

Caffeine and Pregnancy: A Review

1

Supplementary Table 1. Summary of original observational studies of maternal caffeine consumption and pregnancy outcomes published since year 2000.

Authors	Year	Study design	Country	N	Key findings
Miscarriage					
Cnattingius et al. ⁴⁷	2000	case-control	Sweden	562 cases 953 controls	Maternal caffeine consumption associated with increased risk, not confounded by pregnancy-related symptoms, and present in nonsmokers (plasma cotinine confirmed).
Wen et al. ⁴⁸	2001	prospective cohort	USA	650	Maternal caffeine consumption associated with increased risk, not confounded by pregnancy-related symptoms. Results for women experiencing and those not experiencing nausea were examined separately, showing caffeine-related (≥ 300 versus < 20 mg per day) increased risk in the former.
Giannelli et al. ⁴⁹	2003	case-control	United Kingdom	160 cases 314 controls	Maternal caffeine consumption (> 300 mg per day compared to ≤ 150 mg per day) doubled risk, not confounded by pregnancy-related symptoms, and the majority of participants being nonsmokers.
Khoury et al. ⁵⁰	2004	prospective cohort	USA	191	Maternal caffeine consumption among women with type 1 diabetes associated with a 4.5-fold increased risk, not confounded by smoking status. Caffeine-related risk estimated to be greater than that attributable to smoking.
Savitz et al. ⁵⁵	2008	cross-sectional	USA	2,407	“Suggestive” caffeine-related increased risk, discounted due to

Caffeine and Pregnancy: A Review

2

						suspected recall bias.
Weng et al. ⁵¹	2008	prospective cohort	USA	1,063		Maternal caffeine consumption associated with increased risk, more pronounced in nonsmokers, and not confounded by pregnancy-related symptoms.
Stefanidou et al. ⁵²	2011	case-control	Italy	52 cases 260 controls		Maternal caffeine consumption associated with a dose-response increased risk of <i>sine causa</i> recurrent miscarriage of nearly 3-fold for each 100 mg increase in daily caffeine intake, not confounded by pregnancy-related symptoms or smoking status.
Gaskins et al. ⁵³	2018	prospective cohort	USA	11,072		Maternal caffeine consumption (average less than ACOG-advised limit) associated with increased risk, including never smokers, and not confounded by pregnancy-related symptoms.
Purdue-Smithe et al. ⁵⁴	2019	prospective cohort	USA	1,228		Maternal caffeine consumption (biomarker confirmed) associated with increased risk, with no minimum safe threshold of consumption, and not confounded by pregnancy-related symptoms.
Stillbirth						
Wisborg et al. ⁶⁰	2003	prospective cohort	Denmark	18,478		Maternal caffeine consumption associated with increased risk, with similar magnitude for smokers and nonsmokers.
Bech et al. ⁶¹	2006	cross-sectional	Denmark	142 cases 157 controls		Maternal caffeine consumption associated with increased risk, irrespective of genotype for caffeine metabolism.

Caffeine and Pregnancy: A Review

3

Matijasevich et al. ⁶²	2006	case-control	Uruguay	382 cases 792 controls	Maternal caffeine consumption associated with increased risk, with similar magnitude for smokers and nonsmokers, independent of pregnancy-related symptoms.
Greenwood et al. ⁶³	2010	prospective cohort	United Kingdom	2,643	Compared to maternal consumption of less than 100 mg caffeine per day, 300+ mg per day was associated with a five fold (CI: 1.6–16.4) increased risk, not confounded by smoking or pregnancy-related symptoms.
Gaskins et al. ⁵³	2018	prospective cohort	USA	11,072	Caffeine consumption not associated with increased risk.

Low Birth Weight (LBW) and/or Small for Gestational Age (SGA)

Klebanoff et al. ⁷²	2002	prospective cohort	USA	2,515	Maternal caffeine consumption (biomarker confirmed) associated with increased risk of SGA in women who smoked.
Clausson et al. ⁷³	2002	prospective cohort	Sweden	953	Maternal caffeine consumption unrelated to risk of LBW and SGA.
Bracken et al. ⁶⁸	2003	prospective cohort	USA	2,291	Small (28 g) decreased birth weight associated with each increment of 100 mg per day in maternal caffeine.
CARE Study Group ⁶⁹	2008	prospective cohort	UK	2,635	Maternal caffeine consumption associated with decreased birth weight, not confounded by smoking status (salivary cotinine confirmed), with no identifiable threshold of consumption below which the association was absent.

Caffeine and Pregnancy: A Review

4

Caffeine and Pregnancy: A Review

5

Bakker et al. ⁷⁶	2010	prospective cohort	Netherlands	7,346	Maternal caffeine consumption not associated with LBW. High intake (≥ 6 cups of coffee per day) associated with increased risk of SGA.
Sengpiel et al. ⁷⁴	2013	prospective cohort	Norway	59,123	Maternal caffeine consumption associated with LBW and increased risk of SGA.
Hoyt et al. ⁴	2014	case-control	USA	648 cases 7,295 controls	Maternal caffeine consumption associated with SGA.
Bech et al. ⁷⁸	2015	prospective cohort	Denmark	71,000	Maternal caffeine consumption associated with increased risk of LBW and SGA for both smokers and nonsmokers.
Okubo et al. ⁷⁹	2015	prospective cohort	Japan	858	Maternal caffeine consumption associated with neither LBW nor SGA.
Voerman et al. ⁷⁰	2016	prospective cohort	Netherlands	7,857	Maternal caffeine consumption of ≥ 6 cups of coffee per day versus < 2 associated with LBW.
Chen et al. ⁷¹	2018	prospective cohort	Ireland	941	Maternal caffeine consumption associated with LBW, confirmed for both coffee and tea.
Kobayashi et al. ⁷³	2019	prospective cohort	Japan	94,876	Maternal caffeine consumption associated with increased SGA risk.
Modzelewska et al. ⁷⁴	2019	prospective cohort	Norway	67,569	Maternal caffeine consumption associated with increased SGA risk.

Caffeine and Pregnancy: A Review

6

Preterm Birth

Bracken et al. ⁶⁸	2003	prospective cohort	USA	2,291	Maternal caffeine consumption not associated with increased risk.
Chiaffarino et al. ⁸³	2006	case-control	Italy	502 cases 1,966 controls	Maternal caffeine consumption not associated with increased risk.
Okubo et al. ⁷⁹	2015	prospective cohort	Japan	858	Maternal caffeine consumption associated with increased risk.
Kobayashi et al. ⁷³	2019	prospective cohort	Japan	94,876	Increased risk associated with approximate equivalent of >2 cups of coffee per day versus <1 cup.

Childhood Acute Leukemia

Menegaux et al. ⁸⁶	2007	case-control	France	472 cases 567 controls	No overall association, but evidence of maternal caffeine consumption of >3 cups per day associated with increased risk among nonsmokers.
Milne et al. ⁸⁹	2011	case-control	Australia	337 cases 697 controls	No overall association, but evidence of “higher” levels of maternal caffeine consumption associated with increased risk among nonsmokers. Results of a meta-analysis reported in the same study suggested increased risk in children of nonsmoking mothers (see also Milne et al. 2018).
Bonaventure et al. ⁸⁷	2013	case-control	France	764 cases 1,681 controls	Maternal caffeine consumption associated with increased risk.

Caffeine and Pregnancy: A Review

7

Orsi et al. ⁹¹	2015	case-control	France	747 cases 1,421 controls	Role of maternal coffee consumption found to be “unclear”.
Milne et al. ⁸⁸	2018	case-control	Australia, France, Greece, USA	2,552 cases 4,876 controls	Maternal caffeine consumption of >2 cups per day versus no coffee associated with increased risk.
Karalexi et al. ⁹⁰	2019	case-control	France, Greece, Germany, USA	554 cases 1,419 controls	Maternal caffeine consumption of >1 cup per day associated with increased risk.

Childhood Overweight and Obesity

Li et al. ⁹⁹	2015	prospective cohort	USA	615	Maternal caffeine consumption associated with a dose-response increased risk of childhood obesity at 15 years follow-up.
Klebanoff & Keim. ¹⁰²	2015	case-control	USA	1,986 cases 1,986 controls	Maternal caffeine consumption not associated with risk of childhood obesity at 4 and 7 years.
Voerman et al. ⁷⁰	2016	prospective cohort	Netherlands	7,857	Maternal caffeine consumption associated with increased risk of childhood overweight at 6 years.
Papadopoulou et al. ¹⁰⁰	2018	prospective cohort	Norway	50,943	Maternal caffeine consumption associated with increased risk of childhood overweight up to 8 years.
Chen et al. ¹⁰¹	2019	prospective cohort	Ireland	558	Maternal caffeine consumption associated with increased risk of childhood adiposity and obesity at 5 and 9 years.