Use of geographically weighted regression models to inform retail endgame strategies in South Korea: application to cigarette and ENDS prevalence

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ABSTRACT

Background Reducing tobacco retailer availability is a key tobacco endgame policy. The development and evaluation of retail-based policies require spatial methodologies. We modelled the prevalence of adult cigarette and electronic nicotine delivery system (ENDS) use according to tobacco retailer density, considering geographical variations.

Methods Registration data for tobacco retail businesses, a population-representative survey of South Koreans aged ≥19 years, and population and land area data were used. We merged the datasets according to geographical units. Ordinary least squares (OLS) and geographically weighted regression (GWR) analyses were conducted to model cigarette and ENDS use prevalence, respectively.

Findings Tobacco retailer density was associated with increased cigarette use prevalence in the OLS model (β=2.19, p=0.02). A 1.9-fold difference by region was identified for the coefficient, indicating an association with tobacco retailer density (minimum 1.39, maximum 2.65), in the GWR analysis. No significant association was present between tobacco retailer density and ENDS prevalence in either the OLS (β=0.24, p=0.37) or the GWR model (minimum 0.20, maximum 0.28).

Conclusion Our results suggest the importance of using spatial methods to develop and evaluate retail-based endgame policies. The establishment of tobacco retailer databases by the introduction of licensing is necessary to develop and evaluate the effectiveness of tobacco retailer regulations.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Retailer reduction by various measures is a key endgame policy.
⇒ Many nations are committed to implementing retailer reduction policies, but it is unclear *how* policies should be implemented to meet the endgame goal.

WHAT THIS STUDY ADDS

⇒ Tobacco retailer density was positively associated with cigarette smoking prevalence in all regions of South Korea, but the strength of the association varied by region.
⇒ No association was present between tobacco retailer density and electronic nicotine delivery system use prevalence, possibly because of different use and purchase behaviours.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Spatial methods should be used to develop and evaluate policies with geographical features.
⇒ Development of endgame policy implementation schemes must be informed by potential impacts to tobacco use.
⇒ Establishment of a public database of tobacco retailers is a prerequisite for relevant research and policymaking.

INTRODUCTION

The global community of tobacco control advocates and experts called for the tobacco endgame to finally put an end to the tobacco epidemic.[1] Tobacco retailer density restrictions are key measures for the tobacco endgame. There is increasing evidence to support the potential or actual impacts of smoking prevalence reductions, making this approach an effective policy for tobacco control.[2–4] Retailer restrictions effectively reduce tobacco use at the population level, particularly when conventional Framework Convention on Tobacco Control measures are complemented.[5 6]

Specific retail-based interventions include tobacco retailer licensing (TRL), which requires prior approval for retailing, adherence to standards and licensing fees; creating a buffer around youth-oriented facilities or between retailers; limiting the number of retailers according to measures such as population density or area; limiting specific types of retailers such as convenience stores, pharmacies and stores that sell alcohol; and banning sales of specific types of tobacco/nicotine products, such as flavoured tobacco products.[3 6–9] These retail-based interventions are effective for outcomes such as reductions in retailer density, youth access, exposure to tobacco advertising and tobacco product use.[2 9]

Many regions, including New Zealand (NZ)[10] and Finland,[11] aim or are committed to reducing tobacco retailer availability. For example, NZ has established a bold proposal for a regulatory regime to implement tobacco control measures, including reductions in the number of tobacco retailers.[12] The NZ government aims to set the maximum number of retail premises at 600 (a 90% reduction from 6000) and plans to allocate different maximum numbers for rural and urban areas.[12] However, the extent of reduction in smoking prevalence in each area that can result from such policies is unclear. Exploration of the feasibility of achieving the endgame goal through endgame policy must

consider the expected reduction in smoking prevalence; a prevalence goal within a timeframe characterises the endgame goal.[13]

Tobacco retailer density is a geographical construct.[14] Retailers supply tobacco/nicotine products to users or potential users in their respective areas.[14] Additionally, retail establishments are key promotion channels in those geographical areas, with advertising and product displays at the point of sale.[15] Disparities in socioeconomic status among residents and the strength of tobacco control policies contribute to regional variations in tobacco-related prevalence.[16–18] In particular, tobacco retailers are often densely distributed in places with lower socioeconomic status.[19] Thus, explorations of the geographical distribution of tobacco retailers can also help meet equity-related goals in tobacco control.[3 6]

The fact that tobacco retailer densities vary across geographical units underscores the need for spatial methods to inform the development and evaluation of retailer regulations and maximise their effects.[16] Failure to consider spatial heterogeneity in the distribution of tobacco retailers during the implementation of retailer reduction policies may lead to regional concentrations of tobacco retailers. Furthermore, the impact of retail-based interventions may be diluted—there is evidence the tobacco industry offers less expensive products[20] and implements more aggressive promotions[21] in low-socioeconomic status areas. Most previous studies on the impact of tobacco retailer density on tobacco/nicotine use were performed in Canada, Finland, NZ and the USA.[2] Thus, evidence from a high-income Asian country is lacking.

South Korea (hereafter Korea) is a suitable example to provide insights concerning the use of spatial methods to model the association between retailer density and tobacco/nicotine product use. First, because transnational tobacco industries consider Korea an ideal launch market for new products,[22] the use of non-cigarette tobacco/nicotine products (eg, electronic nicotine delivery system (ENDS) and heated tobacco products (HTPs)) is firmly entrenched in the Korean population. Additionally, the prevalence of cigarette smoking in Korea is one of the highest among high-income countries.[23] The overall smoking prevalence in 2020 was 20.6% (men, 34.0%; women, 6.6%)[24] and varied by socioeconomic status (2016, men with less than high school education, 49.7%; men with college education or higher, 34.3%).[25] Also, community-based health statistics are produced yearly to represent each regional site (*sigungu*) in Korea.[26 27] A *sigungu* is a second-level administrative division analogous to a county in the USA and is commonly used as a geographical unit in public health research in Korea.[28] Additionally, a list of registered tobacco retailers in the country is publicly available and updated monthly; one-off registration is required based on a negative licensing scheme. A negative association between tobacco retailer density and quit attempts was reported in 2015 based on the registered retailer list.[29] On average, each *sigungu* had 607.9 outlets (range: 70–2085), equivalent to 1.3–15.5 stores per 1000 residents.[29]

Tobacco/nicotine products in Korea are sold to consumers by retailers, including convenience stores (cigarettes, ENDS and HTPs), supermarkets (primarily cigarettes) and specialised shops selling ENDS, HTPs or both. The overall market share of retailers is unclear. Yet, the Korean Ministry of Health and Welfare (MoHW) reported that most tobacco retailers around universities are convenience stores (67.0%), followed by supermarkets (23.7%).[30] There are more than 50 000 convenience stores in Korea, and the sales revenue proportion of tobacco products among these stores is approximately 40%; it decreased from 43.9% in 2015 to 40.4% in 2022.[31]

The Korean Tobacco Business Act (TBA) states a business must be registered as a tobacco retailer to sell tobacco products to consumers (Article 16), and tobacco products should not be sold by postal sale or electronic transactions (Article 12).[32] However, violations of these acts have been detected by monitoring the enforcement of bans on tobacco advertising, promotion and sales by the MoHW and the Korean Health Promotion Institute in 2019. Among the 278 cases that violated the acts, 31 (11.2%) cases involved online sales.[30] ENDS sales constitute the largest proportion of illegal online transactions.[33] Another loophole in the TBA is that retail sales of products made from synthesised nicotine are not controlled because the TBA defines tobacco as '*what is manufactured in a state suitable for smoking, sucking, inhaling steam, chewing or smelling by using tobacco leaves as all or any part of the raw materials*'.[30] Therefore, products made with synthesised nicotine can be sold in places not registered as tobacco retailers, including online stores.

Retail-based interventions must be informed by spatial methods and address both cigarette and non-cigarette products.[3] Here, we evaluated regional variations in the extent of the association between tobacco retailer density and the use of cigarettes and ENDS. The results can be used to identify regions that should be prioritised for retail-based interventions.

METHODS

Data sources and measures

Three data sources were pooled for this study. First, the number of tobacco retailers as of July 2022 was obtained from the Korean Ministry of Interior and Safety.[34] The registration date, current business status and name and address of each retailer are updated monthly. We could not identify the types of products sold using the dataset of registered tobacco retailers. However, by reviewing the names of registered businesses, we determined the list includes convenience stores, supermarkets and specialised shops for ENDS and/or HTPs. Lists of businesses operating at the time of data collection (July 2022) were used. Tobacco retailer density, defined as the number of tobacco retailers per 10 000 m^2, served as the main exposure measure. Tobacco retailer density calculated as the number of retailers per land area was commonly employed in previous studies.[2]

Second, tobacco/nicotine use and socioeconomic status were obtained from 2021 Korea Community Health Survey (KCHS) (n=229 242). The KCHS is a community-based health survey of Korean adults aged ≥19 years. Approximately 900 individuals participated from each *sigungu* to ensure the statistics were representative. Half of all Koreans live in metropolitan area, which leads to significant variation in *sigungu* population size (2021, median=176 885; range: 8867–887 015).[35] The details of the KCHS are described elsewhere.[26] The *sigungu*-level adult cigarette smoking prevalence and ENDS use prevalence were the primary outcome measures. The cigarette smoking prevalence refers to the proportion of adults who have smoked at least 100 cigarettes in their lifetime and who currently smoke daily or occasionally. The prevalence of ENDS refers to the proportion of adults who have used ENDS in their lifetime and who have used ENDS during the past month. HTP use was surveyed by the 2021 KCHS but was not used in this study because the raw data regarding HTP use were not publicly released given the large margin of error. Age, proportion of women, annual household income and educational level (from 1 (no education) to 8 (higher than graduate school)) were aggregated at *sigungu* levels as covariates. The proportion of women, household income and

educational level were used to adjust for disparities in tobacco/nicotine use prevalence.[25]

Third, daytime and night-time (residential) population,[36] land area[37] and regional gross domestic product (GDP)[38] data were acquired from Statistics Korea. The daytime and night-time populations per 1 000 000 served as covariates to capture urbanisation and urban mobility. Many tobacco retailers in Korea are supermarkets and convenience stores, the distributions of which are greatly affected by urbanisation and population mobility. The regional GDP per resident was included to adjust for regional socioeconomic status.

All these datasets enabled analysis at the *sigungu* level (a total of 250), and all measures evaluated were continuous. Hereinafter, we refer to *sigungu* as 'administrative regions'. This study was exempted from review by the Institutional Review Board of Seoul National University (E2301/001-006).

Statistical analyses

Descriptive analyses

Estimates of the variables used in the study were visualised using a geographical map to provide descriptive statistics. Together with the outcome and exposure measures, additional measures of tobacco retailer density were visualised. The minimum, median, mean and maximum values of the variables were provided in a table. Characteristics of each administrative region are provided in online supplemental table S1. We considered the complex survey designs of the KCHS to derive aggregated estimates for each administrative region. For the outcome measures of cigarette smoking and ENDS use prevalence, Moran's I value based on Monte Carlo simulations was calculated to identify spatial clustering of cigarette smoking and ENDS use, respectively.

Ordinary least squares and geographically weighted regression models

The conventional ordinary least squares (OLS) model assumes spatial stationarity for the relationships between independent and dependent variables. We used OLS regression to assess the association between tobacco retailer density and the cigarette smoking prevalence and ENDS use prevalence. Prior to the model analyses, multicollinearity among the measures was identified by calculating the correlation coefficients and variance inflation factors. High correlations (online supplemental table S2) and variance inflation factor values were identified between daytime and night-time populations, and between educational level and household income; therefore, the night-time population and household income were omitted from the final model.

Using the same set of variables, we constructed geographically weighted regression (GWR) models to explain the locally varying spatial relationships between tobacco retailer density and tobacco/nicotine use prevalence. In contrast to the OLS model, the GWR model allows relationships to vary across regions. The GWR model was fit using an adaptive bandwidth kernel. The optimal bandwidth was determined by the minimum Akaike information criterion (AIC) method. In a comparison between the OLS and GWR models, the better fitting model fit was regarded as the model with a lower AIC value. As a sensitivity analysis, a quadratic term of retailer density was included in the models to explore the possible non-linear relationship between tobacco retailer density and prevalence (online supplemental tables S3 and S4). The results obtained using the standardised variables are also found in online supplemental tables S5 and S6. R was used for all analyses, with packages svy (complex survey designs), tmap (geographical maps) and spgwr (GWR analyses).

RESULTS

Descriptive statistics

The descriptive statistics of the variables are provided in figure 1 and table 1. Large differences between administrative regions were identified for cigarette smoking and ENDS use prevalence. Adult cigarette smoking prevalence for each region ranged from 10.07% to 26.39%. The prevalence of ENDS use was lower than the prevalence of cigarette smoking, and also exhibited differences between regions, ranging from near 0% to 3.55%. The number of retailers in each region differed by more than 20-fold, ranging from 85 to 2002; these values were equivalent to 0.001–1.04 tobacco retailers per 10 000 m^2.

The average age was 51.78 years (range: 43.77–61.41 years). The proportion of women ranged from 42.58% to 53.49%.

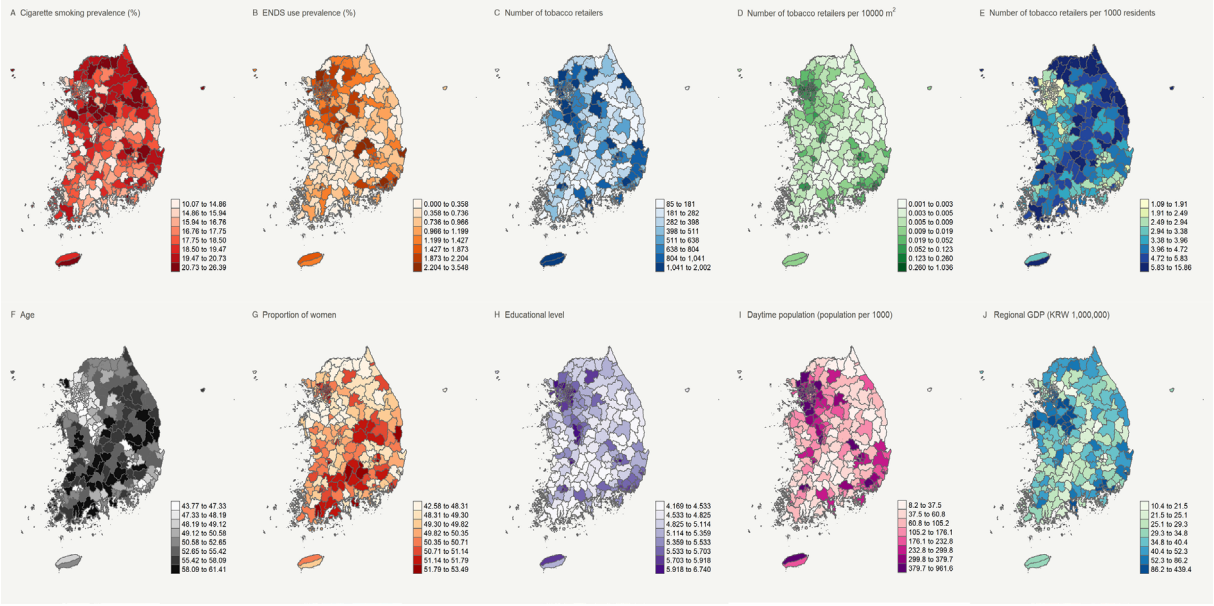

Figure 1 Geographical distributions of the study variables. ENDS, electronic nicotine delivery system; GDP, gross domestic product.

Table 1 Distributions of the study variables

Variables	Minimum	Median	Mean	Maximum
Cigarette smoking prevalence (%)	10.07	17.75	17.73	26.39
ENDS use prevalence (%)	0.00	0.74	1.29	3.55
Number of tobacco retailers	85	511	586.7	2002
Tobacco retailer density (per 10 000 m^2)	0.001	0.02	0.10	1.04
Tobacco retailer density (per 1000 residents)	1.09	3.38	3.83	15.86
Age (years)	43.77	50.58	51.78	61.41
Proportion of women	42.58	50.35	50.11	53.49
Educational level	4.17	5.36	5.29	6.74
Annual household income (KRW10 000)*	2571	4536	4600	8445
Daytime population (population per 1000)	8.20	176.1	200.6	961.6
Night-time population (population per 1000)*	8.16	169.7	200.6	831.9
Regional GDP per resident (KRW1 000 000)	10.39	34.77	49.80	439.4

*Omitted from the final model because of multicollinearity.
ENDS, electronic nicotine delivery system; GDP, gross domestic product.

The average educational level was 5.29 (high school level). The average daytime population per 1000 was equivalent to 200.6 (range: 8.20–961.6). The average regional GDP per resident was KRW49 800 000 (range: KRW10 390 000–KRW439 380 000).

The global Moran's I test for cigarette smoking (index 0.24, $p<0.01$) and ENDS use prevalence (index 0.28, $p<0.01$) indicated that both measures were spatially clustered.

OLS and GWR models

The OLS and GWR models for cigarette smoking prevalence are compared in table 2. In the OLS model, tobacco retailer density ($\beta=2.19$, $p=0.02$), age ($\beta=-0.60$, $p<0.01$), proportion of women ($\beta=-0.75$, $p<0.01$) and educational level ($\beta=-5.29$, $p<0.01$) were significantly associated with cigarette smoking prevalence. No statistically significant associations were identified for daytime population and regional GDP per resident.

The adaptive quartile proportion of observations included in the weighting scheme derived according to the minimum AIC using the Gaussian function was 0.84 (210 of 250 data points). The GWR model showed locally varying coefficients for tobacco retailer density (median=2.25), ranging from a minimum of 1.39 to a maximum of 2.65 ($p<0.01$). The AIC for the GWR model (1050.0) was lower than the AIC for the OLS model (1060.6), indicating a better model fit. Locally varying coefficients for each variable from the GWR model of cigarette smoking prevalence are provided in figure 2 and online supplemental table S7.

The OLS and GWR models for ENDS use prevalence are compared in table 3 and online supplemental figure S1. In the OLS model, no statistically significant association was present except for age ($\beta=-0.07$, $p<0.01$). The GWR model showed locally varying coefficients for tobacco retailer density, but these were insignificant ($p=0.47$) and smaller than the coefficients for cigarette smoking prevalence (minimum, 0.20; maximum, 0.28). Statistically significant locally varying coefficients were identified in age ($p<0.01$), daytime population ($p<0.01$) and regional GDP per resident ($p=0.04$). Local estimates are provided in online supplemental table S8. The AIC for the GWR model (407.4) was lower than the AIC for the OLS model (417.1), indicating a better model fit. The quadratic term of tobacco retailer density showed statistical significance for both cigarette (online supplemental table S3) and ENDS (online supplemental table S4) prevalence in the OLS models, but including the quadratic term did not significantly improve the fit of the models. Following the simplicity principle,[39] our main results only include linear terms for tobacco retailer density.

DISCUSSION

The OLS and GWR models showed that tobacco retailer density and cigarette smoking prevalence were positively associated in each region of Korea. The effect size of tobacco retailer density on cigarette smoking prevalence varied according to region—the effect size in the region with the largest coefficient was 1.9-fold

Table 2 Comparison of the results of OLS and GWR models examining the association between tobacco retailer density and adult cigarette smoking prevalence

	Prevalence of cigarette smoking								
	OLS*			GWR†					
Variable	Coefficient	SE	P value	Minimum	1st quantile	Median	3rd quantile	Maximum	P value
Tobacco retailer density	2.19	0.96	0.02	1.39	2.02	2.25	2.49	2.65	<0.01
Age	−0.60	0.09	<0.01	−0.63	−0.62	−0.60	−0.59	−0.58	0.24
Proportion of women	−0.75	0.11	<0.01	−0.78	−0.77	−0.75	−0.73	−0.72	0.47
Educational level	−5.29	0.67	<0.01	−5.52	−5.45	−5.29	−5.14	−5.03	<0.01
Daytime population	−0.31	1.27	0.81	−0.61	−0.48	−0.31	−0.17	−0.11	0.92
Regional GDP per resident	−0.003	0.003	0.32	−0.004	−0.004	−0.003	−0.002	−0.002	0.01

*AIC for the OLS model: 1060.6.
†AIC for the GWR model: 1050.0.
AIC, Akaike information criterion; GDP, gross domestic product; GWR, geographically weighted regression; OLS, ordinary least squares.

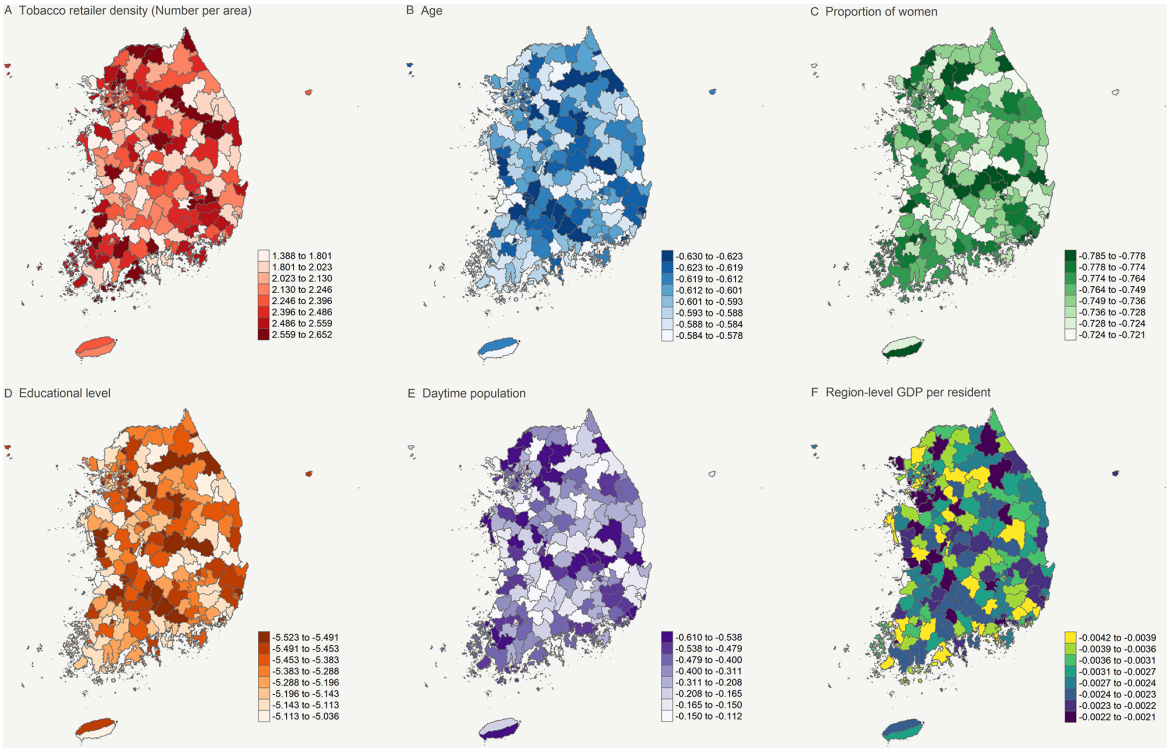

Figure 2 Coefficients of tobacco retailer density (number per 10 000 m^2) and covariates on cigarette smoking prevalence derived from the geographically weighted regression (GWR) model. GDP, gross domestic product.

greater than the effect size in the region with the smallest coefficient. In contrast, the OLS model showed no significant association between tobacco retailer density and ENDS use prevalence. Locally varying coefficients were identified between tobacco retailer density and ENDS use prevalence, but the differences between regions were not statistically significant and smaller than the coefficient differences in the cigarette smoking prevalence model.

The association we found between tobacco retailer density and cigarette smoking prevalence is consistent with the findings of previous studies. A study using the GWR method in Virginia showed that higher tobacco outlet density was associated with cigarette smoking prevalence at the county level.[40] However, the regional distribution of social determinants, including the percentage of women, household income and violent crime rate, primarily explained the association between retailer density and smoking prevalence.[40] In contrast, we identified a significant association between tobacco retailer density and cigarette smoking prevalence, even after adjustment for key covariates. A meta-analysis of 27 studies from Australia, Canada, Finland, NZ, the UK and the USA also indicated that reductions in tobacco retailer density and proximity were associated with lower risks of tobacco use.[2] A scoping review of 35 studies revealed that higher tobacco retailer density in neighbourhoods was associated with higher risk of current adult smoking.[41]

The varying strengths of associations between tobacco retailer density and cigarette smoking prevalence indicate that region-specific targets should be established for the endgame policy that involves restricting the number of retailers. Our findings suggest that the effect of reducing the number of tobacco retailers will differ according to region. More stringent restrictions on tobacco retailer densities are required for regions in which the reductions in tobacco retailer density do not greatly reduce tobacco use. Policies implemented by central governments must be impactful

Table 3 Comparison of the results of OLS and GWR models examining the association between tobacco retailer density and adult ENDS use prevalence

	Prevalence of ENDS use								
	OLS*			GWR†					
Variable	Coefficient	SE	P value	Minimum	1st quantile	Median	3rd quantile	Maximum	P value
Tobacco retailer density	0.24	0.26	0.37	0.20	0.22	0.24	0.25	0.28	0.47
Age	−0.07	0.02	<0.01	−0.08	−0.07	−0.07	−0.07	−0.07	<0.01
Proportion of women	−0.003	0.03	0.92	−0.01	−0.01	−0.003	−0.0001	0.003	0.05
Educational level	0.30	0.18	0.10	0.29	0.30	0.30	0.31	0.32	0.99
Daytime population	0.43	0.35	0.22	0.34	0.39	0.44	0.47	0.50	<0.01
Regional GDP per resident	−0.001	0.001	0.32	−0.001	−0.001	−0.001	−0.001	−0.001	0.04

*AIC for the OLS model: 417.1.
†AIC for the GWR model: 407.4.
AIC, Akaike information criterion; ENDS, electronic nicotine delivery system; GDP, gross domestic product; GWR, geographically weighted regression; OLS, ordinary least squares.

even in areas with weak associations between tobacco retailer density and tobacco use. GWR yields detailed information on regional disparities in association between tobacco retailer density and smoking. Thus, we recommend the use of conventional models and GWR models or other methods that consider spatial heterogeneity before the implementation of retail-based endgame policies. Locally varying estimates must be considered to inform policies sufficient to phase out tobacco use in every geographical unit.

Assessment of the spatial relationship between tobacco retailer density and tobacco use should be followed by registration of tobacco retailers and public dissemination of the retailer list.[42] A database of tobacco retailers is lacking in some regions, and the easiest method to construct such a database is to introduce TRL. Databases for tobacco retailers can be used for both practical and academic purposes. Furthermore, licensing facilitates communication between governments and retailers, improving retailer compliance with required standards and laws.[43] TRL also serves as a precedent for other retailer interventions, including efforts to limit the types of retailers and products, as well as the creation of buffers. Thus, a database of tobacco retailers should include the business name and address, initial and most recent dates of approval, contact details, store type and type of tobacco/nicotine products sold.

We did not find a significant association between tobacco retailer density and ENDS use prevalence. Although our data were limited in explaining this lack of association, the following hypotheses can be tested in future studies. First, people who use ENDS may acquire their products from illegal sources, such as online markets. Illicit online sales of ENDS have been reported in Korea,[33] and synthesised nicotine-containing ENDS may be sold by unregistered retailers. Second, the cycle for purchase may be longer for people who use ENDS than for people who use cigarettes. The average number of cigarettes smoked per day among people who use cigarettes was 12.6, indicating that people who use cigarettes purchase a pack every 2 days[44]; in contrast, people who use refillable pod-based devices may use a bottle of e-liquid for more than 1 week.[45] Additionally, lower use frequency among ENDS users may explain the lack of association.[46] Furthermore, cigarette smoking prevalence is substantially greater than ENDS use prevalence, leading retailers to increase their focus on cigarette sales rather than ENDS sales. It is unclear whether such a landscape will change as the number of tobacco/nicotine product users increases.

The following policy changes are needed to better capture the association between tobacco retailers and ENDS use. First, the databases of tobacco retailers must provide information regarding the types of products that each retailer sells. As mentioned above, this is achievable with the aid of TRL. Considering the increasing popularity of non-cigarette products, the number of people purchasing these products in specialised shops may also increase as these shops offer additional products and promotions.[47] Valid estimates cannot be obtained from databases that lack information regarding the types of tobacco/nicotine products sold. Second, surveillance and robust control of online sales are required. The use of tobacco/nicotine products from unknown sources interferes with the estimation of health effects. These illicit products may contain unacceptable types or amounts of harmful constituents.[48] Third, there is a need for a comprehensive framework of tobacco products that encompasses the constantly proliferating innovations of tobacco/nicotine products. As mentioned in the Introduction section, products containing synthesised nicotine are outside the scope of management and control in Korea.

The limitations of this study include but are not limited to the following. First, this study used a cross-sectional design. Thus, more tobacco retailers may have been established in places with more people who use tobacco/nicotine products. Second, we considered only tobacco retailer density; local variations in terms of proximity, type and licensing should also be measured in the future. Third, some retailers may be operating without registration in the tobacco retailer database in Korea. An incomplete listing of tobacco retailers has been reported in a negative licensing scheme,[49] the type of scheme used in Korea.

The results of this study show that the magnitude of the effect on cigarette smoking prevalence of tobacco retailer density varies according to region. The development and evaluation of retail-based tobacco endgame policies should consider factors such as the number of retailers per population size or land area, as well as the effect of retailer density on smoking prevalence estimates. Tobacco retailer databases are required to record these data, and such databases can be established by TRL. Moreover, tests for hypotheses, including use and purchase patterns, are needed to explore the effect of retailer density on ENDS use.

Contributors HK designed the study, conducted all analyses and drafted the manuscript. All authors interpreted the findings and reviewed and approved the final version of the manuscript. HK is guarantor for the study and manuscript.

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