### RESEARCH ARTICLE







# Sunspot activity and birth defects among Texas births (1999-2016)

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# Abstract

Background: Building on findings that linked higher levels of sunspot (SS) activity with a range of health and adverse birth outcomes, we sought to understand how SS activity over a 17-year time period may be correlated with the occurrence of birth defects.

Methods: Data from the Texas Birth Defects Registry, vital events from the Texas Center for Health Statistics, and mean monthly numbers of sunspots from the National Oceanic and Atmospheric Administration were utilized. Poisson regression was used to calculate crude/adjusted prevalence ratios (cPRs/aPRs) and 95% confidence intervals for three quartiles (Q) of increasing SS activity (compared to a referent of low activity) and 44 birth defects (31 non-cardiac; 13 cardiac) with estimated dates of conception from 1998 to 2016.

**Results:** We found moderately protective aPRs (range: 0.60–0.89) in a little over half of the case groups examined in our quartiles of higher SS activity (19 non-cardiac; 6 cardiac), after adjusting for maternal age, race/ethnicity, and education. Particularly protective aPRs in the highest SS quartiles (O3-4) were noted for: anophthalmia, cataract, gastroschisis, trisomy 18, ventricular septal defects, atrial septal defects, and pulmonary valve atresia or stenosis. Conversely, modestly elevated aPRs were noted for two defect groups (agenesis, aplasia, and hypoplasia of the lung and microcephaly [Q2-3]). Following an additional adjustment of year of conception, results remained similar although many of the estimates were attenuated.

Conclusion: The seemingly protective associations between increasing SS activity may be an artifact of increasing spontaneous abortions that occur following conception during these periods of heightened SS activity.

### KEYWORDS

birth defects, heart defects, pregnancy, solar cycle, sunspots

#### INTRODUCTION 1

Heliobiology, a branch of biophysics that studies how changes in solar activity impact terrestrial organisms,

was founded by Soviet physicist, A. L. Chizhevsky, in the early 20th century. Chizhevsky reported how cyclic variations in solar radiation were found to influence epidemics, epizootics, and exacerbations of nervous and

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mental illnesses (Chizhevsky, 1976). In recent years, periods of both high and low geomagnetic activity from the sunspot cycle (a roughly 11-year cycle) have been associated with myocardial infarction (Cornélissen et al., 2002; Gurfinkel' et al., 1995; Zilli Vieira et al., 2019), blood pressure (Ghione et al., 1998; Wang et al., 2021), suicide (Stoupel et al., 1995), depression (Kay, 1994), and sudden infant death syndrome (SIDS) (Goldwater & Oberg, 2021; O'Connor & Persinger, 1997). Lifespan also appears to be affected. In a recent study utilizing Norwegian data from 1676 to 1878, the authors found that individuals born during solar 'maximums' lived, on average, shorter lives (by  $\sim$ 5 years) compared to those born during solar minimums (Skjærvø et al., 2015). This study follows an earlier analysis by Lowell and Davis (2010) who examined  $\sim$ 58 million death records from the US National Center for Health Statistics (1979-2005) and found that individuals conceived in solar maximum peak years lived approximately two fewer years than those conceived during solar minimum years (Lowell & Davis, 2010).

Although a few proposed mechanisms for these associations in living organisms have been explored, namely: alterations in vitamin D levels and the melatonin pathway (Burch et al., 1999; Weydahl et al., 2001), disruptions in normal calcium ion homeostasis (Blackman et al., 1990; Cleary, 1993), and field-induced changes in free radicals within the body (Cleary, 1993; Sienkiewicz et al., 1993; Sobel et al., 1995), there are many gaps in our understanding of these phenomena. Changes in solar activity induce both magnetic and electromagnetic changes around the earth, for instance, and are known to impact 24-h circadian rhythms—operating primarily through melatonin mediated pathways (Krylov, 2017). Further, diminished folate levels (associated with an array of birth defects; Safi et al., 2012), have also been associated with increasing levels of solar UV radiation (UV-R).

Apart from a limited number of studies on a few selected adverse infant outcomes, little work has examined geomagnetic field variations (GMFVs) attributed to the sunspot cycle and the impact on infant outcomes. A study by Halpern et al. (1995), for instance, found a trend towards an excess incidence of chromosomal abnormalities in infants born during solar maximum versus minimum periods in an Israeli population (2.15% vs. 1.8%) (although results were not statistically significant [Halpern et al., 1995]). More recently, Juckett (2009) found correlations between the solar cycle and both birth defects and cancer across large birth cohorts spanning 180 years (from 1820 to 2000). Similarly, Belisheva et al. (2012) found associations between heightened periods of solar activity, increasing cosmic ray intensity, and later congenital malformations.

While previous work has suggested that cosmic radiation events produced by the Sun may produce adverse biological effects on Earth, other investigators have argued that the ionizing radiation produced by these solar events is insufficient to produce congenital malformations under the current paradigm of ionizing radiation (Overholt et al., 2015). Further, some work has found that a few selected infant outcomes are positively impacted by early pregnancy sun exposure. Merlob et al. (1989) for instance, found that infants born during sunspot maximums were generally heavier and longer in length than those born during solar minimums, and more recently, a study by Megaw et al. (2021) found a protective association between first trimester sun exposure on gestational length. How the influence of these varying levels of background radiation over the course of the solar cycle may ultimately drive a cascade of later biological events during pregnancy is not well understood and little explored.

In light of these gaps, we sought to better understand the potential impacts of sunspot (SS) activity on a range of birth defects utilizing a spectrum approach. Drawing on data from the Texas Birth Defects Registry (TBDR), a large population-based registry, we examined the association between solar maximum and minimum periods, collected from publicly available sunspot data available from the National Oceanic and Atmospheric Administration (NOAA) website over the years 1998-2016 and the occurrence of 44 unique birth defects routinely collected by the TBDR. This is the first study, to our knowledge, to examine solar activity and a wide array of defects using an ecological study design. Better understanding how the internal dynamics of our sun impact biological outcomes over time, such as birth defects, may result in improved models for projected birth prevalence, an improved understanding of temporal trends in birth defects, and indications as to the underlying etiology of various malformations.

# 2 | MATERIALS AND METHODS

The TBDR, established in 1993, is an active statewide surveillance system which collects an array of infant and maternal characteristics as well as defect diagnoses. The TBDR is also routinely linked to state vital event data (collected by the Texas Department of State Health Services [DSHS], Center for Health Statistics [CHS]), such as births and fetal death data, providing useful information on maternal residence and other supplemental demographic information. This study utilized data on infants and fetuses delivered to women residing in Texas from 1999 (the first year the TBDR covered the entire state of

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Texas) to 2016 (the most recent year with complete cleaned data available from the Registry at the time of this study). Infants and fetuses with one of 44 identified structural or chromosomal birth defects—including all live births, fetal deaths, and elective terminations—were included. Cases that are not listed as having a definite diagnosis were excluded—which comprise 4% of all diagnoses in the registry.

# 2.1 | Exposure assessment

This analysis utilized an ecological research design by examining the mean numbers of sunspots (MSS) occurring during the first trimester (assessed as 1 month prior to conception through the third month of pregnancy) categorized as follows: MSS = 0-24th percentile were assigned to quartile 1 (Q1, ref—minimum sunspot activity); MSS = 25th-49th percentile (Q2); MSS = 50th-74th percentile (Q3); and MSS = 75th-100th percentile (Q4—maximum sunspot activity). Sunspot numbers were obtained from the National Oceanic and Atmospheric Administration (NOAA) {American Sunspot Numbers (SSN)}, US Department of Commerce for the years 1998–2016. Observations utilized by NOAA included observations collected by the Solar Division, American

Association of Variable Star Observers (AAVSO)—which only includes high quality observations combined into the 'American Relative Number of Sunspot Numbers' (RA) per instructions outlined in Shapley (1949). Data is publicly available via the following website: (https://www.ngdc.noaa.gov/stp/solar/ssndata.html). Formed in 1807, NOAA provides a variety of public data—from weather forecasting used by the National Weather Services to monitoring space weather and other Earth systems of national and global importance—and was utilized as a secondary data source for this project.

For purposes of this study, we included estimated dates of conception occurring between 1998 and 2016 (see Figure 1). To calculate estimated dates of conception (DOC), we followed an established protocol currently used by the TBDR including a combination of estimates of last reported menstrual period (LMP) and clinical estimates of gestational age at delivery when LMP was missing.

### 2.2 | Outcome assessment

As noted above, 44 unique birth defects were selected for evaluation using the first four digits of the birth defect code—which is roughly equivalent to International

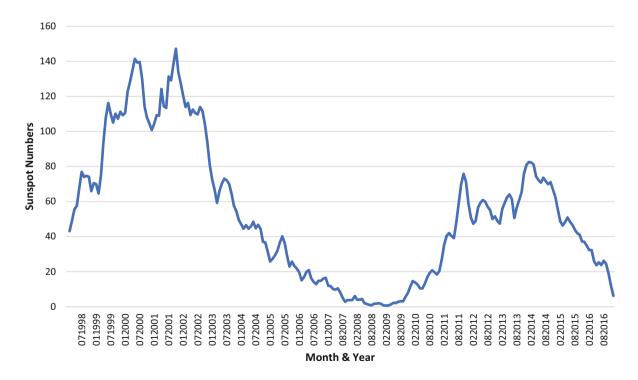


FIGURE 1 Mean sunspot numbers by month and year, NOAA (1998–2016). First trimester mean sunspots (calculated from 1 month pre-conception through first 3 months of pregnancy): Q1 (0 to  $\leq$ 24th percentile) = 7.53; Q2 (25th–49th percentile) = 34.33; Q3 (50th–74th percentile) = 59.41; and Q4 (75th–100th percentile) = 105.05; overall average sunspot numbers across entire time period examined = 53.32; sunspot range = 0.68–147.13. NOAA, The National Oceanic and Atmospheric Administration.



**TABLE 1** Selected birth defects by singleton cases (TBDR, 1999–2016).

999–2016).	
Birth defect	n <sup>a</sup>
Non-cardiac	
Anencephaly	1570
Spina bifida, without anencephaly	2495
Encephalocele	604
Hydrocephaly, without spina bifida	4891
Microcephaly, severe (head circumference < 3rd percentile)	2915
Holoprosencephaly	699
Anophthalmia	191
Microphthalmia	1826
Cataract	1257
Anotia or microtia	2242
Choanal atresia or stenosis	822
Agenesis, aplasia, or hypoplasia of the lung <sup>b</sup>	1992
Cleft palate alone (without cleft lip)	3938
Cleft lip with or without cleft palate	7168
Tracheoesophageal fistula/esophageal atresia	1393
Pyloric stenosis	11,205
Stenosis or atresia of the small intestine	2187
Stenosis or atresia of large intestine, rectum, or anal canal	3471
Hirschsprung disease	948
Biliary atresia	475
Hypospadias (cases and births among males)	20,127
Renal agenesis or dysgenesis	3950
Reduction defects of the upper limbs	2706
Reduction defects of the lower limbs	1268
Craniosynostosis	3465
Diaphragmatic hernia	1847
Omphalocele	1377
Gastroschisis	3525
Trisomy 21 (Down syndrome)	9057
Trisomy 13 (Patau syndrome)	791
Trisomy 18 (Edwards syndrome)	1663
Cardiac	
Common truncus	508
Transposition of the great vessels	2294
Tetralogy of fallot	2540
Ventricular septal defect	38,382
Atrial septal defect	42,743
Atrioventricular septal defect (endocardial cushion defect)	2865
Pulmonary valve atresia or stenosis	6169
	٠.

TABLE 1 (Continued)

Birth defect	n <sup>a</sup>
Tricuspid valve atresia or stenosis	1173
Ebstein anomaly	482
Aortic valve stenosis	1611
Hypoplastic left heart syndrome	1490
Patent ductus arteriosus	40,297
Coarctation of the aorta	3371

Abbreviation: TBDR, Texas Birth Defects Registry.

<sup>a</sup>Exclusions include: multifetal births ( $n=30,501,\sim5\%$ ), birth defects with non-definitive diagnosis codes ( $n=19,265,\sim3\%$ ), and births missing date of conception information (n=1402,<1%), or sunspot number (n=2504,<1%) (*Note*: sunspot data not available for April 2007 from NOAA). <sup>b</sup>Coding for 'agenesis, aplasia, or hypoplasia of the lung' excludes cases of pulmonary hypoplasia or hypoplastic lungs caused by a diaphragmatic hernia.

Classification of Disease 9th Revision (ICD-9) groups. All births with dates of conception occurring between 1998 and 2016 were selected for analysis (including 13 cardiac and 31 non-cardiac defects) (see Table 1).

### 2.3 | Covariates included

Covariate information was obtained from birth and fetal death certificates. The following factors (below) were chosen for our multi-variable analyses because of their association with a wide range of birth defects in the scientific literature and low numbers of missing categories within our selected data repositories: Maternal age [calculated from date of delivery of the index child minus date of mother's birth (10–19, 20–24, 25–29, 30–34, 35–39, 40+)]; maternal race/ethnicity [White non-Hispanic, Black non-Hispanic, Other non-Hispanic, and Hispanic]; and maternal education [<high school, high school, >high school].

# 2.4 | Statistical analyses

Each of the 44 unique birth defects selected for this study were examined with respect to the first trimester during each of the assigned mean sunspot quartiles (Q2-4 vs. Q1 [referent]) as outlined at the beginning of this section (see Section 2.1) using Poisson regression. Denominator data to calculate birth prevalence was obtained from the Texas Department of State Health Services (DSHS) Center for Health Statistics. After excluding multifetal births (associated with an array of birth defects [Tang et al., 2006]), both crude and adjusted prevalence ratios (cPRs/aPRs) and 95% confidence intervals (95%

CIs) were calculated with all adjusted analyses controlling for maternal age, race/ethnicity, and education.

In addition to the covariates above, we also conducted a subanalysis examining the impact of the inclusion of year of conception as a continuous variable in our models to adjust for time varying impacts of increasing birth defects over time (often attributable to improved methods of diagnosis).

Birth defects and birth certificate data were stored and analyzed using SAS® (v.9.4). To protect confidentiality, all data cells with less than five subjects were suppressed. All co-authors with data contact signed Confidentiality Agreements for the TBDR and Center for Health Statistics (CHS). Additionally, this study was approved by the Texas DSHS Institutional Review Board (IRB) and the University of Houston IRB.

# 3 | RESULTS

Total case groups ranged from n=191 (anophthalmia) to n=42,743 (atrial septal defects) (see Table 1). When examining our primary covariates by total births (n=6,652,309), the majority of mothers in our population were 20–29 years old ( $\sim$ 54%), Hispanic ( $\sim$ 49%), and had more than a high school education ( $\sim$ 44%) (see Table 2).

# 3.1 | Non-cardiac defects

In our basic multivariable analyses (adjusting for maternal age, race/ethnicity, and education), first trimester births occurring in the higher quartile ranges (Q3-4) were found to have moderately protective aPRs with respect to a number of the non-cardiac defect groups (19/31 [61%]) examined in this analysis. For instance, the following 17 non-cardiac groupings had aPRs ranging in magnitude from 0.80 to 0.89 in the Q3-4 groupings: anencephaly, microphthalmia, cataract, anotia/ microtia, choanal atresia or stenosis, cleft palate alone (without cleft lip), pyloric stenosis, stenosis or atresia of the small intestine, Hirschsprung disease, renal agenesis or dysgenesis, reduction defects of the upper and lower limbs, craniosynostosis, diaphragmatic hernia, gastroschisis, and trisomies 13 and 18 (Q2). Five defect groupings had aPRs that were even more protective (aPR range: 0.60-0.79) in Q3-4: microcephaly (Q4 only), anophthalmia, cataract, gastroschisis, and trisomy 18 (see Table 3a). A few significantly elevated aPRs in the higher SS categories were noted for microcephaly (Q2-3); and agenesis, aplasia, or hypoplasia of the lung (Q3-4) (Table 3a).

# 3.2 | Cardiac defects

Among cardiac defects, we also observed protective estimates when moving into the higher quartiles of SS activity for close to half of the cardiac defects examined (6/13 [46%]). For instance, four defects had aPRs in the (0.80–0.89) magnitude range in Q3–4: transposition of the great vessels, pulmonary valve atresia or stenosis, aortic valve stenosis, and patent ductus arteriosus—three in the greater aPR protective range of (0.60–0.79): ventricular septal defect, atrial septal defect, and pulmonary valve atresia or stenosis. Little to no change in estimates were noted in the higher quartile ranges across the other selected defects (Table 3b).

# 3.3 | Year of conception adjustment

After additionally adjusting for year of conception across these models, results were similar—with many of the aPRs staying the same or moving closer to the null across both the cardiac and non-cardiac defects examined. A few exceptions would be anopthalmia, pyloric stenosis, and transposition of the great vessels—where Q4 estimates were notably more protective following the additional adjustment of year of conception (Tables 3a,b).

# 4 | DISCUSSION

To better understand the impact of the solar cycle on a range of birth defects, we examined the association between sunspot data from the National Oceanic and Atmospheric Administration (NOAA) and a spectrum of 44 distinct birth defects groupings and found moderately protective aPRs in a little over half of the case groups examined in our quartiles of higher SS activity (19 noncardiac; 6 cardiac) and noted significantly elevated aPRs among two defect groups (agenesis, aplasia, and hypoplasia of the lung (Q3-4) and microcephaly (Q2-3)). Following an additional adjustment of year of conception across our defect categories, many of the estimates were attenuated (Tables 3a,b). To our knowledge, this is the first study to examine solar activity in relation to such a broad range of defects—while also controlling for important maternal demographic factors and year of conception.

As our understanding of the associations between the internal dynamics of our sun and adverse terrestrial health events (including the occurrence of birth defects) continues to evolve, some investigators speculate that better forecasting models of incidence trends and a more coherent understanding of disease etiology could lead to better forecasting of disease specific screening, diagnosis,

**Births** (n=6,652,309)Characteristic<sup>a</sup> % Mean sunspots (SS) during the first trimester<sup>b</sup> Quartile 1: Q1, ref—minimum SS activity 1,638,668 24.6 Quartile 2: Q2, low to medium SS activity 1.556.962 23.4 Quartile 3: Q3, medium to high SS 1,584,571 23.8 activity Quartile 4: Q4, maximum SS activity 1,872,108 28.1 Maternal age 10-19 836,314 12.6 20-24 1798,915 27.0 25-29 1,822,834 27.4 1414,771 30 - 3421.3 35 - 39641,269 9.6 >40 138,203 2.1 0.0 Missing Maternal race/ethnicity White non-Hispanic 2,343,018 35.2 Black non-Hispanic 747,596 11.2 Hispanic 3,236,239 48.7 Other non-Hispanic 325,453 4.9 Missing 3 0.0 Maternal education <High school 1,819,347 274 High school 1,875,343 28.2 >High school 2,919,430 43.9 38,189 Missing 0.6 Year of conception 1998 233,303 3.5 1999 340,344 5.1 2000 346,821 5.2 2001 353,856 5.3 2002 361.759 5.4 2003 363,409 5.5 2004 367,699 5.5 2005 375,868 5.7 2006 393,053 5.9 2007 362,269 5.5 2008 392,972 5.9 375,002 2009 5.6 2010 369,635 5.6 2011 365,963 5.5

TABLE 2 (Continued)

	Births (n = 6,652	2,309)
Characteristic <sup>a</sup>	n	%
2012	372,278	5.6
2013	383,759	5.8
2014	389,734	5.9
2015	390,752	5.9
2016	113,833	1.7

<sup>a</sup>Exclusions include: multifetal births ( $n = 30,501,\sim5\%$ ), birth defects with non-definitive diagnosis codes ( $n = 19,265,\sim3\%$ ), and births missing date of conception information (n = 1402,<1%), or sunspot number (n = 2505,<1%) (*Note*: sunspot data not available for April 2007 from NOAA). <sup>b</sup>First trimester mean sunspots (calculated from one month pre-conception through first three months of pregnancy): Q1 (0 to ≤24th percentile) = 7.53; Q2 (25th–49th percentile) = 34.33; Q3 (50th–74th percentile) = 59.41; and Q4 (75th–100th percentile) = 105.05; overall average sunspot numbers across entire time period examined = 53.32; sunspot range = 0.68–147.13.

treatment and prevention (Hrushesky et al., 2011). Further, while solar UV-R is a known mutagen (and using sunscreen and avoiding over-exposure are important messages for preventing skin cancer) (Dale Wilson et al., 2012), there are instances where periodic exposure is beneficial to human health (e.g., mediating natural synthesis of vitamin D and endorphins in the skin) (D'Orazio et al., 2013; Mead, 2008).

# 4.1 | Solar activity and biophysical pathways of exposure

While all living organisms are influenced by solar activity, how sunspot signals—responsible for solar magnetic storms—induce changes in biophysical pathways remains unclear. Recent speculation has included alterations in UV-R, solar protons, heavy charged particles, geomagnetic storm-induced gravitational field changes, fluctuations, and resonance signals (Hrushesky et al., 2011). One particularly interesting facet of recent research lies in the realm of cosmic ray impacts on the Earth and ionizing radiation. During periods of heightened solar activity, increasing numbers of solar flares and coronal mass ejections are known to cause increased ionization in the Earth's lower ionosphere (D region) (Tsurutani et al., 2009). While ionizing radiation from astrophysical sources is dominated by two secondary cosmic ray sources (i.e., muons and neutrons), how these particles work together during heightened periods of solar activity to penetrate the atmosphere and exert genotoxic damage remains speculative (Overholt et al., 2015). Although rare, muons are subatomic particles

thought to be the highest ionizing radiation threat from heightened solar events due to their high rate of penetration through the upper atmosphere and ability to reach sea level and below (Marinho et al., 2014). Little is known, however, about how muons interact with other forms of cosmic ionizing radiation such as neutrons. One hypothesis is that these two forms of ionizing radiation combine during periods of heightened solar activity to produce effects which are 'additive' and would account for more biological damage than ionization alone would suggest (Overholt et al., 2015). Another speculated mechanism is that following these heightened solar events, increasing ionization of the Earth's atmosphere is thought to deplete stratospheric ozone and subsequently lead to increased levels of ultraviolet B (UV-B) radiation reaching the Earth-known to be especially hazardous to life (Melott & Thomas, 2011).

# 4.2 | Sunspot activity and fetal loss

Although contrary to previous research finding associations between higher levels of solar activity and increasing birth defects, possible explanations for the seemingly protective impact of higher levels of SS activity and lower prevalence of many birth defects examined in this analysis may be related to the influence of increasing levels of solar UV-R on fetal loss early in pregnancy. While not captured in this analysis, other environmental epidemiological investigations have found that an array of known environmental toxicants associated with adverse birth outcomes can often be missed due to the impact of these toxicants on spontaneous abortions (SAs) (loss of a pregnancy <20 weeks gestation) (Bakulski et al., 2019). In particular, those toxicants with a high probability of toxicogenomic responses are often also highly correlated with SAs (Bakulski et al., 2019). With many SAs occurring before women are aware of their pregnancies, a depleted number of fetuses are thus left to be susceptible to later adverse birth outcomes (Bakulski et al., 2019). With evidence mounting with respect to the negative impacts of radiation on adverse birth outcomes (Frangione et al., 2023), the seemingly protective influence of increasing SS activity may be an artifact of increasing SAs that occur following conception during these periods of heightened SS activity. Future studies in this topic area would benefit from the inclusion of fetal deaths as part of their analysis.

# 4.3 | Radiation hormesis

Another alternative hypothesis lies within the realm of radiation hormesis—the hypothesis that low levels of radiation are beneficial and stimulate activation of repair mechanisms within biological organisms (Feinendegen, 2005). Although the subject of considerable debate and not currently accepted by the United States National Research Council (Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2|The National Academies Press, 2006), there appears to be some evidence that low doses of ionizing radiation may, in fact, have beneficial effects on living beings (as seen from protective effects found in some cellular [de Toledo et al., 2006], animal [Sakai et al., 2002], and human studies [Nair-Shalliker et al., 2012]). A recent Australian study, for instance, examining solar radiation and DNA damage found that with increasing sun exposure, the misrepair of DNA strand breaks decreased (Nair-Shalliker et al., 2012). Given the limited evidence to support this hypothesis, however, the linear nothreshold model (LNT) (which relies on the postulate that all ionizing radiation exposure is harmful, regardless of dose) continues to be the dominant model most relied upon by regulatory agencies for human radiation exposure (Hall, 1998).

# 4.4 | Solar UV-R and blood pressure

An additional explanation for the apparent protective impact of UV-R on birth defects may be understood in light of recent research on solar UV-R and blood pressure. Some recent evidence has pointed to associations between solar UV-R and reduced blood pressure—known to enhance nitric oxide release by mobilizing storage forms in the skin and modulating the immune system (Campbell & Soothill, 1993; Hart et al., 2011)—mediators essential to the process of implantation and early placentation with influences on the fetal genome (Lowell & Davis, 2010; Norwitz, 2006; Velauthar et al., 2014). Further, hypertension alone has been independently associated with an array of birth defects (Bellizzi et al., 2016; van Gelder et al., 2015). While modern lifestyles particularly in the developed world—often coincide with spending increasing amounts of time indoors and in automobiles—where much of the natural UV-R (especially UV-B) is blocked (Almutawa et al., 2013), low levels of daily sun exposure may, in fact, be beneficial not only in the context of decreasing blood pressure, but also in the context of improving birth outcomes.

# 5 | STRENGTHS AND LIMITATIONS

While strengths of this analysis include the utilization of a large population-based study incorporating data from

Association between quartiles of average numbers of sunspots during the first trimester and selected (a) non-cardiac and (b) cardiac defects among singletons (Texas, TABLE 3 1999-2016).

Mean sunspots (MSS) during the first trimester					Adjusting for maternal age, race/ethnicity, and education	ternal age, ıd	Adjusting for maternal age, race/ethnicity, education, and year of conception	ernal age, ucation, ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	$p$ -trend $^{\mathbf{b}}$	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
(a) Non-cardiac defects								
Anencephaly	1570			1059				
Q1—minimum SS activity	389	Ref.	.33	278	Ref.	.13	Ref.	.46
Q2—low to medium SS activity	369	1.00 (0.87–1.15)		262	1.00 (0.83-1.21)		0.99 (0.82–1.19)	
Q3—medium to high SS activity	346	0.92 (0.80–1.06)		236	0.90 (0.74-1.10)		0.88 (0.72–1.06)	
Q4—maximum sunspot activity	466	1.05 (0.92–1.20)		283	0.89 (0.74–1.07)		0.98 (0.80–1.19)	
Spina bifida, without anencephaly	2495			2354				
Q1—minimum SS activity	624	Ref.	.61	009	Ref.	80.0	Ref.	.33
Q2—low to medium SS activity	595	1.00 (0.90-1.12)		695	1.00 (0.89–1.13)		1.00 (0.88-1.13)	
Q3—medium to high SS activity	604	1.00 (0.89–1.12)		570	1.00 (0.88–1.12)		0.99 (0.87–1.12)	
Q4—maximum sunspot activity	672	0.94 (0.85–1.05)		615	0.90 (0.80-1.01)		0.93 (0.81–1.07)	
Encephalocele	604			524				
Q1—minimum SS activity	148	Ref.	.90	127	Ref.	.36	Ref.	98.
Q2—low to medium SS activity	149	1.06 (0.84-1.33)		138	1.15 (0.92–1.44)		1.14 (0.88–1.47)	
Q3—medium to high SS activity	140	0.98 (0.78–1.23)		125	1.04 (0.83–1.30)		1.01 (0.78–1.32)	
Q4—maximum sunspot activity	167	0.99 (0.79–1.23)		134	0.93 (0.75–1.17)		1.01 (0.77–1.33)	
Hydrocephaly, without spina bifida	4891			4752				
Q1—minimum SS activity	1195	Ref.	.05	1176	Ref.	.12	Ref.	.42
Q2—low to medium SS activity	1165	1.03 (0.95–1.11)		1146	1.03 (0.94–1.13)		1.01 (0.93-1.10)	
Q3—medium to high SS activity	1228	1.06 (0.98–1.15)		1195	1.06 (0.97–1.16)		1.02 (0.94-1.11)	
Q4—maximum sunspot activity	1195	0.95 (0.88–1.03)		1235	0.92 (0.84-1.01)		1.03 (0.95–1.13)	
Microcephaly, severe (head circumference < 3rd percentile)	2915			2878				
Q1—minimum SS activity	700	Ref.	<.01	669	Ref.	<.01	Ref.	.92
Q2—low to medium SS activity	778	1.17 (1.06–1.30)		692	1.17 (1.04–1.31)		1.09 (0.98–1.21)	
Q3—medium to high SS activity	808	1.20 (1.08–1.32)		800	1.21 (1.08–1.35)		1.06 (0.95–1.18)	
Q4—maximum sunspot activity	628	0.79 (0.70–0.87)		610	0.76 (0.67–0.85)		0.99 (0.88–1.11)	
								(Continues)

TABLE 3

Mean sunspots (MSS) during the first trimester					education		and year of conception	ucation, ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend <sup>b</sup>	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Holoprosencephaly	669			640				
Q1—minimum SS activity	159	Ref.	.59	151	Ref.	.65	Ref.	.65
Q2—low to medium SS activity	161	1.07 (0.86–1.33)		152	1.07 (0.85–1.34)		1.07 (0.86–1.32)	
Q3—medium to high SS activity	170	1.11 (0.89–1.37)		153	1.07 (0.85–1.35)		1.07 (0.86–1.33)	
Q4—maximum sunspot activity	500	1.15 (0.94–1.42)		184	1.06 (0.85–1.32)		1.05 (0.84–1.31)	
Anophthalmia	191			168				
Q1—minimum SS activity	52	Ref.	.31	51	Ref.	.04	Ref.	.01
Q2—low to medium SS activity	51	1.03 (0.70–1.52)		44	0.93 (0.63-1.35)		0.93 (0.64–1.35)	
Q3—medium to high SS activity	36	0.72 (0.46–1.09)		32	0.67 (0.44–1.01)		0.69 (0.46–1.03)	
Q4—maximum sunspot activity	52	0.88 (0.60-1.29)		41	0.72 (0.49–1.05)		0.64 (0.42–0.97)	
Microphthalmia	1826			1790				
Q1—minimum SS activity	492	Ref.	90.0	489	Ref.	0.01	Ref.	0.01
Q2—low to medium SS activity	439	0.94 (0.83–1.07)		432	0.93 (0.81–1.05)		0.92 (0.81–1.05)	
Q3—medium to high SS activity	409	0.86 (0.75-0.98)		396	0.84 (0.73–0.96)		0.84 (0.73–0.96)	
Q4—maximum sunspot activity	486	0.86 (0.76-0.98)		473	0.85 (0.75–0.97)		0.86 (0.74–0.98)	
Cataract	1257			1240				
Q1—minimum SS activity	334	Ref.	<.01	334	Ref.	<.01	Ref.	.02
Q2—low to medium SS activity	333	1.05 (0.90–1.22)		333	1.05 (0.91–1.21)		1.03 (0.89–1.19)	
Q3—medium to high SS activity	246	0.76 (0.65-0.90)		243	0.75 (0.64-0.88)		0.73 (0.62–0.86)	
Q4—maximum sunspot activity	344	0.90 (0.78–1.05)		330	0.87 (0.75–1.01)		0.95 (0.81–1.11)	
Anotia or microtia	2242			2205				
Q1—minimum SS activity	581	Ref.	.01	574	Ref.	.01	Ref.	.22
Q2—low to medium SS activity	552	1.00 (0.89–1.12)		547	1.00 (0.90-1.12)		0.99 (0.88–1.11)	
Q3—medium to high SS activity	548	0.98 (0.87–1.10)		542	0.99 (0.89–1.11)		0.96 (0.86–1.08)	
Q4—maximum sunspot activity	561	0.85 (0.75–0.95)		542	0.85 (0.76–0.95)		0.93 (0.83–1.05)	

Adjusting for maternal age, race/ethnicity, education,	and year of conception	aPRs (95% CIs) <sup>c</sup> p-trend <sup>c</sup>
djusting for maternal age, ace/ethnicity, and	ducation	Crude PRs (95% CIs) p-trend Cases (n) aPRs (95% CIs) <sup>b</sup> p-trend <sup>b</sup>
∢ ii	ō	Cases (n) a
		p-trend
		Crude PRs (95% CIs)
		Cases (n)
	Mean sunspots (MSS) during the first trimester	by quartile (Q) <sup>a</sup>

TABLE 3

					Adjusting for maternal age, race/ethnicity, and education	ernai age, d	Adjusting for maternal age, race/ethnicity, education, and year of conception	ernal age, ucation, otion
Mean sunspots (MSS) during the first trimester by quartile $(Q)^a$	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend <sup>b</sup>	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Choanal atresia or stenosis	822			608				
Q1—minimum SS activity	215	Ref.	.49	215	Ref.	.59	Ref.	.95
Q2—low to medium SS activity	178	0.87 (0.71–1.06)		177	0.86 (0.72–1.03)		0.85 (0.70–1.04)	
Q3—medium to high SS activity	189	0.91 (0.75–1.11)		186	0.89 (0.75–1.06)		0.87 (0.72–1.06)	
Q4—maximum sunspot activity	240	0.98 (0.81–1.18)		231	0.94 (0.80–1.11)		1.01 (0.83–1.23)	
Agenesis, aplasia, or hypoplasia of the lung	1992			1867				
Q1—minimum SS activity	406	Ref.	<.01	393	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	437	1.13 (0.99–1.30)		418	1.13 (0.99–1.29)		1.14 (0.99–1.31)	
Q3—medium to high SS activity	454	1.16 (1.01–1.32)		436	1.16 (1.02-1.33)		1.19 (1.03-1.36)	
Q4—maximum sunspot activity	969	1.50 (1.33-1.69)		620	1.38 (1.22–1.57)		1.27 (1.11–1.47)	
Cleft palate alone (without cleft lip)	3938			3855				
Q1—minimum SS activity	1027	Ref.	.15	1017	Ref.	.01	Ref.	.01
Q2—low to medium SS activity	926	0.95 (0.87–1.04)		911	0.94 (0.86–1.03)		0.94 (0.86–1.03)	
Q3—medium to high SS activity	903	0.91 (0.83-0.99)		888	0.90 (0.82–0.99)		0.90 (0.82–0.99)	
Q4—maximum sunspot activity	1082	0.92 (0.85–1.00)		1039	0.88 (0.81–0.97)		0.88 (0.80–0.97)	
Cleft lip with or without cleft palate	7168			9069				
Q1—minimum SS activity	1696	Ref.	.22	1650	Ref.	.92	Ref.	.70
Q2—low to medium SS activity	1726	1.07 (1.00–1.15)		1665	1.07 (0.99–1.14)		1.07 (1.00–1.14)	
Q3—medium to high SS activity	1727	1.05 (0.98–1.13)		1681	1.06 (0.99–1.14)		1.06 (0.99–1.14)	
Q4—maximum sunspot activity	2019	1.04 (0.98–1.11)		1909	1.01 (0.94–1.08)		1.01 (0.94–1.08)	
Tracheoesophageal fistula/esophageal atresia	1393			1378				
Q1—minimum SS activity	323	Ref.	4	323	Ref.	.67	Ref.	.29
Q2—low to medium SS activity	331	1.08 (0.93–1.26)		329	1.07 (0.90–1.27)		1.06 (0.91–1.24)	
Q3—medium to high SS activity	353	1.13 (0.97–1.31)		351	1.12 (0.95-1.33)		1.11 (0.95–1.29)	
Q4—maximum sunspot activity	386	1.05 (0.90–1.21)		375	1.03 (0.87–1.21)		1.07 (0.91–1.26)	
								(Continues)

.65

Ref.

.79

Ref.

119

.93

1.01 (0.79–1.29) 0.92 (0.71–1.17)

1.01 (0.81–1.26) 0.91 (0.72–1.14)

114 105

1.01 (0.78–1.30) 0.93 (0.72–1.21)

Ref.

119 114 107 0.98 (0.76-1.26)

1.00 (0.80-1.24)

134

0.99 (0.78–1.27)

135

Q3—medium to high SS activity

Q4—maximum sunspot activity

Q2—low to medium SS activity

Q1—minimum SS activity

(Continued)

TABLE 3

p-trend<sup>c</sup> Adjusting for maternal age, race/ethnicity, education, <.01 and year of conception 9 .15 Ξ. aPRs (95% CIs)<sup>c</sup> 0.87 (0.82-0.93) 0.85 (0.80-0.91) 1.04 (0.98-1.11) 0.87 (0.77-0.98) 0.87 (0.77-0.98) 0.92 (0.81-1.04) 1.02 (0.93-1.12) 1.04 (0.94-1.14) 0.96 (0.87-1.06) 1.02 (0.85-1.21) 0.96 (0.80-1.14) 0.88 (0.72-1.06) Ref. Ref. Ref. Ref. Adjusting for maternal age, p-trend .63 22 .01 9. race/ethnicity, and aPRs (95% CIs)<sup>b</sup> 0.85 (0.80-0.91) 0.85 (0.76-0.96) 0.88 (0.78-1.00) 0.89 (0.79-1.01) 1.02 (0.92-1.13) 1.03 (0.93-1.14) (96.0-99) 18.0 1.03 (0.97-1.10) 1.01 (0.95-1.07) 0.97 (0.88-1.07) 1.03 (0.84-1.27) 0.98 (0.80-1.21) education Ref. Ref. Ref. Ref. Cases (n) 11,123 2734 2273 3347 3290 2153 290 502 570 191 795 606 243 818 240 234 225 325 942 472 p-trend <.01 60: .03 71 Crude PRs (95% CIs) 0.84 (0.79-0.88) 0.87 (0.78-0.98) 1.03 (0.98-1.09) 0.89 (0.79-1.00) 0.90 (0.80-1.01) 1.03 (0.94-1.13) 1.04 (0.87-1.25) 1.01 (0.84-1.21) 0.82 (0.68-0.98) 1.02 (0.97-1.08) 1.02 (0.93-1.12) 0.98 (0.89-1.08) Ref. Ref. Ref. Ref. Cases (n) 11,205 2830 2748 2286 3341 2187 3471 290 497 511 589 832 839 243 237 475 948 241 227 951 Stenosis or atresia of large intestine, rectum, or anal Mean sunspots (MSS) during the first trimester Stenosis or atresia of the small intestine Q3—medium to high SS activity Q4—maximum sunspot activity Q4—maximum sunspot activity Q4—maximum sunspot activity Q4—maximum sunspot activity Q2—low to medium SS activity Q1—minimum SS activity Q1—minimum SS activity Q1—minimum SS activity Q1—minimum SS activity Hirschsprung disease Pyloric stenosis by quartile (Q)<sup>a</sup> Biliary atresia canal

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Mean sunspots (MSS) during the first trimester					Adjusting for maternal age, race/ethnicity, and education	ternal age, id	Adjusting for maternal age, race/ethnicity, education, and year of conception	ternal age, tucation, ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Hypospadias (cases and births among males)	20,127			19,966				
Q1—minimum SS activity	4931	Ref.	<.01	4925	Ref.	.02	Ref.	.36
Q2—low to medium SS activity	4803	1.03 (0.99–1.07)		4782	1.02 (0.97–1.06)		1.00(0.96-1.04)	
Q3—medium to high SS activity	5040	1.06 (1.02–1.10)		5005	1.04 (0.99–1.09)		1.01 (0.97–1.05)	
Q4—maximum sunspot activity	5353	0.95 (0.91–0.99)		5254	0.94 (0.90–0.98)		1.02 (0.98–1.06)	
Renal agenesis or dysgenesis	3950			3790				
Q1—minimum SS activity	995	Ref.	<.01	972	Ref.	<.01	Ref.	.15
Q2—low to medium SS activity	296	1.02 (0.94–1.12)		938	1.01 (0.93-1.11)		1.00(0.91-1.08)	
Q3—medium to high SS activity	686	1.03 (0.94-1.12)		953	1.02 (0.93-1.11)		0.98 (0.90–1.07)	
Q4—maximum sunspot activity	666	0.88 (0.80–0.96)		927	0.85 (0.78–0.92)		0.94 (0.85–1.02)	
Reduction defects of the upper limbs	2706			2591				
Q1—minimum SS activity	700	Ref.	.43	684	Ref.	.01	Ref.	80.
Q2—low to medium SS activity	638	0.96 (0.86–1.07)		614	0.95 (0.86–1.06)		0.95 (0.85–1.06)	
Q3—medium to high SS activity	630	0.93 (0.84–1.04)		909	0.93 (0.83-1.03)		0.92 (0.82–1.03)	
Q4—maximum sunspot activity	738	0.92 (0.83-1.02)		289	0.87 (0.79–0.97)		0.91 (0.81–1.02)	
Reduction defects of the lower limbs	1268			1178				
Q1—minimum SS activity	324	Ref.	99.	312	Ref.	.11	Ref.	.22
Q2—low to medium SS activity	307	1.00 (0.85–1.17)		282	0.96 (0.81–1.14)		0.95 (0.81–1.12)	
Q3—medium to high SS activity	288	0.92 (0.78–1.08)		269	0.91 (0.76–1.08)		0.90 (0.76–1.06)	
Q4—maximum sunspot activity	349	0.94 (0.81–1.10)		315	0.88 (0.74–1.04)		0.92 (0.78–1.09)	
Craniosynostosis	3465			3442				
Q1—minimum SS activity	921	Ref.	<.01	921	Ref.	<.01	Ref.	.36
Q2—low to medium SS activity	755	0.86 (0.78–0.95)		752	0.85 (0.77–0.94)		0.83 (0.76-0.92)	
Q3—medium to high SS activity	935	1.05 (0.96–1.15)		933	1.04 (0.95–1.14)		0.99 (0.91–1.09)	
Q4—maximum sunspot activity	854	0.81 (0.74–0.89)		836	0.80 (0.73-0.88)		0.90 (0.81–0.99)	
								(Continues)

TABLE 3

Wean sunsnots (MSS) during the first trimester					race/etnmenty, and education	<b>D</b>	race/etnmenty, education, and year of conception	lucation, ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend <sup>b</sup>	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Diaphragmatic hernia	1847			1798				
Q1—minimum SS activity	493	Ref.	.03	489	Ref.	.04	Ref.	60.
Q2—low to medium SS activity	393	0.84 (0.73–0.96)		384	0.83 (0.73-0.94)		0.83 (0.72-0.95)	
Q3—medium to high SS activity	465	0.98 (0.86–1.11)		458	0.98 (0.86–1.10)		0.97 (0.86–1.11)	
Q4—maximum sunspot activity	496	0.88 (0.78–1.00)		467	0.83 (0.73-0.94)		0.83 (0.73-0.96)	
Omphalocele	1377			1211				
Q1—minimum SS activity	317	Ref.	.45	290	Ref.	.35	Ref.	.15
Q2—low to medium SS activity	317	1.05 (0.90–1.23)		273	0.99 (0.83-1.18)		0.98 (0.82-1.17)	
Q3—medium to high SS activity	338	1.10 (0.95–1.29)		301	1.07 (0.90–1.28)		1.06 (0.89–1.25)	
Q4—maximum sunspot activity	405	1.12 (0.97–1.30)		347	1.06 (0.90–1.25)		1.12 (0.94–1.33)	
Gastroschisis	3525			3363				
Q1—minimum SS activity	1025	Ref.	<.01	266	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	837	0.86 (0.78-0.94)		797	0.89 (0.78–1.01)		0.87 (0.78–0.97)	
Q3—medium to high SS activity	819	0.83 (0.75-0.91)		9//	0.87 (0.77–0.99)		0.82 (0.74-0.92)	
Q4—maximum sunspot activity	844	0.72 (0.66–0.79)		793	0.69 (0.60–0.78)		0.84 (0.74–0.94)	
Trisomy 21 (Down syndrome)	9057			8712				
Q1—minimum SS activity	2275	Ref	.29	2215	Ref	.14	Ref	.23
Q2—low to medium SS activity	2154	1.00 (0.94–1.06)		2098	0.98 (0.91–1.04)		0.97 (0.92–1.03)	
Q3—medium to high SS activity	2156	0.98 (0.92–1.04)		2086	0.95 (0.89–1.02)		0.95 (0.89–1.01)	
Q4—maximum sunspot activity	2472	0.95 (0.90-1.01)		2313	0.96 (0.90–1.02)		0.97 (0.91–1.04)	
Trisomy 13 (Patau syndrome)	791			651				
Q1—minimum SS activity	210	Ref	.29	179	Ref	.15	Ref	.14
Q2—low to medium SS activity	196	0.98 (0.81-1.19)		158	0.92 (0.73-1.16)		0.92 (0.72–1.17)	
Q3—medium to high SS activity	171	0.84 (0.69–1.03)		141	0.80 (0.63-1.02)		0.80 (0.63-1.03)	
Q4—maximum sunspot activity	214	0.89 (0.74–1.08)		173	0.87 (0.69–1.09)		0.87 (0.67–1.12)	

TABLE 3 (Continued)

					Adjusting for maternal age, race/ethnicity, and	ernal age, d	Adjusting for maternal age, race/ethnicity, education, and year of concention	ternal age, lucation,
Mean sunspots (MSS) during the first trimester by quartile $(Q)^a$	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend	aPRs (95% CIs) <sup>c</sup>	$\frac{1}{p\text{-trend}^c}$
Trisomy 18 (Edwards syndrome)	1663			1358				
Q1—minimum SS activity	453	Ref	.01	380	Ref	<.01	Ref	<.01
Q2—low to medium SS activity	398	0.92 (0.81–1.06)		340	0.92 (0.80–1.06)		0.92 (0.79–1.05)	
Q3—medium to high SS activity	396	0.90 (0.79–1.03)		326	0.86 (0.75–1.00)		0.86 (0.74-0.99)	
Q4—maximum sunspot activity	416	0.80 (0.70-0.92)		312	0.75 (0.65–0.87)		0.77 (0.66–0.90)	
(b) Cardiac defects								
Common truncus	208			498				
Q1—minimum SS activity	131	Ref.	06:	130	Ref.	0.73	Ref.	0.95
Q2—low to medium SS activity	113	0.91 (0.71–1.17)		113	0.91 (0.69–1.21)		0.90 (0.68–1.19)	
Q3—medium to high SS activity	121	0.96 (0.75–1.22)		118	0.94 (0.71–1.24)		0.91 (0.69–1.21)	
Q4—maximum sunspot activity	143	0.96 (0.75–1.21)		137	0.94 (0.72–1.23)		1.02 (0.77–1.36)	
Transposition of the great vessels	2294			2261				
Q1—minimum SS activity	613	Ref.	.04	609	Ref.	.07	Ref.	.05
Q2—low to medium SS activity	496	0.85 (0.76-0.96)		495	0.85 (0.76–0.96)		0.86 (0.76–0.97)	
Q3—medium to high SS activity	563	0.95 (0.85–1.06)		555	0.94 (0.84–1.06)		0.95 (0.84–1.07)	
Q4—maximum sunspot activity	622	0.89 (0.79–0.99)		602	0.87 (0.78–0.97)		0.85 (0.75-0.96)	
Tetralogy of fallot	2540			2514				
Q1—minimum SS activity	603	Ref.	.01	601	Ref.	.23	Ref.	.65
Q2—low to medium SS activity	059	1.13 (1.02-1.27)		648	1.13 (1.01–1.26)		1.10 (0.98–1.24)	
Q3—medium to high SS activity	625	1.07 (0.96–1.20)		620	1.06 (0.95–1.19)		1.02 (0.91–1.15)	
Q4—maximum sunspot activity	662	0.96 (0.86–1.07)		645	0.95 (0.85–1.07)		1.06 (0.94–1.19)	
Ventricular septal defect	38,382			38,043				
Q1—minimum SS activity	10,412	Ref.	<.01	10,391	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	9442	0.95 (0.93-0.98)		9406	0.95 (0.92–0.98)		0.93 (0.90-0.95)	
Q3—medium to high SS activity	9241	0.92 (0.89–0.94)		9170	0.92 (0.89–0.95)		0.87 (0.85-0.90)	
Q4—maximum sunspot activity	9287	0.78 (0.76-0.80)		9206	0.78 (0.75–0.80)		0.89 (0.86-0.91)	
								(Continues)

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1.14 (0.89–1.47) 1.05 (0.81–1.38)

1.14 (0.88–1.49) 1.04 (0.80–1.36)

129

1.17 (0.91–1.50) 1.05 (0.82–1.34)

132

Q3—medium to high SS activity Q4—maximum sunspot activity

Mean sunspots (MSS) during the first trimester					Adjusting for maternal age, race/ethnicity, and education	ternal age, nd	Adjusting for maternal age, race/ethnicity, education, and year of conception	ternal age, lucation, ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	$p$ -trend $^{\mathbf{b}}$	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Atrial septal defect	42,743			42,415				
Q1—minimum SS activity	10,886	Ref.	<.01	10,875	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	11,368	1.10 (1.07-1.13)		11,317	1.09 (1.05–1.14)		1.03 (1.00–1.07)	
Q3—medium to high SS activity	11,233	1.07 (1.04–1.10)		11,142	1.06 (1.02–1.11)		0.96 (0.93–0.99)	
Q4—maximum sunspot activity	9256	0.74 (0.72–0.77)		9081	0.74 (0.71–0.77)		0.92 (0.89–0.95)	
Atrioventricular septal defect (endocardial cushion defect)	2865			2818				
Q1—minimum SS activity	711	Ref.	.22	703	Ref.	.41	Ref.	.83
Q2—low to medium SS activity	664	0.98 (0.88–1.09)		629	0.98 (0.87–1.09)		0.97 (0.87–1.08)	
Q3—medium to high SS activity	723	1.05 (0.95-1.17)		712	1.04 (0.93–1.15)		1.03 (0.92–1.14)	
Q4—maximum sunspot activity	192	0.94 (0.85–1.05)		744	0.94 (0.84–1.04)		0.96 (0.86–1.08)	
Pulmonary valve atresia or stenosis	6169			6116				
Q1—minimum SS activity	1758	Ref.	<.01	1751	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	1499	0.90 (0.84-0.96)		1491	0.90 (0.83-0.97)		0.87 (0.81–0.94)	
Q3—medium to high SS activity	1468	0.86 (0.81–0.93)		1460	0.87 (0.80–0.94)		0.82 (0.77-0.89)	
Q4—maximum sunspot activity	1444	0.72 (0.67–0.77)		1414	0.71 (0.66–0.77)		0.81 (0.75-0.88)	
Tricuspid valve atresia or stenosis	1173			1156				
Q1—minimum SS activity	300	Ref.	.59	299	Ref.	.16	Ref.	.73
Q2—low to medium SS activity	287	1.01 (0.86–1.18)		285	1.00 (0.85–1.18)		0.98 (0.83-1.15)	
Q3—medium to high SS activity	569	0.93 (0.79–1.09)		267	0.92 (0.78-1.10)		0.88 (0.75–1.04)	
Q4—maximum sunspot activity	317	0.92 (0.79–1.08)		305	0.90 (0.77–1.07)		1.02 (0.86–1.20)	
Ebstein anomaly	482			474				
Q1—minimum SS activity	117	Ref.	.10	117	Ref.	.33	Ref.	.26
Q2—low to medium SS activity	93	0.84 (0.64–1.10)		92	0.83 (0.62-1.10)		0.82 (0.63-1.08)	

Adjusting for maternal age, race/ethnicity, education, Adjusting for maternal age, race/ethnicity, and

TABLE 3

Mean sunspots (MSS) during the first trimester					education		and year of conception	ption
by quartile (Q) <sup>a</sup>	Cases (n)	Crude PRs (95% CIs)	p-trend	Cases (n)	aPRs (95% CIs) <sup>b</sup>	p-trend <sup>b</sup>	aPRs (95% CIs) <sup>c</sup>	p-trend <sup>c</sup>
Aortic valve stenosis	1611			1596				
Q1—minimum SS activity	422	Ref.	.49	420	Ref.	.31	Ref.	.41
Q2—low to medium SS activity	367	0.92 (0.80–1.05)		367	0.92 (0.79–1.06)		0.91 (0.79–1.05)	
Q3—medium to high SS activity	369	0.90 (0.79–1.04)		363	0.89 (0.77-1.04)		0.88 (0.77-1.02)	
Q4—maximum sunspot activity	453	0.94 (0.82–1.07)		446	0.93 (0.81-1.07)		0.96 (0.84-1.11)	
Hypoplastic left heart syndrome	1490			1468				
Q1—minimum SS activity	358	Ref.	.34	356	Ref.	.54	Ref.	.75
Q2—low to medium SS activity	352	1.03 (0.89–1.20)		349	1.03 (0.88–1.21)		1.02 (0.87–1.19)	
Q3—medium to high SS activity	382	1.10 (0.96–1.27)		379	1.10 (0.94–1.29)		1.08 (0.92–1.26)	
Q4—maximum sunspot activity	398	0.97 (0.84–1.12)		384	0.93 (0.80-1.09)		1.00 (0.85–1.18)	
Patent ductus arteriosus	40,297			40,011				
Q1—minimum SS activity	10,518	Ref.	<.01	10,504	Ref.	<.01	Ref.	<.01
Q2—low to medium SS activity	9842	0.98 (0.96-1.01)		9817	0.98 (0.95-1.01)		0.95 (0.92-0.98)	
Q3—medium to high SS activity	10,395	1.02 (0.99–1.05)		10,330	1.02 (0.98–1.05)		0.95 (0.92-0.98)	
Q4—maximum sunspot activity	9542	0.79 (0.77–0.82)		9360	0.80 (0.77-0.82)		0.93 (0.90–0.96)	
Coarctation of the aorta	3371			3337				
Q1—minimum SS activity	836	Ref.	.22	829	Ref.	.14	Ref.	.73
Q2—low to medium SS activity	831	1.05 (0.95–1.15)		828	1.05 (0.95–1.15)		1.04 (0.94–1.15)	
Q3—medium to high SS activity	800	0.99 (0.90–1.09)		791	0.99 (0.90–1.09)		0.97 (0.87–1.07)	
Q4—maximum sunspot activity	904	0.95 (0.86–1.04)		688	0.95 (0.86–1.04)		1.01 (0.91-1.12)	

\*Mean sunspots (MSS) calculated during the first trimester (1 month pre-conception through first 3 months of pregnancy): <224th percentile assigned to quartile 1 (Q1, ref—minimum sunspot (SS) activity); MSS falling Association of Variable Star Observers (AAVSO)—which only includes high quality observations combined into the 'American Relative Number of Sunspot Numbers' (RA) per instructions outlined in Shapley (1949). percentile assigned to Q4 (maximum SS activity). MSS information was obtained from the National Oceanic and Atmospheric Administration (NOAA), US Department of Commerce website (https://www.ngdc.noaa. between 25th and 49th percentile assigned to Q2 (low to medium SS activity); MSS falling between the 50th and 74th percentile assigned to Q3 (medium to high SS activity); and MSS between the 75th and 100th gov/stp/space-weather/solar-indices/sunspot-numbers/american/lists/list\_aavso-arssn\_monthly.txt). Observations utilized by NOAA include observations collected by the Solar Division, American <sup>b</sup>Adjusted for maternal age, maternal race/ethnicity, and maternal education.

Abbreviations: 95% CI, 95% confidence interval; aPR, adjusted prevalence ratio; Q1, Quartile 1; Q2, Quartile 2; Q3, Quartile 3; Q4, Quartile 4; TBDR, Texas Birth Defects Registry.

'Adjusted for maternal age, maternal race/ethnicity, maternal education, and year of conception.

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the TBDR (with the inclusion of clinically verified cases), the DSHS Center for Health Statistics (incorporating vital events across Texas), and NOAA (providing continual monitoring of solar and space weather conditionsincluding sunspots), this study is not without limitations. Given the spectrum nature of this analysis and numerous statistical associations tested for, we cannot rule out the potential for chance findings. Further, given the ubiquity and broadly defined scope of exposure (SS activity over time), there are numerous avenues for exposure misclassification—a few of which will be discussed in more detail below, alongside some current speculated mechanisms underlying these associations as they relate to the occurrence of birth defects.

### Solar UV-R exposure 5.1 misclassification

As touched on above, in considering this ecological study design, our use of SS exposure can only be considered a proxy for individual UV and other cosmic exposures experienced by our terrestrial population at large (i.e., the ecological fallacy) (Mackenbach, 2000)—thus, we cannot attribute any causal relationships to these findings. Further, we utilized mean monthly exposures across the first trimester broken down into quartiles where peak exposures were not assessed. Future studies would benefit from more accurate methods of assessing exposure accounting for daily exposure across the entire pregnancy period.

Along these lines, individual exposure levels to differing types of solar ultraviolet (UV) radiation (UV-A vs. UV-B) were also not captured in this study. While both types of radiation are known to damage DNA, they have different mechanisms of action. Solar UV-A radiation, for instance, the predominant form of UV-R reaching the Earth, is known to pass through glass (Duarte et al., 2009) and penetrate as deep as the dermis in skin (Guerra et al., 2023). UV-B, on the other hand (shorter in wavelength and largely blocked by glass) penetrates less well through the atmosphere—although is considered more directly damaging to DNA when exposure does occur (Guerra et al., 2023). As discussed in Section 4.1, UV-B exposure penetrating the atmosphere may also be more common during active SS periods—thus being more problematic during solar maximums. Lastly, we were unable to account for the amount of time spent outdoors, type of clothing worn, or utilization of sunscreen in our population—all of which may have had important impacts on the amount of UV-R our population was exposed to.

# UV-R, folate degradation, and birth defects

While previous in-vitro studies have shown that both folate (and its synthetic derivative folic acid) are degraded by both solar UV-A and UV-B radiation, only UV-A radiation (as discussed above) is known to penetrate through to dermal circulation (Guerra et al., 2023)—leaving folate more vulnerable to degradation (Borradale et al., 2014). Further, regarding folate status in particular (important for the prevention of an array of birth defects [Czeizel, 2004; Zhou et al., 2020]), recent research has pointed to a potential interaction between the solar cycle and MSR/MTHFR genotypes influencing embryo viability (Lucock et al., 2012). Lucock et al. (2012), for instance, hypothesized that there is a time specific sensitivity of folate to solar emissions that could predispose specific genotypes to pregnancy loss or developmentally originated disorders. Future studies aimed at better understanding not only frequency and type of UV-R exposure, but also amounts of circulating folate and genotypic interactions in the presence of these exposures could provide greater insight into the mechanisms underlying these associations.

#### 5.3 Global moderators

Further, while solar activity is ubiquitous, variations in UV intensity on a global scale occur due to a variety of factors, including: differences in latitudes (UV rays are less intense further away from the equator due to differences in the orientation and polarity of the Earth's magnetic field [Palmer et al., 2006]), chlorofluorocarbon (CFC) pollution, cloud cover, aerosols, solar wind, Sun-Earth distance, solar zenith, and altitude (Aceituno-Madera et al., 2011; McKenzie et al., 2011; Sabburg et al., 2001). Given that all study subjects included in this analysis resided in Texas, the chance for misclassification due to altitudinal and latitudinal residential differences, in particular, is minimal. Future research would benefit from the inclusion of more complex models accounting for these varying global factors.

#### 5.4 Residual confounders

Lastly, we cannot rule out the potential for residual confounding by other factors such as maternal diabetes, smoking, hypertension, body mass index (BMI), rural/ urban residence, and an array of other sociodemographic and occupational factors that were not included in this analysis and may have had significant impacts on our results.

# 6 | CONCLUSION

While still relatively new to the field of public health and birth defects research, heliobiology may prove increasingly important in the future. As solar radiation levels are expected to increase in the coming years due to climate change and variations in atmospheric ozone (Williamson et al., 2014), better understanding how solar activity influences human health—alongside the mechanisms underlying these changes—will prove to be increasingly important. For the present analysis, we examined 18 years of sunspot data (a proxy for solar activity) and a spectrum of 44 birth defects in a large, population-based study utilizing Texas data. Slightly over half of the defects examined had protective aPR estimates in the presence of increasing SS activity, while two defect groupings included significant elevations. With the additional inclusion of year of conception across our models, results were similar with the exception that a number of the findings were attenuated. Given our overall limited understanding of these solar-terrestrial relationships, future work is needed to replicate and build upon these findings to provide a more coherent picture of these complex relationships.

### CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

# DATA AVAILABILITY STATEMENT

Research data are not shared.

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