FROM MOUSE TO MAN: HOW THE HUMAN POST MORTEM MICROBIOME RELATES TO LOCAL AREA CRIME LEVEL

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ABSTRACT

Violence is a widespread public health and justice system problem with far-reaching consequences for victims, offenders, and their communities. Aggression, the cognitive and behavioral antecedent to violent action, is mainly understood in terms of the psychosocial risk factors that increase the likelihood of aggressive behavioral strategies. Neighborhood context is a principal risk factor for violent crime perpetration, but the mechanisms that mediate the effect of the environment on individual-level aggression behavior are poorly understood, especially the biological factors that may contribute to our understanding of violent behavior. In order to gain a better understanding of mechanisms that precipitate violence in specific geographic contexts, this dissertation explores the relationship between aggression behavior and the gut microbiome, a spatially determined physiological system that affects human health and behavior. In humans, *post mortem* microbiome studies show a loss of biodiversity in high crime census block groups that can be leveraged, alongside indicators of socioeconomic status, to predict block group crime level, supplying critical foundational support to explore how differences in gut microbiome composition relate to human aggression behavior. The overall goal of this research is to connect basic science findings in mice to correlational evidence of a relationship between the human gut microbiome and violent crime exposures, thus revealing how community health affects individuals and supplying a potential target for future intervention.

In honor of my grandfathers, Władysław Kwiatkowski and Anthony Ambroziak, who collectively fought a war, crossed an ocean, and overcame abject poverty to give me this opportunity. Your sacrifices will never be forgotten.

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CHAPTER 1: INTRODUCTION

Introduction

Aggression predicates acts of violence that serve to control, traumatize, maim, or kill victims. According to the Federal Bureau of Investigation (2017), however, a conservative estimate of violent crime (e.g., murder, rape, robbery, and aggravated assault) in Michigan is 450 crimes per 100,000 persons annually, with aggravated assault offenses accounting for approximately 69% of all violent crime. Within clinical populations, the risk of aggression is elevated among those with paranoid psychoses, substance abuse disorder, and antisocial personality disorder (Eronen, Angermeyer, & Schulze, 1998), posing a challenge to patient care within the justice and healthcare systems. Importantly, survivors of violence often suffer long-term health consequences of abuse, such as increased risk for post-traumatic stress disorder, chronic pain, and generally higher health care utilization (Campbell, 2002; Rivara et al., 2019). Thus, aggression and violence represent serious public health problems with negative effects on quality of life, health, and vitality for both perpetrators and victims.

Spatial location is a critical risk factor for crime perpetration, underscoring the importance of contextual, or environmental, factors in driving offender behavior. Crime mapping has thus become a tradition of criminological study in an effort to understand broader patterns of behavior and the local area factors that increase risk of crime. Historically, criminologists of the 19th century first demonstrated the coupling of crime and place (e.g., Guerry, 1833), but it was the work of Shaw and McKay (1942) that first explained the link in terms of social and environmental factors that disrupt community through social disorganization. In particular, residential instability, population heterogeneity, and low socioeconomic status emerged as predictors of neighborhood delinquency that persisted in defining risk across three different time periods irrespective of

shifting neighborhood demographics (Shaw & McKay, 1942), suggesting that factors within a disorganized neighborhood context rather than individual-level traits drive human health and behavioral patterns.

This foundational research led to the identification of a suite of social and environmental risk factors for criminal behavior that are spatially clustered in disadvantaged neighborhoods (Bursik & Grasmick, 1993; Sampson & Groves, 1989; Sampson, Raudenbush, & Earls, 1997; Shaw & McKay, 1942). This has led many to speculate that there is a neighborhood effect wherein mechanisms of social control breakdown (in response to disorganization) to create a social (i.e., low cohesion) and physical environment where crime is more readily perpetrated. However, most individuals who live in neighborhoods that have a high risk of crime do not commit crime or otherwise engage in deviant behavior (Bursik & Grasmick, 1993). Therefore, there is important variation in this so-called "neighborhood effect" on crime that is not accounted for by current explanations of criminal behavior, highlighting a need for additional research to explain individual variation in response to the psychosocial risk factors associated with deviance.

Indeed, research to date is limited in its ability to provide (1) a mechanism through which social and environmental exposures influence individual action and (2) why individuals exposed to similar social and environmental factors vary in their engagement in deviant behavior. Understanding how these factors affect the brain, the final common mediator of risk, is essential for understanding the etiology of deviant/aggressive behavior. Previous research demonstrates that there are significant differences in brain activity between individuals with a history of violent behavior and non-violent controls (e.g., Leutgeb et al., 2015). Specifically, increased risk for human aggression is associated with pathophysiological changes in brain regions underlying emotional regulation and the body's response to stress (e.g., threat). Impairments in the prefrontal

cortex (PFC), the seat of executive function, and the amygdala, the center of fear and aggression (Rosell & Siever, 2015), limit the ability to process and regulate emotion, enabling the expression of violating behaviors (Sapolsky, 2017). Importantly, similar pathophysiological changes are observed in the brains of individuals who grow up living in impoverished socioeconomic conditions (Liberzon et al., 2015). This raises the question as to how exposures in disadvantaged neighborhood contexts affect the brain. Critically, because the brain does not operate in isolation from the rest of the body, consideration of other physiological systems that could mediate the relationship between the physical environment and the brain must be accounted for.

Emerging research about the human microbiome, the communities of microbes that inhabit the body, suggests that it has a role as a physiological regulator in health and behavior (Knight, 2015), an effect that depends on the environment and its spatial location. Moreover, recent evidence suggests a role for the gut microbiome in human psychological disposition and mental health. For example, Borre and colleagues (2014) review how perturbations in the normal developmental trajectory of the human microbiome due to both lifestyle choices (e.g., formula versus breast feeding) and environmental insults (e.g., pathogen exposure) can disrupt physical growth, permanently alter critical brain signaling pathways, and predispose an individual to neurodevelopmental psychiatric disorders. Research also shows that differential microbial community structures in the gut are associated with different temperaments in children (Christian et al., 2015) as well as major depression and anxiety in adults (Jiang et al., 2015; Jiang et al., 2018). Together, these findings suggest that gut dysbiosis (i.e., imbalance) is associated with various expressions of pathological behavior and aberrations in brain health.

Evidence of the specific effect of the gut microbiome on human aggression is limited and does not directly relate to behavior. In one study, changes in inmate diet were associated with

reductions in aggression and prison rule-breaking (Gesch, Hammond, Hampson, Eves, & Crowder, 2002; Zaalberg, Nijman, Bulten, Stroosma, & van der Staak, 2010). This effect was attributed to changes in metabolic function (Gesch et al., 2002), but given recent findings regarding the effect of diet on the gut microbiome (Sonnenburg & Sonnenburg, 2015), the underlying mechanism for this behavioral change among the prisoners remains unclear. More specifically, other work has shown that changes in the gut microbiome are associated with changes in the neurocognitive antecedents of aggressive behavior. For example, a recent human imaging study showed reductions in brain activity related to vigilance (e.g., threat tracking) following probiotic treatment (Tillisch et al., 2013), and other research demonstrated reductions in self-reported aggression in response to probiotics (Steenbergen et al., 2015). Taken together, this research suggests a relationship between the microbiome of the gut and sensitivity to emotional cues that could be important for the manifestation of aggressive behavior in humans.

Importantly, the microbiome of the gut has a known role in sensory and neurochemical pathways that communicate with the brain to modulate behavior (Mayer et al., 2014). Its composition is also highly dependent on lifestyle choices and environmental exposures (Clarke, O'Mahony, Dinan, & Cryan, 2014; von Mutius & Vercelli, 2010). Thus, perturbations in the gut microbiome caused by environmental input, such as those observed in disadvantaged neighborhoods (e.g., low access to nutritional foods, toxin exposure), could have a profound effect on behavior, including deviant behavior. However, research is needed to investigate the potential link between the human microbiome, brain health, and aggression behavior to uncover potential mechanisms that could explain why certain contexts are so risky for both health and behavior.

Though there is increasing interest in studying the biological factors associated with aggressive behavior from a criminal justice perspective (Rafter et al., 2016), only limited work has

been done. Neuroscientific research shows the importance of pathophysiological changes in the brain for the expression of aggression behavior (Bannon, Salis, & O'Leary, 2015), which involves a dynamic interplay of biological, psychological, and social or environmental factors. Given the established contributions of both environmental and social neighborhood factors to individual-level risk for aggressive behavior, the pressing question becomes how context interacts with physiology, and to what extent there is an effect of physiology beyond long-established risk factors like residential instability, population heterogeneity, and low socioeconomic status. One potential mechanism is through the gut-brain axis, which is both shaped by the environment and has a role in human behavior, including pathological behavior. However, the role of the gut-brain axis in aggression and aggressive behavior remains largely unexplored.

The Biopsychosocial Model

In the 1970s, the medical community experienced a paradigm shift with the introduction of George L. Engel's biopsychosocial model (Engel, 1977). Engel (1977) criticized the biomedical model for its cold reductionism, asserting that biology alone could not explain the complexity of human health and behavioral phenomena. As a solution, Engel (1977) proposed the biopsychosocial model as a paradigm to explain human health and behavior with respect to the combination of biological, psychological, and social or environmental risk factors that work together and interact to affect human health and behavior. Naturally, the main tenet of the biopsychosocial model is that complex health and behavioral phenomena cannot be explained by narrowly defined mechanisms. For example, disease may be characterized by pathophysiological changes in the body, but the severity of the illness and its prognosis worsen in the presence of psychosocial risk factors, such as psychological distress or poor living conditions (Engel, 1977). In this view, human health and behavioral phenomena may have a classic presentation, but vary

according to other biological (e.g., comorbidities), psychological, and social or environmental risk factors. This perspective expands the influences of context, or the social and environmental exposures that nuance both human experience and physiology, and supplies a critical framework for integrating natural and social science to advance the study of aggression behavior.

At the onset of an acute social interaction, the actors and their biology arrive conditioned from past experience. They import experience gained through development, socialization, and social learning (i.e. culture) as reference for appropriate behavior. Together, the actors' histories, social abilities, and other factors, such as current emotional and psychological state, frame each actor's perception of environmental and social cues, and shape the behavioral response (Crick & Dodge, 1994). As such, the role of biology is to simply enable an established propensity towards aggression and deviance (Sapolsky, 2017). This comprehensive explanation of aggression can be accounted for within a biopsychosocial framework, creating a critical need to integrate biology in criminological research to understand the full set of factors known to influence aggressive and violent behavior (Fishbein, 1990).

The human microbiome is a primary candidate for integration into a biopsychosocial model of aggression behavior in humans. The microbiome, which varies according to both physical (Afshinnekoo et al., 2015; Yatsunenko et al., 2012) and social (Song et al., 2013) exposures, is an environmental factor that is known to affect host physiology, including the structure and function of the brain (Sherwin, Bordenstein, Quinn, Dinan, & Cryan, 2019). Importantly, the human microbiome is specifically known to vary by socioeconomic conditions with a significantly higher abundance of pathogens and lower biodiversity associated with urban blight and unhealthy living conditions (Pearson et al., 2019), forging another potential link between the human microbiome and disadvantaged neighborhood contexts where crime occurs. Together, these features position

the gut microbiome as a potential novel mechanism through which the environment can affect individual behavior in a spatially determined way.

Background

In an ordinary context, aggression is a behavioral tool used to compete for resources. When aggression is expressed outside the context of competition, it is pathological (Nelson & Trainor, 2007). When it becomes harmful, it is deviant. When a law prohibits the behavior and the individual is caught, it is criminal. Interpersonal aggression is conceptualized in many ways in the literature but can generally be subdivided into two types. Broadly, reactive aggression is considered emotional and impulsive while instrumental aggression is considered calculated and goal-oriented, either for gain or pleasure (J. Haller & Kruk, 2006; Nelson & Trainor, 2007; Sapolsky, 2017). Both reactive and instrumental aggression are associated with pathophysiological changes in several key brain regions in the clinical literature. In particular, areas implicated in emotion and executive control function differently or less optimally preceding deviant behavior. Though many regions are known to participate in processing emotional stimuli, the cortico-amygdala loop is among the most studied. The basic function of this circuitry is to (1) detect emotional stimuli, and (2) properly interpret the stimuli to select an appropriate behavioral response.

Deficits in the structure and function of the amygdala and prefrontal cortex (PFC), critical players in circuits underlying emotional regulation and social behavior, result from changes in the molecular environment of the body. Indeed, brain activity depends on the coordinated signaling of chemicals messengers for normal function. Adverse events (i.e., stressors) can excessively activate biological processes that suppress neural growth factors, limit social learning, and alter developmental trajectory. When activity changes, there is an underlying change in chemical

messaging, or signaling cascades. It is the inimitable set of life experiences garnered through unique social and environmental exposures in combination with unique genetic factors that creates variation in human behavior and adds complexity to understanding behavioral phenomena, like aggression.

Acknowledging that the brain does not operate in isolation, it is critical to examine the relationship between other physiological systems and the brain dysfunction driving behavioral aggression. The human microbiome is one such system, both known for its profound effects on health and behavior as well as its contextually specific (microbial) community structure, positioning it as a likely conduit between environmental exposures, the brain, and spatially determined behaviors (e.g., aggression). The microbiome is an environmental factor that affects host physiology and behavior, potentially via the gut-brain axis (Knight, 2015; Sherwin et al., 2019), a collection of signaling pathways that describes mechanisms through which microbiota can engage in physiological processes throughout the body. For example, the vagus nerve, known for its role in visceral sensation (e.g., cramping), directly innervates the gut where afferent projections interact with microbial metabolites and intermediary enteroendocrine cells that are regulated, in part, by gut bacteria. Moreover, gut bacteria produce neurotransmitters, short-chain fatty acid (SCFA), and other signaling molecules as well as inflammatory agents (e.g., lipopolysaccharide) that induce an immune response. The gut microbiota therefore interact with vital body systems, directly modulating host physiology, and by extension health and even behavior. Critically, although in its infancy, there is evidence to suggest that the gut microbiome plays a role in regulating the function of key aggression-related brain regions.

The Current Study

The current study is an interdisciplinary exploration of the role of the gut microbiome in aggressive behavior, underscoring the translational relevance of my preclinical work with the Michigan State University's Neuroscience Program. Human microbiome data were obtained through collaboration with the Human Post Mortem Microbiome (HPMM) research team who supplied secondary sequencing data from their study of the *post mortem* human microbiome across Wayne County, Michigan (Pechal, Schmidt, Jordan, & Benbow, 2018). Secondary sequencing data from samples representing the digestive track (i.e., mouth and rectum) collected from decedents during routine autopsy in 2014-2015 were used as a proxy measure for the *ante mortem* gut microbiome to investigate the relationship between microbial community structure and local area crime. These data supplied descriptive information, including the diversity and distribution of bacteria, as well as geospatial information for both the (1) death event and (2) home locations of each decedent, placing each subject in the local area where they had known social and environmental exposures. Violent crime data from the Detroit Police Department (DPD) as well as socioeconomic data from the United States Census Bureau (USCB) were paired with microbiome data to examine the relationship between disadvantage, the human gut microbiome, and patterns of local area aggression behavior.

CHAPTER 2: METHODOLOGY

Site Selection

Detroit is a recovering city, trying to regain itself after years of political corruption, rapid population decline, and the mass exodus of industry (LeDuff, 2013). Once considered America's arsenal of democracy for its manufacturing efforts during World War II (Baime, 2014), it is now plagued with healthcare disparities, poverty, and crime. In 2015, Detroit's population was estimated to be approximately 690,074 individuals, accounting for only 7% of the state of Michigan's total population (U.S. Census Bureau, 2015) but a disproportionate amount of its disadvantage. For example, Detroit has a higher mortality rate for seven of the ten leading causes of death in Michigan, including heart disease, cancer, stroke, unintentional injuries, diabetes mellitus, pneumonia/influenza, and kidney disease compared to both Michigan and the United States at large (Michigan Department of Community Health, 2014). The 2015 American Community Survey estimates that 30% of Detroit's 365,528 housing units are vacant. Among the homes that are occupied, only 49% are owner-occupied and a staggering 25% do not have access to a car in a city where there is limited public transportation. The median household income is $25,764, but 49% of households earn less than $25,000 per year. The unemployment rate is high with 25% of Detroit's eligible workforce unemployed (U.S. Census Bureau, 2015). In addition to its poor health and poverty, Detroit has an infamous reputation. Popular media consistently characterizes Detroit as America's most dangerous city, and even rank it among one of the most dangerous places in the world (Fisher, 2015; "The world's most dangerous cities," 2017). According to the Federal Bureau of Investigation, the City of Detroit accounted for 36% of Michigan's violent crime in 2015 and ranked in the top three major cities in violent crime and homicide (Federal Bureau of Investigation, 2017). Detroit is thus characterized by disadvantage,

instability, and crime. Given this unfortunate profile, Detroit is the ideal place to study how patterns of violent crime relate to local area social and environmental risk factors.

Aggregate Data: The United States Census Bureau American Community Survey

In an attempt to reconstruct contextual features at the time of HPMM data collection, 5-year socioeconomic variable estimates for Michigan in 2015 were obtained from the 2015-2019 American Community Survey (ACS). Unlike single-year estimates, five-year survey estimates are drawn from larger sample sizes with sampling at smaller census geographies and have the benefit of years of subsequent data collection to inform estimates, rendering five-year variable estimates the most reliable (Gaquin & Ryan, 2019). The 2015-2019 ACS data are the most recent five-year product release from the USCB and were selected because the majority of the HPMM samples were collected during 2015 (61%). Data from the 2010-2014 ACS were not included to reduce the chance of introducing variation in estimates between ACS surveys related to changing census geographies or question modification. Importantly, 2010 decennial census data were excluded from the current study in an effort to minimize threats to internal validity driven by the profound impact of the 2008 recession on economic security nationwide. The 2010 data reflect a distinct period of history that may inaccurately represent the socioeconomic conditions during 2014 and 2015. Therefore, the 5-year estimates for 2015 from the 2015-2019 ACS were collected for the State of Michigan.

Table 1 | 2015 American Community Survey Variables

Study Variable	Operationalization
Unemployment	Estimate of the total count of work eligible adults not in the labor force
Household Income	Estimate of the median household income during the past 12 months
Population of Black Residents	Estimate of the total count of Black residents
Vacancy	Estimate of the total count of vacant housing units
Tenure	Estimate of the total count of occupied housing units
Population of Ages ≥ 16	Estimate of the total count of population aged 16 years or older
Population	Estimate of the total count of the population
Unemployment Rate	= Unemployment / Population of Ages ≥ 16 Years
Percent of Black Residents	= Population of Black Residents / Population
Vacancy Rate	= Vacancy / (Vacancy + Tenure)

Sociodemographic variables estimating the total population and population aged 16 and older (i.e., eligible workforce), unemployment, median household income, the representation of Black citizens, vacancy status, and total tenure were collected at the census block group level (**Table 1**), the smallest geographic unit of analysis available for the ACS, representing between 600 and 3,000 people clustered in a contiguous area (USCB, 2021a). All demographic measures were recorded by the Census per survey respondent self-identification and report. Census variables were collected in accordance with Office of Management and Budget's Federal Interagency Work Group for Research on Race and Ethnicity. According to the most recent ACS estimates (USCB, 2019), the City of Detroit includes a diverse population that is 77.9% Black or African American, 14.7 White, 1.7% Asian, 0.7% American Indian or Alaskan Native, 3.3% of another race, and 1.7% multi-racial. While 77.9% of Detroit residents self-identify as Black or African American, this ranges from 83.1% to 100% per block group. Due to the current and historical practice of societal underinvestment in residential areas with high Black representation, the percentage Black could be a signal for under-investment not measured by other covariates and is therefore included

in these models. Altogether, these ACS data provide basic social and environmental factors that characterize Detroit block groups and serve as socioeconomic covariates in statistical modeling.

Aggregate Data: Detroit Police Department Open-Source Crime Data

Open-source violent crime data for the City of Detroit were obtained from the city's open data portal. Specifically, victim-based data enumerating the number of aggravated assaults, nonfatal shootings, and homicides reported to the Detroit Police Department (DPD) during 2014-2015 were collected. Aggravated assaults reported to DPD were collected from a larger dataset documenting major crimes reported to DPD during 2011-2014 that were compiled for submission to public safety surveillance programs. To extract aggravated assaults from these data, a crime category and date variable query was used to filter the dataset for aggravated assault crimes that occurred only during 2014. Likewise, data for nonfatal shootings reported to DPD in 2014-2017 were downloaded and filtered for incidents that occurred during 2014 and 2015. Finally, homicide data for incidents reported to DPD in 2014-2017 was downloaded and subset by the incident date variable to obtain years 2014 and 2015. All three datasets included latitude and longitude data, providing the location of where each incident occurred. These data were thus transformed into three separate spatial point datasets.

These spatial point data were assigned to census block group polygons and summed to calculate a raw count of incidents within the block group. Totals were divided by the block group population and multiplied by 1,000 to generate *per capita* aggravated assault, nonfatal shootings, and homicide rates. Each block group was then categorized as having high, medium, or low levels of *per capita* assault, shootings, and homicide using quantile thresholds from variable summary statistics. These categorizations were subsequently used to code block groups as having high, medium, or low overall crime. A block group was considered to have high crime if it was also

coded as having high levels of assaults, shootings, and homicides. Likewise, a block group was considered to have low crime if it was coded as having low levels of assaults, shootings, and homicides. Notably, a designation of "medium" crime level can be interpreted as a variable crime level. Importantly, overall crime rates were not calculated given significant variation reporting across crime type (see Appendix). Together with USCB socioeconomic data, the combined data supplied critical contextual information for the human *post mortem* microbiome data.

Aggregate Data: The Human Post Mortem Microbiome

To examine the relationships between the human gut microbiome and local area crime and sociodemographic factors, secondary 16S ribosomal RNA (rRNA) amplicon sequencing data from the Human *Post Mortem* Microbiome (HPMM) project were obtained through collaboration with HPMM colleagues. In their original work, Pechal and colleagues (2018) collected *post mortem* microbiome samples from the ears, eyes, nose, mouth, and rectum from 188 decedents during routine autopsy with the Wayne County, Michigan, Medical Examiner (ME) between 2014 and 2015[1]. Samples were subsequently characterized via a common genetic marker, allowing for the identification of constituent microbiota. In addition, ME reports provided basic demographic, health, and law enforcement information, detailing circumstances surrounding the individual's death. Accompanying sample metadata therefore included variables for age, race, sex, body mass index (BMI), manner of death (e.g., natural), cause of death (e.g., cardiovascular disease), and the estimated postmortem interval, which leverages milestones in decomposition to determine the estimated time between death and discovery. Central to the current study, decedent death event and home location geospatial information were also collected. Together, these data provide covariates which have a role in shaping the human gut microbiome.

[1] Some 2015 cases were processed in 2016.

The HPMM dataset has broad forensic applications, but principal among them is its ability to represent the *ante mortem* human microbiome. Indeed, the majority of the subjects were sampled within 24-48 hours of death, limiting the effects of decomposition on microbial community composition. Moreover, variation in the manner in which individuals died (i.e., natural, accidental, homicide, and suicide) led to the inclusion of decedents of varying age and health, creating opportunity to evaluate the *post mortem* microbiome as a tool for exploring living human health. As a first step, initial analyses showed stability in microbial community composition during the first 24-48 hours after death, especially among rectal samples, suggesting that decomposition processes do not dramatically shift microbial communities immediately after death. In a further proof of concept analysis, the initial HPMM investigation demonstrated that features of the *post mortem* microbiome of the mouth, such as decreased phylogenetic diversity, significantly predicted the presence of *ante mortem* heart disease among decedents found less than 24 hours after death. Taken together, the overall stability of the *post mortem* microbiome and predictive power of these data suggest that they may serve as an appropriate proxy measure of *ante mortem* microbial communities, rendering the human *post mortem* microbiome a viable tool for examining human health in living populations (Pechal et al., 2018). As such, 16S rRNA amplicon sequencing data from mouth and rectal samples (i.e., digestive track samples) from this study were used as proxy measures to characterize the human gut microbiome among decedents who lived and died across the City of Detroit.

Aggregate Data

United States Census Bureau

To compare the effects of local area socioeconomic factors on the composition of the human *post mortem* microbiome, basic demographic information for the State of Michigan was

obtained from the United States Census Bureau (USCB) using a Census application programming interface (API) key[2] and the *tidycensus* package for R and RStudio (Walker & Herman, 2021). The USCB is the United States federal repository for both the decennial census, a population enumeration effort in accordance with Article I, Section 2 of the United States Constitution, and the American Community Survey (ACS), an annual estimation of the nation's demographic and economic characteristics (USCB, 2021b) for policy decision-making. The *tidycensus* package facilitates digital data collection from both of these surveys.

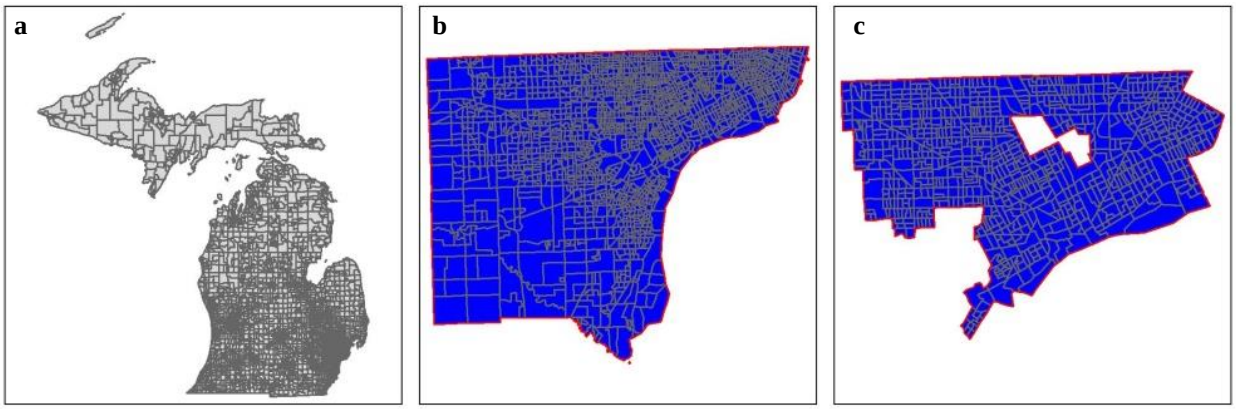

Figure 1 | Maps of Michigan Census Block Groups. a-c) Schematic showing the 2015 ACS census block groups (BG) represented in study geographies. a) Michigan, 8,205 BG; b) Wayne County, MI, 1,822 BG; c) Detroit, MI, 879 BG.

Geospatial information for the State of Michigan was downloaded from USCB using a combination of the *tidycensus* and *tigris* packages for R and RStudio (Walker, 2020; Walker & Herman, 2021). The *tidycensus* package facilitates USCB survey data download with accompanying attribute information, including polygon geometry for the census geography to which the data are assigned (e.g., block group). The *tigris* package, however, facilitates the download of shapefiles for USCB geographies, such as metropolitan areas in specific states, providing critical cartographic information. Shapefiles store geospatial vector data that describe physical space as points (e.g., locations), lines (e.g., streets), and polygons (e.g., neighborhoods),

[2] Census API requests can be made at https://api.census.gov/data/key_signup.html.

defining geographies for data selection and mapping operations. In particular, USCB observes legally bounded small geographies, such as counties and incorporated places, but also creates statistical entities for other small geographies, like census core-based statistical areas (i.e., metropolitan areas), to examine local data trends (USCB, 2012). To access the geographical boundaries observed during the 2015 ACS, geospatial information for counties, core-based statistical areas, and incorporated places in Michigan was collected using the *tigris* package. These data were subsequently integrated with census demographic and economic data to pare down, or clip, census survey data to study-relevant geographies.

A series of data processing steps were conducted to isolate Wayne County and City of Detroit geospatial and ACS survey data (**Fig 1a-c**). Shapefiles for the legal boundaries observed during the 2015 ACS for Michigan counties and incorporated places were downloaded and queried using logical operators searching the "NAME" variable for "Wayne" and "Detroit", respectively. Shapefiles for nationwide core-based statistical areas drawn for the 2015 ACS were also downloaded and similarly queried for "Detroit" to identify its metro area. Each geography was then joined with 2015 ACS demographic and economic data using the *sf* package for R and RStudio (Pebesma, 2018). Importantly, all Michigan ACS survey data that were assigned to block groups that did not fall within the shapefiles were eliminated, thereby "clipping" the census data to areas under study. The resulting geospatial dataset was projected to the World Geodetic System 1984 (WGS84) coordinate reference system for downstream processing and analysis.

Detroit Police Department Open Source Crime Data

The City of Detroit has an open data portal from which three datasets were downloaded (https://data.detroitmi.gov/). Specifically, datasets enumerating the number of aggravated assaults, nonfatal shootings, and homicides reported to the Detroit Police Department (DPD) during 2014-

2015 were collected. Aggravated assaults reported to DPD were collected from a larger dataset documenting major crimes reported to DPD during 2011-2014 that were compiled for submission to state and federal public safety surveillance programs, such as the Michigan Incident Crime Reporting (MICR)[3] and National Incident Based Reporting System (NIBRS) data repositories. To extract aggravated assaults from these data, a crime category and date variable query was used to filter the dataset for aggravated assault crimes that occurred only during 2014. Likewise, a victim-based dataset documenting nonfatal shootings reported to DPD during 2014-2017 calendar years was downloaded and queried for incidents that occurred during 2014 and 2015 using the incident date variable. Finally, a third, victim-based dataset detailing homicides reported to DPD during 2014-2017 calendar years was downloaded and queried for incidents that occurred during 2014 and 2015 using the incident date variable. These data are victim-based, spatial point datasets with latitude and longitude coordinates projected to the WGS84 coordinate reference system, providing the precise location of where each incident occurred for assignment to census block group polygons.

Human Post Mortem Microbiome Data

Secondary 16S rRNA amplicon sequencing data from the Human *Post Mortem* Microbiome (HPMM) project (www.ebi.ac.uk/ena; PRJEB22642) were obtained through collaboration with HPMM colleagues. For the original project, Pechal and colleagues (2018) collected *post mortem* microbiome samples from five different body locations, including the ears, eyes, nose, mouth, and rectum, for 188 decedents during routine autopsy examinations conducted by the Wayne County, Michigan, Medical Examiner (ME) between 2014 and 2015[4]. The ME

[3] The MICR data was extensively evaluated for this project and deemed insufficient due to inadequate address data entry.
[4] Some 2015 cases were processed during 2016.

report also provided basic demographic and health information as well as the circumstances surrounding the individual's death. Sample metadata therefore included variables for age, race, sex, body mass index (BMI), manner of death (e.g., natural), cause of death (e.g., cardiovascular disease), and the estimated postmortem interval, denoting the estimated time between death and discovery. Critically, the metadata include geospatial information for the decedent's home and death event locations. Together, these data constitute the basic factors which could drive the microbial profile reflected in the sample data.

The HPMM dataset provides geospatial information for decedent home and death event locations, both of which were geocoded to examine the distribution of HPMM sample characteristics in physical space. Specifically, location information was provided via geographical coordinates and/or postal address, depending on the nature of the circumstances surrounding the decedent and his death. For example, some decedents were homeless and therefore had no known home location. To avoid excluding these individuals from analysis, their death event locations were duplicated as an approximation of their sleep location, and by extension, home area (Pearson et al., 2019). Additionally, some deaths occurred at locations without postal addresses, like intersections or open fields. These death events were manually assigned the next nearest postal address to the given coordinates or intersection using Google Maps Street View. Together, these strategies facilitated the collection of standard postal addresses for all home and death event locations in the dataset. These standard postal addresses were subsequently formatted for automated geocoding using the *ggmap* package for R and RStudio (Kahle & Wickham, 2013), which leverages Google Maps to generate geographical coordinates for known postal addresses. Together, these strategies yielded geocoordinates for a complete spatial point dataset that was

filtered for locations within Detroit and subsequent block group assignment (see below), thereby rendering characteristics of decedent gut microbiome spatial attributes.

Analytic Strategy

Microbiome Data Analysis (performed with S. Kaszubinski)

To obtain meaningful sample characterizations from raw DNA sequences, a series of computationally-intensive data processing steps were conducted. First, the study team's collaborating HPMM forensic data analyst pulled raw sequences through a standardized data processing pipeline to classify taxa present in the samples using the Quantitative Insights Into Microbial Ecology 2 (QIIME 2) program v2018.11 (Bolyen et al., 2019). Briefly, this entailed assembling paired-end sequence reads from the raw fastq files provided by MSU Genomics Core, removing poor quality sequences, and taxonomic assignment, the details of which are outlined by the HPMM team elsewhere (Kaszubinski, Pechal, Schmidt, et al., 2020). For classification, sequences were binned into operational taxonomic units (OTUs), or working groups of sequences with 99% similarity. From these OTUs, representative sequences were aligned to the SILVA small subunit database v132 (Quast et al., 2013). Non-bacterial sequences were removed from the dataset and final taxonomy tables were exported to CSV files to be used as input data for downstream analysis.

Next, the taxonomy tables were imported into R and RStudio for further data processing. In these final steps, a long-form dataset was created such that each OTU represented a row and every column was one of the decedents' five samples. The OTUs were labeled according to their taxonomic classification (down to the genus level), empty rows were removed, and the reformatted table was merged with combined study metadata using the *phyloseq* package for R and RStudio (McMurdie & Holmes, 2013). In an effort to standardize sample microbial

communities, taxa with less than 0.01% of the mean library size, or the number of sequences, were dropped from the dataset. Sequence libraries were subsequently normalized via rarefaction, whereby sequence libraries were randomly subsampled to a specified minimum library size to prevent the effects of sample size bias on microbial community composition. Guided by rarefaction curves, human and mouse data were rarefied to standardize library size. Using normalized sequence libraries, measures of relative abundance and community diversity metrics were calculated to characterize the decedent's gut microbiome.

Statistics and Model Selection

Statistical analysis was conducted using a combination of R and RStudio version 4.0.5 (R Core Team, 2021; RStudio Team, 2020). Data distributions were examined with Shapiro-Wilks tests of normality and Bartlett's tests of homogeneity of variance to select the appropriate parametric or nonparametric tests.

Dependent and Independent Variables

For this analysis, the primary dependent variable was an ordinal, pseudo-composite crime variable with three levels describing census block groups with high, medium (i.e., fluctuating), and low crime relative to levels of assault, nonfatal shootings, and homicide. To construct this categorical measure of overall crime, quantile thresholds were used to designate each block group as having low, medium, or high levels of *per capita* assault, shootings, and homicide. These designations within each crime type were subsequently used to code block groups as having high, medium, or low overall crime. Importantly, overall crime rates (as opposed to the categorical variable described here) were not calculated given variation in reporting across crime type. This variable was selected from the suite of described crime variables (i.e., *per capita* rates) during the

initial stages of data analysis with exploratory analyses that established the potential microbiome-crime exposure link.

Independent variable collection was informed by criminological research and theory that emphasizes the role of contextual factors in disrupting social processes in human communities. As such, USCB socioeconomic variables, including household income, vacancy rate, unemployment rate, and the percentage of residents who identify as Black in census block groups were used alongside HPMM variables that characterize the human *post mortem* gut microbiome. These included measures of relative abundance as well as alpha and beta diversity metrics. Relative abundance was calculated as a value between 0 and 1, indicating the percentage of the community that each operational taxonomic units (OTUs), or working groups of sequences with 99% similarity, occupies (McGill et al., 2007). This measure was used to compare the distribution of microbiota between samples across different levels of local area crime. Relatedly, diversity metrics were used to describe the structure of microbial community membership. In particular, alpha diversity measures, including observed richness, Chao1 diversity, Shannon diversity, and Inverse Simpson diversity, were used as summary statistics to quantify the richness and evenness of taxa *within* samples. Conversely, beta was used as a summary statistic of (dis)similarity, or the degree of overlap, *among* samples within each crime level condition (Morgan & Huttenhower, 2012). The diversity of each sample was compared to the diversity of every other sample, generating a dissimilarity matrix among the sample microbial communities. Together, measures of relative abundance and community diversity provide basic descriptive statistics for microbiome community structure that were used to determine the extent to which features of the human *post mortem* gut microbiome could predict what type of living crime exposure decedents experienced, accounting for all other socioeconomic factors.

Research Questions

In this cross-sectional, non-experimental investigation of violent crime, characteristics of the human *post mortem* gut microbiome were compared between census block groups[5] with varying levels of violent crime. These comparisons were made with respect to both (1) death event and (2) home locations. In doing so, three primary research questions were answered:

1. Is there a relationship between the human gut microbiome and local area violent crime levels?
2. Does the human gut microbiome vary according to (i) local area crime level and (ii) other socioeconomic factors?
3. Which taxa, if any, drive the relationship between the human gut microbiome and local area socioeconomic factors?

Analysis

Given the exploratory nature of this project, data analysis was conducted in a series of data-driven steps. Sample data were subdivided by body site and rectal and mouth samples were separately analyzed. Model building proceeded with bivariate comparisons between microbiome diversity metrics and structural features and crime variables, including block group crime level as well as *per capita* assault, nonfatal shooting, and homicide rates. The distribution of microbiome sequencing data is unknown but non-normal, zero-inflated, and overdispersed, requiring the use of nonparametric tests. Alpha diversity metrics (i.e., observed richness, Chao1, Shannon diversity, and Inverse Simpson diversity) were calculated for both mouth and rectal samples. Shapiro-Wilks

[5] This analysis was repeated using census tracts and DPD police precincts as the unit of analysis. These analyses returned negative findings, likely due to introducing variation in study variables aggregated to larger geographic areas.

normality tests confirmed the use of nonparametric correlations with Kendall's tau and Kruskal-Wallis tests. Here, a Bonferroni correction was used to correct for multiple comparisons.

For beta diversity, permutational multivariate analysis of variance (PERMANOVA) was used with 999 permutations and concomitant tests for differences in beta dispersion, or homogeneity of variance, between conditions. Permutational analysis of variance is a nonparametric model that tests group differences, similar to parametric analysis of variance (ANOVA). Instead of means testing, however, PERMANOVA evaluates group differences based on user-specified distances that reflect similarities between sample clusters (M. J. Anderson, 2001, 2017). As such, PERMANOVA evaluates differences across centroids of clusters (e.g., block group crime level). Here, dissimilarity matrices were calculated using Unifrac distances, thereby taking phylogenetic relationships into account in exploring differences between samples.

In accordance with other HPMM research (Kaszubinski, Pechal, Smiles, et al., 2020), multinomial logistic regression was selected to model the probability of membership in one of the three block group crime level categories using maximum likelihood estimation. Multinomial logistic regression is an ideal modeling technique because it does not require normally distributed data, linearity, or homoscedasticity. In this case, the model was used to predict block group placement in one of the three crime level categories using a combination of socioeconomic variables and microbiome measures collected from decedents assigned to the block groups as either their death event or home location. Model building was conducted in a stepwise fashion, beginning with diversity metrics and proceeding with the subsequent addition of socioeconomic covariates. Models were evaluated for goodness-of-fit with the Akaike information criterion (AIC) and log likelihood indices relative to a null model. Model performance was assessed via model

rate of correct block group (BG) classification, but models were compared to the null model using a Chi-squared difference test. McFadden's pseudo R^2 was also reported.

To investigate whether specific taxa or socioeconomic predictors drive the relationship between gut microbiome composition and local area crime, a random forest classification model with 500 trees was built (Kaszubinski, Pechal, Schmidt, et al., 2020; Y. Zhang et al., 2019). Random forest modeling is a machine learning strategy that utilizes a supervised learning approach to classify data within large and complex datasets. Briefly, labeled training data that pairs input values (e.g., socioeconomic and OTU data) with their class label (e.g., block group crime level) is used to derive a function to classify novel, unlabeled inputs, or test data. This cross-validation step assigns prediction error to the model, which can be leveraged to generate an importance score for specific taxa (or other metadata) by estimating the increase in error associated with removing them as a predictor. Random forest classification was piloted to identify OTUs and socioeconomic predictors that differentiate the composition of the gut microbiome between high, medium, and low violent crime levels. Given that random forest modeling is sensitive to unbalanced groups, however, alternative modeling strategies were implemented.

In particular, negative binomial mixed models (NBMM) with maximum likelihood estimation were used as a follow-up to random forest modeling to identify specific taxa associated with block group crime level and *per capita* homicide. This modeling strategy was selected to account for features of microbiome data that are poorly dealt with by other analytic strategies (Zhang et al., 2017; Zhang & Yi, 2020). Specifically, microbiome data are count data with natural dependencies created by an inherent structure related to taxonomic levels (i.e., phylum, genus), phylogenetic relationships, gene function, etc. Moreover, the relative abundance of an OTU necessarily affects the abundance of all others in the sample. Together, these features violate the

classic assumption of independence that most statistical tests require. In addition, sample OTU data are nested within each decedent, incorporating unknown host factors that thus become random effects. Models thus included OTUs as the modeled count variable, crime and socioeconomic variables as fixed effects, and sample ID, a decedent indicator, as the random effect. To incorporate the crime level variable, low, medium, and high crime conditions were dummy coded with the low condition as the reference category. Overall, NBMM was utilized to identify microbiota that are differentially abundant, depending on contextual factors.

CHAPTER 3: RESULTS

Overview

The current study demonstrates a potential link between human gut microbiome composition and local area crime level. Secondary sequencing data from both mouth and rectum samples were used to calculate diversity metrics that describe the human *post mortem* microbiome as a proxy measure for the *ante mortem* gut microbiome. These metrics were subsequently assigned to both the decedents' death event and home locations to determine if the structure of the gut microbiome was unique in different physical contexts such that it could be used to predict the local area crime level, and by extension, the types of social and environmental exposures in the block group.

Demographics

The final sample included 98 decedents with a death event or home location in the City of Detroit, 85 of whom both lived and died in Detroit. The full sample (n = 98) was comprised of decedents with an average age of 43.9 years and an average body mass index (BMI) of 27.4. Fifty-nine percent were male and 41% female. There were only two racial identities represented in the sample, 76% of whom were Black and 24% of whom were White. Most cases occurred in the Spring (52%) with the majority of decedents found less than 48 hours *post mortem* (89%). The manner in which decedents died included accident (34%), homicide (33%), suicide (6%), and natural (28%) events, categories that included drug-related (29%), gunshot (26%), cardiovascular (22%), and other (23%) causes. From the full sample, 93 had complete case information on their death event location and 82 had complete case information related to their home location. Table 2 presents basic demographic information on the sample subdivided by block group, or local area, crime level.

Samples

The original HPMM contained 855 samples representing five body areas and 30,906 taxa. From this dataset, 162 rectum and 173 mouth samples were extracted. Libraries with less than 0.01% the mean number of sequences were trimmed, and libraries were rarefied to 5,000 reads. After these quality control and normalization measures, Detroit samples were selected. There were a total of 146 rectum samples, representing 1,191 taxa, and 170 mouth samples, representing 913 taxa, for death event and home locations in the final Detroit HPMM dataset (**Table 3**).

Table 2 | Wayne County Medical Examiner Case Report Data

		Death Event Location			Home Location		
		Low Crime	**Medium Crime**	**High Crime**	**Low Crime**	**Medium Crime**	**High Crime**
		(n = 6)	(n = 75)	(n = 12)	(n = 8)	(n = 72)	(n = 2)
Age	*Mean*	41.3	44.2	42.2	47.1	43.8	46.0
	SD	(11.3)	(14.5)	(15.9)	(16.0)	(13.9)	(26.9)
BMI	*Mean*	26.2	27.6	26.7	26.9	27.5	30.4
	SD	(4.01)	(7.15)	(5.21)	(3.43)	(7.04)	(3.96)
Sex	*Male*	1	31	5	4	44	2
	Female	5	44	7	4	28	0
Race	*White*	3	16	5	2	15	1
	Black	3	59	7	6	57	1
MoD	*Accident*	1	22	9	1	26	2
	Homicide	2	28	1	3	24	0
	Natural	3	21	1	4	19	0
	Suicide	0	4	1	0	3	0
Event Location	*Hospital*	0	16	8	1	19	0
	Indoors	5	42	2	4	41	1
	Outdoors	1	13	1	2	8	1
	Vehicle	0	4	1	1	4	0
PMI	*< 48 HRS*	5	65	11	7	62	2
	> 48 HRS	1	10	1	1	10	0

Table 3 | Human Post Mortem Microbiome Sample Count by Body Site

	Death Event (n = 164)				Home Location (n = 152)			
	Low Crime	Medium Crime	High Crime	Total	Low Crime	Medium Crime	High Crime	Total
Rectum	5	60	11	76	6	60	4	70
Mouth	6	69	13	88	7	70	5	82

Alpha Diversity | Death Event Location Crime Level

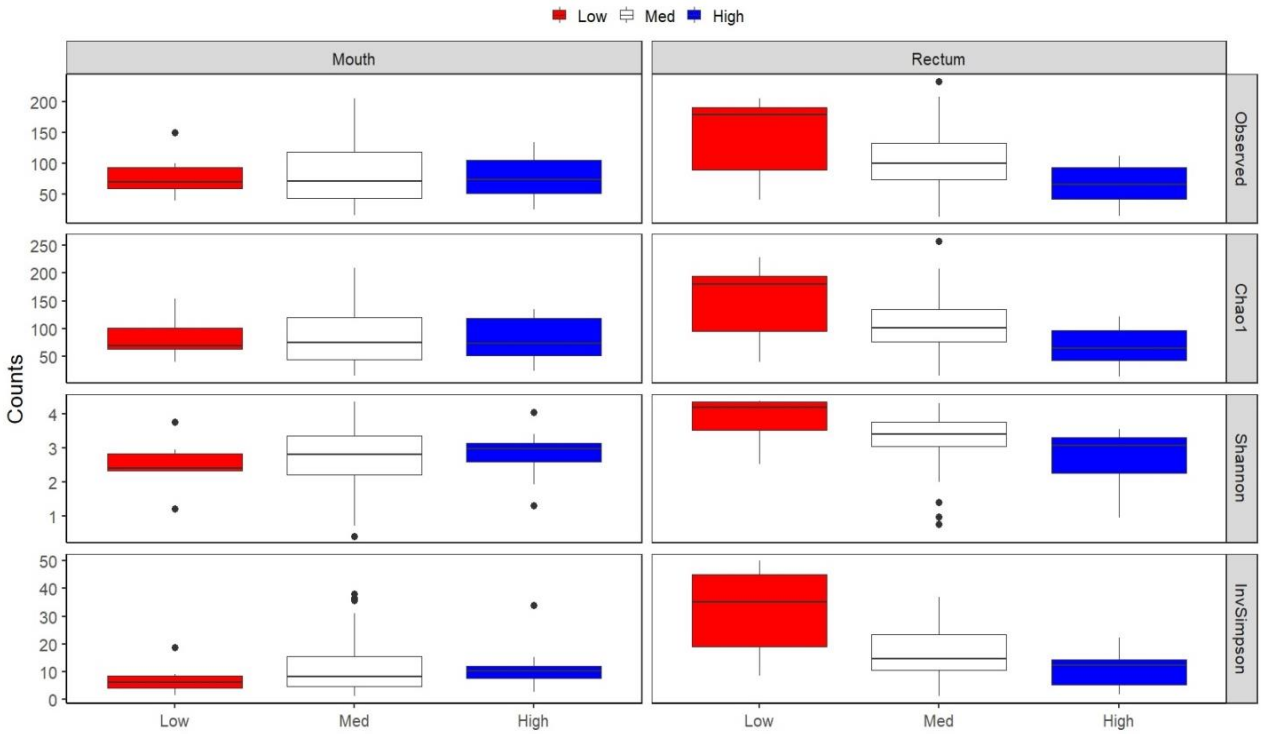

Figure 2 | Alpha Diversity by Death Event Location. Schematic showing the distribution of alpha diversity values for observed richness, Chao1, Shannon diversity, and Inverse Simpson diversity in mouth and rectal samples across low, medium, and high levels of census block group crime at the decedents' death even location. There were significant differences across levels of crime ($p < 0.05$) for each alpha diversity metric.in rectal samples. There were no significant findings in mouth samples.

Alpha diversity is associated with block group crime level at decedent death event location

To compare richness and evenness by local area crime level at the decedent's death event location, Kruskal-Wallis tests were conducted with crime level serving as the grouping variable. Though observed richness in rectum samples and Shannon diversity in mouth samples were normally distributed, sample size within conditions varied markedly between low, medium, and high crime areas, rendering the use of one-way ANOVA tests a less conservative choice. As such,

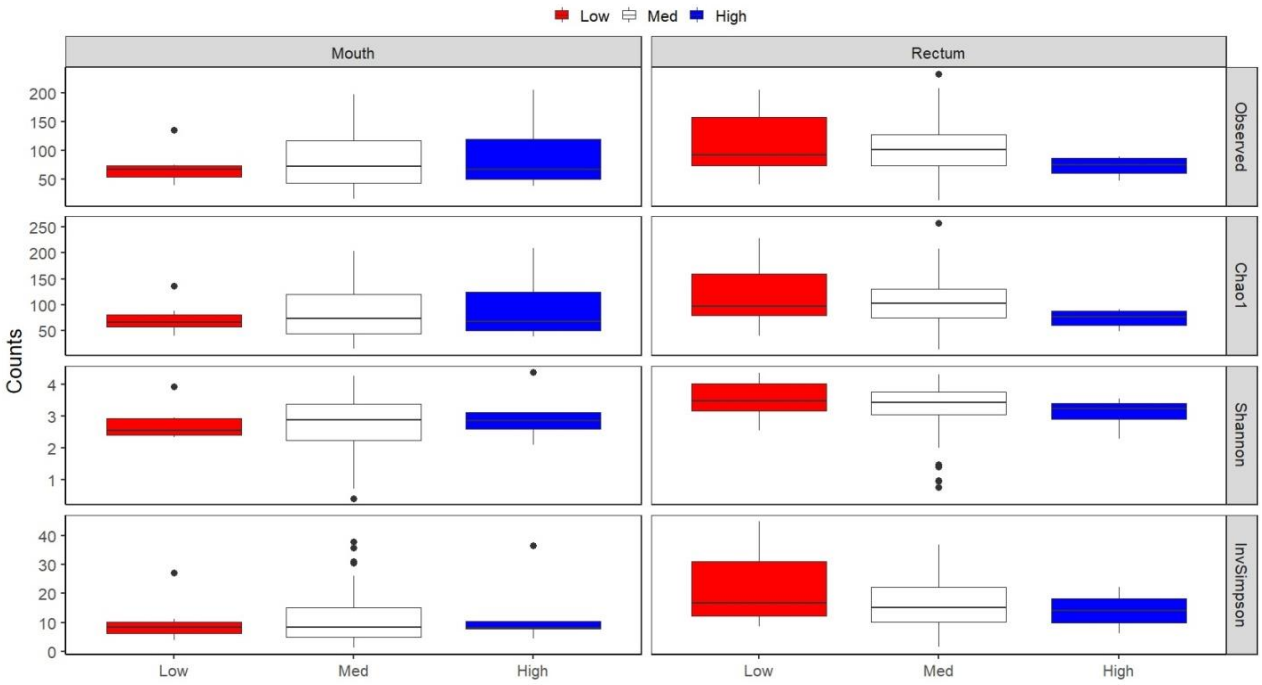

Figure 3 | Alpha Diversity by Home Location. Schematic showing the distribution of alpha diversity values for observed richness, Chao1, Shannon diversity, and Inverse Simpson diversity in mouth and rectal samples across low, medium, and high levels of census block group crime at the decedents' home location. There were no significant differences in alpha diversity ($p > 0.05$) in mouth or rectum samples.

Kruskal-Wallis tests with post hoc Nemenyi tests were globally employed to compare measures of alpha diversity across local area crime level at the death event locations.

Results show a significant difference in the alpha diversity of rectum samples (n = 76) between low (n = 6), medium (n = 59), and high (n = 11) crime areas when comparing the decedents' death event locations. Results indicate that there are significant differences in observed richness ($H(2) = 8.1103$, $p = 0.017$), Chao1 ($H(2) = 7.842$, $p = 0.020$), Shannon diversity ($H(2) = 9.2975$, $p = 0.010$), and Inverse Simpson diversity ($H(2) = 7.3407$, $p = 0.025$) indices among rectum samples across local area crime levels (**Fig 2; Table 4)**. Specifically, observed richness among decedents found in areas with low ($p = 0.036$) and medium ($p = 0.035$) crime was significantly higher compared to high crime areas, but there was no difference between low and

medium crime areas (p = 0.505). Likewise, the Chao1 index, an indicator of sample richness, was significantly higher in low and medium crime areas compared to high crime areas; though, there was no difference in Chao1 index between medium and low crime areas (p = 0.515). Findings for Shannon diversity, an alpha diversity measure that accounts for both the abundance and distribution of taxa, follow the same pattern with significantly higher alpha diversity in low (0.013) and medium (0.038) crime areas compared to high crime areas but no difference between medium and low crime areas (p = 0.275). Finally, results show significantly higher Inverse Simpson diversity, another alpha diversity measure that accounts for richness and evenness, among low crime areas compared to high crime areas (p = 0.022), but no differences between medium and low (0.190) or medium and high crime areas (0.147) were found. There were no significant differences between low (n = 6), medium (n = 69), and high (n = 13) crime areas for any of the alpha diversity metrics among decedent mouth samples (n = 88). In addition, alpha diversity was further investigated by local area crime in the decedents' home location. Repeat analysis according to the decedents' home location showed no significant differences in alpha diversity in either mouth or rectal samples (**Fig 3; Table 5**). In sum, multiple metrics demonstrate significant differences in the alpha diversity of rectum samples between block group crime level assigned to the decedent death event, but not home, locations.

Table 4 | Alpha Diversity by Death Event Location Crime Level

	Rectum M (SD)			Mouth M (SD)		
	Low	Med	High	Low	Med	High
Observed Richness	140.600 (72.189)	104.550 (43.339)	65.455 (34.992)	80.500 (39.399)	82.652 (49.226)	78.385 (36.864)
Chao1 Diversity	147.723 (77.443)	108.791 (46.549)	68.641 (36.913)	84.348 (41.012)	86.538 (51.691)	82.029 (39.401)
Shannon Diversity	3.805 (0.787)	3.320 (0.714)	2.715 (0.863)	2.520 (0.833)	2.783 (0.887)	2.827 (0.706)
Inverse Simpson	31.514 (17.476)	16.702 (8.804)	10.825 (6.475)	7.620 (6.035)	11.167 (9.095)	10.870 (7.930)

Table 5 | Alpha Diversity by Home Location Crime Level

	Rectum M (SD)			Mouth M (SD)		
	Low	Med	High	Low	Med	High
Observed Richness	112.667 (64.920)	102.850 (44.958)	71.500 (19.416)	70.714 (30.939)	82.029 (47.265)	95.800 (68.430)
Chao1 Diversity	119.311 (70.590)	107.227 (48.121)	72.857 (19.817)	74.121 (31.429)	85.938 (49.873)	97.887 (70.579)
Shannon Diversity	3.521 (0.681)	3.272 (0.792)	3.075 (0.556)	2.787 (0.558)	2.768 (0.880)	3.009 (0.854)
Inverse Simpson	22.204 (14.574)	16.399 (8.699)	14.113 (7.029)	10.275 (7.857)	10.706 (8.368)	13.428 (13.116)

Alpha diversity is not correlated with block group per capita assault, nonfatal shootings, or homicide at decedent death event or home locations

To determine if alpha diversity of both rectum and mouth samples was associated with *per capita* rates of aggravated assault, nonfatal shootings, and homicide, nonparametric correlations were conducted using Kendall's tau with a Bonferroni correction to adjust for multiple comparisons. Findings revealed no significant associations between any of the continuous crime measures and observed richness, Chao1, Shannon diversity, or Inverse Simpson diversity in either the decedents' death event (**Fig 4-5**) or home location (**Fig 6-7**), thereby confirming the choice of the categorical crime level variable as the primary dependent variable in subsequent analyses.

In view of these findings, the rectum sample dataset for decedent death event location was selected for further analysis. To foretell any issues of multicollinearity while modeling, relationships between predictor variables were explored via Spearman rank correlation tests (**Fig 8**). Here, p-values were not adjusted to consider every source of potential model contamination. Unsurprisingly, household income was negatively associated with both block group

unemployment rate ($r = -0.345$, $p < 0.0001$) and vacancy rate ($r = -0.247$, $p < 0.0001$). Likewise, block group vacancy rate was also positively associated with unemployment rate ($r = 0.146$, $p < 0.0001$). In addition, there were small but significant correlations between the percentage of Black residents in a block group and socioeconomic and *per capita* crime variables. The percentage of Black residents was significantly associated with household income ($r = -0.193$, $p < 0.0001$), unemployment rate (0.091, $p = 0.01$), and vacancy rate (0.145, $p = 0.01$) as well as reductions in *per capita* nonfatal shootings ($r = -0.222$, $p < 0.0001$) and assault ($r = -0.132$, $p < 0.0001$), underscoring the potential of informal social control mechanisms and guardianship in driving down local area crime. Overall, these data demonstrate important covariation in the dataset that must be further examined during model building.

Alpha Diversity | Rectum Samples by Death Event Location

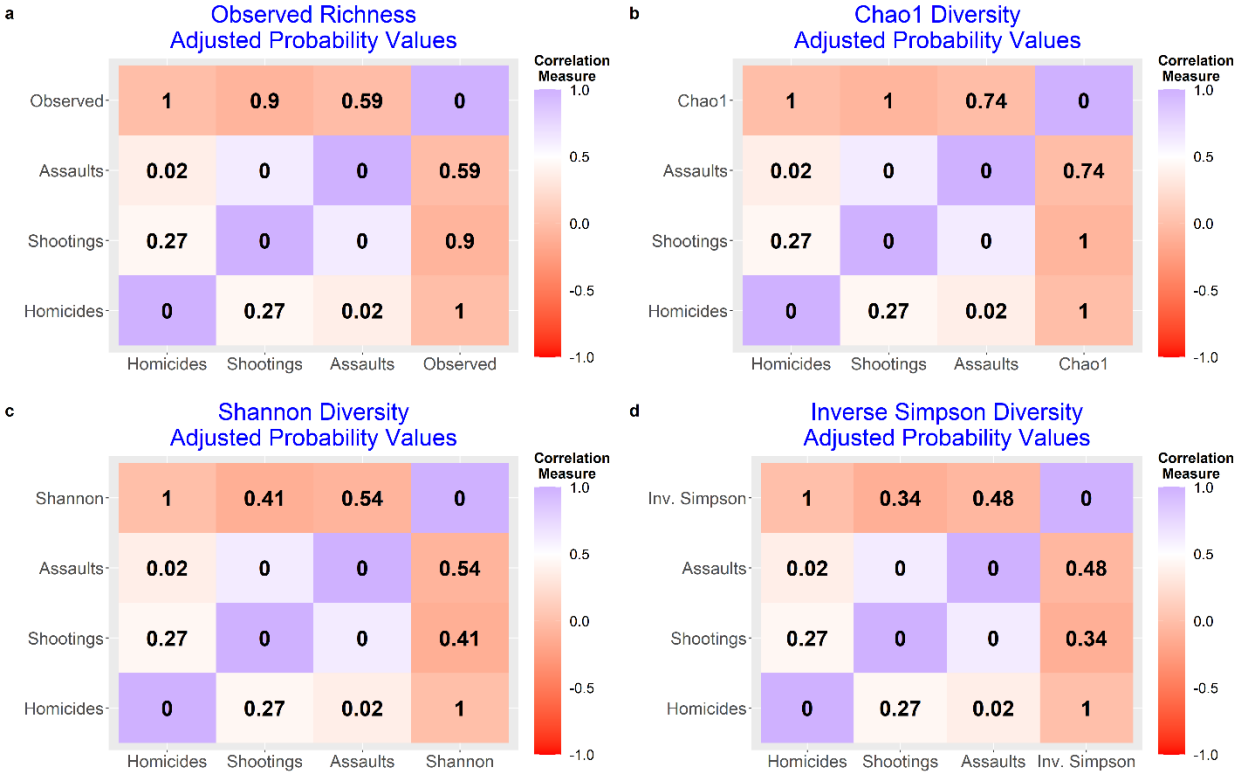

Figure 4 | Rectum Sample Alpha Diversity and *Per Capita* Crime by Death Event Location. a-d) Correlograms depicting correlation results using Kendall's tau to determine the relationship between block group *per capita* assault, nonfatal shootings, and homicide at decedent death event location and a) observed richness, b) Chao1, c) Shannon, and d) Inverse Simpson diversity in rectum samples. The color of the squares represents the strength and direction of the correlation coefficient, and the values represent p-values adjusted with a Bonferroni correction.

Alpha Diversity | Mouth Samples by Death Event Location

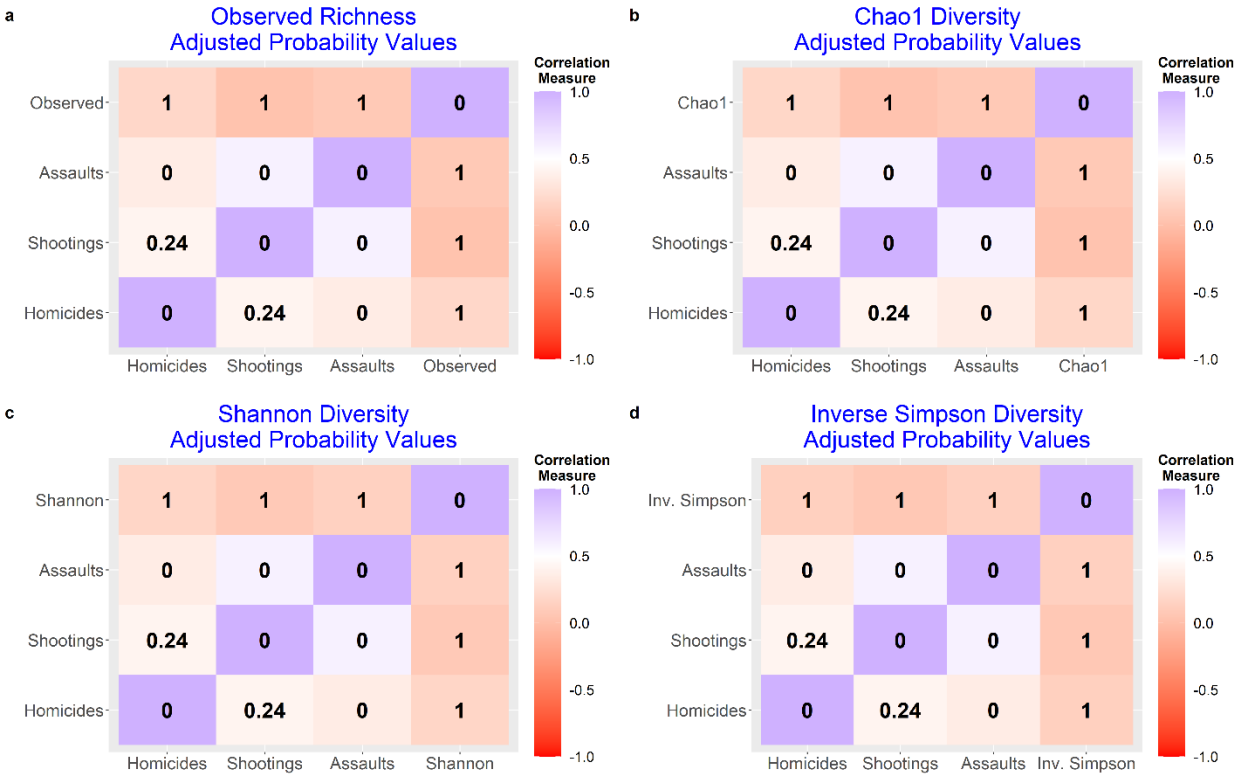

Figure 5 | Mouth Sample Alpha Diversity and *Per Capita* Crime by Death Event Location. a-d) Correlograms depicting correlation results using Kendall's tau to determine the relationship between block group *per capita* assault, nonfatal shootings, and homicide at decedent death event location and a) observed richness, b) Chao1, c) Shannon, and d) Inverse Simpson diversity in mouth samples. The color of the squares represents the strength and direction of the correlation coefficient, and the values represent p-values adjusted with a Bonferroni correction.

Alpha Diversity | Rectum Samples by Home Location

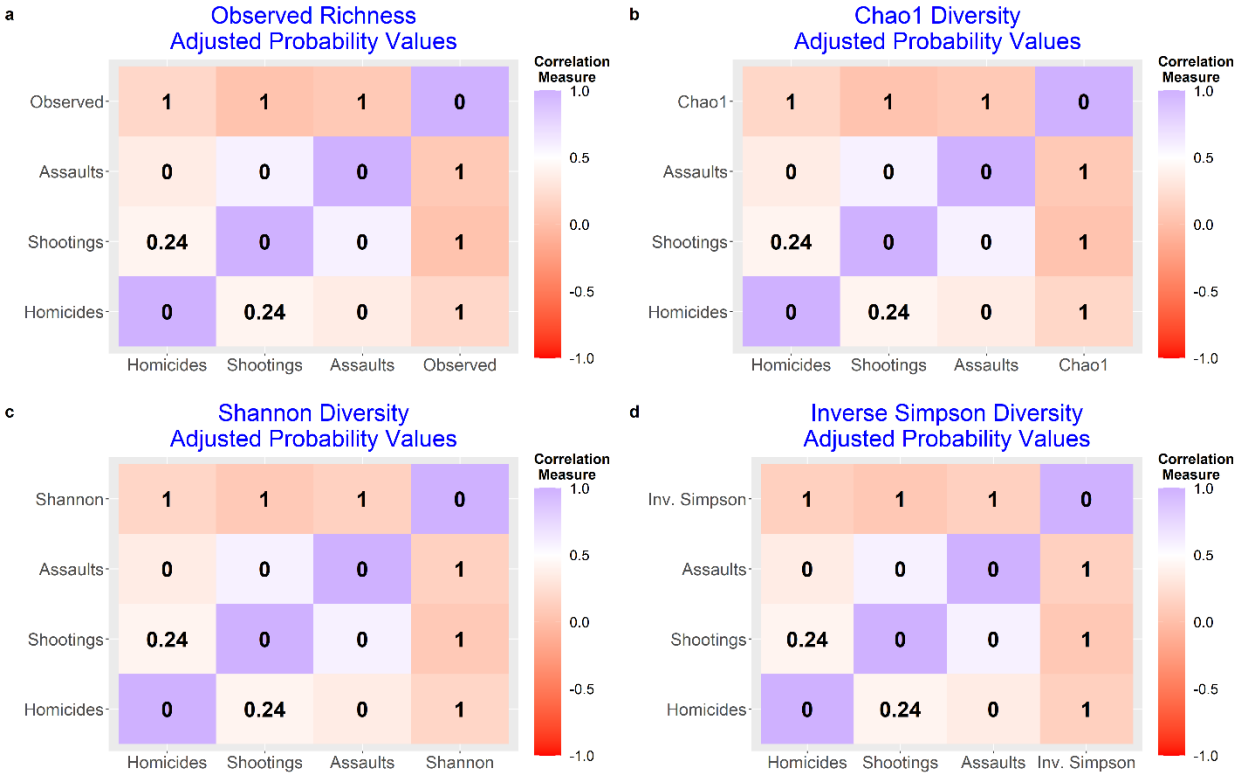

Figure 6 | Rectum Sample Alpha Diversity and *Per Capita* Crime by Home Location. a-d) Correlograms depicting correlation results using Kendall's tau to determine the relationship between block group *per capita* assault, nonfatal shootings, and homicide at decedent home location and a) observed richness, b) Chao1, c) Shannon, and d) Inverse Simpson diversity in rectum samples. The color of the squares represents the strength and direction of the correlation coefficient, and the values represent p-values adjusted with a Bonferroni correction.

Alpha Diversity | Mouth Samples by Home Location

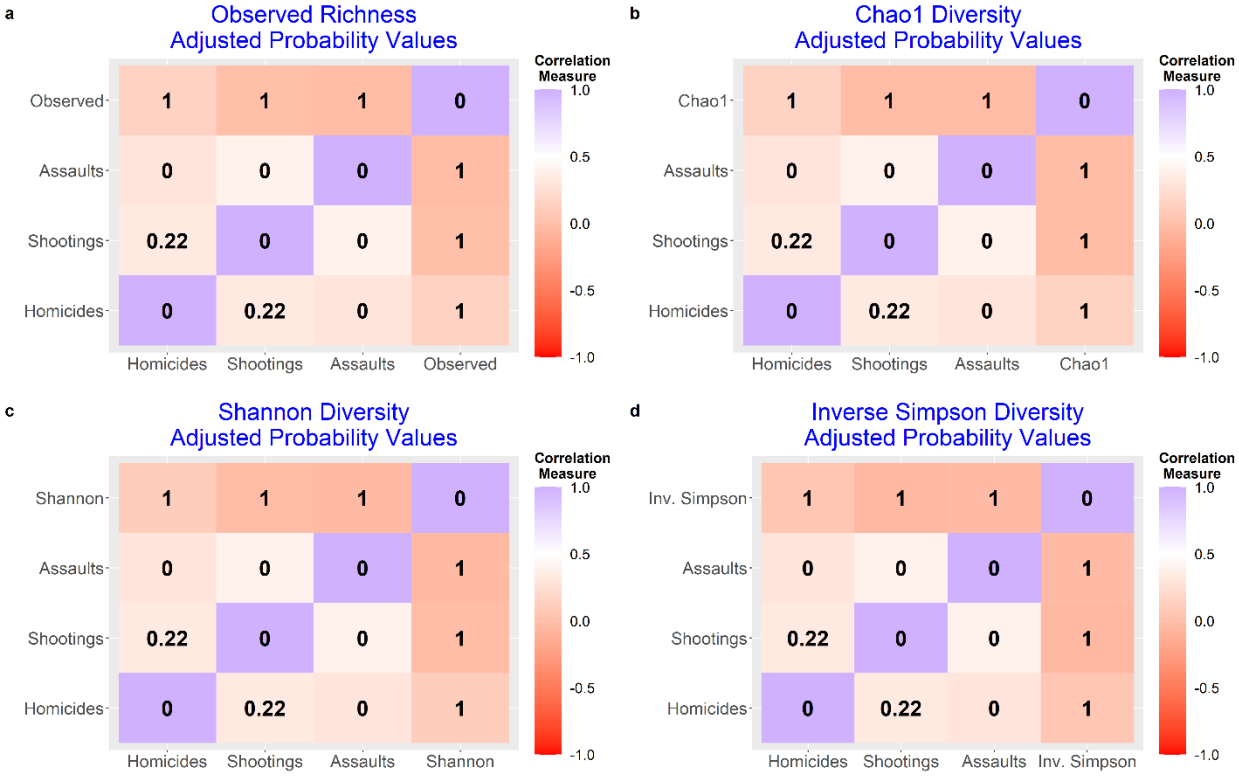

Figure 7 | Mouth Sample Alpha Diversity and *Per Capita* Crime by Home Location. a-d) Correlograms depicting correlation results using Kendall's tau to determine the relationship between block group *per capita* assault, nonfatal shootings, and homicide at decedent home location and a) observed richness, b) Chao1, c) Shannon, and d) Inverse Simpson diversity in mouth samples. The color of the squares represents the strength and direction of the correlation coefficient, and the values represent p-values adjusted with a Bonferroni correction.

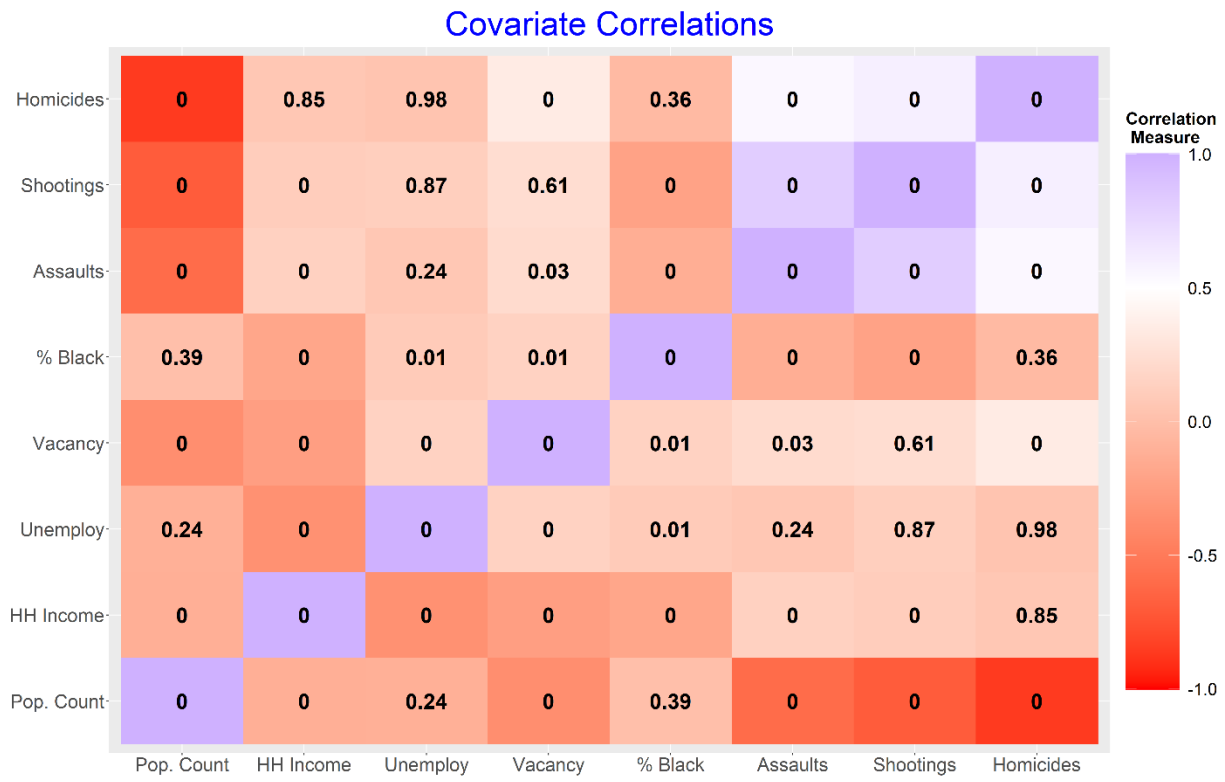

Figure 8 | Correlations for Model Covariates. Correlogram showing significant correlations among model covariates collected for decedent death event locations. Notably, there are significant relationships between household income and i) unemployment rate and ii) vacancy rate. There is also a significant association between unemployment rate and vacancy rate. The color of the squares represents the strength and direction of the correlation coefficient, and the values show unadjusted p-values.

Random forest classification fails with dramatically imbalanced groups

In order to determine the OTUs driving the relationship between alpha diversity in rectum samples and block group crime level at decedent death locations, a random forest classification model was built. For this analysis, decedent demographic metadata and USCB socioeconomic covariates from their assigned block group were included with OTU data as predictors of block group crime level membership. Using 500 decision trees and 92 predictors at each decision tree split, the error estimate was 21.05%, suggesting that model predictors correctly predicted sample membership to its assigned block group 78.95% of the time. However, this low error rate was a result of the low number of cases in the low (n = 5) and high (n = 11) crime conditions being misclassified in the medium (n = 60) crime level group 100% of the time. As such, negative binomial mixed models were used as an alternative strategy to identify taxa that differ in abundance between low, medium, and high crime areas.

Block group vacancy rate and alpha diversity drive block group classification

To investigate the extent to which alpha diversity measures can predict block group placement in one of the three crime level categories beyond known risk factors for neighborhood dangerousness, sets of multinomial logistic regression models were fitted, corresponding to the four alpha diversity metrics presented (i.e., observed richness, Chao1, Shannon diversity, and Inverse Simpson diversity). Models were compared for goodness-of-fit relative to a null model. First, single variable models were fitted to assess standalone performance of model covariates (Models A1-7; **Table 6**). Findings indicate a significant effect of block group unemployment rate, vacancy rate, and Inverse Simpson diversity in predicting block group crime level; however, these models showed only a modest improvement in goodness-of-fit compared to the null model. Therefore, significant covariates from Models A1-7, including unemployment rate, vacancy rate,

and the Inverse Simpson diversity, were selected for further model building, accounting for population homogeneity. These predictors were used to construct Models B-G, comparing model fit to a null model.

The addition of socioeconomic covariates improved model fit and block group classification in low, medium, and high crime conditions (**Tables 7-8**). Models B-G were all significant (**Table 7**), but the overall best performing models were Models D & G. Both Models D & G successfully predicted block group crime level 81.9% of the time. However, model fit was best for Model G. Model G shows a significant effect of block group vacancy rate such that for every one-unit increase in vacancy rate, the odds of classification in a high crime level block group increase ($\beta = 24.3$, $p = 0.03$). Likewise, for every one-unit decrease in decedent Inverse Simpson diversity, the odds of classification in a high crime block group increase ($\beta = -0.17$, $p = 0.02$). Importantly, unlike in random forest modeling, classification was not driven by the imbalanced groups. Block groups in every crime condition were both correctly and incorrectly classified, contributing to overall model performance. Taken together, these data demonstrate that there is a common gut microbiome structure within crime level conditions that drives block group classification.

Table 6 | Single Variable Multinomial Logistic Regression

	Models A1-7 (n = 72)			
	β	SE	p-value	AIC
% Black Residents	1.76	1.33	0.186	47.11
Unemployment Rate	10.85	4.57	0.018	42.19
Vacancy Rate	17.49	6.68	0.009	36.77
Observed	-0.02	0.01	0.053	36.47
Chao1	-0.02	0.01	0.054	36.58
Shannon	-2.08	1.11	0.062	35.52
Inverse Simpson	-0.13	0.05	0.005	30.13

Table 7 | Multivariate Multinomial Logistic Regression with Inverse Simpson Diversity

		Inverse Simpson	% Black	Unemployment	Vacancy
Model B	β	-0.133			
	SE	(0.047)			
	p-value	0.005			
Model C	β	-0.174	4.285		
	SE	(0.064)	2.144		
	p-value	0.006	0.046		
Model D	β	-0.113	--	17.028	
	SE	(0.054)	--	7.262	
	p-value	0.037	--	0.019	
Model E	β	-0.161	4.262	16.693	
	SE	(0.077)	2.539	7.623	
	p-value	0.037	0.093	0.029	
Model F	β	-0.193	2.853	--	23.290
	SE	(0.083)	2.074	--	11.516
	p-value	0.020	0.169	--	0.043
Model G	β	-0.171	--	--	24.304
	SE	(0.071)	--	--	10.858
	p-value	0.016	--	--	0.025

Table 8 | Multivariate Multinomial Logistic Regression Model Fit

Model	Log-likelihood	McFadden R^2	X^2	p	BG Correct	% Correct	AIC
Null	-59.4	0.0	0.0	1.0	NA	NA	46.8
Model B	-41.1	0.14	13.9	0.0	58	80.6%	30.1
Model C	-35.2	0.27	25.8	0.0	54	75.0%	27.3
Model D	-37.0	0.23	22.1	0.0	59	81.9%	23.3
Model E	-31.8	0.34	32.5	0.0	56	77.8%	20.8
Model F	-30.3	0.37	35.5	0.0	59	81.9%	24.8
Model G	-35.5	0.26	25.2	0.0	59	81.9%	21.0

Residential instability, population heterogeneity, and low socioeconomic status are important predictors of gut microbiome composition

Microbiome OTUs, binned sequencing data used to describe bacterial abundance, from rectum samples assigned to decedent death locations were modeled using crime and socioeconomic variables to identify microbiota that have a significant relationship with block

group contextual factors. Given the significant relationships among socioeconomic covariates, four separate models were fitted using a dummy coded block group crime level variable alone (**Fig 9**; Model 1) as well as block group vacancy rate (Model 2), unemployment rate (Model 3), and percentage of Black residents (Model 4) together with block group crime level as fixed effects. In all four models, crime level and socioeconomic factors were significant predictors in modeling OTU data (see Appendix), with socioeconomic factors markedly increasing the number of OTUs predicted by block group contextual factors compared to the crime variable alone. Together, these four models collectively predicted the abundance of 52 different taxa (see Appendix), demonstrating local area contextual factors drive gut microbiome composition. Importantly, these

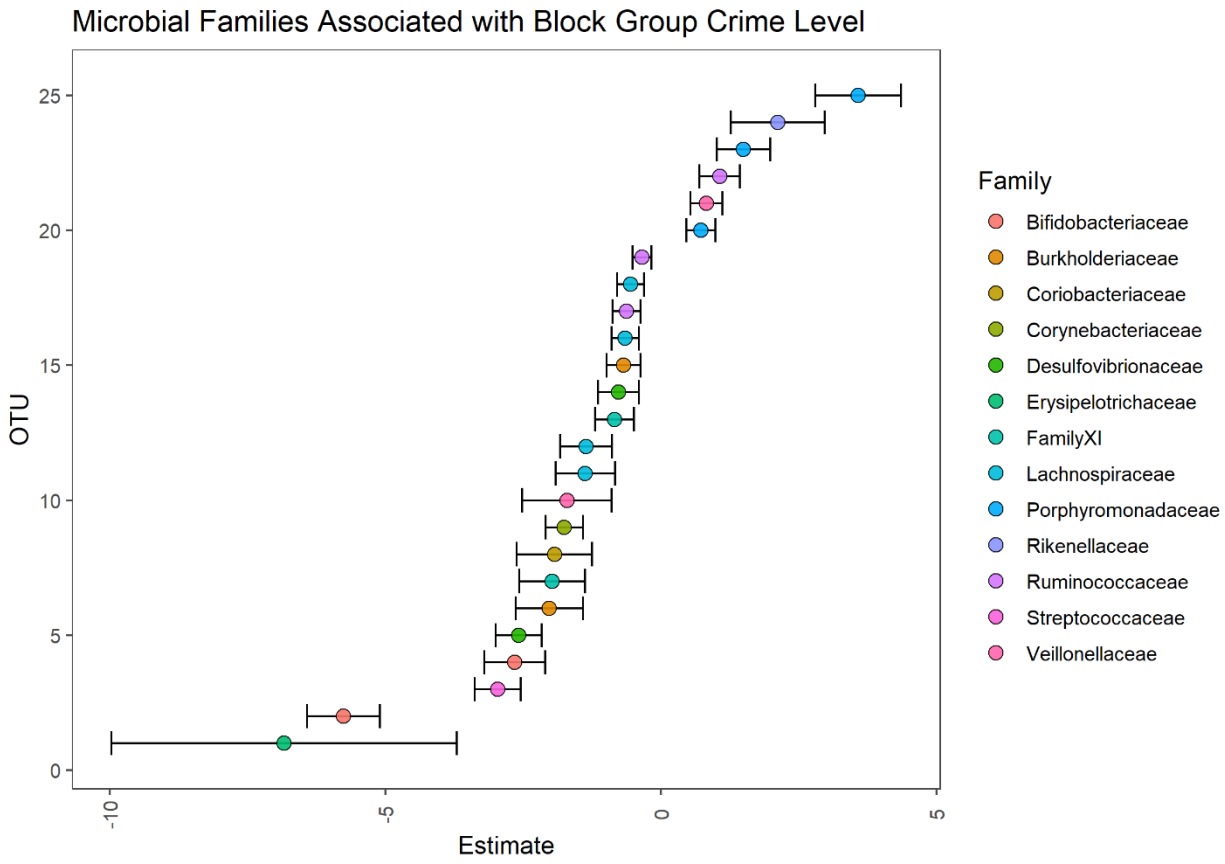

Figure 9 | Microbial Families Associated with Crime Level. Schematic depicting 25 bacteria families significantly associated with block group crime level (Model 1). Each point corresponds to one taxon and its color corresponds the family. The error bars represent standard error of the estimate.

data supply critical evidence that gut microbiome composition varies according to local area crime exposures.

Given that the primary dependent variable is categorical and there are limited cases in the low and high crime conditions, a follow-up NBMM analysis modeling OTU data with block group *per capita* homicide was conducted. *Per capita* homicide was selected for this supplemental analysis because it is considered a reliable indicator of local crime, and subsequently used in place of crime level as the model's fixed effect. Results were similar to finding from Model 1, returning 18 taxa that were significantly associated with block group *per capita* homicide (**Fig 10**).

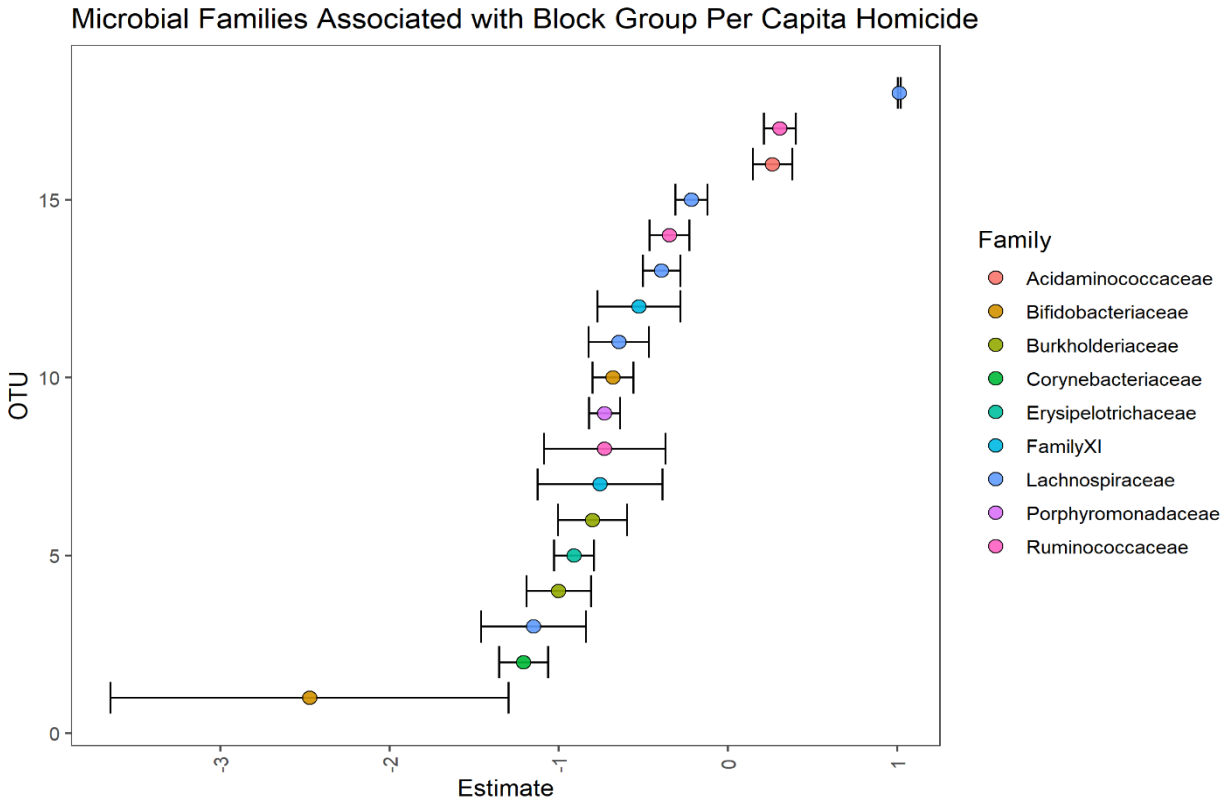

Figure 10 | Microbial Families Associated with *Per Capita* Homicide. Schematic depicting 18 bacteria families significantly associated with block group *per capita* homicide. Each point corresponds to one taxon and its color corresponds the family. The error bars represent standard error of the estimate.

Interestingly, both crime variables have a significant relationship with *Lachnospiraceae* and the Clostridia class, in general, providing a direct connection to the project's preclinical findings.

Beta diversity did not differ between block group crime conditions

To investigate the differences in beta diversity across levels of local area crime, a series of PERMANOVA tests were conducted using Unifrac distances. Results returned no significant difference in beta diversity among rectum samples across levels of block group crime at decedent death event locations ($F(2) = 1.0534$, $R^2 = 1.0534$, $p = 0.307$). There were also no significant differences in beta dispersion among rectal samples between crime conditions ($F(2) = 0.780$, $p = 0.45$). Similarly, there were no significant differences detected for beta diversity of mouth samples by block group crime level at decedent death event locations ($F(2) = 1.1527$, $R^2 = 0.026$, $p = 0.166$), nor any difference in beta dispersion across conditions ($F(2) = 0.6643$, $p = 0549$). A similar pattern emerged from analyses by decedent home location. PERMANOVA results indicated no difference in beta diversity of rectum samples between low, medium, and high crime block groups at decedent home locations ($F(2) = 1.194$, $R^2 = 0.034$, $p = 0.132$). There was also no difference in home location beta dispersion of rectum samples ($F(2) = 0.1468$, $p = 0.874$). Finally, there were no significant differences in beta diversity ($F(2) = 0.8684$, $R^2 = 0.022$, $p = 0.77$) or beta dispersion ($F(2) = 1.1377$, $p = 0.323$) of mouth samples across crime conditions at decedent home locations. Overall, this suggests that there is no significant deviation in microbiome community structure across block group crime level.

CHAPTER 4: DISCUSSION

In this dissertation, findings demonstrate a potential link between human gut microbiome composition and local area crime level. Specifically, secondary sequencing data from mouth and rectum samples were used to calculate diversity metrics that describe the human *post mortem* microbiome as a proxy measure for the *ante mortem* gut microbiome. These metrics were subsequently assigned to both the decedents' death event and home locations in an effort to determine if the structure of the gut microbiome was unique in different physical contexts such that it could be used to predict the local area crime level, and by extension, the types of social and environmental exposures in the block group.

The data show a significant negative relationship between alpha diversity of rectum samples and block group crime level assigned to decedent death event locations. Negative binomial mixed models for rectum samples at the decedent death event location revealed 52 unique taxa that are associated with block group socioeconomic and crime variables. Importantly, subsets of taxa were identified that are associated with both block group crime level and *per capita* homicide. Further analysis (of rectum samples assigned to decedent death event locations) with multinomial logistic regression was used to determine the extent to which the structure of the human gut microbiome is a standalone marker of *ante mortem* social and environmental exposures. In sum, these data suggest that there is a link between human gut microbiome composition and local area violent crime level.

The current study demonstrates an overall loss of gut microbiome diversity and change in distribution of certain taxa as local area crime increases, supplying a novel mechanism through which neighborhood context could affect health and behavior. This finding is in line with criminological research that has already established a link between environmental factors and local

crime patterns. For example, previous research documents that exposures to lead and other toxins in the environment are highest in impoverished areas (Mohai & Saha, 2006, 2007), and that those exposures increase the likelihood of neurocognitive deficits and externalizing behaviors (Denno, 1990; Narag, Pizarro, & Gibbs, 2009). This important criminological research provides well-documented evidence that bridges the first connection between physical context and human physiological states. Complementary neuroscientific research demonstrates that exposure to heavy metals, including lead, induces excitotoxicity and oxidative stress that causes cell death in the brain (Bondy, 2021; Li, Xia, Zorec, Parpura, & Verkhratsky, 2021), adding a molecular mechanism that explains the observed neurocognitive changes and behavioral deficits among those with high toxin exposure in their environment. Importantly, research shows that toxin exposure is positively associated with local violent crime patterns, especially in areas with the highest resource deprivation (Stretesky & Lynch, 2004), showcasing the interaction between human physiology and the environment. The current work shows a relationship between gut microbiome composition and local area crime that is modulated by socioeconomic factors, thereby expanding on this approach by combining criminological and basic neuroscientific research to provide another potential mechanism that may mediate the effect of a disadvantaged neighborhood context.

The data presented here confirm with multiple metrics that the decedents with exposure to high crime areas have overall lower biodiversity in their gut microbiomes. This result is consistent with previous research that demonstrates a reduction in biodiversity associated with urban blighting (Pearson et al., 2019). Multiple studies demonstrate the relationship between crime and urban blight (Bogar & Beyer, 2015; Branas, Rubin, & Guo, 2012; Spelman, 1993), with some showing reductions in certain types of crime secondary to green remediation (Branas et al., 2016; Kondo et al., 2018). It is therefore unsurprising that, along with alpha diversity indicators, the best

model predicting block group crime level was its vacancy rate with high vacancy areas having higher crime rates. Though it is true that reductions in microbial diversity are associated with urban blight and blight is associated with increases in crime, evidence also suggests that environmental exposures drive gut microbiome composition (Afshinnekoo et al., 2015; Von Ehrenstein et al., 2000; von Mutius & Vercelli, 2010; Yatsunenko et al., 2012), raising important questions about other exposures in high crime areas that could affect gut microbiome composition.

Previous work has demonstrated the forensic applications of the HPMM in its ability to predict forensic case attributes; however, the performance of rectal samples in predictions is relatively poor (Kaszubinski, Pechal, Smiles, et al., 2020; Pechal et al., 2018; Y. Zhang et al., 2019). Given that the *post mortem* microbiome of the rectum is especially stable (Pechal et al., 2018), the current study's findings suggest that the microbial profile in *post mortem* rectal samples has potential non-forensic applications. To this end, the current study shows that rectal samples assigned to decedent death event location can be used in tandem with socioeconomic factors to predict local area crime level, establishing a potential gut-brain link related to differential exposures in low, medium, and high crime areas. Interestingly, the current study failed to show a relationship between measures of alpha diversity (i.e., observed richness, Chao1, Shannon diversity, and Inverse Simpson diversity) and any other measure of crime, suggesting that the relationship between the gut microbiome and local crime level exists in severe contexts where crime is very high or very low.

Though the specific effect of crime exposure on gut microbiome composition is unknown, there are two principal mechanisms through which very high crime exposure could negatively affect the human gut microbiome. First, stress has a known role in shaping the gut microbiome both in humans and animal models (Foster, Rinaman, & Cryan, 2017; Moloney, Desbonnet,

Clarke, Dinan, & Cryan, 2014; C. Yang et al., 2017), playing a critical role in brain health. For example, one recent study in children reported that high stress was associated with lower alpha diversity (Michels et al., 2019). Interestingly, this relationship was found with Simpson, but not observed or Chao1 diversity, as shown here, suggesting that richness and evenness are both important in determining the effect of social and environmental exposures. Next, resource deprivation, a stressor in and of itself, may affect gut microbiome composition. While there is an overall dearth of research on this topic, researchers posit that both stress exposure and reduced access to varied sources of dietary fiber (e.g., food deserts) could explain, in part, gut microbiome differences related to inflammatory disease and health across geographic space (Harrison & Taren, 2018; Kau, Ahern, Griffin, Goodman, & Gordon, 2011). Given the connection between violence exposure and stress (Bingenheimer et al., 2005; Cisler et al., 2012), and the relationship of both with disadvantage, the current study supplies evidence that the gut microbiome is a potential candidate to consider as a mediator of the neighborhood effect.

One important facet of the gut microbiome as a mediator of the neighborhood effect is its potential to explain, in part, individual-level variation in behavior within a biopsychosocial framework. Indeed, the structure of the gut microbiome depends on individual-level conditioning in response to psychosocial factors (e.g., stress, diet). In this view, unique social and environmental exposures shape the gut microbiome, changing host physiology and contributing to the variability in health and behavioral outcomes observed in disadvantaged communities. The gut microbiome is thus a biological factor that exerts its effects in accordance with other known psychological and social or environmental risk factors identified in the criminological literature. In addition, the current study identified specific taxa in relation to high crime contexts that were also identified in the project's preclinical studies in relation to territorial, reactive aggression behavior in mice,

raising questions about neighborhood context and the role of the gut microbiome in human aggression that needs to be addressed in future research.

The current study has a number of limitations. Detroit represents 139 square miles of land in Southeast Michigan, yet only 95 of the 185 HPMM subjects died within its city limits. Among those 95 decedents, only 72 had data from rectum samples, further paring down the sample size. Therefore, this study cannot be considered representative of all Detroit block groups. In addition, the current study is ecological research and cannot be used to make inferences about the individuals in the block groups (Zeoli, Paruk, Pizarro, & Goldstick, 2019), but rather, the types of exposures that could occur within a block group.

Individual behaviors may have contributed to the observed findings in both decedent death event and home locations. Given the high number of deaths that occurred at hospitals[6] and accidental deaths recorded in the death event location dataset for high crime areas, it is possible that other factors that affect gut microbiome composition, like drug use, could be driving the observed relationship between block group crime exposures and alpha diversity. Moreover, there may be variation in exposure to the decedent home locations among individuals who may have spent the majority of their time elsewhere (due to work or other lifestyle choices), contributing to the null findings. Because the current study has an ecological design, exploring the effect of individual-level factors on the gut microbiome was outside its scope. Additional observations are needed to improve future modeling that could be hampered by imbalanced groups and overall low number of individuals in the high crime condition.

Another critical limitation of this study is endogeneity in modeling (Zohoori & Savitz, 1997). Environmental and social exposures that are known risk factors for crime, like family

[6] Though there are many hospital deaths recorded in the high crime condition, they did not all occur at the same hospital.

structure (e.g., Bursik & Grasmick, 1993), also have an influence in driving microbial community composition (Song et al., 2013). In particular, the environment has a strong influence in shaping gut microbiome composition (Afshinnekoo et al., 2015; Pearson et al., 2019; Von Ehrenstein et al., 2000; von Mutius & Vercelli, 2010; Yatsunenko et al., 2012). Endogeneity thus becomes a problem when one model covariate (e.g., block group vacancy rate) has theoretical influence on both the outcome and other model covariates (e.g., alpha diversity). This is a particularly difficult limitation to overcome with microbiome and social and environmental research; however, future work should attempt more sophisticated modeling on larger datasets.

Conclusion

The current study shows that the structure of the human gut microbiome varies according to local area crime level and socioeconomic conditions. In particular, these data show that there is lower biodiversity in areas with high crime, an indicator of a less healthy microbiome. Thus, data presented here hypothesize a potential mechanism through which access to a particular diet, water supply, atmosphere, or physical space affects health and behavior. In the United States, socioeconomic deprivation is distributed across geographic space in a racially coded way. As such, the findings presented here demonstrate yet another way through which the persistent lack of investment and marginalization of Black communities has real health consequences that translates into a disproportionate health burden.

Public health research has long shown how local food environments contribute to health disparities (Moore & Diez Roux, 2006; Wallace et al., 2021). Most immediately, the current study's findings provide support for this public health research, providing a novel biomarker to demonstrate the impact of different physical contexts, with varying levels of crime exposure, socioeconomic resources, and healthy dietary choices, as well as how these different living

conditions affect health. This work could therefore provide additional rationale for bolstering greening efforts and urban food programs. Further research is needed to develop the human gut microbiome as a potential target for public health intervention.

CHAPTER 5: CONCLUSIONS AND FUTURE DIRECTIONS

Summary

The work presented in this dissertation contributes to the field of criminology in several ways. Overall, my preclinical data describe a novel connection between the gut microbiome and territorial, reactive aggression behavior in mice that holds translational relevance for human public health. In support of this clinical relevance, the human data show that local area crime level is associated with variation in the human *post mortem* gut microbiome, establishing a critical link in the field of criminology between environmental context and physiology. Together, these findings move toward a biopsychosocial model of aggression behavior, providing foundational information that begins to address a critical gap in criminological research. Though criminological theories discuss the ill effects of concentrated disadvantage, poor social attachment, and their negative psychological sequelae that increase risk for crime perpetration, current research has not elucidated the biological underpinnings of these dispositions or how they convert to behavioral action. That is to say, the mechanisms of how individuals in risky physical and social environments go from *feeling* to *doing* are poorly understood. By combining research in the social and natural sciences, the work of my dissertations demonstrates the relationship between the gut microbiome and aggression behavior that has important connections to human crime patterns, laying the foundation for further exploration of the gut microbiome in human aggression. Given the complexity of aggression behavior and the multitude of factors that increase risk for human aggression, the best solution is to pull aggression-related natural and social science work together into a biopsychosocial model, which this interdisciplinary work begins to do.

To demonstrate the translational relevance of my preclinical work, the presented analysis explored the relationship between violent crime, socioeconomic conditions, and the human *post*

mortem gut microbiome. For these studies, secondary 16S ribosomal RNA (rRNA) amplicon sequencing data were obtained through collaboration with colleagues on the Human *Post Mortem* Microbiome (HPMM) research team, including data analyst Sierra Kaszubinski as well as Drs. Jennifer Pechal and Eric Benbow. These data provide correlational evidence that gut microbiome composition varies according to local area (i.e., census block group) crime level. Importantly, analysis of decedent rectum samples revealed that alpha diversity, the richness and evenness of gut bacteria, corresponding to decedent death event locations was significantly lower in high versus medium and low crime areas. Further investigation showed that, together with block group vacancy rate, alpha diversity could be used to predict block group category placement in low, medium, and high crime conditions. Further examination of bacteria abundance data with negative binomial mixed models identified specific taxa that varied by crime level, some of which belonged in the same *Lachnospiracaeae* family we identified as associated with aggression in male CD-1 aggressor mice described in my *Aggression and the Gut-Brain Axis* work. Taken together, these data provide support for a connection between crime exposure and changes in (gut) physiology that have implications for the future study of aggression behavior and violent crime in humans.

Implications and Future Directions

Biological changes in a disadvantaged neighborhood context

There is a call in criminological research to incorporate biology into the framework of major criminological theories to supply information about the molecular underpinnings of criminal behavior in all its various presentations (Fishbein, 1990). Though not formally tested here, the work in this thesis provides foundational evidence in support of exploring how perturbations in the gut microbiome affect individual-level expressions of aggression behavior. While it is unlikely that all behaviors have a direct gut-brain link, there are a multitude of factors in disadvantaged

neighborhoods that could affect gut microbiome composition, thereby affecting individual physiology and behavior. Importantly, this line of reasoning is consistent with criminological research on neighborhoods and small places showing that structural features impair social and community processes such that psychosocial risk factors aggregate in geographic space to compound risk for negative health and behavioral outcomes.

Living in an economically disadvantaged community, which in this study was associated with a higher block group percentage of Black residents, with high crime is a source of chronic stress, especially among children and adolescents. Among youth exposed to socioeconomic deprivation (i.e., low socioeconomic status; SES), research demonstrates an increase in both self-reported stress and cortisol reactivity (Brenner, Zimmerman, Bauermeister, & Caldwell, 2013; Hackman, Betancourt, Brodsky, Hurt, & Farah, 2012), revealing a direct connection between neighborhood context and a physiological mechanism that also affects (Xu, Lee, Zhang, & Frenette, 2020), and is affected by (Gao et al., 2018), the gut microbiome. Evidence also suggests that exposure to low socioeconomic status is associated with changes in the structure and function of key corticolimbic brain regions (Liberzon et al., 2015; Noble et al., 2015), an effect attributed, in part, to other psychosocial factors, such as maternal health, family relationship quality, and fewer community resources in low SES contexts (Hackman et al., 2010). Critically, such chronic stress exposure is also associated with pathophysiological changes in the structure and function of the corticolimbic brain regions, like the amygdala, shifting physiology towards threat sensitivity and reactivity (Kwiatkowski, Manning, Eagle, & Robison, 2020).

In addition to socioeconomic deprivation, the majority of youth living in high crime areas are also routinely exposed to violence (Berman, Kurtines, Silverman, & Serafini, 1996; Finkelhor, Turner, Ormrod, & Hamby, 2009), which has been directly associated with an impaired stress

response among those affected (Theall, Shirtcliff, Dismukes, Wallace, & Drury, 2017). Altogether, there is overwhelming evidence that living within a crime hotspot has deleterious health consequences, both increasing risk for disease and mood disorders (Lowe et al., 2016; Robinson & Keithley, 2000; Weisburd & White, 2019). Moreover, violence exposure has an interactive effect with exposure to disadvantage, exacerbating the risk for major depression, anxiety, and even post-traumatic stress disorder (Stockdale et al., 2007), all of which are associated with perturbations in the gut microbiome (Foster et al., 2017). Importantly, exposure to socioeconomic deprivation and neighborhood violence is also a risk factor for crime perpetration.

Early life adversity increases risk for criminal offending in a dose-dependent fashion (Appleyard et al., 2005; Hay et al., 2006). In a large cohort study examining adult socioeconomic burden, 81% of the subjects with criminal convictions experienced early life socioeconomic deprivation and other early life adversity (Caspi et al., 2016). In addition, youth who are exposed to violence show immediate deficits in attention and impulse control (Sharkey, Tirado-Strayer, Papachristos, & Raver, 2012), and are significantly more likely to perpetrate serious violence within two years of exposure (Bingenheimer et al., 2005). Though the mechanisms that facilitate this behavioral pattern are poorly understood, there is likely a complex interplay between stress, threat sensitization and reactivity, and other psychosocial factors that increase risk for aggression, raising the question as to how exposure to socioeconomic deprivation and violence in high crime areas changes physiology. In answer to this question, the data presented in this dissertation suggest that exposure to high crime areas affects the composition of the human gut microbiome, potentially mediating the epigenetic effects of social and environmental exposures.

In recent consideration of the link between neighborhood context and aggression behavior, Lesham and Weisburd (2019) proposed that exposures in crime hotspots have epigenetic effects

whereby the chronically stressful social and environmental landscape interacts with individual-level genetic factors to change gene expression, the brain, and behavior. One canonical example comes from Caspi and colleagues (2002) who demonstrated a genetic variant of the monoamine oxidase A (*MAOA*) gene was associated with increased risk of a disposition favorable towards violence as well as antisocial and violent behavior, but only among those who had also experienced childhood maltreatment. Indeed, the environmental effects on gene expression are being more widely recognized in the study of aggression behavior (Tremblay, Vitaro, & Côté, 2018), with some studies estimating that a 50-50 split between genetic and environmental effects in explaining variation of aggression behavior in children (Lacourse et al., 2014; Tuvblad & Baker, 2011; Tuvblad & Beaver, 2013). Moreover, recent research shows multiple methylation sites associated with aggression behavior in humans, explained in part by maternal health behaviors and other chemical exposures (van Dongen et al., 2021), drawing attention to physiological processes that mediate such changes in cell signaling and gene expression, namely epigenetics.

Future Work

Further research is needed to increase the translational relevance of this dissertation with additional human data. Overall, additional HPMM samples are needed to cover a larger study geography and include more cases from distinctly low and high crime areas where the greatest differences in the HPMM analysis were observed. Current HPMM studies should also be supplemented with protein quantification of human brain tissue, potentially collected alongside *post mortem* microbiome samples during routine autopsy. In addition, sampling from living humans across varying levels of neighborhood crime and over repeated measurements could also be conducted. Moreover, self-reported measures of violent crime perpetration, psychosocial stress, socioeconomic status, and other lifestyle factors need to be collected directly from individuals

under study in order to make any direct inferences about human gut microbiome composition and aggression behavior. Together, these efforts could greatly advance a biopsychosocial model of human aggression.

Ethical Considerations

Though many criminologists are concerned about the life sciences bringing reductionism and determinism to the study of crime, this is highly unlikely with the biopsychosocial approach. The biopsychosocial model requires assessment of biological, psychological, and social or environmental factors that combine and interact to drive a behavioral response. This approach showcases several layers of explanation rather than a universal cause of aggression and deviance. Instead of being deterministic, the incorporation of biology in criminological research is a necessary result of the intertwining of these fields. As such, there will likely never be an absolute biomarker of aggression or deviance, or a single cure. To assume otherwise would be ethically and empirically incorrect. Though individual structures, such as the amygdala, PFC, and their circuitry, can change in function in a manner that is conducive to deviant behavior, they are part of a larger, more complicated system that may fail or compensate. There is never a guaranteed response based solely on physiology or solely on psychology or solely on environment. Instead, it is best to view biological processes as enablers of a propensity for aggression and deviance that is cast over time in the light of developing psychology in response to environmental influences. This is most appropriately understood in the context of a biopsychosocial approach where environmental cues and stressors shape psychological and biological function, and the work presented here offers a potential avenue forward for the biopsychosocial model.

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Table 9 | Negative Binomial Mixed Models of OTUs with Crime Level and Socioeconomic Predictors

Family	Genus	Variable	Estimate	SE	p	p-adj	Model
Erysipelotrichaceae	Clostridium:innocuum	Crime Level	-6.841	3.130	0.032	0.180	Model 1
Bifidobacteriaceae	Bifidobacterium	Crime Level	-5.764	0.660	0.000	0.000	Model 1
Streptococcaceae	Streptococcus	Crime Level	-2.963	0.416	0.000	0.000	Model 1
Bifidobacteriaceae	Bifidobacterium	Crime Level	-2.655	0.554	0.000	0.000	Model 1
Desulfovibrionaceae	Desulfovibrio	Crime Level	-2.584	0.420	0.000	0.000	Model 1
Burkholderiaceae	Sutterella	Crime Level	-2.030	0.611	0.001	0.020	Model 1
FamilyXI	W5053	Crime Level	-1.977	0.598	0.001	0.020	Model 1
Coriobacteriaceae	Collinsella	Crime Level	-1.936	0.683	0.006	0.057	Model 1
Corynebacteriaceae	Corynebacterium1	Crime Level	-1.756	0.337	0.000	0.000	Model 1
Veillonellaceae	Unassigned	Crime Level	-1.709	0.811	0.038	0.190	Model 1
Lachnospiraceae	Lachnoclostridium	Crime Level	-1.378	0.540	0.013	0.098	Model 1
Lachnospiraceae	Ruminococcus:torques	Crime Level	-1.359	0.471	0.005	0.054	Model 1
FamilyXI	Anaerococcus	Crime Level	-0.845	0.349	0.018	0.120	Model 1
Desulfovibrionaceae	Bilophila	Crime Level	-0.773	0.367	0.038	0.190	Model 1
Burkholderiaceae	Sutterella	Crime Level	-0.683	0.305	0.028	0.160	Model 1
Lachnospiraceae	Roseburia	Crime Level	-0.651	0.249	0.011	0.088	Model 1
Ruminococcaceae	RuminococcaceaeUCG-002	Crime Level	-0.629	0.256	0.016	0.110	Model 1
Lachnospiraceae	Blautia	Crime Level	-0.559	0.244	0.025	0.150	Model 1
Ruminococcaceae	Subdoligranulum	Crime Level	-0.345	0.171	0.048	0.240	Model 1
Porphyromonadaceae	Porphyromonas	Crime Level	0.722	0.259	0.007	0.058	Model 1
Veillonellaceae	Dialister	Crime Level	0.820	0.291	0.006	0.057	Model 1
Ruminococcaceae	Fastidiosipila	Crime Level	1.063	0.366	0.005	0.054	Model 1
Porphyromonadaceae	Porphyromonas	Crime Level	1.495	0.484	0.003	0.036	Model 1
Rikenellaceae	Alistipes	Crime Level	2.118	0.850	0.015	0.110	Model 1
Porphyromonadaceae	Porphyromonas	Crime Level	3.573	0.780	0.000	0.000	Model 1
FamilyXI	Anaerococcus	Crime Level	-8.415	3.090	0.008	0.094	Model 2

Table 9 (cont'd)

Erysipelotrichaceae	Clostridium:innocuum	Crime Level	-6.429	3.218	0.049	0.300	Model 2
Streptococcaceae	Streptococcus	Crime Level	-3.248	0.504	0.000	0.000	Model 2
Porphyromonadaceae	Porphyromonas	Crime Level	-2.744	0.342	0.000	0.000	Model 2
Prevotellaceae	Prevotella	Crime Level	-2.593	0.593	0.000	0.001	Model 2
Desulfovibrionaceae	Desulfovibrio	Crime Level	-2.377	0.531	0.000	0.001	Model 2
Coriobacteriaceae	Collinsella	Crime Level	-2.219	0.697	0.002	0.034	Model 2
Erysipelotrichaceae	Erysipelatoclostridium	Crime Level	-1.902	0.774	0.016	0.160	Model 2
Lachnospiraceae	Tyzzerella	Crime Level	-1.427	0.291	0.000	0.000	Model 2
Corynebacteriaceae	Corynebacterium1	Crime Level	-1.421	0.327	0.000	0.001	Model 2
Burkholderiaceae	Sutterella	Crime Level	-1.194	0.227	0.000	0.000	Model 2
Lachnospiraceae	Ruminococcus:torques	Crime Level	-1.017	0.372	0.008	0.094	Model 2
Desulfovibrionaceae	Bilophila	Crime Level	-0.887	0.372	0.020	0.170	Model 2
FamilyXI	Anaerococcus	Crime Level	-0.883	0.427	0.042	0.300	Model 2
Porphyromonadaceae	Porphyromonas	Crime Level	-0.463	0.223	0.041	0.300	Model 2
Veillonellaceae	Dialister	Crime Level	0.595	0.290	0.044	0.300	Model 2
Porphyromonadaceae	Porphyromonas	Crime Level	0.613	0.265	0.023	0.180	Model 2
Veillonellaceae	Negativicoccus	Crime Level	0.708	0.277	0.012	0.130	Model 2
Porphyromonadaceae	Porphyromonas	Crime Level	1.205	0.502	0.019	0.170	Model 2
Rikenellaceae	Alistipes	Crime Level	2.286	0.731	0.003	0.036	Model 2
Streptococcaceae	Streptococcus	Vacancy	-10.784	3.727	0.005	0.110	Model 2
Streptococcaceae	Streptococcus	Vacancy	-3.692	1.314	0.006	0.120	Model 2
Peptostreptococcaceae	Criibacteriumbergeronii	Vacancy	-3.629	0.951	0.000	0.036	Model 2
Lachnospiraceae	Tyzzerella	Vacancy	-3.626	1.138	0.002	0.067	Model 2
Lachnospiraceae	Ruminococcus:torques	Vacancy	-3.054	1.458	0.040	0.430	Model 2
FamilyXI	Finegoldia	Vacancy	3.244	1.241	0.011	0.180	Model 2
FamilyXI	Peptoniphilus	Vacancy	3.962	1.596	0.015	0.190	Model 2
Porphyromonadaceae	Porphyromonas	Vacancy	4.911	1.964	0.015	0.190	Model 2
FamilyXI	W5053	Vacancy	7.078	2.160	0.002	0.067	Model 2
Ruminococcaceae	Eubacterium:coprostanoligene	Vacancy	7.331	2.467	0.004	0.100	Model 2
Corynebacteriaceae	Corynebacterium1	Vacancy	27.633	12.757	0.034	0.400	Model 2
FamilyXI	Anaerococcus	Vacancy	40.051	12.100	0.002	0.067	Model 2
FamilyXI	Anaerococcus	% Black	-4.304	2.079	0.042	0.260	Model 3
Corynebacteriaceae	Corynebacterium1	% Black	-3.108	0.970	0.002	0.032	Model 3
FamilyXI	Peptoniphilus	% Black	-2.197	1.087	0.047	0.270	Model 3

Table 9 (cont'd)

Actinomycetaceae	Mobiluncus	% Black	-1.823	0.425	0.000	0.002	Model 3
Lachnospiraceae	Blautia	% Black	0.943	0.313	0.004	0.052	Model 3
Lachnospiraceae	Lachnoclostridium	% Black	1.172	0.472	0.015	0.150	Model 3
Bacteroidaceae	Bacteroides	% Black	1.217	0.451	0.009	0.100	Model 3
Enterobacteriaceae	Escherichia-Shigella	% Black	1.392	0.628	0.030	0.200	Model 3
Erysipelotrichaceae	Erysipelatoclostridium	% Black	1.494	0.569	0.011	0.120	Model 3
Bifidobacteriaceae	Bifidobacterium	% Black	1.497	0.379	0.000	0.005	Model 3
Burkholderiaceae	Parasutterella	% Black	1.986	0.716	0.007	0.090	Model 3
Burkholderiaceae	Sutterella	% Black	2.017	0.573	0.001	0.014	Model 3
Porphyromonadaceae	Porphyromonas	% Black	2.084	0.939	0.030	0.200	Model 3
Erysipelotrichaceae	Holdemanella	% Black	2.688	0.372	0.000	0.000	Model 3
Lachnospiraceae	Blautia	% Black	2.838	1.221	0.023	0.190	Model 3
Bacteroidaceae	Bacteroides	% Black	2.899	1.191	0.017	0.150	Model 3
Lachnospiraceae	Agathobacter	% Black	2.991	0.001	0.000	0.000	Model 3
Erysipelotrichaceae	Clostridium:innocuum	% Black	3.214	1.322	0.018	0.150	Model 3
Veillonellaceae	Dialister	% Black	4.077	1.058	0.000	0.005	Model 3
Lachnospiraceae	Anaerostipes	% Black	6.971	1.247	0.000	0.000	Model 3
Enterobacteriaceae	Unassigned	% Black	11.762	5.234	0.028	0.200	Model 3
Lachnospiraceae	Fusicatenibacter	% Black	12.311	5.845	0.039	0.250	Model 3
Lachnospiraceae	Agathobacter	Crime Level	-6.982	0.001	0.000	0.000	Model 3
Porphyromonadaceae	Porphyromonas	Crime Level	-4.951	0.586	0.000	0.000	Model 3
Acidaminococcaceae	Phascolarctobacterium	Crime Level	-4.628	2.086	0.030	0.170	Model 3
Veillonellaceae	Negativicoccus	Crime Level	-2.810	0.608	0.000	0.001	Model 3
Prevotellaceae	Prevotella	Crime Level	-2.441	0.479	0.000	0.000	Model 3
Porphyromonadaceae	Porphyromonas	Crime Level	-2.015	0.579	0.001	0.014	Model 3
Coriobacteriaceae	Collinsella	Crime Level	-1.787	0.683	0.011	0.095	Model 3
Prevotellaceae	Prevotella	Crime Level	-1.491	0.506	0.004	0.050	Model 3
Streptococcaceae	Streptococcus	Crime Level	-1.476	0.529	0.007	0.066	Model 3
Desulfovibrionaceae	Desulfovibrio	Crime Level	-1.474	0.649	0.026	0.160	Model 3
FamilyXI	W5053	Crime Level	-1.383	0.601	0.024	0.150	Model 3
Lachnospiraceae	Tyzzerella	Crime Level	-1.331	0.376	0.001	0.013	Model 3
Lachnospiraceae	Lachnoclostridium	Crime Level	-1.154	0.523	0.031	0.170	Model 3
Burkholderiaceae	Sutterella	Crime Level	-1.080	0.358	0.004	0.045	Model 3
Lachnospiraceae	Ruminococcus:torques	Crime Level	-1.051	0.267	0.000	0.005	Model 3
Ruminococcaceae	RuminococcaceaeUCG-002	Crime Level	-0.848	0.352	0.019	0.140	Model 3

Table 9 (cont'd)

Desulfovibrionaceae	Bilophila	Crime Level	-0.779	0.373	0.040	0.190	Model 3
FamilyXI	Anaerococcus	Crime Level	-0.771	0.288	0.009	0.085	Model 3
Erysipelotrichaceae	Erysipelatoclostridium	Crime Level	-0.751	0.355	0.038	0.190	Model 3
Burkholderiaceae	Sutterella	Crime Level	-0.719	0.311	0.024	0.150	Model 3
Erysipelotrichaceae	Holdemanella	Crime Level	-0.704	0.232	0.003	0.045	Model 3
Bifidobacteriaceae	Bifidobacterium	Crime Level	-0.676	0.237	0.006	0.060	Model 3
Actinomycetaceae	Varibaculum	Crime Level	-0.640	0.296	0.034	0.180	Model 3
Bacteroidaceae	Bacteroides	Crime Level	0.565	0.281	0.048	0.210	Model 3
Actinomycetaceae	Mobiluncus	Crime Level	0.639	0.265	0.019	0.140	Model 3
Corynebacteriaceae	Corynebacterium1	Crime Level	1.212	0.605	0.049	0.210	Model 3
FamilyXI	Anaerococcus	Crime Level	1.333	0.666	0.049	0.210	Model 3
Porphyromonadaceae	Porphyromonas	Crime Level	1.486	0.386	0.000	0.005	Model 3
Lachnospiraceae	Anaerostipes	Crime Level	1.759	0.778	0.027	0.160	Model 3
Rikenellaceae	Alistipes	Crime Level	2.389	0.987	0.018	0.140	Model 3
Erysipelotrichaceae	Clostridium:innocuum	Crime Level	-7.207	3.182	0.026	0.170	Model 4
FamilyXI	Anaerococcus	Crime Level	-6.592	3.192	0.043	0.220	Model 4
Bifidobacteriaceae	Bifidobacterium	Crime Level	-5.462	0.699	0.000	0.000	Model 4
Veillonellaceae	Negativicoccus	Crime Level	-5.054	0.523	0.000	0.000	Model 4
Porphyromonadaceae	Porphyromonas	Crime Level	-4.178	1.864	0.028	0.170	Model 4
Desulfovibrionaceae	Desulfovibrio	Crime Level	-3.358	0.469	0.000	0.000	Model 4
Erysipelotrichaceae	Holdemanella	Crime Level	-2.828	1.131	0.015	0.110	Model 4
Bifidobacteriaceae	Bifidobacterium	Crime Level	-2.731	0.468	0.000	0.000	Model 4
Erysipelotrichaceae	Erysipelatoclostridium	Crime Level	-2.662	0.903	0.004	0.042	Model 4
Burkholderiaceae	Sutterella	Crime Level	-2.091	0.626	0.001	0.019	Model 4
Coriobacteriaceae	Collinsella	Crime Level	-1.848	0.688	0.009	0.077	Model 4
Veillonellaceae	Unassigned	Crime Level	-1.690	0.810	0.040	0.220	Model 4
Peptostreptococcaceae	Criibacteriumbergeronii	Crime Level	-1.614	0.513	0.002	0.031	Model 4
Prevotellaceae	Prevotella	Crime Level	-1.609	0.534	0.004	0.042	Model 4

Table 9 (cont'd)

Lachnospiraceae	Tyzzerella	Crime Level	-1.518	0.362	0.000	0.001	Model 4
Lachnospiraceae	Dorea	Crime Level	-1.228	0.273	0.000	0.000	Model 4
Lachnospiraceae	Ruminococcus:torquesgroup	Crime Level	-1.061	0.363	0.005	0.042	Model 4
Lachnospiraceae	Lachnoclostridium	Crime Level	-0.759	0.323	0.021	0.150	Model 4
Desulfovibrionaceae	Bilophila	Crime Level	-0.693	0.267	0.011	0.089	Model 4
Burkholderiaceae	Sutterella	Crime Level	-0.660	0.310	0.036	0.210	Model 4
Actinomycetaceae	Varibaculum	Crime Level	-0.649	0.318	0.045	0.220	Model 4
Ruminococcaceae	UBA1819	Crime Level	-0.552	0.263	0.040	0.220	Model 4
Prevotellaceae	Prevotella6	Crime Level	-0.450	0.196	0.025	0.170	Model 4
Veillonellaceae	Dialister	Crime Level	0.901	0.179	0.000	0.000	Model 4
Ruminococcaceae	Faecalibacterium	Crime Level	1.576	0.000	0.000	0.000	Model 4
Rikenellaceae	Alistipes	Crime Level	2.163	0.740	0.005	0.042	Model 4
Ruminococcaceae	Faecalibacterium	Unemploy.	-26.970	0.000	0.000	0.000	Model 4
Ruminococcaceae	Faecalibacterium	Unemploy.	-15.206	5.934	0.012	0.074	Model 4
Veillonellaceae	Dialister	Unemploy.	-11.591	1.035	0.000	0.000	Model 4
Lachnospiraceae	Agathobacter	Unemploy.	-11.515	3.291	0.001	0.009	Model 4
Lachnospiraceae	Anaerostipes	Unemploy.	-11.456	2.847	0.000	0.002	Model 4
Ruminococcaceae	RuminococcaceaeUCG-003	Unemploy.	-10.481	2.435	0.000	0.002	Model 4
Streptococcaceae	Streptococcus	Unemploy.	-9.397	2.298	0.000	0.002	Model 4
Bacteroidaceae	Bacteroides	Unemploy.	-9.284	2.562	0.001	0.007	Model 4
Lachnospiraceae	Ruminococcus:torquesgroup	Unemploy.	-3.403	1.553	0.032	0.130	Model 4
Desulfovibrionaceae	Bilophila	Unemploy.	-2.797	1.141	0.017	0.084	Model 4
Corynebacteriaceae	Lawsonella	Unemploy.	2.079	0.925	0.028	0.120	Model 4
Peptococcaceae	Peptococcus	Unemploy.	2.922	0.912	0.002	0.018	Model 4
FamilyXI	Peptoniphilus	Unemploy.	3.014	1.101	0.008	0.059	Model 4
Porphyromonadaceae	Porphyromonas	Unemploy.	3.116	1.523	0.044	0.170	Model 4
FamilyXI	Peptoniphilus	Unemploy.	3.211	1.551	0.042	0.170	Model 4
Lachnospiraceae	Tyzzerella	Unemploy.	3.862	1.548	0.015	0.081	Model 4
FamilyXI	Peptoniphilus	Unemploy.	4.113	1.611	0.013	0.076	Model 4
Lachnospiraceae	Dorea	Unemploy.	4.437	1.166	0.000	0.004	Model 4
Veillonellaceae	Dialister	Unemploy.	4.654	0.766	0.000	0.000	Model 4
Rikenellaceae	RikenellaceaeRC9gutgroup	Unemploy.	4.973	1.972	0.014	0.079	Model 4
Peptostreptococcaceae	Criibacteriumbergeronii	Unemploy.	5.102	2.194	0.023	0.110	Model 4
FamilyXI	Anaerococcus	Unemploy.	5.565	2.328	0.019	0.091	Model 4
Veillonellaceae	Dialister	Unemploy.	5.854	1.413	0.000	0.002	Model 4
FamilyXI	Peptoniphilus	Unemploy.	5.918	1.834	0.002	0.018	Model 4
Porphyromonadaceae	Porphyromonas	Unemploy.	6.735	2.522	0.009	0.067	Model 4
Burkholderiaceae	Parasutterella	Unemploy.	7.196	2.592	0.007	0.056	Model 4

Table 9 (cont'd)

Erysipelotrichaceae	Holdemanella	Unemploy.	7.253	3.264	0.029	0.120	Model 4
Ruminococcaceae	Eubacterium:coprostanoligene	Unemploy.	7.365	3.028	0.017	0.084	Model 4
Veillonellaceae	Negativicoccus	Unemploy.	9.263	2.240	0.000	0.002	Model 4
Bifidobacteriaceae	Bifidobacterium	Unemploy.	9.601	2.992	0.002	0.018	Model 4
Porphyromonadaceae	Porphyromonas	Unemploy.	10.049	3.207	0.003	0.022	Model 4
FamilyXI	W5053	Unemploy.	17.847	6.910	0.012	0.074	Model 4
Porphyromonadaceae	Porphyromonas	Unemploy.	20.364	7.852	0.011	0.074	Model 4

Table 10 | 52 Unique Taxa Associated with Crime Level and Socioeconomic Predictors

Phylum	Class	Order	Family	Genus
Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus:torques
Actinobacteria	Actinobacteria	Corynebacteriales	Corynebacteriaceae	Corynebacterium1
Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Porphyromonas
Proteobacteria	Gammaproteobacteria	Betaproteobacteriales	Burkholderiaceae	Sutterella
Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Bilophila
Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Collinsella
Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium
Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella
Firmicutes	Clostridia	Clostridiales	FamilyXI	W5053
Firmicutes	Erysipelotrichia	Erysipelotrichales	Erysipelotrichaceae	Clostridium:innocuum
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	RuminococcaceaeUCG-002
Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes
Firmicutes	Negativicutes	Selenomonadales	Veillonellaceae	Unassigned
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Subdoligranulum
Firmicutes	Clostridia	Clostridiales	FamilyXI	Anaerococcus
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnoclostridium
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia
Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Fastidiosipila
Firmicutes	Negativicutes	Selenomonadales	Veillonellaceae	Dialister
Firmicutes	Negativicutes	Selenomonadales	Veillonellaceae	Negativicoccus
Firmicutes	Clostridia	Clostridiales	FamilyXI	Finegoldia
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Tyzzerella
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Eubacterium:coprostanoligene
Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae	Criibacteriumbergeronii
Firmicutes	Erysipelotrichia	Erysipelotrichales	Erysipelotrichaceae	Erysipelatoclostridium
Firmicutes	Clostridia	Clostridiales	FamilyXI	Peptoniphilus
Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Varibaculum
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Agathobacter
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Anaerostipes
Proteobacteria	Gammaproteobacteria	Betaproteobacteriales	Burkholderiaceae	Parasutterella
Firmicutes	Erysipelotrichia	Erysipelotrichales	Erysipelotrichaceae	Holdemanella
Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides
Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Unassigned
Firmicutes	Negativicutes	Selenomonadales	Acidaminococcaceae	Phascolarctobacterium
Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Mobiluncus
Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia-Shigella
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Fusicatenibacter
Firmicutes	Clostridia	Clostridiales	Peptococcaceae	Peptococcus
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	RuminococcaceaeUCG-003
Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella6

Table 10 (cont'd)

Actinobacteria	Actinobacteria	Corynebacteriales	Corynebacteriaceae	Lawsonella
Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	RikenellaceaeRC9gut
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	UBA1819
Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Dorea
Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces
Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminiclostridium5
Firmicutes	Negativicutes	Selenomonadales	Veillonellaceae	Megasphaera
Bacteroidetes	Bacteroidia	Bacteroidales	Marinifilaceae	Odoribacter