Received: 19 July 2022 | Revised: 23 November 2022 | Accepted: 29 December 2022

DOI: 10.1002/hsr2.1054

ORIGINAL RESEARCH

Health Science Reports Open Access WILEY

Preterm birth characteristics and outcomes in Portugal, between 2010 and 2018—A cross-sectional sequential study

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Funding information

The present publication was funded by Fundação Ciência e Tecnologia, IP national support through CHRC, Grant/Award Number: UIDP/04923/2020

Abstract

Introduction: According to the World Health Organization, 11% of all children are born prematurely, representing 15 million births annually. An extensive analysis on preterm birth, from extreme to late prematurity and associated deaths, has not been published. The authors characterize premature births in Portugal, between 2010 and 2018, according to gestational age, geographic distribution, month, multiple gestations, comorbidities, and outcomes.

Methods: A sequential, cross-sectional, observational epidemiologic study was conducted, and data were collected from the Hospital Morbidity Database, an anonymous administrative database containing information on all hospitalizations in National Health Service hospitals in Portugal, and coded according to the ICD-9-CM (International Classification of Diseases), until 2016, and ICD-10 subsequently. Data from the National Institute of Statistics was utilized to compare the Portuguese population. Data were analyzed using R software.

Results: In this 9-year study, 51.316 births were preterm, representing an overall prematurity rate of 7.7%. Under 29 weeks, birth rates varied between 5.5% and 7.6%, while births between 33 and 36 weeks varied between 76.9% and 81.0%. Urban districts presented the highest preterm rates. Multiple births were 8× more likely preterm and accounted for 37%–42% of all preterm births. Preterm birth rates slightly increased in February, July, August, and October. Overall, respiratory distress syndrome (RDS), sepsis, and intraventricular hemorrhage were the most common morbidities. Preterm mortality rates varied significantly with gestational age.

Conclusion: In Portugal, 1 in 13 babies was born prematurely. Prematurity was more common in predominantly urban districts, a surprise finding that warrants further studies. Seasonal preterm variation rates also require further analysis and modelling to factor in heat waves and low temperatures. A decrease in the case rate of RDS and sepsis was observed. Compared with previously published results, preterm mortality per gestational age decreased; however, further improvements are attainable in comparison with other countries.

KEYWORDS
gestational age, morbidities, mortality, multiple, prematurity, urban–rural

1 | INTRODUCTION

According to the World Health Organization (WHO), an estimated 11% of all children are born prematurely, representing 15 million births annually.[1] Prematurity is the most important cause of hospitalization in newborn children, the leading cause of death during the neonatal period, and the second cause of death in children under 5.[2]

Prematurity causes are multifactorial. Prematurity can be associated with spontaneous labor at an early gestational age resulting from several factors such as maternal characteristics, lifestyle, uterine anatomy and infection,[3] or can be caused by iatrogenic labor when, in specific clinical circumstances, a decision is taken to deliver a newborn at an early gestational age.[4] Multiple pregnancies are also an important risk factor for prematurity.[5,6] A seasonality pattern in preterm birth has also been reported, with preterm birth peaks occurring in the Summer or Winter months.[7] Other morbidity and mortality outcomes vary significantly with prematurity; in particular, extreme prematurity survival is significantly connected to gestational age.[8] In Portugal, in 2016, according to the National Institute of Statistics (INE), 6.801 premature births occurred, corresponding to 7.8% of all births.[9]

According to Organisation for Economic Co-operation and Development (OECD), Portugal has the fifth highest proportion of children born with low weight, 8.9%, significantly superior to the OECD average of 6.5% in 2015.[10]

A National Very Low Birth Weight Registration (RNMBP) was implemented in Portugal in 1994.[11] This database includes the prenatal, perinatal, and postnatal data associated with the premature birth of extremely and very low birth weight (VLBW) children in Portugal. According to the RNMBP data, between 2005 and 2012, there were no survivors from births at 22 weeks of gestational age, and an inverse relationship between gestational age and death: 87%, 70%, 43%, and 30% at 23, 24, 25, and 26 weeks, respectively, making gestational age the most important risk factor for death. A sustained reduction in preterm deaths was reported between 1996 and 2012, particularly a decrease from 27% to 15% in preterm deaths with a birth weight under 1500 g.[12]

Prematurity is considered a major cause of mortality and morbidity, and survivors are at increased risk of cognitive delay, cerebral palsy, ophthalmologic and auditory disease, and overall decreased health.[13]

To the authors' knowledge, an extensive analysis on preterm birth characteristics, from extreme to late prematurity and associated deaths, has not been published. In this study, the authors characterize premature births in Portugal, between 2010 and 2018, according to gestational age, birth weight, multiple gestations, comorbidities, and outcomes.

2 | METHODS

2.1 | Design study

To analyze premature births, the authors conducted a sequential, cross-sectional, observational epidemiologic study.

2.2 | Data

Data were collected from the BDMH (Hospital Morbidity Database), an anonymous administrative database containing demographic information, diagnosis, and procedures of all the hospitalizations in Portugal, and coded according to the ICD-9-CM (International Classification of Diseases) until 2016 and ICD-10 subsequently. Data from the National Institute of Statistics was utilized to compare the Portuguese population. Data were statistically analyzed using R software (R Core Team, 2018). Descriptive statistics were performed and statistical analysis using one-sample χ^2 test, Pearson's correlation, Fisher–Freeman–Halton exact test, and linear-by-linear association tests were utilized. Linear regression was algo performed to compare quantitative variables. Statistical significance was considered when $p < 0.05$.

2.3 | Outcomes

All the children born at National Health Service (NHS) hospitals, in Portugal, between 2010 and 2018 were included in our study, and premature births were analyzed subsequently. Prematurity was defined as birth before 37 weeks (36^{+6} weeks of gestation), extreme preterm as birth before 28 weeks (27^{+6}), adapted extreme prematurity as birth before 29 weeks (28^{+6} weeks of gestation), late prematurity as birth between 34 weeks and 36^{+6}, and adapted late prematurity as birth between 33 and 36^{+6} weeks. The adapted extreme preterm groups were created due to gestational age aggregation in ICD-9-CM, meaning preterm data on gestational age was combined in 25–26, 27–28, 29–30, 31–32, 33–34, and 35–36 weeks from 2010 to 2016. Birth weight was analyzed from a variable that presents birth weight in gram, so these were not derived from ICD coding. Low birth weight was defined as <2500 g and very low birth weight as <1500 g. Comorbidities such as necrotizing enteritis (NEC) (77751, 77752, 77753, 7775, P771, P772, P773, P779), respiratory distress syndrome (RDS) (769, P220), sepsis (77181, P360, P361, P362, P363, P364, P365, P368, P369) intraventricular hemorrhage (IVH) (77211, 77212, 77213, 77214, P520, P521, P5221, P5222, P523, P524, P525, P526, P528, P529), and retinopathy of prematurity (ROP) (H351, H3510, H3511, H3512, H3513, H3514,

H3515, H3516, H3517) were defined according to ICD-9 and ICD-10. Due to coding limitations outcomes such as late sepsis or specific ROP stages were not possible to obtain. Deaths were analyzed according to the variable DSP (destination after hospital discharge), with Code 20 (death) referring exclusively to the event of death during the inpatient stay associated with birth. Preterm infants not coded for a specific gestational age were excluded from analysis requiring this information.

2.4 | Ethics

The study utilized an anonymous secondary database; therefore, no ethical approval was required.

3 | RESULTS

3.1 | Prematurity

Between 2010 and 2018, there were 668,171 births at SNS hospitals in Portugal. Of these, 51,316 were preterm, representing an overall prematurity rate of 7.7%, and annual prematurity rates varying from 7.3% to 8.0%. A nonhomogeneous pattern across years was observed but no clear trend emerged in total preterm analysis and according to sex (Table 1 and Figure 1).

A decrease in the absolute number of preterm births was observed and was partnered with an overall birth decrease, maintaining the preterm birth rates at similar levels. Low weight was observed in 61,608 births, yielding a yearly low birth rate varying from 8.9% to 9.5%, values consistently higher than preterm birth rates. A very low birth was observed in 8750 births, corresponding to 1.3% of all births.

A total of 3,305 births occurred before 29 weeks (7.6% of preterm births), and compared among years; these remained stable throughout the study. A total of 38,930 births occurred between weeks 33 and 36^{+6}, corresponding to 89.4% of the preterm births presenting an increasing trend from 76.9% in 2010 to 81.0% of all preterm births.

3.2 | Sex

Prematurity was consistently more frequent in the male sex in all years, corresponding to 52% of preterm birth (Table 2).

3.3 | Gestational age

Globally, preterm births varied yearly from 7.3% to 8.0% of all births. In 2017, extremely preterm birth was 4.0% preterm births and late

TABLE 1 Total births, preterm births, low birth weight births, and very low birth weight births, in absolute and relative value (per 100 births), by year, between 2010 and 2018 at SNS hospitals in Portugal.

	Year										
	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total	*p* Value
Births											
n	84,480	87,023	75,170	68,379	66,310	69,167	73,717	73,356	70,569	668,171	<0.001[a]
											0.068[b]
Preterm births											
n	6301	6352	5877	5384	5120	5515	5825	5681	5261	51316	<0.001[a]
%	7.5	7.3	7.8	7.9	7.7	8.0	7.9	7.7	7.5	7.7	0.716[b]
Male (*n*, %)											
n	3228	3350	3073	2732	2777	2834	3060	3001	2803	26,858	0.007[c]
%	51	53	52	51	54	51	53	53	53	52	0.061[d]
Low birth weight											
n	7514	8121	6837	6326	6110	6547	6707	6929	6517	61,608	0.002[c]
%	8.9	9.3	9.1	9.3	9.2	9.5	9.1	9.4	9.2	9.2	0.019[d]
Very low birth weight											
n	1068	1419	1002	830	806	880	946	949	850	8750	<0.001[c]
%	1.3	1.6	1.3	1.2	1.2	1.3	1.3	1.3	1.2	1.3	<0.001[d]

[a]One-sample χ^2 test.
[b]Pearson's correlation.
[c]Fisher–Freeman–Halton exact test.
[d]Linear-by-linear association test.

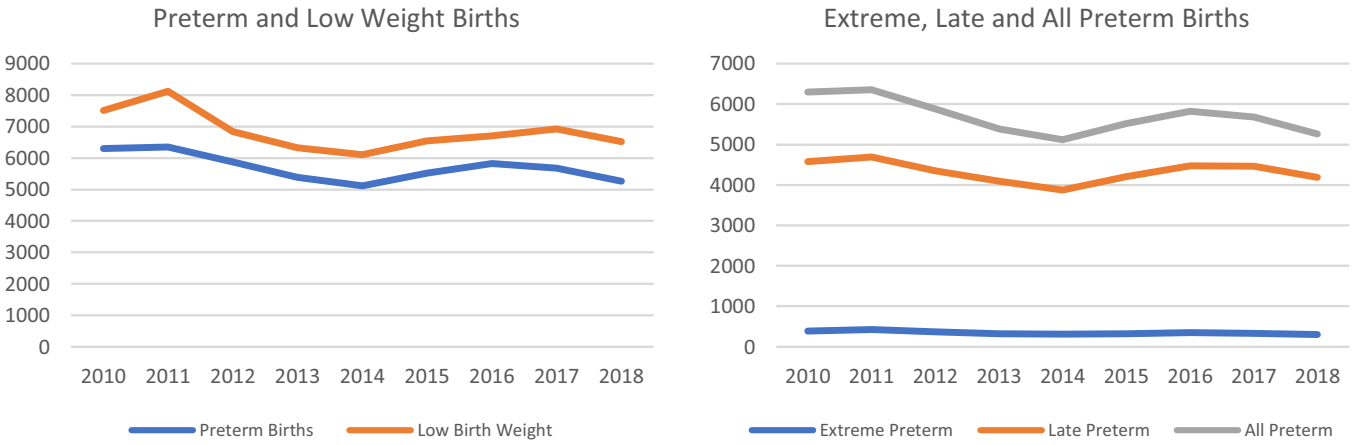

FIGURE 1 (Left) Preterm and low weight births per year and (right) extreme, late, and total preterm births per year, between 2010 and 2018, at SNS hospitals in Portugal.

TABLE 2 Preterm births by gestational week in relative and absolute terms, total births with known gestational week per year between 2010 and 2018, and extreme and late preterm birth between 2017 and 2018, in Portugal.

Gestational age in weeks		2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
<23									2	2	
	<24	15	27	27	27	23	16	18	0.0	0.0	176
		0.2	0.4	0.5	0.5	0.4	0.3	0.3	10	9	
23									0.2	0.2	
24	24	48	46	43	33	27	39	49	43	34	362
		0.8	0.7	0.7	0.6	0.5	0.7	0.8	0.8	0.6	
25									41	43	
	25–26	121	122	127	93	118	102	112	0.7	0.8	982
26		1.92	1.92	2.16	1.73	2.30	1.85	1.92	57	46	
									1.0	0.9	
27									74	73	
	27–28	200	234	175	165	141	160	173	1.3	1.4	1590
28		3.2	3.7	3.0	3.1	2.8	2.9	3.0	103	92	
									1.8	1.7	
29									145	94	
	29–30	357	332	312	253	259	303	272	2.6	1.8	2664
30		5.7	5.2	5.3	4.7	5.1	5.5	4.7	195	142	
									3.4	2.7	
31									217	214	
	31–32	637	633	551	493	520	515	549	3.8	4.1	4957
32		10.1	10.0	9.4	9.2	10.2	9.3	9.4	313	315	
									5.5	6.0	

TABLE 2 (Continued)

Gestational age in weeks	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
33								488	456	
33–34	1348	1316	1273	1167	1135	1228	1283	8.6	8.7	11,235
34	21.4	20.7	21.7	21.7	22.2	22.3	22.0	786	755	
								13.8	14.4	
35								1181	1121	
35–36	3233	3380	3077	2923	2741	2980	3195	20.8	21.3	27,695
36	51.3	53.2	52.4	54.3	53.5	54.0	54.8	2006	1858	
								35.3	35.3	
Total	5959	6090	5585	5154	4964	5343	5651	5661	5254	43,702
Preterm under 29 weeks (*n*, %)	384	429	372	318	309	317	352	433	391	3305
	6.4	7.0	6.7	6.2	6.2	5.9	6.2	7.6	7.4	7.6
Extreme preterm (*n*, %)								227	207	
								4.0	3.9	
33–36 weeks preterm (*n*, %)	4581	4696	4350	4090	3876	4208	4478	4461	4190	38,930
	76.9	77.1	77.9	79.4	78.1	78.8	79.2	78.8	79.7	89.1
Late preterm (*n*, %)								3973	3734	
								70.2	71.1	
Total preterm	6301	6352	5877	5384	5120	5515	5825	5681	5261	51,316
Unknown gestational week (*n*, %)	342	262	292	230	156	172	174	20	7	7614
	5.4	4.1	5.0	4.3	3.0	3.1	3.0	0.4	0.1	14.8

preterm births 70.2%. Unsurprisingly, there was an increase in the absolute and relative birth rates with increasing gestational age. In 2018, for example, 0.2% ($n = 11$) of preterm births were infants with less than 24 weeks, and 56.5% ($n = 2970$) were between 35 and 36 weeks. For most of the years, a small proportion of the preterm births were not coded for a specific gestational age and were excluded from analysis requiring this information.

3.4 | District distribution

In absolute value, preterm births occurred mainly in large urban districts such as Lisbon ($n = 12,859$, 27.0%), Porto ($n = 9580$, 20.1%), and Setubal ($n = 4803$, 10.1%) and the lowest counts were observed in rural districts such as Portalegre, Guarda e Bragança. Considering preterm births from total births, large urban centers maintained an increased rate than the national average (7.7%)—in the Porto district, 8.6%, and in the Lisbon district, 8.2%, of births were preterm. The lowest preterm birth rates, under 5.5%, were observed in mainly rural districts such as Portalegre and Beja. Castelo Branco, an interior and mainly rural district, also reported preterm birth rates of 8.3%.

3.5 | Monthly preterm births

Overall, preterm births were slightly more frequent in February, July, August, and October, corresponding to 7.9%–8.0% of all preterm births. In contrast, extreme preterm birth rates were more common in July at 9.4% and August at 9.7%.

3.6 | Multiple births

A total of 19,975 were multiple births, corresponding to 3.0% of all births and between 2.8% and 3.4% of births per year. Between 97.0% and 99.1% were twins, and the remaining triplets or more. Preterm multiples corresponded to 1.8%–2.2% of all births yearly and importantly corresponded to 35.3%–42.2% of all preterm births. In addition to this, 61.2%–68.4% of multiple pregnancies were associated with premature birth. In 2017, 2.0% of multiples were born preterm and 39.7% were late preterm. Under 29 weeks, preterm multiple births rates appear to present a slight increase over the 9-year analysis (Table 3 and Figure 2).

TABLE 3 Multiple births and preterm multiple births per year and proportion for all births between 2010 and 2018, in Portugal.

Year	Multiple births	Twin births (*n*, %)	Triplets or more (*n*, %)	Preterm multiple births (*n*, %)	Proportion of preterm multiples from all preterm (%)	Proportion of preterm multiples from all multiples (%)	Altered extreme preterm multiples births (*n*, %)	Extreme preterm multiples births (*n*, %)	Altered late preterm multiples birth (*n*, %)	Late preterm multiples birth (*n*, %)
2010	2378 (2.8)	2344 (98.6)	34 (1.4)	1543 (1.8)	37.7	64.9	90 (3.8)		1072 (45.1)	
2011	2450 (2.8)	2394 (97.7)	56 (2.3)	1630 (1.9)	38.6	66.5	104 (4.2)		1216 (49.6)	
2012	2201 (2.9)	2182 (99.1)	19 (0.9)	1506 (2.0)	37.5	68.4	101 (4.6)		1077 (48.9)	
2013	2006 (2.9)	1980 (98.7)	26 (1.3)	1330 (1.9)	37.3	66.3	92 (4.6)		959 (47.8)	
2014	1996 (3.0)	1963 (98.3)	33 (1.7)	1321 (2.0)	39.0	66.2	105 (5.3)		939 (47.0)	
2015	2326 (3.4)	2294 (98.6)	32 (1.4)	1541 (2.2)	42.2	66.3	78 (3.4)		1148 (49.4)	
2016	2054 (2.8)	2003 (97.5)	51 (2.5)	1331 (1.8)	35.3	64.8	89 (4.3)		978 (47.6)	
2017	2384 (3.2)	2335 (97.9)	49 (2.1)	1459 (2.0)	42.0	61.2	84 (5.8)	53 (2.3)	1089 (45.7)	947 (39.7)
2018	2180 (3.1)	2115 (97.0)	65 (3.0)	1378 (2.0)	41.4	63.2	85 (6.2)	68 (3.1)	979 (44.9)	856 (39.3)
Total	19,975	19,610	365	13,039			828		9457	

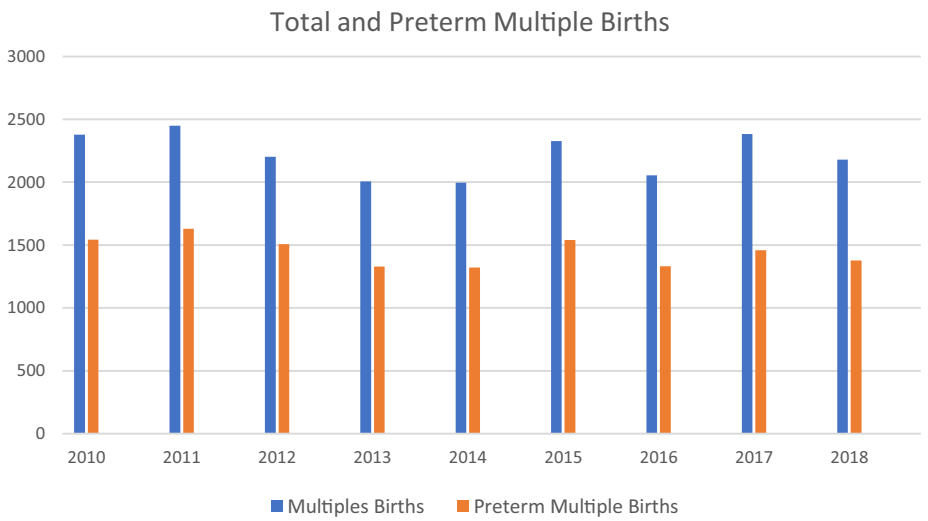

FIGURE 2 Total and preterm multiple births per year between 2010 and 2018 at SNS hospitals in Portugal.

TABLE 4 Mean birth weight and standard deviation for preterm (in g), under 29 weeks preterm, and 33–36 weeks preterm babies, between 2010 and 2018, in Portugal.

	Birth weight						<1000 g			
	Preterm		Under 29 weeks preterm		Preterm 33–36 weeks		Preterm		Under 29 weeks preterm	
Year	μ	SD	μ	SD	μ	SD	*n*	%	*n*	%
2010	2152.7	622.8	932.5	414.8	2364.1	455.8	322	5.1	127	2.0
2011	2134.0	650.1	948.6	452.7	2345.0	483.1	405	6.4	138	2.2
2012	2151.1	624.6	917.3	420.9	2365.6	453.9	348	5.9	112	1.9
2013	2151.6	606.6	918.1	386.5	2352.9	437.4	293	5.4	108	2.0
2014	2126.8	612.8	922.7	401.3	2338.7	451.6	271	5.3	101	2.0
2015	2130.5	605.9	930.3	406.2	2333.0	444.6	275	5.0	108	2.0
2016	2141.7	620.1	922.4	390.1	2350.5	467.0	329	5.6	106	1.8
2017	2151.9	627.9	874.8	283.2	2369.7	467.1	307	5.4	98	1.7
2018	2155.5	621.3	885.8	295.6	2365.4	464.3	269	5.1	98	1.9
Total	2144.0	621.3	916.9	383.5	2353.9	458.3	2819		996	

3.7 | Birth weight

Between 2010 and 2018, mean preterm birth weights remained stable between 2126.8. and 2155.5 g. Extreme preterm birth weights varied between 885.8 and 948.6 g. Under 1000 g births preterm births varied between 5.1% and 6.4%, and approximately 30% of extremely preterm births had a birthweight under 1000 g (Table 4).

3.8 | Preterm complications and ventilation requirements

Between 2010 and 2018, NEC cases varied between 24 (6.1%) and 44 (10.3%), RDS varied between 216 (55.2%) and 318 (74.1%), sepsis between 119 (30.4%) and 200 (46.6%), IVH between 88 (22.9%) and 141 (40.1%), Grade 3 and 4 IVH between 34 (8.7%) and 45 (12.6%), and ROP between 55 (14.1%) and 87 (20.3%). Regarding ventilation requirements, noninvasive ventilation was utilized between 165 (42.2%) and 221 (51.5%) and invasive ventilation between 170 (43.5%) and 265 (71.2%) (Table 5 and Figure 3).

3.9 | Preterm deaths

Overall, 976 deaths were reported in our study, a rate of 1.9% from all preterm births. Preterm deaths varied significantly according to gestational age. During the birth hospital episode, preterm deaths: at 24 weeks ranged from 48.5% (2015) to 75% (2016); between 27 and

TABLE 5 Preterm comorbidities (NEC, RDS, sepsis; IVH, ROP) and ventilation requirements per year between 2010 and 2018 at SNS hospitals in Portugal.

	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total	*p* Value
NEC	43 (11.2)	44 (10.3)	33 (8.9)	32 (10.1)	25 (8.1)	30 (9.5)	31 (8.8)	30 (6.9)	24 (6.1)	292 (8.8)	<0.05
RDS	277 (72.1)	318 (74.1)	281 (75.5)	267 (84.0)	250 (80.9)	256 (80.8)	278 (79.0)	278 (64.2)	216 (55.2)	2421 (73.3)	0.07
Sepsis	168 (43.8)	200 (46.6)	169 (45.4)	163 (51.3)	146 (47.2)	149 (47.0)	157 (44.6)	159 (36.7)	119 (30.4)	1430 (43.3)	<0.05
IVH	88 (22.9)	115 (26.8)	98 (26.3)	92 (28.9)	92 (29.8)	102 (32.2)	141 (40.1)	116 (26.8)	100 (25.6)	944 (28.6)	0.2
IVH Grade 3 and 4	53 (13.8)	54 (12.6)	44 (11.8)	37 (11.6)	36 (11.7)	54 (17.0)	72 (20.5)	45 (10.4)	34 (8.7)	429 (13.0)	0.7
ROP	85 (22.1)	87 (20.3)	77 (20.7)	77 (24.2)	84 (27.2)	79 (24.9)	92 (26.1)	81 (18.7)	55 (14.1)	717 (21.7)	0.98
NIMV	200 (52.1)	221 (51.5)	195 (52.4)	202 (63.5)	199 (64.4)	204 (64.4)	202 (57.4)	172 (39.7)	165 (42.2)	1760 (53.3)	<0.05
Mechanical ventilation	254 (66.1)	284 (66.2)	265 (71.2)	225 (70.8)	207 (67.0)	233 (73.5)	230 (65.3)	215 (49.7)	170 (43.5)	2083 (63.0)	<0.05
Ventilation option coded as other	28 (7.3)	38 (8.9)	33 (8.9)	29 (9.1)	27 (8.7)	26 (8.2)	48 (13.6)	117 (27.0)	133 (34.0)	479 (14.5)	-

Abbreviations: IVH, intraventricular hemorrhage; NEC, necrotizing enteritis; NIMV, non invasive mechanical ventilation; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity.

28 weeks decreased to 10.5% (2010) and 14% (2018); and between 35 and 36 weeks, ranged from 0.1% to 0.2%. Between weeks 29 and 36, death rates decreased from 4.6% to 0.2%. In the yearly death analysis, a decreasing trend was observed in deaths of 31–32 and 33–34 weekers and no particular trend was evident for other gestational ages or overall trend.

The mode day of death for total and extreme preterm was consistently Day 0 of life, whereas in late preterm, the same pattern was observed, but from 2015 onward, the mode varies between Days 2 and 6. A wide variation of the mean, median, and SD was observed for total, extreme, and late preterms (Tables 6 and 7).

4 | DISCUSSION

Over the 9 years analyzed, at NHS hospitals in Portugal, 7.7% (n = 51.316) of all births were preterm, or 1 in 13 babies was born preterm, highlighting the magnitude of prematurity as a present-day public health issue. These values are in line with other national results[14] and international studies.[1] Preterm birth rates were stable throughout our study; a decrease in overall births was associated with a decrease in preterm births rendering a preterm rate between 7.3% and 8.0%. Unsurprisingly, as reported in the literature, preterm births were more common in males.[15] Overall, preterm births under 29 weeks occurred in 0.48% of births and 6.1% of all preterm births. In 2017, our study reports an extreme preterm rate of 0.31% of all births and 4.0% of preterm births. International estimates show higher values than ours; extreme preterm births constitute around 0.42% of all births[16] and 0.55% of all births in the United Kingdom, in 2019.[17] In France, extreme preterm births constituted 5% of all preterm birth,[18] a higher value than the one we report. In 2017, preterm births between 34 and 36 completed weeks were 5.4% of all births and 69.9% of all preterm births. A multicentre Portuguese study on late preterm prevalence showed 5.4% of late singleton births between 34 and 36 weeks, which is in line with our national results.[19]

Prematurity was more frequent in high-density urban districts like Lisbon and Porto and some rural districts such as Castelo Branco and Bragança. The lowest prematurity rates were observed in rural districts like Beja and Portalegre. The authors expected urban districts to be associated with lower prematurity rates as studies have mainly shown an urban maternal residence associated with a longer gestation.[20,21] However, our results show the opposite. This finding is supported by Statistics Portugal (INE) data, where preterm births in Alentejo, a mainly rural region, are consistently inferior to the Lisbon Metropolitan region. A similar description has also been reported in Pennsylvania (USA), where rural preterm rates were lower than urban ones.[22] However, prematurity is multifactorial, and several risk factors may play a role as socioeconomic factors, maternal educational level, ethnicity, or access to health services, which our study did not analyze.[21] Other hypotheses to explain this asymmetry may be associated with other urban pregnancy vulnerabilities, cesarean section rates, or twinning rates in Portuguese urban centers. However, this detailed analysis is beyond the scope of this article, and future studies are required to ascertain the predominant factors associated with this result.

Our analysis shows preterm births were more frequent during the Summer months, July and August, typically two extremely hot months in all of Portugal, and the winter month of February. Several countries have reported seasonality preterm rates with preterm peaks during Summer and or Winter months.[23,24] Greece, with a similar Mediterranean climate as Portugal, has reported these two

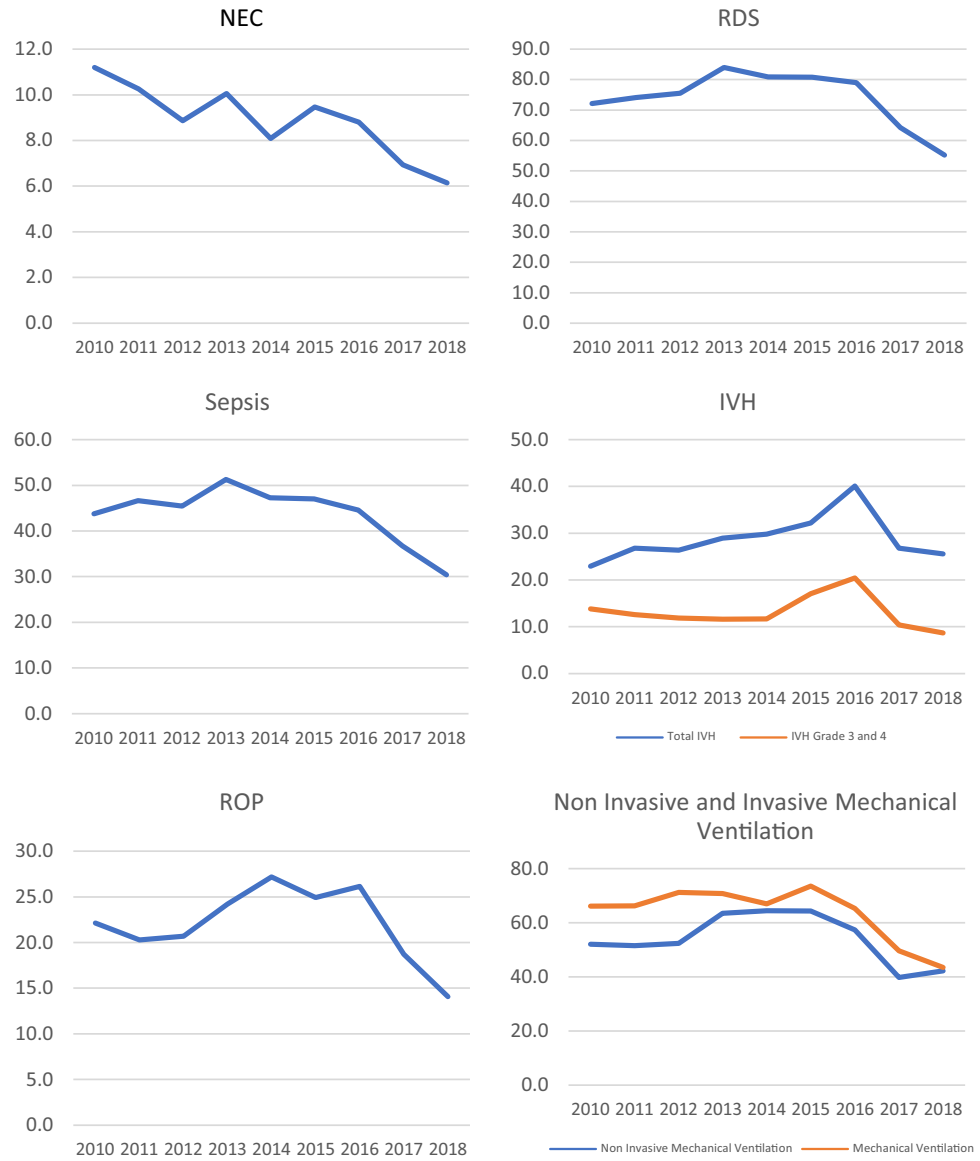

FIGURE 3 Preterm comorbidities (NEC, RDS, sepsis; IVH, ROP) and ventilation requirements per year between 2010 and 2018 at SNS hospitals in Portugal. IVH, intraventricular hemorrhage; NEC, necrotizing enteritis; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity.

peaks and has shown models that include meteorological conditions to optimize preterm birth descriptions.[25] Further analysis on the seasonality of preterm births in Portugal is required, particularly with models to factor in heatwaves and low temperatures.

Multiple birth rates varied from 2.8% to 3.4% of all births yearly, similar to results published in other countries[6,26] accounting for 37% to 42% of all preterm births analyzed. Over 97% of multiple births studied were twins and the remaining triplets. Between 61% and 68% of all multiple births were preterm. In contrast, the overall prematurity rate was 7.9%, which reflects an approximately eight times increase in premature births in multiple pregnancies, similar to what has been shown in other studies.[6] An increase in multiple gestations with associated preterm births has been widely recognized to be connected with increased maternal age and infertility treatment options.[27]

As expected, comorbidities were frequent in extreme preterms: 73.3% were diagnosed with respiratory distress syndrome and 43.3% with sepsis, and in both cases, a statistically significant decrease in cases was observed throughout the study. RDS has been consistently recognized as the most common complication associated with prematurity.[28] Sepsis is documented as a frequent complication and a Swedish study reported sepsis in 66% of preterm infants under 27 weeks gestation, where we reported 43.3% under 29 weeks.[29]

Necrotizing enterocolitis in developed countries is reported to occur in 5%–12% of VLBW infants.[28] In our analysis, we report 8.8% of preterms under 29 weeks, which is in keeping with the literature.

TABLE 6 Absolute and relative deaths per gestational age and year, between 2010 and 2018.

	Gestational age (in weeks)																	Under 29 weeks preterm	33–36 weeks preterm
Year	<23 <24	23	24 24	25 25–26	26	27 27–28	28	29 29–30	30	31 31–32	32	33 33–34	34	35 35–36	36	Total			
2010	9 (60.0)		25 (52.1)	25 (20.7)		21 (10.5)		12 (3.4)		10 (1.6)		5 (0.4)		5 (0.2)		112 (1.78)		80 (71.4)	10 (12.5)
2011	16 (59.3)		26 (56.5)	26 (21.3)		27 (11.5)		17 (5.1)		11 (1.7)		9 (0.7)		7 (0.2)		139 (2.19)		95 (68.3)	16 (16.8)
2012	15 (55.6		25 (58.1)	25 (19.7)		19 (10.9)		8 (2.6)		11 (2.0)		9 (0.7)		4 (0.1)		116 (1.97)		84 (72.4)	13 (15.5)
2013	10 (37.0)		16 (48.5)	16 (17.2)		17 (10.3)		9 (3.6)		10 (2.0)		4 (0.3)		6 (0.2)		88 (1.63)		59 (67.0)	10 (16.9)
2014	10 (43.5)		15 (55.6)	15 (12.7)		15 (10.6)		10 (3.9)		11 (2.1)		8 (0.7)		4 (0.1)		88 (1.72)		55 (62.5)	12 (21.8)
2015	7 (43.8)		19 (48.7)	19 (18.6)		17 (10.6)		12 (4.0)		7 (1.4)		5 (0.4)		4 (0.1)		90 (1.63)		62 (68.9)	9 (14.5)
2016	12 (70.6		30 (75.0)	30 (29.4)		17 (10.6)		14 (4.6)		5 (1.0)		3 (0.2)		7 (0.2)		118 (2.03)		89 (75.4)	10 (11.2)
2017	1 (50.0)	7 (70.0)	25 (58.1)	17 (41.5)	11 (19.3)	11 (14.9)	4 (3.9)	5 (3.4)	5 (2.6)	3 (1.4)	6 (1.9)	1 (0.2)	2 (0.3)	4 (0.3)	4 (0.2)	106 (1.87)		58 (54.7)	11 (19.0)
2018	2 (100.0)	8 (88.9)	24 (70.6)	20 (46.5)	17 (37.0)	12 (16.4)	11 (12.0)	5 (5.3)	8 (5.6)	2 (0.9)	1 (0.3)	2 (0.4)	0 (0.0)	5 (0.4)	2 (0.1)	119 (2.26)		69 (58.0)	9 (13.0)
Total	97		205	221		171		105		77		48		52		976		651	100
p Value	0.2		0.8	0.2		0.3		0.9		<0.05		<0.05		0.2		0.61		0.98	0.14

Severe IVH is typically defined as the combination of Grade 3 IVH, without parenchymal involvement and Grade 4 IVH despite the different outcomes.[30] In our analysis, 13.0% of extreme preterms developed severe IVH (Grades 3 and 4) in keeping with literature reports of 14.3%.[31]

In medical literature, the reported rate of ROP is higher[32,33] than the one reported in this analysis, respectively, 43.5%–60% and 21.7%. It is unlikely that such a wide gap corresponds to decreased rate of disease but is more likely related to coding ROP practices; however, further analysis is required.

From a ventilation requirement point, our analysis showed 53% of admissions required NIVM and 63% mechanical ventilation, highlighting the respiratory burden associated with this condition. However, the ICD coding presented limited applicability, not allowing differentiating of high-flow nasal cannula and continuous positive airway pressure. Furthermore, due to the transition from ICD-9-CM to ICD-10-CM an unexpected increase in the other ventilation options was observed, which warrants caution when interpreting these results.

Overall, as expected, gestational age had a major impact on preterm birth survival rates[30]; preterm mortality rate at 24 weeks was overall 58%, varying between 47.7% and 75% yearly, while between 35 and 36 weeks, the mortality rate varied between 0.1% to 0.2%, which reflects the importance of in utero pregnancy weeks. For the same gestational age, preterm death rates per gestational age presented substantial variability between years. Comparing these results with the RNMBP, where death rates per gestational week between 2005 and 2012 are presented,[34] at 24 weeks, the mortality rate presented in our study showed a slight decrease (58% vs. 65%). At 25–26 weeks, a similar pattern (23% vs. 30%) highlights a decrease in mortality rates.

A total of 976 deaths were observed during our analysis, corresponding to 1.9% of all preterm births. Results from an American regional cohort study from 2008 to 2011 revealed a mortality rate of 1.4%. When comparing mortality per gestational week in both studies, mortality rates are slightly lower at almost all gestational ages. A particular wider gap was observed at 24 weeks, where we report 56.1% when compared to 31.8% in that study.[35]

Infant mortality in Portugal has remained low; 282 children under 1 year of age died in Portugal in 2016, yielding an infant mortality rate was 3.2 per 1000.[9] From these deaths, at least 118 (41%) were preterm infants during their birth hospital admission. This fact suggests that an intervention to reduce infant mortality should necessarily involve reducing mortality associated with prematurity. However, an European article by the EPICE group, comparing the application of evidence-based practices in neonatology, concluded that between 22 and 31 weeks in Portugal, only 32% and 47% of newborns in the Lisbon and Northern Region received all the measures studied, respectively. This result contrasts with a European average of 58.3%.[36] A single Portuguese hospital study, on low birth weight births, to benchmark practices and results also highlights areas needing strengthening to improve outcomes such as the rates of healthcare-associated infection, neurological sequelae,

TABLE 7 Mode, mean, and median age of death (in days) in total, extreme and late preterm, by year between 2010 and 2018 in Continental Portugal.

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	*p* Value
Total preterm										
Mode	0	0	0	0	0	0	0	0	0	
n	33	60	35	30	34	26	29	16	34	
Mean	10.5	7.6	11.2	14.5	7.9	11.9	12.7	13.4	9.2	0.5
Median	4.0	2.0	3.0	6.0	4.0	4.0	4.0	5.0	3.0	
SD	36.0	13.2	24.5	30.9	13.9	22.8	19.00	29.5	18.8	
Extreme preterm										
Mode	0	0	0	0	0	0	0	0	0	
n	42	42	26	19	23	20	25	16	29	
Mean	4.0	6.6	8.7	14.9	7.4	11.5	12.5	14.3	7.9	0.1
Median	7.0	2.0	3.0	6.0	4.0	5.0	4.0	6.0	3.0	
SD	9.7	10.6	16.1	33.8	14.4	20.3	27.2	30.9	11.6	
Late preterm										
Mode	0	0	0	0	0	0 and 2	4	2	6	
n	3	7	5	5	4	2	4	2	2	
Mean	13.9	14.4	4.6	9.3	12.7	6.2	19.6	21.1	23.3	0.9
Median	3	6	2	1	3	4	5	9	6	
SD	30.6	25.1	7.9	15.2	18.1	6.7	14.3	32.9	54.4	

hypothermia control after birth, and neuroprotection with magnesium sulfate.[37]

Our results reinforce the need to decrease preterm birth rates and concomitantly improve the survival and morbidity outcomes of these infants. Increased awareness of prematurity as a serious public health problem partnered with policies aimed at mitigation and involving stakeholders, the public and private sectors, and communication strategies to reach those at risk are required.[38]

5 | LIMITATIONS

There were limitations to our study. First, the data were not obtained specifically for our analysis but for administrative care as a secondary database.

Errors in selecting, collecting, coding, or transferring data are possible. Second, the data presented here correspond to the births at NHS hospitals. However, in recent years, the number of births in private hospitals has increased significantly from 6% in 2000 to 14% in 2016. Neonatal guidelines have imposed a 32-week limit for preterm births in private hospitals, meaning premature births primarily occur in NHS institutions. Consequently, this will lead to a small overestimation of preterm and low-weight birth rates, but less so for the extreme preterm. For example, in 2016, according to INE, 6801 premature births occurred; comparing this result with our analysis where we characterized 5.825 premature births during the same year, we concluded that 976 preterm births likely occurred in private hospitals, corresponding to 14% of preterm births, the majority of which between 32 and 37 weeks.

Third, the aggregation of the gestational age in sets of 2 weeks enables this study to form the typical gestational age limits of 27^{+6} weeks for extreme preterm and 34 weeks to 36^{+6} weeks for late prematurity; however, the authors feel the analysis in itself maintains significant

Fourth, several newborns were not coded by gestational age, and these were excluded from the analysis where specific gestational age was required.

6 | CONCLUSION

In this 9-year national study, the authors found an overall low birth weight rate of 9.2% and a preterm birth rate of 7.7%, meaning 1 in 13 babies in Portugal was born preterm. Low birth weight, prematurity, and under 29 weeks preterm birth rates plateaued, whereas prematurity rates between 33 and 36 weeks increased. Prematurity was more common in predominantly urban districts than in rural ones, which was a surprising finding and warranted further studies by the authors to understand the risk factors related to preterm birth in Portugal. Seasonal preterm variation rates need further analysis and

modelling to factor in heat waves and low temperatures. Multiple births were eight more likely to be preterm and accounted for 37%–42% of all preterm births analyzed. A decrease in the case rate of RDS and sepsis was observed. In comparison with previously published results, preterm mortality per gestational age decreased; however, further improvements are attainable compared with other countries.

AUTHOR CONTRIBUTIONS

Cecília Elias: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; validation; visualization; writing – original draft; writing – review and editing. **Paulo Jorge Nogueira**: Conceptualization; data curation; formal analysis; methodology; software; supervision; validation; writing – review and editing. **Paulo Sousa**: Conceptualization; funding acquisition; methodology; resources; supervision; validation; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data may be obtained from a third party and are not publicly available.

TRANSPARENCY STATEMENT

The lead author Cecília Elias affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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REFERENCES

1. World Health Organization. *Preterm Birth—Key Facts*. World Health Organization; 2018. https://www.who.int/news-room/fact-sheets/detail/preterm-birth
2. Liu JohnsonHL, Cousens S, et al. Global, regional and national causes of child mortality, an updated systematic analysis for 2010 with time trends since 2000 [published correction appears in *Lancet*. 2012;380(9850):1308]. *Lancet*. 2012;9(379):2151-2161. doi:10.1016/S0140-6736(12)60560-1
3. Goldenberg RL, Gravett MG, Iams J, et al. The preterm birth syndrome: issues to consider in creating a classification system. *Am J Obstet Gynecol*. 2012;206(2):113-118. doi:10.1016/j.ajog.2011.10.865
4. Alfirevic Z, Milan SJ, Livio S. Caesarean section versus vaginal delivery for preterm birth in singletons. *Cochrane Database Systematic Reviews*. 2012;6(6):CD000078. doi:10.1002/14651858.CD000078.pub2
5. Schaaf J, Mol B, Abu-Hanna A, Ravelli A. Trends in preterm birth: singleton and multiple pregnancies in the Netherlands, 2000–2007. *BJOG*. 2011;118(10):1196-1204. doi:10.1111/j.1471-0528.2011.03010.x
6. Fuchs F, Senat MV. Multiple gestations and preterm birth. *Semin Fetal Neonatal Med*. 2016;21(2):113-120. doi:10.1016/j.siny.2015.12.010
7. Lee S, Steer P, Filippi V. Seasonal patterns and preterm birth: a systematic review of the literature and an analysis in a London-based cohort. *BJOG*. 2006;113(11):1280-1288. doi:10.1111/j.1471-0528.2006.01055.x
8. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. *Anesth Analg*. 2015;120(6):1337-1351. doi:10.1213/ANE.0000000000000705
9. Instituto Nacional de Estatistica. *Estatísticas Demográficas*. Instituto Nacional de Estatistica; 2016. https://www.ine.pt/ngt_server/attachfileu.jsp?look_parentBoui=307957746%26att_display=n%26att_download=y
10. OECD. *Health at a Glance*. OECD; 2017. doi:10.1787/health_glance-2017-en
11. Cunha M, Cadete A, Virella D, Grupo do Registo Nacional de Muito Baixo. Acompanhamento dos recém-nascidos de muito baixo peso em Portugal. *Acta Pediatr Port*. 2010;41(4):155-161. doi:10.25754/pjp.2010.4337
12. Sociedade Portuguesa de Neonatologia. *Consenso Clínico—Limite Da Viabilidade*. Sociedade Portuguesa de Neonatologia; 2016. https://www.spneonatologia.pt/wp-content/uploads/2016/11/2014-Viabilidade.pdf
13. Rogers LK, Velten M. Maternal inflammation, growth retardation, and preterm birth: insights into adult cardiovascular disease. *Life Sci*. 2011;89(13-14):417-421. doi:10.1016/j.lfs.2011.07.017
14. Sociedade Portuguesa de Neonatologia. *Nascer Prematuro Em Portugal*. Sociedade Portuguesa de Neonatologia; 2016. https://www.spneonatologia.pt/wp-content/uploads/2016/10/Manual-completo.pdf
15. di Renzo GC, Rosati A, Sarti RD, Cruciani L, Cutuli AM. Does fetal sex affect pregnancy outcome. *Gender Med*. 2007;4(1):19-30. doi:10.1016/S1550-8579(07)80004-0
16. Chawanpaiboon S, Vogel JP, Moller AB, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Glob Health*. 2019;7(1):e37-e46. doi:10.1016/S2214-109X(18)30451-0
17. Morgan AS, Mendonça M, Thiele N, David AL. Management and outcomes of extreme preterm birth. *BMJ*. 2022;10:e055924. doi:10.1136/bmj-2021-055924
18. Torchin H, Ancel PY, Jarreau PH, Goffinet F. Épidémiologie de la prématurité: prévalence, évolution, devenir des enfants. *J Gynecol Obstet Biol Reprod*. 2015;44(8):723-731. doi:10.1016/j.jgyn.2015.06.010
19. Barros JG, Clode N, Graça LM. Prevalence of late preterm and early term birth in Portugal. *Acta Med Port*. 2016;29(4):249-253. doi:10.20344/amp.6523
20. Murray SR, Juodakis J, Bacelis J, et al. Geographical differences in preterm delivery rates in Sweden: a population-based cohort study. *Acta Obstet Gynecol Scand*. 2019;98(1):106-116. doi:10.1111/aogs.13455
21. Rai RK, Sudfeld CR, Barik A, Fawzi WW, Chowdhury A. Socio-demographic determinants of preterm birth and small for gestational age in rural West Bengal, India. *J Trop Pediatr*. 2019;65(6):537-546. doi:10.1093/tropej/fmz002
22. Hillemeier MM, Weisman CS, Chase GA, Dyer AM. Individual and community predictors of preterm birth and low birthweight along the rural–urban continuum in central Pennsylvania. *J Rural Health*. 2007;23(1):42-48. doi:10.1111/j.1748-0361.2006.00066.x
23. Keller CA, Nugent RP. Seasonal patterns in perinatal mortality and preterm delivery. *Am J Epidemiol*. 1983;118(5):689-698. doi:10.1093/oxfordjournals.aje.a113679

24. Beltran A, Wu J, Laurent O. Associations of meteorology with adverse pregnancy outcomes: a systematic review of preeclampsia, preterm birth and birth weight. *Int J Environ Res Public Health*. 2013;11(1):91-172. doi:10.3390/ijerph110100091
25. Baroutis G, Mousiolis A, Hoffman D, Antsaklis A. Preterm birth seasonality in Greece: an epidemiological study. *J Matern Fetal Neonat Med*. 2012;25(8):1406-1412. doi:10.3109/14767058.2011.636103
26. Collins J. Global epidemiology of multiple birth. *Reprod Biomed Online*. 2007;15:45-52. doi:10.1016/S1472-6483(10)62251-1
27. Avraham S, Seidman DS. The multiple birth epidemic: revisited. *J Obstet Gynecol India*. 2012;62(4):386-390. doi:10.1007/s13224-012-0309-7
28. Shulhan J, Dicken B, Hartling L, Larsen BM. Current knowledge of necrotizing enterocolitis in preterm infants and the impact of different types of enteral nutrition products. *Adv Nutr*. 2017;8(1):80-91. doi:10.3945/an.116.013193
29. Ohlin A, Björkman L, Serenius F, Schollin J, Källén K. Sepsis as a risk factor for neonatal morbidity in extremely preterm infants. *Acta Paediatr*. 2015;104(11):1070-1076. doi:10.1111/apa.13104
30. Sarkar S, Bhagat I, Dechert R, Schumacher R, Donn S. Severe intraventricular hemorrhage in preterm infants: comparison of risk factors and short-term neonatal morbidities between Grade 3 and Grade 4 intraventricular hemorrhage. *Am J Perinatol*. 2009;26(06):419-424. doi:10.1055/s-0029-1214237
31. Bell EF, Hintz SR, Hansen NI, et al. Mortality, in-hospital morbidity, care practices, and 2-year outcomes for extremely preterm infants in the US, 2013-2018. *JAMA*. 2022;327(3):248. doi:10.1001/jama.2021.23580
32. Yucel OE, Eraydin B, Niyaz L, Terzi O. Incidence and risk factors for retinopathy of prematurity in premature, extremely low birth weight and extremely low gestational age infants. *BMC Ophthalmol*. 2022;22(1):367.
33. Stoll BJ, Hansen NI, Bell EF, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993–2012. *JAMA*. 2015;314(10):1039. doi:10.1001/jama.2015.10244
34. Sociedade Portuguesa de Neonatologia. *Consenso Clínico "Prematuridade Tardia"*. Sociedade Portuguesa de Neonatologia; 2018. https://www.spneonatologia.pt/wp-content/uploads/2018/05/Consenso-PTT-.pdf
35. Manuck TA, Rice MM, Bailit JL. Preterm neonatal morbidity and mortality by gestational age: a contemporary cohort. *Am J Obstet Gynecol Author*. 2017;215(1):103.e1-103.e14. doi:10.1016/j.ajog.2016.01.004
36. Zeitlin J, Manktelow BN, Piedvache A, et al. Use of evidence based practices to improve survival without severe morbidity for very preterm infants: results from the EPICE population based cohort. *BMJ*. 2016;354:i2976. doi:10.1136/bmj.i2976
37. Saldanha J, Moniz C, Machado MC. Recém-Nascido de Muito Baixo Peso numa Unidade de Cuidados Intensivos Portuguesa Comparativamente ao Vermont Oxford Network: 15 Anos de Registo. *Acta Med Port*. 2019;32(11):686-692. doi:10.20344/amp.9130
38. Galson SK. Preterm birth as a public health initiative. *Public Health Rep*. 2008;123(5):548-550. doi:10.1177/003335490812300502

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Elias C, Nogueira PJ, Sousa P. Preterm birth characteristics and outcomes in Portugal, between 2010 and 2018—A cross-sectional sequential study. *Health Sci Rep*. 2023;6:e1054. doi:10.1002/hsr2.1054