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been partly due to underlying health determinants that affected PTB and mortality. These findings suggest that PTB should be recognized as a risk factor for mortality and could inform preventive strategies.

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Canadian provincial and territorial vital statistics registries. Data privacy and confidentiality were upheld throughout the process of data linking and use, with access involving use of deidentified data

Table 1. Characteristics of Individuals Born at Term and Preterm in Unmatched and Matched Cohorts in Canada for Births from 1983 to 1996

Characteristics	Cohort, No. (%) ^a		SMD	Matched (weighted) (N = 4 350 210)	
	Unmatched (N = 4 998 560)			Term birth (n = 4 033 880)	Preterm birth (n = 316 330)
Sex					
Female	2 277 730 (48.9)	156 770 (45.8)	0.06	1 839 490 (45.6)	144 250 (45.6)
Male	2 378 250 (51.1)	185 810 (54.2)		2 194 390 (54.4)	172 080 (54.4)
Birth plurality					
Singleton	4 597 440 (98.7)	293 030 (85.5)	0.51	3 605 150 (89.4)	282 710 (89.4)
Multiple	58 540 (1.3)	49 550 (14.5)		428 720 (10.6)	33 620 (10.6)
Maternal parity					
0	1 999 540 (42.9)	158 450 (46.3)	0.10	1 925 140 (47.7)	150 970 (47.7)
1	1 669 660 (35.9)	108 640 (31.7)		1 289 770 (32.0)	101 140 (32.0)
2	684 860 (14.7)	48 760 (14.2)		553 680 (13.7)	43 420 (13.7)
3	203 080 (4.4)	17 090 (5.0)		175 700 (4.4)	13 780 (4.4)
4	98 850 (2.1)	9640 (2.8)		89 580 (2.2)	7030 (2.2)
Maternal age, y					
<20	277 470 (6.0)	26 240 (7.7)	0.11	311 660 (7.7)	24 440 (7.7)
20-24	1 029 950 (22.1)	77 760 (22.7)		930 470 (23.1)	72 970 (23.1)
25-29	1 735 490 (37.3)	116 650 (34.0)		1 404 930 (34.8)	110 170 (34.8)
30-34	1 199 010 (25.8)	85 070 (24.8)		998 630 (24.8)	78 310 (24.8)
35-39	366 590 (7.9)	31 790 (9.3)		344 870 (8.5)	27 040 (8.5)
40	47 480 (1.0)	5070 (1.5)		43 320 (1.1)	3400 (1.1)
Paternal age, y					
<25	553 490 (11.9)	44 730 (13.1)	0.13	528 460 (13.1)	41 440 (13.1)
25-29	1 415 490 (30.4)	97 230 (28.4)		1 175 120 (29.1)	92 150 (29.1)
30-34	1 424 850 (30.6)	94 970 (27.7)		1 139 050 (28.2)	89 320 (28.2)
35-39	652 540 (14.0)	47 760 (13.9)		546 460 (13.5)	42 850 (13.5)
40	267 740 (5.8)	22 800 (6.7)		237 740 (5.9)	18 640 (5.9)
Missing	341 870 (7.3)	35 090 (10.2)		407 050 (10.1)	31 920 (10.1)
Maternal place of birth					
Africa	30 370 (0.7)	2630 (0.8)	0.11	22 000 (0.5)	1730 (0.5)
Asia	214 530 (4.6)	19 170 (5.6)		210 750 (5.2)	16 530 (5.2)
Canada	3 881 490 (83.4)	274 790 (80.2)		3 324 710 (82.4)	260 720 (82.4)
Central and South America	59 070 (1.3)	5780 (1.7)		52 950 (1.3)	4150 (1.3)
Europe	233 930 (5.0)	16 550 (4.8)		170 430 (4.2)	13 370 (4.2)
North America excluding Canada	85 160 (1.8)	6370 (1.9)		57 700 (1.4)	4530 (1.4)
Other ^b	151 440 (3.3)	17 300 (5.0)		195 340 (4.8)	15 320 (4.8)
Paternal place of birth					
Africa	35 000 (0.8)	2950 (0.9)	0.13	23 600 (0.6)	1850 (0.6)
Asia	211 580 (4.5)	18 300 (5.3)		202 960 (5.0)	15 920 (5.0)
Canada	3 698 460 (79.4)	258 740 (75.5)		3 134 880 (77.7)	245 830 (77.7)
Central and South America	57 900 (1.2)	5390 (1.6)		50 330 (1.2)	3950 (1.2)
Europe	273 180 (5.9)	18 620 (5.4)		196 280 (4.9)	15 390 (4.9)
North America excluding Canada	69 000 (1.5)	5310 (1.5)		46 880 (1.2)	3680 (1.2)
Other ^b	310 880 (6.7)	33 280 (9.7)		378 940 (9.4)	29 720 (9.4)
Maternal marital status at birth					
Married	3 476 020 (74.7)	232 010 (67.7)	0.16	2 777 070 (68.8)	217 770 (68.8)
Other	80 300 (1.7)	7510 (2.2)		65 610 (1.6)	5150 (1.6)
Missing	116 470 (2.5)	14 120 (4.1)		151 460 (3.8)	11 880 (3.8)
Single	983 200 (21.1)	88 950 (26.0)		1 039 740 (25.8)	81 540 (25.8)

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Table 1. Characteristics of Individuals Born at Term and Preterm in Unmatched and Matched Cohorts in Canada for Births from 1983 to 1996 (continued)

Characteristics	Cohort, No. (%) ^a			Matched (weighted) (N = 4 350 210)	
	Unmatched (N = 4 998 560)		SMD	Term birth (n = 4 033 880)	Preterm birth (n = 316 330)
	Term birth (n = 4 655 980)	Preterm birth (n = 342 580)			
Province of birth					
Alberta	527 340 (11.3)	39 250 (11.5)		463 670 (11.5)	36 360 (11.5)
Atlantic provinces	320 610 (6.9)	23 330 (6.8)		272 260 (6.7)	21 350 (6.7)
British Columbia	548 130 (11.8)	37 730 (11.0)		424 630 (10.5)	33 300 (10.5)
Manitoba	207 000 (4.4)	17 200 (5.0)		189 000 (4.7)	14 820 (4.7)
Ontario	1 740 060 (37.4)	133 040 (38.8)	0.05	1 586 220 (39.3)	124 390 (39.3)
Quebec	1 095 210 (23.5)	77 180 (22.5)		931 680 (23.1)	73 060 (23.1)
Saskatchewan	195 930 (4.2)	13 320 (3.9)		151 350 (3.8)	11 870 (3.8)
Yukon, Nunavut, and Northwest Territories	21 710 (0.5)	1530 (0.4)		15 070 (0.4)	1180 (0.4)
Birth year					
1983	317 260 (6.8)	21 250 (6.2)		256 890 (6.4)	20 150 (6.4)
1984	322 000 (6.9)	22 260 (6.5)		267 020 (6.6)	20 940 (6.6)
1985	322 210 (6.9)	21 230 (6.2)		254 650 (6.3)	19 970 (6.3)
1986	320 060 (6.9)	21 300 (6.2)		256 100 (6.3)	20 080 (6.3)
1987	319 100 (6.9)	21 720 (6.3)		259 700 (6.4)	20 370 (6.4)
1988	326 460 (7.0)	23 460 (6.8)		279 540 (6.9)	21 920 (6.9)
1989	335 800 (7.2)	23 460 (6.8)		279 970 (6.9)	21 960 (6.9)
1990	348 390 (7.5)	24 550 (7.2)	0.09	288 300 (7.1)	22 610 (7.1)
1991	349 940 (7.5)	25 600 (7.5)		298 170 (7.4)	23 380 (7.4)
1992	351 620 (7.6)	26 040 (7.6)		304 430 (7.5)	23 870 (7.5)
1993	340 040 (7.3)	26 860 (7.8)		311 560 (7.7)	24 430 (7.7)
1994	341 660 (7.3)	27 680 (8.1)		320 120 (7.9)	25 100 (7.9)
1995	336 000 (7.2)	28 680 (8.4)		330 550 (8.2)	25 920 (8.2)
1996	325 460 (7.0)	28 490 (8.3)		326 900 (8.1)	25 640 (8.1)

Abbreviation: SMD, standardized mean difference.

^b Includes Oceania or Antarctica and adjacent islands and missing or unknown data.

^a All numbers have been rounded to the nearest 10 to preserve confidentiality.

In the unmatched cohort, we estimated the incidence rate of all-cause mortality per 10 000 person-years by PTB (and GA categories) and plotted the unadjusted cumulative incidence of all-cause mortality between the ages of 1 year and 36 years by GA categories. In the matched cohorts, we compared and plotted the cumulative incidence of all-cause mortality during the first year (aged 0-11 months) and between the ages of 1 year and 36 years by PTB status. We used log-binomial regression models to calculate RRs and risk differences (RDs) for mortality between the ages of 1 year and 36 years and in narrower age ranges (ages 0-11 months and ages 1-5, 6-12, 13-17, 18-28, and 29-36 years) among individuals who were still alive at the beginning of the respective age range. These age intervals were chosen to examine associations with mortality in different stages from birth to adulthood. We also estimated and plotted RDs and RRs stratified by age in years (ages 1-36 years). We estimated all associations for PTB as a binary variable and by GA categories. For cause-specific mortality, we estimated hazard ratios (HRs) using Cox proportional hazards regression models in 4 age ranges (0-11 months and 1-5, 6-17, and 18-36 years) to have a sufficient number of events and censored individuals who died from other causes.²⁹ We accounted for clustering of siblings born to the same mother using clustered variance estimates in all models. We used R, version 4.2.1 (R Project for Statistical Computing) for descriptive analyses and matching and Stata, version 16.1 (StataCorp LLC) for graphs and log-binomial regression and Cox proportional hazards regression models. Precision around point estimates was provided using 2-sided 95% CIs, and estimates were considered statistically significant if the 95% CIs did not include the null value. The threshold for statistical significance was 2-tailed $< .05$.

depicts the crude cumulative incidence of all-cause mortality beyond infancy by GA category in the unmatched cohort and highlights that total mortality was higher with decreasing GA.

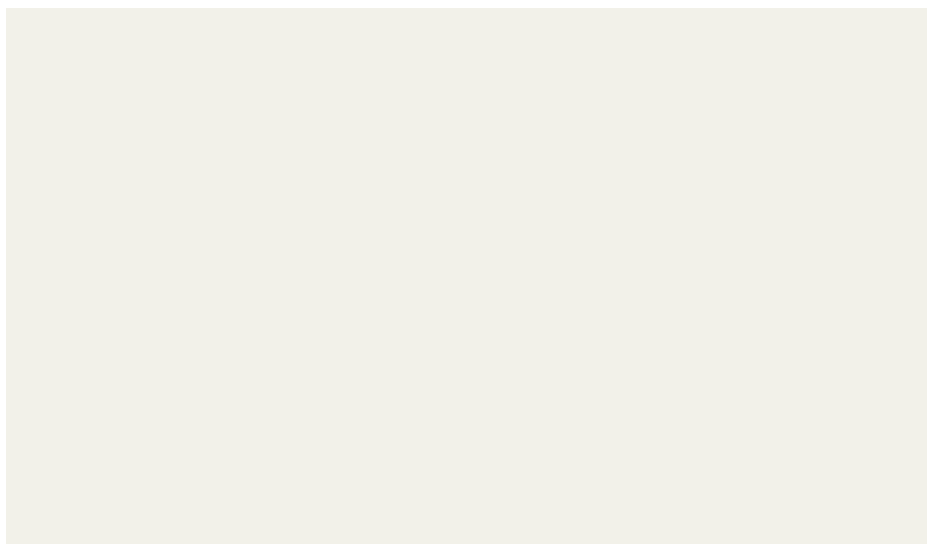
During the first year of life, the unadjusted average monthly incidence of all-cause mortality was 23.9 (95% CI, 23.4-24.42) for those born preterm and 1.82 (95% CI, 1.79-1.86) for those at term per 10 000 child-months. By the end of the first year of life, 2.6% of those born preterm died (26.2% for 24-27 weeks' GA, 6.0% for 28-31 weeks' GA, 2.4% for 32-33 weeks' GA, and 0.9% for 34-36 weeks' GA) compared with 0.2% for those born at term.

PTB and All-Cause Mortality in the Matched Cohorts

patterns were generally consistent across age groups (ages 1-5, 6-17, and 18-36 years) and GA categories, with higher HRs among lower age groups and lower GAs (eTable 4 in [Supplement 1](#)).

PTB and Mortality Among Newborns and Infants in the Matched Cohorts

We found an increased risk of all-cause mortality associated with PTB among newborns and infants (ages 0 to 11 months) (RD, 2.29 [95% CI, 2.23-2.35]; RR, 11.61 [95% CI, 11.09-12.15]), with higher RDs



PTB can disrupt the normal progression of intrauterine growth and maturation in all fetal organs, predisposing individuals who are affected to a range of morbidities and chronic diseases.¹¹ For example, neonates who are born preterm are at increased risk of bronchopulmonary dysplasia, which is associated with subsequent chronic lung diseases.³¹⁻³³ Necrotizing enterocolitis is also common among neonates born preterm, particularly those born at less than 28 weeks' gestation, and it predisposes these children to a range of gastrointestinal problems later in life.^{34,35} PTB also can lead to a range of neurological impairments, including cerebral palsy and epilepsy.^{36,37} PTB is also associated with adiposity in early childhood and adolescence, which can put these individuals at risk of cardiometabolic complications.³⁸⁻⁴⁰ PTB has also been associated with select pediatric cancers, such as hepatoblastoma and nephroblastoma.^{41,42} Some underlying conditions that predispose to PTB may also increase the risk of mortality, such as congenital malformations.^{43,44} Furthermore, a growing literature has shown an increased risk of several chronic illnesses, including diabetes, ischemic heart diseases, heart failure, hypertension, asthma, stroke, mental and behavioral problems, and infections later in life among individuals who are born preterm.^{5,6,45-55} Findings for cause-specific mortality are also aligned with these biologic effects of PTB on various body systems across the lifespan.^{5,6}

In a systematic review by Crump et al¹⁰ that included 8 studies (6 Swedish, 1 Australian, and one European), the authors found that individuals born preterm had a significantly increased risk of mortality from all causes compared with those born at term. The risk of mortality was highest for those born at the lowest gestational ages and for those with the lowest birth weights. The authors also found that the risk of mortality was significantly increased for those born preterm who had one or more of the following conditions: congenital malformations, chronic lung disease, and neurodevelopmental disorders.

ARTICLE INFORMATION

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Author Contributions: Drs Ahmed and Pechlivanoglou had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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eTable 9. Risk Differences (RDs, %) and Ratios (RRs) With 95% CIs for the Association Between PTB and All-Cause Mortality in the Matched Cohort Among a Subsample Linked to Maternal Tax With Matching on Family Income and Rural Residence (1990-1996 Births)

eFigure 1. Kaplan-Meier Plot of Cumulative Incidence of All-Cause Mortality by Gestational Age Categories in the Unmatched Cohort (Ages 1-36 Years)

eFigure 2. Kaplan-Meier Plot of Cumulative Incidence of All-Cause Mortality by Preterm Birth in the Matched Cohort (Ages 1-36 Years)

eFigure 3. Risk Differences (RDs, %) and Ratios (RRs) for the Association Between Preterm Birth and All-Cause Mortality in the Matched Cohort, Stratified by Age in Years (Ages 1-36 Years)

eFigure 4. Kaplan-Meier Plot of Cumulative Incidence of All-Cause Mortality by Preterm Birth in the Matched Cohort (Ages 0-11 Months)

eFigure 5. Risk Differences (RDs, %) and Ratios (RRs) With 95% CIs for the Association Between PTB and All-Cause Mortality in the Matched Cohort, Stratified by Sex

[SUPPLEMENT 2.](#)

[Data Sharing Statement](#)