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Data Availability Statement: Data contain the identifiable information of study participants, and can only be accessed by study team members based on the approval of the Institutional Review Board at Washington University School of Medicine. Any requests for data need to be discussed with Dr. Andrew Heath, the PI of the MOAFTS cohort. Dr. Heath's contact information is listed in the title page of the manuscript.

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**RESEARCH ARTICLE** 

# Geographic Variation in Maternal Smoking during Pregnancy in the Missouri Adolescent Female Twin Study (MOAFTS)

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# Abstract

## Objective

Despite well-known adverse health effects of maternal smoking during pregnancy (MSP), it is still unclear if MSP varies geographically and if neighborhood socioeconomic deprivation (SED) plays an important role in MSP. This study aims to investigate small-area geographic variation in MSP and examine the association of SED with MSP.

## Methods

The Missouri Adolescent Female Twin Study (MOAFTS) is a cohort study of female like-sex twins born in Missouri to Missouri-resident parents during 1975–1985. Biological mothers completed a baseline interview in 1995–1998 and reported MSP with the twins. Residential address of the mother at birth was geocoded. We developed a census tract-level SED index using a common factor approach based on 21 area-level socioeconomic variables from the 1980 Census data. Multilevel logistic regressions estimated geographic heterogeneity (random effect) in MSP and the odds ratios (ORs, fixed effects) of neighborhood SED associated with MSP.

## Results

Of 1658 MOAFTS mothers, 35.2% reported any MSP and 21.9% reported MSP beyond the first trimester. Neighborhood SED was associated with any MSP (the highest vs. the lowest quartile: OR = 1.90, 95% confidence interval [CI] = 1.40-2.57,  $P_{trend} < 0.001$ ) and MSP beyond the first trimester (OR = 1.98, 95% CI = 1.38-2.85,  $P_{trend} = 0.002$ ) in unadjusted analyses. After adjusting for individual covariates (demographics, socioeconomic



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conditions, alcohol use, and parents' cohabitation), neighborhood SED was not associated with MSP, but geographic variation still persisted in MSP (variance = 0.41, P = 0.003) and in MSP beyond the first trimester (variance = 0.82, P < 0.001).

#### Conclusions

Neighborhood SED was associated with MSP in unadjusted analyses but this association could be explained by individual socioeconomic conditions. Nonetheless, significant geographic variation in MSP persisted and was not accounted for by differences in neighborhood SED. To develop effective interventions to reduce MSP, further studies are necessary to explore underlying reasons for its geographic variation.

#### Introduction

Cigarette smoking is an established risk factor for multiple chronic diseases and the leading preventable cause of mortality in the United States [1]. Excess mortality can be attributed to more than 21 common smoking-relevant diseases, including cancer, cardiovascular diseases, and respiratory diseases [2]. Tobacco control is the highest priority for advancing population health [3], which includes maternal smoking during pregnancy (MSP). In addition to hazards to pregnant women themselves, MSP could increase risks of adverse prenatal development [4], preterm birth [5], disruptive behaviors [6-9], socio-psychiatric disorders [10-13], obesity [14-16], and other diseases [17, 18] in their offspring. The U.S. CDC reported that the prevalence of MSP remained relatively stable between 10% and 15% during 2000–2011 in nine states included in the Pregnancy Risk Assessment Monitoring System (PRAMS) [19], while smoking in the general U.S. population has declined [20].

Previous studies have reported individual-level risk factors for MSP [21-31]. While some studies reported that MSP was associated with area-level characteristics [32-35], no previous study has assessed the extent of geographic variation in this behavior. It is also unclear if potential geographic variation in MSP can be attributed to some specific area-level characteristics, such as neighborhood socioeconomic deprivation and neighborhood tobacco environment. Such research could aid in the development of more effective public health interventions to reduce MSP. For example, public health officials could maximize the benefit of public health interventions by targeting specific geographic areas and reasons for elevated MSP prevalence in these areas.

In the current study, we applied a multilevel approach to examine the extent of geographic variation and the role of small-area socioeconomic deprivation (SED) in MSP using a population-representative sample of Missouri female twins.

## **Materials and Methods**

#### **Study Population**

The Missouri Adolescent Female Twin Study (MOAFTS) is a prospective cohort study of female like-sex twins born in Missouri to Missouri-resident parents from July 1, 1975 through June 30, 1985. Monozygotic and dizygotic twins were ascertained through Missouri birth records. Study twins were recruited using a cohort-sequential design [36], and parent interviews were completed in 1995–1998. The twin cohort has been followed prospectively since median age 15, for about 20 years, through seven waves of data collection, to examine the development

of their alcohol and tobacco use, other health behaviors and social/psychiatric disorders. In the current study, using the MOAFTS parent interview data (n = 1658), we investigated the extent of geographic variation and the role of neighborhood SED in MSP. The study, including the consent procedure, was approved by the Institutional Review Board at Washington University School of Medicine. All study participants provided their written informed consent to participant in this study.

#### Study outcomes

Mothers who reported lifetime smoking of at least 100 cigarettes were classified as regular smokers. All regular smokers were asked 1) whether they had smoked during their pregnancy with the twins, including before they realized they were pregnant; and 2) for how many weeks or months they had smoked. We coded a) whether a mother had smoked during the first trimester, and b) whether she had smoked beyond the first trimester (which in most cases meant smoking throughout the pregnancy) to reflect the chronicity of MSP.

#### Measures

**Neighborhood socioeconomic deprivation (SED) index.** The residential addresses from birth records were geocoded to obtain their coordinates and corresponding residential census tract using ArcGIS (version 10.2.2, ESRI Inc., Redland, CA). In all, 798 census tracts were included in the study sample, which study participants ranged from 1 to 9 (median: 2). To explore if geographic variation in MSP can be attributed to specific neighborhood characteristics, we assessed neighborhood socioeconomic deprivation, a commonly used neighborhood measure of area-level characteristic.

Since the twins were born during 1975–1985, we used 1980 Missouri Census data to develop a census tract-level statewide SED index. Similar to our previous study [37], we selected multiple socioeconomic and demographic variables in six domains, including 1) education (the percentage of population with less than high school education); 2) employment and occupation (the percentage of population unemployed, the percentage of population with working class); 3) housing conditions (the percentage of households without ownership, the percentage of households with vacancy, the percentage of households with > = 1 person per room, the percentage of households in poverty, the percentage of households female-headed with dependent children, the percentage of households with family income less than \$30,000, the percentage of households with public assistance, the percentage of households without a car, the percentage of households without a phone, the percentage of households without plumbing, the percentage of households without a kitchen); 4) poverty and income (the percentage of population below the federal poverty line, income disparity); 5) racial composition (the percentage of non-Hispanic African American population, the percentage of Hispanic population); and 6) residential stability (the percentage of population aged 65 or above, the percentage of population living in the same residence in the past five years). We applied a principal component common factor analysis approach to examine the structure of these socioeconomic indicators, and selected seven variables that substantially contributed to the total variation of socioeconomic variables, including the percentage of population unemployed, the percentage of households with at least one person per room, the percentage of households female-headed with dependent children, the percentage of households with public assistance, the percentage of households without a car, the percentage of population below the federal poverty line, and the percentage of non-Hispanic African American population. These seven variables account for 40.5% of overall variation and have high internal consistency (Cronbach alpha = 0.92). After standardization and weighting by factor loading coefficients, these seven variables were summed as the

final SED index. The SED index was categorized into quartiles based on the number of study participants in the census tracts in order to examine nonlinear trends in multilevel analysis. The highest SED quartile represents the most deprived category of neighborhood socioeconomic conditions.

**Individual covariates.** Three groups of individual characteristics during the pregnancy were considered as potential confounders to adjust the multilevel models, including 1) demographics (age and race), 2) individual socioeconomic conditions (mother's education, father's education, and family income), and 3) maternal alcohol use (alcohol drinking during pregnancy, and maternal history of alcohol dependence) and biological parents' cohabitation. These individual characteristics were chosen based on previous literature. Mother's age at twin birth was categorized into three groups: <18 years, 18–29 years, and >30 years. Race was dichotomized into White or African American. Both mother's education and father's education were categorized as <12 or >13 years. Family income was dichotomized at the cutoff of \$45,000 per year based on the income distribution in the study population. The parents' cohabitation was grouped as yes or no. Maternal alcohol dependence was assessed according to Diagnostic and Statistical Manual-IV (DSM-IV) criteria, using a telephone adaptation of the Semi-Structured Assessment for the Genetic of Alcoholism (SSAGA) diagnostic interview [38]. Alcohol dependence was defined as endorsing three or more of seven diagnostic criteria in the same 12-month period, lifetime. Both Alcohol use during pregnancy and maternal history of alcohol dependence were dichotomized as yes or no.

## Statistical analysis

Chi-square tests were used to examine potential differences in individual characteristics across quartiles of the neighborhood SED index. We applied a generalized linear mixed modeling approach to fit the multilevel logistic regression to quantify the geographic variation in and the association of neighborhood SED with MSP. The trend of SED association was tested by using the medians of each SED quartile in the models.

To examine if groups of individual covariates could explain potential geographic variation and the role of neighborhood SED, we fit four multivariate models adjusting for any one or all three groups of individual characteristics. Geographic variation in MSP was quantified using census tract-level variance from the fitted multilevel model. Since this variance has no meaningful unit and is hard to interpret by itself, we computed two heterogeneity measures, median odds ratio (MOR) and interquartile odds ratio (IqOR) to estimate the geographic heterogeneity in MSP based on commonly used odds ratios [39, 40]. Calculation of these two measures is described elsewhere [39, 40]. The fit of the multilevel models was based on the scaled deviance, with lower deviance indicating better fit [41]. The data management and statistical analysis were conducted in SAS System (version 9.3, SAS Institute Inc., Cary, North Carolina).

#### Results

Of 1685 mothers with twins, 584 (35.2%) smoked during pregnancy, and 363 (21.9%) smoked beyond the first trimester of pregnancy. Mothers living in neighborhoods with higher SED were more likely to be younger, African American, with less education and lower family income, not cohabitating with the father of the twins, and with a personal history of alcohol dependence compared to those in neighborhoods with lower SED (Table 1).

#### MSP

The prevalence of MSP was significantly higher for mothers residing in neighborhoods with the highest SED quartile than those in neighborhoods with the lowest SED quartile (40.5% vs.



Table 1. Characteristics of mothers of twins	= 1658) from the Missouri Adolescent Female Twin S	Study (MOAFTS).
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Variable	Neighborhood Socioeconomic Deprivation (SED) Quartile				
	1st (Lowest SED) (n = 414)	2 <sup>nd</sup> (n = 422)	3 <sup>rd</sup> (n = 405)	4th (Highest SED) (n = 417)	
Smoking during pregnancy (MSP)					< 0.001
Yes	111 (26.81)	152 (36.02)	152 (37.53)	169 (40.53)	
No	303 (73.19)	270 (63.98)	253 (62.47)	248 (59.47)	
MSP beyond 1 <sup>st</sup> trimester					0.002
Yes	64 (15.46)	92 (21.80)	102 (25.19)	105 (25.18)	
No	350 (84.54)	330 (78.20)	303 (74.81)	312 (74.82)	
Age at twin birth					<0.001
< 18 Years	5 (1.21)	12 (2.84)	19 (4.69)	27 (6.47)	
18–29 Years	276 (66.99)	324 (76.78)	320 (79.01)	323 (77.46)	
30+ Years	131 (31.80)	86 (20.38)	66 (16.30)	67 (16.07)	
Missing	2	0	0	0	
Race					<0.001
White	408 (98.55)	403 (95.50)	388 (95.80)	249 (59.71)	
AA	6 (1.45)	19 (4.50)	17 (4.20)	168 (40.29)	
Education (Mom)					<0.001
< = 12 years	15 (3.62)	46 (10.90)	47 (11.60)	71 (17.03)	
> = 13 years	348 (84.06)	311 (73.70)	295 (72.84)	267 (64.03)	
Unknown	51 (12.32)	65 (15.40)	63 (15.56)	79 (18.94)	
Education (Dad)	· · ·	. ,	. ,	, , , , , , , , , , , , , , , , , , ,	<0.001
< = 12 years	15 (3.62)	33 (7.82)	49 (12.10)	61 (14.63)	
> = 13 years	345 (83.33)	322 (76.30)	280 (69.14)	249 (59.71)	
Unknown	54 (13.04)	67 (15.88)	76 (18.77)	107 (25.66)	
Household income		. ,	. ,		<0.001
< = \$45,000	168 (40.58)	247 (58.53)	253 (62.47)	324 (77.70)	
> \$45,000	233 (56.28)	167 (39.57)	142 (35.06)	89 (21.34)	
Unknown	13 (3.14)	8 (1.90)	10 (2.47)	4 (0.96)	
Parents' cohabitation	× ,	~ /	· · · · ·	, , , , , , , , , , , , , , , , , , ,	<0.001
Yes	358 (86.47)	353 (83.65)	327 (80.74)	274 (65.71)	
No	7 (1.69)	19 (4.50)	22 (5.43)	70 (16.79)	
Missing	49 (11.84)	50 (11.85)	56 (13.83)	73 (17.51)	
Alcohol use during pregnancy		~ /	, , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,	0.211
Yes	148 (35.75)	125 (29.62)	126 (31.11)	114 (27.34)	
No	264 (63.77)	293 (69.43)	276 (68.15)	298 (71.46)	
Unknown	2 (0.48)	4 (0.95)	3 (0.74)	5 (1.20)	
Maternal history of alcohol dependence	()	(3)			0.023
Yes	12 (2.90)	16 (3.79)	26 (6.42)	28 (6.71)	
No	402 (97.10)	406 (96.21)	379 (93.58)	389 (93.29)	

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26.8%, P < 0.001) (Table 1). Mothers who lived in neighborhoods with the highest SED quartile were more likely to smoke during pregnancy (Table 2 Model 1: odds ratio [OR] = 1.90, 95% confidence interval [CI] = 1.40–2.57,  $P_{\text{trend}} < 0.001$ ) compared with those who lived in neighborhoods with the lowest SED quartile. The associations remained after adjusting for age and race (Model 2) or for parents' cohabitation and maternal alcohol use (Model 4), but not after

Table 2. Geographic variation in and the association of neighborhood socioeconomic deprivation with maternal smoking during pregnancy (MSP) (MOR, median odds ratio; IqOR, interquartile odds ratio). Model 1 was not adjusted for any individual characteristics; Model 2 was adjusted for age and race; Model 3 was adjusted for individual socioeconomic conditions (mom's education, dad's education, and household income); Model 4 was adjusted for biological parents' cohabitation and alcohol use (maternal alcohol use during pregnancy, and maternal history of alcohol dependence); Model 5 was adjusted for all individual covariates.

	Model 1	Model 2	Model 3	Model 4	Model 5
MSP					
Fixed effects	OR (95% CI)				
Socioeconomic Deprivation					
1st (least)	1.00	1.00	1.00	1.00	1.00
2 <sup>nd</sup>	1.54 (1.12–2.11)	1.52 (1.10–2.08)	1.26 (0.91–1.76)	1.63 (1.18–2.25)	1.31 (0.93–1.85)
3 <sup>rd</sup>	1.65 (1.21–2.25)	1.62 (1.18–2.21)	1.24 (0.89–1.72)	1.67 (1.21–2.29)	1.26 (0.89–1.77)
4 <sup>th</sup> (most)	1.90 (1.40–2.57)	1.87 (1.34–2.63)	1.18 (0.85–1.65)	1.88 (1.37–2.60)	1.30 (0.90–1.89)
P for trend	<0.001	0.002	0.621	0.002	0.317
Random effects	Index	Index	Index	Index	Index
Variance	0.26 (P = 0.021)	0.25 (P = 0.023)	0.36 (P = 0.005)	0.27 (P = 0.021)	0.41 (P = 0.003)
MOR	1.62	1.61	1.78	1.65	1.84
IqOR	3.21	3.18	3.99	3.33	4.37
Scaled Deviance	2043	2038	1937	1973	1863
MSP beyond 1 <sup>st</sup> trimester					
Fixed effects	OR (95% CI)				
Socioeconomic Deprivation					
1st	1.00	1.00	1.00	1.00	1.00
2nd	1.54 (1.05–2.25)	1.56 (1.07–2.28)	1.22 (0.82–1.82)	1.56 (1.07–2.28)	1.26 (0.84–1.88)
3rd	1.98 (1.37–2.85)	2.00 (1.38-2.91)	1.46 (0.99–2.16)	1.91 (1.32–2.76)	1.49 (1.00–2.20)
4th	1.98 (1.38–2.85)	2.22 (1.49-3.29)	1.18 (0.79–1.75)	1.85 (1.27–2.70)	1.40 (0.91–2.15)
P for trend	0.002	<0.001	0.758	0.009	0.202
Random effects	Index	Index	Index	Index	Index
Variance	0.65 (P<0.001)	0.66 (P<0.001)	0.89 (P<0.001)	0.64 (P<0.001)	0.82 (P<0.001)
MOR	2.16	2.17	2.45	2.14	2.37
IqOR	6.40	6.46	8.71	6.28	8.03
Scaled Deviance	1745	1737	1673	1713	1629

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adjusting for individual socioeconomic conditions (Model 3) or for all three groups of individual covariates (Model 5). However, considerable geographic variation in MSP remained in Model 5 (MOR = 1.84, IqOR = 4.37). If two mothers with the same individual characteristics were randomly selected from two different neighborhoods, their likelihoods of MSP were 1.84 times different (on average). Meanwhile, a mother, randomly selected from the first quartile of participants living in neighborhoods with the highest likelihood of MSP, was 4.37 times more likely to smoke during pregnancy than a mother randomly selected from the fourth quartile of participants living in neighborhoods with the lowest likelihood of MSP. Model 5 showed that MSP was associated with several individual characteristics, including less education, lower family income, any alcohol use during pregnancy, and maternal history of alcohol dependence (Table 3).

#### MSP beyond the first trimester

Results were similar for MSP beyond the first trimester. The prevalence of continued MSP was significantly higher for mothers residing in neighborhoods with the highest SED quartile than those in neighborhoods with the lowest SED quartile (25.2% vs. 15.5%, P = 0.002) (Table 1).

Variable	OR (95% CI)			
	MSP	MSP beyond 1st trimester		
Age at twin birth				
< 18 Years	0.71 (0.39-1.29)	0.82 (0.44–1.53)		
18–29 Years	1.00	1.00		
30+ Years	0.98 (0.75-1.29)	1.25 (0.93–1.68)		
Race				
White	1.00	1.00		
AA	0.82 (0.56-1.22)	0.64 (0.41–0.99)		
Education (Mom)				
< = 12 years	3.16 (2.19–4.56)	2.84 (1.98-4.08)		
> = 13 years	1.00	1.00		
Education (Dad)				
< = 12 years	1.96 (1.34–2.88)	1.85 (1.26–2.71)		
> = 13 years	1.00	1.00		
Household income				
< = \$45,000	2.07 (1.61–2.65)	2.37 (1.79–3.14)		
> \$45,000	1.00	1.00		
Parents' cohabitation				
Yes	1.00	1.00		
No	1.13 (0.71–1.80)	1.25 (0.77–2.04)		
Alcohol use during pregnancy				
Yes	2.59 (2.04–3.27)	1.61 (1.24–2.07)		
No	1.00	1.00		
Maternal history of alcohol dependence				
Yes	2.15 (1.30–3.55)	2.58 (1.59-4.17)		
No	1.00	1.00		

 Table 3. Associations of individual maternal characteristics with maternal smoking during pregnancy (MSP).

 Both models were adjusted for neighborhood socioeconomic deprivation.

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Neighborhood SED was significantly associated with continued MSP (Table 2 Model 1, the most vs. the least deprived: OR = 1.98, 95% CI = 1.38–2.85,  $P_{trend} = 0.002$ ). The association was not changed after adjusting for demographics (Model 2) or maternal alcohol use and parents' cohabitation (Model 4), but became nonsignificant after adjusting for individual socioeconomic conditions in Model 3 ( $P_{trend} = 0.758$ ) or all individual covariates (Model 5, the most vs. the least deprived quartile: OR = 1.40, 95% CI = 0.91–2.15,  $P_{trend} = 0.202$ ). However, considerable geographic variation remained for MSP beyond the first trimester in Model 5 (MOR = 2.37, IqOR = 8.03). The individual characteristics associated with MSP beyond the first trimester included less education, lower family income, any alcohol use during pregnancy, and maternal history of alcohol dependence (Table 3).

#### Discussion

The prevalence of MSP still remains high in the United States, although its adverse health effects have been well-understood [4-18]. The U.S. CDC reported that the prevalence of MSP decreased from 18.4% to 11.4% during 1990–2002 [42]. However, the prevalence of MSP was significantly higher in Missouri (24.8% in 1990) than in the U.S. Although slightly decreased, the prevalence of MSP remained high in 2002 (18.2%) [42] and remained about stable (15–20%) from 2000–2011 in Missouri [19]. As one of three national objectives relevant to MSP,

the U.S. *Healthy People* 2020 goal (HP 2020) aims to reduce the prevalence rate of MSP to 1.4%.[43] Current rates of MSP are far higher than this goal. There is therefore an urgent need to design and implement more effective public health strategies and policies to achieve this objective. Examining the extent of geographic variation in MSP is one key aspect.

The main purpose of our study was to examine geographic variation in and the association of neighborhood SED with MSP. In the female twin cohort, with uniquely rich data on geographic information and exposures during pregnancy of the mothers of the twins, we observed that MSP varied geographically and that neighborhood SED was associated with MSP in unadjusted models. However, individual socioeconomic conditions explained the relationship between higher neighborhood SED and increased likelihood of MSP. Nonetheless, the measured variables included in our study did not explain the substantial geographic variation in MSP. Similar results were found in continued MSP.

Some studies have investigated individual factors associated with MSP, including older age of mother's first pregnancy [21, 22], low socioeconomic status [21, 22], being unmarried [23], lower educational attainment [24–26], mental health problems [27–29], irregular doctor checkup [21, 22], limited or no religious participation [26, 30], and limited social support [31]. Area-level studies have reported that MSP was associated with higher neighborhood social capital [33], lower area-level education [34], more residential segregation [35], absence of local indoor smoking ordinance [44], and lower state-level cigarette tax rates [45]. No previous study has, to our knowledge, investigated the extent of geographic variation in MSP. In the current study, we found that the neighborhood SED association could be explained by individual socioeconomic status. In other words, mothers in the most deprived neighborhoods were more likely to smoke because they were themselves of lower socioeconomic status.

Both neighborhood- and individual-level socioeconomic conditions did not account for geographic variation in MSP. One potential explanation may be geographic access to tobacco outlets. Previous studies reported that greater concentration of and shorter travel distance to tobacco retailers were associated with higher likelihood of smoking among the general adult population [46, 47]. Better understanding of geographic patterns in MSP and underlying reasons will facilitate prioritizing limited health and intervention resources to neighborhoods with the highest rates of MSP.

Some studies reported the effectiveness of intervention efforts aiming to reduce MSP. Pharmaceutical approaches, such as nicotine replacement therapy, were reported to have limited effects on increasing smoking cessation during pregnancy [48]. Recently, a randomized controlled trial found that a physical activity intervention did not improve smoking cessation during pregnancy [49]. Randomized trials indicated that a 5As-based brief intervention successfully increased smoking cessation during pregnancy [50, 51], while a computer-assisted, simplified, and low-intensity contingency management (CM-Lite) intervention was not effective [50]. Two phase II randomized controlled trials showed that financial incentives could increase smoking cessation during pregnancy [52, 53]. A meta-analysis included 12 trials showed that self-help interventions were more effective in smoking cessation compared to standard care during pregnancy [54]. It was found that physician training and individual counseling was useful in reducing MSP [55]. Similar to the general population, pregnant women were responsive to higher price and taxes of cigarette [56]. These intervention studies did not take into account the impact of geographic heterogeneity in MSP on the effectiveness of the intervention efforts. To control tobacco use and reduce disparities in smoking during pregnancy in a more fruitful way, future tobacco control strategies should be designed in a multilevel framework, including strengthening health communication among primary care providers and OB/GYN physicians and women during pregnancy, geographically restricting tobacco retail outlets, or increasing local cigarette tax, especially in geographic areas with higher risk of MSP.

Our study has strengths and limitations. In the first study of this kind, we quantified geographic variation in MSP and attempted to explore the potential reasons. The recruitment of the MOAFTS cohort was based on official birth records, and we also verified that there was no significant difference between the MOAFTS twin births and entire female births in terms of socioeconomic environment in the state of Missouri in the same birth years. Therefore, our study sample was largely representative of all female births in Missouri. We applied a multivariable approach to develop a composite neighborhood SED index which could capture broader deprivation concepts compared to a single socioeconomic indicator [57]. Although the inaccuracy of residential address might also introduce geocoding bias and misclassification of neighborhood SED, official birth records are less likely subject to this issue. Since the parent interview was conducted after the twin births, it is possible that the information about MSP might have suffered from recall bias. Our previous study showed that mothers are accurate reporters of their MSP based on their twin sister's reports [58]. Prospective observation may be needed to assess longitudinal consistency of self-reported MSP in the future. In addition, due to unavailability of historic information about other neighborhood variables, such as tobacco outlets distribution at the time of the twins' births, we can only use census data to describe neighborhood characteristics. Our analysis of historic data in the MOAFTS cohort may not directly benefit current tobacco control efforts. However, our findings strongly suggest that further studies are needed to investigate the relationship of geographic variation in MSP and neighborhood characteristics other than socioeconomic deprivation. The current findings will also be helpful for us to further investigate the impact of geographic heterogeneity in MSP on the development of smoking behaviors among their children in the MOAFTS cohort.

In conclusion, significant geographic variation in MSP existed in the MOAFTS cohort. Neighborhood SED did not fully account for this geographic variation in MSP. Further studies are necessary to replicate our findings and identify potential mechanisms underlying the observed geographic clustering of tobacco use during pregnancy. This will help public health professionals implement evidence-based public health interventions to reduce disparities in MSP.

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## **Author Contributions**

Conceived and designed the experiments: ML PAM MTL GAC CNL MS ACH. Performed the experiments: ML PAM MTL ACH. Analyzed the data: ML. Contributed reagents/materials/ analysis tools: ML ACH. Wrote the paper: ML PAM MTL GAC CNL MS ACH.

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