High-density poultry operations and community-acquired pneumonia in Pennsylvania : Environmental Epidemiology

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Abstract

Background:

Air pollution from industrial food animal production may increase vulnerability to pneumonia among individuals living in nearby communities. We evaluated the association between individual-level residential proximity to high-density poultry operations and diagnosis with community-acquired pneumonia (CAP).

Methods:

We conducted a nested case–control study among patients of a large health system in Pennsylvania, USA. We used diagnostic codes for pneumonia and chest imaging from electronic health records from 2004 to 2015 to identify 11,910 child and adult cases of CAP and 59,550 frequency-matched outpatient controls. We estimated exposure to poultry operations using data from nutrient management plans, calculating an inverse-distance squared activity metric based on operation and residential addresses that incorporated number, size, and location of operations. Mixed effects logistic regression models evaluated associations between quartiles of the activity metric and CAP diagnosis. Models controlled for sex, age, race/ethnicity, Medical Assistance (proxy for low socioeconomic status), and smoking status.

Results:

Individuals living in the highest (versus lowest) quartile of the poultry operation metric had 66% increased odds of CAP diagnosis (adjusted odds ratio [confidence interval]) Q2, 0.98 [0.74, 1.31]; Q3, 1.17 [0.93, 1.46]; Q4, 1.66 [1.27, 2.18]).

Conclusions:

Findings suggest that living in closer proximity to more and larger poultry operations may increase risk of CAP, contributing to growing concern regarding public health impacts of industrial food animal production.

What this study adds

A nascent body of research links industrial food animal production—a source of air pollution—with adverse respiratory outcomes in nearby communities. This study contributes to the field by analyzing residential proximity to poultry operations and community-acquired pneumonia in Pennsylvania. To our knowledge, no prior studies have assessed this relationship in the United States, despite a high prevalence of industrial poultry production and the substantial burden of pneumonia on mortality and hospitalization rates. Using a more thorough measurement approach than past epidemiologic studies, we found that living closer to more and larger poultry operations may increase individual risk of community-acquired pneumonia.

In the United States, pneumonia is a leading cause of death and illness-related hospitalization.[1,2] Young children and older adults face the highest burden of community-acquired pneumonia (CAP),[3,4] but it is also a common and costly infection among working-age adults.[5] Risk factors for CAP include lifestyle factors (e.g., smoking, poor dental hygiene), inhalation and oxygen therapy, and comorbid conditions (e.g., chronic respiratory disease, HIV infection).[6,7]

Ambient air pollution also increases risk of lower respiratory infections, including CAP.[8–10] Exposure to air pollutants such as particulate matter induces oxidative stress in pulmonary macrophages and epithelial cells, reducing the lung's defenses against bacterial pathogens, thereby increasing susceptibility to respiratory infections.[10,11] Exposure to air pollution may also disrupt the composition of the oropharyngeal microbiota, which is believed to play an essential role in respiratory health. Through the use of available nutrients and niches, a balanced microbiota provides resistance to the acquisition and establishment of pathogens and prevents the overgrowth of pathobionts (potential pathogens endemic to the respiratory tract) such as *Streptococcus pneumoniae*, the most common cause of CAP.[12,13] Prior research found an absence of protective bacteria among pneumonia patients, leading to an imbalanced oropharyngeal microbiota and creating openings for overgrowth of pathogenic bacteria.[14]

As a source of air pollution, industrial food animal production (IFAP) can compromise respiratory health.[15] These large, homogeneous, densely packed livestock operations emit particulate matter, endotoxins, and other pollutants, which spread downwind through ventilation fans and emissions from decomposing manure.[15–18] Adverse effects on lung function and increased respiratory symptoms have been reported among individuals living near IFAP, particularly among susceptible groups.[19–21] A group conducted a series of studies in livestock-intensive areas of the Netherlands to examine associations between living near animal farms and pneumonia.[22–25] These studies reported a largely consistent finding of increased pneumonia risk among individuals living near goat farms and a less consistent relationship for poultry farm exposure. However, three of the four studies used data gathered during a *Coxiella burnetti* outbreak, an infection generally associated with goats, but not poultry, that leads to Q-fever and can manifest in pneumonia.[23–25] In addition to this limitation, only one study accounted for accumulated risk from multiple farms in proximity to individuals' home addresses,[25] and none incorporated animal density in their exposure metrics.

Limited existing evidence in settings with low Q-fever warrants greater understanding of the relationship between living near poultry IFAP and lower respiratory infections, particularly studies that comprehensively account for poultry operation proximity and size. Furthermore, to our knowledge, no studies have examined relationships between poultry IFAP and CAP in the United States, despite a high prevalence of poultry IFAP. Thus, the goal of this study was to evaluate the association between individual-level residential proximity to high-density poultry operations and CAP diagnosis.

Methods

Study population

We conducted a nested case–control study among patients of Geisinger, a large integrated health system in Pennsylvania. To identify CAP cases, we used electronic health record (EHR) data for

501,843 children and adults with an outpatient, inpatient, or emergency department contact between January 2004 and July 2015. The study area included 38 Pennsylvania counties comprising Geisinger's primary care market and bordering counties. Geisinger's primary care patients represent the age and sex distribution of the general population in central and northeastern Pennsylvania.[26] The latitude and longitude of subjects' addresses were geocoded using ArcGIS version 10.1 (Esri, Redlands, CA).[27] The Geisinger Institutional Review Board approved the study and waived informed consent.

Case ascertainment and control selection

We identified incident CAP cases using Geisinger system and International Classification of Diseases (ICD, 9th and 10th Revisions) diagnostic codes. ICD-10 codes were internally converted to ICD-9 during data extraction. Cases were defined as subjects with an ICD-9 diagnostic code for pneumonia (480.x, 481, 482.x, 483.x, 484.x, 485, 486, 487.0) and a Current Procedural Terminology code for chest radiological imaging.[28] We identified cases from codes from the following encounter types: outpatient (53% of cases), inpatient (23%), and emergency department (21%); an additional 3% of cases were identified via medication records. To exclude nosocomial pneumonia cases,[29] we omitted subjects with hospitalization for more than 2 days in the 90 days preceding pneumonia diagnosis; residence in an institution (i.e., nursing home, assisted living facility, residential treatment center, or prison); diagnosis of ventilator-associated pneumonia or *Pneumocystis jirovecii* pneumonia in the year prior to pneumonia diagnosis; diagnosis with an excluding condition (i.e., recurrent pneumonia, solid organ or bone marrow transplant, immunodeficiency, AIDS, hematologic malignancies, primary lung cancer, or tuberculosis); chemotherapy or radiation therapy in the 6 months prior to pneumonia diagnosis; or outpatient dialysis in the 30 days prior to pneumonia diagnosis.

Randomly selected outpatient controls were frequency-matched (5:1) to cases by age category, sex, and encounter in the same year as CAP diagnosis. Exclusion criteria for controls included a prior pneumonia diagnostic code, diagnosis with an excluding condition (listed above), or residence in an institution. Subjects could serve as controls over multiple years, and cases were eligible to serve as controls until the year of CAP diagnosis.

Poultry operation data

Poultry operation data were identified using publicly available nutrient management plans (NMPs), which are required for livestock operations that exceed either: (1) 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 (2) 1000 total AEUs (per US Clean Water Act). Considering AEUs are adjusted for the proportion of time during the year that animals are present on an operation, eight AEUs would be equivalent, for example, to 5050 five-pound broilers (chickens raised for meat) raised over the course of six 6-week cycles (252 production days). We obtained NMPs for the year 2015 for operations in the study area from County Conservation Districts. We used operation addresses to assign latitude and longitude and Google Earth to confirm the presence of a poultry house.[30]

Poultry types included broilers, layers (egg-laying hens), pullets (young hens produced for breeding), turkeys, and ducks. Air pollutant emissions from poultry operations likely vary by poultry type, the local climate of the poultry house, ventilation type, and manure management system.[31]

Poultry operation activity metric assignment

We created a poultry operation activity metric to account for the intensity and proximity of poultry operations using total number of poultry operations in the study area, distance between each subject's residence and poultry operations, and number of poultry AEUs at each operation. We used inverse distance-squared gravity measures[32] to derive the activity metric for each subject as previously reported:[33]

$$\text{Activity metric for subject } j = \sum_{i=1}^{n} \frac{a_i}{d_{ij}^2}$$

where n was the number of operations, a_i was poultry AEUs at operation i, and d_{ij}^2 was the squared-distance (m^2) between operation i and subject j. The activity metric was modeled as quartiles; quartile one represented the lowest activity and served as a reference category. The metric was not time varying as IFAP operations in the region are largely static.[34] We used R version 3.3.1 (R Foundation for Statistical Computing) to compute the metric.

Covariates

We obtained sex, age at diagnosis/encounter, race/ethnicity, history of Medical Assistance (measure of low socioeconomic status[35]), and smoking status from the EHR. We used medication records to create an indicator (yes versus no) for any antibiotic order and orders for a macrolide, tetracycline, or quinolone (antibiotics commonly used to treat CAP[29]) in the 30 days and 6 months prior to diagnosis/encounter. We examined indications for antibiotic orders when available. Covariates created using subjects' geocoded addresses included distance in meters between subject residence and nearest Geisinger clinic or hospital, presence of a Geisinger hospital in the subject's county of residence (yes versus no), community type (i.e., townships, boroughs, cities), and community socioeconomic deprivation (CSD). Community type was identified using a mixed definition of place that generally captures a rural to urban gradient.[27] CSD was based on six US Census indicators as previously described.[36] We defined season of diagnosis as winter (December–February), spring (March–May), summer (June–August), and fall (September–November).

Statistical analysis

The analysis goal was to evaluate associations between the poultry operation activity metric and CAP diagnosis. We used mixed effects logistic regression with a random intercept for subject to account for controls later serving as cases (and thus multiple observations per subject). To account for the spatial dependence of subjects living in the same communities, we used robust standard errors clustered by community. We adjusted models a priori for sex, age (centered and centered squared), race/ethnicity (non-Hispanic white versus black/Hispanic/other), Medical Assistance (yes versus no), and smoking status (never versus former, current, and unknown). Representing a perturbation to the microbiota,[12] we originally hypothesized that prior antibiotic orders may increase risk of CAP but ultimately did not include antibiotics in models because their use in various time intervals before diagnosis of CAP was strongly associated with the CAP diagnosis used as our outcome. We assessed distance to a Geisinger facility and the presence of a Geisinger hospital in the county of residence as potential confounders because long distances could motivate individuals to seek care for pulmonary symptoms at local, non-Geisinger facilities or hospitals. We evaluated CSD as a confounder since it was previously linked to higher CAP incidence.[37] To determine confounding, we assessed whether poultry metric/CAP associations changed by ≥10% when potential confounders were added to regression models. We report results as adjusted odds ratios with 95% confidence intervals and *P* values. Results were considered significant at $P < 0.05$ (two-tailed).

We stratified models by community type, as we hypothesized that the association between the poultry operation activity metric and CAP might vary by community type. Prior studies have demonstrated individual-level and place-level differences by community type.[36,38] We also evaluated effect modification by Medical Assistance, hypothesizing that poorer health status among low-income populations may increase their vulnerability to IFAP-related CAP; age, given higher CAP incidence in young children and children's vulnerability to air pollutants;[4,39] and season of diagnosis, because CAP and exposures from poultry operations vary seasonally.[3] To evaluate effect modification, we included cross-product terms of variables with the poultry operation activity metric. We used Stata version 14.0 (StataCorp, LP, College Station, TX) for analyses.

Results

We identified 11,910 CAP cases between 2004 and 2015, matched to 59,550 controls. CAP diagnoses increased over the study period as the hospital system expanded and EHR use increased (Table 1). Approximately one-third of cases were children under age 12 years and nearly 30% of cases were older than 62 years. The majority of cases were non-Hispanic white, reflecting the region's demographics. Cases were about three times more likely than controls to have received an antibiotic order in the 30 days prior to diagnosis and about seven times more likely to have received a macrolide, tetracycline, or quinolone order. Prior antibiotic orders were primarily linked to diagnostic codes for upper respiratory tract infections (e.g., sinusitis); cases were more likely than controls to have received an antibiotic for bronchitis, chronic airway obstruction, fever, or cough. A slightly larger proportion of cases than controls lived in cities and boroughs.

Characteristic	No. (%) Unless Specified	
	Cases, $n = 11,910$	Controls, $n = 59,550$
Sex, male	6037 (50.7)	30,183 (50.7)
Age at diagnosis, years, median (IQR)		
0–4	2398 (20.1)	11,990 (20.1)
5–12	1462 (12.3)	7310 (12.3)
13–18	477 (4.0)	2385 (4.0)
19–44	1916 (16.1)	9580 (16.1)
45–61	2183 (18.3)	10,915 (18.3)
62–74	1733 (14.6)	8665 (14.6)
≥75	1741 (14.6)	8705 (14.6)
Diagnosis/encounter year		
2004	598 (5.0)	2990 (5.0)
2005	502 (4.2)	2510 (4.2)
2006	594 (5.0)	2970 (5.0)
2007	835 (7.0)	4175 (7.0)
2008	1052 (8.8)	5260 (8.8)
2009	1036 (8.7)	5180 (8.7)
2010	950 (8.0)	4750 (8.0)
2011	1194 (10.0)	5970 (10.0)
2012	1575 (13.2)	7875 (13.2)
2013	1376 (11.6)	6880 (11.6)
2014	1488 (12.5)	7440 (12.5)
2015[a]	710 (6.0)	3550 (6.0)
Race/ethnicity		
Non-Hispanic white	10,997 (92.3)	55,587 (93.4)
Black	351 (3.0)	1509 (2.5)
Hispanic	451 (3.8)	1852 (3.1)
Other	85 (0.7)	459 (0.8)
Missing	26 (0.2)	143 (0.2)
Smoking status		
Current smoker	1690 (14.2)	5970 (10.0)
Former smoker	2677 (22.5)	10,732 (18.0)
Never smoked	3943 (33.1)	23,580 (39.6)
Unknown	3600 (30.2)	19,268 (32.4)
History of medical assistance	3009 (25.3)	11,606 (19.5)
Received an antibiotic order prior to diagnosis/encounter		
Any antibiotic, 30 days prior	2796 (23.5)	3910 (6.6)
Any antibiotic, 6 months prior	5497 (46.2)	13,198 (22.2)
Macrolide/tetracycline/quinolone, 30 days prior	1632 (13.7)	1137 (1.9)
Macrolide/tetracycline/quinolone, 6 months prior	3046 (25.6)	4760 (8.0)
Diagnosis/encounter season		
Winter	3896 (32.7)	15,312 (25.7)
Spring	3137 (26.3)	15,593 (26.2)
Summer	1949 (16.4)	13,450 (22.6)
Fall	2928 (24.6)	15,195 (25.5)
No. of unique counties	34	38
No. of unique communities	649	975
Community type		
Township	6518 (54.7)	35,662 (59.9)
Borough	3743 (31.4)	17,446 (29.3)
City	1649 (13.9)	6442 (10.8)
Community socioeconomic deprivation, SD units, median (IQR)	0.59 (−2.07, 2.55)	0.08 (−2.25, 2.41)
Poultry operation activity metric (range, [AEU/km²] × 10)		
Quartile 1 (0.01–0.08)	2664 (22.4)	15,200 (25.5)
Quartile 2 (0.08–0.17)	2604 (21.9)	15,528 (25.6)
Quartile 3 (0.17–0.60)	2941 (24.7)	14,928 (25.1)
Quartile 4 (0.60–1078.89)	3701 (31.1)	14,164 (23.8)

[a]Patient data collected through July 2015.

AEU indicates animal equivalent units; CAP, community-acquired pneumonia; IQR, interquartile range; SD, standard deviation.

Table 1:

Descriptive statistics of cases with CAP and controls without CAP at time of frequency matching to case

We collected NMPs for 304 high-density poultry operations, located in 16 counties (Figure 1), the majority of which were broiler (53%) or layer (24%) operations. Operations had a median (IQR) of 154 (101, 250) AEUs (e.g., an operation raising 74,000 broilers every 6 weeks for six cycles). A comparison with US Agricultural Census data[40] indicated NMP data accounted for about 95% of broilers, layers, and pullets produced in the study area. Median distances between study subjects' residences and the nearest poultry operation were 61, 29, 10, and 4 km for quartiles 1–4 of the poultry operation activity metric, respectively.

F1

Figure 1.:

Map of study area. Numbers within borders of each county indicate the number of CAP cases. Yellow circles show locations of poultry operations based on 2015 nutrient management plan (NMP) data. Map generated with ArcGIS (10.1, Esri, Redlands, CA).

In an unadjusted model, subjects with a poultry operation activity metric in the fourth quartile (versus first) had significantly increased odds of CAP diagnosis; inferences did not change after adjustment for covariates (adjusted odds ratio [confidence interval]) Q2: 0.98 [0.74, 1.31]; Q3: 1.17 [0.93, 1.46]; Q4:

1.66 [1.27, 2.18]). We found no evidence of confounding by distance to a Geisinger facility, presence of a Geisinger hospital in the county of residence, or CSD (results not shown).

In models stratified by community type (townships and boroughs), associations between the poultry operation activity metric and CAP were confounded by the presence of a Geisinger hospital in the county of residence, which was strongly associated with CAP diagnosis (townships: 3.86 [2.98, 4.98]; boroughs: 4.48 [3.15, 6.39]). After controlling for this variable, we found no evidence of confounding by community type, with the fourth quartile of the poultry operation activity metric positively associated with CAP in both townships and boroughs (Table 2). Cities could not be evaluated in a stratified model due to small cell counts in cross-tabulations of the poultry operation activity metric and presence of a Geisinger hospital in the county of residence.

Table 2:

Unadjusted and adjusted[a] associations of the poultry operation activity metric with CAP, stratified by community type

We observed little evidence of effect modification by Medical Assistance, age, or diagnosis season on associations of the poultry operation activity metric with CAP, so interaction terms for these variables were not included in final models.

Discussion

Using EHR data from a large patient population in a region with many IFAP facilities, we evaluated the association between residential proximity to high-density poultry operations and CAP diagnoses. We found 66% increased odds of CAP diagnosis for individuals living in the highest quartile of the poultry operation activity metric (versus the lowest). Hypothesizing this association might vary across community types (townships, boroughs, cities), which differ on a range of place-level characteristics (e.g., population density, traffic, level of commercial development) and individual-level characteristics (e.g., socioeconomic status, race/ethnicity) in this region, we stratified our analysis but found a consistent relation between the highest quartile of the poultry operation activity metric and CAP diagnosis. The presence of significant elevated associations in only the fourth quartile of the poultry operation activity metric is consistent with a threshold relation. Our findings suggest that living in proximity to a greater number of and larger poultry operations may increase the risk of acquiring CAP, regardless of community type.

Prior research from the Netherlands related to poultry IFAP and CAP showed inconsistent findings. Three studies coincided with a goat-related *C. burnetti* infection outbreak.[23–25] In a large EHR-based study, Smit et al[25] demonstrated that individuals living within 1.15 km of a poultry farm had 11% increased risk per farm of CAP diagnosis, confirming their earlier study results.[24] In contrast, a case–control study of 408 adult CAP patients with laboratory testing found the presence of sheep and number of goats within 1 km of patient home addresses, but not poultry, was associated with CAP caused by *C. burnetii*.[23] The study used a more stringent definition of CAP, likely excluding cases with milder symptoms that Smit et al may have included in their analyses.[23] After the *C. burnetti* outbreak concluded, a cross-sectional study among 2426 adults reported no association between living near poultry operations and pneumonia (defined as either self-reported physician-diagnosed pneumonia or

EHR-recorded pneumonia).[22] However, in a sensitivity analysis, the study reported an association between poultry farms within 1000 m of an individual's residence and EHR-based pneumonia.

Our findings align most closely with those of Smit et al's,[25] perhaps due to similarities in study design. They used a data-driven kernel analysis that assessed accumulated risk from multiple farms in proximity to individuals' home addresses, providing a similar advantage to our gravity measure, which took into account the number, animal density, and distance of all poultry operations in the study area. Additionally, neither study required laboratory or radiographic confirmation of pneumonia. This reduced specificity of case definitions, potentially capturing subjects without CAP or with less severe cases of CAP. Such cases are relevant for assessment if poultry IFAP and CAP associations are explained by increased susceptibility to lower respiratory infections resulting from microbiota dysbiosis due to air pollution, as evidence from Smit et al's[25] research suggests. They found that CAP patients living <1 km to one or more poultry farms had an altered oropharyngeal microbiota, with increased abundance of *S. pneumoniae*, as compared to those living ≥1 km to farms, which they hypothesized reflected an imbalanced oropharyngeal microbiota resulting from farm-related air pollutants. They noted that although poultry farms can be a source of *Chlamydia psittaci* (the cause of psittacosis, a disease resembling pneumonia), very few cases of CAP in their study area were caused by an avian pathogen. Similarly, our findings are not likely explained by avian-transmitted infections, as we found only one instance of psittacosis in our patient population.

Antibiotics also alter the oropharyngeal microbiota composition, creating a disequilibrium that increases vulnerability to colonization by pathogens and susceptibility to pneumonia.[12,13] This could explain why CAP cases in our study were more likely than controls to have received an antibiotic order in the 30 days and 6 months prior to diagnosis. Yet compared to controls, CAP cases were even more likely to have received an order for antibiotics commonly used to treat pneumonia. Additionally, antibiotic orders were largely linked to diagnostic codes for pulmonary symptoms and conditions. This indicates antibiotic orders prior to CAP diagnosis may have reflected a clinical response to a prodromal phase during which subjects experienced symptoms of airway inflammation and other respiratory infections. These prodromal respiratory symptoms could stem from IFAP-related air pollutants, suggesting that residential proximity to poultry operations may be a risk factor for a variety of respiratory health outcomes, as shown for swine and dairy/veal IFAP in this region for asthma.[34]

Strengths of this study include a large sample size and the use of EHR data to classify CAP diagnoses. Additionally, the poultry operation activity metric incorporated information on subjects' residential distance from poultry facilities, as well as the number of facilities and animal density, and comparison with US Agricultural Census data indicated that NMP data accounted for nearly all poultry production in the study area. Our study also had limitations. Although we adjusted for history of Medical Assistance, this measure does not account for all dimensions of socioeconomic status[35]; thus, our results are subject to residual confounding by unmeasured socioeconomic status. If poorer subjects were more likely to live near IFAP and have a CAP diagnosis, as indicated by higher levels of Medical Assistance among CAP cases, then risk associated with IFAP may have been overestimated. However, subjects living in the highest quartile of the poultry operation activity metric had the least Medical Assistance use, suggesting they were not the most socioeconomically disadvantaged. We also did not incorporate information on swine or bovine IFAP that may contribute to air pollution, which could be done in subsequent studies. Additionally, we lacked environmental samples from poultry operations and around residences and subjects' microbiota data, preventing an evaluation of the hypothesis that air pollution from poultry operations increases vulnerability to CAP by altering the oropharyngeal microbiota. Our study provides initial evidence that residential proximity to poultry operations may increase risk for CAP, but additional research is needed to confirm these findings and elucidate the underlying environmental and biological pathways.

In conclusion, this study demonstrated that residing closer to more and larger poultry operations was associated with CAP, a cause of significant morbidity and mortality. As the first study to evaluate associations of poultry IFAP and CAP in the US, our findings highlight the need for additional research on the contribution of IFAP to air pollution and associated health risks for nearby communities. Understanding such localized risks could better inform clinical decision-making, including monitoring of patients susceptible to lower respiratory tract infections living in proximity to IFAP.

Conflict of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

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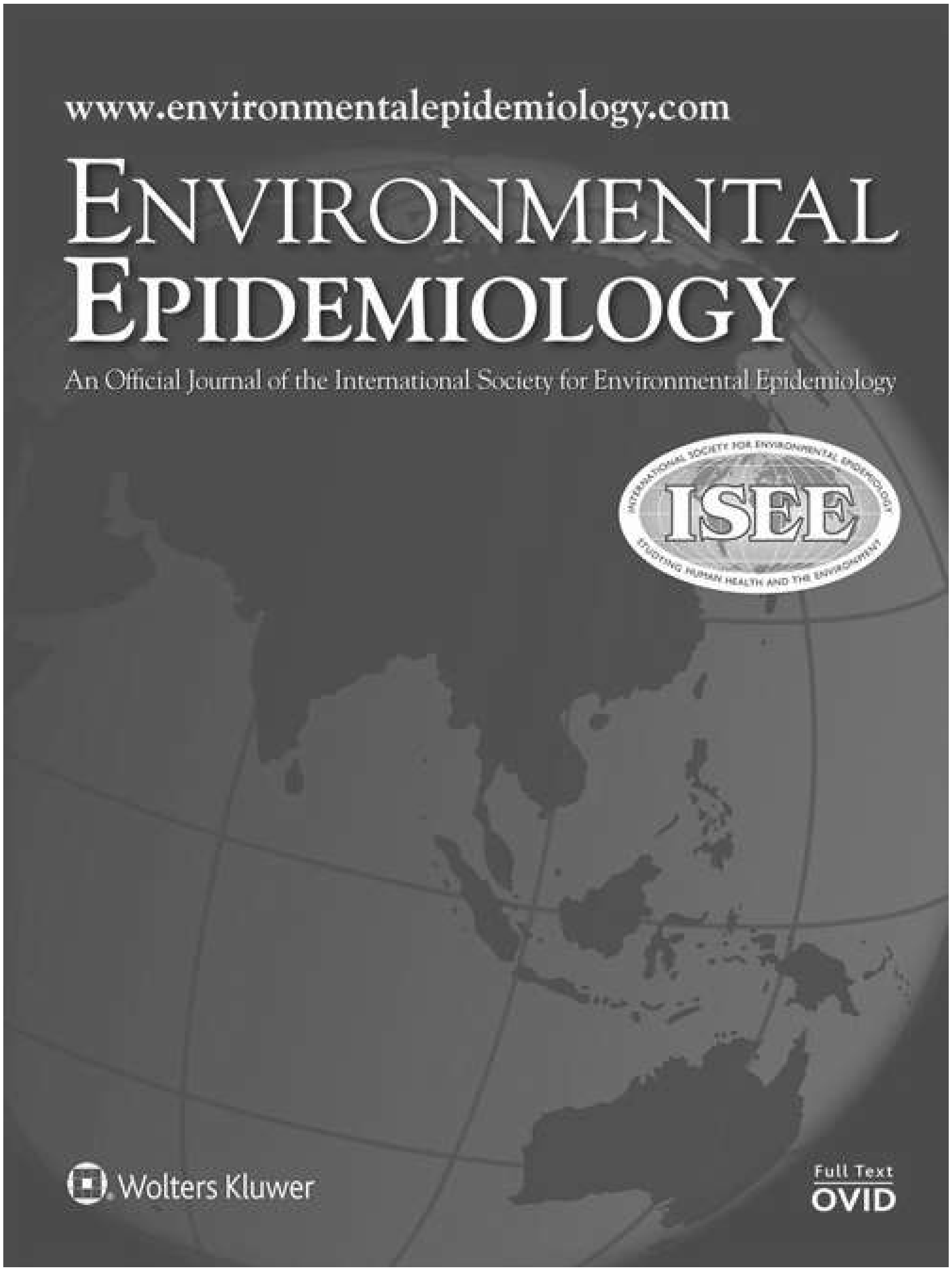
- 

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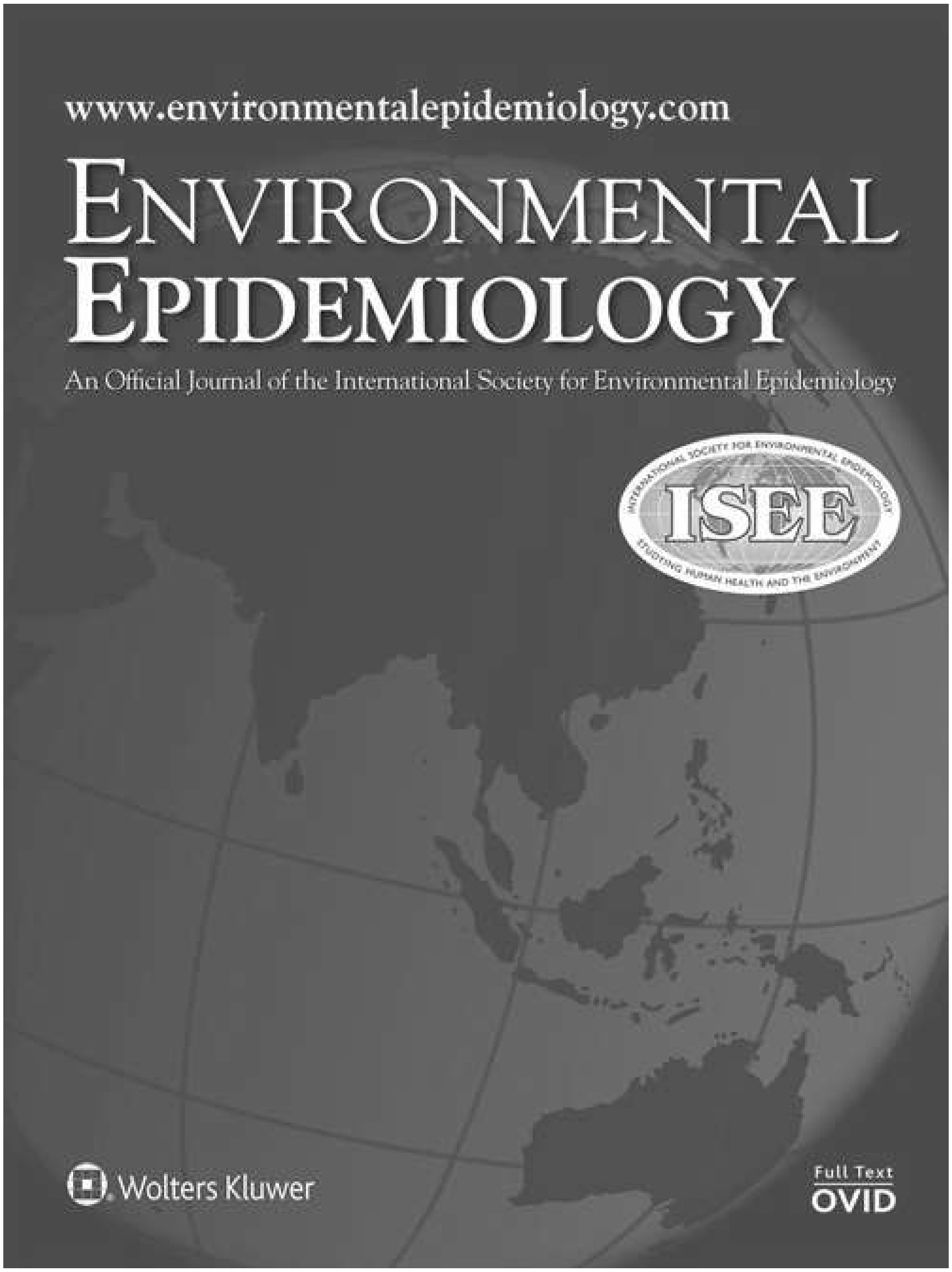
- 

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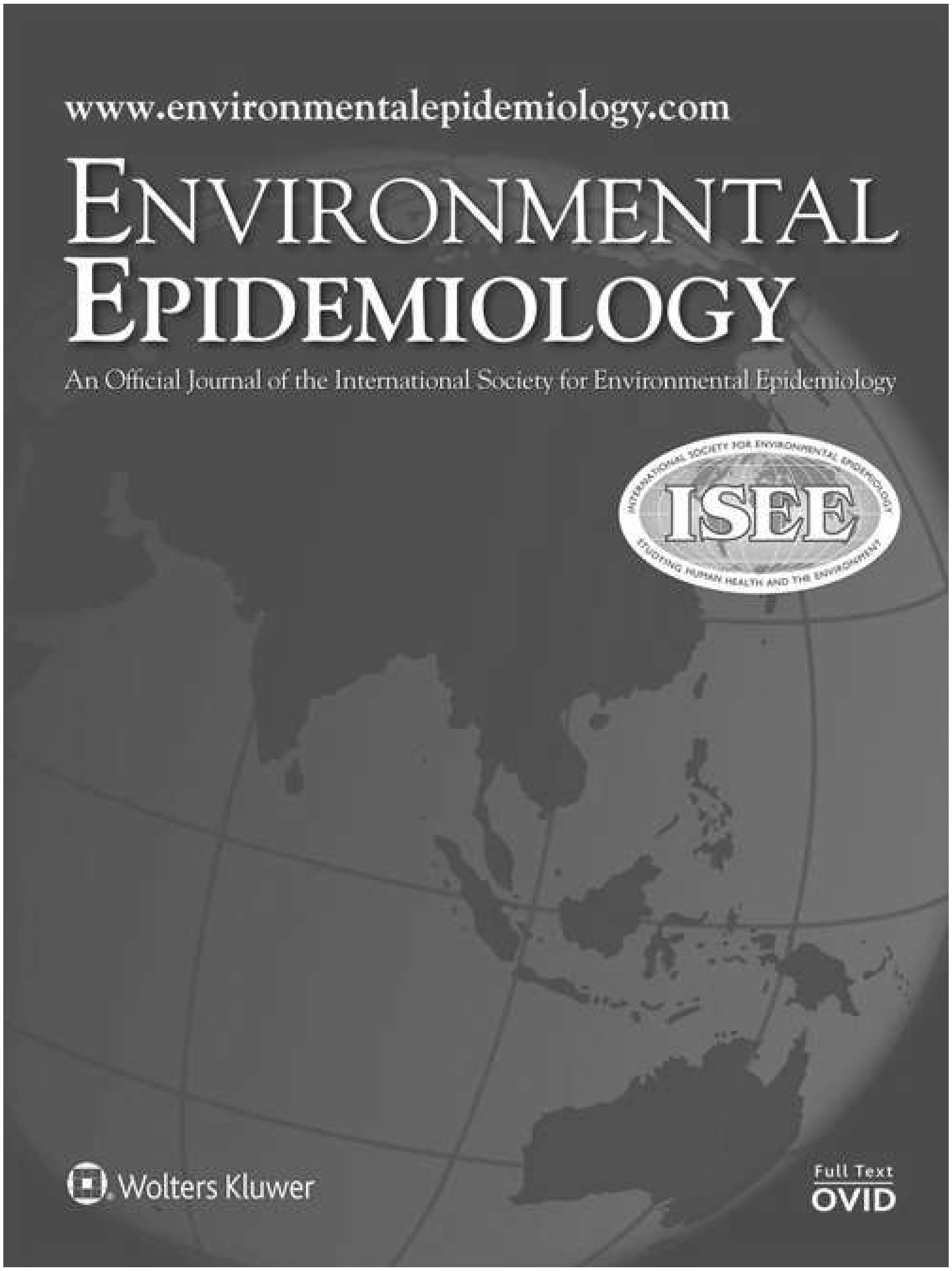
- 

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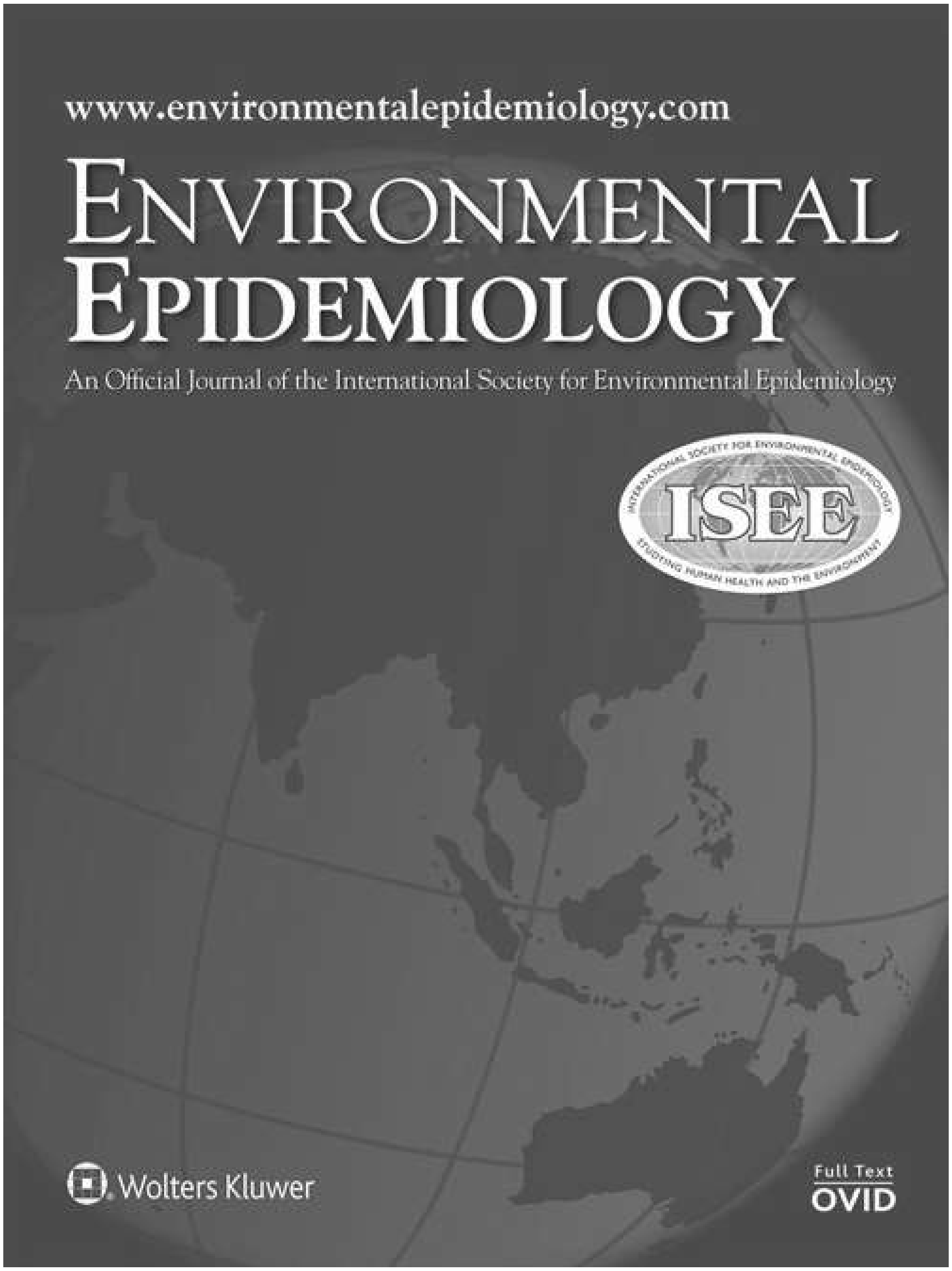
- 

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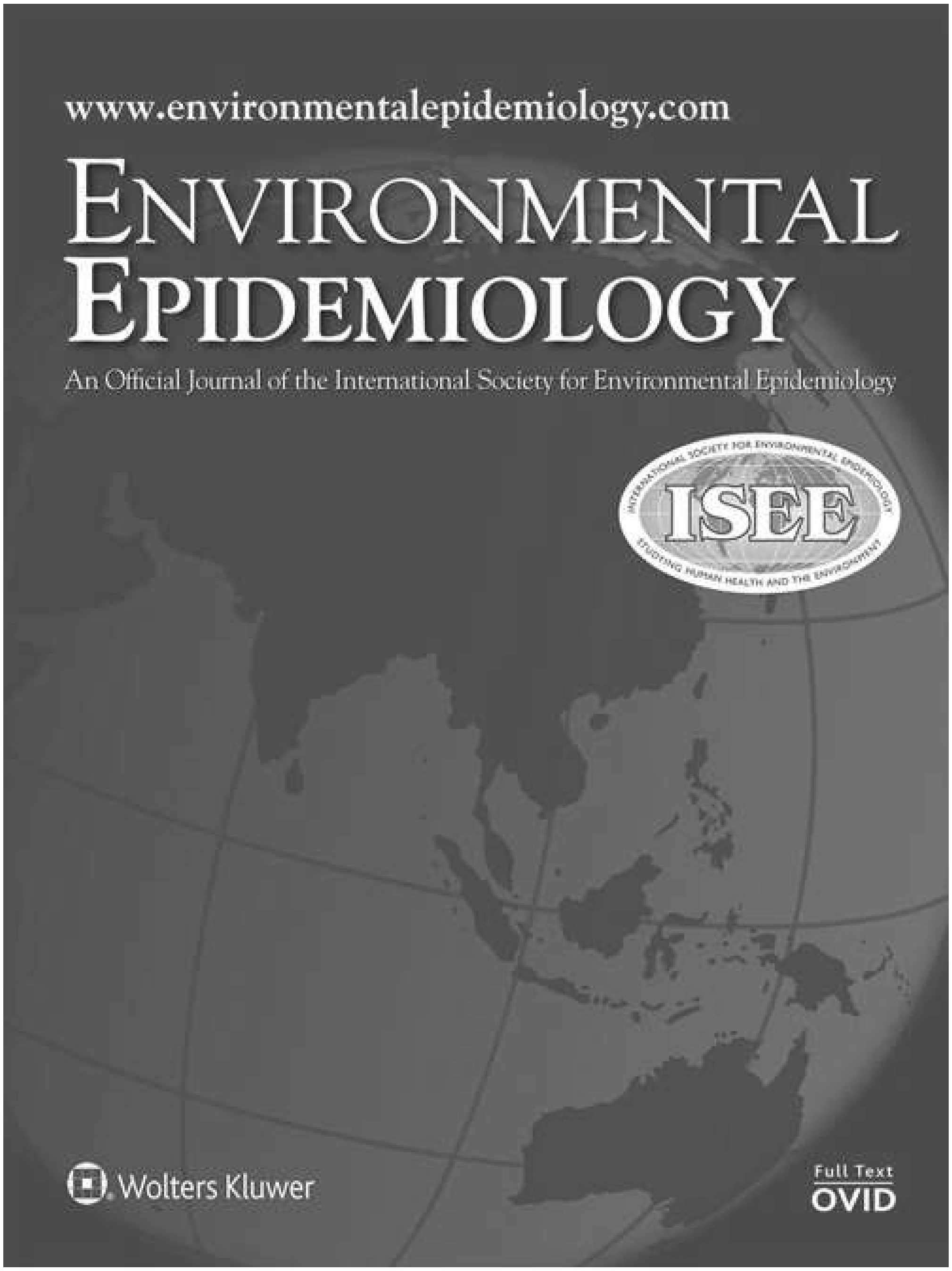
- 

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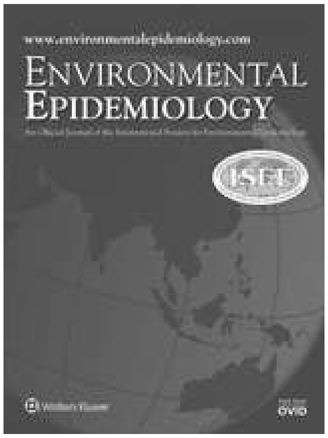
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