

The Effect of Iron Supplements on the Gut Microbiome of Non-pregnant Women of Reproductive Age: A Randomized Controlled Trial

Tim Green,¹ Brittany Hand,² Monika Skubisz,³ Karen Best,³ Luke Grzeskowiak,³ Emma Knight,³ Geraint Rogers,³ and Steven Taylor³

¹South Australian Health and Medical Research Institute; ²Flinders University; and ³South Australia Health and Medical Research Institute

Objectives: Blanket iron supplementation during pregnancy is not recommended in Australia. However, many women take iron as part of a prenatal supplement, often at doses >60 mg/day. Iron supplementation may negatively affect the maternal intestinal microbiome by increasing the abundance of pathogenic bacteria and decreasing commensal bacteria. It is not known if iron supplements alter the microbiome of pregnant women. Here we aim to determine if iron supplementation alters the gut microbiome of non-pregnant women of childbearing age.

Methods: In this two-arm parallel design, double-blind, randomized controlled trial, women (18–45 y) were randomized to take an iron

supplement (60 mg elemental iron) or a placebo capsule for 21 days. The primary outcome was microbiota beta-diversity (paired-sample weighted UniFrac dissimilarity) between iron and placebo groups in stool samples collected at baseline and 21 days. A secondary outcome was to determine the effect of iron on *Escherichia-Shigella* genus relative abundance.

Results: Eighty-two women were randomized, 40 and 42 to iron and placebo groups, respectively. Attrition was < 3% (n = 2) and 97% of women took >80% of their study supplements. On Day 21, there was no difference in mean (95% CI) weighted UniFrac between iron and placebo groups [0.003 (−1.4, 0.7) P = 0.52]. There was no difference in the relative abundance of *Escherichia-Shigella* after 21 days between groups.

Conclusions: For the outcomes we assessed, we did not find an effect of iron supplementation on the microbiome in non-pregnant women. Studies should be carried out in pregnant women, particularly in settings where water and sanitation are poor, and the natural abundance of pathogenic bacteria is higher.

Funding Sources: South Australian Health and Medical Research Institute, Seed Funding Grants for Early/Mid-Career Researchers.