

Maternal gut microbiota influences offspring physical activity levels

Rebecca Schmieley¹, Kevin Gustafson², Zach McAdams², and Aaron C. Ericsson³.

College of Veterinary Medicine, University of Minnesota, St Paul, MN¹

Comparative Medicine Program², Department of Veterinary Pathobiology³, University of Missouri, Columbia MO

Background Information

Obesity is the largest comorbidity affecting 41.9% of adults older than 20 in the United States. Increased food intake and decreased activity levels are key contributors to the development of obesity. The gut microbiome is known to modulate factors such as behavior, weight gain, and metabolism.

Recent investigations have linked the maternal microbiome to lasting changes in offspring body weight.

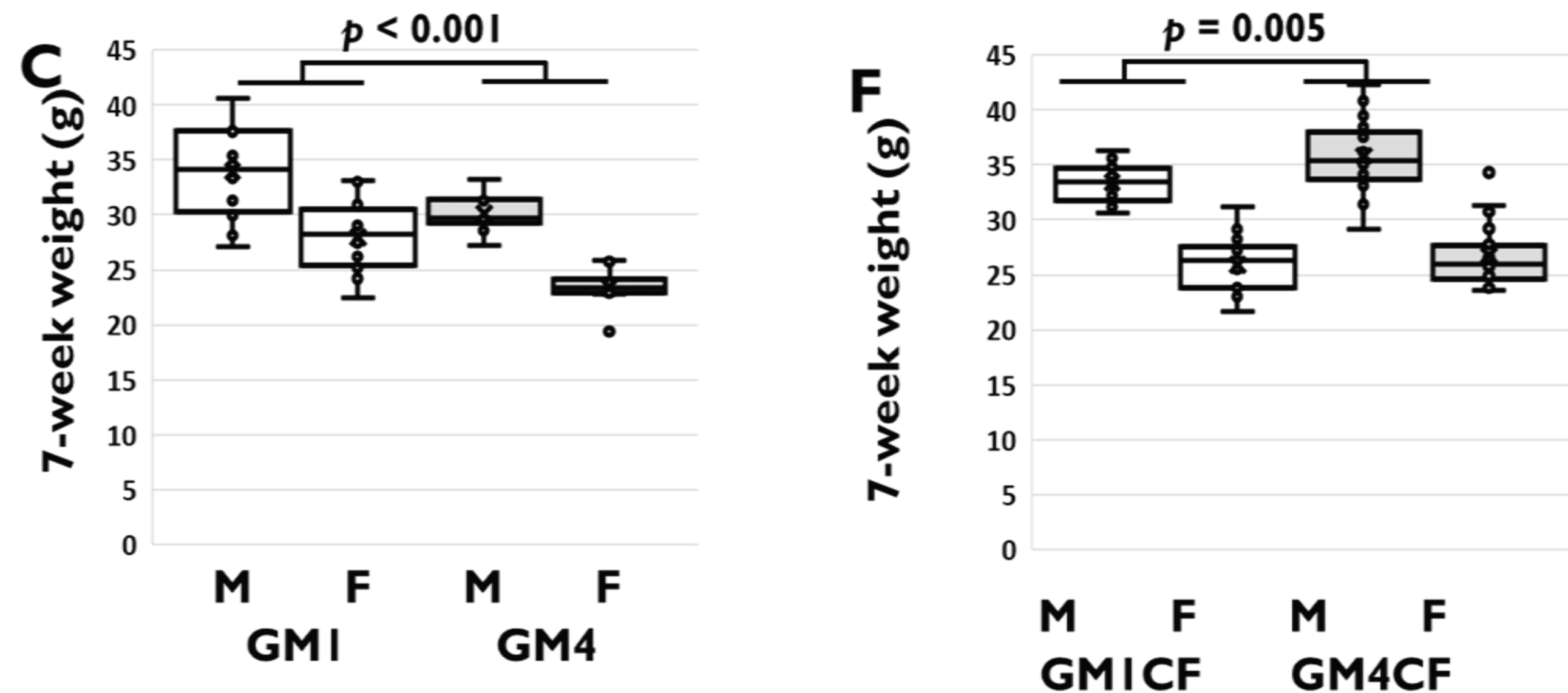


Figure 1. Weight phenotypes are not reversed when pups are cross-fostered to an opposing microbiome. GM1 mice contain a specific low diversity microbiome profile whereas GM4 mice contain a high diversity microbiome profile (n=12/sex/GM). GM1CF mice were born from GM4 dam and were cross-fostered to a GM1 mouse at birth. GM4CF mice were born from GM1 dam and were cross-fostered to a GM4 dam at birth. All microbiomes are hosted in genetically refreshed CD1 mice. This data suggests that the weight gain phenotype is driven by microbiome profiles prior to birth.

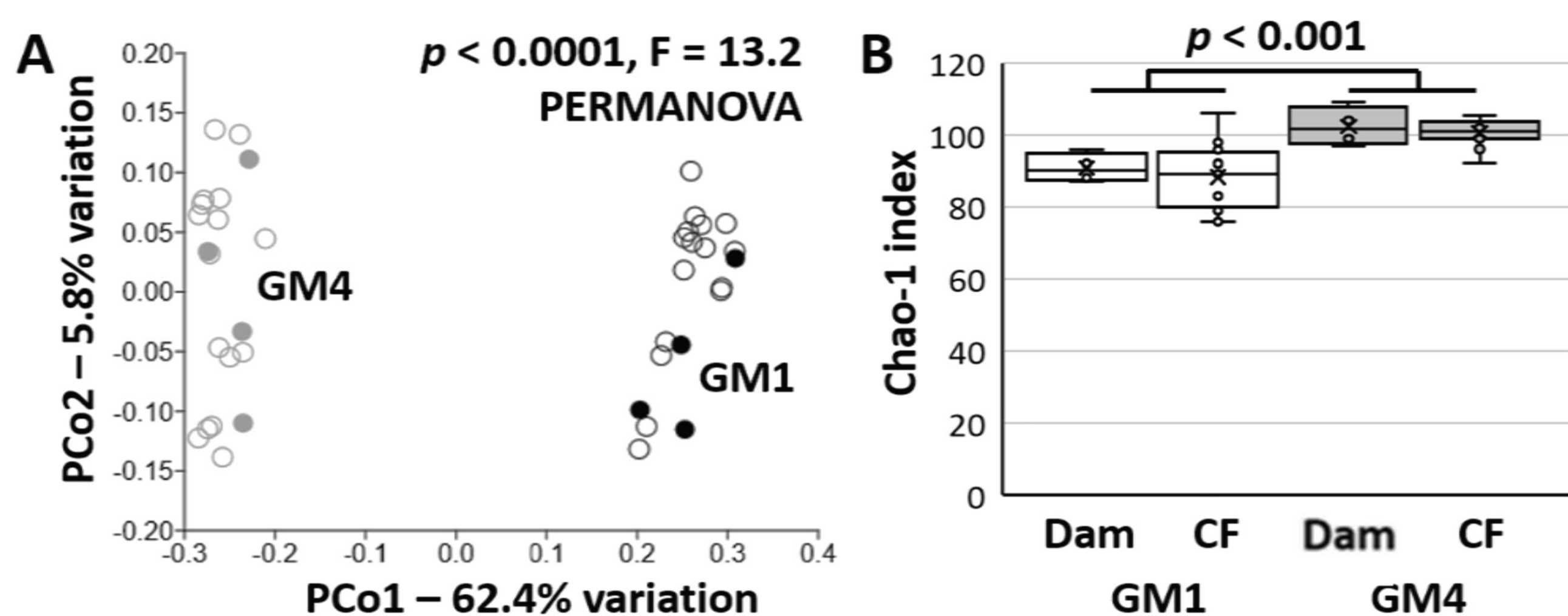


Figure 2. GM1 and GM4 profiles are distinct and can be transferred effectively via cross-fostering. Cross-foster mice (n=16/sex/GM) as seen in figure B, maintain the same level of diversity as their foster dam and are significantly distinct from the cross-foster of the other microbiome profile.

Specific Aims

- Assess voluntary activity as a contributor to the microbiome-associated difference in body weight
- Determine if voluntary activity is determined by the maternal microbiome during fetal development

Experimental Design

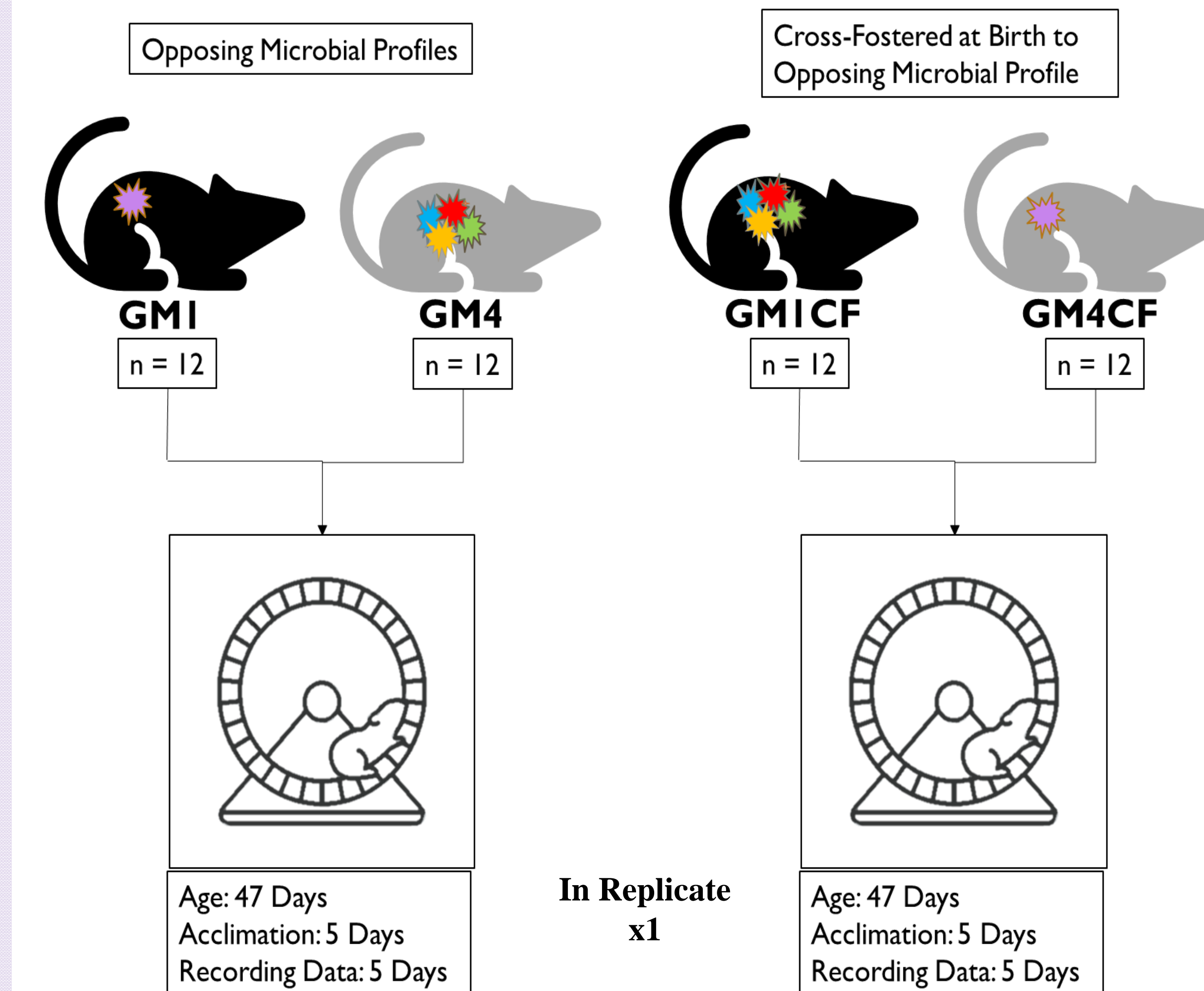


Figure 3: Experimental Diagram. All mice were aged to 47 days and placed single-housed in a cage with an ENV-044 wireless mouse wheel. They were allowed to acclimate for 5 days before an additional 5 days of data was recorded. Each grouping was replicated in a second cohort for a total N=96.

Running Wheel Distances Change with Microbial Profiles

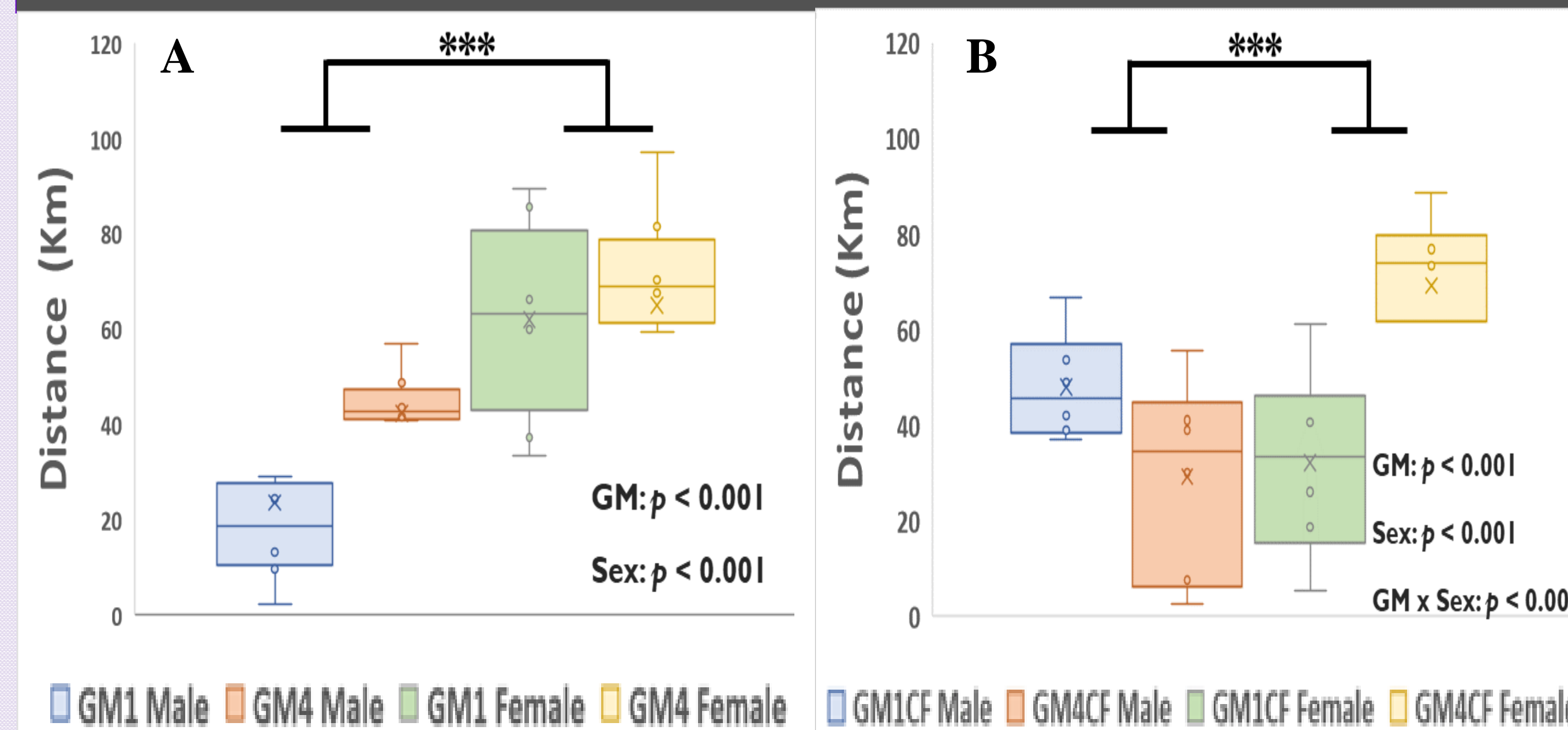


Figure 4 Average Distance Run Over 5 days between GM1, GM4, GM1CF and GM4CF mice. Each GM control group seen in 3A, are significantly different with GM4 mice running the farthest. Sex also impacts total distance with females mice running more than male mice. Figure 3B, details the same data within the cross fostered variants. GM1CF male mice ran significantly more than GM4CF male mice, thus reversing phenotypic expectations seen in 3A. However, GM4CF Female mice maintain expected running patterns covering more distance than GM1CF Female mice. A significant (p<0.001) interaction exists between the cross-fostered mice. All statistics were calculated using 2-way ANOVA in Sigmaplot using the Holm-Sidak method for pairwise comparisons.

Microbiome-driven Phenotype in Males was Driven by Birth Mother

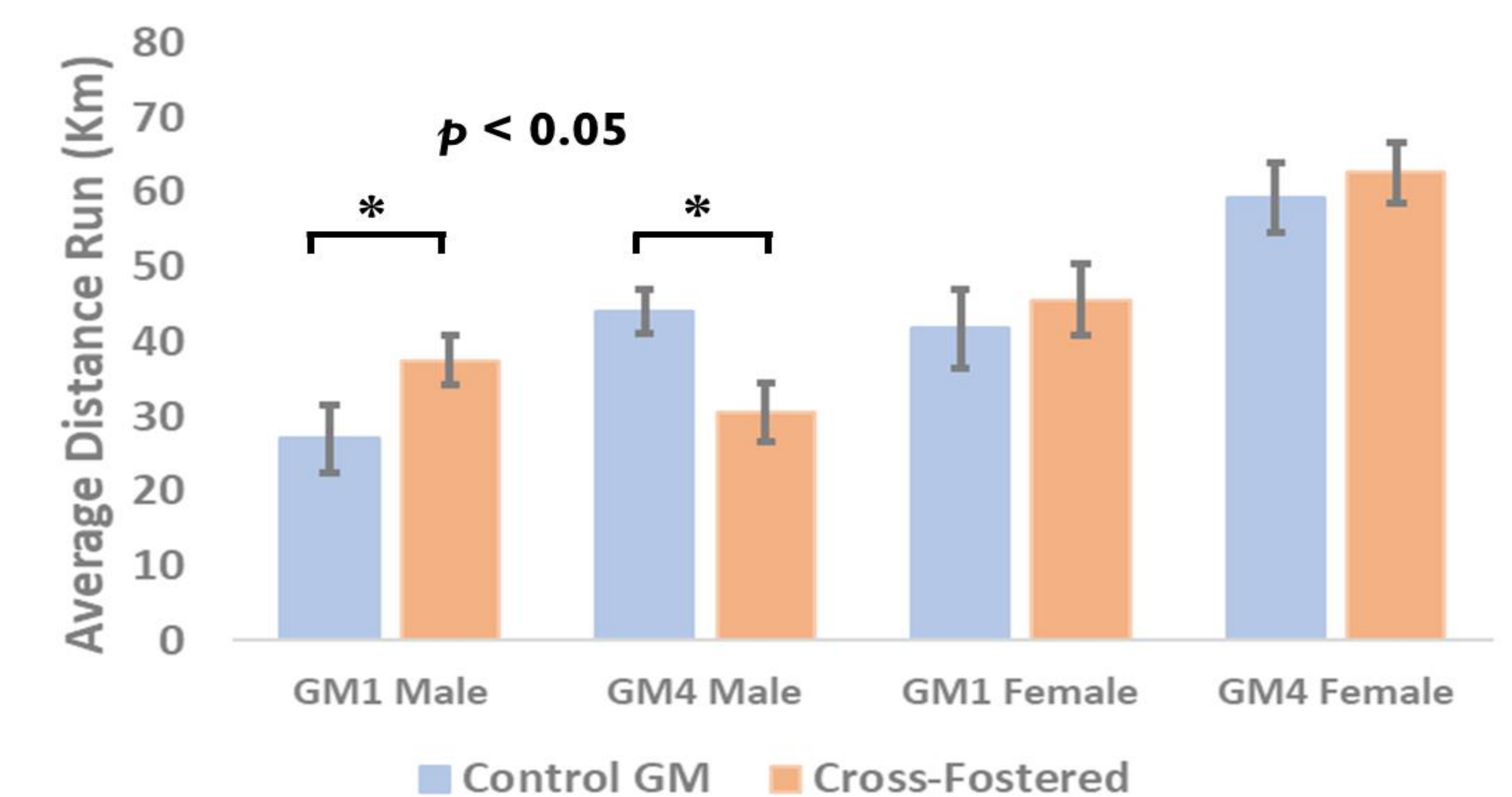


Figure 5 Cross-Comparisons Between Control GM Mice and GM Cross-Fostered Mice. GM1CF male mice ran significantly more than GM1 male mice. GM4 male mice ran significantly more than GM4CF mice. No significance was found between cross-fostered and controlled GM mice. Statistics calculated from Student's T-test with unequal variance. Error bars depict the variance within specific groups (n=12).

Conclusion

- The maternal microbiome can influence physical activity levels in male mice.
- In-utero signalling patterns from the maternal microbiome may be sex-dependent

Future Work

- Future work aims to identify other contributors to this phenotypic weight difference in cross-fostered mice such as: basal metabolic rates, fecal energy loss, and food intake.
- Characterize the mechanism of action and detail signalling molecules.

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