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### **Dietary fat intake and in-vitro fertilization outcomes: saturated fat intake is associated with fewer metaphase 2 oocytes**

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**Introduction:** Dietary fat intake has been shown to affect reproductive health. For example, higher intake of trans fatty acids has been associated with an increased risk of ovulatory infertility, pregnancy loss and endometriosis. Nevertheless, it is still unknown whether dietary fat has an impact on women undergoing in vitro fertilization (IVF). The objective of this study was to evaluate whether fat intake (total, saturated, monounsaturated, polyunsaturated, omega 6, omega 3 and trans) is related to preclinical and clinical outcomes in women undergoing IVF.

**Material & Methods:** Women and men presenting for evaluation at the Massachusetts General Hospital Fertility Center were invited to participate in the EARTH Study, a study on environmental factors and fertility. Participants completed a lifestyle and a validated food frequency questionnaire. One hundred forty seven women, who collectively underwent 198 ART cycles, fulfilled the eligibility criteria to be included in this analysis. Fertilized oocytes were classified as normally fertilized if they had two pronuclei. Embryo quality and cleavage rate were assessed on day 3. Embryos that had 6 to 8 cells were considered to have cleaved at a normal rate, embryos with 5 cells or fewer were considered to be slow cleavage, and embryos with 9 or more cells were considered to have accelerated cleavage. Clinical outcomes were assessed only among couples that underwent an embryo transfer. Women were categorized into tertiles of fat intake and estimates were compared in relation to the lowest tertile. We used 2 different sets of carbohydrate substitution models that included additional terms for all other sources of energy, except for carbohydrates. The first set included terms for age and total energy intake. The second set included additional terms for day 3 FSH, infertility diagnosis, ovarian stimulation protocol, body mass index (BMI) and smoking status. Generalized estimating equations (GEE) were used in order to take advantage of all the available information while accounting for correlated outcomes across cycles within the same couple. We used test for linear trend using the median value for each category of fat intake.

**Result:** In multivariate-adjusted regression models, higher intakes of total fat and saturated fat were related to fewer metaphase 2 (M2) oocytes retrieved. This association was driven by intake of saturated fat. Women in the highest tertile of saturated fat intake had, on average, 9.3 (95%CI: 5.9-14.7) M2 oocytes while women reporting the lowest intake had 11.6 (95%CI: 8.1-16.7) M2 oocytes, (p-trend=0.03). Total fat intake, as well as intake of major types of fat, was unrelated to peak estradiol level or total fertilization rate. Polyunsaturated fat consumption was inversely related to embryo quality. Women in the highest tertile of polyunsaturated fat intake, had a higher proportion of poor quality embryos (p-trend=0.02) and slow cleaving embryos (p-trend=0.001) than women in the lowest tertile

of intake. In addition, higher trans fat consumption was associated with a lower proportion of accelerated cleavage embryos (p-trend=0.03). Fat consumption was also associated with clinical outcomes. Higher intakes of monounsaturated fat were related to higher odds of live birth. The odds ratio of a live birth among women with the highest intake of mono-unsaturated fat was 3.45 (95%CI: 1.12-10.62) when compared to women with the lowest intake (p-trend: 0.03).

**Conclusion:** Saturated fat intake was inversely related to the number of M2 oocytes while polyunsaturated fat consumption was inversely associated with early embryo quality. Monounsaturated fat consumption was associated with increasing odds of a having a live birth.

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