RELATION OF SWINE INDUSTRIAL LIVESTOCK OPERATION AIR EMISSIONS EXPOSURES TO SLEEP DURATION AND TIME OUTDOORS IN RESIDENTIAL HOST COMMUNITIES

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A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology in the Gillings School of Global Public Health.

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ABSTRACT

Nathaniel Scott MacNell: Relation of Swine Industrial Livestock Operation Air Emissions Exposures to Sleep Duration and Time Outdoors in Residential Host Communities
(Under the direction of David Richardson)

Residents of communities hosting swine industrial livestock operations (ILOs) in North Carolina are exposed to mixtures of air pollutants originating from animal confinements, waste lagoons, and waste spray-field systems. To add to the understanding of swine ILO impacts on nearby community residents, I estimated the impact of swine ILO air emissions on sleep and time outdoors. These outcomes have not been formally assessed using epidemiologic methods, but are important components of quality-of-life, have implications for health and disease, and have been raised as concerns by community members.

Acute exposure effects on sleep and time outdoors were estimated by applying discrete-time hazard models to data collected in the Community Health Effects of Industrial Hog Operations (CHEIHO) study. CHEIHO was a community-based, participatory research study that coupled continuous monitoring of pollutant plume markers with twice-daily odor and activity diaries. Dynamic Bayesian network models were used to estimate the total chronic effect of exposures accounting for potential feedback between subsequent exposures and outcomes.

Detectible swine ILO pollutants at night was associated with an average sleep deficit of approximately 15 minutes. Exposure to outdoor odors was associated with decreased odds of being outdoors during the following hour (OR 0.62, 95% interval 0.44 to 0.89). Dynamic models estimated that the total effects of exposures exceeded the expected total effect calculated by summing individual acute effects, suggesting the importance of a feedback mechanism.

The results demonstrate measurable and important impacts of ILO air emissions on sleep and time outdoors among those living nearby. The modeling approaches used were robust to bias from factors that remained constant for each participant over the course of the study and to factors that varied with the time-of-day or the weather, suggesting a causal effect. Policy interventions to reduce community exposures to swine ILO emissions from lagoon-and-sprayfield systems could have positive impacts on public health in rural North Carolina communities.

To Steve.

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LIST OF ABBREVIATIONS

BN	Bayesian network
CHEIHO	Community health effects of industrial hog operations
DAG	Directed acyclic graph
DBN	Dynamic Bayesian network
H_2S	Hydrogen sulfide
H	Hours
HR	Hazard ratio
ILO	Industrial livestock operation
M	Minutes
OE	Odds ratio
PDAG	Probabilistic directed acyclic graph
PPB	Parts per billion
PPM	Parts per million
RH	Relative humidity

CHAPTER 1: BACKGROUND

Swine Industrial Livestock Operations in North Carolina

To date, nearly all of the pork consumed and exported by the United States is produced using Industrial Livestock Operations[1] (ILOs). North Carolina is a leading producer of pork in the United States – with over 2,000 permitted swine operations and 9 million hogs[2,3] – and is second only to Iowa in hog production[4]. Global and national technological and economic shifts led to the rapid development of industrialized pork operations in eastern North Carolina starting in the 1970's, arising in the economic context of dwindling tobacco trade[5]. Economies of scale, geographically concentrated farm loss, and a moratorium on new operations has created an industry densely concentrated in the southeastern part of the state (Figure 1.1)[6]. Duplin and Sampson counties, the top two hog-producing counties in the state, are also the top two hog-producing counties in the entire United States[4].

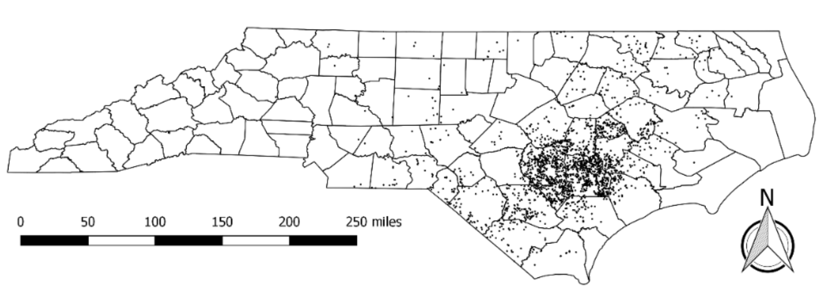

Figure 1.1. Geographical distribution of swine ILOs in North Carolina.

Industrial livestock production systems differ from traditional methods of animal husbandry in their structure and functions. In the case of pork production, technological and organizational innovations have enabled unprecedented gains in production efficiency[7,8]. Selective breeding and genomics has led to the development of swine stocks optimized for rapid gestation, development, and weight gain[9]. Re-organization of the farm system into an industrial model has enabled the use of sequential habitats designed to economically optimize development at different stages of the life course (for instance, farrow-to-weaning, weaning-to-feeder, and feeder-to-finish). Large operations with high animal densities reduce infrastructure capital investment costs per animal and can enable even higher densities through active climate control. Advancements in nutrition and veterinary science have allowed for growth-promoting diets and prophylactic treatment of diseases that might hinder growth[10]. These technological advancements have been made possible by a re-organization of the hog farming business into a franchise model, where individual ILO operators compete for hog-rearing contracts from a centralized integrator[11]. The integrator sets the prices for finished hogs, organizes large-scale supply logistics, and manages the processing and marketing of finished hog products.

The systematic gains in production efficiency made possible by technological and business innovations have come at a cost, which is disproportionately borne by those closer to hog production "on the ground," including farm workers and members of disproportionately minority and low-income host communities unaffiliated with the industry[12]. Workers in hog barns and meat processing spend long hours with large animals in cramped spaces, fast-moving machinery, concentrated agricultural dusts, and strong cleaning chemicals[13]. Many hog industry workers receive above-average salaries for the counties in which they work compared to other workers, but fringe benefits are scarce, job security is limited, injury rates are high, and few hog industry workers are represented in collective bargaining agreements[14–16].

Community Health Impacts of Swine Industrial Livestock Operations

Neighbors of ILOs in host communities face an array of impacts from ILO activities, many of which have been documented by researchers, the press, and community members[17,18]. Transfer of feed and hogs between operations increases heavy truck traffic, which brings noise, bright lights, air pollution, and road wear to the neighborhood day or night. Barn ventilation systems release odorous mixtures of residual feed dusts, animal dander, and dried waste particulates into the air. In some cases, dead animals are left in dumpsters termed “dead boxes” near property boundaries, which putrefy for some time before being disposed of.

Swine waste management activities introduce many other negative impacts. In North Carolina, ILO operations can be issued water quality permits from the State Department of Environmental Quality (DEQ) for lagoon-and-spray field waste management systems, and are used at nearly all swine ILOs in the state[19]. In this system, liquid hog wastes (a mixture of urine, feces, dander, and dusts) fall through slatted floors and flow downhill into a large open cesspool of waste (“lagoon”)[20,21]. In the cesspool, anaerobic bacteria consume nutrients from the wastes and produce mixtures of metabolic byproducts that are added to the waste mixture. Periodically, the waste mixture is sprayed onto adjacent land as an aerosol using high-pressure spray systems. This reduces the quantity of waste in the lagoon and also aerates the waste (increasing subsequent nutrient bioavailability), but also results in the dispersal of waste aerosols in the community[22,23]. These wastes contain strong odorants[24], and ILO neighbors have reported waste aerosols depositing films of hog waste on their homes, vehicles, and property. Genetic tracing has shown that much of this waste ultimately runs off into local waterways[25].

Swine ILO waste aerosols are complex mixtures of pollutants in two functional classes. The first class contains pollutants directly produced by hogs, including allergens present in hog dander, swine intestinal bacteria, heavy metals used as growth promoters in feed, and metabolites from veterinary pharmaceuticals[23]. The second class of pollutants are created as a result of the waste treatment system. Anaerobic decomposition of urine and feces produces microorganisms and microbial metabolites including ammonia and hydrogen sulfide[26], which can be released through passive off-gassing in addition to spraying.

These components of hog waste aerosols have demonstrated physiological impacts. Hog barn dusts have been shown to cause symptoms of respiratory disease in exposed cell cultures[27–30], animals[31–33], hog confinement workers[13,34–50], and healthy volunteers[51–64]. Ammonia and hydrogen sulfide have been historically common occupational exposures in industrial settings and cause respiratory and sensory irritation. Other potential impacts have been hypothesized but not extensively studied. Genetic marker studies suggest that swine ILO workers can become colonized by bacterial strains from their workplace. Limited international evidence suggests that the swine ILO environment could contribute to antibiotic resistance[65]. Active pharmaceutical metabolites could have biological effects but have not been studied in this context.

Odorants in hog waste mixtures are an important pathway of effect, through both chemoreception[26,66] and direct nociception (trigeminal nerve activation)[67,68]. Most odors are processed by specific olfactory neurons with receptors that respond to gas-phase molecules – this corresponds to odors in the popular sense[69]. Exposure to compounds can also trigger the trigeminal and other facial nerves, causing pain. For example, many people are familiar with the idea that exposure to sulfur compounds from a fresh-cut onion stimulates receptors in the trigeminal nerve that result in a sensation of burning in the eyes and nose.

In the epidemiologic context, community exposures to swine ILO pollutant mixtures has been associated with respiratory disease symptoms including excessive coughing[70,71], asthma [72–74], wheezing[71,75], difficulty breathing[71,75], runny nose[70,71], sore throat[70,75], and chest tightness[71,75]. Other observed adverse outcomes associated with exposure include mucosal immunosuppression[76], feelings of loss of control[71], increased mood disturbances[77], increased blood pressure[78], and higher infant mortality[79]. Ethnographic research has also documented a link between ILO emissions and disruption of sleep and outdoor activities[80].

Swine ILO Air Emissions and Sleep

This work aims to quantify the impacts of swine ILO emissions on sleep. Sleep is a primary determinant of health. Sleep quantity and quality influences an array of disease risk factors and diseases, and is also an important component of quality-of-life. Sleep is important for DNA repair[81], cellular metabolism, tissue maintenance, immunological response, mood regulation, and memory consolidation[82,83]. Based on the importance of sleep to health, the National Sleep Foundation recommends 7 to 9 hours of sleep per night for adults 18-65 and 7 to 8 hours per night for adults over 65[84]. Getting less than this recommendation (<7 h) has been linked to increased risks of diabetes and obesity[85–96], cardiovascular disease[97–99], accidents[100,101], poor quality of life[102–107], cancer[108–110], and premature death[111]. Sleep timing, which could be disrupted by unpredictable swine ILO emissions exposures, is also important for supporting health. Studies of shift workers have shown increased risk of mortality, increased disease risks, and reduced quality-of-life among those with inconsistent sleep schedules[112,113].

Sleep is regulated through two main mechanisms: sleep-wake regulation, in which sleep propensity increases with more time spent awake and vice versa; and circadian regulation, in which sleep is regulated based on an internal hormonal clock influenced by environmental time cues like light[114]. In addition to awakenings and sleep timing delays, psychological and environmental stressors can interfere with sleep indirectly by influencing the regulation of sleep homeostasis[115,116]. Effects on homeostatic regulation of sleep also mean that repeated, acute sleep impacts could also have more severe chronic impacts on sleep than might be expected from the sum of individual sleep effects alone[117–119].

Exposure to ILO pollutants is associated with three main categories of health effects and symptoms of disease that could impact sleep duration and outdoor activity: sensory irritation[75,120,121], difficulty breathing[33,34,37,38,75], and psychological stress[77,122] (Figure 1.2, below). Disrupted breathing can make falling asleep difficult[123], cause awakenings from sleep[124], interfere with outdoor activities[125], and produce psychological stress[77,122,126].

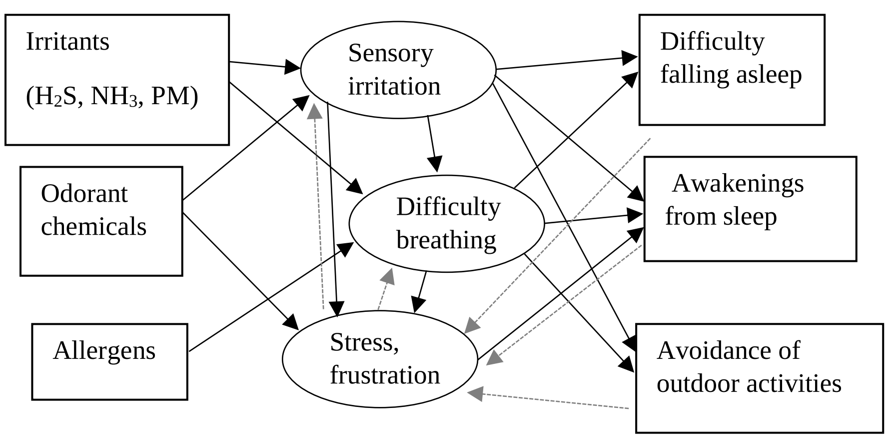

Figure 1.2. Relationship between exposures, potential effects, and mediating factors. Dotted grey arrows show feedback effects, which are difficult to model using traditional methods.

Studies of communities exposed to ILO pollutants have documented sensory effects consistent with olfactory and trigeminal nerve irritation[127] and nausea[71,75], burning nose and eyes[70,71,75], and headaches[70]. These effects could make sleeping difficult. Disease symptoms, the cultural and psychological meanings of malodor[122,128], the inability to control odors, and interference with outdoor functional physical activity and exercise[80] could also make falling asleep more difficult and influence sleep schedules. Exposure to ammonia odorants like those found in swine ILO pollutants have long been known to cause awakenings from sleep; this property is exploited in the clinical context with the use of smelling salts[129].

Swine ILO Air Emissions and Time Outdoors

This work also aims to quantify the impacts of swine ILO emissions on time outdoors. Outdoor activities are an important site for leisure-time and functional physical activity for rural residents, who typically have poor access to indoor facilities like gymnasiums and indoor swimming pools[130]. Rural residents of the U.S. South report more barriers to physical activity and less frequent physical activity[131–135]. Similarly, low-income and Black neighborhoods like those where swine ILOs are concentrated are less likely to have indoor exercise facilities[136]. Physical activity is important for quality of life and lack of physical activity is well-known as risk factor for many diseases including diabetes, heart attack, stroke, and cancer. Physical activity is also important for sleep and its impacts on health – physical activity is associated with acquiring the recommended duration of sleep and better quality sleep[137–143]. Exposures to strong odorants and pollutants from ILO air emissions can make spending time outdoors unpleasant or intolerable. Like a protective sleep environment, access to the outdoors is important for health but also an important component of quality-of-life[144–146]. Particularly in rural contexts, outdoor activities have important implications for health promotion and disease prevention. Rural populations rely on the outdoors for gardening, hunting, fishing, and raising animals to improve access to nutritious foods[80]. Time spent outdoors is an important venue for relaxation, reflection, and stress reduction in the general population, but has a special meaning to those who grew up and live "in the country"[80]. Because rural homes often lack central heating and air conditioning due to their age or design, many rural residents cool their homes in summer months by opening windows – an economically and environmentally sustainable solution that relies on access to clean air. Rural neighborhoods also rely on the outdoors as a space for holding social, cultural, and religious gatherings – which strengthen and enrich both individual and community lives[147].

Estimating Feedback Effects in Modern Epidemiology

Methods for estimating the acute effects of exposure are well developed in epidemiology. In contrast, estimating the total effects of repeated, mutually-influencing exposures and outcomes in epidemiology has proven a difficult problem. In the context of repeated exposures to swine ILO air emissions, a person's experiences of sleep, outdoor activity, and environmental exposures can both mutually oppose and reinforce one another, creating a complex system.

For instance, a sleep disruption event like night-time sleeplessness caused by exposure, which could lead to fatigue the next day. This fatigue effect could cause secondary effects, including reduced outdoor activity, an earlier bedtime, or naps during the next day. Considering just one of these secondary effects in turn, reduced time outdoors could reduce the need for sleep, reduce the potential of subsequent exposure, or increase the need for time outdoors on subsequent days as potential tertiary effects. A model version of this system is shown in Figure 1.3.

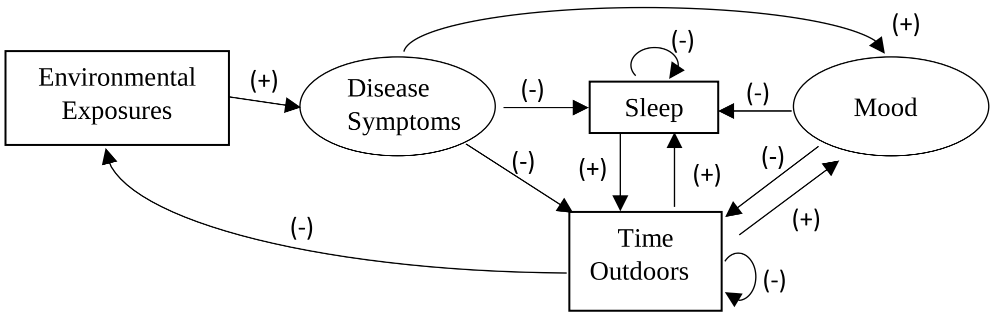

Figure 1.3. Schematic diagram of potential relationships between sleep, outdoor activity, and ILO pollutant exposure. Arrows in this diagram represent effects at a later time point; an equivalent directed acyclic graph (DAG) can be created by drawing a copy of the diagram for each time point *t* and drawing each arrow from t_i to t_{i+1} (see Figure 1.4, below).

Feedback processes are ubiquitous in nature for example, predator-prey dynamics and biological homeostasis – and thus in the study of nature through the biological, medical, physical, chemical, social, and ecological sciences[148] from which public health knowledge is derived. In epidemiology, feedback has been studied in the context of epidemics, where agent-based (stochastic) and compartmental (differential) approaches have been used to model diffusion of effects between units[149]; the general problem of effect diffusion between units of study has been considered as interference in the context of infectious disease[150].

Causal reasoning about systems with feedback has proven difficult in modern epidemiology. This paradigm uses insights from graph theory to reduce complex causal relationships to the simpler problem of comparing outcome distributions among otherwise-similar exposed and unexposed populations. Practically, this amounts to identifying the most appropriate set nuisance factors (“confounders”) that must be included in a data transformation step to make the observed data comparable across exposure categories; popular methods of transformation include participant exclusion, stratification, covariate adjustment, standardization, matching, and weighting. The approach has proven effective for estimating short-term causal effects, but faces limitations in describing complex systems[151]. In the broader context of graph theory, the modern epidemiological approach for selecting adjustment sets is equivalent to the problem of identifying the Markov blanket associated with a particular exposure-outcome relationship if interest[152].

The acute effects of swine ILO emissions exposures on sleep and time outdoors can be assessed using standard epidemiological analysis and repeated measurements data with a few simplifying assumptions (Figure 1.4). The results of this approach are detailed in Chapters 2 and 3. These estimates result from comparing time periods with different exposure and outcome values within participants and are robust to potential confounding biases due to differences between individuals or from time-varying confounders (due to adjustment by time of day).

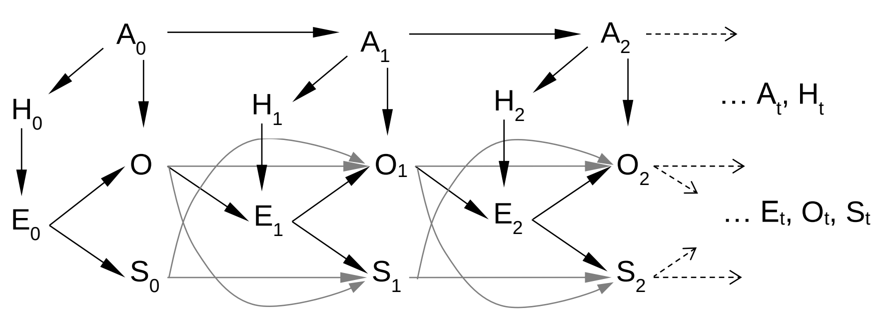

Figure 1.4: Feedback effects can be summarized as a Markov process by a time-indexed directed acyclic graph. Atmospheric conditions (A) influence hog emissions (H) and participants’ time outdoors (O). Hog emissions in turn influence participants’ Exposures (E),

which directly influence future values of time outdoors (O) and sleep (S). Values of outdoors influence future values of outdoors, sleep, and exposure; sleep values influence future values of outdoors and sleep. The acute effects of exposure can be estimated using traditional epidemiological methods.

The limitation of the traditional model in this context is the potential for inaccurate characterization of chronic effects of repeated exposures, which might differ from the sum of individual observed acute effects. If the effect measures observed in periods later in the study are influenced by measures from earlier periods in the study, the overall estimate of acute effect will be biased, although the extent of this bias will depend on several factors including the strength of association between values of the outcome measure as subsequent times. The aim of this dissertation is to estimates average acute effects in a chronically-exposed population, rather than the effect of cumulative chronic exposure in an unexposed population.

To address this limitation, this dissertation used dynamic Bayesian networks, which have seen use in addressing feedback in other contexts. Like the standard epidemiology approach, this approach is guided by a directed acyclic graph but aims to simultaneously estimate multiple parameters. Using these learned parameters, the network can be used to estimate chronic effects by comparing exposure specified exposure regimes – for instance the observed exposures and a counterfactual situation of no exposure. Let the estimation of this effect (of exposure immediately following values of sleep and outdoors) be indicated by the simplified notation

$$E_t \overset{?}{\to} S_{t+1}$$
$$E_t \overset{?}{\to} O_{t+1}$$

to indicate interest in the effect of changes in E at time t on immediately following values of S and O. Using this notation, we can indicate interest in other causal effects – estimable effects that are not represented by arrows in a directed acyclic graph. Consider the effects of a single exposure on subsequent sleep occurring in a following window of length k, offset from exposure by time h:

$$E_t \overset{?}{\to} \sum_{i=h}^{k} O_i$$

This measure could indicate the effect of a single hour's exposure on total sleep during the next 8 hours for $k = 8$ and $h = 1$. Alternatively, consider the total impact of exposures across several time periods on one outcome:

$$\sum_{i=h}^{k} E_i \overset{?}{\to} O_t$$

These example measures estimate the effect of one exposure on multiple outcomes, or of one outcome on multiple exposures. A further formulation considers the effect of exposure regimes (multiple exposures across time) on outcome regimes (multiple, temporally-intersecting outcomes)

$$\sum_{i=0}^{w} E_i \overset{?}{\to} \sum_{j=h}^{k} O_j$$

For instance, suppose that under the scenario of no exposure, a participant sleeps 8 hours per night, on average. Under the scenario of chronic exposure, that participant sleeps for 6 hours on average; 5.5 hours on odor-heavy nights, and 6.5 hours on odor-free nights. A model making comparisons between odor-heavy and odor-free nights might detect a 1-hour deficit effect. A model summing the result of one exposure on a subsequent window might see a reduced estimate of impact (below 1 hour) because the averaged outcomes represent a mixture of more-and-less acute individual effects and the components might influence each other in unforeseen ways. A model estimating the single effect of multiple averaged exposures might also see a reduced estimate of impact (below 1 hour) because the averaged exposure windows would become more similar and might include exposure terms influenced by one another.

This dynamic Bayesian network approach can directly estimate this quantity by comparing the expected outcome distribution under different exposure regimes. Conditional probabilities can be used to perform sequential inference and estimate the total impact of a specified exposure regime. This approach could have wider applicability to other epidemiology studies that using repeated measures of interrelated individual states in the presence of time-dependent confounding.

Swine ILOs and Environmental Justice

Swine ILOs in North Carolina are concentrated in rural, poor, and Black communities[12]. Residents of these communities are more susceptible to environmental exposures because they have higher burdens of chronic disease, fewer health-promoting resources, and poorer access to disease mitigation services[153,154]. In North Carolina and the U.S. South, race and social class are tightly intertwined. This relationship can be traced to history; Black Americans have been economically exploited by Whites for over 300 years[155]. Despite being emancipated by the federal government in the mid-19th century, Black slaves and their descendants have faced an evolving system of exploitation perpetrated by the descendants of enslavers and their White allies. Components of this system have included convict-lease programs[156] coupled with the criminalization of Black life[157], race-specific poll taxes and tests, organized mass murder[158], inequitable provision and restriction of public goods and services, racist public education[159–161], and perpetual debt traps[162]. These efforts have made significant positive contributions to the health and wealth of white communities while systematically degrading the health and life chances of Black Americans[163]. Exploitation has also been met with resistance: community organizing efforts beginning with the abolitionist movement and slave resistance networks have evolved through the Freedman's, Civil Rights, and the recently-developed Black Lives Matter[164] movement.

Health and disease disparities between Black and non-Black populations in the United States have been well documented. Blacks face more life stressors – both at home and at work – including discrimination[165] in housing, education, and employment. Black populations face higher prevalence and severity of chronic diseases – including diabetes, kidney disease, cancer, and cardiovascular disease; unjustly, Black patients also receive poorer care for chronic disease and have higher associated mortality rates. In the context of the present research, Black populations score more poorly on measures of quality of life, sleep duration, nutrition, and physical activity compared to Whites[166]. In the historical context, disrupted Black sleep – and the very concept of an inherently different pattern to Black sleep – is rooted in the use of sleep environments as a weapon to control slaves[167]. Racial differences in sleep duration and quality have been considered as fundamental causes of health disparities in the U.S., particularly for cardiovascular outcomes[168].

Black communities in North Carolina have a higher proportion of the population living below the poverty line than the state as a whole. Poverty has been associated with many of the same health and disease disparities as being Black[169]. The poor have fewer resources to spend on safe housing, nutritious food, meal preparation, transportation, disease care and presentation services, refrigeration for safe food storage, pest control and home sanitation, personal hygiene products, educational activities for children, and socialization. Research has demonstrated that coping with poverty typically requires sacrificing or compromising on these important expenditures – each of which can be important to health and quality of life.

Swine ILOs are also concentrated in rural areas, which have been historically underserved by public health services, facing shortages of healthcare facilities, providers, and funding[170]. Rural areas consistently score poorly on population health indicators[170,171]. Communities in rural areas are experiencing social transitions that create health challenges[172]: a shift to corporate agriculture, job loss, outmigration of young and working people, and poorer access to nutritious food[173].

In parallel to these environmental justice issues, the problems presented by hog ILOs have proven resistant to public health intervention, partially because of the strength and economic importance of the North Carolina's hog industry. Community members are often employed by or have family members employed by the industry, and local governments can be influenced by the industry's presence on boards, relationships with sheriff's departments, and health departments[174]. Institutions that might assist communities in finding solutions, including public universities, might also have conflicts of interest based on their economic and political relationship to the industry[175]. These relationships can make community members doubt the claim that public institutions value their interests, rather than the interests of the industry, and can make research engagement challenging.

Communities affected by hog operations have been actively advocating for public health protections for many years, facing resistance from industry groups and the state government[19]. This advocacy, which has remained firmly grounded in grassroots community organizing, has included civil complaints against the industry in state and federal courts seeking to improve the ILO permitting process[19]. Litigation of these complaints relies heavily on testimony from those impacted by ILOs, but scientific research can also be an important form of evidence in environmental justice court cases[176].

Improved hog waste treatment methods exist and continue to be actively developed[177,178]. But without a legal mandate for their use, these systems have not been widely implemented because their use feasibility has been assessed based on the costs to producers alone[179], without consideration of potential health or environmental impacts. These health and environmental costs of improper waste disposal are externalities of prodution[180] – an economic subsidy that creates higher profits for ILO industry at the public's expense. While the State of North Carolina offers cost-sharing for lagoon conversions programs, the program typically only supports two or three (of the state's over 2,000) system conversions per year[181].

Although externalities of production have been addressed through policies including taxes, production rules, and offsets, purely market-based solutions have also been proposed and have become more popular in the current political climate. Similar to policy interventions, these solutions require more transparency in production so that the market can reflect the true costs of production[182]. For example, disclosure of production costs including avoidance of pesticides and additives, fair labor practices, and appropriate animal stewardship can be appealing to consumers and help pressure other firms to adopt similar practices.

A holistic quantification of the health effects of swine ILO emissions is therefore important for community, industry, policy, and market-based changes that could improve the public's health by reducing exposures to swine ILO pollutants. Scientific evidence about the health impacts of ILOs could help develop strategies to better protect environmental quality and public health by demonstrating the need for more sustainable agricultural production methods.

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CHAPTER 2: AIMS, DESIGN AND METHODS

Specific Aims

Swine Industrial Livestock Operations (ILOs) are a significant source of air pollution in eastern North Carolina. The state's 2,292 permitted swine ILOs[1] are concentrated in rural, poor, and Black neighborhoods[2] with limited resources and access to public health services. Swine ILOs negatively impact rural life by disrupting outdoor activities[3] and causing disease symptoms including respiratory disease[4], stress, negative mood[5], and increased blood pressure[6]. This dissertation fills an important gap in the literature on swine ILO impacts by estimating the effects of ILO pollutant exposures on sleep duration and time outdoors. Sleep is essential for health and the enjoyment of life; less-than-recommended (<7h) sleep duration is associated with mental illness, weight gain, accidents, high blood sugar, high blood pressure, and mortality[7] through circadian, stress, and hormonal pathways. Outdoor activities including physical activity, home and vehicle maintenance, gardening, socialization, and relaxation are important to health and quality of life in rural areas hosting swine ILOs[3], particularly for children. Quantifying the impact of swine ILO pollutants on sleep duration and time-outdoors is important for developing policies that protect public health and promote responsible agricultural production.

I use data from the Community Health Effects of Industrial Hog Operations (CHEIHO) study to estimate the effects of ambient swine ILO pollutant concentrations on sleep duration and time outdoors among those living nearby. CHEIHO was a community-based, participatory research project that has collected repeated assessments of air pollutant concentrations, sleep duration, and time outside over a two-week study period[8]. The study's repeated measurements facilitate effect estimation in the presence of feedback effects between less-than-recommended sleep duration and time outside. Feedback systems are ubiquitous in nature but have not been extensively studied in epidemiology; if unaccounted for, feedback could bias effect estimates. To improve the state of knowledge of how swine ILOs impact public health and to advance the epidemiological study of dynamic systems, I address the following specific aims:

Aim 1 - Association between ambient swine ILO pollutant concentrations and sleep duration. Using measurements from air monitors, odor diaries, and sleep logs, I investigate two hypotheses about ILO exposure effects on sleep: *Greater cumulative ILO odorant exposure during the evening leads to shorter total reported nightly sleep duration the following night (hypothesis 1a), and exposure to higher ILO odorant concentrations at night leads to a greater of rate of awakening from sleep (hypothesis 1b) that night*.

Aim 2 - Association between ambient swine ILO pollutant concentrations and time outdoors. Using measurements from air monitors, odor diaries, and activity logs, I investigate two hypotheses about ILO exposure effects on time outside*: Stronger outdoor odors during morning data collection decrease time outdoors later that day (hypothesis 2a), and time periods during the day with higher odorant concentrations have a lower proportion of time outdoors (hypothesis 2b)*

Aim 3 –Feedback between exposure, time outside, and sleep. Using measurements from air monitors and diaries, I investigate feedback between exposure, time outside, and sleep, to address a hypothesis about bias due potential interrelationships between subsequent values of exposures and outcomes: *The estimated total effect of ILO odorant exposures are of greater magnitude when feedback effects are accounted for (hypothesis 3).*

This dissertation contributes to the literature on community swine ILO impacts by assessing the effect of exposure to swine ILO air pollutants on sleep duration and time outdoors. A better understanding of these impacts is important for guiding policy and technology development to protect the health of communities hosting swine ILOs without hindering sustainable agricultural production. The work should also contribute to understanding the impact of bias on effect estimation.

Methods

Methods Overview

This study used discrete-time hazard models to estimate the effects of ambient concentrations of ILO air pollutants on sleep duration (aim 1) and time outdoors (aim 2). Dynamic Bayesian networks were be used to estimate the effects of chronic exposure, which could differ from the total effect of acute exposures due to feedback (aim 3). The analysis dataset consists of repeated hourly measurements of air pollutant concentrations, odor, sleep status, and time outdoors in communities hosting swine ILOs in Eastern North Carolina. Flexible participant-specific discrete-time hazard functions and covariates for weather conditions were used in discrete hazard models to address potential time-invariant and time varying confounding factors.

This work is oriented within two main theoretical frames: the causal inference paradigm[9], and the ecosocial perspective[10]. The causal inference approach can be classified as a reductionist[1], non-reflexive[2], and positivist[3] program to apply the advantages of the experiment to observational studies to identify causal explanations for disease outcomes. In contrast, the ecosocial perspective combines a multi-level, dynamic, and holistic ("ecological") perspective of health with an acknowledgement that health and disease are socially produced and represent physical embodiments of underlying power dynamics in society. This work attempts to benefit

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[1] *Reductionism* is the belief that a complex system is are best understood by breaking it down into component parts that are more amenable to analysis.
[2] A *non-reflexive* science limits its domain of inquiry to impartial observations of the natural world, excluding the social production of knowledge and the potential biases of the observer as topics of study. This is also known as the *single hermeneutic*.
[3] *Positivity* holds that valid knowledge comes only from direct sensory experience, i.e. experimentation and observation.

from both paradigms to rigorously estimate causal effect measures within theoretical and social contexts.

Data Source and Population

This dissertation uses existing data collected as part of the Community Health Effects of Industrial Hog Operations (CHEIHO) study. CHEIHO was a community-based participatory research study designed in collaboration with community members that aimed to investigate the impacts of industrial hog operations on the general health, disease symptoms, and well-being of those living nearby[8]. The study took place between 2003 and 2005 and enrolled 101 participants living in 16 neighborhoods in Eastern North Carolina that were affected by industrial hog operations[11]; each community participated in the study for a period of at least two weeks. Despite the relatively small number of subjects, the study has a larger effective sample size because repeated measurements were collected for each subject. For instance, participants recorded hourly odor for two weeks – producing 336 potential records for each of 101 participant clusters, or 33,936 potential records total.

Neighborhoods that chose to participate in CHEIHO were identified by community organizers from the North Carolina Environmental Justice Network. Selection of communities using this approach was important for ethical and logistical reasons. Because the swine industry in North Carolina has retaliated against research participants in research studies seen as unfavorable to the industry[12], it was important for communities to be prepared for potential consequences of participation beyond researchers' control. Recruiting interested communities was also important due to historical exploitation of minority study participants by researchers in the United States[8]. This collaborative approach facilitated fair treatment and also contributed to a high response rate among participants (98%)[13].

Although they were not randomly sampled, participating neighborhoods were fairly representative of populations affected by swine ILOs in North Carolina. These neighborhoods had a higher proportion of households in poverty and a higher proportion of residents identifying as Black and a higher proportion of older residents, compared to the state as a whole[2]. Because older individual and minorities typically have greater disease susceptibility and higher existing disease burdens, estimates produced in this analysis might be greater than the effects on the general North Carolina population, but are generalizable to the population affected by swine ILOs air pollutants in North Carolina.

To be eligible for participation, potential study enrollees had to be non-smokers, have a freezer available in their home to store saliva samples, and be able to commit two periods per day to data collection activities. Because non-participant names were not recorded to protect individual confidentiality, the number of excluded participants is unknown. The exclusion of smokers is expected to lead the study to under-estimate the true effect of air pollutants on swine ILO neighbors, if smokers are more susceptible to air pollutants because of existing respiratory system stress. The average age of participants enrolled in the CHEIHO study was 53 and 65% were female. Most (83%) identified as Black[11], 15% identified as white, 1% identified as Latino, and 1% identified as Black/Native American.

Exposure Assessments

This study used ambient air pollutant concentrations and participants' self-reports of odor, instead of direct measurements of human exposure, as the independent variables of interest. During the study period, air monitors located near participants' homes assessed ambient concentrations of hydrogen sulfide (H_2S), a specific marker for swine ILO emissions in the study context, at 15-minute intervals. Twice per day, participants also rated the strength of hog odors they sensed outdoors and recalled the strength of odors they sensed for each of the prior 12 hours (inside or outside, depending on their location during each hour).

Participants rated odors were rated on a scale of 0 (no odor) to 8 (strong odor). Each participants' odor perception was assessed at baseline using a butanol dilution series[11]. In this test, participants were presented with two vials of liquid, one with increasing concentrations of odorants and the other with plain water. The concentration at which a participant could reliably tell the difference between the two vials was used to estimate their odor perception threshold. This threshold might be an effect measure modifier for exposure effect pathways depending on odor perception, but in past CHEIHO research it did not have a significant impact[6]. The exposure and exposure assessment processes are summarized in Figure 2.1, below. A list of the exposure measurements is presented in Table 2.1.

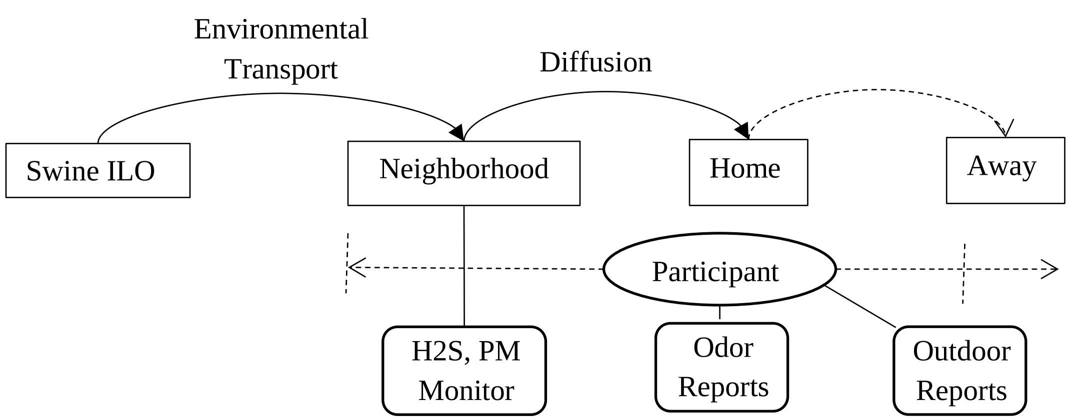

Figure 2.1. Simplified CHEIHO exposure model. Chemical mixtures originating from swine ILOs were carried into participants' neighborhoods by the wind where they could diffuse into homes. Monitor records reflected neighborhood concentrations of hydrogen sulfide and particulate matter "upstream" of human exposure; odor diaries reflected somatosensory "downstream" effects of human exposure to odorant chemicals.

Meteorological instruments on a monitoring trailer were used to simultaneously record temperature, humidity, wind speed, and wind direction during the study. These variables were considered potential confounders because they might influence recent exposures and an individual's propensity to sleep or spend time outdoors.

Assessment	**Type**	**Period**	**Location**	**Units**
H_2S	Monitor	Hourly average	Neighborhood	ppb
Odorant Chemicals (Current location)	Participant Report	Hourly rating (24 per day)	Current Location	Strength (0 to 8)
Odorant Chemicals (Outdoors)	Participant Report	10 minutes (2 per day)	Outdoors (Home)	Strength (0 to 8)

Table 2.1. Summary of CHEIHO exposure assessment methods used in this dissertation.

Outcome Ascertainment

At each of two daily data collection sessions, participants indicated if they were inside (at home), outside (at home), away from home, or asleep for each of the preceding 12 hours using an hourly grid (see example in Figure 5, below). Participant used two identical sheets per day – one for morning data collection and one for nightly data collection. Morning data collection forms were used to assess sleep status on an hourly scale, and the nightly data collection form was used to assess outdoor status on an hourly scale. Night-shift or rotating-shift workers in the population were excluded from the study because their sleep and activity schedules were different from the remainder of the study population.

Compared to the gold standard of polysomnography (multiple-electrode brain and muscle signal measurement), self-reported-sleep is expected to systematically overestimate total sleep duration[14–16], with greater errors for lower sleep duration values. This effect is expected to result in a systematic bias towards a null effect in the study; the bias is expected to make the outcome distribution more similar between exposed and non-exposed groups. Although it is possible that participants' modified their responses to create the appearance of sleep impacts, this is unexpected since assessment of sleep impacts was not an explicit aim of the original study. The Z indicators used to indicate sleep in odor diaries were originally intended to distinguish "skip pattern" missing data during sleep from "true" missing data from participant error (Figure 2.2). An assessment showing that participants' other reports showed high agreement between biometric and environmental measures in the study and suggests that participants accurately reported their sleep status[13].

Participant: 007 **Study Day**: 4 of 14 **Time:** Morning

For each of the <u>*preceding*</u> *twelve hours indicate the strength of livestock odors perceived on a scale of 0 (no odor) to 8 (strong odor) [write "Z" if you were asleep]:*

Hour	9:00p	10:00	11:00	12:00a	1:00	2:00	3:00	4:00	5:00	6:00	7:00	8:00	9:00
Away	0		Z	Z	Z	2	Z	Z	4	1	1	1	1
Outside		3											
Inside			2	Z	Z	6	Z	Z	3	4	5		

Figure 2.2. Hypothetical sleep record showing sleep coding for a person who came home at 10:00pm, spent an hour outside and an hour inside before going to sleep, woke at 2:00am, then slept until 5:00am, and awoke to livestock odors in the morning both inside and outside. This example shows how three different types of sleep disruption - delayed sleep, awakening during the night, and early awakening – might manifest in study records.

Model Selection

The statistical models used for this analysis were chosen using three criteria: (1) models must estimate parameters appropriate for answering the research questions, (2) models must take advantage of the availability of repeated measurements to address potential confounding factors, and (3) model outcome format must match available study data. Based on these criteria, aims 1 and 2 were be assessed using discrete-time hazard models, and aim 3 was addressed using dynamic Bayesian network models. The relationship between the models and the study questions is depicted in Table 2.2.

As a generalized linear model, the discrete-time hazard inherits the assumptions of the linear model (homoscedasticity or common-variance, multivariate normal distribution of transformed residuals, and independence of observations between clusters) but replaces the linearity assumption with the proportional hazards assumption. Since the parameter of interest is a ratio of hazards, it is assumed that the difference in hazards between exposed and unexposed groups is proportional to the baseline hazard[17]. The validity of these assumptions were assessed during the analysis using standard graphical methods, drawing inference from the distribution of model residuals[18].

The dynamic Bayesian network (DBN) models in Aim 3 have several advantages in the context of estimating feedback effects in epidemiology. First, the DBN is modeled as a directed acyclic graph (DAG) in which the probability distribution of each node, based on the values of its parents nodes, is explicitly modeled[19]. This enables the DBN approach to benefit from the same epidemiological paradigm of causal inference, which uses on the relationship between just two nodes on a graph to infer the appropriate conditioning sets for estimating a given exposure-response relationship[20]. Second, the DBN allows flexible modeling for the conditional distributions of nodes. Generalized linear models, also commonly used in epidemiology, can be used for these distributions, generating coefficients with similar interpretations as those used elsewhere in the modern epidemiology literature.

Aim	Inference target	Exposure	Outcome (window)	Regression model (estimate)	MA[1]
1	**Sleep**		**Sleep (hour)**	**Discrete hazard (odds ratio)**	**MN, H CI, M0, PH**
1a	Difficulty sleeping from evening odor	Evening outdoor odor		Model 1a	"
1b	Awakening from sleep from odor	Hourly H_2S		Model 1b	'"
2	**Time Outdoors**		**Outdoor (hour)**	**Discrete-time hazard (odds ratio)**	**MN, H, CI, M0, PH**
2a	Sheltering indoors due to poor air quality	Odors (hour)	Time outdoors (hour)	Model 2a	"
2b	Avoidance of outdoor activities due to poor expected air quality	Outdoor odor (morning)	Hours outdoors (day)	Model 2b	"
3	**Feedback between exposures, sleep, and time outdoors**	Indoor and outdoor H_2S (hour)	Sleep and time outdoors (hour)	**Dynamic Bayesian Network (odds ratio)**	**MN, H, CI, M0**

Table 2.2. Summary of regression models used in this analysis and their relationship to study Aims. Aim 1 and 2 each use one model with a common outcome but two exposure terms to address subaims a and b; Aim 3 is addressed using a dynamic Bayesian network. [1]. *MA: Model Assumptions.* [2]. *MN: Multivariate normality (transformed)* [3]. *H: homoscedastic (common-variance)* [4]. *CI: Cluster independence (between subjects, communities)* [5]. *M0: No measurement error* [6]. *PH: Proportional hazards*

Three classes of alternate models were considered for this analysis. Random-effect models could be used to model each participants' baseline outcome risk (i.e. model intercept) as an independent random variable, but this approach assumes that these baseline risks were independent of the values of the exposures[4]. Generalized Estimating Equations (GEE) could be used to model outcomes in the population using a covariance structure within participants, but this method produces non-collapsible[21] marginal estimates[5] that do not condition on influence of unmeasured participant-specific confounding factors. Marginal structural models were considered for Aim 3, but do not offer the same advantages of the DBN important in this context (similar interpretability to existing models and flexible distributional specification).

Potential Confounding

Analyses can be influenced by confounding bias if there are factors that causally precede exposures and outcomes. Ambient concentrations of ILO air pollutants vary based on production factors, relative ILO location, wind speed, wind direction, time of day[11], and temperature. Sleep and daily outdoor activities could be influenced by temperature and time of day. These potential confounders are time-varying, but the potential for time-invariant confounding factors is also addressed below.

Exposure to ILO emissions in the CHEIHO study can also be broken down into two mechanisms relevant to their potential for confounding: routine life-course exposures, and study-initiated exposures. Routine exposures occurred in participants' lives as a result of industrial

[4] Mean exposures in CHEIHO differed between neighborhoods (and therefore between individuals). The approach ultimately used is comparable to a fixed-intercept approach (within the class hierarchical models) without explicit estimation of these fixed effects.

[5] GEE uses a specified a covariance matrix structure to account for similarity between observations; this approach treats the similarities between individuals' responses in CHEIHO as a nuisance parameter to be eliminated, rather than as a basis for efficient causal inference.

livestock operations nearby. These exposures reflect participants' typical exposures[6] and were the exposures assessed both by air monitors (capturing "upstream" indicators of human exposure) and hourly odor recalls (capturing a "downstream" biomarker of human exposure). Depending on the concentration of ILO air pollutants, this could have resulted in exposure to ILO air pollutants outdoors, indoors, or away from home. While participants did not have control over the concentration of ILO air pollutants at these times, they had some control over their potential for exposure (by going indoors, outdoors, or away from home).

Study-initiated exposures occurred during twice-daily data collection sessions. In the course of data collection, participants were asked to expose themselves to ambient air for 10 minutes and then rate the strength of odors they experienced. For this category of exposure mechanism, participants had control over neither their exposure to outdoor air nor the concentration of ILO pollutants in ambient air.

The difference between these two mechanisms of exposure is relevant to confounding potential because routine daily exposures had the potential to be influenced by other factors while exposures to air occurring during data collection aren't influenced by the same set of factors because they occurred every morning and evening. For morning and evening exposures required by the study design, participants' received exposures could depend on the emissions source or on weather conditions, but not on participants' behavior history. This reduced the potential for confounding bias among exposures occurring during data collection. In both cases, whenever participants were exposed to outdoor air, their exposures to ILO emissions also depended on the concentration of ILO pollutants in the air at that time.

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[6] There was evidence that ILO operators reduced waste spraying (and therefore participants' exposures) in response to seeing the monitoring trailers during the course of the study. This would suggest that the routine exposures recorded during CHEIHO are lower than typical exposures, although the extent of this difference was not formally assessed.

Unmeasured confounding factors that remained constant throughout the study period for each participant were handled using conditional logistic regression models (conditioned on individual hazard functions). The conditional logistic approach uses a partial likelihood calculation that conditions out the influence of unmeasured individual factors (modeled as a flexible discrete-time hazard function). Potential time-varying confounding factors were addressed using covariate adjustment. Temperature and time of day were considered potential confounding factors because they can influence ambient ILO air pollutant concentrations, sleep, and time outdoors.

Effect measure modification

Odor perception threshold can be considered a potential effect-measure modifier. Pathways that depend on individuals' perceptions of odor (for instance, mood changes caused by frustration with odors or avoidance of outdoor activities due to odors) could be reduced among individuals less able to perceive odors, resulting in a dampened response to ambient ILO air pollutant concentrations. On the other hand, individuals with low odor sensitivity might be better able to avoid exposures if they are better able to detect them, which could lead to increased response to air pollutant concentrations among those with poorer sensitivity. Odor perception could also be associated with factors that could affect participants' susceptibility to exposures in other ways. For example, odor perception could be lower in older participants and participants with respiratory disease symptoms.

The potential for effect measure modification was assessed by stratifying participants by odor sensitivity threshold. Odor sensitivity thresholds was assessed at baseline using a butanol dilution series. In this procedure, participants were presented with a series of two vials containing different concentrations of an odorant chemical and scored based on their ability to consistently identify the vial containing a higher concentration by smell. Participants were stratified based on a butanol perception threshold of 40 ppm (parts per million). This level was chosen to maintain an adequate sample size in each of the stratification groups.

Missing data

Prior CHEIHO analyses have indicated that data completeness and quality are high, but considered measures that were important to the original study design, including disease symptoms and biometric measurements. In the context of this work, the completeness of the exposures and outcomes are less complete. Some variables, like indoor odor, outdoor odor, and sleep were mutually incompatible and thus can be considered missing by design in this analysis. For example, participants could not record odors while they were asleep, and also could not report outdoor odors while indoors. Other variables may have had less completeness than expected because they were not the main focus of the study. For example, sleep status was estimated using a missing data code for odor diaries.

Missing data was addressed by the study design, exclusion, and multiple imputation when necessary. First, the conditional models used in this analysis enabled data missing “by design” to fall out of analyses as necessary. For instance, comparisons for the effect of outdoor odor on time outdoors during the next hour only used hours during which participants recorded outdoor odors (and thus were outdoors); although the hourly data might appear “missing” in an hour-by-hour dataset, these data are not truly missing in the design since the effect of interest only occurs during certain time periods.

Data that could not be meaningfully imputed, based on stratification by subject, were excluded to preserve the conditional-on-participant method of analysis. For example, one participant did not record any sleep missing value codes. Participants with too many missing observations for sleep, odor, or time outdoors (>50%) were excluded from the analysis.

Imputation was used for missing data for which there was sufficient data to build an imputation model. This approach reduces potential biases presented by missing data using bootstrapping; the distribution missing values is characterized using a predictive model built from non-missing data, and resampling is used to propagate the effect of this uncertainty on the final effect estimates[22].

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CHAPTER 3: EFFECTS OF REPEATED EXPOSURES TO AIR EMISSIONS FROM SWINE INDUSTRIAL LIVESTOCK OPERATIONS ON SLEEP DURATION AND AWAKENINGS

OVERVIEW

Waste from swine industrial livestock operations (ILOs) produces air pollutants that have been associated with negative health impacts among those living nearby. This study aims to assess the impact of odor emissions on sleep duration and awakenings, important components of health and quality-of-life that affects morbidity and mortality. Following a repeated-measured design, study participants from communities in eastern North Carolina hosting swine ILOs completed twice-daily diaries in which they rated the strength of hog odors and indicated their sleep status every hour for two weeks. Simultaneously, a monitoring trailer placed in each community measured the atmospheric concentration of hydrogen sulfide (H_2S) nearby. Subject-conditional fixed-effects regression models were used to estimate associations between two markers of swine ILO pollutant exposures (H_2S and swine odor) and two sleep outcomes (nightly sleep duration and awakening from sleep). Nightly swine odor was associated with decreased nightly sleep duration (mean -14.3 minutes, 95% interval -25.0 to -3.3 minutes) and nightly hydrogen sulfide concentration was associated with an increased hazard of awakening (*HR* = 1.23, 95% interval 0.98 to 1.55). These results suggest that emissions reductions and odor abatement are important public health goals in designing policy and technology solutions to the problems of livestock production and waste management.

INTRODUCTION

Swine Industrial Livestock Operations (ILOs) are a prevalent source of air pollutants in eastern North Carolina. Today, nearly all of the pork consumed and exported by the United States is produced by industrial livestock operations[1] and North Carolina is a leading producer - with over 2,000 permitted operations and 9 million swine[2,3]. The industry is highly concentrated in the southeastern part of the state[4], where the two top-producing counties are also the two top-producing counties in the entire United States[5].

This context has produced an environment where communities hosting swine ILOs can face concentrated industrial air emissions not typically associated with rural areas. Rural areas consistently score poorly on population health indicators[6,7], and rural communities are experiencing social transitions that create health challenges[8]: a shift to corporate agriculture, job loss, outmigration of young and working people, and poorer access to nutritious food[9]. Air pollution produced by swine ILOs contains complex mixtures of particulate matter, aerosols, and gasses that can vary by facility, time of day, weather, and season. A large proportion of these air pollutants are produced by lagoon-and-sprayfield systems, which are used for waste management at swine ILOs in North Carolina[10]. In this system, wet swine wastes flow through the slatted floors of confinement buildings into open pits where they decompose anaerobically to produce mixtures of microbial metabolites including ammonia and hydrogen sulfude[11]. These wastes are sprayed onto adjacent fields to encourage aerobic decomposition, but this process also produces waste aerosols that spread liquid pollutants into the air and groundwater.

Exposure to ammonia odorants like those found in swine ILO pollutants have long been known to cause awakenings from sleep[12]; this property has been exploited in the clinical context as smelling salts[13]. In ethnographic research conducted in communities near swine ILOs, neighbors have reported that swine ILO air pollutants interfere with sleeping and time outdoors

[14] but these associations have not been quantified statistically. Many of the disease symptoms linked to swine ILO air emissions in past research are consistent with sleep impairment. Disrupted breathing can make falling asleep difficult[15], cause awakenings from sleep[16], interfere with outdoor activities[17], and produce psychological stress[18–20]. Respiratory disease symptoms, the cultural and psychological meanings of malodor[18,21], and the inability to control odors could make falling asleep more difficult.

This study seeks to expand the understanding of the health effects of ILO pollutant exposures by assessing their impact on sleep. Associations between two exposure markers (swine odors and atmospheric hydrogen sulfide concentration) and two outcome measures (nightly sleep duration and sleep instability) are estimated.

METHODS

Study population. This study uses data collected as part of the Community Health Effects of Industrial Hog Operations (CHEIHO) study. Potential CHEIHO communities were identified in collaboration with community organizations and had at least four residents interested in study participation. 101 CHEIHO participants were recruited from 16 North Carolina communities hosting industrial swine operations from 2003 to 2005[22]. To be eligible for CHEIHO, participants had to live within 1.5 miles of an active ILO containing swine, not smoke, be at least 18 years old, and have access to a freezer to store saliva samples collected as part of the study. An initial training session in each community was used to obtain informed consent and train study participants in data collection procedures. A baseline assessment of odor sensitivity was conducted for each participant at baseline using a butanol dilution series[23].

Exposure assessments. Swine ILO pollutant exposures were characterized using participants' hourly swine odor ratings, participants' twice-daily outdoor swine odor ratings, and hydrogen sulfide concentrations recorded by monitors. Over a two-week study period, each participant completed a twice-daily diary form containing questions on the strength of swine odors. Each participant completed two diary data-collection sessions per day at times identified in conjunction with research staff. Each participants' daily diaries were made 12 hours apart between 7 and 9 am and 7 to 9 pm (e.g. 8am and 8pm), providing 24-hour coverage if all diary entries were completed but allowing data collection to occur at convenient times for each participant. At the beginning of each diary session, participants rated the odor from swine operations during the preceding twelve hours using a 9-point scale (0-8); for each rated hour, participants also indicated if the rated odor was indoors, outdoors, or away from home. Participants then spent ten minutes outside and rated the current strength of outdoor odor from swine operations on the same scale.

Simultaneously, a mobile air monitoring trailer was used to make meteorological measurements (temperature, humidity, wind direction, and wind speed) and record atmospheric concentrations of hydrogen sulfide (H_2S). Atmospheric hydrogen sulfide (H_2S) is produced by the anaerobic decomposition of swine waste and has been used as a specific marker of ILO emissions plumes. The monitor was placed in a central location in each community, on average 0.2 miles from participants' homes. H_2S was measured as a chemical marker specific to the complex mixtures of air pollutants produced by liquid swine waste management systems in rural areas. Mean 15-minute H_2S accumulations were originally measured by an MDA Scientific Single Point Monitor (Zellweger Analytics, Inc.) using a chemcasette with a detection limit of 1 part-per-billion volume (ppb) and converted to hourly averages to align with participants' odor records. A HOBO microstation datalogger (Onset Computer Corporation) with temperature and humidity sensors was used to measure meteorological conditions.

Outcome ascertainment. During twice-daily data collection sessions, participants indicated if they were asleep during each of the preceding 12 hours on a diary form (Table 3.5) Each participants' daily diaries were made 12 hours apart between 7 and 9 am and 7 to 9 pm (e.g. 8am and 8pm), providing 24-hour coverage of sleep status if all diary entries were completed, but allowing data collection to occur at convenient times for each participant. Sleep status was classified as a binary variable on an hourly scale in each participants' diary. These hourly values were summed by night to produce a variable representing the number of hours of sleep each evening. Sleep instability (awakening) was defined as a period when a participant reported at least one hour of wake time, following at least one hour of sleep time.

Statistical methods.

Sleep duration each night was modeled as a Poisson distributed outcome following the form

$$\ln n_{ij} = \delta_i + X_{ij}\beta \qquad (1)$$

where n_{ij} is the number of hours of sleep, i is the participant index, j is the night index, X is a vector of exposures and covariates, and δ_i represents a subject-conditional fixed effect[24] for each participant that is conditioned out of the model likelihood by using a conditional likelihood function. In this fixed-effect model form, potential confounding factors are limited to those that vary with time and are associated with odor and nightly sleep duration. The combination of high relative humidity and hot temperature (humid heat) was treated as a potential confounder because it has the potential to disrupt sleep[25] and odorant production[23]. Based on experimental data, humid-heat was defined as a dry-bulb temperature above 80 °F and relative humidity above 60%[26]. Therefore, in our fitted model the X vector consists of the potential confounder, humid-heat, and the exposure of primary interest. We estimated associations with hourly hydrogen sulfide level, nightly average swine odor, or evening outdoor odor. To facilitate interpretation of model parameters, average sleep duration for all study participants was substituted into the model using the formula $\hat{n} * (exp(\beta) - 1)$ to yield an estimate of the average exposure effect in the total population at the reference level of the confounder.

We also fitted a model for sleep stability (i.e., discrete time hazard of awakening from sleep). Sleep stability was modeled as a binary outcome variable using a discrete-time hazard model following the logistic form

$$logit\big(P(y_{i,j,t})\big) = \alpha_{i,} + \lambda_t + X_{i,j}\beta \qquad (2)$$

where y_{ij} is sleep stability (taking a value of 1 if a person is awakened at hour j, conditional on having been asleep at hour j-1, and 0 otherwise), *i* is the participant index, *j* is the hour index, α_i are an participant-specific fixed-effects conditioned out of the likelihood, $\lambda_t$are used to model the baseline hazard as a function of time-asleep, and X is the vector of humid-heat and hydrogen sulfide. We report estimates of association between sleep stability and current hydrogen sulfide exposure, as well as associations with hydrogen sulfide exposure in the preceding hour (i.e., one-hour lagged exposure),

Given the highly skewed distribution of hydrogen sulfide, with 92% of hourly measured below the limit of detection, in current analyses hydrogen sulfide level was modeled as a binary variable coded as 1 if above the limit of detection, and 0 otherwise. Model precision is reported using 95% intervals, rather than 95% confidence intervals, as the data do not come from a random sample.

RESULTS

Of a potential 26,880 person-hours, 24,552 (91.3%) were used due to missing outcome data, covering 1023 day/night person-periods. 21 participants' records were excluded due to insufficient exposure or outcome data (11 participants) or atypical sleep patterns (10 participants), including apparent night-shift work. Demographic characteristics of the 101 original study participants and 80 eligible participants are shown in Table 3.1. The CHEIHO cohort and the analytic sample had similar distributions of age, gender, and race but a smaller proportion of participants in the analytic sample had a butanol odor detection threshold below 40 ppm (35% versus 39.6%). Due to missing data, a higher proportion of study records were from non-Black participants (21.4%) compared to the proportion of non-Black participants in the original CHEIHO study (15.8)

The distributions of sleep and odorant exposures are described in Table 3.2. Hydrogen sulfide was above detection threshold 8.2% of all study hours and participants reported odors 14.5% of their time awake. Evening outdoor odorants were higher on average than morning outdoor odorants (1.50 vs. 1.34). Participants experienced at least one odor episode on 46.8% of days and 50.0% of nights. Atmospheric temperature ranged from 31 °F to 87 °F (mean 62 °F) and relative humidity ranged from 40.7% RH to 100% RH (mean 80.4% RH); 12.4% of nights were classified as hot-humid. Participants slept 7.3 hours per night on average, and 8.3% of days contained at least one nap episode.

Nightly detection of H_2S, nightly swine odor, and evening outdoor ratings were each associated with lower nightly sleep duration (Table 3.3). Models estimated that the presence of nightly swine odor decreased nightly sleep duration in the study population by 14.3 minutes (3.3

to 25.0, 95% interval) on average. Through a similar calculation, the presence of nightly hydrogen sulfide decreased nightly sleep duration by 5.0 minutes on average (-5.8 to 15.6, 95% interval). These estimated associations did not differ by participants' sensitivity to odors.

Detection of hourly H_2S concentration was associated with a greater hazard of awakening from sleep (Table 3.4). The presence of hydrogen sulfide above increased the discrete time hazard of awakening by 24% during that hour (HR=1.24, 95% interval: 0.99 to 1.55) and by 23% (HR=1.23; 95% interval: 0.98 to 1.55) during the following hour (i.e., a 1-hour lagged analysis). An increased hazard of awakening was observed among participants with higher sensitivity to odor (threshold <40 ppm; HR=1.62, 95% interval 1.10 to 2.40) compared to participants with a lower sensitivity to odor (threshold >=40 ppm; HR=1.08, 95% interval 0.82 to 1.43).

DISCUSSION

This study estimated the effect of exposures to swine ILO pollutants on sleep. Night-time ILO pollutant exposures (hydrogen sulfide and odor from swine operations) were associated with adverse sleep effects. Episodes of nightly hydrogen sulfide exposure and odor, two markers of swine ILO pollutant exposures, decreased participants sleep by 14.2 minutes on average and increased the hazard of awakening from sleep by 23%. In the context of chronic daily exposures, these impacts could lead to substantial sleep losses over time.

Observed associations between ILO pollutants and sleep could be attributable to several causes. Hydrogen sulfide, amines, and other emissions components could have direct chemical effects - prompting awakening[12] or disrupting homeostatic (sleep-wake) or circadian regulation[27]. Studies of communities exposed to ILO pollutants have documented sensory effects consistent with olfactory and trigeminal nerve irritation[28] including nausea[29,30], burning nose and eyes[29–31], and headaches[31] that could cause awakenings from sleep. Inability to control exposures during the day and night could also cause annoyance, stress, negative thoughts, and anger that could make sleeping difficult. Respiratory effects of exposures could have secondary effects on sleep by lowering lung function or exacerbating existing conditions like asthma, obstructive pulmonary disease, or sleep apnea[16]. Respiratory symptoms consistent with sleep impairment have been linked to ILO pollutant exposures in Western Europe and the United States, including excessive coughing[29,31], asthma[32–34], wheezing[29,30], difficulty breathing[29,30], runny nose[29,31], sore throat[30,31], and chest tightness[29,30].

Due to the repeated-measures design, observed associations cannot not be explained by factors that remained constant for participants over the study period. For instance, neither participants' pre-existing medical conditions nor seasonal effects could not create an association between ILO pollutant exposures and sleep loss because they remained fixed over the study period for each participant. As potential participants were excluded from the study if they smoked or were unable to participate, it is possible that the true effect is stronger than estimated here due to participants being healthier than the population exposed to swine ILO air emissions. Similarly, participants were excluded if they had atypical sleep schedules, which could have made the analytic sample appear healthier than the general population. Replicating the analysis without any participant exclusions yielded similar (estimated effect direction and magnitude) but less precise results.

The study is limited by the quality of exposure and outcome data. The study used two exposure assessments: participants' perceptions of odor from swine operations, and hydrogen sulfide concentrations measured in participants' neighborhoods. In the present study context, odor perception can be understood as a biomarker of exposure and is limited by potential hysteresis, between-person variability, and non-linearity. Although environmental monitors were placed close to participants' homes (mean 0.2 mi), they only measured one marker of a complex mixture of pollutants and did not quantify individually-received exposures. The outcome data used for this study were collected from self-report in a parent study that was not originally designed to assess sleep disturbances, and are less complete compared to other study data. Self-reported sleep duration data has been shown to over-report actual sleep duration; the correlation between self-reported sleep duration and actigraphy-measured sleep was 0.29 in Black participants in the Multi-Ethnic Study of Atherosclerosis[35]. Sleep under-report in the Chicago site of the Coronary Artery Risk Development in Young Adults Study was inversely proportional to sleep duration, as participants with less sleep under-reported their sleep more[36]. This measurement error could mask observed sleep impacts, as those with the largest sleep deficits may appear more similarly to those with more sleep. A study design using more objective, personal, and comprehensive exposure assessment and an automated method of recording sleep data with improved temporal specificity (e.g. personal accelerometers) could help overcome these limitations.

The repeated-measures models used for the study address some of these limitations and also reduces the potential for confounding biases. These models estimated associations between within-person variations in exposure and outcome and are comparable to models adjusted by participant. This design removed the influence of factors that remained constant for each participant throughout the two-week study period, including demographic characteristics, season, odorant sensitivity, baseline sleep quality, and home permeability to odorants. Of the remaining potential time-varying potential confounding factors, heat-humidity was the most concerning and could be adjusted for in each model.

The associations observed between swine ILO emissions exposure markers and sleep in this study suggest that ILO emissions have negative impacts on sleep among those living nearby. Sleep influences an array of disease risk factors and diseases, but is also an important part of health in its own right. Sleep is important for DNA repair[37], cellular metabolism, tissue maintenance, immunological response, mood regulation, and memory consolidation[38]. Based on the importance of sleep to health, the National Sleep Foundation recommends 7 to 9 hours of sleep per night for adults 18-65 and 7 to 8 hours per night for adults over 65[39]; the American Academy of Sleep Medicine and the Sleep Research Society recommend at least 7 hours of sleep per night for health adults[40]. Getting less than this recommendation (<7 h) has been linked to increased risks of diabetes and obesity[41–52], cardiovascular disease[53], accidents[54,55], poor quality of life[56–61], and premature death[62]. The average sleep duration observed among participants in this study (7.3 hours per night) was not far from the 7-hour recommended minimum.

The social context of pollutant production in swine industrial livestock operations has proven resistant to public health intervention. Swine industrial livestock operations offer economic benefits to a select few that can use their political influence to secure their legal right to pollute[63], leading to regulatory capture favoring larger operations[64,65]. Emissions abatement through technology or policy improvements could offer relief[66–68], but have proven difficult to implement through traditional regulatory channels[10]. In conjunction with existing data on the community health impacts of industrial animal operations, this study could help guide public policy recommendations on health-based emissions controls for livestock waste treatment systems[69]. Odor abatement, in addition to nutrient management, should be an important consideration in designing systems to manage large-scale animal wastes.

Although this study focused on odor and hydrogen sulfide from industrial livestock operations, environmental odorants from industrial sources in other areas could also be important for sleep hygiene and the secondary health effects associated with sleep. From a public health perspective, greater community control over local industrial development could help reduce the high concentrations of swine ILOs and other facilities that create environmental pollutants and positively impact population health. Scientific evidence about the health impacts of ILOs could help facilitate meaningful public engagement around the health effects of environmental quality and promote public health by demonstrating the need for more sustainable methods of production.

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Table 3.1. Distributions of demographic characteristics of study participants by grouped by eligibility and number of records

	Participants		Person-time	
Variable	CHEIHO (n=101) n (%)	Current Study (n=80) n (%)	Person-hours (n=24552) n (%)	Person-days (n=1023) n (%)
Age				
≥65	24 (23.8)	20 (25.)	6768 (27.6)	282 (27.6)
24-64	77 (76.2)	60 (75.)	17784 (72.4)	741 (72.4)
Gender				
Women	66 (65.3)	54 (67.5)	16656 (67.8)	694 (67.8)
Men	35 (34.7)	26 (32.5)	7896 (32.2)	329 (32.2)
Race				
Black	85 (84.2)	66 (82.5)	19296 (78.6)	804 (78.6)
non-Black	16 (15.8)	14 (17.5)	5256 (21.4)	219 (21.4)
Odor Sensitivity				
≤40 ppm	40 (39.6)	28 (35.)	8256 (33.6)	344 (33.6)
>40 ppm	57 (56.4)	48 (60.)	15360 (62.6)	640 (62.6)
Missing	4 (4.)	4 (5.)	936 (3.8)	39 (3.8)

Table 3.2. Distributions [n (%)] of odor ratings, hydrogen sulfide concentration (H_2S) and sleep, on hourly, daily, and nightly scales.

Variable (Unit)	Hourly (0-8) n (%)		Daily[a] (0-8) n (%)		Nightly[b] (0-8) n (%)	
Odor (0-8)	Average (1h)		Outdoor (10m)		Outdoor (10m)	
0	14566	(59.3)	474	(46.3)	465	(45.5)
1-2	1254	(5.1)	273	(26.7)	278	(27.2)
3-4	681	(2.8)	142	(13.9)	123	(12.)
5-8	527	(2.1)	71	(6.9)	107	(10.5)
Missing[c]	7524	(30.6)	63	(6.2)	50	(4.9)
H_2S (ppb)	Average (1h)		Average (12h)		Average (12h)	
0	20804	(84.7)	826	(80.7)	663	(64.8)
0-2	1143	(4.7)	189	(18.5)	319	(31.2)
>2	726	(3.)	8	(.8)	41	(4.)
Missing	1879	(7.7)	0	(.)	0	(.)
Sleep (hrs)	Sleep (1h)[d]		Naps (12h)		Sleep (12h)	
1-3	239	(1.)	69	(6.7)	7	(.7)
4-6	1488	(6.1)	10	(1.)	251	(24.5)
7-9	5554	(22.6)	6	(.6)	728	(71.2)
10-12	365	(1.5)	0	(.)	37	(3.6)
Awake	16906	(68.9)	938	(91.7)	0	(.)

[a] *9am to 9pm* [b] *9pm to 9am* [c]*Participants did not record odors during sleep*
[d]*Proportion of all hours by sleep episode length*

Table 3.3. Estimated change in daily sleep duration by hydrogen sulfide, evening, and nightly odors in the Community Health Effects of Industrial Hog Operations (CHEIHO) study, North Carolina.

All Participants	**β**[a]	**(95% Interval)**	**n**	**RD**[b] **(minutes)**	
H_2S	-0.012	(-0.036, 0.013)	865	-5.0	(-15.6, -5.8)
Odor (swine ILO)					
Evening (outdoor)	-0.005	(-0.029, 0.020)	883	-2.0	(-12.4, 8.7)
Nightly	-0.033	(-0.059, -0.008)	933	-14.3	(-25.0, -3.3)
Low Odor Sensitivity	**β**	**(95% Interval)**	**n**	**RD (Minutes)**	
H_2S	-0.023	(-0.053, 0.008)	541	-9.8	(-22.6, 3.4)
Odor (swine ILO)					
Evening (outdoor)	-0.006	(-0.036, 0.024)	557	-2.6	(-15.2, 10.4)
Nightly	-0.043	(-0.074, -0.012)	596	-18.3	(-30.1, -5.2)
High Odor Sensitivity	**β**	**(95% Interval)**	**n**	**RD (Minutes)**	
H_2S	0.018	(-0.028, 0.064)	285	8.1	(-12.0, 29.1)
Odor (swine ILO)					
Evening (outdoor)	-0.007	(-0.053, 0.040)	287	-2.3	(-22.7, 17.9)
Nightly	-0.024	(-0.075, 0.026)	298	-10.5	(-31.5, 11.6)

Model design adjusts for all time-invariant factors and heat-humidity.
[a] Quasipoisson rate parameter . [b]RD = estimated absolute change in sleep duration per night.

Table 3.4. Estimated association between awakening from sleep[a] and pollutant exposure indicators

All Participants	**HR**[b]	(95% Interval)	n[c]
H_2S (current measure)	1.23	(0.98, 1.55)	6643
H_2S (lagged 1-hour)	1.24	(0.96, 1.53)	6645
Low Odor Sensitivity			
H_2S (current measure)	1.08	(0.82, 1.43)	4119
H_2S (lagged 1-hour)	1.08	(0.81, 1.44)	4118
High Odor Sensitivity			
H_2S (current measure)	1.62	(1.10, 2.40)	2270
H_2S (lagged 1-hour)	1.57	(1.04, 2.38)	2273

[a] Night-time interruption in sleep (≥1 hr) preceded by one or more hours of sleep; model design adjusts for all time-invariant factors, heat-humidity, and time-asleep. [b] Hazard ratio. [c] Number of sleep periods during which awakening could have occurred.

Table 3.5. Hypothetical sleep and odor record for a study participant. This example shows how three different types of sleep instability - delayed sleep, awakening during the night, and early awakening – might manifest in study records.

Participant: 007 **Study Day**: 4 of 14 **Time:** Morning

For each of the preceding twelve hours indicate the strength of livestock odors perceived on a scale of 0 (no odor) to 8 (strong odor) [write "Z" if you were asleep]:

Hour	9:00p	10:00	11:00	12:00a	1:00	2:00	3:00	4:00	5:00	6:00	7:00	8:00a
Away	0											
Outside		3										4
Inside			2	Z	Z	6	Z	Z	3	4	5	

CHAPTER 4: EFFECTS OF REPEATED EXPOSURES TO AIR EMISSIONS FROM SWINE INDUSTRIAL LIVESTOCK OPERATIONS ON TIME OUTDOORS

OVERVIEW

Communities hosting industrial hog operations have reported adverse health and quality-of-life impacts from swine industrial livestock operations (ILOs). This study aims to quantify the impact of swine ILO air emissions exposures on the amount of time community residents spend outdoors. Following a repeated-measured design, 88 study participants from communities in eastern North Carolina with swine ILOs completed twice-daily diaries in which they rated the strength of hog odors and indicated their time spent outdoors every hour for two weeks. Simultaneously, a monitoring trailer placed in each community measured the atmospheric concentration of hydrogen sulfide (H_2S) nearby. Fixed-effects conditional regression models were used to estimate associations between three exposure markers (morning odor, daily odor, and H_2S concentration) and time outdoors. Morning outdoor swine odor (OR=0.82, 95% interval 0.59 to 1.12), hourly outdoor swine odor (OR=0.62, 95% interval 0.44 to 0.89), hourly indoor swine odor (OR=0.47, 95% interval 0.18 to 1.25), and hourly H_2S concentration (OR=0.78, 95% interval 0.56 to 1.11) were associated with reduced time spent outdoors. These observed associations suggest that swine ILO emissions exposures have significant impacts on neighbors' access to the outdoors. Technology and policy developments aimed at reducing air pollutants in rural areas, including swine ILOs pollutants, should consider quality-of-life impacts like time outdoors.

INTRODUCTION

North Carolina hosts over 2,000 permitted swine industrial livestock operations (ILOs) containing around 9 million hogs[1]. Wastes produced by these operations are treated using lagoon-and-sprayfield systems that emit complex mixtures of air pollutants into surrounding communities, including ammonia, hydrogen sulfide (H_2S), dander, dusts, and microbial components[2,3]. Ethnographic research in communities hosting swine ILOs has documented a variety of negative quality-of-life impacts stemming from rural residents' relationship to the outdoors. The presence of outdoor air pollutants and odorants can make spending time outdoors unpleasant, or even unbearable. The outdoors is an important venue for relaxation, reflection, and stress reduction in the general population, but also has a special meaning to those who grew up and live "in the country"[4]. Rural residents rely on access to the outdoors for important health behaviors including functional physical activity, food provisioning, home climate control, and socialization.

Although swine ILO neighbors have reported that swine ILO air pollutants interfere with time outdoors in ethnographic research[4], these effects have not been quantified. This study aims to quantify the impacts of air emissions from swine industrial livestock operations on time outside among those living nearby.

METHODS

Study population. This study uses data originally collected in the Community Health Effects of Industrial Hog Operations (CHEIHO) study, which recruited 101 study participants from communities in Eastern North Carolina hosting industrial swine operations. To be eligible for the study, participants had to be at least 18 years old, live within 1.5 miles of a swine ILO, not smoke, and have access to a freezer for storing saliva samples. For the present study, participants were also excluded if they did not engage in any outdoor activities, aside from the 10 minutes each morning and evening required for study participation. Participants were also excluded if they experienced odors on one or fewer days during the study due to lack of exposure contrast.

Exposure assessments. Exposure to swine ILO pollutants was assessed using two markers specific to swine ILOs in the context of rural environmental exposures: self-reported strength of hog odor, and atmospheric hydrogen sulfide (H_2S) concentration. As part of the CHEIHO study, participants completed a twice-daily diary session during which they recorded the strength of hog odors they sensed for each of the preceding twelve hours (on a 0 to 8 scale). After each diary session, participants spent ten minutes outdoors and rated the strength of outdoor odors on the same scale. Each participant chose their own consistent times to complete their odor logs (e.g. 7 to 9 am, and 7 to 9 pm), providing full 24-hour coverage if all diary entries were completed, but enabling participants to collect data at convenient times. Participants' sensitivity to odors at baseline was assessed using a butanol dilution series[5].

During the study, a mobile air monitoring trailer was placed in a central location in each community. Mean 15-minute H_2S accumulations were measured by an MDA Scientific Single Point Monitor (Zellweger Analytics, Inc.) using a chemcasette with a detection limit of 1 part-per-billion volume (ppb) and were converted to hourly averages to match the timing of participants' odor records. A HOBO microstation datalogger (Onset Computer Corporation) with temperature and humidity sensors was used to measure meteorological conditions.

Outcome ascertainment. Time outdoors per day and the length of outdoor episodes were ascertained from information collected twice daily regarding location (indoors, outdoors, or away from home) for each of the preceding twelve hours. Daily time outdoors was calculated by summing all hourly outdoor values between the bounds of morning and early data collection for all participants (9am to 6pm). Morning and afternoon time outside were calculated by splitting eligible day hours in half (morning 9am to 1pm, afternoon 2pm to 6pm) and summing the number of hours in each time period

Statistical Methods. Cumulative time spent outdoors per day was modeled as a Poisson-distributed variable following the formula

$$\log(n_{i,j}) = \alpha_i + X\beta + Z\gamma$$

where n is the number of hours spent outside, i indexes study participant; j indexes day in study; α is fixed individual effect (conditioned out of the likelihood function); X is an indicator of either morning H_2S exposure, morning 10-minute outdoor odor rating, or daily outdoor odor; and Z is a vector of temperature and wind speed (potential confounders); β and γ are corresponding coefficient vectors. Extremes of outdoor temperature and wind speed have the potential to influence participants' time outside per day and temperature and wind speed also influence swine industrial livestock emissions. Temperature and wind speed were modeled as binary variables (65° F - 85° F versus <65° F or >85° F, and ≤0.58 mph versus >0.58 mph) to capture atmospheric stability and effect on outdoor activity. H_2S and odor were modeled as binary variables (detect/non-detect and odor/no odor). To assess effect-measure modification by time of day, separate models were also used for morning (9am-1pm) and afternoon periods (2pm-6pm). Sensitivity to odor was also considered as a potential effect-measure modifier.

In addition, we also fitted a model for discrete time probability of being outdoors each hour. A binary indicator of location (outdoors versus not outdoors) was used to model whether a person was outdoors each hour (during daytime hours) as a binomial-distributed variable following the formula

$$y_{i,j,k} = \alpha_{i,k} + X\beta + Z\gamma$$

where y is a binary indicator of outside location at hour k, for study participant i, on study day j; $\alpha_{i,k}$ is a fixed individual effect conditioned out of the likelihood function; X is hourly H_2S exposure or hourly odor rating; Z denotes a vector of temperature and wind speed on the hour scale; and β is the corresponding coefficient vector. As above, temperature and wind speed were modeled as binary variables, H_2S and odor were modeled as binary variables (detect/non-detect and odor/no odor), and time-of-day and odor sensitivity were considered as potential effect-measure modifiers. To assess the sensitivity of the hourly model, several lags (1-hour, 2-hour, and 3-hour) of the hydrogen sulfide term and a term for prior number of hours outside per day were also used in separate models.

RESULTS

88 participants' records were used for the analysis, covering a total of 21,408 person-hours. Thirteen participants from the CHEIHO parent study were excluded due to insufficient exposure or outcome data. Due to data entry errors or missing data, 12,418 hourly records were excluded. The demographic characteristics of CHEIHO and present study participants, along with daily and hourly record-weighted distributions of these characteristics, are shown in Table 4.1. The distributions of age, sex, race, and estimated odor sensitivity in the present study were similar to those from the parent study.

Participants' odor ratings, neighborhood H_2S concentrations, and time outside values are described in Table 4.2. Participants were outside for at least one hour of consecutive time on 95.2% of study days. They experienced morning outdoor swine odors during data collection on 42.4% of study days. Atmospheric hydrogen sulfide was detected in participants' neighborhoods during 41.2% of study days. Morning outdoor odors and were lower on average than outdoor odors reported later in the day (mean 1.26 vs. 1.36). Participants experienced morning outdoor swine odors during 42.9% of the study hours that they were outside. Atmospheric hydrogen sulfide was detected during 6.7% of daytime study hours.

We examined the association between the number of hours spent outside each morning and self-assessed morning outdoor odor (Table 4.3). A negative association was observed between morning outdoor 10-minute odor rating and subsequent time outdoors during the morning. Participants spent 20% fewer hours outdoors on mornings when they reported outdoor swine odors during their 10-minute morning data collection (β= -0.069, 95% interval -0.218 to 0.077). A weak negative association was observed between morning hydrogen sulfide detection and number of hours spent outdoors (β= -0.198, 95% interval -0.515 to 0.101). In contrast, a weak positive association was observed between morning 10-minute outdoor swine odor and the number of hours spent outside that afternoon (β = 0.106, 95% interval -0.053 to 0.265).

Next we examined the association between markers of ILO emissions and the probability of being outdoors each hour. Negative associations were observed between markers of swine ILO emissions exposures and hourly time outside. Participants' odds of being outside during an hour following perception of swine odor were lower compared to periods without swine odors (outdoor odor OR=0.62, 95% interval 0.44 to 0.89; indoor odor OR=0.47, 95% interval 0.18 to 1.25). Participants' hourly odds of being outside were also lower during periods when hydrogen sulfide was detected (OR=0.78, 95% interval 0.56 to 1.11) and on days when hog odors were detected outdoors during morning data collection (OR=0.82, 95% interval 0.59 to 1.12).

Associations between exposure markers and time outside were stronger among participants with greater sensitivity to odors at baseline (butanol sensitivity ≤ 40 ppm; Table 4.4). More odor-sensitive participants were less likely to spend time outside hours with hydrogen sulfide detection (OR=0.45, 95% interval 0.26 to 0.79) and during hours following perception of outdoor odors (OR=0.39, 95% interval 0.23 to 0.68) compared to hours without pollutant marker detection. Models for hydrogen sulfide lag terms and models with adjustment for prior time outside per day showed similar results to those reported above (data not shown).

DISCUSSION

This study estimated the effect of exposure to swine ILO air emissions on time outside. Markers of greater exposure (higher atmospheric H_2S concentration and higher rated swine odors) were associated with reduced odds of spending time outdoors. Most prominently, perceiving outdoor swine odor reduced the odds of going outside the following hour by 38% (OR=0.62, 95% interval 0.44 to 0.89), while the detection of hydrogen sulfide in ambient air reduced the odds of going outside during that hour by 22% (OR=0.78, 95% interval 0.56 to 1.11).

While participants' perceptions of odor and their time outdoors were self-reported, atmospheric concentrations of hydrogen sulfide (H_2S) were objectively measured and these readings were not available to participants during the study. Misclassification of time outdoors by H_2S concentration due to reporting errors is therefore expected to be non-differential with respect to the exposure and attenuate the observed associations.

Similarly, odor sensitivity was objectively measured using a butanol dilution series at baseline. The stronger observed associations between exposure indicators and outcomes among participants with a higher sensitivity to odors at baseline suggests that participants accurately recorded odors, since more exposure misclassification in the lower sensitivity group could attenuate the association between odor and time outdoors. Modification of the association between H_2S exposure and time outdoors by odor perception threshold further suggests that odor perception could be an important mechanism through which ILO emissions influence time outdoors, since odor perception threshold could not influence the atmospheric concentration of H_2S.

A causal association between ILO emissions exposures and time outside could be explained in several ways, including participants' avoidance of unpleasant sensory stimuli and protective actions (sheltering indoors) taken to avoid the effects of exposure. Sulfuric and ammonic components of swine waste can cause unpleasant olfaction and also stimulate facial trigeminal nociception, causing physical pain typically described as burning of the eyes and nose. In past research, swine ILO emissions exposures have been linked to disease symptoms that could make outdoor activities unpleasant or more difficult, including coughing[6,7], asthma[8–10], wheezing[7,11], difficulty breathing[7,11], runny nose[6,7], sore throat[6,11], and chest tightness[7,11]. In the context of cyclic and chronic exposures, those living near swine ILOs could be both psychologically and physiologically sensitized to exposures, leading to greater negative effects than might be expected in the general population.

Associations were weaker when considered on the day scale; this could be due to increased measurement error caused by poorer spatial resolution. The difference in associations observed for morning and evening outcomes could suggest that effects could be concentrated on morning hours, that participants changed the timing of outdoor activities to avoid odors, or that participants showed greater variability in time outdoors in the afternoon. Stronger negative associations observed among participants with greater sensitivity to odor is consistent with swine ILO neighbors' reports that odor perception is an important way in which swine ILO pollutants impact outdoor activities.

Disruption of time outdoors could have negative secondary impacts in population exposed to swine ILO emissions. In rural areas, outdoor activities are important for leisure time and functional physical activity. Compared to urban areas, rural communities are less likely to have indoor exercise facilities[12] like pools, tracks, game courts, and gymnasiums. Rural residents of the U.S. South report more barriers to physical activity and less frequent physical activity[13–17] compared to their urban counterparts. Physical activity is important for quality of life and lack of physical activity is well-known as risk factor for many diseases including diabetes, heart attack, stroke, and cancer.

Rural populations rely on access to the outdoors for other health behaviors, including gardening, hunting, fishing, and raising animals to improve access to nutritious foods[4]. Because rural homes often lack central heating and air conditioning systems due to their age or design, many rural residents cool their homes in hot months by opening windows – an economically and environmentally sustainable solution that relies on access to clean air. Residents of rural neighborhoods rely on the outdoors as a space for holding social, cultural, and religious gatherings, which strengthen and enrich both individual and community lives[18].

Compared to the general population, communities hosting swine ILOs in North Carolina also have a higher proportion of low-income and Black residents, who face higher burdens of disease and poorer access to public health and medical care services compared to the general population. Differences in life stressors including discrimination[19] in housing, education, and employment, as well as disparities in the prevalence and severity of chronic diseases, the quality of care received from health care providers, and mortality rates highlight the need for improved access to health resources in Black neighborhoods. In the context of the present research, limitations on outdoor activity might be particularly damaging to Black communities, which already score more poorly on measures of quality of life and physical activity compared to White communities[20].

In the historical context of the U.S. South, agricultural production has harmed Black communities for centuries. Despite being emancipated by the federal government in the mid-19th century, Black slaves and their descendants in the U.S. have faced an evolving system of exploitation predicated on controlling Black activities, perpetrated by the descendants of White enslavers and their allies. Components of this system have included convict-lease programs[21] coupled with the criminalization of Black life[22], race-specific poll taxes and tests, organized mass murder[23], inequitable provision and restriction of public goods and services, racist public education[24–26], perpetual debt traps[27], and disproportionate application of lethal force by representatives of the State. Like these past systems, harm caused to Black communities is used to reap economic benefits for a small elite group; in this case, money saved through insufficient investments in pollutant control systems comes at the expense of health and quality-of-life in predominantly Black communities hosting swine ILOs. And like past systems of Black exploitation, swine ILOs have proven difficult to address as a public health problem because profits are used by exploiters to secure legal protections, gain political favor, sway public opinion, and undermine investigations.

A strength of the study is control of many potential time-invariant confounding factors by the study design. The fixed-effect regression models used for analysis condition out factors that remained constant for participants across the two-week study, including sex, age, race, and sensitivity to odorants. Heat-humidity, the most prominent time-varying potential confounding factor, was addressed using measured temperature and wind speed data and including these factors as model covariates. Hourly models could condition on past history outside, further limiting potential confounding bias. This study inherited several advantages of the parent study. Due to the community-based participatory research design of the original study, this study was able to benefit from the high-quality data collected by engaged community members[28]. Similarly, the research questions addressed in this study were informed by the lived experiences of those experiencing swine ILO air exposures.

A limitation of the study is measurement error. Although the hydrogen sulfide air monitors used in this study were placed close to participants' homes, they measured a marker of neighborhood-level emissions, not individually-received emissions exposures. Similarly, outdoor odors were self-reported and only recorded during time periods that participants were outside. Assessment of time outside was not part of the original study design and was indirectly derived from odor logs.

This study could have implications for technology and policy interventions to improve health and quality of life in communities impacted by swine ILOs. Innovations in swine waste treatment or science and health-based emissions controls for industrial livestock operations could be evaluated using health impacts assessments including quality-of-life, rather than static emissions thresholds. The social and economic value of organizational changes in meat production firms or legal changes to the relationship between producers and host communities could be more fairly evaluated if the breadth of community exposure effects are accounted for. Further, inviting input from community members who are actually affected by the day-to-day operations of swine ILOs improves the relevance of the work to public health. These developments could have long-term positive consequences for health and quality of life in rural communities.

Table 4.1. Distributions [n (%)] of demographic characteristics of study participants grouped by eligibility and number of records

		Participants				Person-time			
		CHEIHO		Eligible		Person-hours		Person-days	
Variable		(n=101)		(n=88)		(n=21408)		(n=1197)	
Age									
	≥65	24	23.8	18	20.5	4653	21.7	260	21.7
	24-64	77	76.2	70	79.5	16755	78.3	937	78.3
Gender									
	Women	66	65.3	61	69.3	14691	68.6	821	68.6
	Men	35	34.7	27	30.7	6717	31.4	376	31.4
Race									
	Black	85	84.2	75	85.2	17862	83.4	998	83.4
	Non-Black	16	15.8	13	14.8	3546	16.6	199	16.6
Odor Sensitivity									
	≤40 ppm	40	39.6	33	37.5	8145	38	456	38.1
	>40 ppm	57	56.4	51	58.0	12474	58.3	697	58.2
	Missing	4	4.0	4	4.5	789	3.7	44	3.7

Table 4.2. Distributions [n (%)] of persons and person-hours by odor rating, hydrogen sulfide concentration (H_2S), and time outdoors.

Variable (Unit)		Hourly (persons)		Daily[a] (person-hours)	
Odor (0-8)		Outdoor (1h)		Morning Outdoor (10m)	
0		2389	11.2	508	42.4
1-2		849	4	394	32.9
3-4		499	2.3	150	12.5
5-8		444	2.1	88	7.4
Missing[b]		17227	80.5	57	4.8
H_2S (ppb)		Average (1h)		Average (10h)	
0		18949	88.5	674	56.3
0-2		924	4.3	457	38.2
>2		441	2.1	15	1.3
Missing		1094	5.1	51	4.3
Outdoors (hrs)		Outdoors (1h)		Total (10h)	
Outdoors	1-2	4181	19.5	454	37.9
	3-4	-	-	381	31.8
	5-6	-	-	188	15.7
	7+	-	-	117	9.8
Indoors	0	17227	80.5	57	4.8

[a] 6am to 9pm [b]Only reported when outdoors

Table 4.3. Model coefficients for regression models of associations between exposure indicators and time outside.

Period	Daily[a]			Morning[b]			Afternoon[c]		
Model Form	Poisson[d,e]			Poisson[d,e]			Poisson[d,e]		
All Participants	**β** (SE)		z-value	**β** (SE)		z-value	**β** (SE)		z-value
H_2S Detected	-0.0690	0.0752	-0.917	-0.1976	0.1568	-1.260	-0.0326	0.1209	-0.270
Morning Odor	-0.0198	0.0660	-0.300	-0.2255	0.1138	-1.982	0.1061	0.0809	1.310
High Odor Sensitivity									
H_2S Detected	-0.1834	0.1129	-1.642	-0.4504	0.2335	-1.929	-0.2477	0.2047	-1.210
Morning Odor	-0.0478	0.1002	-0.477	-0.4080	0.1798	-2.269	0.1357	0.1210	1.122
Low Odor Sensitivity									
H_2S Detected	0.0310	0.1033	0.300	0.0460	0.2185	0.210	0.0984	0.1560	0.631
Morning Odor	-0.0028	0.0895	-0.032	-0.0759	0.1505	-0.504	0.0575	0.1113	0.516

[a] 9:00 am to 6:00 pm [b] 9:00 am to 1:00 pm [c] 2:00 pm to 6:00 pm [d] model design adjusts for all time-invariant factors. [e] model adjusted by outdoor temperature and wind speed. [f] 10-minute morning outdoor odor rating

Table 4.4. Model coefficients for regression models of associations between exposure indicators and time outside among participants with low butanol sensitivity (>40 ppm)

Participant Group	All Participants			High Sensitivity			Low Sensitivity		
Exposure Indicator	**β**	**(SE)**	**z**	**β**	**(SE)**	**z**	**β**	**(SE)**	**z**
H_2S Detected	-0.2402	0.1760	-1.365	-0.7807	0.2810	-2.778	0.2838	0.2395	1.185
Swine Odor Detected									
Morning[f]	-0.2029	0.1636	-1.240	-0.2894	0.2322	-1.246	-0.1245	0.2344	-0.531
Outdoor	-0.4721	0.1803	-2.618	-0.9340	0.2796	-3.341	-0.1730	0.2482	-0.697
Indoor	-0.7538	0.4998	-1.508	0.2448	0.7857	0.312	-1.1561	0.6336	-1.824

[a] 9:00 am to 1:00 pm [b] 2:00 pm to 6:00 pm [c] 9:00 am to 6:00 pm [d] model design adjusts for all time-invariant factors. [e] model adjusted by outdoor temperature and wind speed. [f] 10-minute morning outdoor odor rating

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CHAPTER 5: ESTIMATING CHRONIC EXPOSURE EFFECTS IN REPEATED-MEASURES STUDIES BY G-ESTIMATION USING DYNAMIC BAYESIAN NETWORKS.

OVERVIEW

The effect of an acute exposure in an environmental setting is readily assessed using standard epidemiologic methods allowing for potentially complex relationships between exposure, outcome, and covariates over time. Recent approaches have clarified estimation of causal effects of acute exposures in a cohort study. In contrast, in studies of chronic or repeated environmental exposures, estimates of effects may be complicated due to feedback processes, and such processes have not been well characterized in environmental epidemiology. I propose estimating total effects of a chronic exposure, allowing for potential feedback, by extending g-estimation to the general case of exposure *regimes* using dynamic Bayesian networks. Using the example of community exposures to swine Industrial Livestock Operation (ILO) air pollutants in rural North Carolina, I show that the total chronic effect of observed exposures on sleep differs from what would be expected from marginal acute effects alone, suggesting the importance of a feedback mechanism. This method could be widely applicable to longitudinal epidemiology studies with more than two time points and potentially resonant outcome-exposure mechanisms.

INTRODUCTION

Chronic exposures present unique challenges to epidemiologists in occupational and environmental health contexts. Complex causal relationships between sequential values of exposures, responses, and covariates can lead to seemingly-paradoxical situations where a response may be confounded by (past) values of the response, possibly affected by prior exposure. Solutions to this problem have been proposed, including marginal structural models and repeated-measures designs[1]. These approaches can estimate unconfounded direct causal effects of exposure contrasts, but gain these advantages by narrowing their focus to the acute effects of exposure. For instance, a repeated-measures study of the effect of an outdoor exposure on sleep duration could draw a comparison between subject-standardized sleep values (-0.5 hours average on exposed nights and +0.5 hours average on unexposed nights, relative to each participant's mean) and estimate an effect of exposures on sleep duration. While this estimate cannot be confounded by factors remaining constant for each participant over time, it cannot easily estimate the effects of chronic exposure.

These existing solutions leave open the question of estimating chronic exposure effects from longitudinal data. Here I propose the use of a Dynamic Bayesian Network (DBN) model to address research questions in such settings[2]. To illustrate the utility of this approach, I consider the example of chronic community exposures to hog ILO air pollutants in the Community Health Effects of Industrial Hog Operations (CHEIHO) study[3]. In this context, community members have described how the unpredictability, timing, and lack of control over pollutant and odorant exposures leads to stress and disruption of life - including negative impacts on sleep (due to awakening from sleep and difficulty falling asleep) and time spent outdoors (due to sheltering from unpleasant odors).

METHODS

Chronic effects can be practically modeled as n-order feedback effects - a generalization of second-order effects. In the sleep example, a single exposure's disruption of sleep is a first order-effect. Second-order effects could include downstream effects affecting subsequent values of the exposure (if fatigue resulting from lack of sleep leads to less time spent outdoors on the subsequent day) and outcome (if this fatigue and/or sleep deprivation affect future nights' sleep); n-order effects extend this idea to include the "total effect" of a single exposure on all time periods, perhaps until a reasonable washout period is reached.

Feedback captures the idea that these n-order effects could potentially outweigh first-order effects under conditions of residual system memory and effect self-reinforcement. For instance, feedback enables even a soft noise to send a microphone-speaker system into a spiral of increasing volume resulting on the blowout of the speaker system. Famously, feedback caused the destruction of the Tacoma Narrows Bridge from relatively modest (but repeated) wind gusts[4]. Similarly, feedback effects in the chronic exposure context could potentially lead to self-amplifying (or self-limiting) effects of exposure. The total effect of an exposure sequence or *regime* could differ from what might be expected from the sum of the individual effect components.

Dynamic Bayesian networks for causal inference by exposure regime

A dynamic Bayesian network model can be used to address research questions about n-order total causal effects (chronic effects) and distinguish them from first-order (acute) effects. Specifically, this framework extends the approach of g-estimation to the case of estimating the total effects of exposure regimes in study context. The DBN model can be understood as a probabilistic directed acyclic graph (pDAG) in which the relationship between nodes is parametrized at the node level by an empirical probability distribution of values conditional on that node's parents. As an extension to the DAG, the DBN retains features of the DAG essential for causal inference – directionality (preservation of temporal specificity) and a network-based representation of conditional dependence (and independence) between events. DAGs used in causal inference epidemiology correspond to a DBN simplified to the parents and descendants of one edge of interest; the statistical properties of nodes about this edge can be used to derive the unconfounded direct causal effect of the upstream node on the downstream node.

The benefit of the extending the DAG to the DBN is the ability to specify complex counterfactual regimes. Traditionally, a counterfactual is drawn (or alternatively, an intervention is simulated) by changing the value of a single exposure node and estimating the effect on the distribution of the outcome node. Unitary measures, like model-adjusted odds ratios estimating a causal effect, are derived from the DAG model mathematically by fixing the distributions of relevant covariate nodes (e.g. a minimal sufficient adjustment set) and comparing the resulting conditional distribution of the outcome node value under contrasting distributions of the exposure node (Fig 1). G-estimation extends this approach by specifying contrast distributions, rather than set values, for the exposure. The DBN model demonstrated here further extends g-estimation by enabling simultaneous specification of multiple exposure nodes in counterfactuals and thus calculating total effects of contrasted exposure regimes[5].

The DBN model can be thought of an extension of the generalized linear model approach with a conditional structure. The traditional regression model is estimated by finding the parameter vector β that maximizes the likelihood

$$L(\beta|X, y) = \prod_{i=1}^{n} p(y_i|X_i)$$

Given covariate matrix X and outcome vector y. In the case of logistic regression, the log odds of an individual's outcome $p(y_i)$ are modeled as a linear parametric function of an intercept and one or more covariate terms that can be interpreted log-odds ratios:

$$log\left(\frac{p(y_i|X_i)}{1-p(y_i|X_i)}\right) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik} + \varepsilon_i$$

In the DBN, the likelihood function does not use an explicit outcome and but is based on past data for each individual:

$$L(\beta|Z) = \prod_{j=1}^{k}\prod_{i=1}^{n} p_j(Z_i|Z_{i,j-1})$$

Where $Z_{i,j-1}$ includes variables for participant i at prior time points and the function p_j represents a node on the directed acyclic including 1 ... ρ parents in the general form

$$log\left(\frac{p_j(Z_i|Z_{i-1})}{1-p_j(Z_i|Z_{i-1})}\right) = \beta_{j0} + \beta_{j1} Z_{i-1,1} + \beta_{j2} Z_{i-1,2} + \cdots + \beta_{\rho} Z_{i-1,\rho} + \varepsilon_{ij}$$

In this formulation, the difference in exposure regime can be estimated from the set of all $\beta_{j\rho}$ representing conditional probabilities using a Monte Carlo approach substituting values of no exposure for observed values.

Empirical Example

To illustrate this approach I use data from 88 participants of the CHEIHO study, enrolled from rural communities in Eastern North Carolina hosting industrial swine operations. CHEIHO participants had to be at least 18 years old, be able to read and write, and have a freezer for storing saliva samples. For the present study, participants were excluded if they spent no time outdoors or if there was evidence or reporting errors in sleep logs during the study. I have previously reported the estimated acute effects of exposures on sleep from this study using fixed-effects model in a repeated-measures design. I compare the chronic total estimated effects of observed exposure regimes to the total estimated effect derived from replicated marginal (acute-effect) models to estimate the magnitude of feedback effects in determining the total chronic effect of exposure.

Exposure Assessments

From the complex mixture of air pollutants and odorants comprising swine ILO air pollutant plumes, two marker chemicals were used to assess exposures: neighborhood-level atmospheric hydrogen-sulfide (H_2S) concentration measured near participants' homes (ppb), and participant-reported swine odor (on a scale of 0 to 8). In CHEIHO these measures were well-correlated, even though participants had no access to atmospheric data. For this analysis, the H_2S concentration was considered the underlying exposure due to its near-universal availability in the time series data (odors could not be recorded during sleep); odor perception was considered a pathway of exposure impact in the network model.

Outcome Ascertainment

Hourly sleep and time outdoor outcomes were ascertained from odor diaries kept by the participants during the study. Twice per day, participants rated the strength of hog odors they perceived each hour over the past twelve hours; in this process participants also indicated if they were indoors, outdoors, or asleep during each of past twelve hours.

Statistical Method

A dynamic Bayesian network (DBN) model was used to estimate the causal structure of relationship between variables across time. Instead of using a network structure (DAG) to represent each time point of the study across participants (i.e. 88 participants' over 336 hours =

29,568 time points), a more extended network structure including multiple time slices (or "panel data") was used. To observe the effect of different network structures on estimated chronic effects, two network types were used: a "marginal" dynamic network without belief propagation mimicking a traditional regression model with lag terms, and a dynamic Bayesian network with belief propagation between subsequent time points capturing chronic feedback effects.

After the DBN was trained from the observed data, counterfactual values of total sleep and time outdoors could be computed for each participant by setting the underlying exposures values to zero and aggregating the predicted DBN outcomes by participant. Credible intervals for these expected outcomes were computed using the bootstrap method. To illustrate the flexibility of the DBN model, three potential exposure regimes are compared: observed (full) exposures, eliminated exposure (none), and mitigated exposures (reduced by half) that could result from implementation of environmentally-superior technology. DBN models were fit using the R package *bnlearn*[6].

RESULTS

The demographic characteristics of study participants and the distributions of key study variables are shown in Table 5.1. The parsimonious network structure refined to facilitate comparison to marginal models is shown in Figure 5.2. The predicted sleep and time outdoor outcomes for each exposure regime and DBN type, as well as marginal acute estimates, are shown in Table 5.2. DBN models showed an estimated increase in sleep duration and time outdoors with reduced exposures. Across DBN models for both outcomes, the expected total effect of observed exposures on sleep was higher than the total marginal effect, suggesting the importance of a feedback mechanism; compared to observed exposures, this difference for sleep was 3.94 minutes per night (95% interval 1.46 to 5.83) in the marginal model and 4.78 minutes per night (95% interval 1.76 to 7.00) in the model accounting for feedback.

DISCUSSION

In this empirical example, the total chronic effect of exposures to swine ILO air emissions differed from the sum of total individual exposure effects, suggesting the importance of feedback effects. In this model, these feedback effects were modeled as potential disruption of participants' daily and nightly schedules, since sleep and time outdoors could be influenced by lagged values. In the case of swine ILO emissions, the effects of chronic exposures could also differ due to other (not modeled) factors including sensitization, accumulative effects (allostatic load), or interactions of effects across multiple domains (respiratory disease, stress, etc.). Feedback could also occur as participants take protective actions against exposures – if sheltering indoors reduces exposures, exposure effect estimates made form observational data might underestimate the harmful effects of exposure if this protective behavior is not accounted for.

Neighbors of swine ILOs face chronic exposures to air emissions as source operations are ongoing and immobile. Those affected have little control over exposures; sheltering outdoors does not always provide relief as odors can seep indoors. Acute effects of swine ILO emissions exposures on health and quality of-life include increased risks of respiratory and neurological disease symptoms, increased blood pressure, and negative mood. Chapters 3 and 4 aimed to estimate the magnitude of two quality-of-life impacts that should also be considered – sleep and time outdoors. Sleep is essential to health and inadequate sleep is associated with increased disease incidence and mortality. Time outdoors is particularly relevant to health in rural areas, as access to the outdoors is important for health-promoting activities like gardening, functional physical activity, leisure, temperature control in homes, and socialization. The Chronic effects resulting from repeated exposures assessed in this chapter, including disruption of daily activities and sleep schedules, should also be considered in reckoning the total impacts of swine ILOs.

In the present empirical example, the use of a DBN enables estimation of feedback effects by modeling the propagation of effects through first-order lag terms. In a traditional epidemiology model, these lag terms are set to the observed values of the outcome at past time points. In the dynamic model, lag terms for future time points are instead set to the estimated value they would take under a counterfactual exposure regime. This could represent the effect last night's sleep on tonight's sleep, the effect of yesterday's time outdoors on today's time outdoors. Thus, all prior lag terms have the potential to influence the estimated outcomes even though only one lag term is explicitly modeled at each node.

The approach detailed here can be used to estimate the effect of defined interventions in the context of chronic, repeated exposures. Traditional approaches like marginal structural models and repeated-measures designs are powerful tools for estimating short-term, acute effects of single exposures, but the summation of these acute effects may not be equal to the total chronic effect of repeated exposures in the presence of system feedback. The DBN provides a unified approach to estimating acute effects, chronic effects, and the effects of counterfactual exposure regimes. In this example, exposure regime effects were compared to acute effects to estimate the relative importance of feedback and this method could be generally applicable to studies of repeated exposures.

A fully-study DBN might be feasible with a large sample size, but in this example of 88 participants (optimized for a repeated-measures marginal effect estimation design), a simplified time-slice model incorporating one day of feedback offered improved precision relative to a full-study model. This approach also enabled a conditional-on-participant design, which addresses potential confounding factors that remained constant for each participant over the study period.

A secondary benefit of the DBN approach, even in the estimation of acute effects in more traditional study designs, is that the network can deduce conditional dependencies without manual intervention, given the temporal ordering of variables. This underscores the possibility for applying machine-learning to causal inference in the design phase, as well as the analysis phase of epidemiology research. For instance, a DBN could identify potential confounders in a complex study design with hundreds or thousands of covariates that could then be reviewed by an analyst in the process of model specification. Similarly, a proposed causal model (and the focus of arguments for or against such a model) for an epidemiology study could be compared to the "machine-null" model, rather than a "saturated null" model of universal dependence that proves unmanageable in complex study designs.

The DBN, an extension of the DAG that is easily amenable to g-estimation, could have wide applicability to studies of repeated exposures. The ability to identify and quantify feedback effects could also provide strong evidence for interventions focused on controlling the timing of exposures or the identification of windows of increased susceptibility to exposure.

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Table 5.1. Distributions [n (%)] of demographic characteristics, exposures, and outcomes of interest among study participants

	Participants				Hourly Records		
Variable	CHEIHO (n=101)		Eligible (n=88)		(n=21,408)		
Age					Swine Odor		
≥65	24	23.8	18	20.5	Absent	2389	11.2
24-64	77	76.2	70	79.5	Present	1792	8.3
Gender					Missing[a]	17227	80.5
Women	66	65.3	61	69.3	H_2S (ppb)	Average (1h)	
Men	35	34.7	27	30.7	0	18949	88.5
Race					>0	1365	6.4
Black	85	84.2	75	85.2	Missing	1094	5.1
non-Black	16	15.8	13	14.8	State		
Odor Sensitivity					Indoors	TD	TD
≤40 ppm	40	39.6	33	37.5	Outdoors	4148	TD
>40 ppm	57	56.4	51	58	Asleep	TD	TD
Missing	4	4	4	4.5	Missing	TD	TD

[a]Participants did not record odors during sleep.

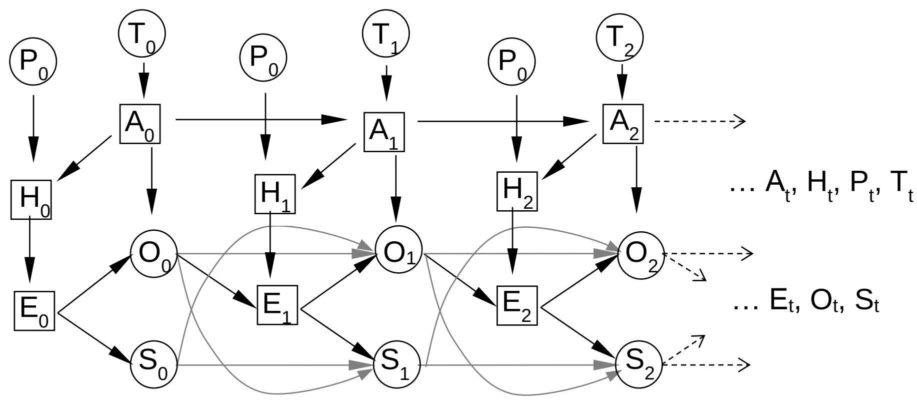
Table 5.2. Estimated differences in sleep and time outdoors by exposure model.

Network Scale	Sleep (Min)			Outdoors (Morning)			Outdoors (Afternoon)		
Replicates (n)	916			916			916		
Exposure Regime	**Mean**	**L95 %**	**U95 %**	**Mean**	**L95 %**	**U95 %**	**Mean**	**L95 %**	**U95 %**
Marginal BN									
As exposed	0	(ref)		0			0		
No Exposures	3.94	1.46	5.83	9.92	9.36	10.59	12.90	12.50	13.30
Mitigated Exposures	1.96	-0.11	3.89	10.04	9.41	10.59	13.37	13.33	13.91
Dynamic BN									
As exposed	0	(ref)		0			0		
No Exposures	4.78	1.76	7.00	9.85	9.57	10.27	12.90	12.48	13.33
Mitigated Exposures	2.40	0.11	4.40	10.02	9.59	1.039	13.37	13.33	13.94

[a] Calculated as the total effect divided by the total number of nodes, to estimate a comparable marginal effect including feedback. [b] Calculated using the marginal effect multiplied by the total number of nodes, to estimate a comparable total effect without feedback.

Figure 5.1. Comparison of the dynamic Bayesian network approach to the directed acyclic graph. The DBN (a) contains a collection of nodes covering multiple time slices, including nodes not directly related to the exposure and outcome. The DAG (b) subsets the DBN to a series of nodes directly related to the exposure-outcome model, enabling analysis with traditional statistical methods.

(a)



(b)

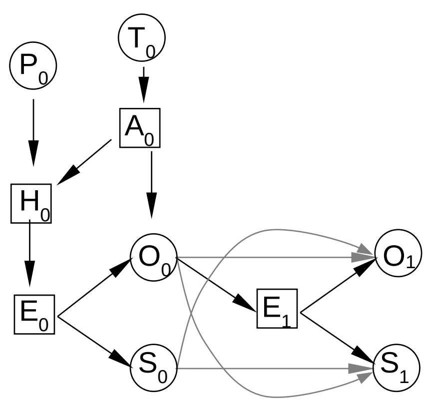
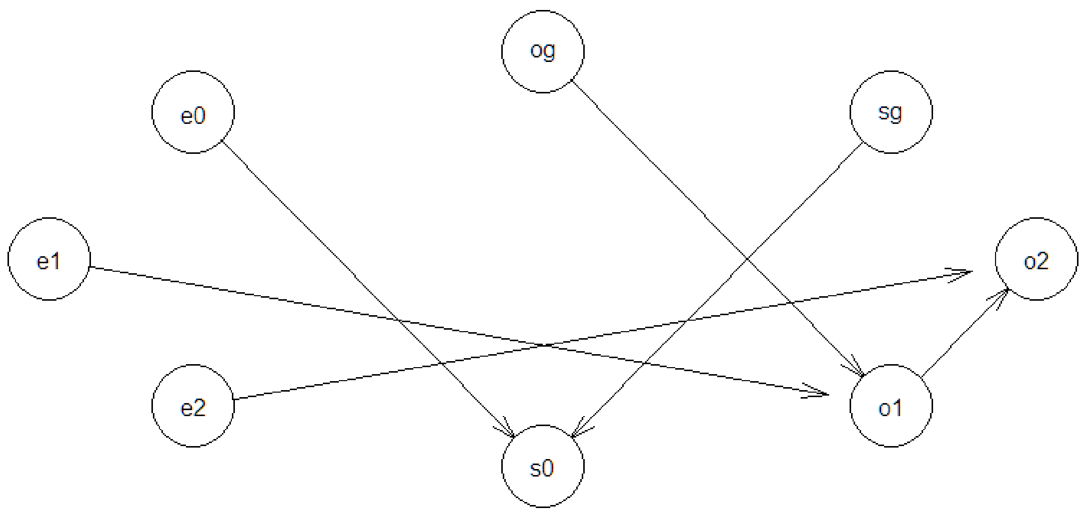


Figure 5.2. Directed acyclic graph of one time slice from the simplified Bayesian network model.



e0	night H_2S exposure
e1	morning H_2S exposure
e2	afternoon H_2S exposure
s0	nightly sleep duration
sg	nightly sleep duration (lagged by one day)
o1	time outdoors (morning)
o2	time outdoors (afternoon)
og	daily time outdoors (lagged by one day)

CHAPTER 6: DISCUSSION

This study aimed to estimate the acute and chronic impacts of swine ILO air emissions exposures on sleep and time outdoors in rural communities hosting swine ILOs. Acute impacts on sleep (Aim 1) and time outdoors (Aim 2) were estimated using discrete hazard modeling of repeated measurements from the Community Health Effects of Industrial Hog Operations (CHEIHO) study. Chronic impacts, which might differ from acute impacts due to feedback effects, were estimated by applying dynamic Bayesian network modeling to CHEIHO data (Aim 3).

Synthesis of Findings

In Chapter 3, associations were observed between swine ILO air emissions exposures indicators and sleep. H_2S detection was associated with reduced nightly sleep duration (14.2 minutes, 95% interval 3.3 to 25.0 minutes), and an increased hazard of awakening (HR 1.24, 95% interval 0.99 to 1.55). The hazard ratio for awakening was greater for participants with higher sensitivity to odors at baseline (HR 1.62, 95% interval 1.10 to 2.40), suggesting the importance of odor perception to the mechanism of impact. Due to the importance of sleep timing to sleep quality and the impact of sleep on health, these awakenings could have higher impacts than might be expected from the difference in sleep duration alone.

Although no studies have assessed the relationship between swine ILO air emissions and sleep, these results are consistent with the literature on sleep and odor and fit with the known effects of exposure to swine ILO emissions. Strong odorants can cause awakening from sleep[1] and hydrogen sulfide is a nociceptive neurotransmitter[2,3]. Exposure to swine ILO emissions has been linked to symptoms of respiratory disease[4], which could cause sleep impairment[5]. Sleep impacts mortality and influences a wide array of health and disease outcomes[6].

In Chapter 4, associations were observed between swine ILO air emissions exposures indicators and time outdoors. Perceiving outdoor swine odor reduced the odds of going outside the following hour by 38% (OR=0.62, 95% interval 0.44 to 0.89), and this effect was stronger among participants with higher sensitivity to odor (OR=0.39, 95% interval 0.23 to 0.68). Similarly, participants were less likely to go outdoors when H_2S was detected (OR=0.78, 95% interval 0.56 to 1.11) and this effect was stronger among participant with higher odor sensitivity (OR=0.46, 95% interval 0.26 to 0.79).

Few studies have explored the impact of odors on time outdoors, although these impacts have been qualitatively described in past CHEIHO research[7]. Odorant chemical and H_2S emissions from swine ILOs have been well-documented[8–12]. Malodorous pollution can cause annoyance[13], stress[14], and increased frustration[15]. Malodors could make time outdoors less enjoyable, and avoidance of symptoms resulting from exposures could lead to rescheduling or avoiding time outdoors[16]. Time outdoors in rural settings supports a variety of health-promoting behaviors including gardening, functional physical activity, leisure, and socialization.

In Chapter 5, the chronic effect of swine ILO emissions exposures was estimated to be greater than the sum of acute effects, when disruption of sleep and activity schedules was accounted for using a dynamic model. Other factors like sensitization to odors or cumulative impact of exposures could cause further differences between estimated acute effects and real-world chronic effects in exposed populations living near swine ILOs. These differences could cause effect estimates derived from traditional epidemiology models to underestimate the true impact of exposures on those living nearby.

Strengths and Weaknesses of Design and Methodology

The design of the parent CHEIHO study was unique in several ways. First, the research design arose and research questions were developed in collaboration with community members[17]. This enabled the research to directly address community concerns, promoted the ethical treatment of participants and the protection of confidentiality in the context of intimidation by the swine industry[18], and improved the quality and completeness of self-reported data[19]. The collaborative nature of the study set the groundwork for future scientific collaborations, helped provide community members access to public health tools, and provided learning opportunities for both professional researchers and citizen scientists.

Second, the study combined self-reports of exposures and outcomes with machine-collected atmospheric and biometric data. The use of self-reported data enabled more specific capture of individual exposure (odor) and outcomes (activity and sleep) with higher temporal resolution than would have been possible with monitoring equipment alone. For example, personal air monitors could not feasibly deployed at each participants' home, and biometric monitors like automated blood pressure cuffs could not be left on around the clock. The availability of machine-recorded atmospheric and biometric data enabled validation of self-reported data. Validated self-reported measures could be used in future research and exposure assessments at low cost.

The environmental exposure assessments used in this study were based on the principle that hydrogen sulfide and odorant chemicals serve as markers of pollutant plumes arising from swine ILOs. The independent effects of these complex mixtures components could not be assessed and could differ from the impacts estimated here. Similarly, other potential pollutants arising from swine ILOs – such as noise and light – could impact sleep in nearby communities but were not assessed here.

Third, CHEIHO used a repeated-measurements design in which each participant recorded data repeatedly twice daily for a period of at least two weeks. This design offers several potential analytic advantages. The availability of multiple data points for each participant enables the use of conditional or stratified models in which estimates can be computed within person. This can produce conditional averages that cannot be influenced by differences between participants that remained constant over the study period. The collection of time-dependent covariates, including weather conditions and health symptoms, also enables adjustment for factors that changed over the study period that could have potentially confounded the relationship between swine ILO emissions exposures and sleep or time outdoors.

This study design used for Aims 1 and 2 was focused on reducing potential confounding bias, at the expense of precision. The design of the original CHEIHO study, as well as the methods of analysis presented here, enable accounting for potential cofounding factors that might otherwise bias estimated associations. These differences – for example age, sex, lung function, occupation, income, and race – could be relevant in a study of environmental sources of exposure since they could potentially influence the severity of exposures and the severity of outcomes. The inclusion of model intercept terms for time-of-day and weather conditions reduced the potential impact of factors that varied periodically by time-of-day. Previous research has demonstrated the high quality of self-reported data in CHEIHO, a direct result of participants' commitment to the study's participatory design.

The original CHEIHO design trades these advantages for several limitations. In epidemiology research, effects of exposures in chronically exposed populations can be difficult to estimate, even when using a repeated measures design. While acute effects can be estimated by making comparisons between time points within the same participant, this approach limits the range of exposures available in each comparison, since each person's own experiences tend to be more similar to one another than as compared to others' experiences. For example, a heavily-exposed participant always experiencing negative exposure effects and a lightly-exposed participant experiencing few exposure effects would contribute little information to a study conditioned on participant. This differs from an unconditional model in which the most and least-heavily exposure participants typically contribute the most information. In this sense, the CHEIHO design is focused primarily on estimation of acute effects of exposure and these effects can be difficult to precisely estimate if there are insufficient exposure contrasts observed over the study period.

A second potential limitation is the selection of CHEIHO participants. Due to concerns with confidentiality and participant protection, as well as the typically tightly-coupled interpersonal social structure of rural communities, potential participants were enrolled from swine ILO host communities that expressed interest in participating. This could be compared to a two-stage sampling design in which selection biases could occur in the selection of blocks or in the enrollment of participants within blocks. At the participant level, exclusion of participants due to inability to complete study protocols could have removed sicker or more susceptible potential participants from cohort of those eligible. At the community level, lack of common awareness of swine ILOs as a problem could have removed less-exposed communities from the eligible pool. CHEIHO, therefore, could be expected to be representative of healthier residents of neighborhoods impacted by heavier swine ILO emissions.

The present study attempts to leverage the benefits of the CHEIHO design while addressing the limitations. The dynamic Bayesian network model shown here improves the estimation of chronic effects in addition to acute effects by accounting for feedback. The limitation of this approach is that if inferences about chronic effects are derived from observed conditional distributions of exposures and outcomes, they still express the magnitude of these effects in the context of other potential effect-measure modifiers – potentially including history of exposure. Thus, while this model can estimate the additional total effects of exposure due to feedback effects, it cannot estimate the full effect of exposure in a truly unexposed population due to sensitization or acclimation to exposures.

Despite the high general quality of self-reported data in CHEIHO, the self-reported sleep and time outdoors data used in the study are indirectly inferred from missing data codes on odor diaries and were not independently validated using a sub-study or biometric equipment. Self-reported sleep data can over-estimate actinographic sleep duration[20–23], which in this study could have biased effect estimates towards a null effect if this classification was non-differential. Although the accuracy of self-report of time outdoors has not been as extensively studied, participants' reports are expected to differ somewhat from actual values since they could only be reported in 1-hour increments.

Outcome ascertainment could have been improved for sleep and time outdoors by providing participants with passive electronic activity trackers[24], which have imperfect accuracy but good intra-device reliability. Accelerometer (movement) readings can be used to estimate periods of activity and inactivity, including sleep, and would have minimal impact on participant confidentiality, since the data only includes the magnitude of movements with time and not the participants' location. Activity trackers are widely available at low cost, can be worn by participants discreetly, need no maintenance over a month or more, and are common enough to have an element of plausible deniability even if they are discovered by antagonists. Similarly, GPS-enabled mobile phone applications[25] could be used to autonomously record masked relative participant positions (e.g. transmitting a participant's distance from a user-specified "home location") and sleep (by recording wake and sleep time through alarms or prompts). Future research assessing community-scale sleep, activity, and time outdoors could be improved by incorporating these methods of semi-automated data collection.

Statistical Methods

Dynamic Bayesian models (DBNs) have wide potential applicability to epidemiology. These models use directed acyclic graphs as a basis of model presentation and assumption encoding, which are quickly becoming more popular in epidemiology as a tool for guiding analysis decisions. The approach takes advantage of a specified causal structure to simultaneously model multiple conditional dependencies in the data, many of which can have causal interpretations. It also enables estimation of novel effects, including the impact of exposure regimes through time on ranges of outcomes.

In lived experience, individuals' exposures and outcomes are not as neatly arranged as might be expected from an epidemiology study. In the modern epidemiological paradigm, departures from this real-world experience are seen as necessary because they provide the basis for causal inference. For example, a randomized controlled trial exposing volunteers to swine ILO air emissions in a clinical sleep study would only leave causal explanations for observed associations between exposure and outcomes, but this design does not match the lived experience of swine ILO neighbors. A randomized experiment with healthy volunteers would not account for any number of potential effect measure modifiers: co-exposures, the psychological meanings of malodor and lack of control, or the cumulative effect of past exposures.

Similarly, a cohort study comparing populations in communities exposed and unexposed to swine ILO air emissions could use inverse probability-of-allocation weighting to produce pseudo-populations which could be compared to estimate a causal effect of acute exposure. But this design depends on the assumption that the two communities, if standardized to have similar distributions of demographic characteristics and risk factors, are fair counterfactuals (similar in all aspects except the exposure). Some factors unique to the exposed community, like history of exposure, or sensitization to exposures, could not be equalized between the two groups.

Generalizing effect estimation to a full DAG structure, rather than focusing on two nodes as in the modern epidemiology approach, can bring the model closer to reality while still allowing estimating of analogous causal effects. Because the likelihood function used for Bayesian networks is equal to the product of each node probability, the likelihood function used in a traditional epidemiology model is equivalent to a "partial likelihood" of the full BN model, with the remaining nodes conditioned out. In the example of the randomized experiment, this partial likelihood is conditional on the observed distribution of covariates within the experimental sample. If this distribution is equivalent to the distribution of covariates within a target population (as in the case of a random, representative sample), the conditioning can be ignored and the estimate is generalizable.

Basic software for fitting DBN models is available both as free and open-source software (FOSS) and in commercial statistical software packages, but is not yet user-friendly for a general audience. Development of diagnostic tools for understanding model behavior, performance, and the validity of model assumptions could help DBNs become more commonplace in epidemiology. Currently, these tasks require development of custom software as default settings do not match common epidemiological methods. For instance, a popular use of DBNs is to estimate network structure from data using criteria of statistical significance in conditional associations. While this data-driven approach works well for outcome prediction, decisions about network structure in epidemiology are typically based on a combination of *a priori* subject-matter knowledge and *a posteriori* evaluations of parsimony, observed associations, and bias-precision tradeoffs. While methods for algorithmically deriving and simplifying DAG structures from observed data are popular in artificial intelligence research, epidemiologists might be expected to prefer structures that accurately represent the study design and hypothesized relationship of interest. Broader use of DBNs in epidemiology will require working out the appropriate modeling approach in different study contexts.

Public Health Significance

The observed impacts of swine ILOs on sleep and outdoor activities have implications for environmental justice and health disparities. North Carolina's swine ILOs are disproportionately concentrated in Black communities[26], meaning that exposure effects from swine ILOs worsen both environmental injustice and health disparities. In this context, loss of control over daily activities and sleep can be understood as an externalities of production – increased profits made off cost savings for hog waste treatment are obtained at the expense of nearby community residents. Historically, control over Black lives in the United States has been turned to profit in variety of evolving systems of exploitation including chattel slavery, discriminatory tenant farming, discriminatory incarceration coupled with convict lease programs, and debt traps[27].

In the face of this environmental injustice, public interest in swine ILOs and community organizing around swine ILOs are on the rise. Public demonstrations and recent high-profile civil cases, featuring the ILO integrators and the State of North Carolina as defendants, consider concerns about community health impacts but also the civil rights impacts of disproportionate impacts concentrated in communities of color[28]. Although a moratorium on new lagoon-and-sprayfield systems has remained in place since last action in 2007, existing operations remain a concern for host communities. Surprisingly, only a handful of operations have adopted improved environmentally superior technology (EST) treatment systems despite a 75% cost-sharing program offered by the North Carolina General Assembly through the Lagoon Conversion Program (LCP)[29]. While these improvements do not address air emissions from swine confinements, they could substantially reduce total emissions if appropriately implemented.

Reductions to emissions produced by swine waste treatment lagoons could produce public health gains by reducing the environmental exposures experienced by rural North Carolinians and others living in communities hosting swine ILOs[26]. The development of environmentally superior technology for waste treatment could also have secondary benefits for communities, including energy production and job creation. Policy changes to improve the competitiveness of smaller and locally-owned swine herds could improve the sustainability and economic resilience of these rural communities.

Networked Sensors in Repeated-Measures Designs

In the fifteen years since the CHEIHO study began, new developments in sensor and instrumentation technology have enabled improved ways to record repeated measurements of various dimensions of exposure and outcomes. Networked, low-cost environmental monitors for temperature, humidity, wind, barometric pressure have become commonplace; basic sensors for atmospheric pollutants like hydrogen sulfide have become available to the budget-conscious hobbyist. These sensors could add rich covariate and contextual data that could improve repeated-measures like those use here. Similarly, sensors for noise and light pollution could also enhance holistic assessments of community impacts of industrial facilities, including industrial livestock operations.

Sensors for assessing sleep duration, awakenings from sleep, and daily physical activity could similarly improve impact assessments by offering real-time outcome measures. Integrated actigraphy could be accomplished with wearable accelerometers now available from many manufacturers; some devices offer pulse-rate measurements or other biometric data. These high-resolution outcome measures could be used to explore the temporal scale of potential exposure effects with unprecedented specificity. The use of networked sensors, capable of securely recording and transmitting data with minimal intervention could improve data quality and improve patient protections. The ubiquity and small size of these sensors could help protect the confidentiality of participants.

Final Conclusions and Summary

The results demonstrate measurable impacts of ILO air emissions on sleep and time outdoors among those living in residential communities nearby. The modeling approaches used were robust to bias from factors that remained constant for each participant over the course of the study and also to factors that varied with the time-of-day or the weather, suggesting acute causal effect of exposures to ILO air emissions on sleep and time outdoors. Policy interventions to reduce community exposures to swine ILO emissions from lagoon-and-spray field systems could have positive impacts on public health in rural North Carolina communities.

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