breast cancer risk and NO_2 and NO_x, markers for traffic-related air pollution, although there was little evidence supporting associations for proxy measures of traffic exposure or for PM. More research is needed to understand the role of specific PM components and whether associations vary by tumor receptor subtype and menopausal status at diagnosis.

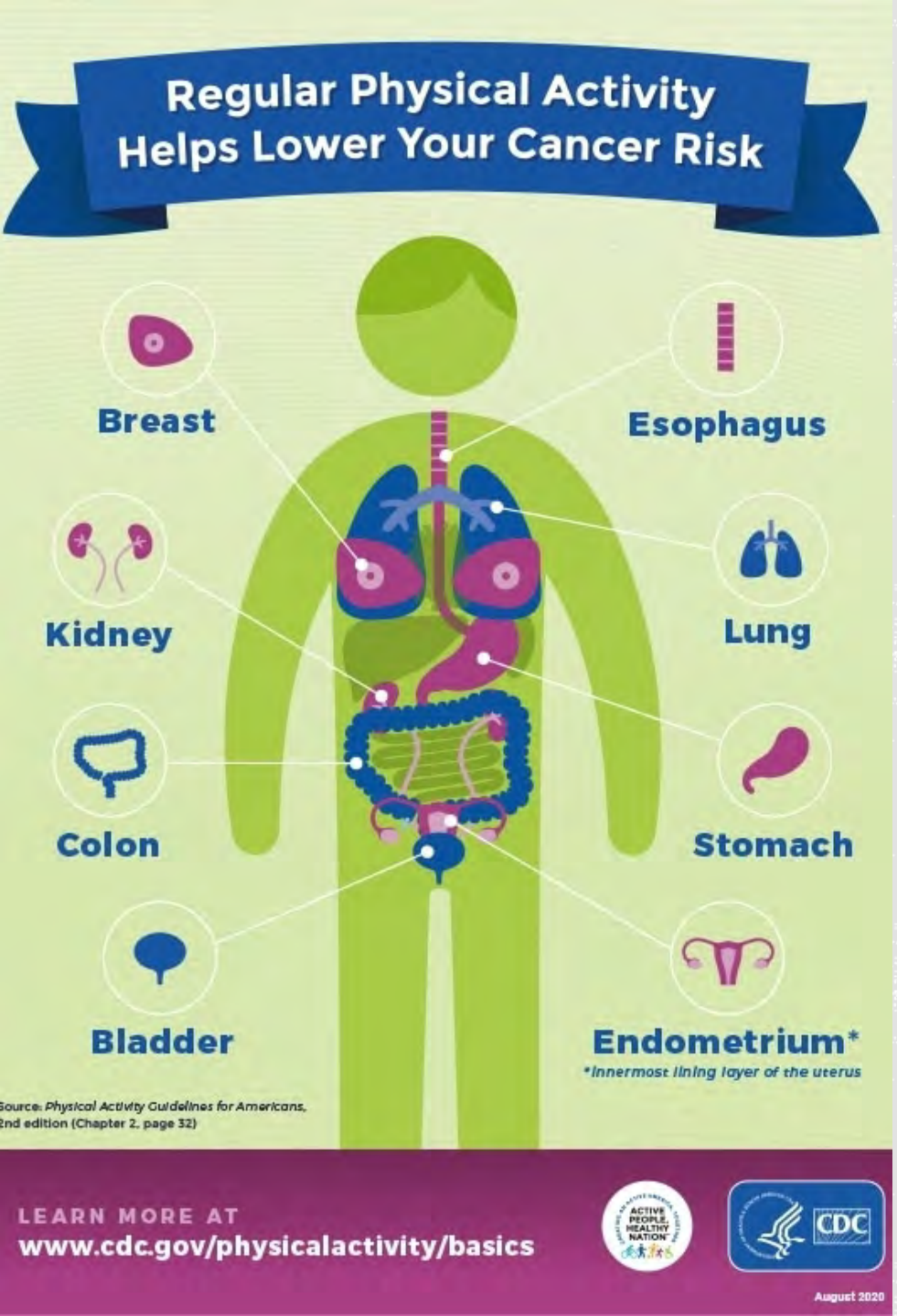
A Congener-specific and Mixture Analysis of Plasma Polychlorinated Biphenyl Levels and Incident Breast Cancer

Humberto Parada Jr,[a,b] Tarik Benmarhnia,[c] Lawrence S. Engel,[d,e] Xuezheng Sun,[d] Chiu-Kit Tse,[d] Eunha Hoh,[f] Andrew F. Olshan,[d,e] and Melissa A. Troester[d,e]

Review

Environmental Exposures during Puberty: Window of Breast Cancer Risk and Epigenetic Damage

Rama Natarajan [1,2], Dana Aljaber [1,†], Dawn Au [1,†], Christine Thai [1,†], Angelica Sanchez [1,†], Alan Nunez [1,†], Cristal Resto [1,†], Tanya Chavez [1], Marta M. Jankowska [3], Tarik Benmarhnia [4], Jiue-An Yang [3], Veronica Jones [1], Jerneja Tomsic [1], Jeannine S. McCune [1], Christopher Sistrunk [1], Stacey Doan [1,5], Mayra Serrano [1], Robert D. Cardiff [1,6], Eric C. Dietze [1] and Victoria L. Seewaldt [1,*]



PHYSICAL ACTIVITY AND CANCER RISK

- Physical activity is a critical determinant of population health
- Recreational physical activity is influenced by several multi-level factors such as:
  - Access to green space
  - Walkable and safe environments
  - Urban forms
- Non-mutually exclusive role of sedentary behaviors
- Higher levels of physical activity are linked to lower risk of several types of cancer

PHYSICAL ACTIVITY AND THE RISK OF CANCER

WCRF/AICR GRADING		DECREASES RISK		INCREASES RISK	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing	Physical activity[1]	Colorectum (colon) 2017[2]		
	Probable	Physical activity[1]	Breast (postmenopause) 2017[3] Endometrium 2013		
		Vigorous-intensity physical activity	Breast (premenopause) 2017[3] Breast (postmenopause) 2017[3]		
LIMITED EVIDENCE	Limited – suggestive	Physical activity[1]	Oesophagus 2016[4] Lung 2017 Liver 2015 Breast (premenopause) 2017[3]	Sedentary behaviours	Endometrium 2013[5]
STRONG EVIDENCE	Substantial effect on risk unlikely	None identified			

1 The exposure of physical activity includes evidence for all types of activity and all intensity levels.

2 The evidence for physical activity and colorectum is for colon cancer only – no conclusion was drawn for rectal cancer.

3 In addition to physical activity, there was sufficient evidence for the Panel to make a separate judgement for vigorous-intensity physical activity and breast cancer (pre and postmenopause).

4 The evidence for physical activity and oesophageal cancer includes unspecified, adenocarcinoma and squamous cell carcinoma.

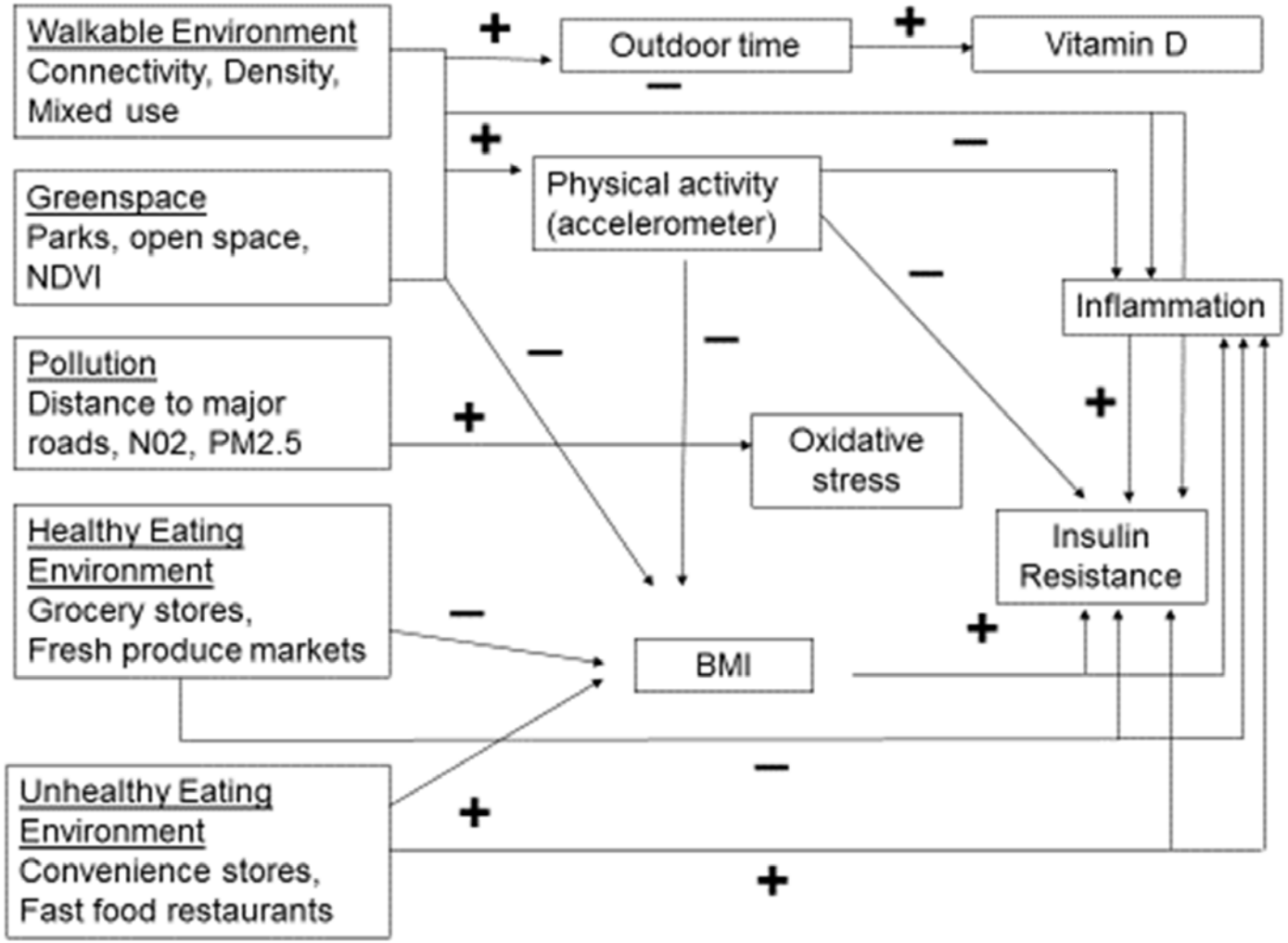
5 The evidence for sedentary behaviours and endometrial cancer was marked by sitting time.

HOW MIGHT PHYSICAL ACTIVITY BE LINKED TO REDUCED RISKS OF CANCER?

- Physical activity has many biological effects on the body, some of which have been proposed to explain associations with specific cancers:
  - Preventing high blood levels of insulin, which has been linked to cancer development and progression [**breast**, colon]
  - Reducing inflammation
  - Helping to prevent obesity, which is a risk factor for many cancers
  - Altering the metabolism of bile acids, decreasing exposure of the gastrointestinal tract to these suspected carcinogens
  - Improving immune system function

- McTiernan A, Friedenreich CM, Katzmarzyk PT, et al. Physical activity in cancer prevention and survival: A systematic review. Medicine and Science in Sports and Exercise 2019; 51(6):1252-1261
- Winzer BM, Whiteman DC, Reeves MM, Paratz JD. Physical activity and cancer prevention: a systematic review of clinical trials. Cancer Causes and Control 2011; 22(6):811-826

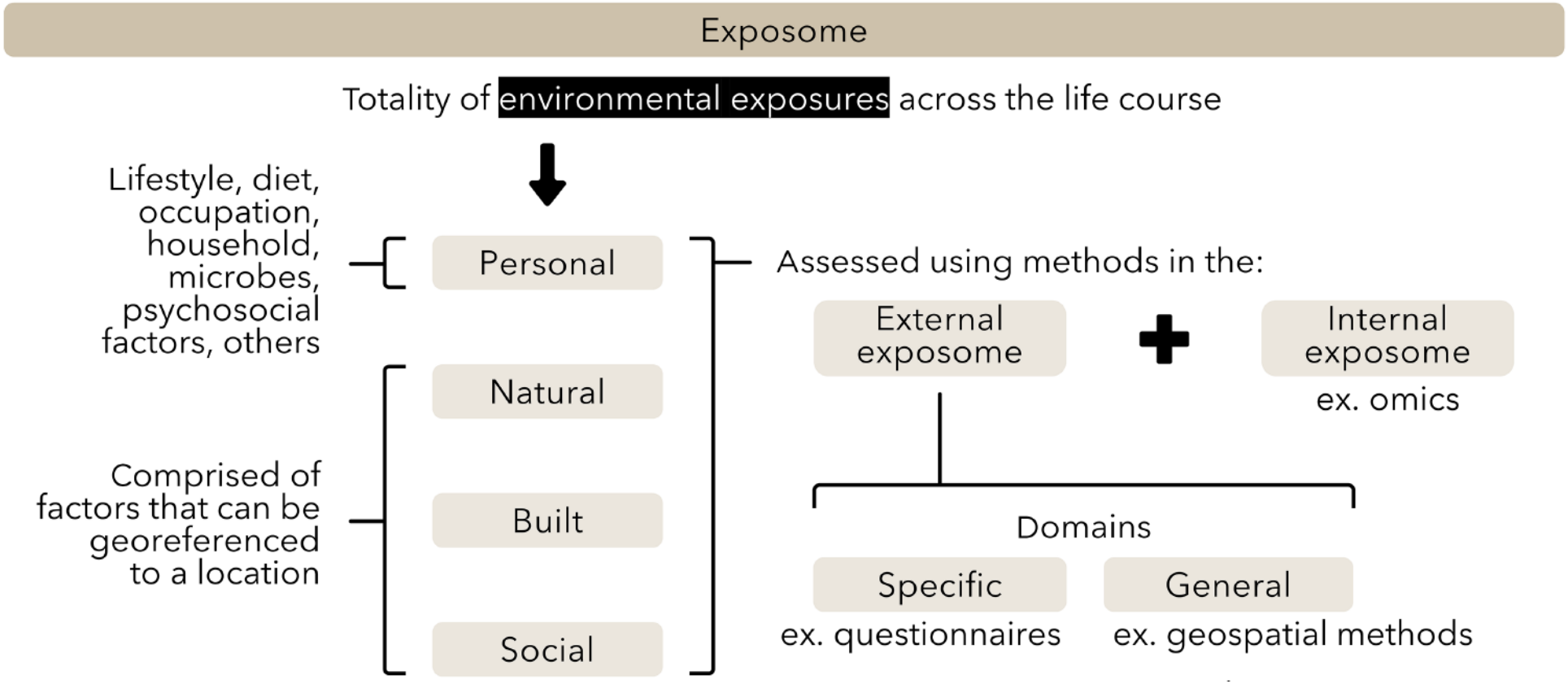
The role of built environments on biomarkers of cancer risk



MECHANISMS BY WHICH BUILT ENVIRONMENT EXPOSURES CAN INCREASE CANCER RISK

1. **Promotion of healthy behaviors**
2. **Reducing exposures to environmental stressors**

EXTERNAL EXPOSOME AND CANCER RISK



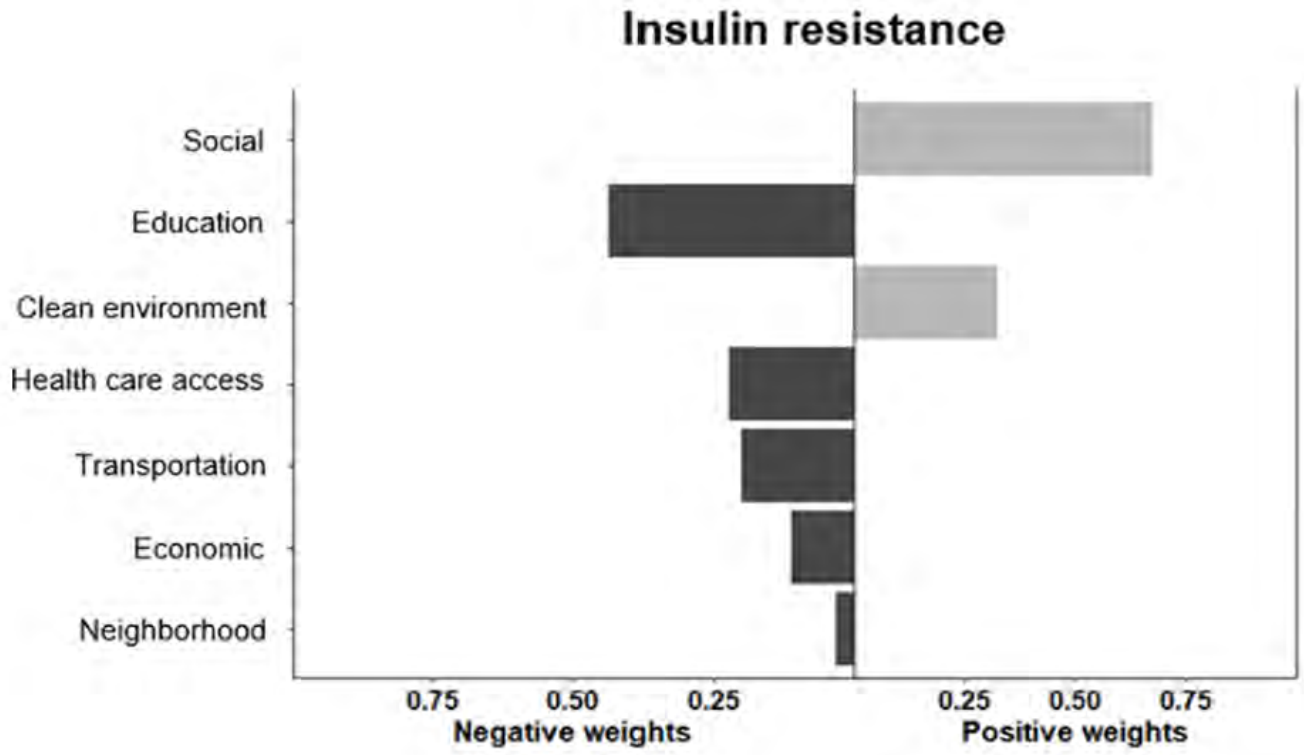
How do environmental characteristics jointly contribute to cardiometabolic health? A quantile g-computation mixture analysis

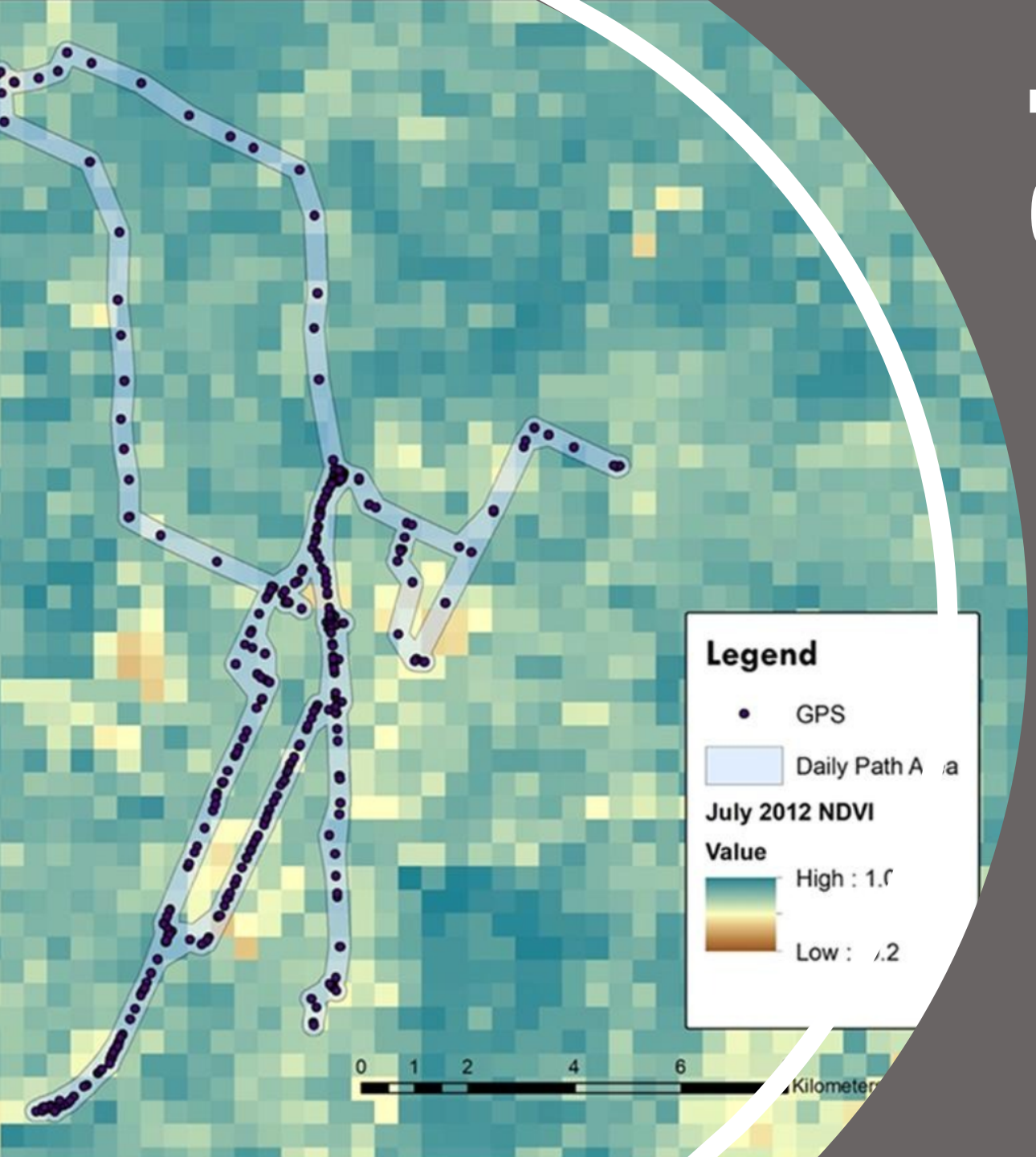
Noémie Letellier [a,*], Steven Zamora [a], Jiue-An Yang [b], Dorothy D. Sears [c,d,e], Marta M. Jankowska [b], Tarik Benmarhnia [a]

Table 3
Quantile g-computation estimates for the association between increasing all the environmental characteristics by a quartile within the overall mixture (N = 570).

Cardiometabolic outcomes	Quantile g-computation estimates*
	β (95 % CI)
Insulin Resistance (N = 566)	−0.09 (−0.18–0.01)
	RR (95 % CI)
Hypertension	0.93 (0.69–1.24)
Obesity	0.81 (0.64–1.02)
Diabetes (N = 566)	0.59 (0.36–0.98)
MetS (N = 565)	0.87 (0.64–1.19)

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; MetS: Metabolic Syndrome.





THE IMPORTANCE OF CONSIDERING ACTIVITY SPACE

- The general principle of an activity space is that it provides a dynamic measure of the environment by describing the locations and spaces an individual interacts with as a result of their activities
- Around key points including home and work locations and extends to locations such as food outlets, child's schools, parks, and social meeting points.
- **Locations may be weighted by the frequency, regularity, and duration at which they are visited (Perchoux et al., 2013).**
- The concept of the activity space was introduced in 1970 when space-time geography was used to assess daily travel behaviours (Hägerstraand, 1970)
- Critical to understand social inequities in health

INTRODUCING THE CONCEPT OF FUNCTIONAL EXPOSOMICS

- Price et al. (2022) defined an environmental exposure as " *a contact between external factor(s) (agent) and a biological entity occurring at an (exposure) interface*"
- The "exposome" can also be seen as the measure of the totality of contact events that a person experiences
- Contact events are dynamic in space and time and can occur in aggregate such as with exposure mixtures (e.g., multiple types of external factors) and/or multiple contact events, which are characteristic of real-world experiences.
- **Functional exposomics** is then defined as the "systematic and comprehensive study of environmental exposure–phenotype interaction over a defined time-period"

Price EJ, Vitale CM, Miller GW, David A, Barouki R, Audouze K, et al. Merging the exposome into an integrated framework for "omics" sciences. iScience 2022; 25:103976.

MEASURING DYNAMIC EXPOSURES

VARIOUS APPROACHES
(INDIVIDUAL INFERENCE)

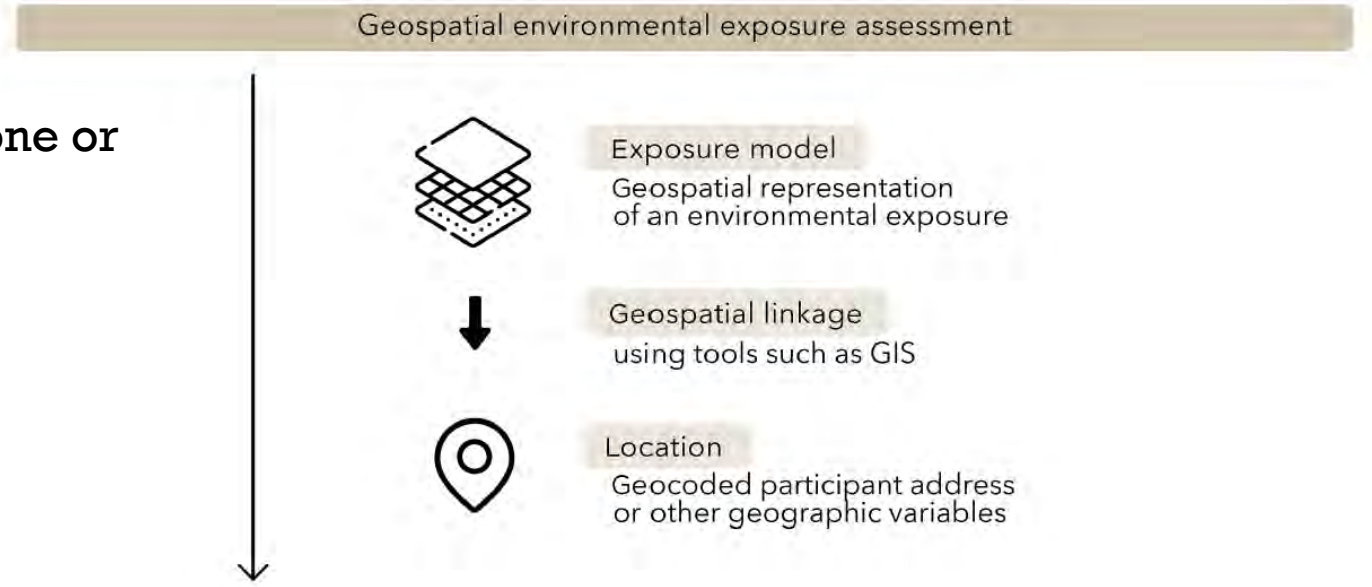
https://www.sensortips.com/

- Direct approaches
  - Using diaries coupled with GPS devices
  - Web mapping applications and interviews
  - We can design studies based on wearable sensors and collect dynamic exposure to various external factors (PM2.5, humidity, noise..)

Pros & Cons

- Indirect approaches
  - Using **passively collected data** from smartphone or using secondary data in which GPS and accelerometer data has been collected

Pros & Cons



Accounting for space, time, and behavior using GPS derived dynamic measures of environmental exposure

Marta M. Jankowska [a,*], Jiue-An Yang [a], Nana Luo [b], Chad Spoon [c], Tarik Benmarhnia [b]

- We compared 3 time-weighted spatial averaging approaches to model dynamic exposures to various environmental exposures
  - Kernel Density Estimation (KDE), Density Ranking (DR), and Point Overlay (PO)
- Relying on routinely collected data based on GPS and accelerometers (smartphones)

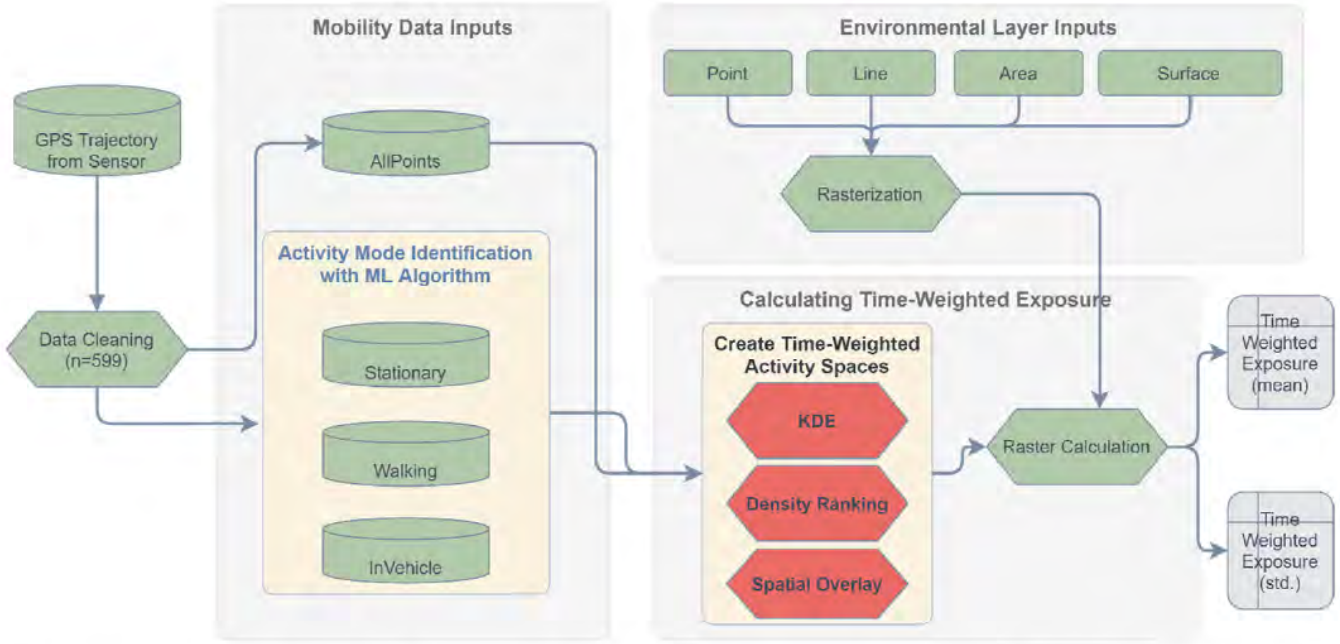
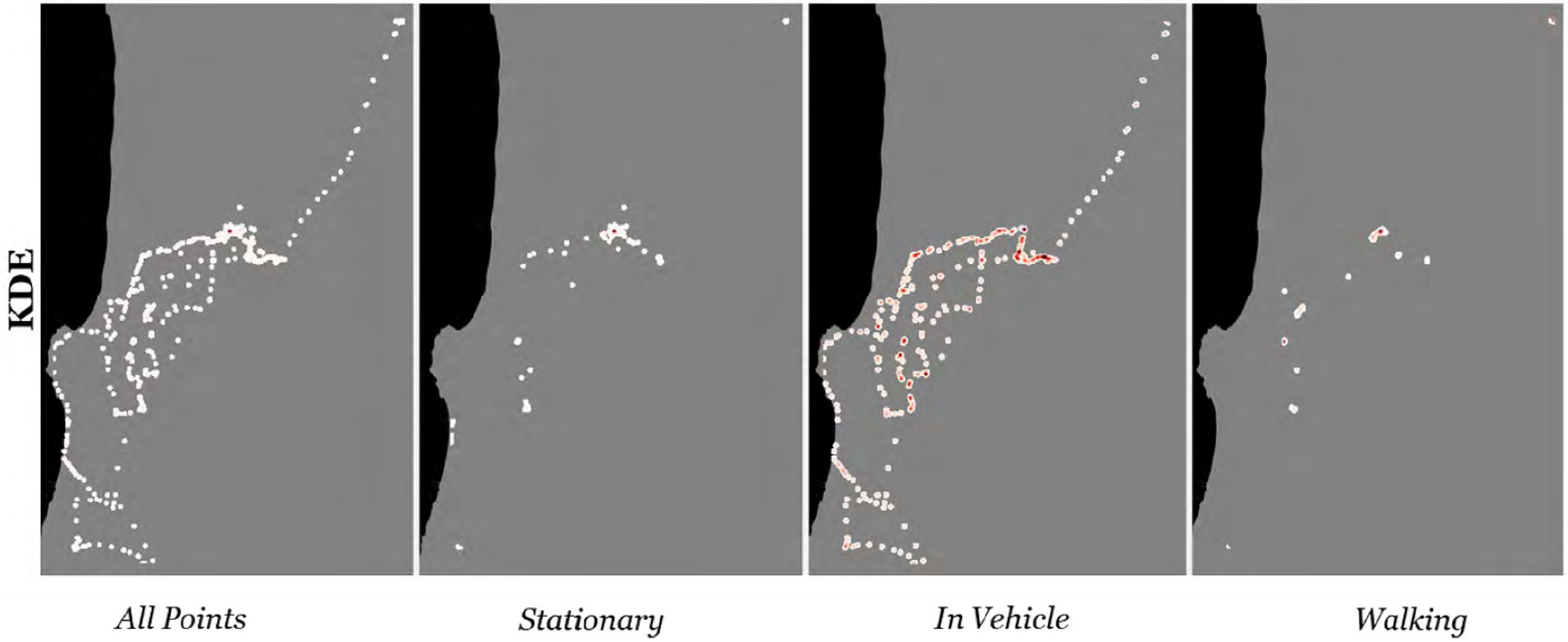


Fig. 1. Analysis workflow for calculating time-weighted measures of environmental exposure across TWSA method, mobility data input, and environmental layer input.

KERNEL DENSITY ESTIMATION



Areas with darker red indicate greater weighted time spent in location during the study period for a particular data type.

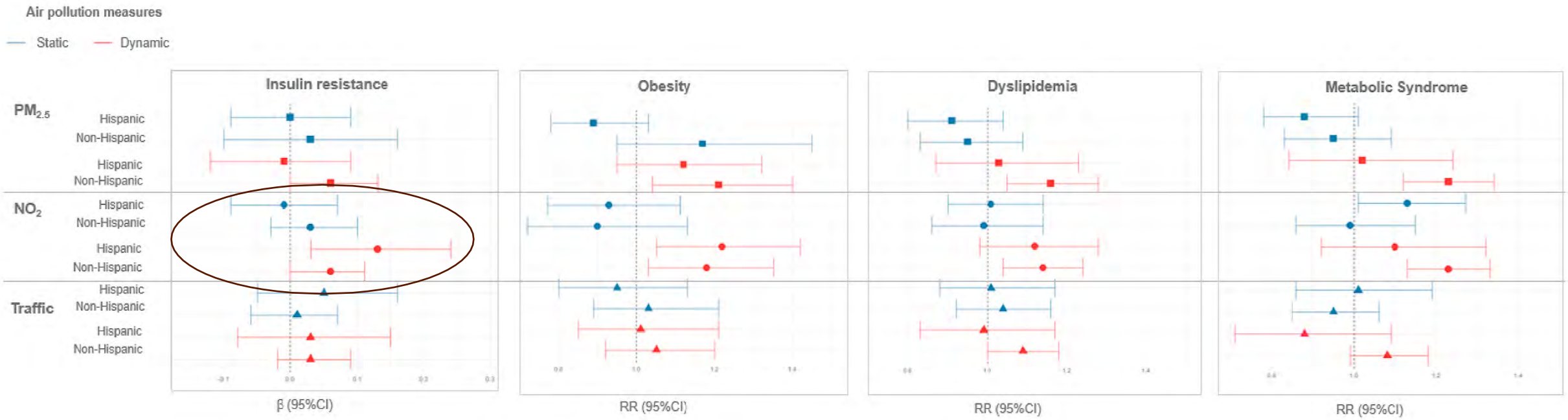
THE COMMUNITY OF MINE STUDY

- Primary objective:
  - Advance methods of cancer risk exposure assessment focusing on physical activity and walkable environments
- Multiple biomarkers collected among 602 participants:
  - Insulin resistance (fasting plasma insulin and glucose levels, and the HOMA-IR index (fasting plasma insulin x fasting plasma glucose/22.5)
  - Average 24 h circulating glucose (measuring HbA1c)
  - Adipose tissue inflammation and insulin resistance are gauged by measuring the adipokines, adiponectin and leptin
  - Systemic inflammation is gauged by levels of CRP
- **But GPS coordinates can be used to study multiple environmental and social exposures**

Jankowska, Marta M., et al. "Protocol for a cross sectional study of cancer risk, environmental exposures and lifestyle behaviors in a diverse community sample: the Community of Mine study." BMC Public Health 19 (2019): 1-9.

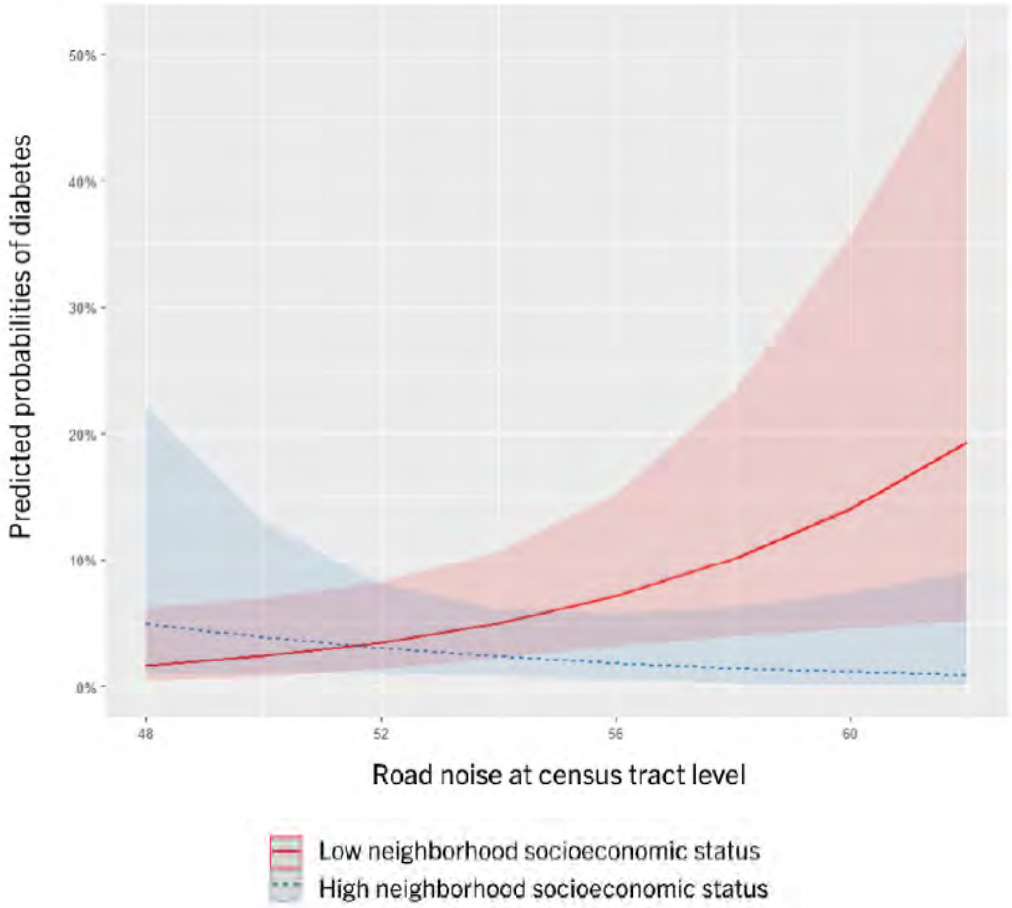
Air pollution and metabolic disorders: Dynamic versus static measures of exposure among Hispanics/Latinos and non-Hispanics

Noémie Letellier [a,*], Steven Zamora [a], Chad Spoon [b], Jiue-An Yang [c], Marion Mortamais [d], Gabriel Carrasco Escobar [e], Dorothy D. Sears [b,f,g,h], Marta M. Jankowska [c], Tarik Benmarhnia [a]



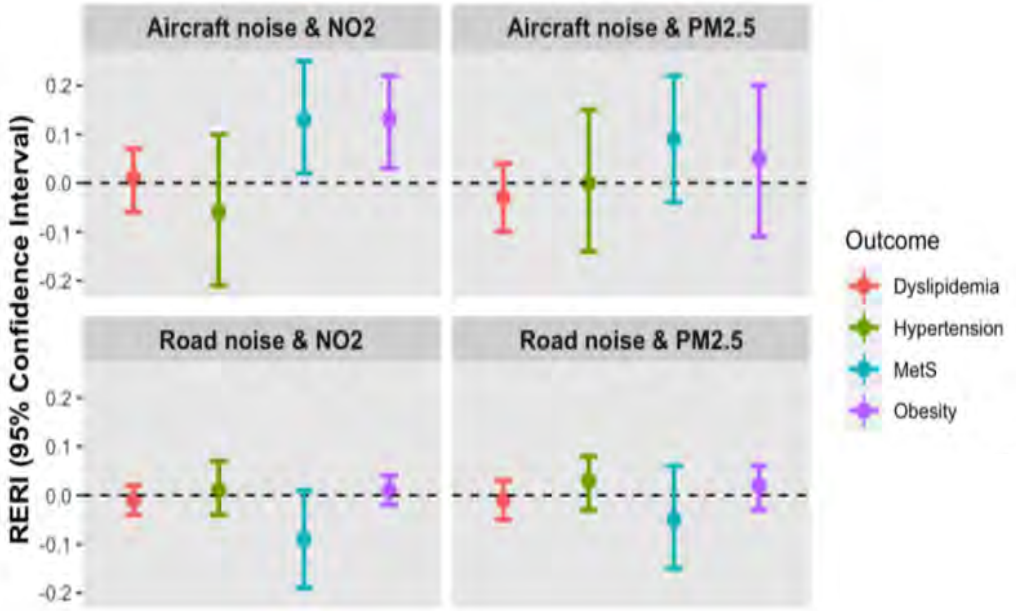
Aircraft and road traffic noise, insulin resistance, and diabetes: The role of neighborhood socioeconomic status in San Diego County☆

Noémie Letellier [a,*], Jiue-An Yang [b], Clémence Cavaillès [c], Joan A. Casey [d], Gabriel Carrasco-Escobar [e], Steven Zamora [a], Marta M. Jankowska [b], Tarik Benmarhnia [a]



Title: Combined impact of dynamic air pollution and transportation noise on cardiometabolic disorders in San Diego County

Authors: Blanche Berneron, Jiue-An Yang, Marta M. Jankowska, Tarik Benmarhnia, Noémie Letellier

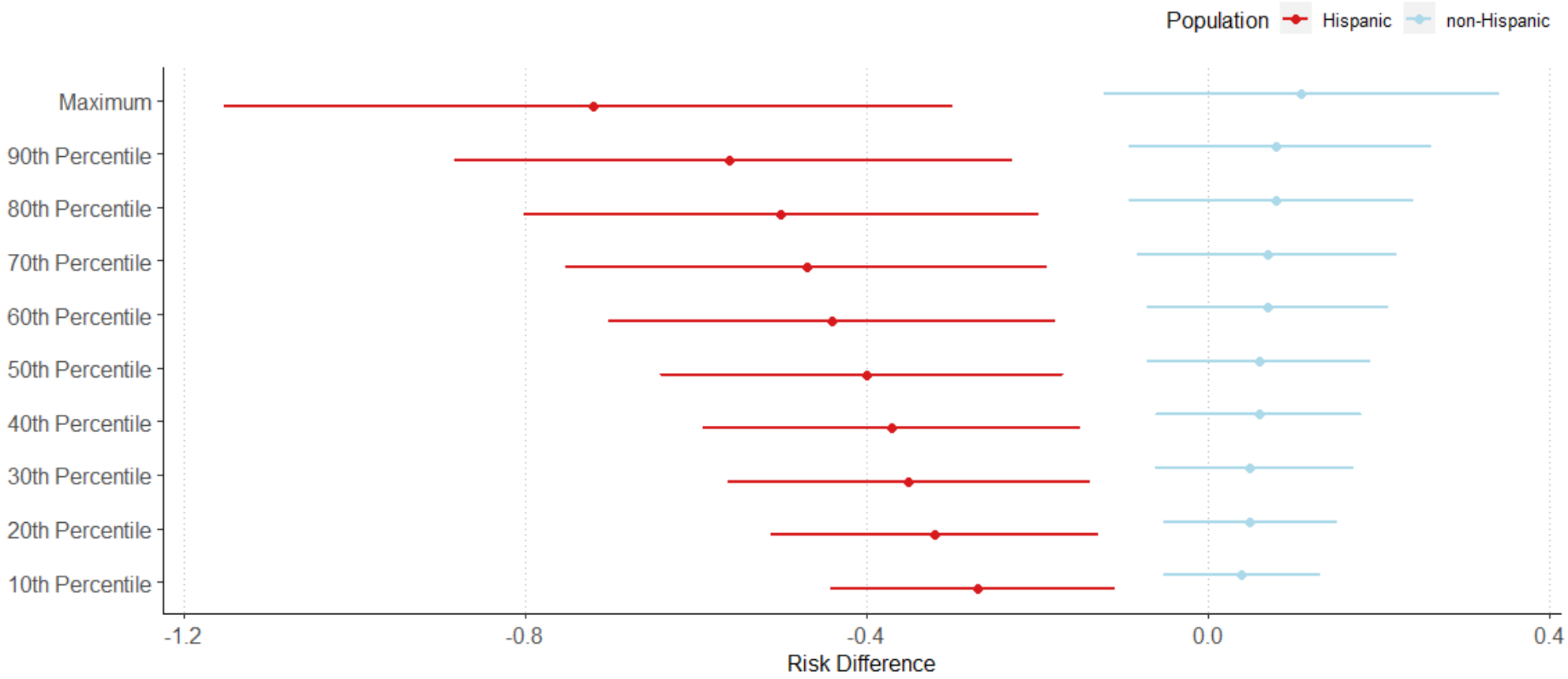


Interaction between dynamic exposures on the additive scale (using Relative Excess Risk due to Interaction)

Simulating the impact of greenspace exposure on metabolic biomarkers in a diverse population living in San Diego, California

A g-computation application

Anaïs Teyton[a,b,c,*], Nivedita Nukavarapu[d], Noémie Letellier[c,e], Dorothy D. Sears[f,g,h,i], Jiue-An Yang[d], Marta M. Jankowska[d], Tarik Benmarhnia[c,e]



Example: insulin resistance

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