



RCM Expert Clinical Advisory Group (ECAG) briefing

Caffeine in pregnancy

Why are we publishing this briefing now?

On 25 August 2020, the BMJ Evidence based medicine published a paper by a psychologist from Reykjavik University, Professor Jack E James. BMJ EBM is an online journal which publishes research, insights and opinion pieces.

The paper strongly advocates that the current UK and international guidance, that women are safe to consume up to 200mg of caffeine daily, should be revised and that women should avoid all caffeine during pregnancy.

The publication led to a great deal of media interest which could lead to anxiety among women and families about caffeine in pregnancy and concern among midwives and other professionals about the evidence base for their current advice to women. This briefing summarises the current evidence base to support health professionals when advising women to make informed decisions.

This briefing is based on a review of key organisations websites offering expert advice on their topic area and an RCM MIDIRS search on caffeine and pregnancy, undertaken on 25 August 2020. The MIDIRS search yielded 183 articles, dating back to 1980. For this briefing, 65 papers published since January 2010 were reviewed. Eleven were excluded as they were out of scope, were news reports or opinion pieces, leaving 54 papers.

Key 'take home' messages about Caffeine in pregnancy 31 August 2020

- Current international guidance from the NHS, Tommy's, WHO and the RCOG is that women can safely consume up to 200mg of caffeine daily. James' paper does not provide new evidence to support his recommendation that this guidance should be changed.
- Research evidence shows that there is a link between high caffeine consumption (>300mg a day) and lower birthweight. The UK and international guidance is currently based on this.
- Current research evidence finds that there is **no** link between high caffeine consumption and preterm birth.
- There is no current evidence of sufficient strength that low maternal caffeine intake in pregnancy (<200mg) is linked to adverse pregnancy outcomes.
- Research evidence is mixed in relation to any relationship between high caffeine consumption (>300mg a day) and other outcomes (these are discussed in more detail below). More research is underway and is needed in these areas to inform guidance.
- Midwives should ensure that women are informed in early pregnancy of the risks of high caffeine intake to the fetus. For example, in addition to tea and coffee (75-277mg), caffeine is present in chocolate (+/-50mg), some soft drinks (+/-80mg) and medications (e.g. Anadin extra 45mg). It is important that women are aware that their total intake from all dietary sources each day should not exceed 200mg (NHS Choices 2018).
- As any new, robust evidence emerges on this topic, this should be considered when reviewing the current guidance.

Discussion

James identifies that 'it is important that women receive sound evidence-based advice about potential caffeine-related harm' (2020:1) a view the RCM agrees with. He continues that 'the cumulative scientific evidence supports pregnant women and women contemplating pregnancy being advised to avoid caffeine' (James, 2020:6). However, to understand whether this recommendation is correct, it is necessary to explore the limitations of the paper:

1. The paper does not describe original research or a systematic review, but a 'narrative review.' There is no description of an established search process to ensure that the studies discussed are of high quality. Nor is there robust description of the analytical approach to the papers chosen to avoid the risk of selecting only studies that support the author's view and bias. The databases used for the search were PubMed and Google Scholar.
2. The paper does not include or reference all key studies in the topic area. For example, to support its position on the risk of high doses of caffeine crossing the placenta, the paper references a 1975 study, but not a recent study which explored a method to quantify the concentration of caffeine in the fetal circulation (Pemathilaka et al, 2019); it does not reference the most recently published studies in this area which indicate that low to moderate caffeine consumption are not associated with adverse outcomes (Berglundh et al, 2020; Lamy et al, 2020; Voerman et al, 2020).
3. The paper does not address the risk of bias or other confounding variables in the studies included (for example, the potential impact of smoking and alcohol intake accompanying caffeine intake and that higher caffeine intake may be accompanied by being overweight and smoking) nor does it adequately differentiate between the impact of high and low caffeine intake (Lehtonen et al, 2020; Leviton, 2018).
4. The paper overstates the strength of the evidence in relation to the risks of caffeine intake in relation to stillbirth, miscarriage, childhood leukaemia and childhood obesity. The paper uses only relative risk figures, expressing them in percentages, rather than describing absolute risk associated with the behaviour. This can lead to an overstatement of the impact of a particular behaviour or intervention.

What is known about the impact of caffeine in pregnancy?

Link between high caffeine intake and low birthweight

A range of observational studies and systematic reviews of studies have identified a link between high caffeine consumption (>200mg or >300mg a day) and lower birth weights (Bakker et al, 2010; Bech et al 2015; CARE study group, 2008; Chen et al 2014; Chen et al, 2019; Karalexi et al, 2020; Kobayashi et al, 2019; Modzelewska et al, 2019; Rhee et al, 2015).

There is only one Cochrane review analysing two randomised controlled trials which compare the outcomes for women randomised to caffeinated versus decaffeinated coffee (Jahanfar and Jaafer, 2015). This review concluded that the intervention, of reducing the intake of caffeinated coffee did not have an impact on birthweight, preterm birth or small for gestational age rates.

Several studies found **no** link between low caffeine intake (\leq 200mg) and reduced birth weight (Jarosz et al 2015, Lu et al, 2017; Wierzejska et al 2019).

The link between high caffeine intake and low birth weight is well established and has been included in UK and international guidance on the topic.

The link between caffeine intake and fertility and miscarriage

There appears to be an increased risk of this adverse outcome with high (>300mg per day) intake.

Expert advice:

The Miscarriage Association (2020) find the key risks linked with increased risk of miscarriage are maternal age over 30, being overweight (BMI>30) or underweight (BMI <18.5) and high alcohol intake. Caffeine intake is not included in their description of key risks, although the recommendation to keep daily caffeine intake to below 200mg a day is included in their publication on planning another pregnancy (Miscarriage Association, 2013).

The RCOG (2020) also highlights these key risk factors from Nilsson et al's (2014) birth cohort study of 91,427 pregnancies: regularly lifting weights of over 20kg and night work, as the key risk factors. Caffeine was included as a potential risk factor and consumption of more than 8 cups of coffee a day was associated with an increased risk of miscarriage. However, the risk factors of maternal age, weight, alcohol intake, lifting of heavy weights and night working were all more strongly associated with miscarriage than caffeine.

The Tommy's website highlights the following lifestyle factors as key in reducing the risk of miscarriage:

- not smoking
- a healthy, balanced diet
- gaining and keeping a healthy weight before and during pregnancy
- avoiding infections, including rubella
- avoiding foods such as raw and undercooked meat, unpasteurised milk and dairy etc
- not drinking alcohol or taking illegal substances
- staying active
- limiting caffeine intake to <200mg a day and supply a caffeine calculator to enable women to watch their daily intake (Tommy's, 2020).

The evidence base:

A systematic review has found a link between high caffeine intake (>300mg) and spontaneous abortion (Lyngso et al, 2017) but **no** association with fertility or length of time to becoming pregnant.

Other studies have found a link between high caffeine intake and miscarriage, but not lower intake (Cnattingius et al, 2000; Gianelli et al 2003; Wen and Shu, 2001). Gianelli et al (2003) found no link between maternal pre-pregnancy caffeine intake and risk of miscarriage.

Other studies have shown conflicting results in relation to higher caffeine intake and increased spontaneous abortion – with some finding a relationship and others not (Hahn et al, 2015; Li et al, 2015; Pollack et al, 2010).

Fernandes et al (1998) found an association between intake of >150mg daily and increased miscarriage rates but was not able to modify for other confounding variables including maternal age, smoking or alcohol intake. Chen et al (2014) found that women who regularly drank >300mg caffeine a day were also more likely to smoke and drink alcohol. It cannot therefore be said with certainty that caffeine alone is associated with an increased risk of miscarriage as found in these studies.

Other variables such as links between the effect of caffeine on IVF success rates could not be made (Choi et al, 2011) however there did seem to be a link between that and increased bleeding in early pregnancy (Choi et al, 2020).

Caffeine intake and preterm birth

The consensus from the evidence is that maternal caffeine intake is not associated with higher rates of preterm birth (Jarosz et al, 2012; Sengpiel et al 2013).

Caffeine intake and stillbirth

Expert advice

Tommy's, the UK's largest charity funding research into the causes of miscarriage, stillbirth and premature births, current campaign calls for more research into their causes and lists the following key factors to reduce the risk of stillbirth:

- smoking cessation
- women sleeping on their side in the third trimester
- monitoring fetal movements
- attending all antenatal appointments and scans to identify problems early
- staying a healthy weight
- avoiding alcohol and drugs (Tommy's, 2020).

The evidence base

Gardosi et al (2013) UK based population study of 92,218 singleton pregnancies found the following key modifiable factors associated with stillbirth:

- maternal obesity
- smoking; and
- undetected fetal growth restriction.

One study in our MIDIRS search and referenced in James' paper found a link between caffeine and later miscarriage and stillbirth (Greenwood et al, 2010); their cohort study of 2,643 pregnant women found that those with higher caffeine intakes in the first trimester had a higher risk of late miscarriage and stillbirth. This was particularly marked for those with an intake of over 300mg a day.

It is of interest to note that James' paper identifies Chen et al (2016) meta-analysis as showing significant associations, with increased risk of stillbirth per 100mg per day estimated in one study to be 9%. In the original study conclusion however, the author describes the results as 'inconclusive' and likely to have been affected by publication bias (where studies that show positive results are more likely to be published than those showing no association) and with the risk of other confounding factors such as smoking not being completely accounted for. Chen's conclusion is 'to avoid high caffeine intake during pregnancy appears prudent' (Chen et al, 2016:1242), rather than recommending no caffeine.

Longer term impacts on the newborn and child

James describes a link between acute childhood leukaemia (ALL) and maternal caffeine intake in pregnancy. However, the author of one of the papers quoted to support this link concludes: 'There was little evidence of an overall association between maternal coffee consumption and risk of ALL' (Milne et al, 2011:217). This study also found that antenatal tea consumption was inversely related to childhood leukaemia, which is not described in James' paper.

It is interesting to note that UK organisations which focus on childhood leukaemia, do not propose caffeine intake in pregnancy as a risk factor for childhood leukaemia; these are identified as:

- genetic inheritance,
- family history,

- inherited immune diseases,
- alcohol in pregnancy and
- environmental factors, particularly exposure to radiation

(Children with Cancer UK, 2020; Blood cancer UK, 2020).

Studies show inconsistent results in relation to any association between childhood IQ and high maternal caffeine intake; with some suggesting a link and others finding no association (Galera et al 2016; Klebanoff and Keim, 2015).

Mikkelsen et al (2017) found extremely high caffeine consumption (>8 cups a day) at 15 weeks' gestation to be associated with a higher rate of attention and behaviour disorders in children although this has not been replicated elsewhere (Del-Ponte et al, 2016; Loomans et al, 2012).

Some studies have suggested links between high or higher caffeine consumption (>300mg or >600mg) and childhood obesity (Papadopoulou et al, 2018; Voerman et al, 2016). Links have not been established between maternal caffeine intake and newborn irritability in low birthweight babies or cryptorchidism (Maeda, et al, 2019 Kjersgaard et al, 2018).

Conclusion

The current UK and international guidance that women should avoid high caffeine intake (>200mg a day) continues to be supported by the current evidence base.

Useful links, references and bibliography

Links

[MIDIRs search approach and databases accessed](#)

Miscarriage Association (2020) www.miscarriageassociation.org.uk website accessed 31 August

Royal College of Obstetricians and Gynaecologists (RCOG) www.rcog.org.uk website accessed 31 August 2020

[Tommy's response to the paper by Jack E James](#), August 2020, including a radio interview from Prof Andrew Shennan

Tommy's www.tommys.org website accessed 31 August 2020

RCOG guidance:

Response to publication of Jack E James' paper: Dr Daghni Rajasingam, RCOG spokesman, said: 'Women do not need to completely forgo tea and coffee while pregnant – advice that will not change in light of the review. Other, and potentially more reliable, research has found that pregnant women do not need to cut caffeine out entirely because these risks are extremely small, even if the recommended caffeine limits are exceeded. The Royal College of Obstetricians and Gynaecologists' advice to limit caffeine intake to 200mg per day – the equivalent to two cups of instant coffee – still stands.'

Patient information [here](#)

References

- Bakker, R., Steegers, E. A., Obradov, A., *et al*, (2010). [Maternal caffeine intake from coffee and tea, fetal growth, and the risks of adverse birth outcomes: the Generation R Study](#) *The American Journal of Clinical Nutrition* vol 91(6): 1691-1698
- Bech, B.H., Frydenberg, M., Henriksen, T.B., *et al*, (2015) Coffee consumption during pregnancy and birth weight: does smoking modify the association? *Journal of Caffeine Research* vol 5(2):65-72 June
- Berglundh, S., Vollrath, M., Brantsæter, A. L., *et al*, (2020) [Maternal caffeine intake during pregnancy and child neurodevelopment up to eight years of age-Results from the Norwegian Mother, Father and Child Cohort Study](#) *European Journal of Nutrition* 26 May online
- Blood Cancer UK (2020) [What is childhood acute lymphoblastic leukaemia \(ALL\)?](#) (Accessed 31 August 2020)
- CARE Study Group (2008) [Maternal caffeine intake during pregnancy and risk of fetal growth restriction: a large prospective observational study](#) *BMJ* 337:a233.
- Chen, L., Bell, E. M., Browne, M. L., *et al*, (2014). [Exploring maternal patterns of dietary caffeine consumption before conception and during pregnancy](#). *Maternal and Child Health Journal* vol 18 (10):2446-2455 December
- Chen, L-W., Wu, Y., Nelakantan, N., Chong, M., *et al* (2016) [Maternal Caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose-response meta-analysis of prospective studies](#), *Public health nutrition*
- Chen, L-W., Murrin, C.M., Megegan, J., *et al*, (2019) [Maternal, but not paternal or grandparental, caffeine intake is associated with childhood obesity and adiposity: The Lifeways Cross-Generation Cohort Study](#) *The American Journal of Clinical Nutrition* vol 109(6):1648-1655 June
- Childhood with Cancer UK (2020) [What causes childhood cancer?](#) (Accessed 31 August 2020)
- Choi, J. H., Ryan, L. M., Cramer, D. W., *et al*, (2011) Effects of caffeine consumption by women and men on the outcome of in vitro fertilization *Journal of Caffeine Research* vol 1(1):29-34 7 April
- Choi, H., Koo, S., Park, H-Y., (2020) Maternal coffee intake and the risk of bleeding in early pregnancy: a cross-sectional analysis *BMC Pregnancy and Childbirth* vol 20(121) 21 February
- Cnattingius, S., Signorello, L. B., Anneren, G., *et al* (2000) Caffeine intake and the risk of first-trimester spontaneous abortion *New England Journal of Medicine* vol 343(25):1839- 1845 21 December
- Del-Ponte, B., Santos, I. S., Tovo-Rodrigues, L., *et al*, (2016) Caffeine consumption during pregnancy and ADHD at the age of 11 years: a birth cohort study *BMJ Open* vol 6(12):e012749 5 December
- Feodor Nilsson, S., Andersen, P. K., Strandberg-Larsen, K., Nybo Andersen, A-M., (2014) Risk factors for miscarriage in a prevention perspective: a nationwide follow-up study. *BJOG* 10.1111/1471-0528.12694.
- Fernandes, O., Sabharwal, M., Smiley, T., *et al*, (1998) Moderate to heavy caffeine consumption during pregnancy and relationship to spontaneous abortion and abnormal fetal growth: a meta-analysis *Reproductive Toxicology* vol 12(4):435-444

- Galéra, C., Bernard, J.Y., van den Waerden, J., et al, (2016) Prenatal caffeine exposure and child IQ at age 5.5 years: The EDEN Mother-Child Cohort *Biological Psychiatry* vol 80(9):720-726 1 November
- Gardosi, J., Madurasinghe, V., Williams, M., et al, (2013) [Maternal and fetal risk factors for stillbirth: population based study](#), *BMJ*
- Giannelli, M., Doyle, P., Roman, E., et al, (2003) The effect of caffeine consumption and nausea on the risk of miscarriage *Paediatric and Perinatal Epidemiology* vol 17(4):316-323 October
- Greenwood, D.C., Alwan, N., Boylan, S., et al, (2010) Caffeine intake during pregnancy, late miscarriage and stillbirth *European Journal of Epidemiology* vol 25(4):275-280 April
- Hahn, K. A., Wise, L. A., Rothman, K. J., et al, (2015) Caffeine and caffeinated beverage consumption and risk of spontaneous abortion *Human Reproduction* vol 30(5):1246-1255 May
- James, J. E., (2020) [Maternal caffeine consumption and pregnancy outcomes: a narrative review with implications for advice to mothers and mothers-to-be](#) *BMJ Evidence-Based Medicine* March
- Jahanfar, S., Jaafar, S. H., (2015) *Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcome (Cochrane Review)* (Assessed as up-to-date: 16 January 2015) The Cochrane Database of Systematic Reviews Issue 6,
- Jarosz M; Wierzejska R; Siuba M., (2012) Maternal caffeine intake and its effect on pregnancy outcomes *European Journal of Obstetrics and Gynecology and Reproductive Biology* vol 160(2):156-160.
- Karalexi, M. A., Dessypris, N., Clavel, J., et al, (2019) Coffee and tea consumption during pregnancy and risk of childhood acute myeloid leukemia: A Childhood Leukemia International Consortium (CLIC) study *Cancer Epidemiology* vol 62(101581) October
- Klebanoff, M. A., Keim, S. A., (2015) Maternal Caffeine Intake During Pregnancy and Child Cognition and Behavior at 4 and 7 Years of Age *American Journal of Epidemiology* vol 182(12):1023-1032
- Kjersgaard, C., Arendt, L. H., Ernst, A., et al, (2018) Lifestyle in pregnancy and cryptorchidism in sons: a study within two large Danish birth cohorts *Clinical Epidemiology* vol 2018(10) 19 March
- Kobayashi, S., Sata, F., Murata, K., et al, (2019). Dose-dependent associations between prenatal caffeine consumption and small for gestational age, preterm birth, and reduced birthweight in the Japan Environment and Children's Study *Paediatric and Perinatal Epidemiology* vol 33(3):185-194 May
- Lamy, S., Houivet, E., Benichou, J., et al, (2020) [Caffeine use during pregnancy: prevalence of use and newborn consequences in a cohort of French pregnant women](#) *European Archives of Psychiatry and Clinical Neuroscience* 21 February online
- Lehtonen, A., Uusitalo, L., Auriola, S., et al, (2020) [Caffeine content in newborn hair correlates with maternal dietary intake](#) *European Journal of Nutrition* 3 April online
- Leviton, A. (2018) [Biases Inherent in Studies of Coffee Consumption in Early Pregnancy and the Risks of Subsequent Events](#) *Nutrients* vol 10(9):1182 23 August
- Li, J., Zhao, H., Song, J. M., et al, (2015) A meta-analysis of risk of pregnancy loss and caffeine and coffee consumption during pregnancy *International Journal of Gynecology and Obstetrics* vol 130(2): 116-122 August

Loomans, E. M., Hofland, L., van der Stelt, O., *et al*, (2012) Caffeine intake during pregnancy and risk of problem behavior in 5- to 6-year-old children. *Pediatrics* , vol 130(2):e305-13 August

Lu, J-H., He, J-R., Shen, S-Y., *et al*, (2017) Does tea consumption during early pregnancy have an adverse effect on birth outcomes? *Birth* vol 44(3):281-289 September

Lyngsø, J., Ramlau-Hansen, C.H., Bay, B., *et al*, (2017) Association between coffee or caffeine consumption and fecundity and fertility: a systematic review and dose–response meta-analysis. *Clinical Epidemiology* vol 2017(9) 15 December

Maeda, T., Sekiguchi, K., Wasada, R., *et al*, (2019) Caffeine not associated with irritable behaviour in very low-birth-weight infants. *Early Human Development* vol 137:104835 October

Milne, E., Royle, J. A., Bennett, L. C., *et al*. (2011) Maternal consumption of coffee and tea during pregnancy and risk of childhood ALL: results from an Australian case-control study. *Cancer Causes Control* 22:207–18

Miscarriage Association (2013) [Thinking about another pregnancy](#) (Accessed 31 August 2020)

Modzelewska, D., Bellocco, R., Elfvin, A., *et al*, (2019) [Caffeine exposure during pregnancy, small for gestational age birth and neonatal outcome – results from the Norwegian Mother and Child Cohort Study](#) *BMC Pregnancy and Childbirth* vol 19(80) 26 February

NHS Choices (2018) [Should I limit caffeine during pregnancy?](#) (Accessed: 4 September 2020)

Pemathilaka, R. L., Caplin, J. D., Aykar, S. S., *et al*, (2019) [Placenta-on-a-chip: in vitro study of caffeine transport across placental barrier using liquid chromatography mass spectrometry](#). *Global Challenges*, 18 February

Rhee, J., Kim, R., Kim, Y., *et al*, (2015) [Maternal Caffeine Consumption during Pregnancy and Risk of Low Birth Weight: A Dose-Response Meta-Analysis of Observational Studies](#) *PLoS ONE* vol 10(7) 20 July e0132334.

Pollack, A. Z., Buck Louis, G. M., Sundaram, R., *et al*, (2010) Caffeine consumption and miscarriage: a prospective cohort study *Fertility and Sterility* vol 93(1):304-306

Papadopoulou, E., Botton, J., Brantsaeter, A-L., *et al*, (2018) Maternal caffeine intake during pregnancy and childhood growth and overweight: results from a large Norwegian prospective observational cohort study *BMJ Open* vol 8(3):e018895 23 April

Sengpiel, V., Elind, E., Bacelis, J., *et al*, (2013) Maternal caffeine intake during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study *BMC Medicine* vol 11(42) 19 February

Tommy's (2020) [Check your caffeine intake in pregnancy](#) (Accessed 31 August)

Voerman, E., Jaddoe, V. W., Gishti, O., *et al*, (2016). Maternal caffeine intake during pregnancy, early growth, and body fat distribution at school age *Obesity* vol 24(5):1170-1177 May

Voerman, E., Jaddoe, V. W., Hulst, M. E., *et al*, (2020) [Associations of maternal caffeine intake during pregnancy with abdominal and liver fat deposition in childhood](#), *Pediatric Obesity*, vol 15 (5) May e12607 <https://onlinelibrary.wiley.com/doi/full/10.1111/ijpo.12607>

Wen, W., Shu, X. O., (2001) High caffeine intake increased the risk of first-trimester spontaneous abortion in non-smoking women *Evidence-Based Obstetrics and Gynecology* vol 3(4):174-175 December

Wierzejska R., Jarosz, M., Wojda, B., (2019) Caffeine Intake During Pregnancy and Neonatal Anthropometric Parameters *Nutrients* vol 11(4):e806 April

Bibliography

Adams, S. Hough, A. (2011) Wake up to caffeine levels in your espresso, scientists urge. *Telegraph* 1 December

American College of Obstetricians and Gynecologists, (2010). ACOG Committee opinion no. 462: Moderate caffeine consumption during pregnancy *Obstetrics and Gynecology* vol 116(2) part 1:467-468 August

Anon; (2011) [Coffee shop caffeine: pregnancy health risk?](#) *NHS Choices* 1 December

Anon; (2012) Can consuming caffeine while breastfeeding harm your baby? An interview with Ruth Lawrence, PhD *Journal of Caffeine Research* vol 1(4):192-194, December

Aranda, J. V. Beharry, K. Valencia, G. B. et al, (2011) Caffeine impact on neonatal morbidities *Journal of Maternal-Fetal and Neonatal Medicine* vol 23(S3):20-23, October

Fletcher, J. (2018) [What to avoid during pregnancy](#) *Medical News Today* 24 August

Gray, P.H. Flenady, V. J. Charles, B.G. et al (2011) Caffeine citrate for very preterm infants: Effects on development, temperament and behaviour. *Journal of Paediatrics and Child Health* vol 47(4):167-172, April

Kraaijenga, J. V. Hutten, G. J. de Jongh, F. H. et al (2015) The effect of caffeine on diaphragmatic activity and tidal volume in preterm infants *Journal of Pediatrics* vol 167 no1:170-75 July

Lee, B. H. Park, T. C. Lee, H. J. (2014) Influence of caffeine on the expression of human chorionic gonadotropin and progesterone receptors in human trophoblast cell lines. *Acta Obstetrica et Gynecologica Scandinavica* vol 93(12):1334-1335

Morgan, S. Koren, G. Bozzo, P. (2013) Motherisk update: [Is caffeine consumption safe during pregnancy?](#) *Canadian Family Physician* vol 59(4):361-362 April