Geographical clustering and socioeconomic factors associated with hypoglycemic events requiring emergency assistance in Andalusia (Spain)

Fernando Gomez-Peralta ¹, Cristina Abreu,¹ Manuel Benito,² Rafael J Barranco³

To cite: Gomez-Peralta F, Abreu C, Benito M, *et al*. Geographical clustering and socioeconomic factors associated with hypoglycemic events requiring emergency assistance in Andalusia (Spain). *BMJ Open Diab Res Care* 2021;**9**:e001731. doi:10.1136/bmjdr-2020-001731

► Supplemental material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/bmjdr-2020-001731>).

Received 26 June 2020
Revised 26 November 2020
Accepted 5 December 2020

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Endocrinology and Nutrition Unit, Hospital General de Segovia, Segovia, Spain

²Department of Urbanism, School of Architecture, Polytechnic University of Madrid, Madrid, Spain

³Department of Health Sciences, University of Jaén, Jaén, Spain

Correspondence to

Dr Fernando Gomez-Peralta; fgomezperalta@gmail.com

ABSTRACT

Introduction The geographical distribution of hypoglycemic events requiring emergency assistance was explored in Andalusia (Spain), and potentially associated societal factors were determined.

Research design and methods This was a database analysis of hypoglycemia requiring prehospital emergency assistance from the Public Company for Health Emergencies (*Empresa Pública de Emergencias Sanitarias* (EPES)) in Andalusia during 2012, which served 8 393 159 people. Databases of the National Statistics Institute, Basic Spatial Data of Andalusia and System of Multiterritorial Information of Andalusia were used to retrieve spatial data and population characteristics. Geographic Information System software (*QGIS* and *GeoDA*) was used for analysis and linkage across databases. Spatial analyses of geographical location influence in hypoglycemic events were assessed using Moran's I statistics, and linear regressions were used to determine their association with population characteristics.

Results The EPES attended 1 137 738 calls requesting medical assistance, with a mean hypoglycemia incidence of 95.0±61.6 cases per 100 000 inhabitants. There were significant differences in hypoglycemia incidence between basic healthcare zones attributable to their geographical location in the overall population (Moran's I index 0.122, z-score 7.870, p=0.001), women (Moran's I index 0.088, z-score 6.285, p=0.001), men (Moran's I index 0.076, z-score 4.914, p=0.001) and aged >64 years (Moran's I index 0.147, z-score 9.753, p=0.001). Hypoglycemia incidence was higher within unemployed individuals (β=0.003, p=0.001) and unemployed women (β=0.005, p=0.001), while lower within individuals aged <16 years (β=-0.004, p=0.040), higher academic level (secondary studies) (β=-0.003, p=0.004) and women with secondary studies (β=-0.005, p<0.001). In subjects aged >64 years, lower rate of hypoglycemia was associated with more single-person homes (β=-0.008, p=0.022) and sports facilities (β=-0.342, p=0.012).

Conclusions This analysis supports the geographical distribution of hypoglycemia in the overall population, both genders and subjects aged >64 years, which was affected by societal factors such as unemployment, literacy/education, housing and sports facilities. These data can be useful to design specific prevention programs.

Significance of this study

What is already known about this subject?

- Hypoglycemic events are serious acute diabetes complications that often require emergency department visits and hospital admissions.
- Our previous assessment of out-of-hospital emergency care due to hypoglycemic episodes experienced by a large population dwelling in Andalusia (Spain) revealed their high resource utilization and costs for the Spanish healthcare system.

What are the new findings?

- Spatial analyses showed significant differences in the incidence of hypoglycemic events requiring emergency assistance between the basic healthcare zones of Andalusia in the overall population, women, men and subjects aged >64 years.
- Linear regression analyses showed that hypoglycemia was higher within unemployed individuals, while lower within those aged <16 years and higher academic level. In subjects aged >64 years, hypoglycemia was less detected in those living in single-person homes.
- These analyses support that distribution of hypoglycemia is affected by societal factors such as unemployment, literacy/education and housing.

How might these results change the focus of research or clinical practice?

- Spatial analyses using Geographic Information System software are useful to characterize health outcomes in prevalent diseases such as diabetes mellitus.
- This information can be useful to design specific healthcare programs to prevent hypoglycemic events according to their geographical distribution and societal characteristics.

INTRODUCTION

Diabetes is a lifelong disease that has become a global concern worldwide due to its increasing prevalence and a wide range of potential complications that may impact both patient daily living and national healthcare systems.¹ The occurrence of hypoglycemic

events is one of the most serious acute complications in patients with diabetes, which may entail sequelae and fatal consequences if the glycemic state is not controlled.² These episodes often require emergency department visits and hospital admissions,^{3,4} especially when patients are elderly.^{3,5} Insulin-related hypoglycemia was responsible for nearly 100 000 visits per year to US emergency departments.³ In Spain, a self-reported survey in patients with diabetes showed that 30% of responders with severe hypoglycemia required emergency hospital care and 19% hospital admission.⁶ Our previous assessments of out-of-hospital emergency care due to hypoglycemia also supported high resource utilization and costs for the Spanish healthcare system.⁷ Indeed, it showed that hypoglycemic episodes experienced by a large Spanish population dwelling in Andalusia (Spain) were common emergencies requiring in situ emergency care, transfer and hospital care for less than 24 hours that accounted for an annual cost of over €6 000 000.

As diabetes management mainly lies in outpatient care, complications derived from the uncontrolled disease may also depend on factors outside the hospital setting.⁴ These may include cultural and socioeconomic barriers that affect healthcare delivery, such as low literacy, social support or communication with healthcare providers.⁸ Geographical distribution of diabetes complications may, therefore, contribute to clarify the existence of patterns that may be affected by societal peculiarities. In fact, spatial analyses have been widely used to explore the influence of location and its potentially associated factors in the occurrence of events in health science.⁹ In the diabetes field, several methods have been used to assess the geographical variation of disease prevalence, distance to the primary care provider, patient–endocrinologist ratio, glycemic control or other clinical outcomes.^{10–13} From these assessments, it emerged that sociodemographic factors such as population-dense areas, poor environmental quality, population aging, more deprived places, low socioeconomic status and low neighborhood education were associated with a higher prevalence of diabetes.^{10–13} The neighborhood socioeconomic status was also associated with glycemic control,¹⁰ and prophylactic measures to reduce weight, eliminate detrimental habits and normalize metabolism or arterial pressure decreased diabetes complications.¹⁰

In light of the above, we used spatial analyses to explore the geographical distribution of hypoglycemic events in a large population from Spain, as well as determining societal factors that may be associated with their occurrence.

METHODS

Study design

The Emergency Assistance of the Person with Diabetes Project (*Proyecto de Atención Urgente Extrahospitalaria del Paciente Diabético*) carried out in Andalusia (Spain) comprised a data collection from the Andalusian Public Company for Health Emergencies (*Empresa Pública de*

Emergencias Sanitarias (EPES)) database on all registered calls requesting emergency assistance due to hypoglycemia from 1 January 2012 to 31 December 2012.⁷ This retrospective study brought together the hypoglycemia incidence data obtained from each basic healthcare zone, geographical location and local societal factors. The requirement for informed consent was waived based on the study nature.⁷ All authors had access to the database population used to create the study population.

Data sources and measures

EPES database

The EPES provide comprehensive care for emergencies and accidents in the prehospital setting within the whole Andalusian region (Spain),¹⁴ which included an overall population of 8 393 159 inhabitants in 2012.¹⁵ As cases attended by other Andalusian emergency healthcare providers with a final diagnosis of hypoglycemia must be reported to EPES, its database contained information on all calls requesting emergency assistance due to hypoglycemic episodes. It included unique identifiers for tracking specific individuals and additional details such as their gender and location of residence. With regard to their location, only their basic healthcare zones could be accessed due to personal data protection regulations. These basic healthcare zones were used to link the information contained in the different databases considered in the analysis (online supplemental figure 1).

The diagnosis of hypoglycemic events was based on the criteria proposed by the American Diabetes Association,² when blood glucose levels were <70 mg/dL (3.9 mmol/L).⁷ These episodes were coded using the ninth edition of the International Classification of Diseases-Clinical Modification,¹⁶ which included the following codes: 249.3, 250.3, 249.8, and 250.8.

Basic spatial data of Andalusia

The Basic Spatial Data of Andalusia (*Datos Espaciales de Referencia de Andalucía*) is a set of geographical databases of the whole Andalusian region that enable spatial analyses to be conducted.¹⁷ It provided data on administrative divisions (eg, basic healthcare zones) and geographical information (eg, surface and geometry) that were used for Geographic Information System (GIS) analysis in this study. Basic healthcare zones are the territorial units for the effective provision of primary healthcare services in Andalusia and may include one or more primary care centers.

Spanish National Statistics Institute

The National Statistics Institute provides a wealth of official statistics on its webpage, including overall data for Spain and for the different Spanish regions. It was used to obtain data on the population and housing census of Andalusia registered as of 1 November 2011.¹⁸ These data were used to calculate the population, gender distribution, age, literacy/education level, single-person homes, dependence index (ie, proportion of dependent

population: aged <18 and >65 years with respect to aged 18–64 years), foreign population and marital status in each basic healthcare zone. The incidence of hypoglycemic events was calculated taking into account the cases described in the EPES database and the overall population of the basic healthcare zone obtained from the population and housing census of Andalusia.

System of Multiterritorial Information of Andalusia

The System of Multiterritorial Information of Andalusia (*Sistema de Información Multiterritorial de Andalucía*) is a database of the Institute of Statistics and Cartography of Andalusia (*Instituto de Estadística y Cartografía de Andalucía*) that offers multithematic and multiterritorial statistical information.¹⁹ We used this database to identify information on homes with pending payments, annual net income, unemployed individuals, pharmacies, sports facilities and deaths from endocrine, nutritional or metabolic diseases in all basic healthcare zones throughout 2012.

Statistical analyses

Spatial autocorrelation

In this work, spatial autocorrelation measurements have been made for local identification of clusters on the chosen data and scale. Local study metrics of spatial clusters on variables associated with geographic locations (formatted as spatial data) used by GIS assume that all observations and their spatial dimension influence and relate to each other, but those closest to each other do so more intensely than those who are more distant.²⁰ By establishing a priori geographical relationships of proximity between statistical observations, the finding of the degree to which this statement is true is usually addressed by the application of spatial autocorrelation, which is defined as the measure to which we can reject the null hypothesis that the spatial distribution of a variable is completely random. The statistics used in this study are local Moran's I. This metric compares each observation of the universe with all of its 'next' observations to indicate the degree to which, statistically, the values of a particular variable seem to be grouped locally. This measurement (in its local version) returns, for each observation, z-values that establish the degree to which high or low values relate to their neighborhood and p values describing their significance, the degree to which the null hypothesis of complete spatial randomness can be rejected. The combination of both continuous variables generates, for each observation, a discrete variable of qualitative type, indicating the cluster class to which it belongs. Then, the geospatial study provided the following main data: local Moran's I index, z-score, p value and cluster types.²¹ For this study, the basic healthcare zones are the territorial units to compare its hypoglycemic events incidence (cases per 100 000 inhabitants) using clusters (contiguous pairs) of them by proximity and calculating randomness at each cluster. The clustering types included statistically significant clusters of

high values surrounded by high values (high–high) or low values surrounded by low values (low–low), clusters of high values surrounded by low values (high–low), clusters of low values surrounded by high values (low–high) and non-significant clusters.

Association of sociodemographic factors

Linear regression analyses were performed to assess the association of sociodemographic factors with hypoglycemic events, including hypoglycemia incidence as the dependent variable and the following factors as independent variables: age; individuals aged <16, 16–64 and >64 years; women and men; illiterates, individuals without studies and with primary, secondary or tertiary studies; single-person homes and homes with pending payments; dependence index; net income per inhabitant; married, unemployed and foreign individuals; deaths from endocrine, nutritional or metabolic diseases; pharmacies and sports facilities per 100 000 inhabitants; and inhabitants per hectare.

Statistical approach

The analyses were conducted in the overall population and according to gender and the following age ranges: <16 years, 16–64 years and >64 years. In addition, hypoglycemia incidence was compared among these subgroups using Mann-Whitney tests. A significance level of 0.001 was used for Moran's I statistics and 0.05 for multivariate regressions and subgroup comparisons. Missing data were not considered in the analyses, which were performed using the GIS software (*QGIS* and *GeoDA*²²) and the Statistical Package for the Social Sciences V.22.

RESULTS

The EPES emergency coordination centers attended 1 137 738 calls requesting medical assistance during 2012, 8683 (0.8%) of which were due to hypoglycemia.⁷ The population characteristics in the 216 basic healthcare zones of Andalusia are described in table 1. The calculated mean ($\pm$ SD) incidence of hypoglycemic events in the overall Andalusian population was 95.0 $\pm$ 61.6 cases per 100 000 inhabitants (table 1). Comparisons according to gender showed that hypoglycemia incidence was higher in women than in men, overall and according to age groups except for 16–64 years (figure 1A and online supplemental table 1). Comparisons according to age ranges showed that hypoglycemia incidence increased with age, reaching its highest value when age was >64 years (figure 1B and online supplemental table 2).

Geographical distribution

The geographical distribution of hypoglycemic events in the different basic healthcare zones of Andalusia is depicted in figure 2. Spatial analyses showed that there were significant differences in hypoglycemia incidence between basic healthcare zones attributable to their geographical location (significant spatial autocorrelation) (Moran's I index 0.122, z-score 7.870, p=0.001),

Table 1 Overall characteristics of the Andalusian population (N=216)*

Characteristics	Mean±SD
Overall age (years)	39.9±1.6
Individuals within each age group	
Individuals aged <16 years per 100 000 inhabitants	17 059.4±2449.7
Individuals aged 16–64 years per 100 000 inhabitants	66 330.9±2585.2
Individuals aged >64 years per 100 000 inhabitants	16 606.4±4562.3
Gender	
Men per 100 000 inhabitants	50 450.4±1096.8
Women per 100 000 inhabitants	49 541.1±1104.4
Literacy/education level	
Illiterates per 100 000 inhabitants	3585.4±1562.6
Individuals without studies per 100 000 inhabitants	12 684.9±4423.0
Individuals with primary studies per 100 000 inhabitants	14 796.8±2971.8
Individuals with secondary studies per 100 000 inhabitants	42 056.4±3896.0
Individuals with tertiary studies per 100 000 inhabitants	9762.0±4154.0
Housing	
Single-person homes per 100 000 homes	20 065.7±4809.5
Homes with pending payments per 100 000 inhabitants	24 568.7±10 3830.0
Dependence index	51.0±6.0
Net income per inhabitant (euros)	15 899.3±11 4180.9
Married individuals per 100 000 inhabitants	47 742.7±2726.4
Unemployed individuals per 100 000 inhabitants	15 015.8±4367.3
Foreign individuals per 100 000 inhabitants	7231.1±7743.0
Deaths from endocrine disease per 100 000 inhabitants	27.4±18.4
Pharmacies per 100 000 inhabitants	45.7±23.7
Sports facilities 100 000 inhabitants	151.3±130.3
Inhabitants per hectare	3.2±8.9
Hypoglycemic events per 100 000 inhabitants	95.0±61.6

*Characteristics of the population from the 216 basic healthcare zones of Andalusia are presented.

with one cluster of high values (high–high) and two clusters of low values (low–low) (figure 2A).

This spatial autocorrelation was also observed when the analyses were conducted in women (Moran's I index 0.088, z-score 6.285, $p=0.001$; figure 2B) and men (Moran's I index 0.076, z-score 4.914, $p=0.001$; figure 2C).

In these cases, up to two clusters with high values (high–high) and three clusters with low values (low–low) were identified, some of which partly coincided (figure 2B and C).

When the analyses were conducted according to age groups, the correlation was found in the age group >64 years (Moran's I index 0.147, z-score 9.753, $p=0.001$), with one cluster of high values (high–high) and three clusters of low values (low–low) (figure 2F). No significant spatial patterns were observed in age groups <16 years (Moran's I index 0.010, z-score 2.262, $p=0.029$; figure 2D) and 16–64 years (Moran's I index 0.060, z-score 4.203, $p=0.002$; figure 2E).

Additional data on spatial distribution of sociodemographic population characteristics are provided in online supplemental figures 2–13.

Linear regression analyses

Linear regression analyses showed that hypoglycemia incidence was directly associated with the number of unemployed individuals ($\beta=0.003$, $p=0.001$) and inversely associated with the number of individuals aged <16 years ($\beta=-0.004$, $p=0.040$) and those with secondary studies ($\beta=-0.003$, $p=0.004$) (table 2).

Similarly, hypoglycemia incidence was directly associated with the number of unemployed women ($\beta=0.005$, $p=0.001$) and inversely associated with the number of women with secondary studies ($\beta=-0.005$, $p<0.001$), though no association was found in men (table 2).

With regard to age, hypoglycemia incidence was directly associated with the number of unemployed ($\beta=0.002$, $p=0.039$) and foreign individuals ($\beta=0.002$, $p<0.001$) and inversely associated with the number of single-person homes ($\beta=-0.004$, $p=0.001$) and homes with pending payments ($\beta=-0.002$, $p<0.001$) in subjects aged <16 years (table 2). Hypoglycemia incidence was also directly associated with the number of unemployed individuals ($\beta=0.002$, $p=0.001$) and those without studies ($\beta=0.002$, $p=0.009$) in those aged 16–64 years (table 2). In subjects aged >64 years, hypoglycemia incidence was inversely associated with the number of single-person homes ($\beta=-0.008$, $p=0.022$) and sports facilities ($\beta=-0.342$, $p=0.012$) (table 2).

DISCUSSION

Our spatial analysis of hypoglycemic events requiring prehospital emergency assistance in Andalusia performed by the Local Moran's I statistic supported the existence of geographical patterns in the overall population, both genders and subjects aged >64 years. The maps generated considering these populations pointed at different areas according to the incidence of hypoglycemic events, unmasking up to two regions with high and up to three regions with low hypoglycemia incidence. As diabetes management mainly lies in outpatient care, the significant gathering and dispersion of hypoglycemic events may be affected by out-of-hospital factors.

Figure 1 Comparison of hypoglycemic events per 100 000 inhabitants according to gender (A) and age ranges (B).

Indeed, socioeconomic variables such as unemployment, literacy/education, housing and sports facilities were associated with hypoglycemia incidence in our linear regression analyses.

The hypoglycemia distribution in the overall population may be driven by its higher incidence in women, especially those unemployed and with low literacy/education. Linear regression findings supported the direct association of hypoglycemia incidence with the number of unemployed individuals and its inverse association with the number of those with secondary studies in

the female and overall populations. The clustering maps agreed with these findings as the cluster with high hypoglycemias partly overlapped that of high unemployment and the cluster with low hypoglycemias almost completely overlapped that with higher rates of secondary studies in both women and overall populations. However, these variables seem to be unrelated to the hypoglycemia incidence in men, despite its distinct geographical pattern, suggesting the effect of other factors or more complex interactions that are still pending clarification.

With regard to the association between the hypoglycemia incidence and the number of individuals aged <16 years in the overall population, the lower representativity of their hypoglycemic events and the type of diabetes that usually affect this age group should be noted; while adult and elderly patients are mainly affected by type 2 diabetes, young patients are mostly cases of type 1 diabetes.²³ In addition, our geographical analysis revealed no significant pattern of hypoglycemic events in this subset of younger subjects, in contrast to the geographical pattern seen in those aged >64 years. Even considering that hypoglycemic events in this age range are few in the whole dataset, they are, unfortunately, very frequent in the daily life of people with type 1 diabetes due to their need for complex insulin regimens. Therefore, the influence of external factors in the occurrence of hypoglycemia events in this group could be less discriminating.

On the contrary, the distinct distribution of hypoglycemic events in the older population may be affected by societal factors, such as the number of single-person homes and sports facilities. However, the inverse association of hypoglycemia incidence and single-person homes contrasts with our expectation and merits reflection. Our previous report,⁷ which showed a clearly lower incidence of severe hypoglycemic episode emergency calls during the night and a peak during the first morning hours, suggests absence of detection during the night and, perhaps, another person other than the patient noticing the condition after the night. We can speculate that our finding (less severe hypoglycemic events in single-person

Figure 2 Geographical distribution of hypoglycemic events per 100 000 inhabitants in the overall population (A), women (B), men (C), aged <16 years (D), aged 16-64 years (E) and aged >64 years (F). HH, high-high cluster; HL, high-low cluster; LH, low-high cluster; LL, low-low cluster; NS, non-significant.

Table 2 Sociodemographic factors associated with hypoglycemia incidence in linear regression analyses

Sociodemographic factors	Standardized β	Unstandardized β (95% CI)	P value	R ²
Overall population				
Individuals aged <16 years per 100 000 inhabitants	−0.148	−0.004 (−0.007 to 0.000)	0.040	0.073
Individuals with secondary studies per 100 000 inhabitants	−0.209	−0.003 (−0.006 to −0.001)	0.004	
Unemployed individuals per 100 000 inhabitants	0.248	0.003 (0.001 to 0.006)	0.001	
Men*	—	—	—	
Women				
Individuals with secondary studies per 100 000 inhabitants	−0.259	−0.005 (−0.008 to −0.002)	<0.001	0.074
Unemployed individuals per 100 000 inhabitants	0.246	0.005 (0.002 to 0.009)	0.001	
Aged <16 years				
Single-person homes per 100 000 homes	−0.270	−0.004 (−0.006 to −0.002)	0.001	0.143
Homes with pending payments per 100 000 inhabitants	−0.341	−0.002 (−0.003 to −0.001)	<0.001	
Unemployed individuals per 100 000 inhabitants	0.146	0.002 (0.000 to 0.004)	0.039	
Foreign individuals per 100 000 inhabitants	0.233	0.002 (0.001 to 0.003)	<0.001	
Aged 16–64 years				
Individuals without studies per 100 000 inhabitants	0.187	0.002 (0.001 to 0.004)	0.009	0.062
Unemployed individuals per 100 000 inhabitants	0.243	0.002 (0.001 to 0.003)	0.001	
Aged >64 years				
Single-person homes per 100 000 homes	−0.171	−0.008 (−0.016 to −0.001)	0.022	0.096
Sports facilities per 100 000 inhabitants	−0.188	−0.342 (−0.609 to −0.076)	0.012	

Optimal multivariate models are shown.

*No optimal model could be obtained.

homes) is an issue of non-detection rather than a real protective factor.

There was a partial overlap of the high-value and one of the low-value hypoglycemia clusters with a low-value and a high-value cluster of sports facilities, respectively. Although the fear of hypoglycemia can be a major barrier to physical activity,⁸ its relationship with the number of sports facilities remains unclarified. Complex interactions with other indirect indicators are likely involved in these associations, and further analyses are therefore needed to shed light on these issues. Indeed, the R² coefficient values of the statistically significant associations with societal factors could be considered of mild to medium effect,²⁴ which highlight the underlying multifactorial nature of the hypoglycemia incidence distribution.

To our knowledge, only one report has used spatial and multivariate analyses to understand the geographical clustering and socioeconomic factors associated with hypoglycemic events.²⁵ Its findings unmasked 21 local government areas with increased risk of hypoglycemia attended by prehospital emergency medical service and also revealed the influence of area-level factors such as the proportion of overseas-born residents and access to a motor vehicle in the state of Victoria in Australia. Other studies have investigated the geographical distribution of diabetes prevalence and cardiac, neurologic, renal and lower extremity diabetic complications, revealing significant clustering in many countries worldwide.^{10–13 26–39}

Reported data in European countries showed the influence of area deprivation, population density, educational attainment, income level and green urban areas in diabetes prevalence.^{10 32} Sociodemographic and environment-related variables were also associated with diabetes prevalence in some areas of the USA, Canada, New Zealand and China,^{11–13 27 28 33 35 38} including age, race/ethnicity, economic status, physical inactivity, active commuting, recreation facilities, unhealthy lifestyle, natural amenities, lone-parent families, vacant houses, literacy/education, smoking, unemployment and criminality. In addition, population characteristics such as elderly residents also predicted the higher rates of moderate to severe cardiac, neurologic, renal and lower extremity complications in New York City, as well as the proportion of certain races/ethnicities, insurance rates and poverty.²⁶ Areas of increased prevalence of lower extremity complications such as diabetic foot ulceration and amputation have also been associated with local deprivation considering employment, income, crime, housing, health, education and access in Scotland.³¹ Although comparisons among study findings are limited by the outcome and methodologic differences, the identification of local variability using geographical analyses highlights its suitability to promote and monitor public policies for diabetes management. Furthermore, the incidence rate of severe hypoglycemia reported in our project is within the range evidenced by different studies

performed using distinct reporting methods worldwide (online supplemental table 3).^{7 40–45}

Despite the crucial role of diabetes care in delaying disease-related complications, the different local context of patient groups within regions or countries also seems to unevenly affect their appearance.^{26 31 37} Understanding spatial variations of diabetic outcomes and their relationships with societal factors can identify high-risk areas and ground-specific programs prioritizing interventions to improve healthcare delivery to involved communities.^{10 11 25 26 36 37} The identification of successful clusters in obtaining proposed goals may serve as an example of actions that may be considered when promoting and delivering healthcare,^{13 37} though reasons for distinct healthcare needs in specific communities warrant further research to achieve optimal results.^{11 26} Thus, we consider that our analysis represents a suitable approach to identify hypoglycemia patterns and population peculiarities that can be used to tailor targeted interventions and improve preventive healthcare programs.

We nonetheless acknowledge certain limitations that should be considered when interpreting our findings, including the retrospective collection of information available in several databases and the inherent spatial analysis bias derived from its geometric and graphic nature. Although spatial autocorrelation techniques reduce the subjectivity of data visualization in space and spatial analysis is an appropriate method for descriptive and exploratory purposes, it cannot provide satisfactory explanations. We therefore performed linear regression analyses to provide further insight into the association of hypoglycemia with a broad range of socioeconomic factors retrieved from different databases. However, medical charts of people who called requesting assistance could not be accessed and the potential influence of other unconsidered factors such as those related to diabetes management could not be assessed. Despite the fact that it was not a nationwide study, it included all calls requesting emergency assistance from one of the largest regions in Spain with more than 8 million inhabitants. Additional studies are still needed to confirm its applicability to other regions or countries.

In conclusion, our geographical analysis revealed differences in the risk of hypoglycemic events requiring emergency assistance in the different geographic areas, which seems to be affected by age and associated with societal factors such as employment, literacy/education, housing and sports facilities. These findings warrant further research to more deeply understand spatial patterns of hypoglycemia and design-specific prevention programs according to its geographical distribution and societal characteristics.

Acknowledgements The authors would like to thank Esther Álvarez-García, of the Scientific Advisory & Medical Writing Department at Dynamic Science S.L., for her writing assistance in the preparation of this manuscript.

Contributors All authors have participated sufficiently in the work presented by the article to take public responsibility for the content. FG-P contributed

to conception of the work presented by the article, acquisition, analysis and interpretation of data, and drafting of the article. MB was the main person responsible for Geographic Information System analysis. CA, MB and RJB contributed to the analysis and interpretation of data and revised the article for critically important content. All authors provided their final approval of the version to be published.

Funding Menarini Laboratories, S.A. supported the editorial assistance by means of an unrestricted grant. The conception and design, acquisition of data or analysis and interpretation of data were conducted thanks to the unconditional effort of all participating investigators.

Map disclaimer The depiction of boundaries on the map(s) in this article does not imply the expression of any opinion whatsoever on the part of BMJ (or any member of its group) concerning the legal status of any country, territory, jurisdiction or area or of its authorities. The map(s) are provided without any warranty of any kind, either express or implied.

Competing interests FG-P has taken part in advisory panels for Sanofi and Novo Nordisk; he has received research support from Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals and Lilly, and he has acted as a speaker for Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company and Lilly. CA has received research support from Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals and Lilly, and she has acted as a speaker for Sanofi, Novo Nordisk, Boehringer Ingelheim Pharmaceuticals, AstraZeneca Pharmaceuticals LP and Bristol-Myers Squibb Company.

Patient consent for publication Not required.

Ethics approval This study is embedded in the Emergency Assistance of the Person with Diabetes Project (PAUEPAD, for its initials in Spanish). Institutional review board approval was obtained through the Empresa Pública de Emergencias Sanitarias and Investigation Committee (approval number: PAUEPAD26032013), and the requirement for informed consent was waived based on the nature of the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplemental information. Further data are available on reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Fernando Gomez-Peralta <http://orcid.org/0000-0003-0106-0091>

REFERENCES

- 1 International Diabetes Federation. IDF diabetes atlas: international diabetes Federation, 2017. Available: <http://diabetesatlas.org/resources/2017-atlas.html> [Accessed 13 Mar 2018].
- 2 Seaquist ER, Anderson J, Childs B, *et al.* Hypoglycemia and diabetes: a report of a Workgroup of the American diabetes association and the endocrine Society. *Diabetes Care* 2013;36:1384–95.
- 3 Geller AI, Shehab N, Lovegrove MC, *et al.* National estimates of insulin-related hypoglycemia and errors leading to emergency department visits and hospitalizations. *JAMA Intern Med* 2014;174:678–86.
- 4 Kim S. Burden of hospitalizations primarily due to uncontrolled diabetes: implications of inadequate primary health care in the United States. *Diabetes Care* 2007;30:1281–2.
- 5 Budnitz DS, Lovegrove MC, Shehab N, *et al.* Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med* 2011;365:2002–12.

- 6 Orozco-Beltrán D, Mezquita-Raya P, Ramírez de Arellano A, *et al.* Self-Reported frequency and impact of hypoglycemic events in Spain. *Diabetes Ther* 2014;5:155–68.
- 7 Barranco RJ, Gomez-Peralta F, Abreu C, *et al.* Incidence and care-related costs of severe hypoglycaemia requiring emergency treatment in Andalusia (Spain): the PAUEPAD project. *Diabet Med* 2015;32:1520–6.
- 8 Ahola AJ, Groop P-H. Barriers to self-management of diabetes. *Diabet Med* 2013;30:413–20.
- 9 Koch T. *Cartographies of disease: maps, mapping, and medicine*. Redlands, USA: ESRI Press, 2005.
- 10 Baker J, White N, Mengersen K. Spatial modelling of type II diabetes outcomes: a systematic review of approaches used. *R Soc Open Sci* 2015;2:140460–12.
- 11 Hipp JA, Chalise N. Spatial analysis and correlates of county-level diabetes prevalence, 2009–2010. *Prev Chronic Dis* 2015;12:140404.
- 12 Siordia C, Saenz J, Tom SE. An introduction to macro- level spatial nonstationarity: a geographically weighted regression analysis of diabetes and poverty. *Human Geogr* 2012;6:5–13.
- 13 S. Shrestha Set *al.* Spatial clusters of county-level diagnosed diabetes and associated risk factors in the United States. *Open Diabetes J* 2012;5:29–37.
- 14 Council of Health of Andalusia. Public company for health emergencies (Empresa Pública de Emergencias Sanitarias, EPES), 2018. Available: <http://www.epes.es/> [Accessed 20 Feb 2018].
- 15 National Statistics Institute. Census of population and housing. population figures as of January 1, 2013. Spain, 2013. Available: <http://www.ine.es/jaxit3/Datos.htm?t=9681> [Accessed 20 Feb 2018].
- 16 Ministry of Health Social Policy and Equality. *CIE-9 MC. coding, information and health statistics manual 2011*. Madrid, Spain: Ministry of Health, Social Policy and Equality, 2011.
- 17 Statistical and Cartographic Institute of Andalusia. Basic spatial data of Andalusia (DERA), 2017. Available: <http://www.juntadeandalucia.es/institutodeestadisticaycartografia/DERA/index.htm> [Accessed 20 Feb 2018].
- 18 National Statistics Institute. Census of population and housing. population figures as of November 1, 2011. Spain, 2011. Available: http://www.ine.es/censos2011_datos/cen11_datos_inicio.htm [Accessed 20 Feb 2018].
- 19 Institute of Statistics and Cartography of Andalusia. System of Multiterritorial information of Andalusia (SIMA), 2011. Available: <http://www.juntadeandalucia.es/institutodeestadisticaycartografia/sima/index2.htm> [Accessed 20 Feb 2018].
- 20 Tobler W. Spatial interaction patterns. *J Environ Sci* 1976;6:271–301.
- 21 Anselin L. Local indicators of spatial Association-LISA. *Geogr Anal* 1995;27:93–115.
- 22 Anselin L, Syabri I, Kho Y. GeoDa: an introduction to spatial data analysis. *Geogr Anal* 2006;38:5–22.
- 23 Tao Z, Shi A, Zhao J. Epidemiological perspectives of diabetes. *Cell Biochem Biophys* 2015;73:181–5.
- 24 Ellis PD. *The essential guide to effect sizes: statistical power, meta-analysis, and the interpretation of research results*. Cambridge: Cambridge University Press, 2010.
- 25 Villani M, Earnest A, Smith K, *et al.* Geographical variation of diabetic emergencies attended by prehospital emergency medical services is associated with measures of ethnicity and socioeconomic status. *Sci Rep* 2018;8:5122.
- 26 Lee DC, Long JA, Sevvick MA, *et al.* The local geographic distribution of diabetic complications in New York City: associated population characteristics and differences by type of complication. *Diabetes Res Clin Pract* 2016;119:88–96.
- 27 Zhou M, Astell-Burt T, Bi Y, *et al.* Geographical variation in diabetes prevalence and detection in China: multilevel spatial analysis of 98,058 adults. *Diabetes Care* 2015;38:72–81.
- 28 Green C, Hoppa RD, Young TK, *et al.* Geographic analysis of diabetes prevalence in an urban area. *Soc Sci Med* 2003;57:551–60.
- 29 Minozzo M, Fruttini D. Loglinear spatial factor analysis: an application to diabetes mellitus complications. *Environmetrics* 2004;15:423–34.
- 30 Wrobel JS, Mayfield JA, Reiber GE. Geographic variation of lower-extremity major amputation in individuals with and without diabetes in the Medicare population. *Diabetes Care* 2001;24:860–4.
- 31 Hurst JE, Barn R, Gibson L, *et al.* Geospatial mapping and data linkage uncovers variability in outcomes of foot disease according to multiple deprivation: a population cohort study of people with diabetes. *Diabetologia* 2020;63:659–67.
- 32 Faka A, Chalkias C, Montano D, *et al.* Association of Socio-Environmental determinants with diabetes prevalence in the Athens metropolitan area, Greece: a spatial analysis. *Rev Diabet Stud* 2018;14:381–9.
- 33 Myers CA, Slack T, Broyles ST, *et al.* Diabetes prevalence is associated with different community factors in the diabetes belt versus the rest of the United States. *Obesity* 2017;25:452–9.
- 34 Yang L, Shao J, Bian Y, *et al.* Prevalence of type 2 diabetes mellitus among inland residents in China (2000–2014): A meta-analysis. *J Diabetes Investig* 2016;7:845–52.
- 35 Shrestha SS, Thompson TJ, Kirtland KA, *et al.* Changes in disparity in County-Level diagnosed diabetes prevalence and incidence in the United States, between 2004 and 2012. *PLoS One* 2016;11:e0159876.
- 36 Curtis AJ, Lee W-AA. Spatial patterns of diabetes related health problems for vulnerable populations in Los Angeles. *Int J Health Geogr* 2010;9:43.
- 37 Nucci LB, Gomes Sandrin ACL. Spatial analysis of hospitalization rate for diabetes mellitus and its complications in the Brazilian population, 2007–2011. *Int J Diabetes Dev Ctries* 2016;36:228–34.
- 38 Warin B, Exeter DJ, Zhao J, *et al.* Geography matters: the prevalence of diabetes in the Auckland region by age, gender and ethnicity. *N Z Med J* 2016;129:25–37.
- 39 Ccorahua-Ríos MS, Atamari-Anahui N, Miranda-Abarca I, *et al.* Type 2 diabetes mellitus prevalence between 2005 and 2018 in population under 30 using data from the Ministry of health of Peru. *Medwave* 2019;19:e7723.
- 40 Dornhorst A, Lüddecke H-J, Sreenan S, *et al.* Safety and efficacy of insulin detemir in clinical practice: 14-week follow-up data from type 1 and type 2 diabetes patients in the predictive European cohort. *Int J Clin Pract* 2007;61:523–8.
- 41 Khunti K, Alsifri S, Aronson R, *et al.* Rates and predictors of hypoglycaemia in 27 585 people from 24 countries with insulin-treated type 1 and type 2 diabetes: the global HAT study. *Diabetes Obes Metab* 2016;18:907–15.
- 42 Pathak RD, Schroeder EB, Seaquist ER, *et al.* Severe hypoglycemia requiring medical intervention in a large cohort of adults with diabetes receiving care in U.S. integrated health care delivery systems: 2005–2011. *Diabetes Care* 2016;39:363–70.
- 43 Sharma SK, Joshi SR, Kumar A, *et al.* Efficacy, safety and acceptability of biphasic insulin aspart 30 in Indian patients with type 2 diabetes: results from the present study. *J Assoc Physicians India* 2008;56:859–63.
- 44 UK Hypoglycaemia Study Group. Risk of hypoglycaemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. *Diabetologia* 2007;50:1140–7.
- 45 Zilov A, El Naggar N, Shah S, *et al.* Insulin detemir in the management of type 2 diabetes in non-Western countries: safety and effectiveness data from the Achieve observational study. *Diabetes Res Clin Pract* 2013;101:317–25.