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Supplemental Material

Early Biological Aging and Fetal Exposure to High and Low Ambient Temperature: A Birth Cohort Study

Dries S. Martens, Michelle Plusquin, Bianca Cox, and Tim S. Nawrot

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Figure S2. Shape of the association between placenta TL and ambient temperature in different weeks of pregnancy. Estimates provided as a percent difference in TL (with 95% CI) relative to the reference (median) temperature of 11.1°C. Models were adjusted for date of delivery, gestational age, maternal pre-pregnancy BMI, maternal age, paternal age, newborn sex, newborn ethnicity, season of birth, parity, maternal smoking status, maternal education, pregnancy complications, maternal PM_{2.5} exposure, and batch.

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Supplemental Table S1. Sensitivity analyses for placental TL

Model	n	% difference (95% CI) in placenta TL	
		Heat effect	Cold effect
Main model	1,103	-0.84 (-2.77, 1.13)	0.76 (0.47, 1.06)
Unconstrained lag structure	1,103	-0.97 (-3.05, 1.16)	0.74 (0.44, 1.05)
Adjustment for month delivery	1,103	-1.14 (-3.11, 0.87)	0.79 (0.49, 1.10)
Adjustment humidity	1,103	-1.43 (-3.40, 0.58)	0.50 (0.19, 0.82)
No PM _{2.5} adjustment	1,103	0.00 (-1.91, 1.96)	0.41 (0.14, 0.67)
Adjustment fruit and vegetables consumption ^a	1,076	-0.94 (-2.92, 1.07)	0.77 (0.47, 1.07)
Adjustment physical activity ^b	1,048	-1.09 (-3.07, 0.94)	0.75 (0.45, 1.06)
Adjustment cord plasma vitamin D ^c	937	-0.40 (-2.56, 1.80)	0.67 (0.35, 0.99)
Adjustment maternal plasma vitamin D ^d	764	-1.20 (-3.79, 1.45)	0.49 (0.12, 0.86)
Excluding non-European	958	-0.63 (-2.74, 1.53)	0.74 (0.42, 1.05)
Excluding low educated	979	-1.17 (-3.24, 0.96)	0.72 (0.40, 1.04)
Excluding current and former smokers	709	-0.76 (-3.22, 1.77)	0.93 (0.55, 1.31)
Excluding pregnancy complications	964	-1.13 (-3.23, 1.03)	0.76 (0.44, 1.08)
Excluding cesarean sections	1,060	-1.01 (-2.97, 0.98)	0.70 (0.40, 1.00)
Excluding all of the above	471	-1.28 (-4.38, 1.91)	0.63 (0.18, 1.09)
Newborn boys	574	-1.71 (-4.47, 1.13)	0.85 (0.43, 1.27)
Newborn girls	529	0.34 (-2.51, 3.28)	0.63 (0.20, 1.07)

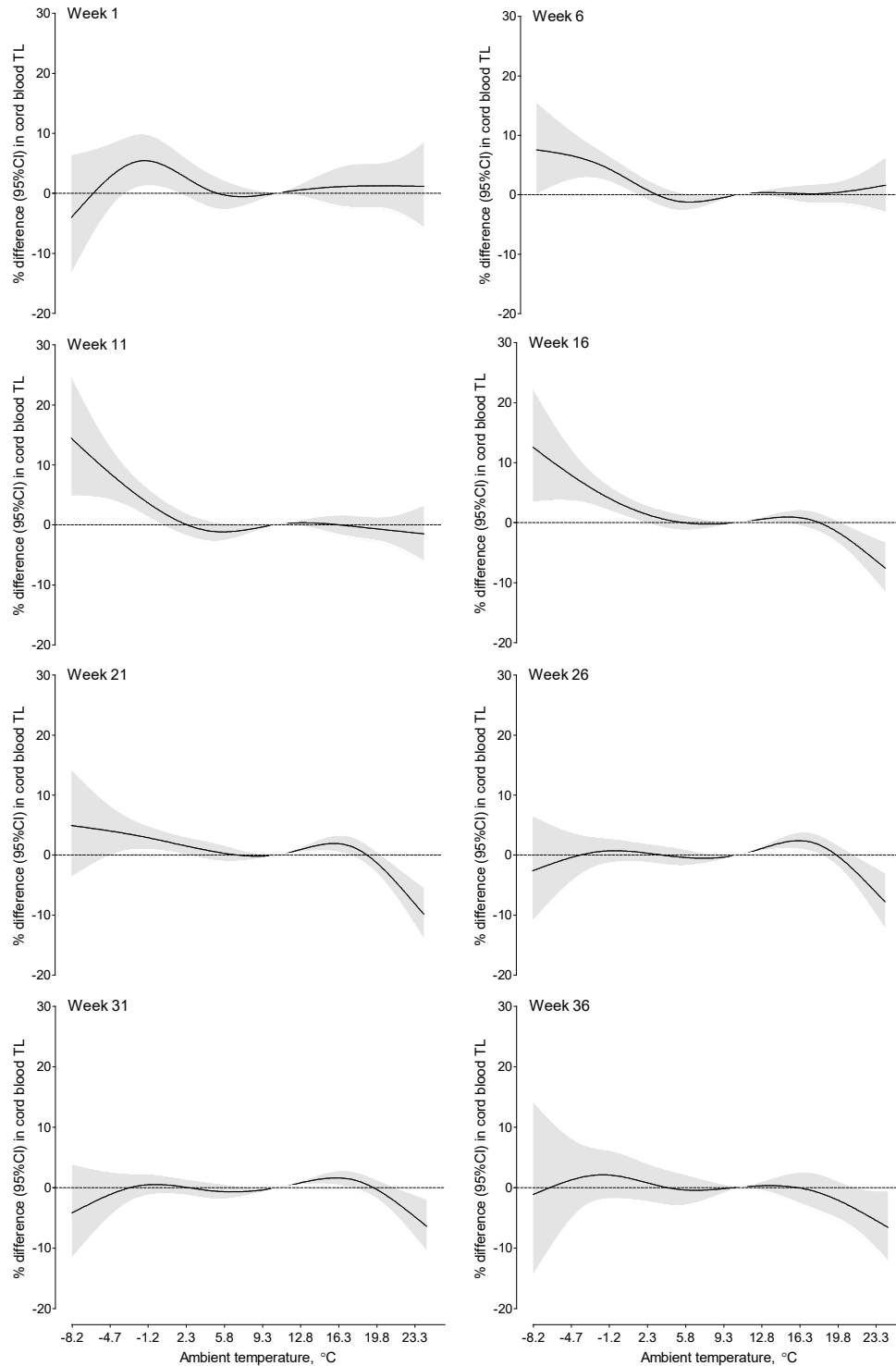
Estimates are averaged week specific estimates over the entire pregnancy. Estimates provided as a % difference (95%CI) in TL for a 1°C increase in ambient temperature above the heat threshold (21.5°C) for associations with heat and a 1°C decrease in ambient temperature below the cold threshold (2.5°C) for associations with cold. Models were adjusted for date of delivery, gestational age, maternal pre-pregnancy BMI, maternal age, paternal age, newborn sex, newborn ethnicity, season of birth, parity, maternal smoking status, maternal education, pregnancy complications, maternal PM_{2.5} exposure and batch. The season of birth was removed from the model adjusting for month of delivery.

^aMissing data on n= 27

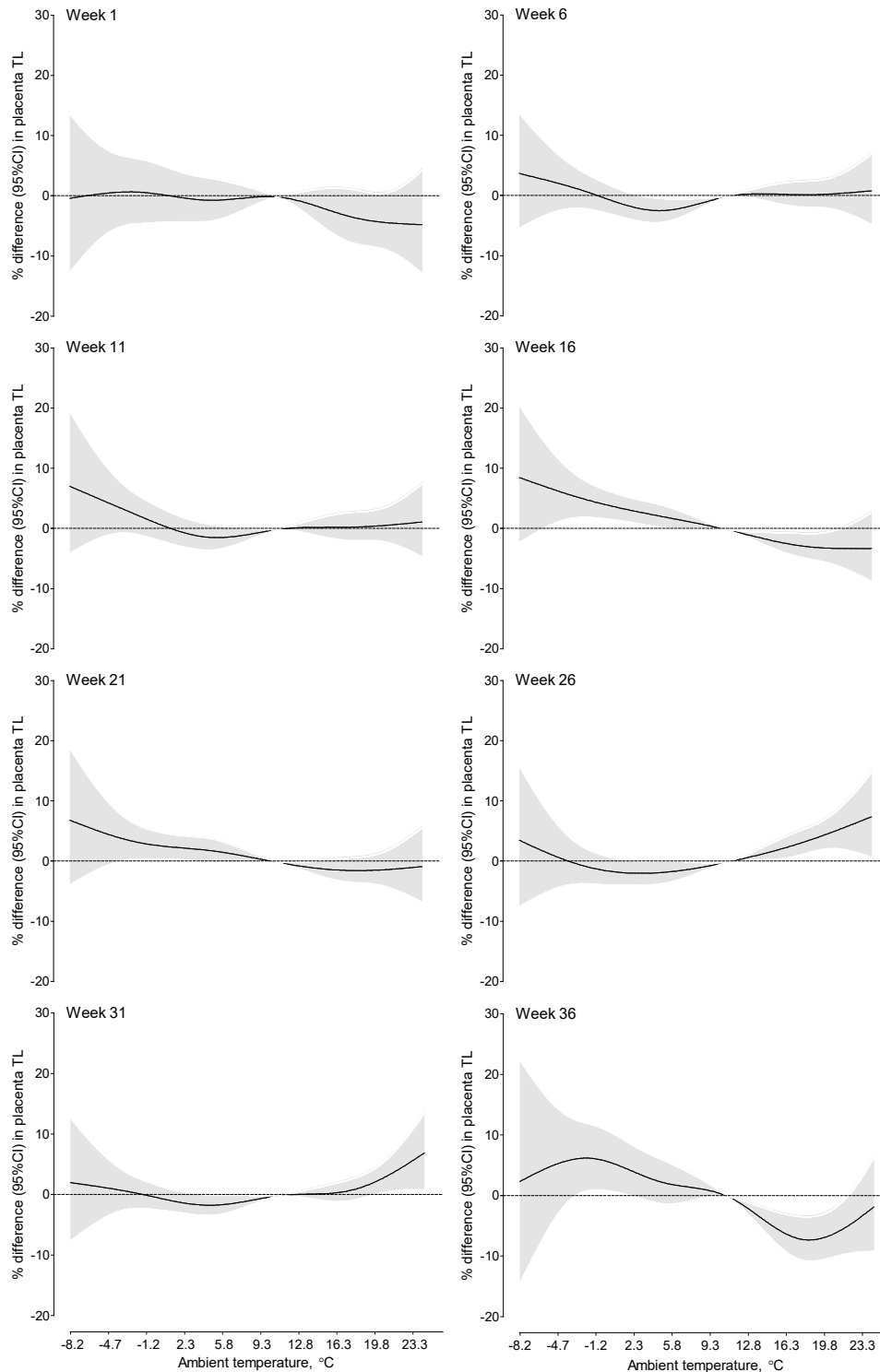
^bMissing data on n= 55

^cMissing data on n= 166

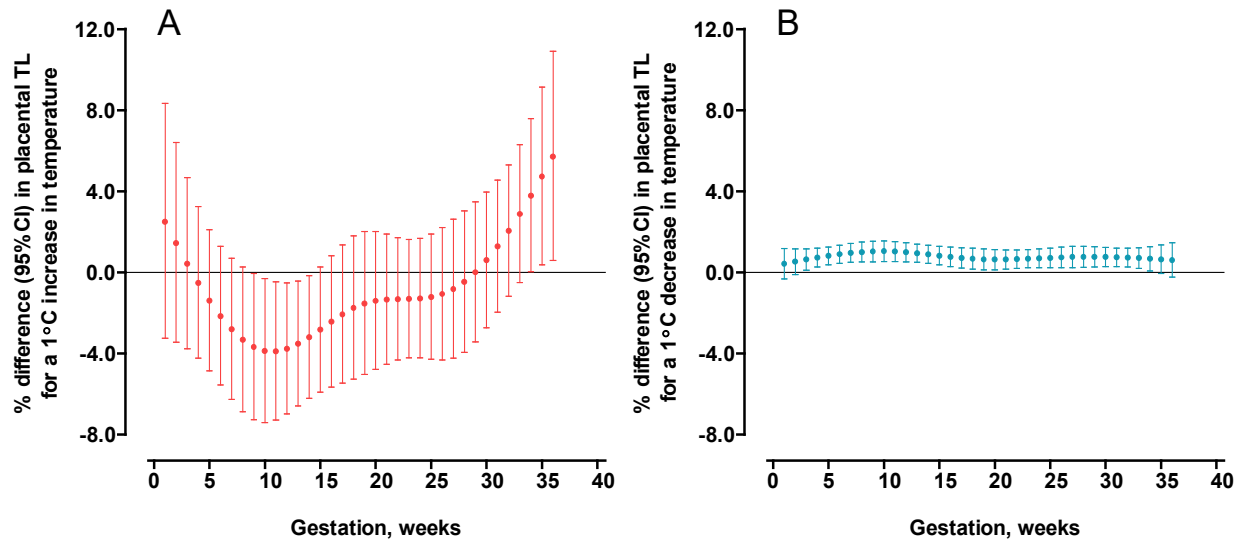
^dMissing data on n= 339



Supplemental Figure S1. Shape of the association between cord blood TL and ambient temperature in different weeks of pregnancy. Estimates provided as a percent difference in TL (with 95% CI) relative to the reference (median) temperature of 11.1°C. Models were adjusted for date of delivery, gestational age, maternal pre-pregnancy BMI, maternal age, paternal age, newborn sex, newborn ethnicity, season of birth, parity, maternal smoking status, maternal education, pregnancy complications, maternal PM_{2.5} exposure and batch.



Supplemental Figure S2. Shape of the association between placenta TL and ambient temperature in different weeks of pregnancy. Estimates provided as a percent difference in TL (with 95% CI) relative to the reference (median) temperature of 11.1°C. Models were adjusted for date of delivery, gestational age, maternal pre-pregnancy BMI, maternal age, paternal age, newborn sex, newborn ethnicity, season of birth, parity, maternal smoking status, maternal education, pregnancy complications, maternal PM_{2.5} exposure, and batch.



Supplemental Figure S3. Cold and heat effect estimates on placental TL.

Week specific estimates provided as a % difference in average relative TL (with 95% CI) for a 1°C increase in ambient temperature above the heat threshold (21.5°C) for associations with heat (A), and a 1°C decrease in ambient temperature below the cold threshold (2.5°C) for associations with cold (B). The combination of temperatures minimizing the residual deviance in the double-threshold DLNM for placental TL was 21.5°C (heat threshold) and 2.5°C (cold threshold). Models were adjusted for date of delivery, gestational age, maternal pre-pregnancy BMI, maternal age, paternal age, newborn sex, newborn ethnicity, season of birth, parity, maternal smoking status, maternal education, pregnancy complications, maternal PM_{2.5} exposure and batch.