

A Game of T Cells: Interactions between the microbiome and immune recovery

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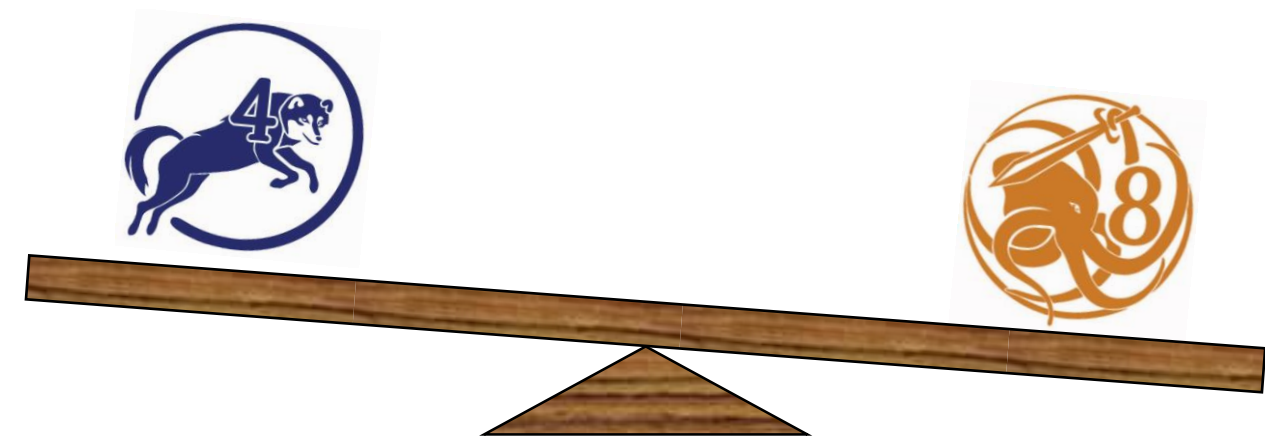


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Background

- Historically, absolute CD4 has been used as a measure both in people living with HIV (PLHIV) and uninfected individuals of how competent the immune system is.
- Now that most PLWH are on treatment, there is a movement to replace absolute CD4 with a more nuanced biomarker: the CD4:CD8 ratio¹.
- Ratios below the “normal” range likely correlate with disease in both the aged and PLWH.
- McFall-Ngai has theorized that the adaptive immune response developed in vertebrates to manage complex microbiomes². Therefore, manipulating the CD4:CD8 ratio may require a deep understanding of the relationship between ratio imbalance and microbiomes.



Burning Questions

- How do the fecal and oral microbiomes interact with the CD4:CD8 ratio and to what degree? Does the decline or recovery of one influence the decline or recovery of the others?
- If there is a relation between ratio recovery and HIV reservoir disappearance, does the microbiome play a role? Who is in the driver’s seat?



Acknowledgements

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Ethiopian Cohort

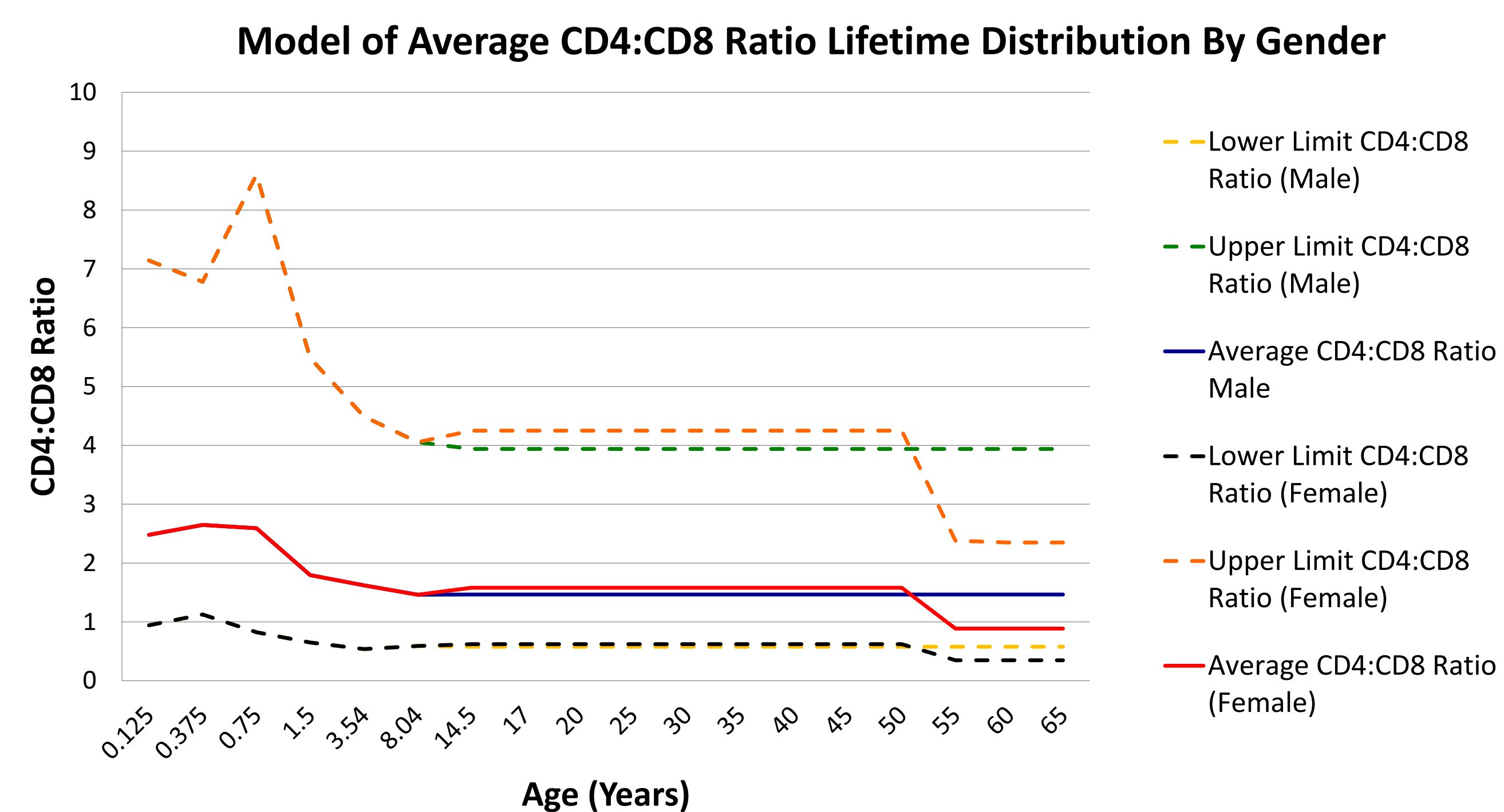


Figure 2. In female mice and humans, the ratio changes with fertility status and age. The normal ratio range for healthy elderly individuals is unknown.

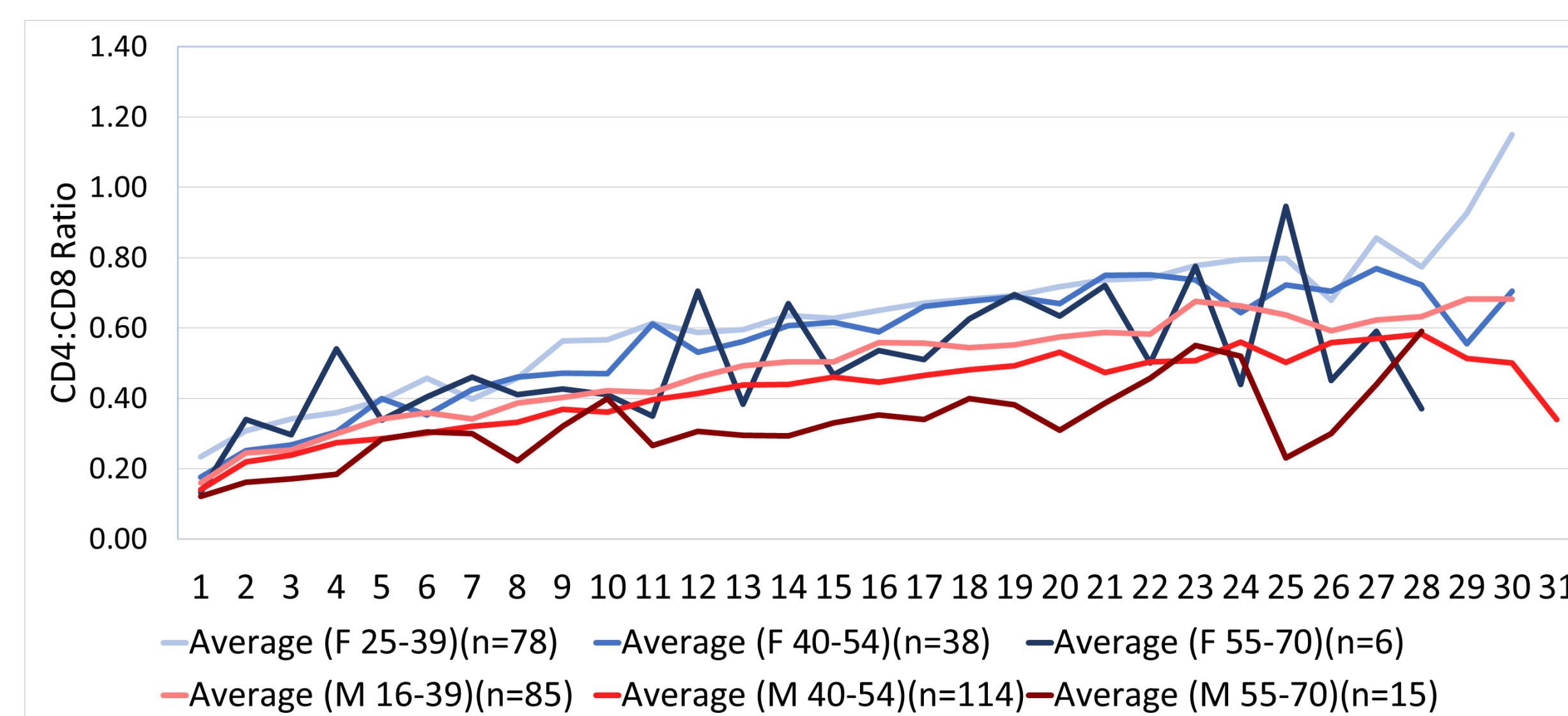


Figure 3. Composite of 336 HIV+ Ethiopian patients on ART therapy comprised of 2/3 males and 1/3 females over approximately 15 years. Young women show better ratio recovery than other groups.

Spoilers

- Microbial dysbiosis may depend upon both gender and ratio recovery.
- If *Prevotella* is associated with HIV fecal dysbiosis AND MSM behavior, could we see ratio changes in non-HIV MSM from Multicenter AIDs Cohort (MACs)?
- The order and coincidence of estrogen falling, ratio falling, and change in microbiome can be tracked in the Women’s Interagency HIV Study (WIHS).

Relevant Microbiome Data

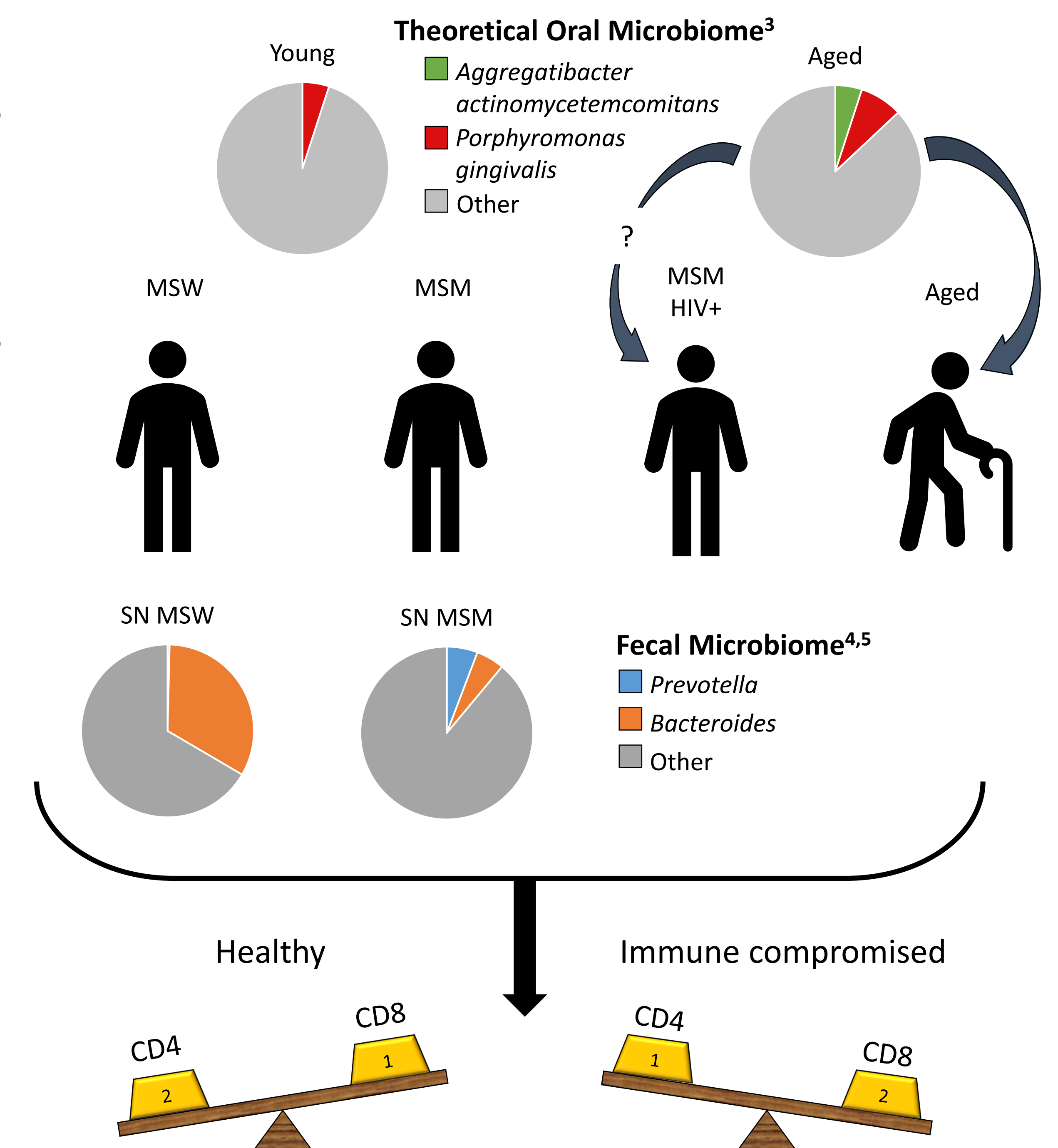


Figure 1. Both the oral and fecal microbiome may impact the CD4:CD8 ratio differently for different groups of people. Theoretical oral microbiome data was influenced by Papantonopoulos *et al*³. Fecal microbiome data was adapted from Neff *et al*⁵. The mean OTU count for each genera was used from supplemental tables 2 and 6.

References

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