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Large-scale societal factors and noncommunicable diseases: Urbanization, poverty and mortality spatial patterns in Argentina

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A B S T R A C T

Introduction: In developing countries, the rapid increase in noncommunicable diseases burden has been accompanied by socio-demographic changes, such as rapid urbanization, with persistence of considerable socio-economic gaps between populations. In Argentina, cardiovascular diseases (CVD) and cancer are leading causes of death. The aim of this study was to identify geographic clustering of mortality rates related to both diseases in Argentina and to assess their association with two large-scale societal factors, urbanization and poverty contexts.
Materials and methods: We performed an ecological study in Argentina (n = 525 counties), 2009–2011 period. Using spatial analysis techniques we identified and mapped spatial clusters of high and low values for age-standardized mortality rates (ASMR) of cancer or CVD and for selected urbanization and poverty indicators. We estimated incidence-rate ratios using two-level *Poisson* regression models, which accounted for rates distribution spatial variability.
Results: Cancer and CVD mortality rates distribution were spatially dependent. Population growth showed an inverse association with ASMR from these causes, for both sexes. We detected an additive interaction of effects between urban scale and poverty level, being the "rural poverty" associated with an increasing risk of mortality by cancer (in both sexes) or by CVD (only men), compared to contexts with high urban scale and low poverty level. Counties with an intermediate urban scale seem to present the most favorable context, even when their socio-economic conditions are more unfavorable than those with higher urbanization levels.
Conclusions: Geographical differences in urban and socioeconomic contextual conditions can explain spatial variation in NCD mortality burden in Argentina.

1. Introduction

Noncommunicable diseases (NCD) are the leading mortality cause of death worldwide, with the majority of death occurring in low- and middle-income countries. In Argentina, NCD account for 81% of total deaths, being cardiovascular diseases (CVD) and cancer responsible for almost half of all deaths (World Health Organization, 2014a).

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While common behavioral or metabolic/physiological risk factors for NCD are well established at the individual level, currently researchers are looking at the role of large-scale societal forces that drive NCD, including ageing, the globalization of unhealthy lifestyles, and rapid urbanization (World Health Organization, 2014b). Nevertheless, pathways underlying these "upstream" determinants of NCD are not completely understood, especially in low- and middle-income countries (Ebrahim et al., 2013).

Although the growing epidemic of NCD has been described as a global phenomenon, the spatial distribution of their burden indicators varies greatly both between and within countries. Based on the idea that people's lifestyles and the conditions in which they live strongly influence their health (Wilkinson and Marmot, 2003), the Spatial Epidemiology assumes that geography defines the spatial context and character in which health risks occur (Beale, Abellan, Hodgson, & Jarup, 2008). Thus, it may be thought that behind the spatial patterns of diseases burden often underlie some health inequities, reflecting, in turn, inequitable distribution of its determinants.

Particularly, the Social Determinants of Health (SDH) approach puts its interest in those conditions in which individuals live, work and age, and the wider set of forces and systems shaping the conditions of daily life (World Health Organization), as main determinants of health outcomes in populations. From this perspective, models have been proposed which, in general, identify constituents ranging from the most distal factors at societal-level to a set of individual-level influences (behavioral/physiological) (Graham, 2004). It is remarkable that the conception of nested and correlated data structures that underlie the conceptual model of SDH is the basis of multilevel analytical approach (Kawachi, Subramanian, & Almeida-Filho, 2002). Accordingly, our study focused on two large-scale societal factors, urbanization and poverty, addressed from the multilevel modeling framework and mapping.

The influence of urbanization on health is complex, context-specific and closely related to socioeconomic determinants. In fact, if we assume that it is linked to economic growth and development, we would expect a favorable impact on health due to its potential to minimize socioeconomic disadvantages. However, urban life has also been associated with environmental risk exposures (i.e., air pollution and occupational hazards) (Gong et al., 2012) and risks conferred by behavioral changes such as unhealthy diet and sedentary life (Angkurawaranon, Jiraporncharoen, Chenthanakij, Doyle, & Nitsch, 2014a, Angkurawaranon, Jiraporncharoen, Chenthanakij, Doyle, & Nitsch, 2014b; Gong et al., 2012; Leon, 2008). In addition, it should be noted that, although there is strong evidence that poverty has traditionally been deeper in rural areas than in cities, nowadays, the growing concentration of harsh poverty within cities, especially in developing countries (UNFPA, 2007), reinforces the importance of disentangling the complex linkage between urbanization, poverty and health.

In Latin America and the Caribbean, the most urbanized region in the world, rapid urban growth in the last decades has been highlighted as a megatrend that affects people's well-being (PAHO, 2012). In turn, Argentina is among the countries with a long-standing process of urbanization and with a highly urban population (UN & CELADE, 2009). Even when census results indicate that 91% of population is living in urban areas, there is a notable heterogeneity in the country, which has been related to quality of life in this population (Velázquez, 2010). Besides, the last national census reports that over a million households have at least one basic need unsatisfied, 83.5% of which belong to urban areas.

Socio-demographic scenario in the Latin American region has been widely studied. However, little is still known about large-scale societal factors underlying the spatial distribution of NCD burden statistics in developing countries. Therefore, our aims were: a) to identify geographic clustering of mortality rates of cancer and CVD in Argentina (2009–2011), and b) to assess their association with two larger-scale societal factors, urbanization and poverty contexts.

2. Materials and methods

2.1. Study design and data

We performed an ecological study, including two hierarchical administrative divisions of Argentina: 525 counties (510 departments and 15 communes in Buenos Aires City), nested into 24 provinces (23 plus the Autonomous City of Buenos Aires, excluding Argentine Antarctica and the South Atlantic Islands). We calculated sex-specific and age-standardized mortality rates (ASMR, *per* 100,000 persons/year) by direct method (national population of 2010 census as standard) for selected causes (ICD-10th revision codes: C00-C97 for cancers and I00-I99 for CVD) and for each geographical unity (county). The average of 2009–2011 ASMR was used to control the influence of small-area estimation, which is expected in counties with small population size.

Beyond the simplified notion of urbanization as the proportion of people living in areas defined as urban, this phenomenon represents a complex demographic process that involves several aspects, such as the population distribution on the urban-rural space, the speed and scale of urban growth, and the organization of the urban system. Thus, our convention for "urbanization" encompasses two main features: the speed of population growth (as *proxy* of urban population growth) and the organization of the urban system measured by county urban scale. We include the following indicators: a) average annual population growth (defined by the National Institute of Statistics and Censuses -INDEC- as the average annual change of population size during the 2001–2010 period, *per* thousand inhabitants) and b) urban scale (category based on the largest urban agglomeration within each administrative division in 2010). We define urban scale variables taking into account the six category scale proposed by Velázquez et al. (2016). For interpretation, we transformed this scale as follows: a) big cities and large middle-sized cities (of 400,000 or more inhabitants); b) intermediate middle-sized cities (399,999-50,000 inhabitants); c) small cities and villages (49,999-2000 inhabitants); and d) towns and rural population (less than 2000 inhabitants).

We chose the percentage of households with Unsatisfied Basic Needs (UBN) as poverty indicator for each sampling unit. This indicator is extensively used as a structural poverty index in Latin American counties. From the basic needs approach, poverty was defined on the basis of socially determined needs that an individual, and hence her households, must satisfy in order to participate fully in society (ECLAC & UNICEF, 2005). Thus, if the access of previously established basic needs, such as housing, sanitation facilities, attendance to school and livelihood, are not met by households, they are considered poor.

No ethical review was required as it involved anonymized records and datasets existing in the public domain.

2.2. Data sources

In order to calculate ASMRs, we used the number of certified deaths provided by the National Health Ministry and estimated the population size by exponential interpolation of 2001 and 2010 population census data, published by the INDEC. Population growth information was obtained through the INDEC Report of the 2010 National Population, Household and Housing Census final results. Poverty indicator was obtained by processing of this official census database using REDATAM software (Redatam + SP, ECLAC/United

Nations). Velázquez et al. (2016). provided the urban-scale database (at the county level), based on aggregated census data obtained by official sources.

2.3. Spatial analysis and mapping

Spatial autocorrelation was assessed performing Moran's Index (MI) test using the inverse-distance spatial weight matrix with power 1 (Chi & Zhu, 2008). MI is a common statistical measure of the degree to which a set of spatial features and their associated data values tended to be clustered or dispersed (Stopka, Krawczyk, Gradziel, & Geraghty, 2014). The global MI is defined as the equation:

$$MI = \frac{\sum_{i=1}^{N} \sum_{j=1}^{N} w_{ij}(x_i - \overline{x})(x_j - \overline{x})}{\sum_{i=1}^{N} (x_i - \overline{x})^2},$$

where N is the number of spatial units (counties); x_i and x_j are the values of variable x in county i and j; $\overline{x}$ is the average over all spatial units of the variable; w_{ij} is the spatial weight that measures the strength of the relationship between two spatial units (Zhao, Huang, & Liu, 2012). The statistical significance of MIs was checked considering the Normal asymptotic distribution of MIs under null hypothesis (Kelejian & Prucha, 2001). Since this global indicator may be too crude as a measure of the actual spatial autocorrelation for data across a region that could be expected in several spatial regimes (Chi & Zhu, 2008), we calculated a local indicator of spatial association, the Getis-Ord Gi* statistic (Getis & Ord, 1992). This statistic is given as:

$$G_i^* = \frac{\sum_{j=1}^{n} w_{ij}x_j - \overline{X}\sum_{j=1}^{n} w_{ij}}{S\sqrt{\left[n\sum_{j=1}^{n} w_{ij}^2\right]}}$$

where x_j is the attribute value for county j, w_{ij} is the spatial weight between county i and j, n is equal to the total number of counties and $\overline{X}$ and S are the mean and standard deviation of x_j, respectively.

Thus, we performed the Getis-Ord Hot Spot Analysis tool (Gi* statistic) of the ArcMap central application of ArcGIS 10.2.2 software (Esri Inc. 1999–2014, US) for all variables (except for urban scale as categorical variable). This tool identifies statistically significant spatial clusters of high values (hot spots) and low values (cold spots) for each variable, considering each county within the context of neighboring county and against all counties in the dataset (Stopka, Krawczyk, Gradziel, & Geraghty, 2014). Thus, z-scores and p-values are estimated indicating whether the observed spatial clustering of high or low values is more pronounced than one would expect in a random distribution of those same values (ESRI, 2016). We illustrated the clustering for each variable using thematic maps with statisitically significant hot spot and cold spots.

2.4. Statistical modeling

Due to the hierarchical structure of our dataset (counties nested into provinces), we estimated associations of urbanization and poverty indicators with NCD mortality using a two-level *Poisson* regression model. A random effect (intercept) was incorporate at province level accounting for that source of "not observed" spatial variability of rates distribution, which we suppose that could be originate the possible correlation between counties within each province. Thus, county i as level 1 ($i = 1, \ldots, 525$) and province j as level 2 ($j = 1, \ldots, 24$) were considered for modeling, being the linear predictor of proposed model:

$$\log[E(y_{ij})] = \zeta_{ij} + \beta_1 x_{1ij} + \beta_2 x_{2ij} + \beta_3 x_{3ij} + \beta_4 x_{4ij} + \beta_5\, x_{2ij} * x_{3ij} + \beta_6\, x_{2ij} * x_{4ij}$$

In this model, we defined ASMR for cancers or cardiovascular diseases (CVD) by sexes, as the response variable (y_{ij}), the average annual population growth (x_{1ij}), urban scale (x_{2ij}) and percentage of households with UBN by tertiles (being x_{3ij} and x_{4ij} dummy covariates for this categorical variable) as explanatory variables with fix effects (linear coefficients), and ζ_{ij} as a random intercept term. We also included additive interaction terms to represent joint effects between scale urban and poverty level. We estimated incidence-rate ratios (exponential of coefficients) for interpretations. We used Stata v13 software (StataCorp LP 1985–2013, USA) for all statistical analysis.

3. Results

Estimated mortality rates and large-scale societal characteristics of counties are presented in Table 1. There were 122.9 and 157.0 cancer deaths *per* 100,000 women and men, respectively (the average of 2009–2011 ASMR equals to 118.3 and 181.8 *per* 100,000) in Argentina. The mortality rate was higher for CVD than cancer, with crude rates of 190.1 (ASMR: 169.4) and 214.3 (ASMR: 268.8) *per* 100,000, in the female and male populations, respectively. Most Argentinean counties had an increase in the annual population growth up to 20%, while about 10% of them had a null or negative population growth. Besides, more than half of the counties present an urban scale of small cities and villages (64.57%) and had a percentage of households with UBN greater than 10% (53.52% of counties). The proportion of counties with high level of poverty (upper tertile of UBN) tends to increase with a decreasing urban scale (Table 1).

Based on MI estimates, we found that distribution of cancer (MI: 0.02 in women and 0.12 in men) and CVD ASMRs (MI: 0.09 in both populations), as well as population growth (MI: 0.04) and poverty indicator (MI: 0.26) were spatially dependent in Argentina ($p < 0.05$). All MI values were positive and statistically significant, showing that the spatial distribution of high and low values is more spatially clustered than expected if underlying spatial processes were random. The greatest spatial clustering (higher MI) was observed in male cancer rates and UBN indicator.

Fig. 1 shows clustering maps of the cancer or CVD mortality distributions. Similar locations of the cold spot clusters of cancer ASMR were observed for women and men (Fig. 1A and B); they showed distinguished clusters in the northwest region of the country. In contrast, differences between sexes were found for high-value clusters of cancer ASMR across Argentina. In men (Fig. 1-B), two major local hot spot clusters of counties were located in the Pampa region (east-central area) and the southern Patagonia. For women (Fig. 1-A), less clear spatial pattern of hot spots was observed, showing significantly clusters with disperse location across the country (Fig. 1-A). A similar spatial pattern for cancer and CVD mortality was observed, with hot spots in east-central areas and cold spots in northwestern areas for both diseases. However, CVD mortality pattern (Fig. 1C and D) shown no differences between sexes, as opposed to cancer mortality, and reveals a statistically significant cold spot cluster in Patagonia region (Southern area), which was not observed in cancer spatial patterns (Fig. 1A and B).

Fig. 2-A and B show that there is a considerable heterogeneity in terms of both urban scale and population growth within the country. Highest population growth seems to be concentrated in the southern region of Argentina (north and southern Patagonia), whereas the lowest growth was located west of Buenos Aires (Fig. 2-B).

Table 1
Characteristics of cancer and CVD mortality and selected variables in Argentina (525 counties).

Variables	Mean (SD) or Frequency (%)
- Cancer mortality (average of 2009–2011 rates)[a]	
CMR in women	122.9 (52.2)
ASMR in women	118.3 (1.5)
CMR in men	157.0 (67.8)
ASMR in men	181.8 (2.3)
- CVD mortality (average of 2009–2011 rates)[a]	
CMR in women	190.1 (102.8)
ASMR in women	169.4 (2.4)
CMR in men	214.3 (92.0)
ASMR in men	268.8 (3.7)
- Average annual population growth in 2001–2010 period[b]	
Null population growth, or 1% or more annual decrease	54 (10.29)
0.1–9.9% annual increase	267 (50.86)
10–19.9% annual increase	140 (26.67)
20–29.9% annual increase	39 (7.43)
30–39.9% annual increase	18 (3.43)
40% or higher annual increase	7 (1.33)
- Urban scale (2010)[b]	
Big cities and large middle-sized cities (>400,000 inhabitants)	77 (14.67)
Intermediate middle-sized cities (399,999 to 50,000 inhabitants)	60 (11.43)
Small cities and villages (49,999 to 2000 inhabitants)	339 (64.57)
Towns and rural population (<2000 inhabitants)	49 (9.33)
- % households with UBN (2010)[b]	
Under 10%	244 (46.48)
10–19%	195 (37.14)
20–29%	73 (13.90)
30% or more	13 (2.48)
- Urban scale by poverty level[b] (percentage of households with UBN tertiles)	
Big cities and large middle-sized cities	
Lower tertile of UBN	31 (40.26)
Middle tertile of UBN	40 (51.95)
Upper tertile of UBN	6 (7.79)
Intermediate middle-sized cities	
Lower tertile of UBN	29 (48.33)
Middle tertile of UBN	22 (36.67)
Upper tertile of UBN	9 (15.00)
Small cities and villages	
Lower tertile of UBN	110 (32.45)
Middle tertile of UBN	101 (29.79)
Upper tertile of UBN	128 (37.76)
Towns and rural population	
Lower tertile of UBN	5 (10.20)
Middle tertile of UBN	12 (24.49)
Upper tertile of UBN	32 (65.31)

SD indicates standard deviation; CMR, crude mortality rate; ASMR, age-standardized mortality rates; UBN, Unsatisfied Basic Needs.
[a] Mean (SD).
[b] Frequency (%).

On the contrary, Fig. 2-C shows a strong spatial clustering (hot spots), with a high proportion of households with UBN in the northern area of the country. Besides, low values for this poverty indicator (cold spots) were located in the Pampa region (Fig. 2-C).

Tables 2 and 3 summarizes the results of modeling by sex, both for cancer and CVD mortality series, respectively. The multilevel modeling was able to quantify unobserved heterogeneity on mortality dataset attributable to the spatial variability in rates distribution. In fact, estimated variances of random effect of the clustering variable "province" were significant in all models. This implies that there was a non-random spatial distribution of NCD ASMR. Individual and joint effects of selected covariates were significant for both cancer and CVD ASMRs. For that, deviations from additivity of covariate effects are only described here.

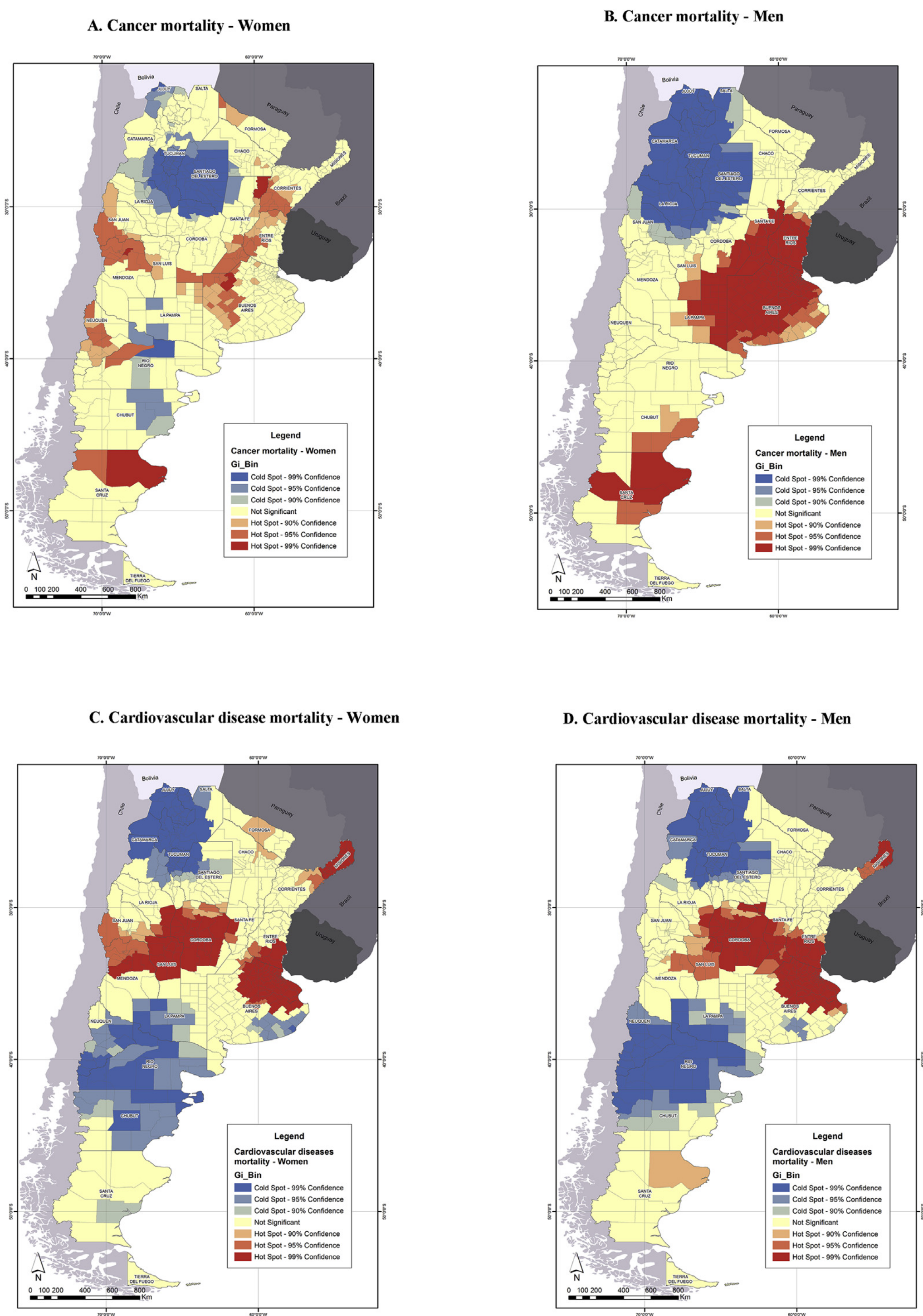
As shown in Tables 2 and 3, there was a decreasing risk of mortality associated to an increase in the average annual population growth and a significant interaction between urban scale and the selected poverty indicator for both cancer and CVD. Overall, using the highest urban scale (big cities and large middle-sized cities) combined with low poverty (low tertile of UBN indicator) as a baseline interaction category, there was an indirect effect of intermediate categories (urban scale between 2000 and 399,999 inhabitants with medium or high tertile of UBN) on cancer and CVD ASMRs (Tables 2 and 3). This mean that living in intermediate middle-sized cities or small cities and villages would be more advantageous than residing in big cities, even in conditions of greater poverty. Additionally, we found that higher mortality risk of cancer (in both sexes) and CVD (in men) were associated with the smallest urban scale (towns and rural population) coupled with medium or high level of poverty (medium or high tertile of UBN) (Table 2 and 3-B). According to the estimated IRRs, counties characterized with low urban scale and poverty contexts had a risk increment of almost 43% of cancer mortality (IRR for towns and rural population, tertile III of UBN = 1.43 and 1.72 for male and female population, respectively), and of 16% or more for male CVD mortality (IRR 1.16, 95% CI 1.06–1.28), compared with reference category. Only for women, this effect was the opposite (significant protective effect) when CVD ASMR was fitted (Table 3-A).

4. Discussion

This study presents a current spatial pattern of the mortality rates for the most prevalent NCD in Argentina. Our results suggest that geographical differences in urban and socioeconomic conditions are associated with spatial variation in cancer or CVD mortality rates. We found that increasing population growth at the county-level seems to have a favorable impact on mortality rates from these causes, for both sexes. Besides, there was additive interaction between urban scale and UBN level, showing that the rural poverty is associated with an increasing risk of death by cancer (in both sexes) or by CVD (only men), compared to counties with the highest urban scale and low poverty level. Instead, counties with an intermediate urban scale seem to present the most favorable context, even when households have more unfavorable socioeconomic conditions than those located in the largest-sized cities.

Globally, there is evidence suggesting that the urban transition has been favorable for economic development (Gong et al., 2012; UNFPA, 2007) and that urban growth population has benefited many local economies, due to the prosperities linked to economies of scale, pooling of talent and availability of services and technologies (Friel et al., 2011). Southern Argentinean provinces, where our study identified a hot spot of population growth, were previously classified as typically "receptors" of population that exhibited favorable Gross Geographic Product (GGP) growth along time (Velázquez, 2016). In health, this feature may reflect favorable macro-economic circumstances that assure, for example, availability of medical services and technology for cancer or CVD screening or health care at the county level.

Urbanization constitutes a contextual factor associated to the rising burden of NCD in the last years (Angkurawaranon et al., 2014a, 2014b; Gong et al., 2012). Overall, researchers proposed that both material mechanisms (structural determinants and material conditions of daily life) and psycho-social mechanisms (psychological stressors or depression, health behaviors) may mediate associations between social determinants of macro-levels (as urbanization) and NCD outcomes (Havranek et al., 2015). Public health research on urbanization typically comes from developed countries and focuses on the rural-urban dichotomy, even when abundant evidence points to the complexity and multifactorial



Note: Features at the highest level of color intensity reflect statistical significance with a 99 percent confidence level; features at the intermediate level of color intensity reflect a 95 percent confidence level; features at the lowest level of color intensity reflect a 90 percent confidence level; and the clustering for features in yellow is not statistically significant.

Fig. 1. Clustering maps of high values (hot spots in red) and low values (cold spots in blue) of AMSR *per* 100,000 (average of 2009–2011 rates) for cancer (A and B) and cardiovascular diseases (C and D), by sexes (women on the left; men on the right) in Argentina. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

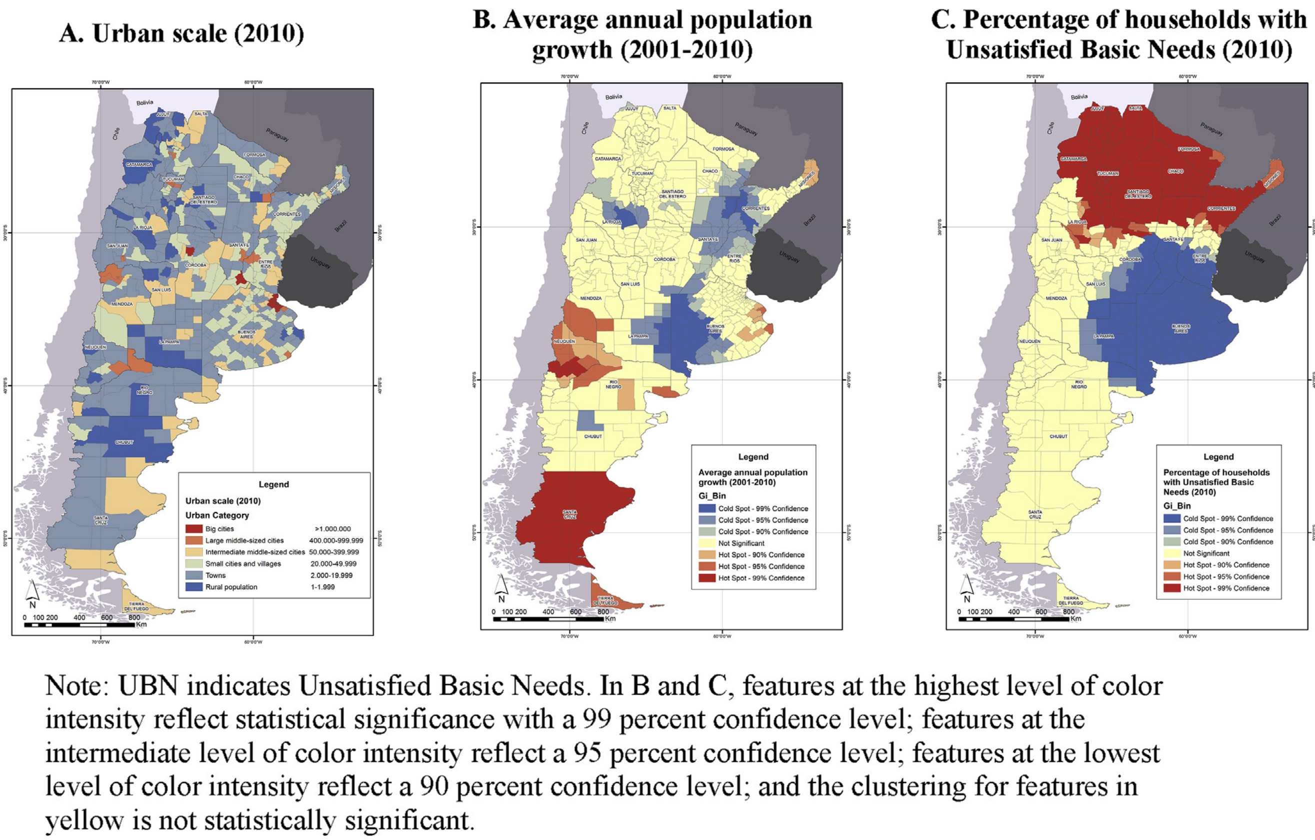


Fig. 2. Urban scale distribution (A), clustering maps of high values (hot spots in red) and low values (cold spots in blue) of population growth (2001–2010) (B), and poverty indicator (C) by counties in Argentina in 2010. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Estimates of association measures (IRR) between urbanization and poverty indicators and the cancer mortality in Argentina (average of 2009–2011 ASMR). Multilevel Poisson models results.

	A. Female population		B. Male population	
	IRR (95% CI)	p value	IRR (95% CI)	p value
Covariables (Fixed effects)[a]				
- Average annual population growth, *per* thousand inhabitants (*continuous* variable)	0.995 (0.995–0.996)	<0.001	0.998 (0.997–0.998)	<0.001
- Urban scale (categorical variable)				
Big cities and large middle-sized cities	1	–	1	–
Intermediate middle-sized cities	1.11 (1.06–1.17)	<0.001	1.18 (1.14–1.24)	<0.001
Small cities and villages	1.13 (1.08–1.17)	<0.001	1.23 (1.19–1.27)	<0.001
Towns and rural population	0.40 (0.35–0.45)	<0.001	0.53 (0.48–0.58)	<0.001
- % households with UBN (categorical variable by tertiles)				
Tertile I	1	–	1	–
Tertile II	1.04 (0.99–1.08)	0.127	1.02 (0.99–1.06)	0.228
Tertile III	1.06 (0.98–1.16)	0.162	1.06 (0.99–1.13)	0.111
- Interaction (categorical variables)				
Urban scale * % households with UBN				
Big cities and large middle-sized cities, tertile I of UBN	1	–	1	–
Intermediate middle-sized cities, tertile II of UBN	0.95 (0.88–1.01)	0.107	0.85 (0.80–0.89)	<0.001
Intermediate middle-sized cities, tertile III of UBN	0.87 (0.78–0.97)	0.015	0.82 (0.75–0.89)	<0.001
Small cities and villages, tertile II of UBN	0.96 (0.91–1.01)	0.093	0.84 (0.81–0.88)	<0.001
Small cities and villages, tertile III of UBN	0.87 (0.80–0.95)	0.002	0.73 (0.68–0.78)	<0.001
Towns and rural population, tertile II of UBN	1.48 (1.27–1.72)	<0.001	1.98 (1.78–2.20)	<0.001
Towns and rural population, tertile III of UBN	1.72 (1.47–2.01)	<0.001	1.43 (1.28–1.61)	<0.001
Clustering variable (random effects)	**Area level variance (covariance)**			
Intercept	0.014 (0.001)		0.008 (0.001)	

ASMR indicates age-standardized mortality rates; IRR, incidence-rate ratios; CI, confidence interval; UBN, Unsatisfied Basic Needs.
[a] Constant (95% CI): 125.47 (121.24–129.86) and 186.69 (181.79–191.73) in the female and male models, respectively.

Table 3
Estimates of association measures (IRR) between urbanization and poverty indicators and the cardiovascular diseases mortality in Argentina (average of 2009–2011 ASMR). Multilevel Poisson models results.

	A. Female population		B. Male population	
	IRR (95% CI)	p value	IRR (95% CI)	p value
Covariables (Fixed effects)[a]				
- Average annual population growth, *per* thousand inhabitants (*continuous* variable)	0.997 (0.996–0.998)	<0.001	0.996 (0.995–0.996)	<0.001
- Urban scale (categorical variable)				
Big cities and large middle-sized cities	1	–	1	–
Intermediate middle-sized cities	0.92 (0.88–0.96)	<0.001	0.98 (0.95–1.00)	0.096
Small cities and villages	0.91 (0.88–0.94)	<0.001	0.98 (0.95–1.00)	0.055
Towns and rural population	0.90 (0.84–0.98)	0.010	0.54 (0.50–0.58)	<0.001
-% households with UBN (categorical variable by tertiles)				
Tertile I	1	–	1	–
Tertile II	1.15 (1.11–1.19)	<0.001	1.18 (1.15–1.21)	<0.001
Tertile III	1.30 (1.22–1.39)	<0.001	1.39 (1.32–1.46)	<0.001
- Interaction (categorical variables)				
Urban scale * % households with UBN				
Big cities and large middle-sized cities, tertile I of UBN	1	–	1	–
Intermediate middle-sized cities, tertile II of UBN	0.90 (0.85–0.95)	<0.001	0.90 (0.86–0.94)	<0.001
Intermediate middle-sized cities, tertile III of UBN	0.87 (0.80–0.95)	0.001	0.80 (0.75–0.86)	<0.001
Small cities and villages, tertile II of UBN	0.93 (0.89–0.96)	<0.001	0.87 (0.84–0.90)	<0.001
Small cities and villages, tertile III of UBN	0.82 (0.77–0.88)	<0.001	0.76 (0.72–0.80)	<0.001
Towns and rural population, tertile II of UBN	0.86 (0.78–0.94)	0.001	1.33 (1.22–1.45)	<0.001
Towns and rural population, tertile III of UBN	0.73 (0.66–0.81)	<0.001	1.16 (1.06–1.28)	0.001
Clustering variable (random effects)	**Area level variance (covariance)**			
Intercept	0.018 (0.001)		0.021 (0.001)	

ASMR indicates age-standardized mortality rates; IRR, incidence-rate ratios; CI, confidence interval; UBN, Unsatisfied Basic Needs.
[a] Constant (95% CI): 197.97 (192.80–203.29) and 275.35 (269.57–281.26) in the female and male models, respectively.

pathways through which urbanization affects health (Gong et al., 2012; Whiting & Unwin, 2009).

Our results support the hypothesis that urbanization (measured by urban scale), coupled with poverty levels, represents a large-scale societal factor underlying the spatial patterns of NCD mortality in Argentina. Multilevel analysis perspective allows distinguishing between “collective” and “contextual” effects on health (Kawachi, Subramanian, & Almeida-Filho, 2002). Hence, the poverty index used in our work provide an explanation for spatial differences in mortality rates based on aggregated group properties that produce a “collective effect”. Instead, urban scale and population growth represent features that are intrinsic to places, and therefore, related to upper-level “contextual effects” (Kawachi et al., 2002). Regarding NCD mortality there is a comprehensive body of knowledge about the variations attributable to collective effects of factors such as poverty level by residence area (Havranek et al., 2015; Merletti, Galassi, & Spadea, 2011), but contextual heterogeneity linked to urbanization process has not been extensively studied in developing regions.

The recognition of poverty as a main social determinant of health inequities is not new. Concerning NCD, the socioeconomic position has been previously related to cancer (Hiatt & Breen, 2008; Merletti et al., 2011) or CVD mortality (Harper, Lynch, & Smith, 2011; Havranek et al., 2015), even in Argentina (Diez Roux, Green Franklin, Alazraqui, & Spinelli, 2007; Matos, Loria, & Vilensky, 1994). However, the socioeconomic pathways underlying health inequalities are not always fully understood. For instance, consistent evidence from developed regions reports higher risks of several types of cancers among socially disadvantaged people and a direct relation of such cancers as colon, breast and ovarian cancer, among others, with social status (Merletti et al., 2011). It should be noted that mortality rates of breast and colon cancer in Argentina are comparable to the mortality rates in developed countries (Justo, Wilking, Jönsson, Luciani, & Cazap, 2013; Pou, Osella, Eynard, Niclis, & Díaz, 2009).

Although current research suggests that urban poverty is a worldwide emerging concern of public health (UNFPA, 2007; PAHO, 2012), our results provide evidence that supports more traditional perspectives, whereby rural poverty is at a greater disadvantage than big cities. In fact, these ones usually concentrate several benefits (better access to health system, education, basic infrastructure, information and knowledge) (UNFPA, 2007) and greater possibilities of employment to meet basic needs (Leon, 2008). Argentine urban system is formed as an urban macrocephaly (Velázquez, 2016), which is particularly significant for cancer patients, since oncologists work mainly in urban areas and the distribution of medical technology used for cancer screening or treatment is unequally distributed.

In view of our findings, the classic “socioeconomic gradient” (higher risks for higher poverty level) seems to be expressed mainly in rural areas (except for woman in CVD), but this does not appear to be evident for the areas with intermediate urban scale. It has been suggested that the so-called “medium-sized” cities in the Latin American region may be instruments of territorial development (UN & CELADE, 2009). In fact, they represent more balanced urban structures than big cities, with increasing challenges derived from a rapid and unplanned urbanization on a large scale. Moreover, the fact that intermediate urban scale areas showed a protective effect on cancer or CVD mortality -even when coupled with medium or high-level of poverty-suggests that factors other than socioeconomic ones influence health outcomes. Psycho-social and behavioral mechanisms mediating the effects of urbanization-related factors on NCD mortality risk have been proposed. For CVD, it has been described that there are macro-social forces, such as the urbanization proposed here, that influence the prevalence of major risk factors (diet quality and tobacco smoking), which in turn are also differentially distributed across social groups (Harper et al., 2011). Additionally, psychological stressors in urban environments (noise, social isolation and anxiety) have been linked to the development of cardiovascular risk factors (hypertension and atherosclerosis) (Gong et al., 2012; Havranek et al., 2015). This hypothesis could explain the lower risk observed in an intermediate urban scale compared to the largest cities discussed in our work.

Regarding cancer, certain environmental factors more common in urban areas than rural ones (for example, air pollution or some occupational exposures) could be clustered in specific geographical regions (Kanavos, 2006), explaining in part the urban-rural distribution of rates. Moreover, there is strong evidence about the major role of urbanization on obesity prevalence (Popkin, 2014). In Argentina, some studies have reported in last years that specific unhealthy dietary patterns and sedentary habits are associated to specific cancer burden (Pou, Díaz, & Osella, 2012), with some differences related to the urban-rural context of residence (Pou, Niclis, Eynard, & Diaz, 2014).

In contrast to what has been observed for cancer mortality, we found that in contexts of rural poverty there is a protective effect on CVD mortality in women. Whereas there is general agreement on the fact that proximity to health centers is a major concern in rural areas (PAHO, 2012), this argument does not seem to be sufficient to explain our result. So, it should be noted that people worldwide living in poverty conditions in rural areas have shown higher total fertility rates than their counterparts with better socio-economic position in urban contexts (UNFPA, 2007). Argentina also follows this trend. Thus, it is possible that women in rural areas have more frequent contacts with reproductive or child health services than those living in cities, and consequently have greater opportunities of early control of risk factors of CVD. It is remarkable that in Argentina the routine control for hypertension is done during pregnancy by nurses or other health care professionals, but for the accurate diagnosis of breast cancer (the most common incident form of cancer in our population) (Ferlay et al., 2013) skilled health personnel and equipment is required, without which delays in diagnosing and treating this disease can occur, impacting in mortality rates.

This study had some limitations. First, the so-called ecological "fallacy" is a bias inherent to its ecological design. So, inferences cannot be made at the individual level based on the associations observed on attributes from aggregated levels. Second, the modifiable areal unit problem (MAUP) has been referred to as an important issue in spatial data analysis. The MAUP occurs when the results of statistical analysis are highly influenced by the selected geographic scale (Chi & Zhu, 2008). Our study considered two administrative geographic scales from the multilevel analysis (counties nested in provinces), in order to control the correlation and to incorporate hierarchical variability. Finally, data quality may be a major issue in studies based on secondary data. Even when vital events registration and censuses coverage in Argentina could be considered acceptable, it is possible that misclassification of causes of death occur (especially for CVD categories); therefore if census undercounts exist, these are more pronounced in socioeconomically disadvantaged areas (Diez Roux et al., 2007). In that case, the observed associations may be slightly underestimated.

5. Conclusions

Our study shows that there are health inequities among Argentina's geographic regions, and that urbanization and poverty are interrelated large-scale societal factors underlying cancer and CVD mortality spatial distributions. In turn, the observed mortality geographical differences reflect "social inequalities" (Krieger, 2001) and help the identification of subpopulations that would most benefit from potential interventions. Thus, we highlight the need to encourage further interdisciplinary research about social determinants of health in developing countries, aimed to disentangle psychosocial, behavioral and material pathways that could mediate unequal health experiences across sub-populations exposed to diverse urban-rural contexts and socioeconomic circumstances.

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References

Angkurawaranon, C., Jiraporncharoen, W., Chenthanakij, B., Doyle, P., & Nitsch, D. (2014a). Urban environments and obesity in southeast Asia: A systematic review, meta-analysis and meta-regression. *PLoS One, 9*(11), e113547. http://dx.doi.org/10.1371/journal.pone.0113547.

Angkurawaranon, C., Jiraporncharoen, W., Chenthanakij, B., Doyle, P., & Nitsch, D. (2014b). Urbanization and non-communicable disease in southeast Asia: A review of current evidence. *Public Health, 128*, 886–895. http://dx.doi.org/10.1016/j.puhe.2014.08.003.

Beale, L., Abellan, J. J., Hodgson, S., & Jarup, L. (2008). Methodologic issues and approaches to spatial epidemiology. *Environmental Health Perspectives, 116*, 1105–1110. http://dx.doi.org/10.1289/ehp.10816.

Chi, G., & Zhu, J. (2008). Spatial regression models for demographic analysis. *Population Research and Policy Review, 27*, 17–42. http://dx.doi.org/10.1007/s11113-007-9051-8.

Diez Roux, A. V., Green Franklin, T., Alazraqui, M., & Spinelli, H. (2007). Intraurban variations in adult mortality in a large Latin American city. *Journal of Urban Health, 84*, 319–333. http://dx.doi.org/10.1007/s11524-007-9159-5.

Ebrahim, S., Pearce, N., Smeeth, L., Casas, J. P., Jaffar, S., & Piot, P. (2013). Tackling non-communicable diseases in low- and middle-income countries: Is the evidence from high-income countries all we need? *PLoS Medicine, 10*(1), e1001377. http://dx.doi.org/10.1371/journal.pmed.1001377.

Economic Commission for Latin America and the Caribbean (ECLAC), & United Nations Children's Fund (UNICEF). (2005). *Child poverty in Latin America. Challenges newsletter 1*. United Nations publication, UN. http://www.unicef.org/lac/Desafios_1_ing%285%29.pdf (Accessed 1 Jul 2016).

Environmental Systems Research Institute (ESRI). Hot Spot Analysis (Getis-Ord Gi*). http://desktop.arcgis.com/en/arcmap/10.3/tools/spatial-statistics-toolbox/hot-spot-analysis.htm (Accessed 30 May 2016).

Ferlay, J., Soerjomataram, I., Ervik, M., Dikshit, R., Eser, S., Mathers, C., et al. (2013). *GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide: IARC CancerBase No. 11*. Lyon, France: International Agency for Research on Cancer. http://globocan.iarc.fr (Accessed 29 Jan 2016).

Friel, S., Akerman, M., Hancock, T., Kumaresan, J., Marmot, M., Melin, T., et al. (2011). Addressing the social and environmental determinants of urban health equity: Evidence for action and a research agenda. *Journal of Urban Health, 88*, 860–874. http://dx.doi.org/10.1007/s11524-011-9606-1.

Getis, A., & Ord, J. K. (1992). The analysis of spatial association gy use of distance statistics. *Geographical Analysis, 24*, 189–206. http://dx.doi.org/10.1111/j.1538-4632.1992.tb00261.x.

Gong, P., Liang, S., Carlton, E. J., Jiang, Q., Wu, J., Wang, L., et al. (2012). Urbanisation and health in China. *Lancet, 379*, 843–852. http://dx.doi.org/10.1016/S0140-6736(11)61878-3.

Graham, H. (2004). Social determinants and their unequal distribution: Clarifying policy understandings. *Milbank Quarterly, 82*, 101–124.

Harper, S., Lynch, J., & Smith, G. D. (2011). Social determinants and the decline of cardiovascular diseases: Understanding the links. *Annual Review of Public Health, 32*, 39–69. http://dx.doi.org/10.1146/annurev-publhealth-031210-101234.

Havranek, E. P., Mujahid, M. S., Barr, D. A., Blair, I. V., Cohen, M. S., Cruz-Flores, S., et al. (2015). Social determinants of risk and outcomes for cardiovascular disease: A scientific statement from the American heart association. *Circulation, 132*, 873–898. http://dx.doi.org/10.1161/CIR.0000000000000228.

Hiatt, R. A., & Breen, N. (2008). The social determinants of cancer: A challenge for transdisciplinary science. *American Journal of Preventive Medicine, 35*, S141–S150. http://dx.doi.org/10.1016/j.amepre.2008.05.006.

Justo, N., Wilking, N., Jönsson, B., Luciani, S., & Cazap, E. (2013). A review of breast cancer care and outcomes in Latin America. *Oncologist, 18*, 248–256. http://dx.doi.org/10.1634/theoncologist.2012-0373.

Kanavos, P. (2006). The rising burden of cancer in the developing world. *Annals of Oncology, 17*(Suppl 8). http://dx.doi.org/10.1093/annonc/mdl983. viii15–viii23.

Kawachi, I., Subramanian, S. V., & Almeida-Filho, N. (2002). A glossary for health inequalities. *Journal of Epidemiology & Community Health, 56*, 647–652.

Kelejian, H. H., & Prucha, I. R. (2001). On the asymptotic distribution of the Moran I test statistic with applications. *Journal of Econometrics, 104*, 219–257.

Krieger, N. (2001). A glossary for social epidemiology. *Journal of Epidemiology & Community Health, 55*, 693–700.

Leon, D. A. (2008). Cities. urbanization and health. *International Journal of Epidemiology, 37*, 4–8. http://dx.doi.org/10.1093/ije/dym271.

Matos, E. L., Loria, D. I., & Vilensky, M. (1994). Cancer mortality and poverty in Argentina: A geographical correlation study. *Cancer Epidemiology, Biomarkers & Prevention, 3*, 213–218.

Merletti, F., Galassi, C., & Spadea, T. (2011). The socioeconomic determinants of cancer. *Environmental Health, 10*(Suppl 1), S7. http://dx.doi.org/10.1186/1476-069X-10-S1-S7.

Pan American Health Organization (PAHO). (2012). *Health determinants and inequalities. Health in the Americas*. http://www2.paho.org/saludenlasamericas/dmdocuments/hia-2012-chapter-2.pdf (Accessed 10 Jun 2016).

Popkin, B. M. (2014). Synthesis and implications: China's nutrition transition in the context of changes across other low and middle-income countries. *Obesity Reviews, 15*(Suppl 1), 60–67. http://dx.doi.org/10.1111/obr.12120.

Pou, S. A., Díaz, M. D., & Osella, A. R. (2012). Applying multilevel model to the relationship of dietary patterns and colorectal cancer: An ongoing case-control study in Córdoba, Argentina. *European Journal of Nutrition, 51*, 755–764. http://dx.doi.org/10.1007/s00394-011-0255-7.

Pou, S. A., Niclis, C., Eynard, A. R., & Diaz, M. P. (2014). Dietary patterns and risk of urinary tract tumours: A multilevel analysis of individuals in rural and urban contexts. *European Journal of Nutrition, 53*, 1247–1253. http://dx.doi.org/10.1007/s00394-013-0627-2.

Pou, S. A., Osella, A. R., Eynard, A. R., Niclis, C., & Díaz, M. P. (2009). Colorectal cancer mortality trends in Córdoba, Argentina. *Cancer Epidemiology, 33*, 406–412. http://dx.doi.org/10.1016/j.canep.2009.09.009.

Stopka, T. J., Krawczyk, C., Gradziel, P., & Geraghty, E. M. (2014). Use of spatial epidemiology and hot spot analysis to target women eligible for prenatal women, infants, and children services. *American Journal of Public Health, 104*(Suppl 1), S183–S189. http://dx.doi.org/10.2105/AJPH.2013.301769.

United Nations (UN), & Latin American and Caribbean Demographic Centre (CELADE). (2009). *Urbanization prospects. Demographic observatory of Latin America*. Santiago, Chile: CELADE.

United Nations Population Fund (UNFPA). (2007). *State of world population 2007, unleashing the potential of urban growth*. New York: UNFPA. http://www.unfpa.org/publications/state-world-population-2007 (Accessed 15 May 2016).

Velázquez, G. A. (2016). *Geografía y calidad de vida en Argentina. Análisis regional y departamental 2010*. Tandil: Universidad Nacional del Centro de la Provincia de Buenos Aires.

Whiting, D., & Unwin, N. (2009). Cities, urbanization and health. *International Journal of Epidemiology, 38*, 1737–1738. http://dx.doi.org/10.1093/ije/dyn152.

Wilkinson, R. G., & Marmot, M. (Eds.). (2003). *Social determinants of health: The solid facts* (2nd. Edition). Denmark: World Health Organization. http://www.euro.who.int/__data/assets/pdf_file/0005/98438/e81384.pdf (Accessed 16 May 2016).

World Health Organization. Social determinants of health. http://www.who.int/social_determinants/en/. (Accessed 29 Jun 2016).

World Health Organization. (2014a). *Noncommunicable diseases country profiles*. http://www.who.int/nmh/publications/ncd-profiles-2014/en/ (Accessed 06 May 2016).

World Health Organization. (2014b). *Global status report on noncommunicable diseases*. http://www.who.int/nmh/publications/ncd-status-report-2014/en/ (Accessed 20 Feb 2016).

Zhao, X., Huang, X., & Liu, Y. (2012). Spatial autocorrelation analysis of Chinese inter-provincial industrial chemical oxygen demand discharge. *International Journal of Environmental Research and Public Health, 9*, 2031–2044. http://dx.doi.org/10.3390/ijerph9062031.