

SUPPLEMENTARY MATERIAL

Perinatal Photoperiod and Childhood Cancer:

Pooled results from 182,856 individuals in the International Childhood Cancer Cohort Consortium (I4C)

Cohorts

ALSPAC dates of birth were set to the 15th of each month as only month and year of birth were available for reasons of confidentiality. The closest whole latitude to Bristol (52°N) was set as perinatal location. Fourteen non-cases and two cases were dropped due to presence of Down syndrome or no data on sex. Missing data were imputed with the following additional variables: mother's age, father's age, ethnicity, paid childcare, paid work for the mother, and instances of binge drinking in the previous month.

CPP perinatal location was set as the latitude of the hospital of birth. Seventy-six non-cases were dropped due to presence of Down syndrome or missing sex data, and 8,131 non-cases were dropped due to missing date-of-birth or insufficient information to calculate follow-up time. Missing data were imputed from the following additional variables: mother age, father age, socioeconomic status, and maternal smoking.

DNBC perinatal location was set as nearest 0.5 degree latitude of perinatal residence using the y-coordinate of WGS 1984 UTM Zone 33N geocodes. Eleven non-cases were dropped due to

presence of Down syndrome. Missing data were imputed from the following additional variables: mother's age, father's age, birth-length, caesarean section, socio-occupational status, annual income, number of previous pregnancies, maternal diabetes pre-pregnancy, gestational diabetes, number of cigarettes per day, partner smokes, alcohol consumption during pregnancy, and breast-feeding.

JPS perinatal location was set as 32°N, the closest whole latitude to the city of Jerusalem. Thirty-five non-cases were dropped due to the presence of Down syndrome or missing date-of-birth information. Missing covariate data were imputed from the following additional variables: father's age, mother's age, mother work, illness during pregnancy, Caesarean-section, gestational diabetes, socioeconomic status, suspected toxemia during pregnancy, father's place of birth, mother's place of birth, and current diabetes.

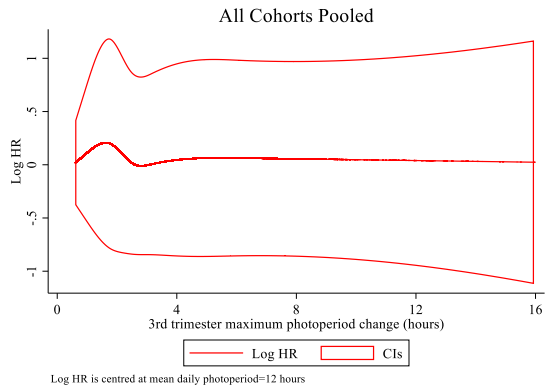
MOBA perinatal location was set as the midpoint of the municipality in which the mother resided in the prenatal period. The y-coordinates of WGS 1984 UTM Zone 33N geocodes were converted to the nearest 0.1 degree of latitude. Seventeen non-cases were dropped due to missing sex data or presence of Down syndrome, and 241 non-cases were dropped due to no location data. Some sparsely populated municipalities were merged with others to reduce possibility of individual identification. Missing data were imputed from the following additional variables: father's age, mother's age, birth-order, child length at birth, mother exposure to passive smoking at home (30 weeks gestation), mother smoking now (30 weeks gestation), mothers frequency of alcohol consumption during pregnancy, sessions of binge drinking from 0-12 weeks gestation, caesarean section, plurality.

TIHS perinatal location was determined by use of postcodes collected at 4 days and 4 weeks post-birth. The 4 days post-birth postcode was considered as residential postcode during the prenatal period and up to 1-month post-birth. The 4-week post-birth postcode was considered as residential

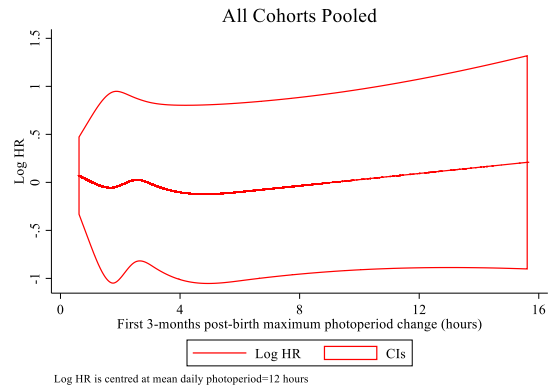
postcode from 1-month post-birth onward. Each postcode was assigned to the nearest latitude. Where the latitudes differed, both were considered when assigning PLICCS metrics (i.e. prenatal and 30 days postnatal mean daily photoperiod corresponded to the prenatal latitude and the 31-90 days postnatal mean daily photoperiod corresponded to the 1-month postnatal latitude). Where one postcode was missing, the other was used. Where both are missing, the latitude of the hospital of birth was used. Four non-cases were excluded having moved residence outside of ~41-43°S latitudinal range during the perinatal period. Missing data were imputed from the following additional variables: first child, work during pregnancy, foetal distress, placental state, intubation, public or private healthcare, and father age.

FIGURES

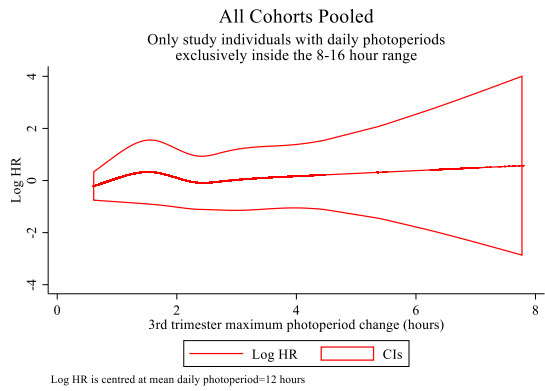
A.



B.



C.



D.

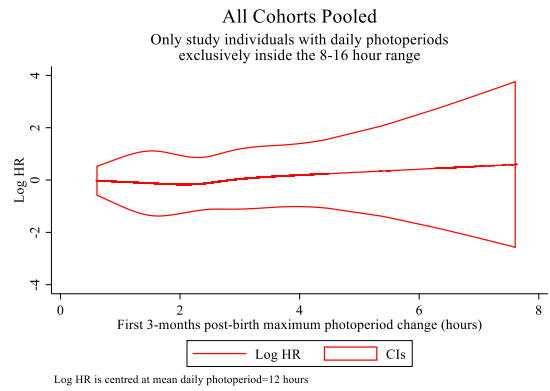


Fig. S1

Splines of maximal seasonal change for all individuals in (A) 3rd trimester and (B) first 3-months post-birth and for those individuals who experience photoperiods exclusively inside the 8-16 hour range in (C) 3rd trimester and (D) first 3-months post-birth.

TABLES

Table S1: Hazard ratios (HR) and 95% confidence intervals (CI) for individual cohorts and all cohorts pooled stratified by cohort for both PLICCS metrics and both time windows of interest for individuals who experience photoperiods exclusively inside the 8-16 hour range

	3 rd Trimester				First 3-months post-birth Trimester			
	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a
	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)
ALSPAC	0.65 (0.28-1.53)	0.63 (0.17-2.30)	*	*	1.04 (0.34-3.21)	1.11 (0.25-4.75)	*	*
CPP	0.89 (0.76-1.04)	0.90 (0.77-1.05)	0.98 (0.73-1.33)	0.96 (0.63-1.47)	1.01 (0.86-1.18)	1.01 (0.86-1.18)	1.06 (0.79-1.42)	0.99 (0.67-1.47)
DNBC	1.05 (0.52-2.12)	0.89 (0.44-1.82)	1.34 (1.93-9.21)	*	0.47 (0.20-1.09)	0.45 (0.21-0.98)	0.44 (0.07-2.81)	*
JPS	0.93 (0.83-1.05)	0.94 (0.83-1.07)	0.99 (0.79-1.22)	1.43 (0.73-2.82)	1.00 (0.89-1.12)	0.98 (0.87-1.10)	1.04 (0.83-1.30)	1.38 (0.70-2.74)
MOBA	*	*	0.09 (0.00-9.86)	*	*	*	*	*
TIHS	0.87 (0.70-1.08)	0.88 (0.70-1.10)	0.75 (0.49-1.14)	0.41 (0.14-1.19)	1.09 (0.91-1.31)	1.10 (0.90-1.33)	1.20 (0.76-1.91)	0.56 (0.18-1.75)
Pooled	0.91 (0.84-0.99)	0.91 (0.82-1.00)	0.94 (0.80-1.11)	0.97 (0.58-1.59)	1.01 (0.93-1.09)	0.93 (0.84-1.03)	1.06 (0.90-1.25)	1.66 (1.03-2.66)

HRs and CIs correspond to risk change per one-hour increase in mean daily photoperiod of per one-hour increase in maximal photoperiod change.

^aAdjusted for sex, gestational age, birthweight, parental education, PLICCS metric from adjacent time window, and direction of photoperiod change

*No convergence, no cases in these cohorts, or too few cases/individuals to provide realistic estimates.

Note: adjusting for direction of photoperiod change excludes those individuals whose mid-points of the respective time windows fall on either equinox but these individuals are few.

Table S2: Hazard ratios (HR) and 95% confidence intervals (CI) for individual cohorts and all cohorts pooled stratified by cohort for both PLICCS metrics and both time windows of interest for cancer types for individuals who experience photoperiods exclusively inside the 8-16 hour range								
	Blood Cancers							
	3 rd Trimester				First 3-months post-birth Trimester			
	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a
	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)
ALSPAC	*	*	*	*	0.87 (0.82-0.92)	1.10 (0.26-4.73)	*	*
CPP	0.77 (0.60-0.99)	0.80 (0.60-1.07)	0.98 (0.62-1.55)	1.10 (0.46-2.61)	0.89 (0.70-1.14)	1.08 (0.90-1.31)	1.09 (0.70-1.69)	0.92 (0.59-1.45)
DNBC	0.51 (0.18-1.42)	0.52 (0.16-1.69)	0.27 (0.02-4.52)	*	0.30 (0.07-1.35)	0.38 (0.14-1.07)	0.18 (0.01-5.26)	2.16 (0.32-1.58)
JPS	0.96 (0.80-1.14)	1.00 (0.79-1.27)	1.04 (0.75-1.45)	1.03 (0.27-3.98)	0.96 (0.80-1.15)	1.02 (0.89-1.17)	1.00 (0.71-1.41)	1.49 (0.67-3.33)
MOBA	*	*	*	*	*	*	*	*
TIHS	0.75 (0.52-1.08)	0.73 (0.49-1.09)	0.98 (0.40-2.43)	0.27 (0.03-2.83)	0.93 (0.63-1.39)	1.15 (0.93-1.42)	0.84 (0.37-1.92)	0.74 (0.19-2.82)
Pooled	0.87 (0.76-0.99)	0.82 (0.67-1.00)	1.01 (0.78-1.31)	1.28 (0.59-3.31)	0.92 (0.81-1.05)	0.97 (0.86-1.10)	0.99 (0.76-1.28)	1.79 (0.99-3.26)
	Solid Cancers							
	3 rd Trimester				First 3-months post-birth Trimester			
	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a	Individual Mean Daily Photoperiod	Individual Mean Daily Photoperiod ^a	Individual Maximal Photoperiod Change	Individual Maximal Photoperiod Change ^a
	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)	HR (CI)
ALSPAC	0.65 (0.28-1.53)	0.63 (0.17-2.30)	*	*	1.09 (0.27-4.35)	*	*	*
CPP	0.97 (0.80-1.19)	0.94 (0.79-1.13)	0.98 (0.66-1.45)	0.91 (0.56-1.47)	1.09 (0.89-1.34)	0.88 (0.68-1.14)	1.04 (0.70-1.53)	1.15 (0.52-2.57)
DNBC	1.59 (0.64-3.93)	1.20 (0.42-3.45)	3.07 (0.27-34.91)	*	0.63 (0.23-1.69)	0.59 (0.14-2.35)	0.82 (0.10-6.46)	*
JPS	0.92 (0.79-1.07)	0.93 (0.81-1.07)	0.95 (0.71-1.26)	1.61 (0.74-3.50)	1.03 (0.88-1.19)	0.86 (0.68-1.09)	1.07 (0.79-1.44)	1.11 (0.29-4.28)
MOBA	*	*	*	*	*	*	*	*
TIHS	0.92 (0.70-1.21)	0.93 (0.71-1.23)	0.67 (0.41-1.08)	0.50 (0.16-1.60)	1.16 (0.95-1.42)	0.96 (0.60-1.53)	1.41 (0.80-2.50)	0.32 (0.03-3.06)
Pooled	0.94 (0.84-1.04)	0.95 (0.84-1.08)	0.90 (0.73-1.11)	0.77 (0.43-1.36)	1.07 (0.96-1.18)	0.83 (0.67-1.04)	1.11 (0.89-1.38)	1.40 (0.58-3.39)

HRs and CIs correspond to risk change per one hour increase in mean daily photoperiod of per one hour increase in maximal photoperiod change.

^aAdjusted for sex, gestational age, birthweight, parental education, PLICCS metric from adjacent time window, and direction of photoperiod change; *No convergence, no cases in these cohorts, or too few cases/study individuals to provide realistic estimates. Note: adjusting for direction of photoperiod change excludes those individuals whose mid-points of the respective time windows fall on either equinox but these individuals are few.