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Residential proximity to high-density poultry operations associated with campylobacteriosis and infectious diarrhea

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ABSTRACT

Poultry carry zoonotic bacteria that can cause gastroenteritis in humans. Environmental transmission of pathogens from poultry operations may increase gastrointestinal infection risk in surrounding communities. To evaluate associations between residential proximity to high-density poultry operations and individual-level diarrheal illnesses, we conducted a nested case-control study among 514,488 patients in Pennsylvania (2006–2015). Using electronic health records, we identified cases of five gastrointestinal outcomes: three pathogen-specific infections, including *Escherichia coli* (n = 1425), *Campylobacter* (n = 567), and *Salmonella* (n = 781); infectious diarrhea (n = 781); and non-specific diarrhea (2012–2015; n = 28,201). We estimated an inverse-distance squared activity metric for poultry operations based on farm and patient addresses. Patients in the second and fourth (versus first) quartiles of the poultry operation activity metric had increased odds of *Campylobacter* (AOR [CI], Q2: 1.36 [1.01, 1.82]; Q3: 1.38 [0.98, 1.96]; Q4: 1.75 [1.31, 2.33]). Patients in the second, third, and fourth quartiles had increased odds of infectious diarrhea (Q2: 1.76 [1.29, 2.39]; Q3: 1.76 [1.09, 2.85]; Q4: 1.60 [1.12, 2.30]). Stratification revealed stronger relations of fourth quartile and both *Campylobacter* and infectious diarrhea in townships, the most rural community type in the study geography. Increasing extreme rainfall in the week prior to diagnosis strengthened fourth quartile *Campylobacter* associations. The poultry operation activity metric was largely unassociated with *E. coli*, *Salmonella*, and non-specific diarrhea. Findings suggest high-density poultry operations may be associated with campylobacteriosis and infectious diarrhea in nearby communities, highlighting additional public health concerns of industrial agriculture.

1. Introduction

Poultry are reservoirs of several zoonotic bacteria that cause acute gastroenteritis in humans, including *Campylobacter*, *Salmonella*, *Escherichia coli*, and *Listeria* (Berghaus et al., 2012; Blaak et al., 2015; Dahshan et al., 2016; Lee et al., 2016; Sahin et al., 2015). Among the most common causes of foodborne illness in the U.S., these pathogens cause significant morbidity and mortality, with serious sequelae such as Guillain-Barré syndrome (*Campylobacter*), reactive arthritis and irritable bowel syndrome (*Campylobacter* and *Salmonella*), end-stage renal disease (*E. coli*), and pre-term labor and fetal infection (*Listeria*) (Humphrey et al., 2007; Scallan et al., 2015). The risk of illness due to foodborne transmission of pathogenic bacteria from poultry meat is well documented (Batz et al., 2012). Environmental transmission of these pathogens from poultry operations to humans presents an additional, though far less-studied risk.

Research has previously linked industrial food animal production (IFAP)—which is characterized by large, homogeneous, and densely packed livestock operations—to increased risk of zoonotic diseases in nearby communities (Casey et al., 2015). In terms of zoonotic bacteria associated with gastroenteritis, a case-control study conducted in counties with high cattle density found that living or working on a dairy

Abbreviations: IFAP, industrial food animal production; NMP, Nutrient Management Plan; AEU, animal equivalent unit

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farm was positively associated with campylobacteriosis, with strong overlap between human and bovine bacterial isolates (Davis et al., 2013). A study conducted across multiple states that linked *Campylobacter* cases with socioeconomic and environmental data by zip code found that in top poultry and dairy producing regions, campylobacteriosis incidence rates were significantly higher in zip codes with broiler operations or dairy operations compared to zip codes without operations (Rosenberg Goldstein et al., 2016). Other ecological studies using disease surveillance data have reported associations of farm animal density and *Campylobacter*, and the percent of the population living on a farm with risk of *E. coli* infection (Chang et al., 2009; Green et al., 2006). Studies have also found that rural residents living in areas with swine or dairy IFAP experience greater occurrence of diarrhea as measured by interviews with area residents (Arnold, 1999; Wing and Wolf, 2000), although these studies did not assess specific pathogens and are subject to recall bias.

While studies have shown living or working on a poultry farm and contact with live poultry to be a risk factor for *Campylobacter* and antibiotic-resistant *E. coli* infection (Davis et al., 2013; Price et al., 2007; Studahl and Andersson, 2000; Thorsteinsdottir et al., 2010; Wilson 2004), individual-level associations of poultry operations with risk of human infections in surrounding communities are largely unstudied. Environmental contamination from poultry operations has the potential to spread pathogens to nearby communities (Jonsson et al., 2010). Bacterial pathogens colonize animals at an early age and spread quickly through a flock (Blaak et al., 2015; Friese et al., 2013; Hermans et al., 2012; Sahin et al., 2015). From poultry houses, bacteria enter the community environment via aerosolized particles or in dust emitted through ventilation fans, through pests such as flies, and through land-disposal of poultry waste (Blaak et al., 2014, 2015; Bull et al., 2006; Friese et al., 2013; Graham et al., 2009a, 2009b; Skora et al., 2016). Heavy rainfall can facilitate further transport of pathogens into surface and groundwater and is independently associated with gastrointestinal illness (Gleason and Fagliano, 2017; Levy et al., 2016).

Given the limited research related to poultry IFAP and risk of relevant human infections in surrounding communities, the aim of this study was to evaluate associations between residential proximity to poultry operations and individual-level diarrheal illnesses. We conducted a case-control study of the association between residential proximity to poultry operations and five gastrointestinal outcomes. While past research utilized gravity models to analyze zoonotic disease risk in swine and bovine operations (e.g. Casey et al., 2013), to our knowledge this is the first study to use this geospatial method to assess infectious disease risks related to poultry IFAP and to evaluate associations of IFAP with gastrointestinal outcomes. We evaluated three pathogen-specific intestinal infection diagnoses that have been linked to poultry operations: *E. coli, Campylobacter,* and *Salmonella*. In addition, since the majority of patients seeking medical care for diarrhea are not tested for specific pathogens (Scallan et al., 2005), we sought to ascertain the relation of poultry operation proximity to less severe or persistent diarrheal illnesses by evaluating two other diagnoses, specifically infectious and non-specific diarrhea.

2. Methods

2.1. Study population

Using electronic health record (EHR) data, we identified child and adult patients with one of five gastrointestinal outcomes from Geisinger, an integrated health system in Pennsylvania, USA. Geisinger primary care patients represent the age and sex distribution of the general population in central and northeastern Pennsylvania (Casey et al., 2016a, 2016b). The study area comprised 38 counties in Pennsylvania, including the health system's primary care market and bordering counties (Fig. 1). The latitude and longitude of patients' addresses were geocoded using ArcGIS version 10.1 (Esri, Redlands, CA). For four of our study outcomes, we utilized EHR data from 514,488 patients who had contact with Geisinger from January 2006 to July 2015; for non-specific diarrhea, we limited data to 455,364 patients with contact from January 2012 to July 2015 due to inconsistencies in coding prior to 2012. The Geisinger Institutional Review Board approved the study and waived informed consent.

2.2. Case ascertainment and control selection

We identified cases from the five diagnostic groups using Geisinger system diagnostic codes and text descriptions cross-linked to International Classification of Diseases (ICD, 9th and 10th Revision) codes from outpatient, emergency department, and medication records. Indications from medication records were used to identify cases with potential call-in orders for diarrhea not associated with a patient encounter and to enhance incomplete coding from encounters. Diagnoses were identified as follows (ICD-9 codes, ICD-10 codes not documented as they were internally converted to ICD-9 during data extraction): intestinal infection related to *Salmonella* (003.0), *E.coli* (008.0, 008.00, 008.09, 041.4, 041.41, 041.49), or *Campylobacter* (008.43), infectious diarrhea/bacterial enteritis (008.5, 009.2, 009.3, excluding codes with text descriptions indicating travelers' diarrhea), and non-specific diarrhea (787.91, 564.5). We used positive fecal sample laboratory test results to identify *Salmonella* and *Campylobacter* cases in addition to those identified through codes; negative test results received one week before or after a diagnostic code were used to exclude patients as cases. For *Salmonella* and *Campylobacter* cases, 28% and 36% had both a code and positive laboratory test, 25% and 19% had a code only, and 47% and 45% had a laboratory test only, respectively. There were an insufficient number of *Listeria* cases to evaluate. Patients with an inpatient diagnosis for infectious diarrhea and non-specific diarrhea were excluded as potential cases for one year following diagnosis to avoid counting hospital-acquired infections as cases. Given the ambiguity of the non-specific diarrhea ICD-9 code, we used additional exclusion criteria for these cases. Specifically, we did not include cases with text descriptions for "frequent defecation" or "frequent stool," and we excluded cases for one-year after EHR notations for causes of non-infectious diarrhea (e.g., "chemotherapy-induced diarrhea," "antibiotic-associated diarrhea") or if there was a diagnosis for an acute condition associated with diarrhea (i.e., cholera, typhoid, Norwalk virus, receiving chemotherapy). All outcome analyses only included first incident cases. For all outcomes except non-specific diarrhea, 4% or less of cases had repeat diagnoses in subsequent years; 10% of non-specific diarrhea cases had repeat diagnoses, most of which had just one repeat diagnosis.

We randomly selected outpatient controls with no history of diarrhea diagnoses and frequency-matched them to cases by age category (< 1, 1, 2–4, 5–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80–99, ≥100), sex, and year of encounter. If a control had multiple encounters in a year, one encounter was randomly selected for the activity metric assignment date.

2.3. Poultry operation data

Livestock operations are required to develop a Nutrient Management Plan (NMP) for manure handling if they exceed two animal equivalent units (AEUs, 1000 pounds of live weight on an annualized basis) per acre and have greater than eight AEUs (per Pennsylvania Act 38), or if they exceed 1000 total AEUs (per U.S. Clean Water Act). Operations can also voluntarily develop an NMP. NMPs provide information on livestock operation location and animal type and quantity. We obtained NMPs for poultry operations in the 38-county study area from County Conservation Districts. We located the latitude and longitude of poultry operations using Google Earth with visual confirmation of a poultry house on-site.

The study area contained five types of poultry operation: broilers