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Pollen counts and suicide rates. Association not replicated

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Abstract

Objective: To replicate a previously reported association between pollen counts and county suicide rates in the continental United States, across space and time.

Method: The authors evaluated the relationship between airborne pollen counts and suicide rates in 42 counties of the continental United States, containing a pollen-counting station participating in the Aeroallergen Monitoring Network in the United States (N = 120 076 suicides), considering years' quarter, age group, sex, race, rural/urban location, number of local psychiatrists, and median household income, from 1999 to 2002. The county-level effects were broken into between-county and within-county.

Results: No within-county effects were found. Between-county effects for grass and ragweed pollen on suicide rates lost statistical significance after adjustment for median income, number of psychiatrists, and urban vs. rural location.

Conclusion: Future research is necessary to reappraise the previously reported relationship between pollen levels and suicide rates that may have been driven by socioeconomic confounders.

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Declaration of interest
None.

Keywords

suicide; pollen; allergy; seasonal variation

Introduction

Suicide is a major public health problem with almost a million people dying annually worldwide (1). It is the 10th leading cause of death worldwide (2) and 11th in the United States (US), and ranked as second or third among the younger American population (3).

Recently, two of the authors (PQ, TTP) reported that patients who had suffered from severe allergic illness have higher suicide rates based on a population-based nested case–control design (4). Previously, Timonen et al. (5) documented that, in women, atopic disorders are associated with depression, the most common psychiatric condition associated with suicide (6, 7). Patients with allergic rhinitis experience higher levels of general and mental fatigue, components of a depressive syndrome (8). Furthermore, cross-sectional and prospective studies confirmed that patients with allergy sufferers are more than twice as likely to also suffer from major depression (9, 10).

A peak of suicide in spring has been consistently reported, with less replicated and less robust late summer/early fall peaks (11–14). Seasonality is greater for violent suicides (14, 15) and suicide attempts, in interaction with gender (16) and for suicides in victims with a history of mood disorders (17).

While we lack an understanding of the mechanisms driving the seasonal peaks of suicide, one hypothesis is that seasonal triggers of airway inflammation lead to increased production of mediators of inflammation that reach the brain and impair its effective emotional and behavioral modulation. As pollen is the most important seasonal aeroallergen it has been postulated that airborne pollen may act as an environmental trigger for suicide in vulnerable individuals. Consistent with this hypothesis, as a result of a previous ecological study in the United States, Postolache et al. (2004) reported that relative rates of non-violent suicide in women are increased during the tree pollen peaks in spring (13). Likewise, a greater seasonality in suicide completion is associated with previously diagnosed atopy (18). Recently, a significant association between history of seasonal allergies and suicidality in a nationally representative sample of adults in the United States was also reported (19). A significant spring peak in hospital admissions for allergy-related asthma has also been previously reported (20), with allergic asthma as well as other allergic manifestations (allergic rhinitis in particular) being found associated with suicide completion (4).

Consistent with a possible affective mediation, self-reported mood worsening with high pollen concentration is significantly associated with seasonality of mood (6). Furthermore, in the laboratory, an aeroallergen sensitization and exposure induced increased levels of aggressive and anxiety-like behaviors and altered social interaction in rodents (21, 22) and increased mRNA for certain allergy-related cytokines in the brain of sensitized and allergen-exposed animals (21, 22). Although suicide cannot be modeled in rodents, aggression has been previously proposed as an intermediate phenotype for suicidal behavior (23, 24), and anxiety has also been centrally implicated in suicidality (25–28). Moreover, the increase in mRNA for certain allergy-related cytokines that were found in the brain of pollen-sensitized and pollen-exposed rodents has also been previously found increased in the prefrontal cortex in suicide victims (29).

To attempt to replicate the results of our previous study based on the 4-year interval 1995–1998 (13) in the subsequent 4-year interval 1999–2002, with adjustment for previously unmeasured confounders, we tested the hypothesis of positive association between pollen counts trees, grass, and ragweed, and quarterly county suicide rates in the continental United States.

Aims of the study

The goal of this research is to investigate the hypothesized association between pollen counts and suicide rates across the United States. Both between-county and within-county (over time) associations were estimated. Differences between counties can be confounded with many unmeasured factors ranging from population density, access to quality mental health care, socioeconomic factors, etc. Data within counties related changes to pollen counts to changes in suicide rates within the same county and, therefore, adjust for between-county confounders. Our analysis separated the between-county and within-county effects, so that our statistical inferences could focus on the association between changes in pollen counts and changes in suicide rates in ecologically distinct areas and are, therefore, not confounded by measured and unmeasured differences in locations. We used counties because this is the smallest ecological unit for which suicide rates are reported by the Centers for Disease Control and Prevention.

Material and methods

Data source

Monthly suicide-rate data were derived from state vital record systems based on local death certificate registries for the years 1999–2002 for each US county. Suicide is coded as (*U03, X60–X84, Y87.0) based on the 10th Revision, Death Age-adjusted International Classification of Diseases, 1992. Suicide rates were broken down by year (1999–2002), quarter of the year (1 = January–March, 2 = April–June, 3 = July–September, 4 = October–December), age group (1 = 0–14, 2 = 15–24, 3 = 25–44, 4 = 45–64, 5 = 65≤), sex (1 = male, 2 = female), and race (1 = black, 2 = non-black) for 42 locations. Each location had 4×4×5×2×2 = 320 entries in the data set.

Exposure variables of interest were pollen counts of three types (tress, grasses and ragweed). UMass SPHHS- Aerobiology Lab categorized daily pollen counts as follows (Table 1).

From these data, the daily pollen counts were approximated as the midpoint of the interval; for example, category ‘Moderate’ for tree pollen is translated as (15 + 90)/2 = 52.5 m^3. The category of ‘No Sample’ was treated as missing.

Using the daily values of pollen counts calculated as earlier, we created two variables ‘average pollen counts’ and ‘deviation from average’ for each pollen type: $t1$ = average tree pollen count for the period 1999–2002 and *d_t*1 = deviation from the average tree pollen count for each quarter for the period 1999–2002. For grass and ragweed pollen, *g*1 and *d_g*1, and *r*1 and *d_r*1 are similarly created respectively. When included simultaneously in the Poisson regression model, the mean pollen counts (*t*1, *g*1, and *d*1) describe between-county effects and the deviations from the mean (*d_t*1, *d_g*1, and *d_r*1) describe within-county effects (i.e., the relationship between changes in pollen counts from quarter to quarter and corresponding changes in suicide rate).

Potential confounders adjusted for one or more of the statistical models included year's quarter, age group, sex, race, rural/urban location (1 = metropolitan, 2 = non-metropolitan), number of local psychiatrists, and log(median household income).

Statistical analysis

To relate pollen count and suicide rate, we estimated the log-linear Poisson model:

$$\log(\text{suicide}_{ij}) = \log(\text{population}_{ij}) + \mathbf{X}_{ij}{}'\beta$$

for $i = 1, 2, \ldots, 42$ locations and $j = 1, 2, \ldots, 320$ within-county measurements, **X** is the vector of covariates and β is the corresponding coefficient vector. …

The quantity $\log(\text{population}_{ij})$ is the offset. Each location has four different levels of population for 1999–2002. Using the generalized estimating equations (GEE) methodology, a working correlation must be specified. Because there are 320 data points in each location, the unrestricted model has too many correlation parameters, so we used an exchangeable correlation structure (i.e., a constant correlational -structure).

We examined whether the relationship between pollen counts and suicides remained stable as we adjusted the model for potential confounders in a sequential manner. The following three models were estimated.

i. Model 1 has only exposure (pollen) variables:

$$\log(\text{suicide rate}) = \alpha + \beta_1 t_1 + \beta_2 d\_t_1 + \beta_3 g_1 + \beta_4 d\_g_1 + \beta_5 r_1 + \beta_6 d\_r_1;$$

ii. Model 2 adds quarter and within-county effects to Model 1:

$$\log(\text{suicide rate}) = \text{Model 1} + \beta_7 \text{quarter} + \beta_8 \text{agegrpx} + \beta_9 \text{sex} + \beta_{10} \text{race};$$

iii. Model 3 adds county-level (i.e., between-county) characteristics to Model 2:

$$\log(\text{suicide rate}) = \text{Model 2} + \beta_{11} \text{rural/urban} + \beta_{12} \text{psych} + \beta_{13} \log(\text{income});$$

Proc Genmod of sas (SAS Institute Inc., Cary, North Carolina, USA) was used to fit these models.

Results

Table 2 (Model 1) presents results of the simplest model that includes within-county and between-county pollen effects.

Table 2 reveals significant between-county effects of grass and ragweed, but no significant effects of tree pollen, and no significant within-county associations.

Table 3 (Model 2) presents results of the model that adds within-county covariates of time, age, sex, and race to Model 1.

Table 3 reveals that the between-county effects of ragweed and grass are quite similar to what was observed for Model 1 that did not include within-county covariates. The covariates of quarter, age, sex, and race were all significant and in the expected directions.

Table 4 (Model 3) presents results of the model that adds between-county covariates of urban/rural location, number of local psychiatrists, and median income to Model 2.

Table 4 reveals that when we adjust for the three between-county effects, none of the pollen effects, either within-county or between-county, are statistically significant. The covariates of urban/rural location, number of local psychiatrists, and median income are all statistically significant.

No significant within-county effects (d_t1, g_t1, d_r1) were found in any of the three statistical models.

We estimated the same model (model 3) using two total pollen count variables: total pollen count (pol_sum = $t1 + g1 + r1$) and its deviational form from average (dev_pol = $d\_t1 + d\_g1 + d\_r1$). As shown in Table 5, the coefficients of the new two total variables are insignificant as they were before and effects of the covariates are unchanged.

Discussion

We tested the hypothesis of a positive ecological association between pollen counts and suicide rates as suggested by Postolache et al. (2004) in women in the United States (13), and recently confirmed in both genders in Denmark (31). This hypothesis received further indirect support from recent reports on a relationship between allergy and suicide (4), and an association between intranasal corticosteroids, medications that are used to treat allergic rhinitis, and lower suicide rates (32), as well as the relationship between seasonal allergies and suicidal ideation (19). We did not confirm the results of our previous studies (13, 31) as we found no significant within-county association. Moreover, while there was evidence of a between-county association for grass and ragweed, these appear to be the result of previously unmeasured confounding by certain socioeconomic variables including the number of local psychiatrists, urban–rural environment and income.

How could this divergence be explained? First, by differences in temporal and spatial resolutions between this study and the previous studies. In Postolache et al. (13), we evaluated the relative rates of suicide using temporal windows of high pollen approach. We selected three periods (pre-peak, peak, and postpeak) for each allergen in time unit of a quarter month (7.6 days) in the USA and Canada and discarded all the other intervals. Second, the characteristics of pollen release have to be considered. Pollen release is periodic, with separation by zero pollen periods, and day-to-day variation can be massive. Threshold and ceiling effects are likely. Third, what really matters are the immunological mediators that reach the human brain from the airways, or produced *in situ* by brain cells such as glia or even neurons (21, 22, 29), not airborne pollen *per se*. Specifically, airborne pollen induces allergic reactions in sensitized individuals that can result, via molecular and cellular mediators of inflammation, in changes in brain function leading to affective and behavioral dysregulation. However, this relationship could be far from linear. There may be certain thresholds at which pollen count cause qualitatively different reactions. Mild elevations in pollen counts might not result in behavioral changes, and thus not be associated with elevated suicide rates (31). Fourth, some factors may dampen or antagonize the effects of exposure to allergens and allergic illnesses. An interaction of allergic illness with diagnosis, follow up and treatment of mood disorders is suggested, as, in Denmark, allergy patients with history of hospitalization for mood disorder were less, rather than more, likely to commit suicide in contrast to patients without history of hospitalization for mood disorders (4). By extension, it might be possible that if patients have not been under psychiatric care for mood disorders, allergy may elevate risk for suicide, while if the patient has been under psychiatric care for mood disorders, allergy may be protective. One possible explanation of this interaction is the reversal by psychiatric treatment of the pro-suicidal effects of allergic inflammation, in addition to potential protective effects of certain allergy treatments. Specifically, we have recently reported that prescription volume of intranasal corticosteroids, medications known to reduce local production of inflammatory mediators, is associated with decreased rates of suicide (32). An increased density of local psychiatrists could flatten the association between allergy and suicide by an increased diagnosis and treatment of mood disorders and a more sophisticated approach to identifying and addressing vulnerabilities and triggers of suicide.

Suicide results from a complex interaction of many factors including biological predispositions, a psychiatric illness, stressful events, and socioeconomic factors (33, 34). Gibbons et al. (2005) previously reported higher suicide rates in association with less available mental health care, rural location, and lower per capita average income in the United States (35). Therefore, these results raise the possibility that the previously reported relationship between pollen level and suicide rates is not causal possibly generated by socioeconomic confounders.

Regarding the between-county effects, access to mental health care with respect to number of local psychiatrists and household income is a contributing factor to suicide rate. Healthcare access in general is important for suicide prevention (36). Tondo et al. (37) found a strong negative correlation between state suicide rate in the United States and the number of psychiatrists per 100 000 population. They also found that household income, as one of the indices to indicate the level of accessibility to the healthcare systems, is negatively associated with suicide rate. With increasing levels of household income, an individual is more likely to consult a mental health provider to obtain appropriate healthcare services (38, 39). On the contrary, low income, a rural environment, and inadequate health care may lead to undertreated allergies and undertreated mood disorders; and non-specifically an increased risk for suicide.

The results of this study have to be interpreted cautiously, as ecological models are based on the information measured at the aggregate level, and thus provide information on groups of individuals in geographically determined area. Inferences regarding individual-level associations are not supported. The lack of adjustment for confounders in the previous US study (13) may account for differences in outcome. However, in our recent study in Denmark that confirmed the relationship using an individually linked, population-based approach, accounted for several socioeconomic variables, the rurality was relatively constant over time and the availability of psychiatric care was relatively homogenous (31).

Unmeasured factors that vary periodically and may alter the inflammation mediating mechanisms implicated in our hypothesis could explain difference of study outcome. One such factor could be the upper respiratory viral infections – influenza B IgG antibody titers, for instance, have been associated with suicide attempts (40). Additionally, common neurotropic infections with *Toxoplasma gondii* may be associated with suicide completions (41) and attempts (42–44). Reduced atopic sensitization has been described in environments with high microbial burden, including *T. gondii* (45). The immune responses to *T. gondii* partially overlap with and partially compete with immune responses that mediate allergic reactions. Moreover, a confounding effect of rural environment and poor socioeconomic conditions may in fact be mediated by low-grade immune activation induced by environmental microbial burden. Specifically, *T. gondii* has been designated by the Centers for Disease Control and Prevention as a neglected infection of poverty (46), and considering the high prevalence of the chronic latent neurotropic infestation with the parasite may represent an important source of unmeasured confounding in our model. Finally, socioeconomic status and the urban vs. rural environment are associated with differential exposure to particulate air pollutants that have been recently associated with increased suicide risk (47). These pollutants have an adjuvant effect on allergic inflammation, increasing prevalence and morbidity of allergy (48). As pollutant exposure was not measured, differences in exposure could have explained divergent results between studies.

Our hypothesis was not confirmed, as suicide rates appeared to be independent of overall pollen levels and even more importantly, changes in pollen levels over time. Instead, we found that adjusting for availability of psychiatric care and median income rendered statistically insignificant any apparent between-county relationship of suicide rates to pollen levels. The current report does not support that seasonal aeroallergen exposure contributes to the highly replicated seasonal peaks in suicides, across countries, continents, and hemispheres (49). Adjusting for number of psychiatrists, rural vs. urban environment, and income, as well as for measures of pollution and, if possible, neurotropic pathogen exposure is strongly recommended for future work. The allergens-as-suicide-triggers hypothesis, at least for those individuals with dual vulnerability for allergy and suicidal behavior, should not be, however hastily rejected, considering inherent limitations of the current ecological approach and the potential to prematurely lose a promising lead to identifying modifiable suicide risk factors.

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Significant outcomes

- Adjusting for previously unmeasured confounders, we failed to replicate the results of our previous study based on the four-year interval 1995–1998, in the subsequent four-year interval 1999–2002.
- Airborne pollen counts were not significantly associated with suicide rates after adjustment for certain confounders such as rural vs. urban location, income, and number of local psychiatrists. If not controlled for, these factors may generate spurious environmental associations with suicide.

Limitations

- Our results are based on an ecological approach; thus, inferences regarding individual-level associations are not supported.

Table 1.

The category of pollen counts

	Pollen grains per cubic meter of air		
Category	**Tree**	**Grass**	**Ragweed**
No sample	–	–	–
Absent	0	0	0
Low	0–15	0–5	0–10
Moderate	15–90	5–20	10–50
High	90–1500	20–200	50–500
Very high	>1500	>200	>500

Table 2.

Result of the simplest model that includes within-county and between-county pollen effects (unadjusted estimation)

	Estimate	SE	95% CI	*Z*	Pr > |*Z*|
Intercept	−10.795	0.1846	−11.1569, −10.4331	−58.46	<0.0001
Average tree pollen count	−0.0003	0.0009	−0.0020, 0.0015	−0.31	0.7595
Deviation from average tree pollen count	0.0001	0.0001	−0.0000, 0.0002	1.73	0.0833
Average grass pollen count	0.0210	0.0066	0.0080, 0.0340	3.17	0.0015
Deviation from average grass pollen count	0.0008	0.0008	−0.0007, 0.0023	1.06	0.2879
Average ragweed pollen count	0.0053	0.0025	0.0005, 0.0102	2.15	0.0318
Deviation from average ragweed pollen count	0.0002	0.0004	−0.0005, 0.0009	0.53	0.5977

SE, standard error; CI, confidence interval.

Table 3.

Result of the second model controlling for within-county covariates

	Estimate	SE	95% CI	*Z*	Pr > |*Z*|
Intercept	−11.165	0.1301	−11.420, −10.910	−85.84	<0.0001
Period					
January–March	0.0991	0.0397	0.0213, 0.1768	2.50	0.0125
April–June	0.1506	0.0324	0.0871, 0.2141	4.65	<0.0001
July–September	0.0441	0.0222	0.0006, 0.0876	1.99	0.0469
October–December (reference)					
Age					
0–14	−3.8259	0.1738	−4.1667, −3.4852	−22.01	<0.0001
15–24	−0.7430	0.1172	−0.9728, −0.5133	−6.34	<0.0001
25–44	−0.3699	0.0919	−0.5500, −0.1898	−4.03	<0.0001
45–64	−0.2549	0.0576	−0.3677, −0.1420	−4.43	<0.0001
65 or more (reference)					
Sex					
Male	1.4150	0.0237	1.3685, 1.4614	59.73	<0.0001
Female (reference)					
Race					
Black	−0.4003	0.0536	−0.5053, −0.2953	−7.47	<0.0001
Non-black (reference)					
Average tree pollen count	−0.0004	0.0007	−0.0018, 0.0010	−0.58	0.5649
Deviation from average tree pollen count	−0.0001	0.0001	−0.0002, 0.0001	−0.82	0.4144
Average grass pollen count	0.0157	0.0058	0.0044, 0.0271	2.71	0.0067
Deviation from average grass pollen count	−0.0008	0.0009	−0.0026, 0.0010	−0.88	0.3811
Average ragweed pollen count	0.0053	0.0024	0.0006, 0.0101	2.20	0.0276
Deviation from average ragweed pollen count	0.0003	0.0004	−0.0006, 0.0012	0.63	0.5265

SE, standard error; CI, confidence interval.

Table 4.

Result of the third model controlling for both within-county and between-county covariates

	Estimate	SE	95% CI	*Z*	Pr > |*Z*||
Intercept	−2.2071	1.5834	−5.3105, 0.8962	−1.39	0.1633
Period					
January–March	0.0895	0.0393	0.0124, 0.1666	2.27	0.0230
April–June	0.1390	0.0325	0.0753, 0.2026	4.28	<0.0001
July–September	0.0442	0.0224	0.0004, 0.0881	1.98	0.0481
October–December (reference)					
Age					
0–14	−3.8157	0.1819	−4.1723, −3.4592	−20.98	<0.0001
15–24	−0.7259	0.1192	−0.9594, −0.4924	−6.09	<0.0001
25–44	−0.3433	0.0955	−0.5303, −0.1562	−3.60	0.0003
45–64	−0.2386	0.0591	−0.3546, −0.1227	−4.04	<0.0001
65 or more (reference)					
Sex					
Male	1.4172	0.0236	1.3709, 1.4635	59.97	<0.0001
Female (reference)					
Race					
Black	−0.4349	0.0578	−0.5482, −0.3217	−7.53	<0.0001
Non-black (reference)					
Area					
Urban	0.2825	0.0684	0.1485, 0.4165	4.13	<0.0001
Rural (reference)					
Number of psychiatrists	−0.0001	0.0000	−0.0001, −0.0000	−5.88	<0.0001
Median household income (log-transformed)	−0.8314	0.1491	−1.1237, −0.5391	−5.58	<0.0001
Average tree pollen count	−0.0005	0.0006	−0.0016, 0.0006	−0.88	0.3808
Deviation from average tree pollen count	−0.0000	0.0001	−0.0002, 0.0001	−0.40	0.6922
Average grass pollen count	0.0042	0.0052	−0.0059, 0.0143	0.81	0.4173
Deviation from average grass pollen count	−0.0007	0.0009	−0.0025, 0.0011	−0.79	0.4268
Average ragweed pollen count	−0.0018	0.0024	−0.0065, 0.0030	−0.73	0.4682

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	Estimate	SE	95% CI	Z	Pr > |Z|
Deviation from average ragweed pollen count	0.0002	0.0005	−0.0007, 0.0012	0.48	0.6278

SE, standard error; CI, confidence interval.

Table 5.

Result of estimating the third model using two total pollen count variables: total pollen count and its deviational form from average

	Estimate	SE	95% CI	Z	Pr > |Z|
Intercept	−2.2676	1.3362	−4.8866, 0.3513	−1.70	0.0897
Period					
January–March	0.0919	0.0392	0.0152, 0.1686	2.35	0.0189
April–June	0.1257	0.0335	0.0600, 0.1914	3.75	0.0002
July–September	0.0473	0.0228	0.0026, 0.0920	2.08	0.0379
October–December (reference)					
Age					
0–14	−3.8124	0.1831	−4.1712, −3.4537	−20.83	<0.0001
15–24	−0.7251	0.1191	−0.9586, −0.4916	−6.09	<0.0001
25–44	−0.3428	0.0953	−0.5295, −0.1560	−3.60	0.0003
45–64	−0.2380	0.0591	−0.3538, −0.1222	−4.03	<0.0001
65 or more (reference)					
Sex					
Male	1.4167	0.0238	1.3702, 1.4633	59.64	<0.0001
Female (reference)					
Race					
Black	−0.4324	0.0569	−0.5440, −0.3207	−7.59	<0.0001
Non-black (reference)					
Area					
Urban					
Rural (reference)	0.2998	0.0675	0.1676, 0.4320	4.44	<0.0001
Number of psychiatrists	−0.0001	0.0000	−0.0001, −0.0001	−8.65	<0.0001
Median household income (log-transformed)	−0.8226	0.1248	−1.0672, −0.5779	−6.59	<0.0001
Total pollen count*	−0.0006	0.0005	−0.0015, 0.0004	−1.19	0.2340
Deviation from average†	−0.0000	0.0001	−0.0002, 0.0001	−0.65	0.5136

SE, standard error; CI, confidence interval.

*Total pollen count (pol_sum = $t1 + g1 + r1$).

†Deviation from average (dev_pol = *d_t*1 + *d_g*1 + *d_r*1).