




# Temporal and Spatial Trends of Adverse Pregnancy and Birth Outcomes in a Sample of Births from a Public Hospital in Chile

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**Abstract** Understanding temporal and spatial trends in pregnancy and birth outcomes within an urban area is important for the monitoring of health indicators of a population. We conducted a retrospective cohort study of all births in the public hospital of Temuco, a medium-sized city in Southern Chile between 2009 and 2016 ( $n=17,237$ ). Information on adverse pregnancy and birth outcomes, as well as spatial and maternal characteristics (insurance type, employment, smoking, age, and overweight/obesity), was collected from medical charts. Home addresses were geocoded

and assigned to neighborhood. We tested whether births and prevalence of adverse pregnancy outcomes changed over time, whether birth events were spatially clustered (Moran's  $I$  statistic), and whether neighborhood deprivation was correlated to outcomes (Spearman's rho). We observed decreases in eclampsia, hypertensive disorders of pregnancy, and small for gestational age, while gestational diabetes, preterm birth, and low birth weight increased over the study period (all  $p<0.01$  for trend), with little changes after adjusting for maternal characteristics. We observed neighborhood clusters for birth rate,

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preterm birth, and low birth weight. Neighborhood deprivation was negatively correlated with low birth weight and preterm birth, but not correlated with eclampsia, preeclampsia, hypertensive disorders of pregnancy, small for gestational age, gestational diabetes, nor stillbirth. Several encouraging downward trends and some increases in adverse pregnancy and birth outcomes, which, overall, were not explained by changes in maternal characteristics were observed. Identified clusters of higher adverse birth outcomes may be used to evaluate preventive health coverage in this setting.

**Keywords** Pregnancy complication · Birth outcomes · Temporal trends · Spatial analysis · Chile

## Introduction

Worldwide, maternal and perinatal health has improved markedly in the last half century. Despite decreases in maternal mortality [1], maternal morbidity has remained high and some maternal and perinatal adverse outcomes (e.g., preterm birth (PTB), pre-eclampsia, and gestational hypertension) have increased in most areas of the world including Latin America and the Caribbean [2, 3]. As a whole, Latin America has experienced rapid development and rising incomes with

concomitant improvements in population health in the last decade [4]. On the other hand, other changes, for example, the postponement of maternity to older ages, environmental pollution, and obesogenic environments [5, 6] all increase risk of obstetric pathologies and adverse perinatal outcomes [7, 8]. Some of the most common adverse pregnancy outcomes include pregnancy induced hypertension, pre-eclampsia, gestational diabetes, low birthweight (LBW), and PTB.

Improving the health of women of childbearing age, pregnancy, and perinatal outcomes is a focus of governments, as improvements directly affect the health and long-term wellbeing of current and future generations. Maternal and perinatal morbidity can compromise the future health of women and children, with both short- and long-term consequences, including maternal and neonatal mortality, neurological impairment in children, and chronic noncommunicable disease in the dyad [9, 10]. There are economic consequences as well, with morbidity related to increased hospitalization risk in intensive care, which is important both for the individual and also the health system [11].

Understanding how indicators of maternal and child health change over time is necessary for population surveillance. In addition, a spatial analysis provides information on how geographic location may influence health outcomes may be useful for the targeting of public policies aimed at improving community health. Here, we report the prevalence, temporal and spatial trends of several adverse pregnancy, and birth outcomes using a maternal cohort obtained from a public hospital in the South of Chile.

## Materials and Methods

As part of a larger study on pregnancy air pollution exposure and pregnancy and birth outcomes, we conducted a retrospective cohort study of births delivered in the regional public hospital in Temuco, Chile between 2009 and 2016. A chart-abstraction team of health professionals, led by a midwife, digitized information from paper medical charts of births which underwent several data quality checks. The study was approved by the Ethical Committee of the Servicio de Salud Araucanía Sur (#1179).

The urban area of Temuco (population 379,000) [12] is situated in southern Chile in the Araucanía

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Region, approximately 700 km from Chile's capital, Santiago, and includes two neighboring municipalities, Temuco and Padre Las Casas. The population has a life expectancy of 81.7 years, and 32% of the population identifies as having indigenous, mainly Mapuche, origins. The Araucanía Region is the poorest of the 16 regions of Chile with 17% of the population living in poverty, higher levels of illiteracy and low levels of schooling compared to national averages [13]. Additionally, Temuco, like most cities in southern Chile, suffers from high air pollution episodes during the winter due to residential wood-burning [14].

We conducted our study in the regional health center, which is the only tertiary public hospital in the area. In Chile, health insurance is a two-tiered (public and private) system. Public health insurance is available to all via the Fondo Nacional de Salud (FONASA) with differential costs based on income. Those with relatively higher incomes (FONASA B, C and D) are provided the option to receive treatment as part of the private system with a discounted co-pay, while those with lower and no income (FONASA A) are not and thus pay out of pocket if they choose to seek services in the private sector. Private health insurance is available for purchase and clusters among those with higher incomes [15, 16]. Health service infrastructure is separate, with public hospitals often situated close to private ones. In 2017, 75% and 98% of the population of Temuco and Padre Las Casas, respectively, were part of the public (FONASA) system [17, 18].

### Cohort Selection

Of the 26,198 births recorded in the study period, 17,237 were included in the current study (see supplementary Fig. 1 for more details). Because of the nature of air pollution in Temuco [14], this study focused on urban-residing women, and hence, most exclusions were due to living outside of the urban area.

### Outcomes

Preeclampsia, per standard diagnosis practice in Chile, is defined as elevated blood pressure (systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg) at or after 20 weeks' gestation in an individual with previously normal blood

pressure accompanied by one or more of the following new-onset conditions: proteinuria, other maternal organ dysfunction, or uteroplacental dysfunction [19]. Women with clinical diagnosis of preeclampsia without laboratory or Doppler ultrasonography confirmation were presumed not to have the condition. Eclampsia (preeclampsia-induced generalized seizure or coma that cannot be attributed to other causes) was also obtained from clinical chart. Hypertensive disorder of pregnancy was identified from maternity records as those having any of the following four diagnoses: preeclampsia, gestational hypertension, chronic hypertension, and chronic hypertension with superimposed preeclampsia. Chronic hypertension was diagnosed before pregnancy, with gestational hypertension diagnosed during pregnancy. Superimposed preeclampsia was diagnosed as chronic hypertension in association with preeclampsia. Gestational diabetes is defined as values of fasting glucose between 100 and 125 mg/dL on two different days at any point in the pregnancy or fasting glucose  $\geq 140$  mg/dL measured in the second or third trimester of pregnancy [20].

Birth outcomes were identified from records following standard diagnosis practice in Chile: PTB (gestational age  $< 37$  weeks), LBW (birthweight  $< 2500$  g), term LBW (LBW among those born  $\geq 37$  gestational weeks, tLBW), stillbirth (fetal death at or after 20 weeks' gestation), and small for gestational age (SGA, birthweight  $< 10$ th percentile according to gestational age for the Chilean population) [21]. Gestational age was determined using reported date of last menstrual period and via ultrasound conducted in the first trimester in the primary care setting.

### Exposures

Delivery date and the following maternal characteristics were recorded from clinical birth charts: health insurance type, organized as public, public with access to private, and private; smoking status; employment; highest education level completed (none/primary, secondary, or higher education); height; pre-pregnancy weight; and age, organized as  $< 20$ , 20–34, and  $\geq 35$  years [22]. Pre-pregnancy BMI was calculated using height and weight and overweight/obesity was defined as having BMI  $\geq 25$  kg/m<sup>2</sup>.

Maternal residential address was geocoded as previously described [23] using search engines in this order: Bing, Google Earth, and Google Maps for Temuco, and Google Earth only for Padre Las Casas. Both Bing and Google Earth geocoding were implemented using a code in R, using RJSONIO and RCurl packages to automatically download data from the web, while Google Maps geocoding were implemented using QGIS software. Addresses that were not found using automated methods were geocoded manually using Google Street View and a GPS receiver.

Geocoded addresses were aggregated at the neighborhood level using 47 neighborhood units (*unidades vecinales*); administrative units inside municipalities that tend to represent homogeneous neighborhoods [24]. We obtained information on population in the urban area from the most recent census with spatial data [25] and used the multiple deprivation index (MDI) as an overall composite measure of neighborhood deprivation [26]. The MDI is constructed with data from public entities that considers the following six components: crime, education, surrounding green areas, housing, demographics, and Mapuche population [26]. A higher MDI score indicates greater neighborhood deprivation with possible ranges between 5 and 38.

### Statistical Analysis

For temporal trend analysis, we estimated the prevalence of each adverse pregnancy and birth outcome by year, calculated 95% confidence intervals (95% CI) and tested for a linear trend using log binomial regression. We repeated the procedure for the maternal characteristics of interest. Subsequently, we fitted log binomial regression models for each adverse outcome to test whether potential temporal trends in outcomes could be explained by changes in maternal characteristics. For spatial analysis, the prevalence of adverse outcomes was estimated for each neighborhood (number of adverse events / number of births  $\times 100$ ). We calculated birth rate using number of births in our sample as the **numerator, and population in each neighborhood as the denominator  $\times 1000$** . We then tested whether birth rate and adverse events present overall spatial clustering using the Global Moran's  $I$  statistic and identified spatial clusters at the local level using Local Indicators of Spatial

Association (LISA) (e.g., identifying high birth rate neighborhoods next to other high birth rate neighborhoods). Finally, we evaluated the correlation between birth rate and adverse outcomes by neighborhood and whether birth rate and adverse outcomes were correlated with neighborhood deprivation, using Spearman's rho. An alpha level of 0.05 was established. Analyses were conducted using R software.

### Results

Table 1 describes the sample of pregnant women in the cohort. The most frequent adverse pregnancy and birth outcome was hypertensive disorders of pregnancy (9.9%) and PTB (10.4%).

#### Temporal Trends

Figure 1 illustrates prevalence by year of each outcome. Preeclampsia remained relatively stable over the study period ( $\sim 3\%$ ), whereas eclampsia decreased from 0.3 to 0%, and hypertensive disorders of pregnancy decreased from 13.7 to 10% (both  $p < 0.001$  for trend). Gestational diabetes tended to increase, although this trend did not appear to be linear. For birth outcomes, a slight increase was observed in PTB and LBW during the study period, with PTB increasing from 9 to 11.8% ( $p < 0.001$ , for trend) and LBW from  $\sim 6$  to 9% ( $p = 0.007$ , for trend). Stillbirth and tLBW remained mostly stable over time with prevalence below 2% for both outcomes, while SGA decreased from  $\sim 8$  to  $\sim 4\%$  ( $p < 0.001$  for trend).

**Women who reported having paid employment, those who reported having completed higher education, and the prevalence of overweight/obesity increased over the study period, while smoking decreased (all  $p < 0.001$  for trend, Supplementary Fig. 2).** Despite these trends in maternal characteristics, temporal trends in health outcomes remained largely similar after adjustment (Table 2). Some moderate changes in slope when comparing unadjusted and adjusted models were observed for eclampsia (from 35 to 41% reduction per year) and gestational diabetes (18 to 15% increase per year), while more modest changes were observed for PTB (5 to 2% increase per year) and LBW (3 to 1% increase per year). Only changes in LBW over time appeared to be explained by changes in maternal characteristics (RR contained null value in adjusted model).

**Table 1** Maternal characteristics and adverse pregnancy and birth outcomes in a retrospective birth cohort, Temuco, Chile (2009–2016),  $n = 17,237$ 

	Missing	$n$ (%)
Age	0	
< 20		3377 (19.6)
20–34		11,126 (64.5)
≥ 34		2734 (15.9)
Education	30	
≤ Primary		2345 (13.6)
High school		11,419 (66.4)
≥ Secondary		3443 (20.0)
Health insurance type	0	
Public		9515 (55.2)
Public with access to private		7372 (42.7)
Private		350 (2.0)
Marital status	95	
Married		3864 (22.6)
Cohabiting		6842 (39.9)
Single		6296 (36.7)
Other		140 (0.8)
Paid employment	214	5038 (29.6)
BMI category	0	
Underweight		1325 (7.7)
Normal weight		7017 (40.7)
Overweight/obese		8895 (51.6)
Smoking	575	1004 (6.0)
<i>Adverse pregnancy outcomes</i>		
Preeclampsia	0	583 (3.4)
Eclampsia	6	16 (0.9)
Hypertensive disorders of pregnancy	2	1711 (9.9)
Gestational diabetes	0	1363 (7.9)
<i>Adverse birth outcomes</i>		
Preterm birth	23	1782 (10.4)
Low birthweight	11	1294 (7.5)
Term low birthweight	34	268 (1.6)
Stillbirth	96	181 (1.1)

### Spatial Trends

Table 3 shows a summary of spatial statistics and correlations. We observed a range of prevalence estimates by neighborhood and identified evidence of spatial clustering using Moran's  $I$  for birth rate, PTB, and LBW only. Variability in neighborhood deprivation by neighborhood can be appreciated in Supplementary Fig. 3; however, in terms of correlations

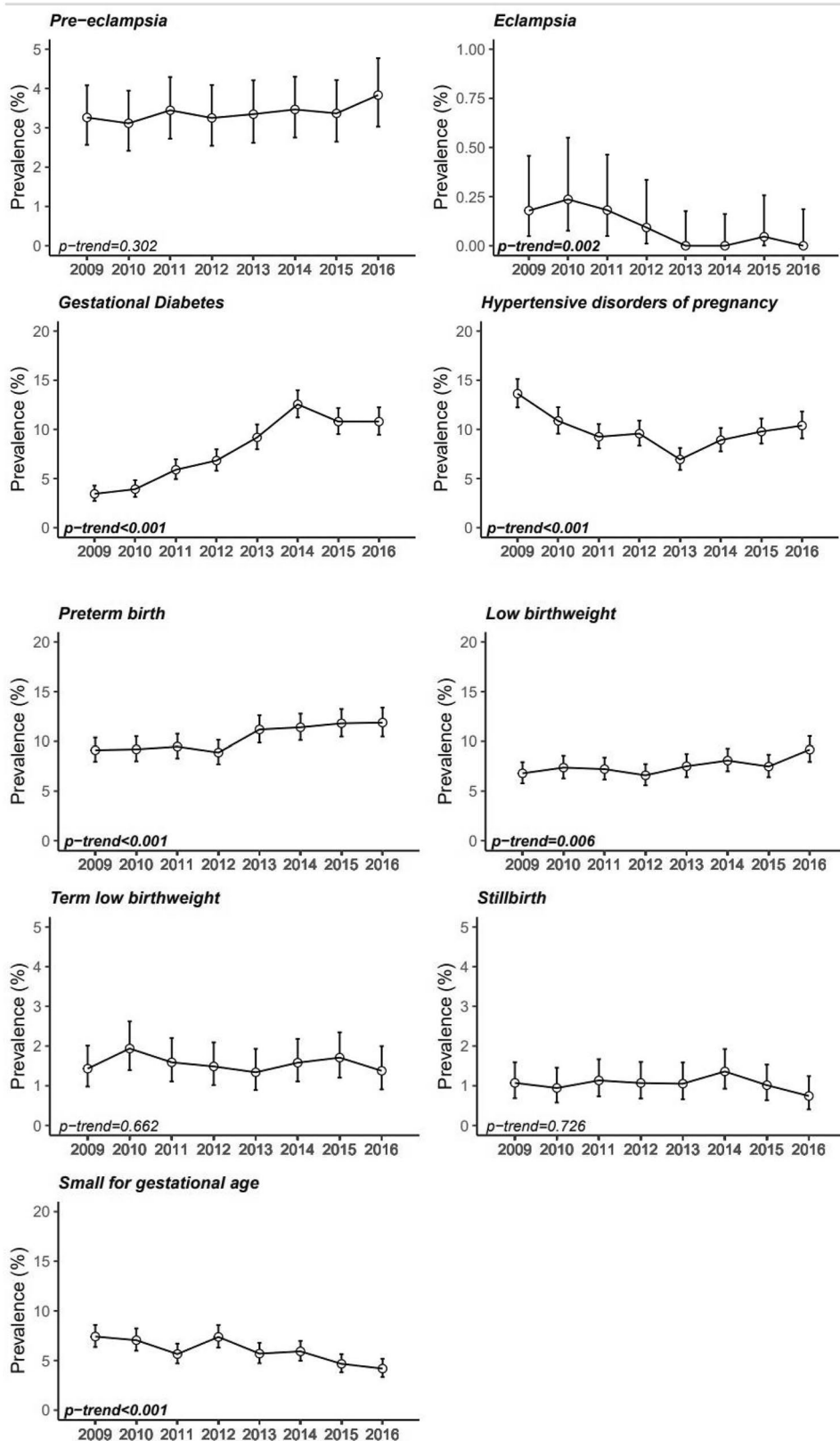
between adverse outcomes and neighborhood deprivation, we observed weak correlations for most outcomes (Table 3), with no clear direction of effect. For birth rate, we observed a moderate positive correlation, indicating greater birth rates in neighborhoods with greater deprivation (Spearman's  $\rho = 0.64$ ), and negative correlations of similar magnitude for PTB and LBW. For most adverse outcomes, we identified weak correlations with neighborhood birth rate and no clear pattern of direction of effect. Birth rate and PTB and LBW were negatively correlated, indicating higher prevalence of these outcomes in neighborhoods with lower birth rates.

For the three outcomes for which spatial clustering was identified (birth rate, PTB, and LBW), Fig. 2 highlights differences in rate and prevalence by neighborhood and where and what type of clusters were identified. For all other outcomes, prevalence estimates are spatially summarized in Supplementary Fig. 4. Two neighborhoods were identified as clusters of high prevalence (neighborhoods close to other high prevalence neighborhoods) of both PTB and LBW: José Miguel Carrera and Millaray (Fig. 2). The neighborhoods of Sofo and Porvenir were clusters of PTB (high-high) and, for LBW, Universidad.

### Discussion

In our retrospective cohort of over 17,000 births to women from a sample of the public hospital in Temuco over an 8-year period, we highlight four primary findings. First, the prevalence of some of the most important adverse pregnancy and birth outcomes was broadly consistent with national reports and within ranges estimated for the region. Second, we observed temporal trends, both increasing and decreasing, in the period from 2009 to 2016, mostly in agreement with other publications. Third, trends were not explained by changes in maternal characteristics, known to influence both maternal and birth outcomes. And, finally, we observed some spatial clustering of adverse outcomes not previously reported in the literature. We discuss these findings and their implications for future research and policy in more detail below.

Our estimates were slightly higher than national rates for PTB [27], but within the estimated range of likely values for the Latin American and Caribbean





◀**Fig. 1** Adverse pregnancy and birth outcomes by year with *p*-value for trend over time, Temuco, Chile, 2009–2016

region [28] for preeclampsia, PTB, LBW, and similar to previous reports for SGA [29]. Rather than discuss each outcome separately, we highlight a few. Although we observed a prevalence of PTB higher than national reports for the same period (10.1% versus 7.8%), prevalence was nearly identical to worldwide estimates [30] and within the range reported for the Latin American and Caribbean region in a recent systematic review and meta-analysis [28]. PTB is the most common cause of death in newborns (first 4 weeks of life) and, when infants survive, is associated with high hospitalization costs and long-term sequelae [3]. Thus, it is vital to maintain surveillance at various administrative levels (within a hospital, city, region, and country).

Reports of prevalence of SGA vary greatly worldwide, in the Latin American region, prevalence in 2010 was estimated as 20%, although much lower (7%) in Chile [29]—a level similar to what we reported here for the 2009 to 2016 period. There is a paucity of information on prevalence of gestational diabetes in many countries, due to the gross underestimation of this adverse pregnancy event [10] and changing definitions and criteria; however, a study conducted in a public hospital in the capital of Chile reported a nearly identical prevalence for the period 2009 to 2015 compared to our study [31]. Because we evaluated only urban-dwelling women from a public hospital, we would expect rates to be similar to those reported in a public hospital in Santiago.

We observed important decreases in eclampsia, hypertensive disorders of pregnancy, and SGA. Because of the small number of cases, our reported downward trend of eclampsia should be interpreted with caution. Specifically, there were no cases of eclampsia in 2013 and 2014, likely due to improved management of pre-eclampsia, and few cases in all other years (prevalence < 0.25%). With respect to hypertensive disorders of pregnancy, our results are in accordance with a recently published report of worldwide trends that found age-adjusted incidence rate decreases between 1990 and 2019 [32]. Decreases are likely related to improved medical interventions and awareness on the part of clinicians. While additional decreases are likely possible, it is important to monitor trends overtime, especially as maternity continues

to be delayed and advanced maternal age is an important risk factor for this pathology. For SGA, a similar downward trend has been reported in Spain starting in 2002, although rates began increasing again after 2009 which coincided with an economic crisis [33]. On the other hand, pre-eclampsia, tLBW, and stillbirth remained low and relatively constant in the period. Like eclampsia, tLBW and stillbirth were also rare (< 2% in all years), making identification of temporal or spatial trends in the studied period difficult. Future studies should consider evaluating trends for a larger administrative area (region or country-wide trends). That said, further reducing these uncommon outcomes remain a challenge to the obstetric community.

We report increases over time in prevalence of gestational diabetes, PTB, and LBW that were largely unaffected by concomitant changes in maternal characteristics. In Chile, the definition of gestational diabetes changed during the study period. Before 2015, pregnant women with fasting glucose between 140 and 200 mg/dL were categorized as glucose intolerant, but as having gestational diabetes after June 2015. We maintained the same definition of gestational diabetes; thus, our findings should not be affected by the change. However, we note that prevalence was in lower in 2015 and 2016 compared to previous years, warranting continued monitoring of this trend. Our findings are consistent with the work of Garmendia and colleagues previously mentioned conducted in a large public hospital in Santiago [31]. Similar to our study, increasing trends have been identified for PTB in Chile and worldwide [30]. Because LBW and PTB often co-occur, it is not surprising that we also observed an increasing trend for LBW. However, we note that the prevalence of tLBW, which may be more indicative of an underlying fetal growth restriction unrelated to PTB, remained somewhat stable and low over the studied period.

Other reports of temporal trends, both increases and decreases, have cautioned against over interpretation of results, as large multiple-country studies are often unable to adjust for changes in maternal characteristics occurring within the study duration [30]. For example, Sebastian and colleagues reported that the 46% decrease in SGA among women in India may relate to reductions in risk factors, for example, increases in the percent of women with higher education and changes in maternal anthropometry [34]. In

**Table 2** Associations between year of birth and adverse pregnancy and birth outcomes, Temuco, Chile (2009–2016),  $n = 17,237^1$ 

	Unadjusted model RR (95% CI)	Adjusted model <sup>2</sup> RR (95% CI)
<i>Pregnancy</i>		
Preeclampsia	1.02 (0.98, 1.05)	0.99 (0.95, 1.02)
Eclampsia	0.65 (0.49, 0.86)*	0.59 (0.42, 0.82)*
Hypertensive disorders of pregnancy	0.96 (0.94, 0.98)*	0.94 (0.92, 0.96)*
Gestational diabetes	1.18 (1.15, 1.21)*	1.15 (1.12, 1.18)*
<i>Birth</i>		
Preterm birth	1.05 (1.03, 1.07)*	1.02 (1.00, 1.04)*
Low birthweight	1.03 (1.01, 1.06)*	1.01 (0.98, 1.03)
Term low birthweight	0.99 (0.94, 1.04)	1.00 (0.94, 1.05)
Stillbirth	0.99 (0.93, 1.05)	0.98 (0.92, 1.05)
Small for gestational age	0.93 (0.91, 0.96)*	0.93 (0.90, 0.95)*

<sup>1</sup>Relative risk represent risk per 1-year change<sup>2</sup>Adjusted for health insurance, maternal smoking, employment, higher education, overweight/obesity, and age category\*  $p$ -value < 0.05

our case, decreases in the period were virtually unaffected by adjustment by these variables. Interestingly, the only temporal trend that attenuated to the null was LBW. While we accounted for several characteristics known to influence adverse maternal and birth outcomes, a future study should attempt to explain these trends using, for example, information from prenatal visits.

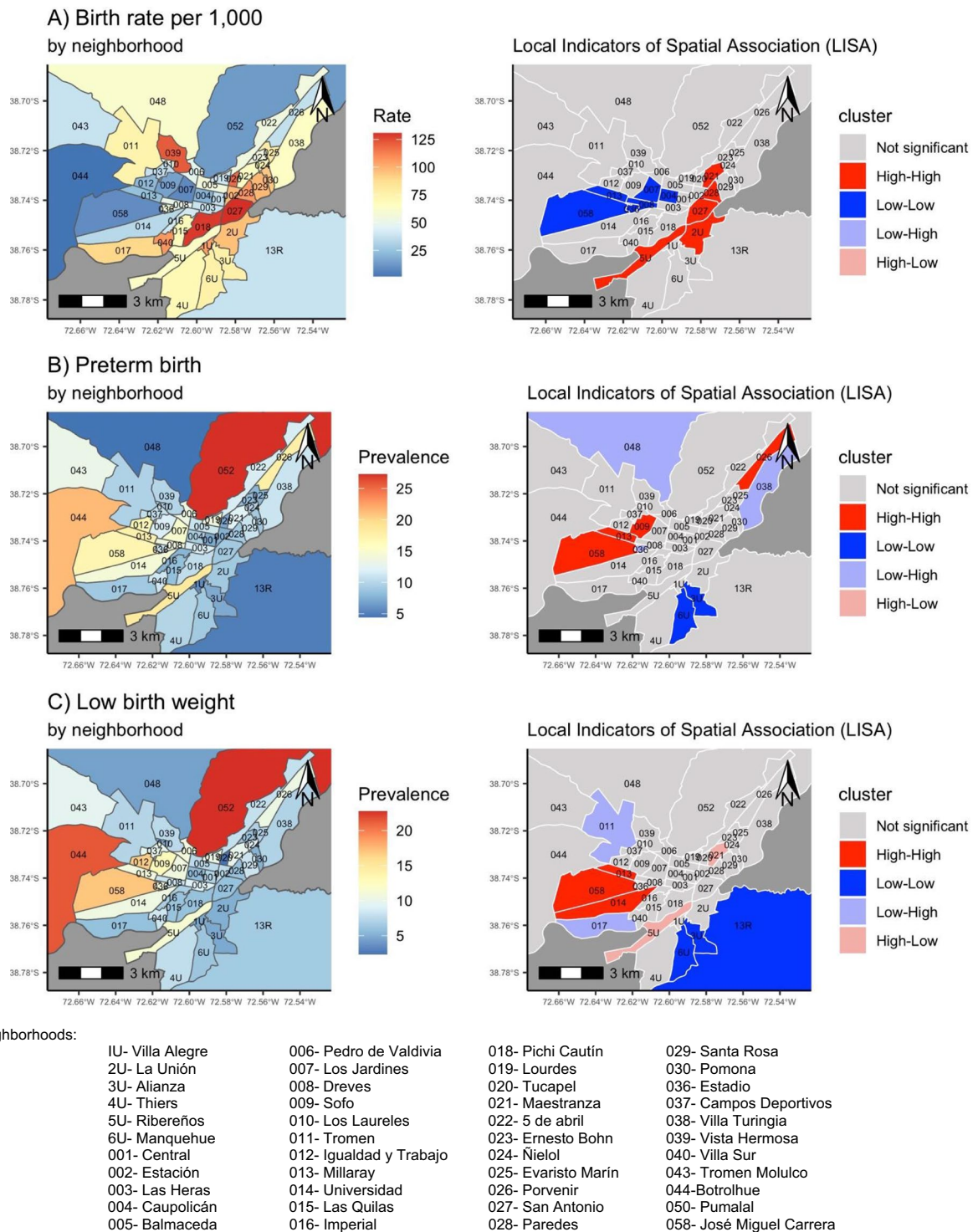
We identified important spatial clusters of birth rate, LBW, and PTB. High-high clusters (i.e., neighborhoods with high rates or prevalence surrounded by other high neighborhoods with high rates of prevalence) identified may be useful for healthcare administrators interested in ensuring vulnerable populations have adequate preventive care coverage. Known risk factors for LBW and PTB could be more closely

**Table 3** Spatial statistics for health outcomes, Temuco, Chile ( $n = 17,237$ )

Health outcome	Min	Max	Moran $I$	Correlation <sup>1</sup> with deprivation index	Correlation <sup>1</sup> with birth rate
Birth rate <sup>2</sup>	1.7	130.7	0.31*	0.64*	–
<i>Pregnancy</i>					
Preeclampsia	0	9.8	0.01	–0.13	–0.02
Eclampsia	0	0.7	–0.06	0.08	0.19
Hypertensive disorders of pregnancy	0	17.7	<0.01	–0.04	–0.09
Gestational diabetes	0	13.1	0.07	0.11	0.04
<i>Birth</i>					
Preterm birth	4.4	27.3	0.16*	–0.58*	–0.55*
Low birthweight	2.3	22.7	0.17*	–0.66*	–0.63*
Term low birthweight	0	7.1	–0.02	–0.32	–0.27
Stillbirth	0	2.7	–0.10	–0.17	0.18
Small for gestational age	1.2	12.3	–0.12	0.11	–0.23

<sup>1</sup>Spearman's rho<sup>2</sup>Births per 1000\*  $p$ -value < 0.05





**Fig. 2** Spatial distribution of select health outcomes by neighborhood and correlations with SES, Temuco, Chile, 2009–2016

monitored among women in the neighborhoods identified as having high rates of these outcomes.

We also explored spatial correlations between neighborhood deprivation and adverse birth outcomes and observed weak correlations for most. This may indicate that prevalence is influenced more by individual, rather than neighborhood, characteristics. Contrary to what has been found in reports from the USA [35], we observed that neighborhoods with a higher LBW and PTB prevalence correlated with lower deprivation index (more affluent neighborhoods). We speculate that this may be explained by the two-tiered system of health care in Chile, where women with higher incomes can choose where to receive care (public or private centers). We conducted our study in the public hospital in Temuco; however, a private hospital is close by, which caters to both private and public health insurance patients with higher income. Given the choice, a woman with pregnancy complications may opt to or be encouraged by her clinician to deliver in the public hospital because of more advanced neonatal and specialty care availability and decreased potential cost. Because we did not have access to prenatal care information, we were unable to explore this hypothesis further. This also shows a limitation of our study since information on prenatal and postnatal outcomes of the more affluent population who chose to undertake their pregnancies and delivery in the private hospital is not included in the current study. Prospective studies of pregnant women of different income levels or the inclusion of information from private health centers might clarify these findings.

There are several strengths worth highlighting. Information was abstracted from medical charts by a team of trained medical professionals led by a senior midwife researcher. A subset (around 10%) of charts were chosen at random for double entry and checking by the senior researcher. In addition, the study was conducted at the only tertiary care public hospital in the area, where the majority of births in the region take place. We were also able to adjust for several individual characteristics that are known to influence the risk of maternal and birth outcomes.

We observed high levels of primary adverse birth and pregnancy outcomes and identified both increasing and decreasing trends that are in accordance with national and international reports. Trends were virtually unaffected after adjusting for maternal characteristics. While the decreasing trends identified are

encouraging, continued surveillance is needed, especially in light of increases in maternal risk factors (e.g., obesity and age at pregnancy). We also identified spatial clusters of adverse birth outcomes which may benefit administrators of local healthcare centers to design targeted public health policies and encourage similar analyses in other cities.

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**Data Availability** Data is available upon request to the corresponding author.

## Declarations

**Disclaimer** The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Sponsors did not influence in any way in the design, the data collection, the analysis, the writing, and the decision to publish these results.

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