Age and Early Life Adversity in the Wild Baboon Gut Microbiome

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Abstract

by

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Mammalian gut microbiomes are highly individualized, dynamic microbial communities. They serve essential functions for their hosts by breaking down complex carbohydrates, producing vitamins, training the immune system, and resisting pathogens. These communities also change substantially throughout life in response to host environment, diet, and sociality. Age and early life experiences have also been shown to influence the composition of the gut microbiome in cross-sectional studies. These changes are proposed to be important markers of individual development and senescence. However, to date, scientific understanding of host-microbe dynamics is hampered by the fact that most microbiome research is cross-sectional. Without fine-grained longitudinal data on microbiome composition across the host's life, we do not know how gut microbiomes change in individuals over time, what factors drive variation in gut microbiome development and aging, or whether these changes serve as markers of maturational milestones or mortality risk.

To address this gap, my PhD research leverages long-term, longitudinal data from a wild population of baboons (*Papio cynocephalus*) monitored by the Amboseli Baboon Research Project (ABRP) in Kenya. My dissertation objective was to characterize how the gut microbiome changes in response to early life experi-

ences and age across the lifespan, understand what host and environmental factors predict these changes, and determine whether microbial changes are linked to host maturation and survival. To accomplish this objective, I combine the ABRP's 50 years of demographic, environmental, social, and genetic data with a corresponding gut microbiome data set consisting of over 17,000 16S gut microbial profiles collected from 601 known individually-known, wild baboons over a 14-year period. Using a subset of these data, I have shown that the gut microbiome changes predictably with age and found that individuals who were socially low-ranked exhibit faster rates of microbial aging relative to high-ranked peers. Next, I found that individuals who aged faster attain certain maturational milestones earlier. Last, I discovered that specific types of early life adversity are correlated with changes in microbial composition or decreased stability late in life. Together, my research improves our understanding of how the gut microbiome adapts to and influences its mammalian host's life course.

To our little family.

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ACKNOWLEDGMENTS

It's astounding how much work goes into a dissertation. As new graduate students, we go in with some understanding that the next 5+ years are going to be a slog, but it is really difficult to describe all the parts that don't appear in the papers, the presentations, the dissertation. Yes, a lot of this is good - the friendships, the personal and professional growth, the gaining of new knowledge and skills - but some of it is...less good: the sweat, the blood, the tears, the systemic racism and undervaluing of labor disproportionately carried out by female academics of color, some cat pee. In this limited space, I will try to encompass some of the contributions my mentors, collaborators, friends, and family made to this process.

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"I love you."

Summertime Magic, Childish Gambino

CHAPTER 1

INTRODUCTION

The mammalian gut microbiome is the most plastic organ in a vertebrate host. It consists of a dense, complex microbial community, where microbes interact with each other and with their host to accomplish a number of essential functions. From a host perspective, these functions include breaking down complex carbohydrates, producing vitamins and amino acids, training the immune system, and resisting pathogens (Clayton et al., 2018; Foster et al., 2017; Hooper and Gordon, 2001). As the host ages and develops, these functions vary in their importance (e.g. much of the active immune system preparation happens when the host is first being exposed to pathogens and becomes more passive as the host and their immune system develop). As such, the gut microbiome has been proposed to adapt with the host and be reflective of the host's needs (Foster et al., 2017).

To date, several studies have shown that the gut microbiome changes considerably with age and developmental stage. For example, in humans, gut microbial diversity and stability rise after birth through weaning as the microbiome is assembled and the host's diet shifts to solid foods (Bergström et al., 2014; Bäckhed et al., 2005; Cong et al., 2016; Koenig et al., 2011; Yassour et al., 2016). During adulthood and old age, dynamic patterns are variable across people and populations, but several studies find age-related changes in diversity and taxonomic abundances (Biagi et al., 2016; Claesson et al., 2011; Mueller et al., 2006; Odamaki et al., 2016; Yatsunenko et al., 2012). Specifically, Yatsunenko et al. (2012) found that children attain their adult gut microbial stability and composition by the age of

three, irrespective of geography, but adults have significantly different phylogenetic compositions based on their geographic population. While in this study alpha diversity appears to plateau in adulthood, other studies have found that diversity may increase in the elderly compared to younger adults (Odamaki et al., 2016). Similarly, if we examine specific taxonomic changes with age we have mixed results: Claesson et al. (2011) found Bacteroidetes increase with greater chronological ages, while Bian et al. (2017) and Biagi et al. (2010) find the opposite or no trend. Importantly, these age- and development- related changes in the gut microbiome have been observed not just in humans, but across a range of host taxa (Smith et al., 2017; Tarpy et al., 2015; Xiang et al., 2020; Xu and Zhang, 2021; Zhang et al., 2018).

A major challenge in studying the relationship between the gut microbiome and host development and aging is the plasticity of the gut microbiome: microbial communities may change in response to host aging as well as in response to an aging host's diet, environment, and social interactions. As a host reaches higher chronological ages, their body ages biologically due to the breakdown of their tissues, organs, and immune system (Bosco and Noti, 2021). The degradation of these physiological processes may impact the constraints governing gut microbiome dynamics —the gut microbiome is, after all, "an ecosystem on a leash" (Foster et al., 2017) —and explain the relationship between the gut microbiome and age-related diseases such as atherosclerosis, type 2 diabetes, and various metabolic or neurodegenerative disorders (Vaiserman et al., 2017). Age-related changes to behavior will also strongly impact the signature of aging on the gut. Host diet in particular has been shown to influence the gut both over long and short term intervals – e.g. vegetarians have compositionally divergent microbiomes from those who partake in more omnivorous diets, but even lifelong vegetarians rapidly adapt if given a meat-based diet (Amato et al., 2015; David et al., 2014b). Diet

is also related to development-related changes, including the switch from milk to adult foods in mammals (Gopalakrishna and Hand, 2020; Lundgren, 2019). Aside from diet, aspects of host environment and lifestyle greatly impact the types of microbes a host may encounter (Bennett et al., 2016; Bierlich et al., 2017; David et al., 2014a; Grieneisen et al., 2019; Hernández-Pérez et al., 2021; Rothschild et al., 2018; Song et al., 2013). Specifically, the move to residential care facilities and cohabitation with other elderly individuals has been shown to not only change the gut microbiome, but also increase the antibiotic uptake and thereby the incidence of gut dysbiosis (Araos et al., 2018; Haran et al., 2018; Jeffery et al., 2016; Le Bastard et al., 2020; Roghmann et al., 2017). Relatedly, social interactions and genetics greatly influence what microbes hosts are exposed to and similar cause some level of compositional convergence outside of the other aspects discussed here (Grieneisen et al., 2017; Moeller et al., 2016; Orkin et al., 2019; Trosvik et al., 2018; Tung et al., 2015).

The gut microbiome is not only impacted at near-daily scales by our diet, environment, and lifestyle but also highly individualized based on a host's early life experiences and genetics. Early life experiences in particular may cause priority effects in a developing host's community: one well identified example of this is in human birth style, where infants born by caesarean section (C-section) have different gut microbiomes compared to infants delivered vaginally (Fukami, 2015; Martin et al., 2016; Reyman et al., 2019). Further, these communities have been shown to be difficult to alter even with concerted seeding efforts (Wilson et al., 2021). Gut microbial taxa have also been shown to be highly heritable, so vertical transmission between parent and offspring will also impact gut microbial historical contingencies (Grieneisen et al., 2021). The confluence of priority effects, historical contingencies, and daily dispersal dynamics combined with high levels of functional redundancy means that relying on cross-sectional data hinders our un-

derstanding of how host environments and behaviors contribute to inter-host differences in the gut microbiome. Birth-to-death longitudinal data, in combination with accompanying data on demographics, diet, and sociality, would allow us to trace microbiome trajectories across complete lifespans and connect these trajectories to markers of development and survival.

However, longitudinal data on gut microbiome dynamics are rare. Nearly all such research is conducted in human subjects and tends to focus on the first few years of life, from birth to a few years old, when samples are easiest to collect, and diet and environment are much more stable (Bergström et al., 2014; Bäckhed et al., 2015; Cong et al., 2016; Galazzo et al., 2020; Koenig et al., 2011; Yassour et al., 2016). While some research on adult human subjects exists, the research thus far is made up of small sample sizes (typically fewer than 30 subjects) with few samples per subject (typically less than 10) and limited to short periods of time (typically less than 1 year) (David et al., 2014b; Faith et al., 2013). Johnson et al. (2019), for example, is one of the best longitudinal studies to date; this study profiled the diet and gut microbiomes of 34 adults daily over a 17-day period and found that, despite diet choice ranging widely, gut microbiome macro and micro nutrient profiles did not change significantly over the study period - the taxonomic composition of the gut microbiome was highly individualized. Prospective data collection, in which researchers follow a cohort over time and measure health outcomes may be better suited to capture these microbial dynamics.

Prospective, longitudinal, population-based approaches that can connect microbiome composition and dynamics to health from natural populations can provide useful models of understanding the evolutionary drivers of the gut microbiome. Ren et al. (2017), for example, studied a wild population of red squirrels over a two-year period and found that environmental factors exerted a much stronger influence on the gut microbiome than host factors like age and sex did.

Rojas and Link to external site (2021) found that across a wild population of spotted hyenas, functional aspects of the gut microbiome are highly consistent despite high variability in taxonomic composition over time.

Thus, in order to explore the relationship between gut microbial composition and host behavior, aging, and development, I leveraged 13,476 gut microbiome compositional profiles collected from 479 known-age wild baboons (*Papio cynocephalus*) over 14 years. This birth-to-death longitudinal data was collected from a wild population of baboons monitored by the Amboseli Baboon Research Project (ABRP) and represents part of a dataset consisting of over 17,000 gut microbial profiles (Grieneisen et al., 2021). Accompanying these profiles is a wealth of information on the baboon hosts: the ABRP has been collecting continuous, individual-based data on numerous aspects of this population, including demographic, environmental, social, and genetic information since 1971 (Alberts and Altmann, 2012). This data on baboon life histories, behavior, and environments is key to correlating microbiome changes over time with aging and developmental outcomes.

Moreover, the Amboseli population is model system for many different aspects of human evolution. Like humans, baboons are omnivorous, terrestrial primates who evolved in the savannahs of East Africa (Melnick and Pearl, 1987). Due to these similarities, baboons and humans may have experienced shared selection pressures over the course of their evolution. Baboons experience well-defined life history stages that mirror human developmental stages, including an extended juvenile period prior to sexual maturation and predictable age-related changes in behavior and physiology in adulthood (Alberts and Altmann, 1995; Altmann et al., 2010; Charpentier et al., 2008; Onyango et al., 2013). Further, prior research in Amboseli has revealed several social and environmental conditions that affect these patterns of aging, including social dominance rank, early life adversity, and

the strength of supportive social bonds in adulthood (Alberts and Altmann, 1995; Altmann et al., 2010; Bronikowski et al., 2011; Charpentier et al., 2008; Lea et al., 2015; Tung et al., 2016). The Amboseli population is also a leading model in understanding the effects of early life adversity on aspects of host health, aging, and fitness (Anderson et al., 2021; Lea et al., 2015; Rosenbaum et al., 2020; Tung et al., 2016; Weibel et al., 2020; Zipple et al., 2019).

The goal of my dissertation is to characterize the relationship between primate hosts and their gut microbiomes across the host life course. To accomplish this objective, I used data from the Amboseli population to identify changes in response to early life experiences and age across the life course, understand what host and environmental factors predict these changes, and determine whether microbial changes are linked to host maturation and survival. Below, I summarize the goal and major findings of each chapter.

While initially proposed as separate chapters, **Chapter 2** is an unusually extensive journal article, in preparation for submission to *eLife*. In this Chapter, I determined if the gut microbiome changes predictably with age. To do this, I created a ”microbiome aging clock” by comparing a suite of machine learning approaches: an elastic net regression, a random forests regression, and a Gaussian process regression to predict host age based on over 9,500 microbiome features. Due to the nested nature of our microbial data, the random forest regression under-performed. The elastic net regression and Gaussian process regression performed similarly at first, but the Gaussian process regression included much more flexible parameters and resulted in the best performance overall after optimization. Using this Gaussian process regression based microbiome aging clock, I tested the behavioral predictors of metrics of microbial aging derived from the microbiome aging clock, and tested the developmental consequences of inter-individual differences in microbial aging metrics. Specifically, I developed the mi-

crobial age acceleration and pace of microbial aging metrics and tested if different aspects of the host's environment and behavior impact their rate of aging. I found that animals who were low-ranked exhibit faster rates of microbial aging relative to high-ranked peers. Next, I examined if inter-individual differences in aging had consequences on host development and found that animals who age faster do attain certain maturational milestones earlier. In sum, Chapter 2 demonstrates that the gut microbiome is a useful, noninvasive biomarker of host aging.

In **Chapter 3**, I investigated whether harsh early life experiences have long term impacts on the gut microbiome. Building on prior research investigating the impacts of early life adversity on fitness in the Amboseli population Tung et al. (2016), I found that there were compositional differences in animals that experienced specific types of early life adversities as compared to those who did not experience any early life adversity. These differences were primarily discernable in adulthood or later in life, but not during the juvenile period. Similarly, I calculated microbial stability and found that specific types of early life adversity were correlated decreased stability only after the juvenile period or over lifespan.

Altogether, my dissertation provides unprecedented insight into the link between microbiome dynamics and host health. My dissertation data contributes the largest longitudinal data set on vertebrate gut microbiome dynamics to date, spanning multiple life history stages for hundreds of individuals. In addition, my research contributes one of the first prospective, longitudinal, population studies to link microbiome data to health and fitness outcomes. This contribution will be significant because it will provide foundational knowledge for understanding what features define healthy microbiomes as well as how these features predict biodemographic markers of host health, including the timing of development, fertility, and survival.

CHAPTER 2

EVALUATING THE MAMMALIAN GUT MICROBIOME AS A MARKER OF BIOLOGICAL AGING

2.1 Abstract[1]

Vertebrate gut microbiomes are highly individualized, dynamic communities that change substantially throughout life and help the host adapt to its developmental stage. These age-related changes may serve as meaningful markers of host development and senescence, but the degree to which they do remains unknown. To fill this gap, we created a "microbiome aging clock" using a unique longitudinal data set spanning 13,563 16S rRNA gut microbial profiles from 479 individual baboons in the Amboseli ecosystem, Kenya over 14 years. The resulting clock predicted host chronological age with an R^2 of 0.488 and a median age prediction error of only 2 years, with males exhibiting faster microbiome aging than females. Using the results of our clock, we calculated sample-specific microbiome age acceleration and longitudinal pace of aging. We then used these metrics to identify potential social and environmental drivers of microbiome aging processes. We found striking effects of host social rank: in both males and females, low social rank was linked to low microbiome age acceleration (i.e. microbiota that were young for their host's chronological age). Further, in females only, low social rank across life was linked to a fast pace of gut microbiome aging. Microbiome age ac-

[1]This chapter is formatted for submission to the journal *eLife*. I am the lead author, and my coauthors include Roche K, Jansen D, Anderson J, Gilbert J, Barreiro L, Altmann J, Alberts SC, Blekhman R, Mukherjee S, Tung J, and Archie EA.

celeration also predicted age of first rank attainment in both sexes. Together, our results suggest powerful connections between host social status and microbiome aging processes.

2.2 Introduction

For most species, physical and cognitive declines with age are inevitable. These changes define biological aging, a phenomenon caused by changes in cellular, tissue-, and organ-level function, which in turn lead to rising disease and mortality risk with age (Komanduri et al., 2019; López-Otín et al., 2013). The pattern and pace of biological aging are different in each individual: an individual's age in years, sometimes called their "chronological age", often does not reflect the timing and pace of physical changes with age (Belsky et al., 2015; Gems and Partridge, 2013; Hayward et al., 2015; Nakamura and Miyao, 2007). Understanding what factors drive these individual differences in biological aging is essential to learn why some individuals age faster than others and may point towards therapies that prolong healthy life.

One under-appreciated marker of biological aging may lie in the composition and dynamics of the mammalian gut microbiome (Ghosh et al., 2020; Heintz and Mair, 2014). In humans and other mammals, gut microbiomes are diverse, dynamic ecosystems that help their hosts digest food, enhance the immune system, resist pathogens, and generate essential vitamins and amino acids (Clayton et al., 2018; Foster et al., 2017). Gut microbiomes are also sensitive to host physiology, environments, and behaviors, and many components of these traits change with age, including immunity, diet, hygiene practices, and social relationships (Bengmark, 1998; Claesson et al., 2011; Gerber, 2014; Palmer et al., 2007; Reese et al., 2020). As such, the gut microbiome has considerable potential to

reflect a wide range of age-related dynamics for their host. In support, the gut microbiome often exhibits predictable changes with age. For example, in humans, gut microbial diversity and stability rise after birth through weaning as the microbiome is assembled and the host's diet shifts to solid foods (Bergström et al., 2014; Bäckhed et al., 2005; Cong et al., 2016; Koenig et al., 2011; Yassour et al., 2016). During adulthood and old age, dynamic patterns are variable across people and populations, but several studies find age-related changes in diversity and taxonomic abundances (Biagi et al., 2016; Claesson et al., 2011; Mueller et al., 2006; Odamaki et al., 2016; Yatsunenko et al., 2012). Recent research conducted in chimpanzees indicates that metrics of the gut microbiome vary significantly with age but, in contrast to results from human studies, diversity was highest when animals were young and lower as animals aged (Reese et al., 2020).

Further, some age-related changes in the gut microbiome predict developmental trajectories and survival. In humans, undernourished children exhibit developmentally immature gut microbial communities that, when transplanted into mice, lead to impaired growth and altered bone morphology (Blanton et al., 2016; Gehrig et al., 2019; Smith et al., 2013; Subramanian et al., 2014). Experiments in short-lived animal models such as flies, mice, and killifish find that the gut microbiome mediates longevity (Clark et al., 2015; Langille et al., 2014; Smith et al., 2017; Tian et al., 2017). Despite these compelling results, we lack longitudinal data that trace microbiome aging trajectories across complete lifespans and connect these trajectories to known drivers of biological aging (e.g. social status and resource limitation) as well as markers of development and survival.

Here, we fill this gap using 13,476 gut microbiome compositional profiles, collected from 479 known-age, wild baboons (*Papio cynocephalus*) over 14 years (Figure 2.1). Our subjects are members of the well-studied baboon population in the Amboseli ecosystem, Kenya (Alberts and Altmann, 2012). Since 1971, the Am-

Figure 2.1. Longitudinal fecal samples collected for (A) female and (B) male baboons in the Amboseli ecosystem. Host age at the time of sample collection is indicated on the x-axis and individual baboons are represented on the y-axis. Each point represents a fecal sample collected from an individual baboon. The fill color of each point reflects the subject's sexual maturation state, with lighter colors reflecting samples collected prior to menarche for females and prior to testicular enlargement for males (for more information on how these milestones are measured, see Table A.8. Plot A contains 8,245 samples from 234 individual females. Plot B contains 5,231 samples from 197 individual males.

boseli Baboon Research Project has collected continuous, individual-based data on baboon life histories, behavior, and environments that are correlated with microbiome changes and predict health and mortality (Alberts et al., 2014; Archie et al., 2014a,b; Grieneisen et al., 2017; Ren et al., 2015; Tung et al., 2015). Baboons are a useful comparative system because they experience well-defined life history stages that mirror human developmental stages, including an extended juvenile period prior to sexual maturation and predictable age-related changes in behavior and physiology in adulthood (Alberts and Altmann, 1995; Altmann et al., 2010; Charpentier et al., 2008; Onyango et al., 2013). Further, prior research in Amboseli has revealed several social and environmental conditions that affect these patterns of aging, including social dominance rank, early life adversity, and the strength of supportive social bonds in adulthood (Alberts and Altmann, 1995; Altmann et al., 2010; Bronikowski et al., 2011; Charpentier et al., 2008; Gesquiere et al., 2011; Lea et al., 2015; Tung et al., 2016).

To identify age-related changes in the gut microbiome, we adopt methods from epigeneticists who use machine learning to build DNA methylation-based predictors of chronological age, also known as ”epigenetic clocks” (Anderson et al., 2021; Binder et al., 2018; Chen et al., 2016a; Horvath, 2013; Marioni et al., 2015). When applied to longitudinal microbiome data, the result is a ”microbiome aging clock” that may reveal young- or old-for-age microbiomes and individual pace of microbiome aging phenomena that may be driven by environmental and social conditions and can be linked to maturational milestones, health, and survival. To date, three microbiome clocks have been built for humans that predict sample-specific age with median error of 6 to 11 years (Cuesta-Zuluaga et al., 2019; Galkin et al., 2020; Huang et al., 2020). However, none of these studies have used longitudinal sampling to measure the pace of microbiome aging, test the social and environmental drivers of microbiome aging, or link interindividual variation in the pattern

and pace of microbiome aging to individual health and survival.

Our objectives were to integrate diverse microbiome features to build a microbiome aging clock and, ultimately, test whether the clock could serve as a marker of biological aging. We began by identifying which microbiome features change the most with host age. We then compared the performance of several machine learning algorithms for our microbiome aging clock, ultimately settling on a Gaussian process regression approach. We then evaluated the clock's performance for male and female baboons, tested which microbiome features were most important to its age predictions, and identified which microbiome features were most strongly correlated with host age. We next used the predicted microbiome ages from the microbiome aging clock (age_m) to test whether the baboons' social and environmental conditions predict two metrics of microbiome aging: (1) *microbiome age acceleration* (i.e. the difference between age_m and chronological age in a given sample) and (2) individual *pace of microbiome aging* (the slope of microbiome age acceleration across an animal's life, accounting for dominant population-level drivers of microbiome change). We hypothesized that harsh conditions (e.g. low rank, high adversity, social isolation) would be linked to gut microbial immaturity in early life and age acceleration in adulthood. To test our hypothesis, we used social/environmental predictors of aging focused on four variables with known links to health, reproduction and/or and survival in the Amboseli baboon population: low social dominance rank, the dry season, social isolation, and early life adversity (Archie et al., 2014a,b; Gesquiere et al., 2011; Lea et al., 2015, 2018; Tung et al., 2016). Alternatively, the gut microbiome's high level of inter-individual variation in taxonomic composition may make it difficult to identify consistent drivers of microbiome aging across the population. Finally, we test whether baboons with young-for-age gut microbiomes or slow paces of gut microbial development mature later and live longer compared to animals with old-for-age microbiomes. Establish-

ing whether the gut microbiome can serve as a noninvasive biomarker of biological aging will contribute to a comprehensive picture of the evolutionary role of the gut microbiome in an aging mammalian host.

2.3 Results

2.3.1 Many microbial features are predicted by host age.

We began by identifying age-related changes in microbiome taxonomic and community features. To do this, we characterized microbiome taxonomic composition using 16S rRNA gene sequencing-based gut microbiome profiles generated from 13,476 fecal samples, collected from 479 known-age individual baboons over 14 years (Figure 2.1; (Grieneisen et al., 2021)). The subjects included 215 males (5,231 samples, 26 mean samples per individual) and 264 females (8,245 samples, 35 mean samples per individual) whose ages ranged from 7 months to 26.5 years (Figure 2.1).

Our analyses focused on 9,575 microbiome features from these samples (Table A.1). These features included: (i) five metrics of alpha diversity; (ii) the top 10 principle components of microbiome compositional variation (which collectively explained 57% of the variation in microbiome community composition); (iii) centered log ratio transformed abundances of each microbial phyla (n = 30), family (n = 290), genus (n = 747) and individual ASVs (n = 8,493). For each feature, we tested whether it was predicted by host age, modeled using both linear and quadratic terms, while controlling for covariates known to explain variation in microbiome composition in our population as fixed effects, including: the season in which the sample was collected (wet or dry), the average maximum temperature for the month prior to sample collection, and the average rainfall total for the month prior to sample collection. Further, the social group the baboon belonged to on the

day the sample was collected, the identity of the baboon the sample was collected from, and the hydrological year (hydrological years are shifted to begin with the onset of the rains in November and conclude at the end of the dry season in October) at time of collection were modeled as random effects. Features present in at least 25% of samples were modeled using a Gaussian error distribution (1,619 features, including all the features in the alpha diversity, composition, phylum, family, genus categories as well as 537 ASVs). The remaining 7,956 ASVs present in less than 25% of samples were modeled using a binomial error distribution.

We found that 757 of the 1619 features modeled with a Gaussian error distribution exhibited significant linear or quadratic relationships with age (Figure 2.2; FDR threshold = 0.05). For all feature types except alpha diversity, a larger proportion of features exhibited significant linear relationships with age compared to quadratic relationships with age (Figure 2.2). In terms of community features, every alpha diversity metric except richness changed significantly with age and exhibited a convex shape. (Figure 2.3, Figure A.1). Seven of the ten principal components (PCs) of microbiome composition also changed significantly with age, with four of the seven PCs exhibiting a solely linear relationship with age. Specifically, PC1 and PC2, which together represent 30.8% of the variation in the data, exhibited a negative linear relationship with age (Figure A.1). PC4 exhibited the only positive linear relationship with age. Principal components five and six exhibited a concave relationship with age, and principal component eight showed a convex relationship with age.

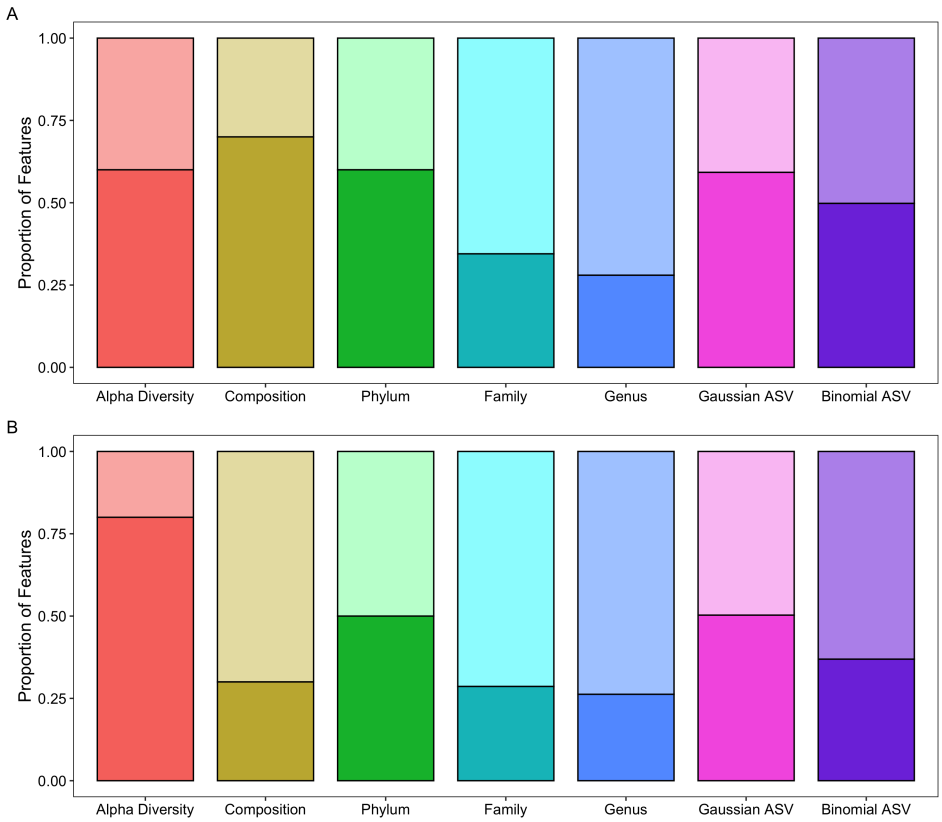

Figure 2.2. The proportion of microbiome features that were significantly predicted by host age, where age was modeled as (A) a linear term, or (B) a quadratic term in a linear mixed model (significance is FDR corrected using the Benjamini-Hochberg procedure with a threshold of 0.05). All features were modeled using Gaussian error distributions, except the features labeled 'binomial ASVs', which were modeled using a binomial error distribution (see Section 2.5).

As animals aged, only three microbial phyla exhibited significantly higher abundances with age: Kiritimatiellaeota and Chlamydiae increased linearly and Firmicutes increased in a concave relationship with age (Table A.2). In contrast, 20 phyla decreased significantly with age, with Cyanobacteria, Elusimicrobia, Epsilonbacteraeota exhibiting the strongest convex relationships with age and Actinobac-

teria exhibiting the strongest negative linear relationship with age (Table A.2). Similarly, of the 139 families with significant associations with age, 30.2% (42 of 139) showed some positive relationship with age the families: *Clostridiaceae*, *Peptostreptococcaceae*, and *Enterobacteriaceae* and many other families in the order Clostridiales exhibited concave relationships with age, but *Campylobacteraceae*, *Elusimicrobiaceae*, and an uncharacterized family within order Gastranaerophilales exhibited convex relationships with age (Table A.2). 36.8% of the 315 significant genera (116 of 315) had a positive relationship with age, with uncharacterized genera in *Clostridiaceae* and *Enterobacteriaceae* and genus *Romboutsia* exhibiting concave relationships and uncharacterized genera in Firmicutes, uncharacterized genus in *Peptostreptococcaceae*, and genus *Ruminococcaceae UCG-011* showing the strongest positive linear relationships with age (Table A.2). Conversely, *Camplylobacter*, *Elusimicrobium* , and an uncharacterized genus within order Gastranaerophilales all exhibited convex relationships with age and *Prevotella*, *Catenibacterium*, and uncharacterized genus in family *Veillonellaceae*, all declined linearly in abundance with age (Table A.2).

Figure 2.3. Linear associations between mean-centered age and community metrics or the 50 taxa whose abundances exhibited the strongest effect sizes. Plot shows the 50 largest linear estimates for taxa that had significant associations with age. Points are colored by category of feature, and category of feature is also indicated in parentheses, where D is for diversity metrics, C for position, P for phylum, F for family, G for genus, and ASV for ASV. Features that also had a significant quadratic age term are indicated by a *.

2.3.2 A Gaussian process model-based microbiome clock accurately predicts chronological age in wild baboons.

We next turned our attention to building our microbiome aging clock. In developing the clock, we compared the performance of elastic net, random forests, and Gaussian process (GP) regression approaches and found that the most accurate predictor of age was produced by a GP model with a kernel customized to account for heteroscedasticity (Figure 2.4; Figure A.6; Table A.4; see Appendix A.1.2 for details). This GP model predicted chronological age (age_c), with an adjusted R^2 of 0.488 and a median error of 1.96 years across all individuals and samples (Figure 2.4A, Table 2.1). As has been observed in previous aging clocks (Anderson et al., 2021; Galkin et al., 2020; Horvath, 2013), microbial age estimates (age_m) were compressed relative to the 1:1 line, leading the model to systematically over-predict the ages of young individuals and under-predict the ages of old individuals (Figure 2.4).

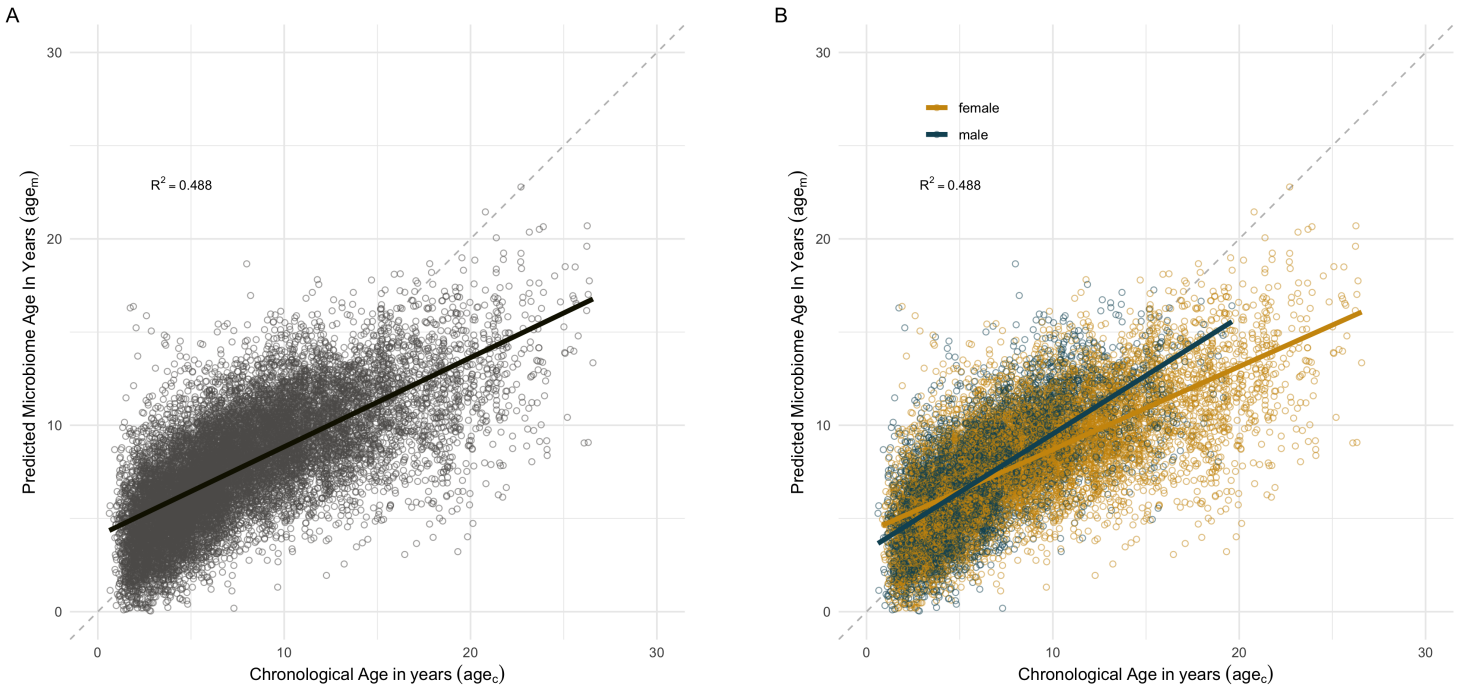

Figure 2.4. A microbiome clock of aging in wild baboons. Plots show predicted microbiome age in years (age_m) from a Gaussian process regression model, relative to each baboon's true, chronological age in years (age_c) at the time of sample collection. (A) Shows a linear fit for all subjects in the model, and (B) shows separate linear fits for each sex. On each plot, the dashed lines indicate a 1-to-1 relationship between age_c and age_m.

TABLE 2.1

A COMPARISON OF GAUSSIAN PROCESS REGRESSION MODELS USING MICROBIOME COMPOSITION TO PREDICT BABOON AGE FOR ALL BABOONS, FEMALES ONLY, AND MALES ONLY.

Subset	**Sample Size**	**R^2**	**Pearson's R**	**Median Error (years)**
All Animals	13476	0.488	0.698	1.962
Females Only	8245	0.489	0.699	2.15
Males Only	5231	0.5	0.707	1.706

NOTE: Model accuracy was determined by regressing the sample's age_c against age_m and determining the correlation coefficient R^2, Pearson's correlation coefficient, and median error, or the median absolute difference between age_c and age_m (Horvath, 2013).

When we subset our age_m estimates by sex, we found that the microbiome aging clock was slightly more accurate for males than females (Figure 2.4B, Table 2.1). In support, we found that the adjusted R^2 for the correlation between age_c and age_m for males was 0.50, with a median error, or median absolute difference between age_c and age_m, of 1.71 years, as compared to an adjusted R^2 of 0.489 and median error of 2.15 years for female baboons (Table 2.1). Male baboons exhibit faster gut microbial aging than females (Figure 2.4B, chronological age by sex interaction: β = 0.18, p $<$0.001, Table 2.2). Specifically, across the lifespan, males show a 1.4 fold-higher rate of change in age_m as a function of age_c compared to females (relationship between age_c and age_m in males only: β = 0.63, p $<$0.001; relationship between age_c and age_m in females only: β = 0.45, p $<$0.001; Table A.5). Interestingly, this effect is only present after maturity: when we subset the model results to samples collected prior to the median age sexual maturity

(age 5.4 years for testicular enlargement in males and age 4.5 years for menarche in females (Onyango et al., 2013) there was no significant interaction effect between sex and age (age_c by sex interaction prior to median age of maturity: β = -0.09, p = 0.203; age_c by sex interaction after median age of maturity: β = 0.15, p $<$0.001; Table 2.2). After maturity, males had a 1.4 fold-higher rate of change than females (relationship between age_c and age_m in males only: β = 0.53, p $<$0.001; relationship between age_c and age_m in females only: β = 0.38, p $<$0.001; Table A.5).

Overall, the microbiome clock was moderately successful in predicting baboon age compared to other markers of aging in the Amboseli baboons. age_m performed favorably compared to female early- or late-aged body mass index (BMI), male late-aged BMI, blood cell composition by flow cytometry, and differential white blood cell counts from blood smears (Table 2.3, (Anderson et al., 2021)). However, the microbiome clock was less accurate than dentine exposure (males, females respectively: adjusted R^2 = 0.73, 0.85; median error = 1.11 years, 1.12 years; Table 2.3) and a recent epigenetic clock (males, females respectively: adjusted R^2 = 0.74, 0.60; median error = 0.85 years, 1.62 years; Table 2.3) (Anderson et al., 2021).

2.3.3 Phyla Firmicutes and Bacteroidetes are important for accurate age predictions.

We hypothesized that including or removing microbial features that were age predictive would correlate with overall model performance. To test this hypothesis, we first took a leave-one-out approach: we removed a taxon and its related features, transformed the remaining features as if the feature was not part of the dataset, ran the Gaussian process regression, and assessed model performance as before. For example, if we removed phylum Actinobacteria, we removed the

TABLE 2.2

LINEAR MIXED MODEL RESULTS ILLUSTRATING AGE BY SEX INTERACTIONS IN AGE_M

Timeframe	**n samples**	**Predictor**	**Estimate**	**SE**	**p-value**
Prior Maturity	4362	Intercept	2.829	0.176	$<$0.001
Prior Maturity	4362	Chronological Age	0.710	0.056	$<$0.001
Prior Maturity	4362	Sex	0.257	0.229	0.263
Prior Maturity	4362	Age*Sex Interaction	-0.087	0.068	0.203
Post Maturity	9114	Intercept	5.131	0.073	$<$0.001
Post Maturity	9114	Chronological Age	0.378	0.006	$<$0.001
Post Maturity	9114	Sex	-0.879	0.160	$<$0.001
Post Maturity	9114	Age*Sex Interaction	0.154	0.017	$<$0.001
Lifespan	13476	Intercept	4.201	0.050	$<$0.001
Lifespan	13476	Chronological Age	0.449	0.005	$<$0.001
Lifespan	13476	Sex	-0.970	0.083	$<$0.001
Lifespan	13476	Age*Sex Interaction	0.182	0.010	$<$0.001

NOTE: Data were subset to three timeframes: prior to maturity, post maturity, and over the entire lifespan. In each of those subsets, age_m was our response variable, as predicted by the variables in the predictor column.

TABLE 2.3

TABLE COMPARING THE MICROBIOME AGING MODEL IN THIS PAPER TO OTHER METRICS OF AGING IN THE AMBOSELI BABOON POPULATION.

Measure	**Sex**	**n samples**	**individuals**	**Adjusted R^2**	**Median Error**
Adult BMI	Females	154	154	0.3	3.25
Adult BMI	Males	139	139	0.21	1.18
Blood Smear	Females	56	56	0.04	2
Blood Smear	Males	77	77	0.04	2
Dentine Exposure	Females	204	34	0.85	1.12
Dentine Exposure	Males	234	39	0.73	1.11
Epigenetic Clock	Females	142	126	0.6	1.62
Epigenetic Clock	Males	135	121	0.74	0.85
Flow Cytometry	Females	26	26	0	4.27
Flow Cytometry	Males	35	35	0.24	2.66
Immature BMI	Females	154	154	0.33	2.3
Immature BMI	Males	139	139	0.81	1.43
Microbiome Clock	Females	8245	234	0.49	2.15
Microbiome Clock	Males	5231	197	0.5	1.71

family, genera, and ASVs that mapped to that phylum and ran the model.

Of the 1081 non-ASV features tested in this analysis, nine features changed the Gaussian process regression's R^2 by more than half a percent when removed from the model (Figure 2.5). Specifically, the removal of the phylum Firmicutes represented the largest drop in R^2, reducing it from 47.8% to 42.4%. The removal of phylum Bacteroidetes was the next most important feature for model performance, reducing performance to 45.3%. Within Firmicutes, the removal of families *Veillonellaceae* and *Ruminococcaceae* hurt model perfomance by nearly 1% and 1.5%, respectively. In Bacteroidetes, the removal of family *Prevotellaceae*, and specifically an uncharacterized genus within *Prevotellaceae*, hurt model performance by 1.3% and 0.6% respectively. For results from all 1081 non ASV taxa, see Table A.6.

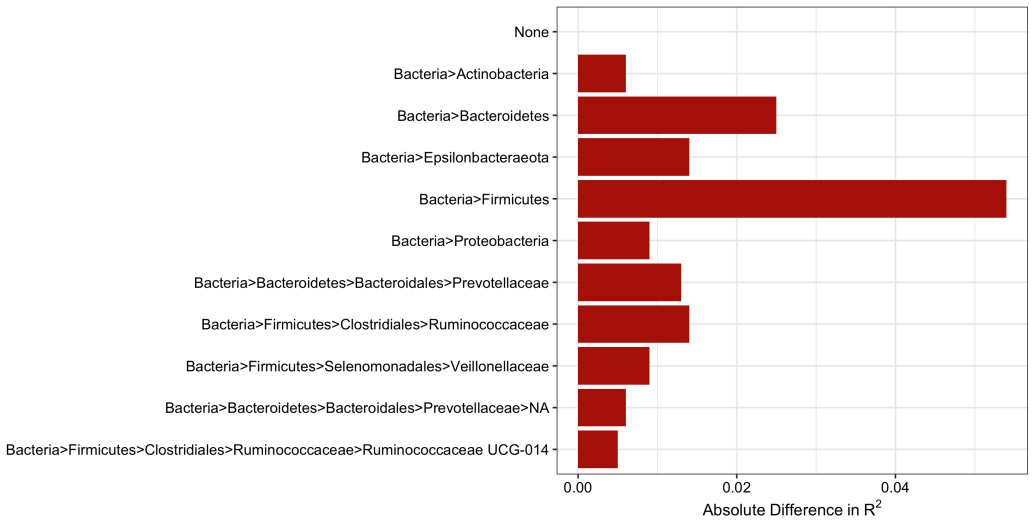

Figure 2.5. Microbiome features that changed the Gaussian process regression's R^2 predicting host age by more than half a percent when removed from the model.

If we compare the two methods of analyzing feature importance, there's little correlation between the difference in R^2 and the linear estimate obtained from the linear mixed model regressing age on the feature of interest (Pearson's correlation: 0.06, Figure A.7). This suggests that while the individual features may appear to change significantly with age, there may be interactions between features that can be assessed using more holistic methods like machine learning algorithms.

2.3.4 Lower ranked animals have young-for-age microbiomes.

While the microbiome clock produced an accurate age_m for the population as a whole, there was considerable variation in age_m estimates across samples (Figure 2.4), suggesting that some subjects had microbiomes that were young- or old-for age. To test whether these deviations were correlated with known predictors of health, reproduction, or mortality risk in Amboseli, we calculated two metrics of aging derived from the microbiome aging clock: the microbiome age acceleration of individual samples, defined as the difference between each sample's age_m and age_c (Figure 2.6A), and the pace of microbiome aging, which reflects longitudinal increase or decrease in individual microbiome age, controlling for chronological age (to account for model compression), and the dominant population-level drivers of microbiome composition in the Amboseli population, such as season, weather, and social group membership (Figure 2.6B) (Ren et al., 2015; Tung et al., 2015).

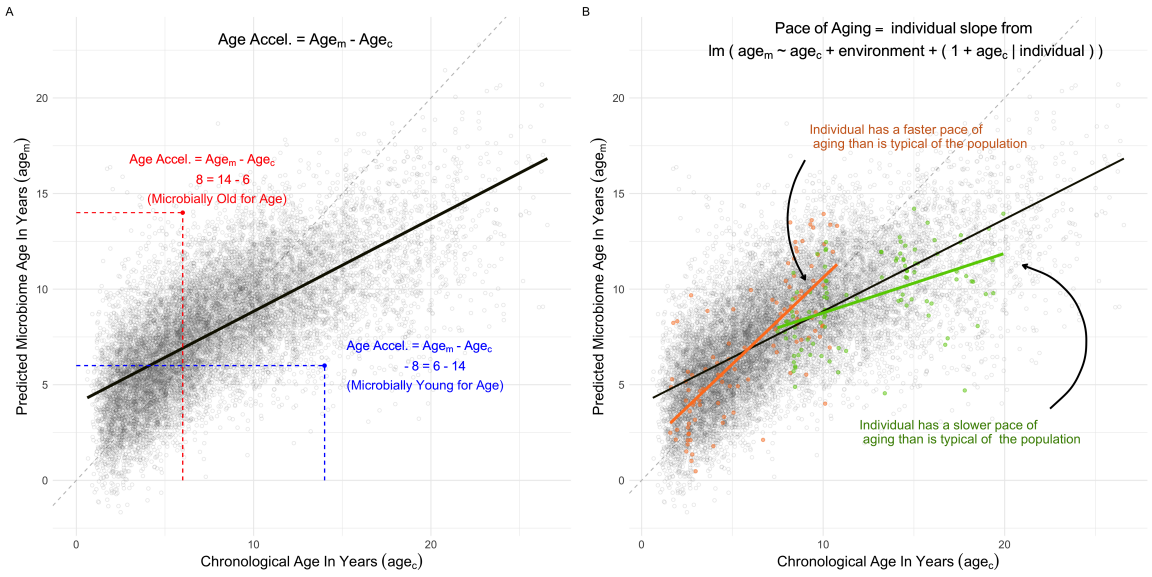

Figure 2.6. Plots illustrating the measurement of (A) sample specific microbiome age acceleration and (B) pace of microbiome aging in individual baboons. (A) Age acceleration is calculated for each microbiome sample as the difference between age_m and age_c. Samples with positive values of age acceleration (e.g. the red sample) have older predicted microbiome age estimates than their true chronological age and would be considered microbially old-for-age. Samples with negative values of age acceleration (e.g. the blue sample) are microbially young-for-age. (B) Pace of microbiome aging reflects longitudinal change in microbiome age acceleration in individuals, controlling for chronological age and environmental variables known to explain variation in gut microbiome composition in Amboseli (Björk et al.; Ren et al., 2015; Tung et al., 2015). Specifically, microbiome pace of aging for a given individual was calculated as the individual's random slope, controlling for the subject's chronological age on the day of sample collection, season on the day of sample collection, average maximum temperature the month prior to sample collection, and total rainfall the month prior to sample collection, with random intercepts for the hydrological year of sample collection and the social group membership on the day of sample collection. High values of microbiome pace of aging above the population median reflect individuals who have steep slopes and therefore fast paces of microbiome aging.

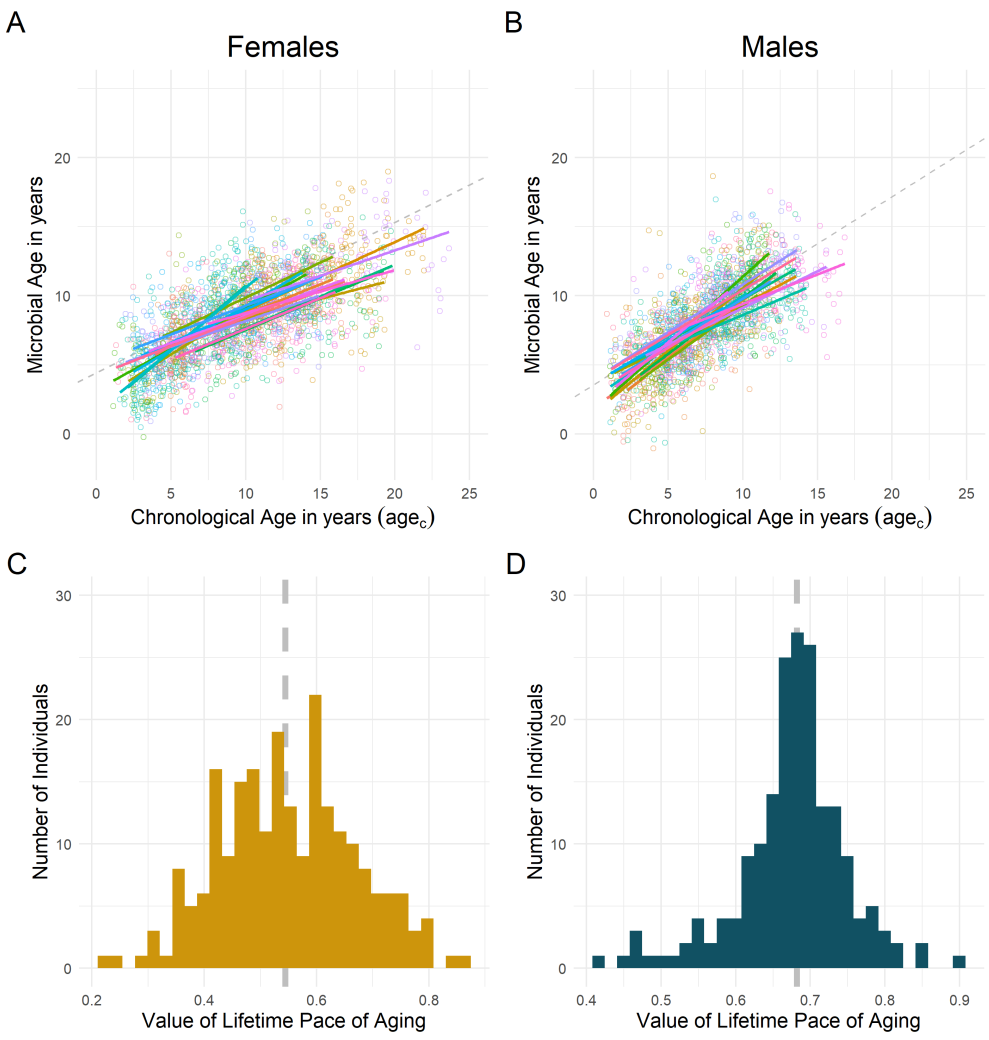

Figure 2.7. Pace of microbiome aging in female and male baboons. Plots A and B depict the pace of microbiome aging in the 20 best-sampled (A) females and (B) males (average number of samples for the 20 best-sampled females = 105 samples; range = 87-135 samples; average number of samples for the 20 best-sampled males = 89 samples; range = 61-135 samples). The plots in C and D are histograms depicting the distribution of pace of microbiome aging for (C) all females (N = 225) and (D) males (N = 187) across the life course. Pace of aging was more variable in females as compared to males (standard deviation in lifetime slope for females = 0.12; standard deviation in lifetime slope for = 0.07). Grey dotted line indicates the median slope of the population pictured.

Individual baboons varied considerably in microbiome age acceleration and pace of microbiome aging. For instance, in mixed effects models, individual identity explained 50% to 25% of the variance in age acceleration for females and males respectively over the course of their lives (Table A.19). Further, some individuals' microbiomes exhibited faster or slower age acceleration, becoming progressively older- or younger-for age over the course of their life, indicating variation in the pace of microbiome aging (Figure 2.7A-B). Consistent with the observed compression in our GP model's age estimates, the mean pace of aging was 0.549 for females and 0.675 for males, indicating that females gain approximately half of a "microbiome-year", and males gain two thirds of a "microbiome-year" per 1-year increase in chronological age. The variation in pace of aging was wider in females than males (standard deviation in females: 0.122; males: 0.073; Figure 2.7C-D).

We first investigated the effects of social status (i.e., dominance rank) on microbiome aging. In baboon societies, individuals are ranked in strict, linear, sex-specific hierarchies, and in females, these hierarchies are nepotistic with few opportunities for social mobility (Melnick and Pearl, 1987). Low-ranking females have low priority of access to food resources and exhibit later maturation and slower reproduction than high-ranking females (Altmann and Alberts, 2005; Charpentier et al., 2008; Gesquiere et al., 2018). We therefore expected that low social status in females would be linked to (i) high age acceleration (i.e. old-for-age gut microbiomes), (ii) slow pace of aging prior to maturity and (iii) fast pace of aging in adulthood (in all analyses, the signs of coefficients are adjusted such that positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals). However, across the life course, we found that low-ranking females exhibited low microbial age acceleration (i.e. young-for-age microbiomes; β = 1.745, p $<$0.001; Table 2.4 and Figure 2.8A) and a fast pace of gut microbial aging compared to high-ranking females (β = - 0.181, p $<$0.001; Table 2.4, Figure

2.8C). These effects may be a consequence of different effects of rank on pace of aging before and after maturity; consistent with the idea that low-ranking females mature more slowly than high-ranking females, females with lower maternal rank at birth were microbially young for age and have a slower pace of microbial aging prior to the median age of menarche compared to females with higher maternal rank (age acceleration: β = 0.422, p = 0.035, Table A.12; pace of aging: β = 0.088, p = 0.005, Table A.14). After the median age of menarche, however, average proportional rank is no longer a significant predictor of age acceleration or pace of aging (age acceleration: β = 0.383, p = 0.256, Table A.15; pace of aging: β = -0.033, p = 0.070, Table A.17).

TABLE 2.4

SIGNIFICANT SOCIO-ENVIRONMENTAL PREDICTORS OF LIFETIME MICROBIOME METRICS OF AGING.

Sex	**Microbial Metric**	**Fixed Effect**	**Estimate**	**p-value**	**Interpretation**
Females	Age Acceleration	Chronological Age	-0.55	$<<$0.001	All model estimates are compressed compared to chronological age
Females	Age Acceleration	Season	-0.18	0.021	Samples taken from the dry season are microbially old-for-age
Females	Age Acceleration	Proportional rank	1.745	$<<$0.001	Lower ranked females are microbially young for age.
Females	Pace of Aging	Average proportional rank	-0.181	$<<$0.001	Lower ranked females have a faster pace of aging than higher ranked females.
Males	Age Acceleration	Chronological age	-0.404	$<<$0.001	All model estimates are compressed compared to chronological age
Males	Age Acceleration	Ordinal rank	0.033	$<<$0.001	Lower ranked males are microbially young for age.
Males	Age Acceleration	Early adversity: Born during a drought	-0.451	0.021	Males born during a drought are microbially young for age
Males	Age Acceleration	Early adversity: Large group size at birth	0.471	0.033	Males born into a group with many individuals are microbially old for age
Males	Age Acceleration	Early adversity: Low maternal social connectedness	-0.395	0.006	Males with a socially isolated mother are microbially young for age

NOTE: Social and environmental factors predicting microbiome age acceleration and pace of aging in females and males across the life course. For females, age acceleration was calculated using 6,743 samples from 192 animals and pace of aging was calculated using 188 females. For males, age acceleration was calculated using 4,355 samples from 168 animals and pace of aging was calculated using 161 males. There were no significant predictors of males pace of aging model. Model results reflect the best-supported model for each sex and aging using an information theoretic approach. In males, rank coefficients were multiplied by -1 for easier interpretation. Full models are shown in Tables A.18, A.19, and A.20.

In contrast to female rank, male rank is determined by strength and fighting ability. Thus, rank changes considerably with age: males achieve their highest rank in young adulthood and their rank declines in middle and old age (Alberts et al., 2003). High-ranking males experience high energetic costs of mating effort and have altered immune responses compared to low-ranking males (Anderson et al., 2021; Gesquiere et al., 2011). Consistent with these energetic costs, we found that low rank in males was associated with lower age acceleration, both across the lifespan and after maturity (lifespan: β = 0.033, p $<$0.001, Table A.20, Figure 2.8B; after median age of maturity: β = 0.044, p $<$0.001, Table A.15). However, rank did not explain variation in age-acceleration prior to maturity: low maternal rank was not associated with gut microbial immaturity in males. This indicates that the energetic costs associated with high rank also result in higher age acceleration. There were also no effects of average rank on pace of microbiome aging in males over lifespan or prior to maturity (see Tables A.14 and A.20), and a very small effect of rank post maturity (β = - 0.003, p = 0.050, Table A.17, Figure 2.8D). As rank changes considerably with age in males, these results were unsurprising: age acceleration is the more flexible measure that can account for rank changes, while pace of aging averages over much of that variation in rank.

We next tested the effect of adverse events in early life, or early life adversity, on microbiome aging. Prior research in Amboseli has identified six sources of adversity (Table 2.5) whose cumulative effects, and sometimes individual effects, lead to high mortality and lower fitness in adulthood (Lea et al., 2015; Tung et al., 2016; Zipple et al., 2019). These six sources included maternal loss prior to age 4, experiencing drought in the first year of life, being born into an especially large social group, the presence of an especially close-in-age competing younger sibling, and having a low-ranking or socially isolated mother (Table 2.5). We also tested the effect these sources may have in summation as ”cumulative early life adver-

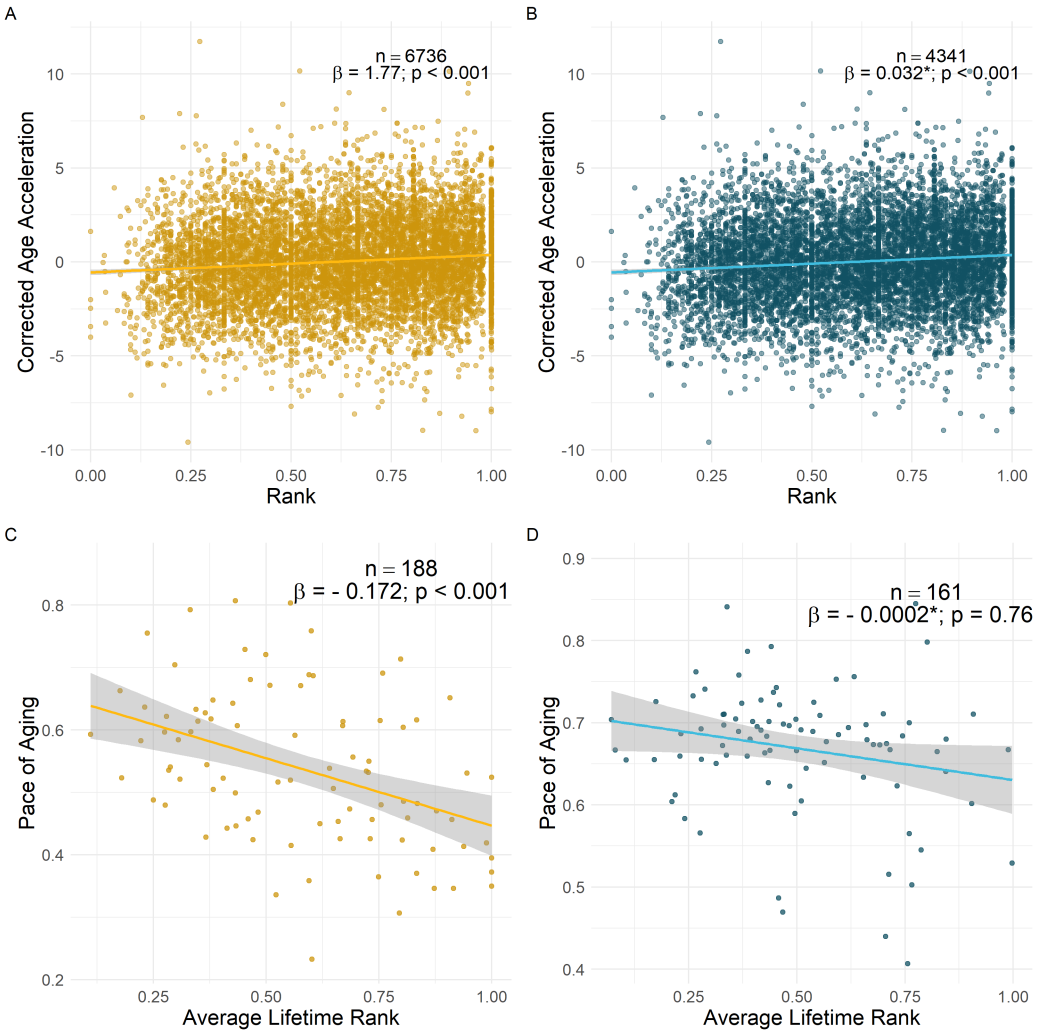

Figure 2.8. Rank predicts lifetime microbial aging in both sexes. Plots with yellow points (on the left; A,C) show microbial metrics of aging in females and plots with blue points (on the right; B,D) show microbial metrics of aging in males. Corrected age acceleration was corrected represents the residuals of the relationship between age m and age c . For side by side comparison, both sexes are shown here with proportional rank values, which are derived from ordinal rank assessments. High ranked individuals are ranked closer to 1 and low ranked individuals are ranked closer to 0. However, males were modeled using ordinal rank values, as reflected by the * in the model output depicted.

TABLE 2.5

DESCRIPTION OF SOURCES OF EARLY LIFE ADVERSITY IN THE AMBOSELI POPULATION

Early life experience	**Description of experience**
Maternal loss	Individual's mother died before the individual reached age 4. While infants are weaned prior to age 2, mothers teach their offspring how to forage and provide social connections.
Born during a drought	During the individual's first year of life, rainfall did not exceed 200 mm. Droughts are associated with nutrient scarcity.
Large group size at birth	Individual was born into a group in the population's highest quartile of group size. Larger groups may be associated with increased resource limitations.
Competing sibling	Individual had a younger sibling born with an age gap of less than 1.5 years. A competing sibling may cause the mother to avert resources away from the focal animal towards their new, more vulnerable sibling.
Low maternal rank	Individual's mother had a social rank in the population's lowest quartile of female social rank. Maternal rank also dictates preferred resource availability and social connections.
Low maternal social connectedness	Individual's born to a mother with a social connectedness rating in the population's lowest quartile of female social connectedness. Offspring social networks are largely based on their mother's network.

sity." We expected that (increased) instances of early life adversity would be linked to low age acceleration and slow pace of aging prior to maturity, but fast pace of aging in adulthood.

Contrary to these predictions, cumulative early life adversity was never an important predictor of microbiome aging in females. However, we did find that specific sources of early life adversity were linked to gut microbial immaturity in the juvenile period. Prior to sexual maturity, females who experienced maternal loss and low maternal rank exhibited young-for-age gut microbiota (maternal loss: β = - 0.360, p = 0.049; low maternal rank: β = 0.422, p = 0.035 Table A.12). However, we found no effects of sources of early life adversity on gut microbial age acceleration

or pace of aging in adulthood for females (Tables A.15 and Table A.17).

In males, the impacts of early life adversity were more complex and spanned the entire life course. Cumulative early life adversity was only an important predictor of pace of aging: prior to maturity, males showed a faster pace of aging with increasing cumulative adversity (β = 0.013, p = 0.036, Table A.14), but after maturity, males with higher cumulative adversity exhibited slower microbiome aging. (β = - 0.022, p = 0.014, Table A.17). With respect to specific sources of early life adversity, the most pervasive effects were linked to experiencing drought in early life. Across lifespan, drought was linked to young-for-age microbiota across the lifespan (β = - 0.451, p = 0.021, Table 2.4) and fast pace of aging prior to sexual maturity (β = 0.040, p = 0.018, Table A.14). Low maternal social isolation at birth was the next most pervasive source of early life adversity. Like drought, low maternal social connection was linked to microbiome ages that were 5 months younger for age across lifespan (β = - 0.395, p = 0.006, Table A.20), with the strongest effects in adulthood (β = - 0.599, p = 0.009, Table A.15). Other sources of early life adversity were less consistent. High group size at the time of birth resulted in males that were 5.4 months older for age across the entire life course than those born in smaller groups (β = 0.471, p = 0.033, Table A.20). The last important but inconsistent source of early life adversity was the birth of a competing sibling; in males, this source of adversity resulted in a slower pace of aging, but this was only perceivable in adulthood (β = - 0.050, p = 0.012, Table A.17).

Next we tested the effects of season. The Amboseli ecosystem is a semi-arid savannah with highly seasonal rainfall. The dry season lasts 5 months and is linked to nutritional hardship; hence we predicted that samples in the dry season would be associated with accelerated aging (we could not test effects of season on pace of aging because all same-aged animals experience the same number of dry seasons). In support, we found that, for females, but not males, samples collected

in the dry season exhibited small, but significant evidence for age acceleration such that samples from females were 2 months younger for age if they were collected in the dry season as compared to the wet season (β = - -0.180, p = 0.021, 2.4). This effect was driven by samples collected during adulthood; we observed no significant effects of season on age acceleration in prior to maturity (prior to median age of maturity: β = - 0.112, p = 0.440, Table A.12; post median age of maturity: β = - 0.223, p = 0.015, Table A.15). Season did not significantly predict microbiome age acceleration in males.

Lastly, for adult females only, we tested whether social isolation leads to age acceleration and fast pace of aging. Social connectedness data for males was not included, as males are more transient, immigrating between groups in order to attain higher ranks, and thus form fewer strong social bonds. Indeed, prior research in Amboseli finds that social isolation is linked to short lifespans in adult females (Archie et al., 2014b). In contrast with our hypothesis, social connectedness was not an important predictor of female age acceleration or pace of aging (age acceleration: β = - 0.057, p = 0.297, Table A.15; pace of aging: β = - 0.009, p = 0.108, Table A.17).

2.3.5 Microbiome age acceleration predicted age of first rank attainment in both sexes.

We next tested whether variation in microbiome age acceleration and pace of aging predicted the timing of maturational milestones and longevity. For females, these milestones included the age at which females attained their first adult rank, menarche, and the age at which they gave birth to their first live offspring. For males, these milestones included the age at which males attained testicular enlargement, dispersal from their natal social group, and attained their adult rank. We also tested if age acceleration and pace of aging predicted juvenile survival to age

4 in both sexes and adult survival in females. We hypothesized that animals that were microbially old for age or exhibited a faster pace of aging would reach maturational milestones earlier and exhibit shorter adult lifespans than those that were young for age or exhibiting a slower pace of aging. For many subjects, we had multiple microbiome observations both before and after maturational milestones (Tables A.10 and A.11), which allowed us to test whether patterns of microbiome aging prior to the milestone versus microbiome aging across the lifespan (including samples after the milestone) was more predictive of maturational timing. We expected that samples collected before the milestone would be more predictive of maturational timing than those collected from across the entire lifespan.

Microbial metrics of aging predicted some developmental milestones, but did not predict juvenile or adult survival. Specifically, age acceleration predicted the timing of rank attainment in both sexes such that individuals with young-for-age microbiomes attained their adult rank sooner than those with old-for-age microbiomes (females: β = 0.370, hazard ratio = 1.447, p = 0.024, Figure 2.9A, Table 2.6; males: β = 0.406, hazard ratio = 1.501, p = 0.025, Figure 2.9B, Table 2.6). While age acceleration was not predictive of any other milestones, pace of aging predicted the timing of menarche and male dispersal. Specifically, females who exhibited a faster pace of aging reached sexual maturation sooner than females with slow pace of aging (Figure 2.10A, β = 4.475, hazard ratio = 87.808, p = 0.045, Table A.21)), but males who exhibited a slower pace of aging dispersed from their natal group later than males with a faster pace of aging (Figure 2.10B, β = -4.038, hazard ratio = 0.018, p = 0.037, Table A.31). While the female results support our hypothesis that animals exhibiting a faster pace of aging will develop sooner than those who exhibit a slower pace of aging, the males show the opposite: animals that exhibit a slower pace of aging will disperse from their natal group sooner. Results for other developmental milestones and survival are available as Appendix

Tables A.21-A.35.

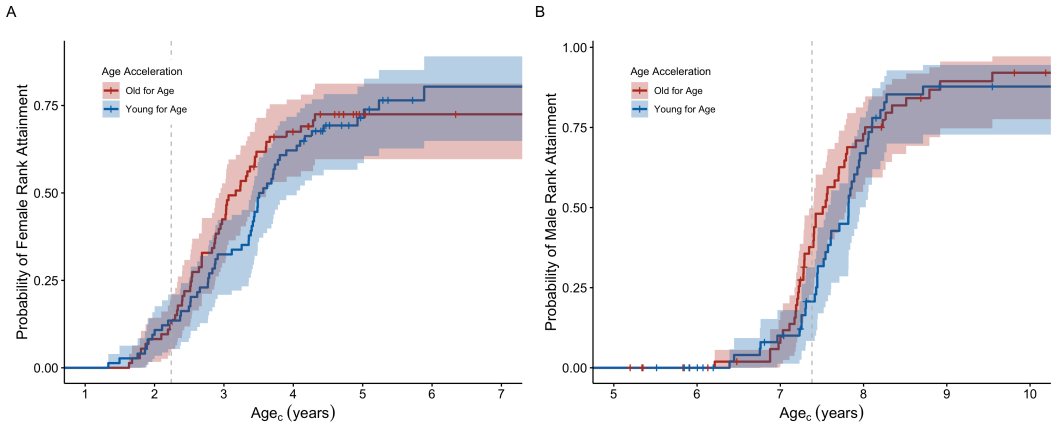

Figure 2.9. Microbiome age acceleration predicts the timing of adult rank attainment in both sexes. The plot in (A) shows the probability of rank attainment as a function of age in females and (B) shows the same relationships for males. The red and blue lines represent animals whose age acceleration was above (red) or below (blue) the median for subjects in this analysis. Grey dotted lines indicate the median age of the milestone occurring in the population (Charpentier et al., 2008).

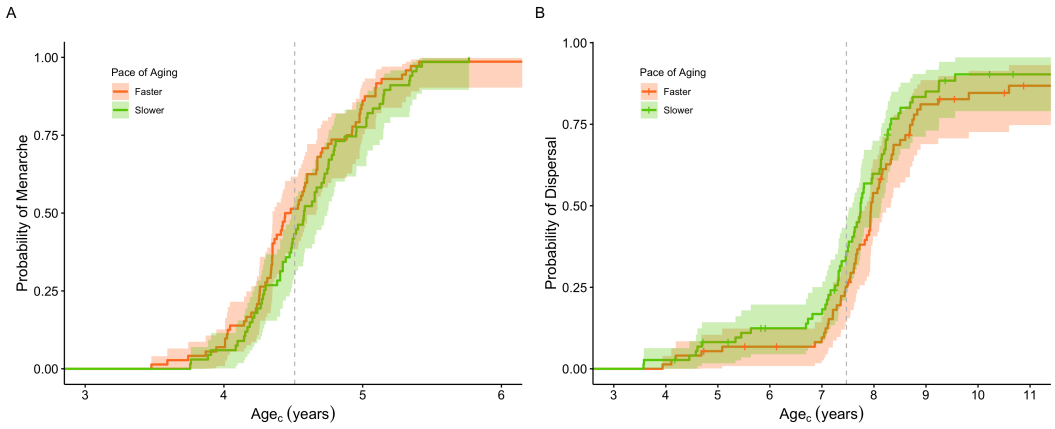

Figure 2.10. Pace of aging predicts the timing of menarche in female baboons and natal dispersal in males. The plot in (A) probability of menarche as a function of age for females, while (B) shows the probability of natal dispersal as a function of age in males. The orange and green lines represent animals whose pace of microbiome aging was above (orange) or below (green) the median for subjects in this analysis. Grey dotted lines indicate the median age of the milestone occurring in the population (Charpentier et al., 2008).

TABLE 2.6

PREDICTING AGE AT RANK ATTAINMENT PRIOR TO MILESTONE

Sex	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Females	Age acceleration averaged prior to milestone	0.37	1.447	1.049 - 1.996	0.024	Animals who are old for age will attain the milestone sooner.
Females	Pace of aging prior to milestone	-2.516	0.081	0.001 - 9.816	0.304	
Females	Mean chronological age of samples	-0.381	0.683	0.468 - 0.997	0.048	Animals with a higher mean chronological age will attain the milestone later.
Females	Mother in same group during approximate timing of milestone	-0.297	0.743	0.435 - 1.268	0.276	
Females	Average number of maternal sisters in group prior to milestone	0.115	1.122	0.955 - 1.319	0.162	Animals with a higher number of maternal sisters in group will attain the milestone sooner.
Females	Low maternal rank at birth	-1.329	0.265	0.143 - 0.489	0	Animals born to mothers with lower ranks will attain the milestone later.
Females	Average number of adult females in group prior to milestone	0.055	1.056	1.015 - 1.1	0.008	Animals in groups with more adult females will attain the milestone sooner.
Females	Average rainfall prior to milestone	0	1	0.996 - 1.004	0.981	

TABLE 2.6 CONTINUED FROM PREVIOUS PAGE

Sex	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Females	Hybridization score	-0.673	0.51	0.199 - 1.31	0.162	
Males	Age acceleration averaged prior to milestone	0.406	1.501	1.051 - 2.142	0.025	Animals that are microbially old for age will attain the milestone sooner.
Males	Pace of aging prior to milestone	-3.527	0.029	0 - 2.527	0.121	
Males	Mean chronological age of samples	-0.052	0.95	0.822 - 1.097	0.484	
Males	Mother in same group during approximate timing of milestone	-0.168	0.846	0.467 - 1.53	0.579	
Males	Average number of maternal sisters in group prior to milestone	-0.29	0.748	0.592 - 0.945	0.015	Animals with a higher number of maternal sisters in group will attain the milestone later.
Males	Low maternal rank at birth	-0.866	0.421	0.219 - 0.807	0.009	Animals born to lower ranking mothers will attain the milestone later.
Males	Average number of excess cycling females in group prior to milestone	0.162	1.176	0.971 - 1.425	0.097	
Males	Average rainfall prior to milestone	-0.002	0.998	0.99 - 1.007	0.7	

TABLE 2.6 CONTINUED FROM PREVIOUS PAGE

Sex	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Males	Hybridization score	2.057	7.82	2.953 - 20.71	0	Animals with higher hybrid scores (more anubis) will attain the milestone sooner.

NOTE: Cox proportional hazards model results showing the predictors of rank attainment in females and males prior to the milestone. For female rank attainment, data from 2,346 samples representing 147 individuals total were used. Complete data was available for 94 females: 25 were censored and data was incomplete in 28 other cases. For male rank attainment, data from 3,918 samples representing 121 individuals total were used. Complete data was available for 78 males: 0 were censored and data was incomplete in 43 other cases.

2.4 Discussion

Our results reveal profound effects of aging in the gut microbiome of wild baboons. This study represents the first longitudinal microbiome aging clock in any species. Further, this is the first study to test the social and environmental factors that predict aging within the gut microbiome, and its consequences for host development and survival. We found that gut microbiome taxonomic features exhibit a clock-like association with age. Our estimates of microbial aging were also consistent with well-known patterns of sex-specific senescence in humans and other primates (Lemaître et al., 2020). Specifically, males exhibited a faster rate of microbial aging than females after maturity.

As the first longitudinal microbiome aging clock in any species, our results contrast with some of the findings from other microbiome aging clocks based on cross-sectional human data. After evaluating a suite of machine learning algorithms, we focused on the Gaussian process regression as the best performing clock, as it had an R^2 of 0.488 and median error of just 1.96 years for a population aged 6 months to 27 years. Galkin et al. (2020) used a similar methodology and compared 4 different types of machine learning algorithms before moving forward with a deep neural network. Using this deep neural network on a publically-available cohort of 1,165 humans aged 18-90 years, they had a considerably lower R^2 value (0.21) but comparable median error (10.6 years in cross-validation) considering the difference in scale between the groups. While our work solely consister of gut microbiome profiles from one population of wild baboons, Huang et al. (2020) used random forests on a large cross-sectional human cohort aged 18-90 years and spanning at least four geographically distinct populations years to compare how different body site microbiomes could be used to predict age. They found that the oral and skin microbiomes resulted in stronger age predictions than the gut microbiome but that there were sex-specific differences in the gut microbiome that

were not discernable in the mouth or skin microbiomes. Lastly, Cuesta-Zuluaga et al. (2019) examined the differences in microbiome diversity using a random forest regression model across four large cohorts of human adults and found that there were sex-specific differences in alpha diversity - females exhibited a slightly higher relative microbiome age than men. This is in direct contrast with our finding that males age faster than females, but our result is also confirmed by other biological markers of aging (Lemaître et al., 2020). These studies are all important proofs of concept for microbiome aging clock. However, our use of longitudinal sampling on a wild baboon populations allows us to not only measure population level differences in microbiome aging, but also test the social and environmental drivers of microbiome aging and link inter-individual variation in the pattern and pace of microbiome aging to individual health and survival.

Our gut microbiome aging clock performed well, compared to other markers of aging commonly used in the Amboseli baboons. Further, as a metric of aging, gut microbial profiles are the least invasive and most easily replicated measure of assessing biological aging (Anderson et al., 2021). Fecal samples can be collected without interfering with the animals directly. In comparison, the other markers of aging require animals to be sedated and measured in a labor-intensive manner – for example, calculating BMI requires sedation, measurements, and weights to be taken and can thus only be calculated infrequently.

In addition to creating an accurate clock estimating microbial aging, we also showed that the microbiome age acceleration and pace of aging were predicted by an individual's social and environmental conditions, especially social dominance rank. Across lifespan, low-ranking animals were microbially young for age. As dominance rank can have direct impacts on the nutritional resources available to an animal, this may corroborate that low-ranking animals are nutritional limited as compared to higher ranked animals. This is consistent with results from stud-

ies showing that undernourished children exhibited young for age microbiomes relative to healthier peers (Subramanian et al., 2014). Further, when these undernourished microbiomes were transplanted into mice, mouse development was hindered: the affected mice exhibited decreased bone density and reduced weight gain relative to those given microbiomes from healthy children. Similarly, our results showed that females born to low-ranking mothers exhibited a slower pace of aging prior to maturity. Females essentially inherit their rank from their mothers, so we might have expected that they remain slow after maturity as well. In contrast, low-ranking females exhibited a faster pace of aging after maturity and across lifespan, suggesting that their gut microbiomes are trying to catch up after a slow development period. Low-ranking males were also young for age and exhibited a faster pace of aging after maturity, suggesting that low-ranking males are likely to be undernourished or otherwise unable to physiologically compete with high-ranking males.

Similar to the effects of rank in females, sources of early life adversity related to nutritional limitation were also linked to patterns of gut microbial aging in males. For example, males born during a drought were microbially young for age. As male offspring may be associated with increased energetic costs, mothers pregnant with sons during drought years may not be able to provide the nutritional resources required by a male infant (Gesquiere et al., 2018). Similarly, males born during a drought year experience a faster pace of aging prior to maturity and a slower pace of aging after maturity, which may be an attempt to "catch up" to their peers developmentally.

In evaluating the usefulness of microbial aging as a predictor of developmental milestones, we found that metrics of microbial aging were predictive of a few specific developmental milestones. The type of metric important for each milestone also varied: milestones related to social standing, such as rank attainment, were

predicted by age acceleration, and milestones related to physiological development, such as menarche or dispersal, were predicted by pace of aging and not age acceleration. This is likely due to the temporal difference between these metrics: age acceleration represents a smaller time scale and thus milestones related to social standing and physical ability may be more impacted by age acceleration. Pace of aging represents longer term trajectories, so milestones that require longer periods of physiological build up may be better represented by it. Specifically, animals that had a faster pace of aging attained menarche sooner than animals with slower paces of aging. Importantly, this result is consistent with results from epigenetic clocks in human studies – girls who had higher epigenetic values of age acceleration (old for age) reached puberty earlier than those who were epigentically young for age (Binder et al., 2018). In males, while testicular enlargement is considered the point at which a male is physically able to produce offspring, their reproductive potential is often not realized until after a male undergoes a growth spurt and is able to physically compete for reproductive females. Thus, rank attainment is the age at which a male is considered an adult and begins rapidly climbing the dominance hierarchy (Alberts and Altmann, 1995). This suggests that to attain their first rank, males must be around their physiological peak, but animals that are young for age are developmentally behind their peers. This idea is echoed if we examine the predictors of pace of aging after sexual maturity. These predictors include sources of early life adversity that could be associated with nutrient limitation – birth in a drought year and a competing sibling – that would play a role in a slower developmental trajectory.

Together, our results highlight the usefulness of the gut microbiome as a biomarker predictive of age. These findings lend important support to the hypothesis that the gut microbiome could serve as a noninvasive biomarker of host aging (Bana and Cabreiro, 2019), with potentially important consequences for the development of

microbiome therapies (Shetty et al., 2017). By leveraging microbial, social, environmental, and life history data on individual hosts followed from birth to death, we have been able to demonstrate that gut microbial aging is an amalgam of an individual's life history predictive of developmental milestones. Together, our results bolster microbiome clock studies that follow human populations (Cuesta-Zuluaga et al., 2019; Galkin et al., 2020; Huang et al., 2020). These results also reinforce that the primate gut microbiome is highly individualized, but predicted by seasonal variation and age group (Björk et al.; Reese et al., 2020). Lastly, we were able to show that the gut microbiome was a predictive biomarker of host aging at the taxonomic level, despite the fact that the gut microbiome is incredibly diverse and exhibits a high level of functional redundancy. A further investigation into the functional properties of the gut microbiome and what pathways change over the course of aging could reveal additional nuance regarding the timing of development. Investigating the influence of the gut microbiome on measures of health that occur multiple times over life, such as the incidence of illness or the rate of wound healing, may also provide insight on the mechanistic role of the gut microbiome in host health and physical functioning.

2.5 Methods

2.5.1 Study population and subjects

Study subjects were 479 wild baboons (215 males and 264 females) living in the Amboseli ecosystem in Kenya between April 2000 to September 2013. The population is primarily composed of yellow baboons (*Papio cynocephalus*) with some admixture from nearby anubis baboon (*Papio anubis*) populations. Prior research in our population finds no link between host hybrid ancestry and microbiome composition (Grieneisen et al., 2019). The baboons are monitored as part

of a long-term monitoring project conducted by the Amboseli Baboon Research Project (ABRP) (Alberts and Altmann, 2012). Since 1971, the ABRP has been collecting continuous observations of the baboons' demography, behavior, and environment. The baboons are individually identified by expert observers who visit and collect data on each social group 3 to 4 times per week (the subjects lived in up to 12 different social groups over the study period). During each monitoring visit, the observers conduct group censuses and record all demographic events, including births, maturation events, and deaths, allowing us to calculate age at maturity and lifespan with precision.

2.5.2 Sample collection, DNA extraction, and 16S data generation

The 13,476 gut microbiome compositional profiles in this analysis represent a subset of 17,277 profiles, which were previously published in Grieneisen et al. (2021). Specifically, this subset of 13,476 fecal samples encompassed samples from individuals where age was known with the greatest precision, where birthdates were known with just a few days of error. Each baboon had on average 33 samples collected across 6 years of their life (Figure 2.1; range = 3 to 135 samples per baboon; median days between samples = 44 days).

Samples were collected within 15 minutes of defecation, homogenized, and preserved in 95% ethanol. Samples were freeze-dried and sifted to remove plant matter prior to long term storage at -80C (Khan et al., 2002; Lynch et al., 2003). DNA from 0.05 g of fecal powder was manually extracted using the MoBio (Catalog No. 12955-12) and QIAGEN (Catalog No. 12955-4) PowerSoil HTP kits for 96-well plates using a modified version of the MoBio PowerSoil-HTP kit. Briefly, we increased the amount of PowerBead solution to 950 μL/well to increase the hydration of the freeze-dried samples, and incubated the plates at 60C for 10 minutes after the addition of PowerBead solution and lysis buffer C1.

Following DNA extraction, a 390 bp region of the V4 region of the 16S rRNA gene was amplified and libraries prepared following standard protocols from the Earth Microbiome Project (Gilbert et al., 2014). Libraries were sequenced on the Illumina HiSeq 2500 using the Rapid Run mode (2 lanes per run). Sequences were single indexed on the forward primer and 12 bp Golay barcoded. The resulting sequencing reads were processed following a DADA2 pipeline (Callahan et al., 2016). After quality filtering with DADA2, we imposed an additional set of quality filters, such that samples were removed for low DNA extraction concentrations ($<$4 times the plate's blank DNA extraction concentration), low read counts ($<$1000 reads), and amplicon sequence variants were removed if they only appeared in one sample. See Grieneisen et al. (2021) for details. This pipeline produced 17,167 samples and 10,720 amplicon sequence variants, which we further limited to 13,476 samples based on the animal's birth status. We filtered out singleton ASVs one further time to produce the 8,492 amplicon sequence variants in our data set. The number of sequencing reads per sample ranged from 1,017 to 427,454 with a median of 51,839 reads. ASVs were assigned to microbial taxa using the IdTaxa(...) function in the DECIPHER package, against the Silva reference database SILVA_SSU_r132_March2018.RData (Quast et al., 2013; Wright et al., 2012).

2.5.3 Identifying microbiome features that contribute to age predictions and that change with age.

To identify microbiome features that change with host age, we ran linear mixed models on 9,575 microbiome features (Table A.1). Linear mixed models were run using the R package lmer4, with p-value estimates from lmerTest. These features included: (i) five metrics of alpha diversity; (ii) the top 10 principle components of microbiome compositional variation; (iii) center log ratio transformed abundances

of each microbial phyla (n = 30), family (n = 290), genus (n = 747) and individual ASVs (n = 8493). Alpha diversity metrics were calculated using the R package vegan and principle components of microbiome compositional variation were calculated using the R package labdsv (Dixon, 2003; Roberts, 2019).

For each feature, we modeled chronological age using both linear and quadratic terms. In order to make our quadratic terms more easily interpretable, we centered our age estimates on zero by subtracting the mean of age from each age value. We also included season (wet or dry) and z-scored rainfall and temperature as fixed effects as well as individual identity, social group at time of collection, hydrological year, and the DNA extraction/PCR plate identity as random effects. All community features (i.e. alpha diversity and principal components), all taxa, and ASVs present in 25% or more of samples (537 ASVs) were modeled using a Gaussian error distribution. Features present in less than 25% of samples (7,956 ASVs) were modeled as present/absent in a given sample with a binomial error distributions. For both types of models, we extracted the coefficient, standard error, and p-value for the age term, then corrected for multiple tests using a Benjamini-Hochberg procedure.

2.5.4 Building the gut microbiome aging clock

We created a microbiome aging clock by fitting Gaussian process (GP) regression model (with a kernel customized to account for heteroskedasticity) to predict each baboon's chronological age at the time of sample collection using our 9,575 microbiome compositional and taxonomic features (Table A.1). The GP regression model with heteroskedasticity correction was the best-performing of four supervised machine learning approaches we considered (elastic net, random forests, and Gaussian process regression with and without the heteroskedasticity kernel; See Appendix Section A.1.2 for a comparison of other algorithms).

Gaussian process regressions were conducted in Python 3 using scikit-learn (Pedregosa et al., 2011; Van Rossum and Drake, 2009). As a nonparametric, Bayesian approach that infers a probability distribution over all the potential functions that fit the data, the Gaussian process regression does not assume a linear relationship between chronological age and predicted age (Rasmussen and Williams, 2005). For the prior distribution in the Gaussian process regression, we used a radial basis function as our kernel and set the scale parameter to the mean Euclidean distance of the dataset, as calculated in vegan (Dixon, 2003). Because initial, exploratory models exhibited heteroskedasticity (Figure A.5), we multiplied the variance in the training data by the radial basis function, which distributed the higher variance in later life more evenly across lifespan.

To calculate a microbial age estimate for every sample, and estimate generalization error, we used nested five-fold cross validation. To calculate a microbial age estimate for every sample and estimate generalization error, in each of the five model runs, 80% of the data was used to train the model, and the remaining 20% of the dataset as the test data. Because host identity can have a strong effect on microbiome composition, we distributed samples from each host across the five test/training data sets by randomly assigning each sample a test set without replacement. For each model run, 4 of the test datasets were treated altogether as training data and the 5th set was the validation test set. We then took the estimates from all 5 model runs and estimated global model accuracy on the aggregated estimates.

We assessed the accuracy of our microbiome clock by regressing each sample's chronological age (age_c) against the model's predicted microbial age (age_m) and determining the R^2 correlation coefficient and Pearson's correlation between age_c and age_m. We also calculated the median error of the model fit as the median absolute difference between age_c and age_m across all samples (Horvath, 2013).

To test how each microbiome feature contributed to the accuracy of the microbiome clock, we took a leave-one-out approach: for each of the features above the ASV level in turn, we removed the feature, centered and log ratio transformed the remaining features, re-ran the Gaussian process regression, and assessed the new model's R^2, Pearson's R correlation coefficient, and median error. For each of the resulting models, we assessed feature importance by comparing the leave-one-out model's R^2 to the model with all features included.

2.5.5 Calculating microbiome age acceleration and pace of aging

To characterize patterns of microbiome aging from our microbiome aging clock, we calculated two metrics of aging: sample-specific microbiome age acceleration and baboon-specific pace of aging. Microbiome age acceleration was calculated as the difference between a sample's age_m and age_c. Higher values of age acceleration indicate old-for-age microbiomes, as $age_m > age_c$, and lower values (which are often negative) indicate a young-for-age microbiome, where age_c ¿ age_m.

Pace of aging was estimated as each individual baboon's random slope from a linear mixed effects model of age_m, predicted by the sample-specific age_c and known environmental drivers of microbiome composition: the average maximum temperature during the month of collection, total rainfall during the collection month, and the season (wet or dry) during sample collection (Grieneisen et al., 2019; Maurice et al., 2015). Social group at the time of collection and hydrological year were also included as random effects (Grieneisen et al., 2017; Tung et al., 2015). For descriptions of all predictors, see Table A.7. Pace of aging was calculated separately for males and females by subsetting the age_m estimates by sex prior to running the linear mixed effects model. In order to reduce noise in the random slope terms, we only calculated pace of aging in baboons that had three or more samples available for the timeframe of interest.

2.5.6 Testing sources of variation in microbiome age acceleration and pace of aging

Many social and environmental factors have been shown to predict fertility and survival in the Amboseli baboons (Altmann and Alberts, 2005; Altmann et al., 2010; Archie et al., 2014b; Gesquiere et al., 2018; Tung et al., 2016). In **order** to test if these factors also predict patterns of microbiome aging, we used a linear mixed modeling approach to test predictors of sample-specific microbiome age acceleration and pace of aging over different phases of life, separately for males and females. The phases of life were: (i) the juvenile period (prior to 4.5 years of age for females, which is the median age of menarche; prior to 5.4 years of age, which is the median age of testicular enlargement in males; (Charpentier et al., 2008; Onyango et al., 2013), (ii) adulthood (post sexual maturity) and (iii) across the full lifespan. See Table A.9 for the number of subjects and samples included in each analysis; these samples vary somewhat across analyses depending on whether the subject's samples spanned the life stage of interest and having complete data on predictor variables (described below and in Table A.7).

Our models varied slightly based on the microbial aging metric and timeframe of interest. For models of age acceleration, the response variable was the sample-specific measure of age_m - age_c. All models included the following fixed effects: (i) individual chronological age at the time of sample collection, to correct for model compression; (ii) the average maximum temperature during the 30 days before the sample was collected, (iii) total rainfall during the 30 days before the sample was collected, and (iv) the season (wet or dry) during sample collection. Every model also included measures of early life adversity the individual experienced prior to 4 years of age as fixed effects. These could be present as either the (v) cumulative early life adversity an animal experienced or the individual six sources of adversity: (vi) loss of mother before age 4, (vii) a sibling born within 1.5 years

of focal individual, (iix) presence of drought in early life, (ix) high group size, (x) maternal social isolation, (xi) and low maternal rank) (Tung et al., 2016). Random effects included individual identity, the social group the individual lived in at the time of collection, and hydrological year. The effects of social dominance rank were modeled differently for each life stage. Prior to maturity, we modeled rank effects as a 0/1 indicating whether the mother was in the bottom quartile of ordinal ranks (variable xi above). For models testing age acceleration later in adulthood or over the entire lifespan, we used sex-specific measures of social rank: for males this was ordinal rank, and for females this was proportional rank (Levy et al., 2020). To make model interpretation more intuitive (high rank corresponds to higher values), we multiplied the coefficients for ordinal rank and low maternal rank by -1. In all female age acceleration models, the number of adult females in the group at collection was included as female-specific measure of resource competition, and in female adulthood models we also included dyadic social connectedness to other females as a measure of female social bond strength (Charpentier et al., 2008; Tung et al., 2016). For full descriptions of all predictors, see Table A.7.

Pace of aging models included followed the same structure as the age acceleration models with certain predictors averaged over the time period being modeled. Environmental and social drivers of microbiome composition (variable i-iv above and the random effects other than individual identity) were not included as these drivers are regressed out during the calculation of the metric itself. Thus, pace of aging models only included measures of early life adversity the individual experienced prior to 4 years of age as fixed effects (v-xi) (Tung et al., 2016). As in the age acceleration models, the effects of social dominance rank were modeled differently for each life stage. Prior to maturity, we modeled rank effects as a 0/1 indicating whether the mother was in the bottom quartile of ordinal ranks. For models testing age acceleration later in adulthood or over the entire lifespan,

we averaged the sex-specific measures of social rank (ordinal rank in males and proportional rank in females) over the time period of interest (Levy et al., 2020). To make model interpretation more intuitive (high rank corresponds to higher values), we multiplied the coefficients for ordinal rank and low maternal rank by -1. In all female pace of aging models, the average number of adult females in the group over the time period of interest was included as female-specific measure of resource competition, and in female adulthood models we also included average dyadic social connectedness to other females as a measure of female social bond strength (Charpentier et al., 2008; Tung et al., 2016). For full descriptions of all predictors, see Table A.7.

2.5.7 Testing whether microbiome age acceleration and pace of aging predict baboon maturation and survival

We used Cox proportional hazards models to test whether microbiome age acceleration and pace of aging predicted the age at which females and males attained maturational milestones and the age at death for juveniles and adult females. We were only able to measure adult survival in females because males disperse between social groups, often repeatedly across adulthood; hence, when males disappear from our population, we cannot determine if they dispersed or died. For females, the maturational milestones of interest were the age at adult rank attainment (median age 2.24 in Amboseli), age at menarche (median age 4.51 in Amboseli), and the age at which she produced her first live offspring (median age 5.82 in Amboseli). For males, these milestones were the age of testicular enlargement (median age 5.38 in Amboseli), the age of dispersal from natal group (median age 7.47 in Amboseli), and the age at which he first out-ranked an adult male baboon in the dominance hierarchy (i.e. adult rank attainment; median age 7.38 in Amboseli) (Charpentier et al., 2008; Onyango et al., 2013). See full de-

scriptions of each milestone in Appendix Table A.8. In order to be included in these analyses, animals must have reached the milestone after the onset of sampling (April 2000) and had at least three samples available in the timeframe of interest. The number of subjects and censored data points in each analysis is presented in Tables SA.10 and SA.11.

Our models varied based on the event of interest and timeframe of interest. All models included (i) age acceleration averaged over the timeframe, (ii) pace of aging calculated for the timeframe, and (iii) mean chronological age of the samples to correct for inter-individual differences in sampling.

All milestone models also included important variables tested in Charpentier et al. (2008): (iv) maternal presence at the time of the milestone, (v) the number of maternal sisters in group averaged over the timeframe, (vi) rainfall averaged over the timeframe, and (vii) whether the animal's mother was low ranked (was in the lowest quartile for female ordinal rank). For female-specific milestones, we also included (ix) the average number of adult females in the group averaged over the timeframe, and for male-specific milestones we included the number of excess cycling females in the group averaged over the timeframe, or the difference between the number of cycling females and the number of mature males within an animal's social group. Last, we included (x) the animal's hybrid score, or an estimation the proportion of an individual's genetic ancestry attributable to anubis or yellow baboon ancestry (Tung et al., 2008). Hybrid score is only available for a subset of the individuals within this dataset, so we included this variable in an analogous set of models in order to protect our sample sizes (Table A.10).

All juvenile survival models included variables (i-iii) from above, as well as measures of early life adversity the individual experienced prior to 4 years of age. These could be present as either the (xi) cumulative early life adversity an animal experienced or the individual six sources of adversity: (xii) loss of mother before

age 4, (xiii) a sibling born within 1.5 years of focal individual, (xiv) presence of drought in early life, (xv) high group size, (xvi) maternal social isolation, (xvii) and low maternal rank) (Tung et al., 2016). Additionally, we ran three versions of this analysis - two subset to each sex, and one version that included both sexes. In the both sexes juvenile survival model, we included (xix) sex as a predictor.

Adult survival was only assessed in females as males often disperse outside of the study population. Like juvenile survival models, adult female survival models included variables (i-iii), and measures of early life adversity (xi-xvii). Last, we included (xx) average lifetime dyadic social connectedness to adult females, (xxi) average lifetime dyadic social connectedness to adult males, and (xxii) average lifetime proportional rank. Full descriptions of all predictors are available in Table A.7.

CHAPTER 3

EARLY LIFE ADVERSITY LEAVES A LONG-TERM IMPACT ON THE BABOON GUT MICROBIOME.

3.1 Abstract[1]

In both free-living and host associated communities, events early in the formation of the community can have consequences for subsequent community assembly and dynamics. For instance, in the human gut microbiome, a handful of studies show that malnutrition or birth style (vaginal vs caesarean) influence microbiome composition. However, few studies have been able to test whether events that occur in early life influence variation in the gut microbiome across the life span using prospective, longitudinal data. To fill this gap, we evaluated whether the gut microbiome changes in response to adverse early life experiences, and whether these changes occurred at the time of the adversity or appeared later in life. We did so using a unique longitudinal data set spanning 12,298 16S rRNA gut microbial profiles from 431 individual baboons in the Amboseli ecosystem, Kenya over 14 years. We found that the gut microbiome changed in response to specific types of adversity, and that these changes were detectable primarily later in life. Further, we found that one measure of gut microbiome stability was also impacted by certain types of early life adversity. Specifically, experiencing a drought or high group size in early life were correlated decreased stability only after the juvenile period or

[1]I am the lead author, and my coauthors include Jansen D, Gilbert J, Barreiro L, Altmann J, Alberts SC, Blekhman R, Tung J, and Archie EA.

over lifespan. Together, our results demonstrate that there are long-term impacts of early life adversity on the baboon gut microbiome, representing a first step towards understanding whether these effects have consequences for host health and physical functioning.

3.2 Introduction

Harsh conditions in early life have important, long-term effects on an individual's behavior, cognition, physiology, and fitness (Lindström, 1999; Snyder-Mackler et al., 2020). For instance in humans, early life adversity is associated with a range of health outcomes, including higher risk of psychiatric disorders, heart disease, cancer, stroke (Dube et al., 2003; Famularo et al., 1992; Felitti et al., 1998; Kessler et al., 2010). However, to date much less is known about the mechanisms linking early life events to health and survival. The dominant hypotheses include evolutionary explanations, such as those proposed by developmental constraints or predictive adaptive response models (Gluckman et al., 2005; Lindström, 1999; Monaghan, 2008), to more proximate mechanisms such as those encompassed by the biological embedding hypothesis (Hertzman, 1999; Miller et al., 2011). These models link early life events to multiple aspects of individual development, physiology, inflammation and immune function, hypothalamic-pituitary-adrenal axis responses, and patterns of DNA methylation. However, few models have considered the role played by the gut microbiome. In this paper, we develop and test this concept.

In humans and other mammals, gut microbiomes are diverse, dynamic ecosystems that help their hosts digest food, enhance their immune system, resist pathogens, and generate essential vitamins and amino acids (Clayton et al., 2018; Foster et al., 2017). In humans, changes in the gut microbiome have been correlated

with a number of health problems ranging from inflammatory bowel disease and hypertension to diabetes and different types of cancers (Chassaing et al., 2017; Manor et al., 2020; Mottawea et al., 2016; Zackular et al., 2014). Despite its importance in host physical functioning and health, gut microbiomes are also sensitive to host physiology, environments, behaviors, and early life experiences (Bengmark, 1998; Gerber, 2014; Palmer et al., 2007). The best studied type of early life experience impacting the human gut microbiome is that of birth style: infants born by caesarean section have a gut microbiome more similar to the mother's skin microbiome, as compared to infants delivered vaginally (Dominguez-Bello et al., 2010). This effect may persist for a period of time after birth, resulting in adverse health outcomes in childhood (Bäckhed et al., 2015; Cong et al., 2016; Mueller et al., 2015; Reyman et al., 2019; Sevelsted et al., 2015). Beyond birth style, other types of early life experiences, including acute malnutrition, stress, maternal separation, and other forms of microbial disruption, have also been shown to exhibit marked changes in gut microbiome composition across a diverse range of host taxa (Billiet et al., 2017; Cowan et al., 2019; Kirschman et al., 2020; Knutie et al., 2017; Rhoades et al., 2019; Subramanian et al., 2014; Videvall et al., 2020; Wilkinson et al., 2020; Xiang et al., 2020). Together, these provide strong evidence that the gut microbiome may play key roles in mediating early life effects on health outcomes. However, research linking early life events to gut microbiome composition across the life course – from the juvenile period through old age – is very rare. Most studies have only followed individuals for a few weeks to a few years (Blanton et al., 2016; Rhoades et al., 2019; Videvall et al., 2020); hence no studies have tested for early life effects as they occur or how these effects persist in the gut.

Here, we fill this gap using 12,298 gut microbiome compositional profiles, collected from 431 known-age, wild baboons (*Papio cynocephalus*) over 14 years. Our subjects are members of a well-studied wild baboon population located in the

Amboseli ecosystem, Kenya and have been studied by the Amboseli Baboon Research Project (ABRP) since 1971 (Alberts and Altmann, 2012). In the last 50 years, the ABRP has collected continuous, individual-based data on baboon life histories, behavior, and environments, many of which can be correlated with microbiome changes or used to predict health and mortality (Alberts et al., 2014; Archie et al., 2014a,b; Grieneisen et al., 2017; Ren et al., 2015; Tung et al., 2015). Baboons are a useful model system for humans because they experience well-defined life history stages that mirror human developmental stages, including an extended juvenile period prior to sexual maturation and predictable age-related changes in behavior and physiology in adulthood (Alberts and Altmann, 1995; Altmann et al., 2010; Charpentier et al., 2008; Onyango et al., 2013).

Prior research in the Amboseli baboons has shown that adverse events in early life can have profound effects on the rest of these animals' lives. Tung et al. (2016) identified six sources of adversity whose cumulative effects led to profound effects on lifespan; females who experienced three or more sources of adversity had median lifespans that were 10 years shorter than females who experienced none of the six sources. The six sources of adversity included maternal loss, maternal social isolation, low maternal social status, early life drought, high group density, and the presence of a competing sibling who diverted maternal attention, with the strongest effects linked to maternal loss and maternal social isolation. In addition to impacting the individual's lifespan, further research has showed that mothers who experienced early life adversity themselves have offspring with significantly reduced survival (Zipple et al., 2019). In addition to more specific health and survival outcomes, the Amboseli population has been used to test whether harsh conditions in early life lead to changes in developmental or reproductive trajectories (Lea et al., 2015; Weibel et al., 2020). Recent work has also examined the mechanistic relationship between early life experiences and an animal's fitness

trajectory: cumulative adversity was not predictive of variation in epigenetic aging, but specific sources of adversity were important predictors of variation in microbial aging (Anderson et al., 2021; Dasari et al.).

Building on this prior research, our objective was to characterize the long-term impacts of early life adversity on the baboon gut microbiome. We hypothesized that the experience of early life adversity – especially adversities that have the strongest effects on adult survival – would be linked to consistent differences in microbiome composition and stability across hosts. Alternatively, because gut microbiomes are highly sensitive to a host's current environment, microbiomes may be resilient to adversity, such that adverse events in early life may have few detectable, long-term consequences for gut microbial composition (Allison and Martiny, 2008; Relman, 2012). Indeed, a host's current environment and behavior is often a strong predictor of gut microbial composition, although the relative effects of early life events are largely unknown. To test this hypothesis, we investigated whether early life experiences, including the six individual sources and their cumulative effects, were linked to predictable differences in gut microbial community composition, abundances of individual microbes, and microbiome community stability, both in early life as the adversity is occurring, and in adulthood. Establishing how the gut microbiome is impacted by early life adversity will contribute to a comprehensive picture of the evolutionary role of the gut microbiome in a mammalian host. Understanding how early adversity gets "under the skin" is key to developing interventions that can mitigate long-term health consequences.

3.3 Methods

3.3.1 Study population and subjects

Study subjects were 431 wild baboons (264 females and 215 males) living in the Amboseli ecosystem in Kenya between April 2000 to September 2013. The population is primarily composed of yellow baboons (*Papio cynocephalus*) with some admixture from nearby anubis baboon (*Papio anubis*) populations, although research in this population finds no link between host hybrid ancestry and microbiome composition (Grieneisen et al., 2019). The baboons studied have been part of a long-term monitoring project conducted by the Amboseli Baboon Research Project (ABRP) (Alberts and Altmann, 2012). The subjects lived in up to 12 different social groups over the study period. These social groups were derived from two original study groups that underwent natural processes of group fission/fusion since the onset of monitoring in 1971. Hence, continuous observations of the baboons' demography, genetics, behavior, and environment are available for nearly 50 years. The baboons are individually identified by expert observers who visit and collect data on each social group 3 to 4 times per week. During each monitoring visit, the observers conduct group censuses and record all demographic events, including births, maturation events, and deaths.

3.3.2 Defining the sources of early life adversity

The metrics for early life adversity follow the same definitions as in Tung et al. (2016). Specifically, we tested six different types of adversity that could be linked to either early life nutritional limitation or psychosocial stress: (1) drought in the first year of life, which may lead to low food availability; (2) high social density, measured by large group size at time of birth, which may lead to competition for resources among group members; (3) low maternal dominance rank, which is

associated with lower access to resources; (4) maternal social isolation, which is associated with decreased social support; (5) maternal death before age of 4 years, which removes maternal social and nutritional support; and (6) the birth of a competing sibling within 1.5 years of the focal animal's birth, which could divert maternal attention. Each source of adversity was treated as a binary variable that indicated whether an individual either experienced the adversity or not (in most cases, experiencing the adversity was defined as being in the worst quartile of the variable in question). Cumulative adversity was thus the sum total of these binarized sources.

3.3.3 Sample collection, DNA extraction, and 16S data generation

The 12,298 gut microbiome compositional profiles in this analysis represent a subset of 17,277 profiles, which were previously published in Grieneisen et al. (2021). Specifically, this subset of 12,298 fecal samples encompassed samples from 431 individuals where age was known with just a few days of error, and where we had complete data on all six metrics of early life adversity. Each baboon had on average 28 samples collected across 5 years of their life (Figure 3.1; range = 1 to 135 samples per baboon; median days between samples = 45 days). The subjects included 234 females (7,321 samples, mean of 31 samples per individual) and 197 males (4,977 samples, mean of 24 samples per individual) whose ages ranged from 7 months to 26.5 years old (Figure 3.1).

Following DNA extraction, a 390 bp region of the V4 region of the 16S rRNA gene was amplified and libraries prepared following standard protocols from the Earth Microbiome Project (Gilbert et al., 2014). Libraries were sequenced on the Illumina HiSeq 2500 using the Rapid Run mode (2 lanes per run). Sequences were single indexed on the forward primer and 12 bp Golay barcoded. The resulting sequencing reads were processed following a DADA2 pipeline (Callahan

Figure 3.1. Longitudinal fecal samples collected for (A) 7,321 samples from 234 female baboons and (B) 4,977 samples from 197 male baboons in the Amboseli ecosystem. Host age at the time of sample collection is indicated on the x-axis and individual baboons are represented on the y-axis. Each point represents a fecal sample collected from an individual baboon. The fill color of each point reflects the cumulative early life adversity an individual experienced: dark blue for animals that experienced no adversity, light blue for those that experienced 1 source, orange for those that experienced 2 sources, and red for those that experienced 3 or more sources.

et al., 2016). After quality filtering with DADA2, we imposed an additional set of quality filters, such that samples were removed for low DNA extraction concentrations ($<$4 times the plate's blank DNA extraction concentration), low read counts ($<$1000 reads), and amplicon sequence variants were removed if they only appeared in one sample. See Grieneisen et al. (2021) for details. This pipeline produced 17,167 samples and 10,720 amplicon sequence variants. We filtered singleton ASVs one additional time to produce the 8,492 amplicon sequence variants in our data set. Last, we filtered our samples based on the animal's birth and early adversity status, resulting in a final count of 12,298 samples. The number of sequencing reads per sample ranged from 1,017 to 427,454 with a median of 51,840 reads. ASVs were assigned to microbial taxa using the IdTaxa(...) function in the DECIPHER package, against the Silva reference database SILVA_SSU_r132_March2018.RData (Quast et al., 2013; Wright et al., 2012).

3.3.4 Identifying adversity-related differences in microbial composition using PERMANOVA

To test whether early life experience explains significant variance in microbiome community composition, we performed PERMANOVA (Permutational Multivariate Analysis of Variance) on a matrix of Bray-Curtis dissimilarities between all samples. Specifically, we tested whether Bray-Curtis dissimilarities were predicted by either (a) the presence or absence of individual sources of adversity ("type" of adversity) or (b) cumulative adversity (the total number of adversities an individual experienced; hereafter, "quantity" of adversity). For each PERMANOVA, we also controlled for covariates known to explain technical and biological variation in microbiome composition (Grieneisen et al., 2017; Kartzinel et al., 2019; Tung et al., 2015; Wang and LêCao, 2020). These variables included the (i) DNA extraction plate, (ii) the season in which the sample was collected (wet or dry), (iii) the hy-

drological year (hydrological years are shifted to begin with the onset of the rains in November and conclude at the end of the dry season in October) at time of collection, (iv) the sex of the individual, (v) the age of the individual at collection, (vi) the social group the baboon belonged to on the day the sample was collected, and (vii) the identity of the baboon from which the sample was collected. Because PERMANOVA tests for variance sequentially, the order in which these covariates were added to the model was important. Specifically, early life experiences is correlated individual identity and thus needed to be evaluated prior to the addition of variables vii. Thus, we included variables i-vi first, which allows us to control for variables related to both population level drivers (i-iii) and host-specific variation in the microbiome (iv-vi), followed by either the types or quantity of adversity (a or b) and ending with host identity (vii). In the case of the type of adversity models, we randomized the order of the adversities.

As sex is an important predictor of microbial variation, we ran models for females and males separately. Age is another important predictor of microbial variation and to identify how early adversity may manifest later in life we further binned the data into discrete four-year age categories (eg. 0 to 4 years, 4 to 7 years, etc) and tested the effect of diversity within those categories. At advanced ages, we had considerably fewer samples available and thus binned all available samples after a specific age: over 19 for females and over 13 for males. Sample sizes are available for each model in Table B.1.

3.3.5 Understanding the contribution of early life adversity to the presence or abundance of microbiome features.

We next used linear mixed models to test whether the experience of adversity was linked to changes in community composition or differential abundance of 9,575 microbiome features. These features were (i) five metrics of alpha diversity;

(ii) the top 10 principle components of microbiome compositional variation (which collectively explained 57% of the variation in microbiome community composition); (iii) centered log ratio transformed abundances of each microbial phyla (n = 30), family (n = 290), genus (n = 747) and individual ASVs (n = 8,493; described in Table A.1). Alpha diversity metrics were calculated using the R package vegan and principle components of microbiome compositional variation were calculated using the R package labdsv (Dixon, 2003; Roberts, 2019). For each feature, we tested whether it was predicted by either the types or quantity of early life adversity while controlling for covariates known to explain variation in microbiome composition in our population as fixed effects, including: the season in which the sample was collected (wet or dry), the average maximum temperature for the month prior to sample collection, the average rainfall total for the month prior to sample collection, and the host's age. Further, the social group the baboon belonged to on the day the sample was collected, the identity of the baboon the sample was collected from, and the hydrological year at time of collection were modeled as random effects. Features present in at least 25% of samples were modeled using a Gaussian error distribution (1,619 features, including all the features in the alpha diversity, composition, phylum, family, genus categories as well as 592 ASVs). The remaining 7,573 ASVs present in less than 25% of samples were modeled using a binomial error distribution. For both types of models, we extracted the coefficient, standard error, and p-value for the age term, then corrected for multiple tests using a Benjamini-Hochberg procedure.

3.3.6 Testing the predictors of microbiome community stability

In order to test how early life adversity impacts the stability of the gut microbiome, we calculated stability as the coefficient of variation of an individual's between-sample Bray-Curtis dissimilarities for three time periods: the juvenile pe-

riod (prior to age 4), adulthood, and across the lifespan. To reduce noise in estimates of coefficients of variation, individuals had to have 10 or more samples per time period to be included in this analysis. We specifically tested whether adversity predicted stability using a linear modeling approach. Coefficient of variation for the time period of interest was our response variable, and fixed effects included either (a) the presence or absence of individual sources of adversity ("type" of adversity) or (b) cumulative adversity (the total number of adversities an individual experienced; hereafter, "quantity" of adversity). We also included (i) mean age of the individual's samples, (ii) total number of samples in the time period, and (iii) sex as additional fixed effects because coefficient of variation is sensitive to changes in sample size and our sample sizes are positively correlated with age and sex (due to sex-based differences in dispersal).

3.4 Results

3.4.1 Presence of a competing sibling and low maternal rank predict microbiome composition.

Our PERMANOVA analyses identified two types of adversity that had small but significant effects on microbiome composition across all samples. The presence of a competing sibling and low maternal rank respectively explained 0.018% ($F = 2.26$, adjusted $p = 0.032$, Table 3.1) and 0.02% ($F = 2.48$, adjusted $p = 0.016$, Table 3.1) of the variation in microbial composition.

Because sex predicted microbiome variation in our initial analyses ($F = 1.77$, $R^2 = 0.014\%$, $p = 0.043$, Table B.2)), we also investigated sex-specific responses to early life adversity by running separate PERMANOVAs for each sex. For females, the presence of a competing sibling contributed a small but significant amount of variation ($F = 2.12$, $R^2 = 0.029\%$, adjusted $p = 0.045$, Table 3.1). For males,

the presence of a competing sibling and low maternal rank were linked to significant differences in gut microbiome composition (competing sibling: $F = 3.01$, $R^2 = 0.06\%$, adjusted $p = 0.006$; low maternal rank: $F = 3.18$, $R^2 = 0.063\%$, adjusted $p = 0.005$; Table 3.1). In contrast to these individual sources of adversity, the quantity of adversity experienced was never a significant predictor of variation in microbiome composition (Table B.2).

Because we expected that the effects of early life adversity might be strongest during the juvenile period and weaken with age, we also ran our models on 4-year age windows. Contrary to our expectation that the effects of early life adversity would be strongest in early life, we found that for the sources of adversity linked to microbiome changes—competing sibling, low maternal rank, and cumulative adversity—their effects grew stronger with host age. Specifically, the presence of a competing sibling becomes a significant predictor of microbiome composition from ages 7-10 and after age 19 ((7-10]: $F = 2.50$, $R^2 = 0.10\%$, adjusted $p = 0.032$; (19-30]: $F = 2.12$, $R^2 = 0.8\%$, adjusted $p = 0.032$; Table B.2, Figure 3.2). Low maternal rank predicted of microbiome composition in all animals between ages 13 and 16 ($F = 2.51$, $R^2 = 0.28\%$, adjusted $p = 0.016$, Table B.2, Figure 3.2). Similarly, in females the presence of a competing sibling explained microbiome composition between ages 10 and 13, and after age 19 ((10-13]: $F = 2.01$, $R^2 = 0.17\%$, adjusted $p = 0.045$; (19-30]: $F = 2.11$, $R^2 = 0.8\%$, adjusted $p = 0.045$; Table B.2). Low maternal rank had the strongest effects on microbiome composition between the ages of 13 and 16 ($F = 2.41$, $R^2 = 0.34\%$, adjusted $p = 0.005$, Table B.2). In males, the presence of a competing sibling and low maternal rank were significant contributors to variation in gut microbiome similarity after age 7 (competing sibling: $F = 2.68$, $R^2 = 0.25\%$, adjusted $p = 0.012$; low maternal rank: $F = 2.90$, $R^2 = 0.28\%$, adjusted $p = 0.005$; Table B.2).

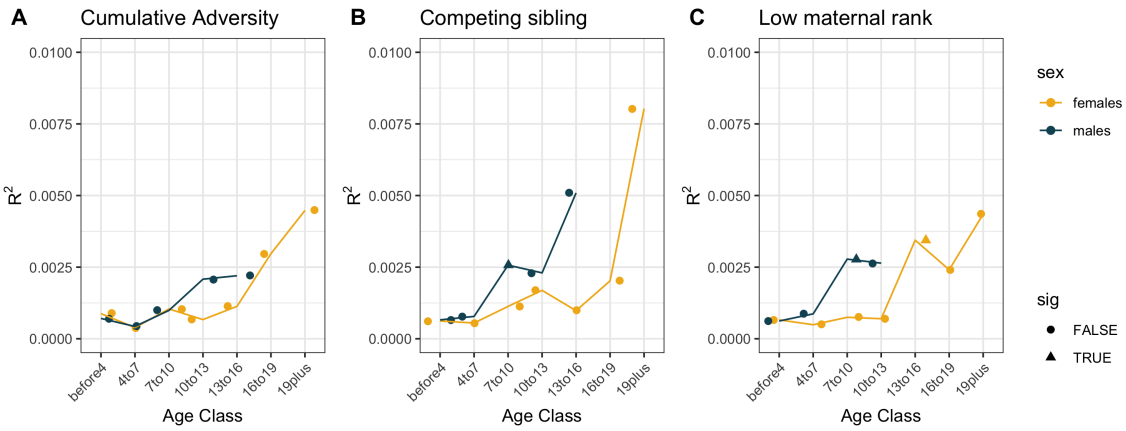

Figure 3.2. Change in the variance explained (R^2) in microbiome Bray-Curtis dissimilarities as a function of host age and the type of early adversities hosts experienced. The three panels show the effects of (A) cumulative adversity; (B) the presence of a competing sibling, and (C) low maternal rank. Colors represent host sex (yellow represents females and blue represents males). Point shape indicates whether the relationship was significant after adjusting for multiple tests using the Benjamini-Hochberg procedure. Other types of early life adversity are visualized in Figure B.1.

TABLE 3.1

STATISTICALLY SIGNIFICANT EFFECTS FROM PERMANOVA ANALYSES TESTING THE RELATIONSHIP BETWEEN INDIVIDUAL SOURCES OF ADVERSITY AND MICROBIOME BRAY-CURTIS DISSIMILARITIES.

Age Class	**Sex**	**Variable**	**F**	**R^2**	**P-value**	**Adjusted P-value**
Lifespan (0,30)	Both	Social group at time of collection	2.72206	0.0024	0.001	0.0016
Lifespan (0,30)	Both	Presence of a competing sibling	2.26006	1.8e-4	0.012	0.032
Lifespan (0,30)	Both	Lowest quartile maternal rank	2.48335	2e-4	0.003	0.016
Lifespan (0,30)	Both	Individual identity	1.30551	0.0443	0.001	0.00133
Lifespan (0,30)	Females	DNA extraction plate	1.0937	0.02988	0.001	0.008
Lifespan (0,30)	Females	Social group at time of collection	2.7547	0.00408	0.001	0.0032
Lifespan (0,30)	Females	Chronological age at time of collection	2.9581	4e-4	0.003	0.024
Lifespan (0,30)	Females	Presence of a competing sibling	2.1245	2.9e-4	0.015	0.04533
Lifespan (0,30)	Females	Individual identity	1.2872	0.03881	0.001	0.008
Lifespan (0,30)	Males	Social group at time of collection	1.3131	0.00287	0.003	0.014
Lifespan (0,30)	Males	Presence of a competing sibling	3.0798	6.1e-4	0.001	0.006
Lifespan (0,30)	Males	Lowest quartile maternal rank	3.1773	6.3e-4	0.002	0.005
Lifespan (0,30)	Males	Individual identity	1.2697	0.0479	0.001	0.006
(0 - 4]	Both	Social group at time of collection	1.53496	0.00554	0.001	0.0016

TABLE 3.1 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Variable	F	R^2	P-value	Adjusted P-value
(0 - 4]	Both	Individual identity	1.09717	0.13145	0.001	0.00133
(4 - 7]	Both	Social group at time of collection	1.86332	0.0054	0.001	0.0016
(4 - 7]	Both	Individual identity	1.11627	0.07796	0.001	0.00133
(7 - 10]	Both	Presence of a competing sibling	2.50344	0.00105	0.007	0.032
(7 - 10]	Both	Individual identity	1.14019	0.08112	0.001	0.00133
(10 - 13]	Both	Individual identity	1.17083	0.06443	0.001	0.00133
(13 - 16]	Both	Social group at time of collection	1.59682	0.0201	0.001	0.0016
(13 - 16]	Both	Lowest quartile maternal rank	2.50746	0.00287	0.004	0.016
(13 - 16]	Both	Individual identity	1.20037	0.07142	0.001	0.00133
(16 - 19]	Both	Social group at time of collection	1.46647	0.03082	0.001	0.0016
(19 - 30]	Both	Presence of a competing sibling	2.11659	0.00801	0.009	0.032
(0 - 4]	Females	Individual identity	1.06065	0.12104	0.025	0.03333
(4 - 7]	Females	DNA extraction plate	1.06513	0.10998	0.01	0.04
(4 - 7]	Females	Social group at time of collection	1.47334	0.00833	0.002	0.0032
(4 - 7]	Females	Individual identity	1.09239	0.07463	0.004	0.008
(7 - 10]	Females	Social group at time of collection	1.24832	0.01022	0.017	0.02267
(7 - 10]	Females	Individual identity	1.13082	0.06734	0.003	0.008
(10 - 13]	Females	Social group at time of collection	1.39466	0.01172	0.002	0.0032
(10 - 13]	Females	Presence of a competing sibling	2.01097	0.00169	0.017	0.04533

TABLE 3.1 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Variable	F	R^2	P-value	Adjusted P-value
(10 - 13]	Females	Individual identity	1.10753	0.05584	0.023	0.03333
(13 - 16]	Females	Social group at time of collection	1.67931	0.02642	0.001	0.0032
(13 - 16]	Females	Lowest quartile maternal rank	2.40841	0.00344	0.005	0.04
(13 - 16]	Females	Individual identity	1.22317	0.06123	0.002	0.008
(16 - 19]	Females	Social group at time of collection	1.54391	0.03465	0.002	0.0032
(19 - 30]	Females	Presence of a competing sibling	2.11659	0.00803	0.013	0.04533
(0 - 4]	Males	DNA extraction plate	1.06735	0.14816	0.008	0.048
(0 - 4]	Males	Social group at time of collection	1.33913	0.00925	0.006	0.014
(0 - 4]	Males	Individual identity	1.09922	0.13057	0.004	0.008
(4 - 7]	Males	Social group at time of collection	1.32461	0.00712	0.007	0.014
(4 - 7]	Males	Individual identity	1.11845	0.07338	0.002	0.006
(7 - 10]	Males	Presence of a competing sibling	2.68396	0.00257	0.004	0.012
(7 - 10]	Males	Lowest quartile maternal rank	2.90441	0.00278	0.001	0.005
(7 - 10]	Males	Individual identity	1.10492	0.08156	0.019	0.0285

NOTE: PERMANOVAs testing the effects of individual types of adversity on Bray-Curtis dissimilarities. PERMANOVAs were run on lifespan and age class subsets of the data. Only significant variables across these models are shown. In addition to the variables below, models also included plate, season, hydrological year, sex (if both sex model), individual identity, chronological age, and social group. Models were run for 999 permutations, and p-values were corrected for multiple tests using the Benjamini-Hochberg procedure. Full results available in Appendix Table B.2.

3.4.2 The presence of many microbial features was predicted by type or quantity of adversity.

We next tested whether individual community metrics and taxa were predicted by either the type or quantity of adversity an animal experienced using a linear mixed modeling approach. We found that of the 1619 features modeled with a Gaussian distribution (i.e. those present in at least 25% of samples), none of the microbial feature counts were predicted by the type or quantity of adversity represented in the model after correcting for multiple tests. However, 21% of ASVs (1,683 of 7,956 ASVs) tested with a binomial error distribution were predicted by cumulative adversity (Table B.3). To check if there were commonalities between ASVs, we aggregated them at higher taxonomic levels. At the phyla level, there were 23 phyla significantly predicted by cumulative adversity: 37.9% of these ASVs (638 of 1,683 ASVs) belonged to Firmicutes, followed by 14.3% (240 ASVs) in Proteobacteria and 13.6% (229 ASVs) in Bacteroidetes. Each of the six sources of adversity were also predictive of between 600-700 ASVs each (though with some overlap between adversities, Figure 3.3). When we examine the 30 taxa with the greatest absolute estimates for each adversity (Figure 3.4, Table B.4), we find there are 22 families that are predicted by multiple adversities. Of these, the families *Lachnospiraceae* and *Prevotellaceae* each represent 18.5% of shared ASVs (30 of 162 shared ASVs each). Of these, 18 of the 30 ASVs in *Prevotellaceae* decreased with early adversity, while 16 of the 30 ASVs in *Lachnospiraceae* decreased with early adversity.

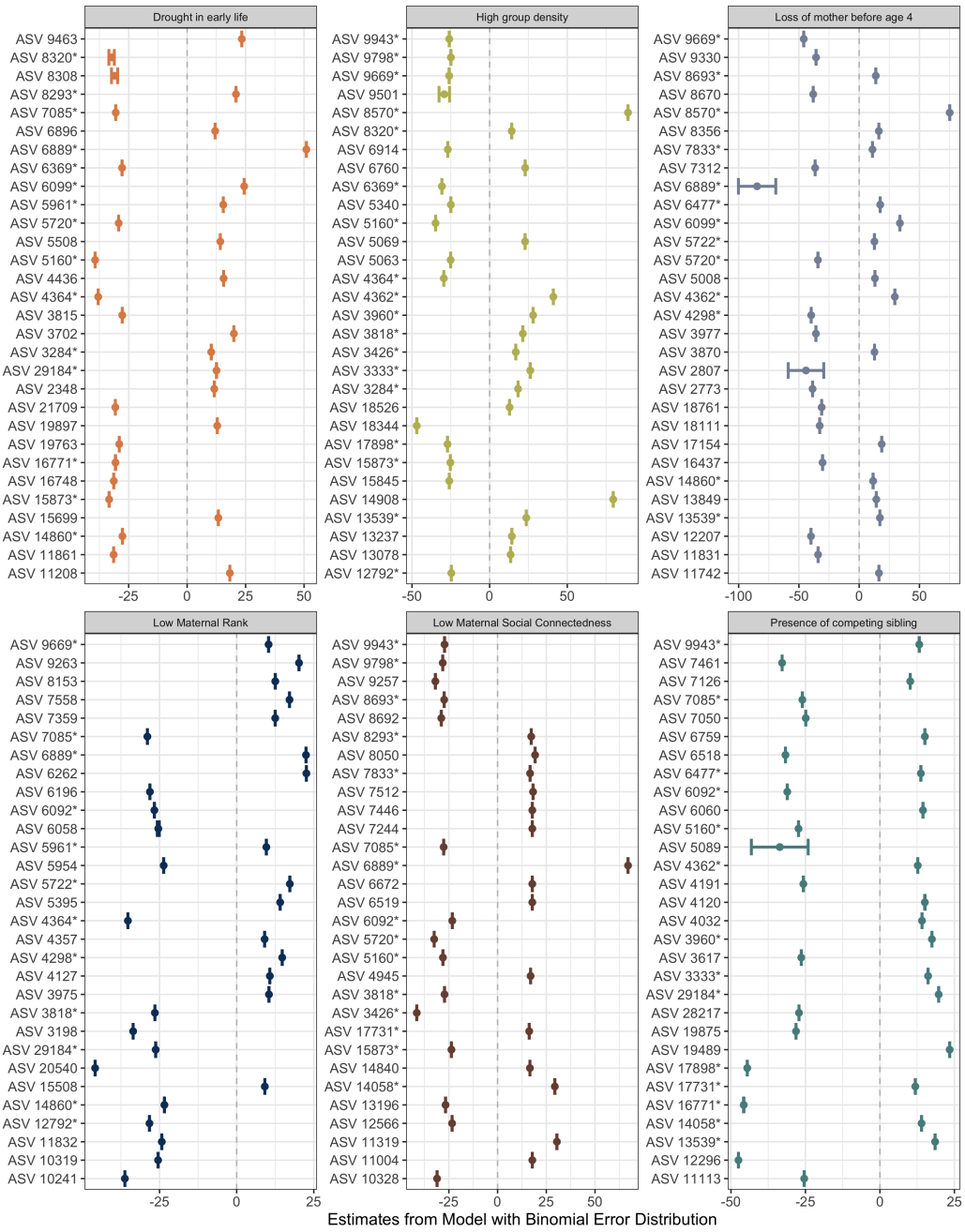

Figure 3.3. Each panel shows the 30 microbiome ASVs that were most strongly associated with each individual source of early life adversity. The x-axis shows the model estimate for one of the six sources of adversity, and the y-axis shows the microbiome ASV in question. ASVs were modeled using a binomial error distribution. Taxa with an * indicate an ASV found in the top 30 of one of more other adversities.

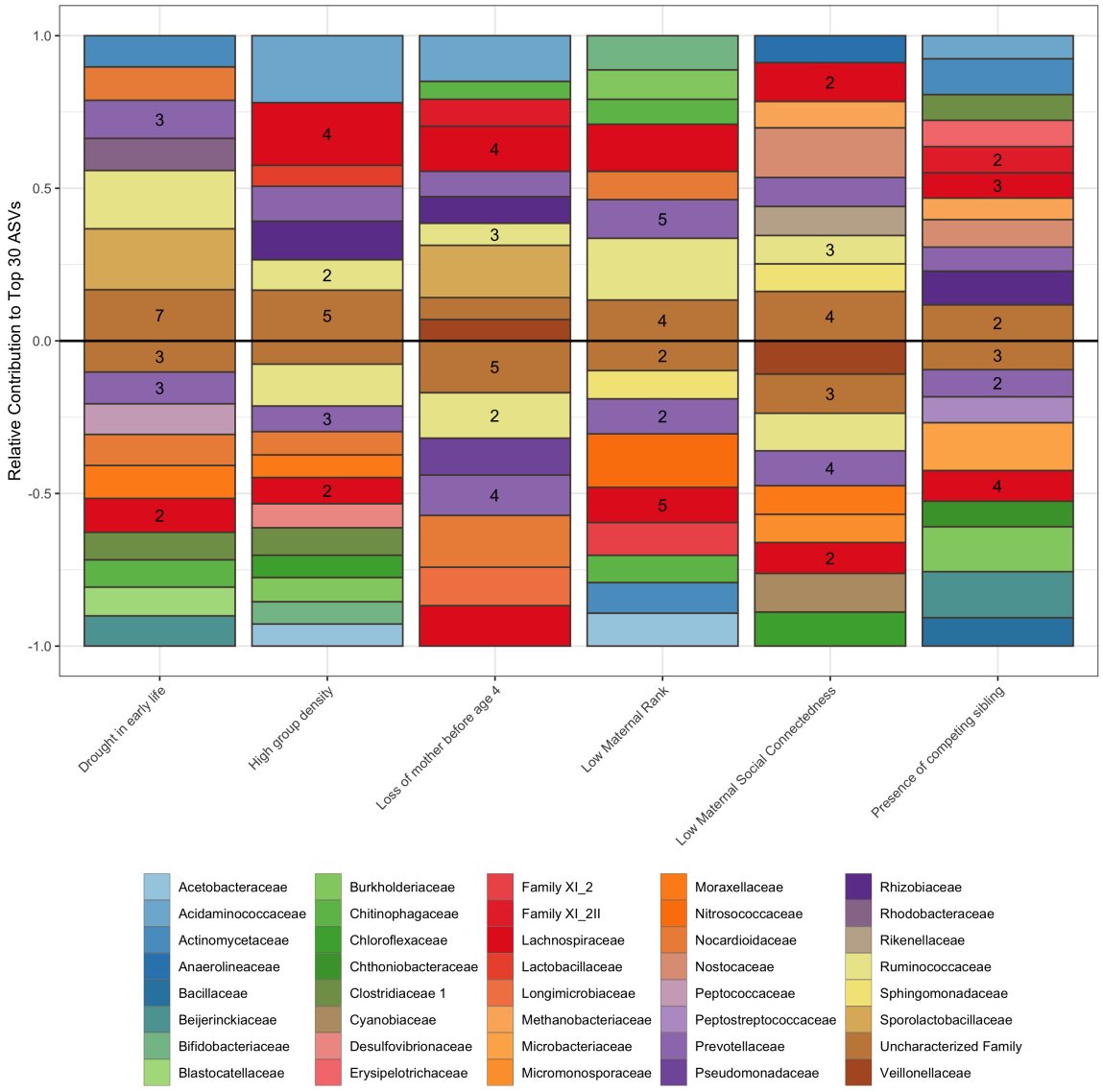

Figure 3.4. Families represented in the top 30 ASVs predicted a type of early life adversity. Each bar represents the family level designation of the 15 highest and lowest ASVs, and the height of the bar represents the relative estimate contribution. Bars with numbers on them indicate multiple ASVs from that family.

3.4.3 Drought and high social group size are linked to low microbiome stability across the lifespan

For these analyses, we tested whether the coefficient of variation (CV) in an individual's between-sample Bray-Curtis dissimilarities was predicted by the type or quantity of adversity at three time periods: early in life (prior to age four), in adulthood (after age four), and across the lifespan. Similar to the age class analysis, the effects of adversity were only evident later in life (Table B.5). Specifically, in early life, neither quantity nor type of adversity predicted stability, but experiencing a drought in early life was predictive of decreased stability in adulthood (β = 0.083, p $<$0.001, Figure 3.5, Table 3.2). Additionally, experiencing a drought or high group densities in early life was linked to increased coefficients of variation, and thus decreased stability over life (drought: β = 0.012, p = 0.005; high group size: β = 0.019, p = 0.005; Figure 3.5, Table 3.2). Across all three time periods, average sampling age and total samples available were correlated with a reduction in CV and thus an increase in stability (Table 3.2). Sex was not predictive of a change in CV (Table B.5).

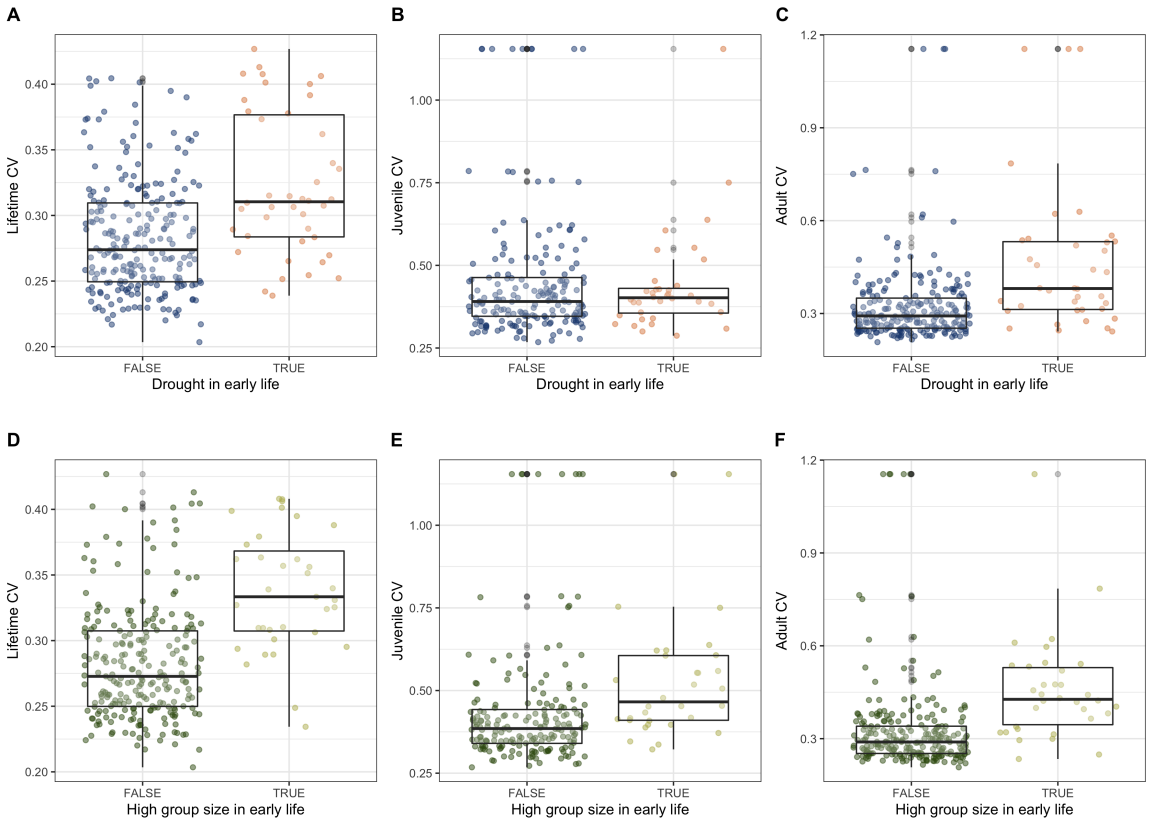

Figure 3.5. Coefficient of variation (CV) in microbiome Bray-Curtis dissimilarities across the lifespan for individual baboons who experienced early life drought and large group sizes at birth. Panels A-C show the relationship between early life drought (x-axis) and Bray-Curits CV (y-axis). Panels D-F show the relationship between large group size at birth (x-axis) and Bray-Curits CV (y-axis).

3.5 Discussion

Our study represents the first longitudinal, birth to death, test of the effects of early life adversity on gut microbiome. We found that specific types of adversity,

TABLE 3.2

SIGNIFICANT LINEAR PREDICTORS OF THE COEFFICIENT OF VARIATION IN BRAY-CURTIS MICROBIOME DISSIMILARITY FOR INDIVIDUAL BABOONS

Time period	Model Version	Variable	Estimate	SE	P-value
Juvenile	Quantity	Mean chronological age	0.13526	0.03007	1e-5
Juvenile	Quantity	Number of samples	-0.00192	4.7e-4	7e-5
Juvenile	Type	Mean chronological age	0.12943	0.03116	5e-5
Juvenile	Type	Number of samples	-0.00164	5e-4	0.00122
Adult	Quantity	Mean chronological age	-0.01219	0.00277	2e-5
Adult	Quantity	Number of samples	-0.00231	3.3e-4	0
Adult	Type	Experienced a drought in early life	0.08363	0.02359	4.7e-4
Adult	Type	Mean chronological age	-0.0127	0.00277	1e-5
Adult	Type	Number of samples	-0.00196	3.4e-4	0
Lifespan	Quantity	Mean chronological age	-0.00195	5.5e-4	5.2e-4
Lifespan	Quantity	Number of samples	-0.00115	7e-5	0
Lifespan	Type	Experienced a drought in early life	0.01226	0.00504	0.01572
Lifespan	Type	Experienced high group size in early life	0.01898	0.00562	8.5e-4
Lifespan	Type	Mean chronological age	-0.00189	5.5e-4	6.5e-4
Lifespan	Type	Number of samples	-0.00107	8e-5	0

NOTE: Significant linear predictors of ”stability” in Bray-Curtis dissimilarity. Stability is defined as the coefficient of variation in Bray-Curtis dissimilarity across an individual’s samples, was calculated across three time periods of interest. We then tested if type or quantity of early life adversity impacted CV using linear models. Full results available in Table B.5.

but not the overall number of sources of adversity, have small but important impacts on microbiome composition and stability. Interestingly, the types of early life adversity that were important to composition were not significant predictors of microbiome stability, or vice versa. Specifically, the presence of a competing sibling or having a low-ranking mother significantly changed the composition of the microbiome, especially after the juvenile period has passed. In contrast, a decrease in microbiome stability was correlated with experiencing a drought or high density group in early life. The lack of overlap in type of adversity between composition and stability may be related to individual vs. population effects: the presence of a competing sibling and low maternal rank are individual level adversities that will not change over life, while drought and high group size are adversities related to cyclical social and environmental changes. These results therefore provide indirect support for the developmental constraints hypothesis, as the animals that experienced poor environmental conditions early in life show decreased microbial stability later in life. These results are in congruence with the existing literature: while Tung et al. (2016) found profound effects on lifespan based on quantity of adversity, Zipple et al. (2019) found that loss of the mother prior to age 4 and the presence of a competing sibling were both related to lower individual survival, as well as lowered survival in the affected individual's offspring. Additionally, Lea et al. (2015) found support for the developmental constraints hypothesis where females born into a low-quality environment had lower fertility during drought than females who had been born into a high-quality environment. Thus our hypothesis that adversities that have the strongest effects on survival would be linked to differences in microbiome composition and stability was partially supported.

Further, our hypothesis stated that early life adversity would have marked and consistent effects on microbiome composition and stability. Indeed, the presence of a competing sibling and low maternal rank were both important to microbiome

composition, while drought or high group size in early life were important to stability in both adulthood and across the entire life course, but not detectable in the juvenile period. Our alternative hypothesis was that gut microbiomes that experience a disturbance such as early life adversity may temporarily be altered by that disturbance but exhibit resilience such that the community returns to its original composition (Allison and Martiny, 2008). Our results show that the microbiome appears to resist change early on, but may be influenced by other physiological consequences of adversity that only impact the microbiome later in life. However, our sample sizes for the oldest age classes are small (Table B.1), and further analyses should be done to ensure that these results are not an artifact of low sample size. One approach would be to subsample our data down to smaller sample sizes, implementing sliding age window subsets, or, given more time and resources, focused sample collection on older individuals. However, there may also be an interaction between survival and specific types of early life adversity such that animals that experience them may have lower overall survival. Careful, controlled experiments in similar model systems of early life adversity would thus complement the current research.

When we examined what taxa were predicted by the type and/or quantity of early life adversity, we found that all definitions of adversity were predictive of the presence or absence of many ASVs. Some of the ASVs with the largest effect sizes belonged to the families *Lachnospiraceae* and *Prevotellaceae*. *Lachnospiraceae* is one of the main producers of short-chain fatty acids in the gut microbiome and has been implicated in early life neural development in humans (Oliphant et al., 2021; Vacca et al., 2020). Similarly, *Prevotellaceae* is important in the breakdown of complex carbohydrates and the production of short-chain fatty acids, and reductions in *Prevotellaceae* have also been implicated in the progression of Parkinson's disease. While in some forms of adversity we see either of

these families solely increase or decrease, in other forms of adversity we see certain taxa within these families both increasing and decreasing. As we only have taxonomic resolution and not functional resolution, in order to better understand the impacts of early life adversity on the gut future research should include shotgun or metagenomic sequencing that can uncover what functions are being up or down regulated in individuals experiencing early life adversity.

Together, our results show that there are marked, long-term effects of early life adversity on both the composition and stability of the gut microbiome. By leveraging microbial, social, and environmental data on individual hosts followed from birth to death, we have been able to demonstrate that the gut microbiome warrants further investigation as a mechanism for the biological embedding of early life adversity. Together, our results bolster microbial studies that follow human populations during the first years of life or shorter lived animal populations (Billiet et al., 2017; Blanton et al., 2016; Bäckhed et al., 2015; Kirschman et al., 2020; Knutie et al., 2017; Reyman et al., 2019; Subramanian et al., 2014; Wilkinson et al., 2020). Lastly, we were able to show that the gut microbiome was a predictive biomarker of early adversity at the taxonomic level, despite the fact that the gut microbiome is incredibly diverse and exhibits a high level of functional redundancy. A further investigation into the functional properties of the gut microbiome and what pathways change based on the types and quantity of early life adversity may help in the development of microbiome therapies for the mitigation of long-term health consequences.

CHAPTER 4

CONCLUSION

For my dissertation, I leveraged an unprecedented gut microbiome dataset consisting of over 17,000 gut microbial profiles collected from a wild population of baboons (*Papio cynocephalus*) monitored by the Amboseli Baboon Research Project to characterize the relationship between the gut microbiome and host age (Chapter 2) and development (Chapter 3). Overall, my dissertation provides new evidence that the gut microbiome is an amalgam of an individual's life history and thus predictive of developmental milestones. Specifically, I created a microbiome aging clock and demonstrated that microbiome aging predicts the age at which baboons attain developmental milestones. Further, I showed that gut microbiome composition and stability are altered in response to specific types of early life adversity, but that these effects primarily manifest later in life. Together, my results illustrate that host behavior and experiences strongly impact the gut microbiome with consequences on host developmental trajectories and potentially fitness.

4.1 The gut microbiome changes predictably with age

For most species, physical and cognitive declines with age are inevitable. These changes define biological aging, a phenomenon caused by changes in cellular, tissue-, and organ-level function, which in turn lead to rising disease and mortality risk with age (Komanduri et al., 2019; López-Otín et al., 2013). An understudied aspect of aging is the that of the gut microbiome: these host-associated ecological communities have considerable potential to reflect a wide range of age-related

dynamics for their host. Specifically, while the gut microbiome's composition is, in part, controlled by its host and dependent on host health, successional theory from community ecology predicts that communities will have their own dynamics that emerge from species interactions; hence, as ecological communities develop and age, they should pass through predictable compositional stages such as increase in diversity or compositional stability (Christian et al., 2015; Connell and Slatyer, 1977; Costello et al., 2012; Dini-Andreote et al., 2015; Fierer et al., 2010). Thus, as hosts develop, senesce, and exhibit changing physical function with age, I expected that their gut microbiomes would correspondingly exhibit changes with age.

To identify age-related changes in the gut microbiome, I adopted methods from epigeneticists who use machine learning algorithms to build DNA methylation-based predictors of chronological age, also known as "epigenetic clocks" (Anderson et al., 2021; Binder et al., 2018; Chen et al., 2016b; Horvath, 2013; Marioni et al., 2015). I built a series of clocks based on algorithms popular in both the epigenetic and microbiome literature and evaluated their fit not only compared to the animal's actual chronological age, but also compared to one another. While all algorithms were consistent in the direction of results and effects, the Gaussian process regression included much more flexible parameters and resulted in the best performance overall after optimization. This is a novel application of this algorithm to both big data and microbiome data, as this type of regression is known to slow considerably with increased feature quantity. Each algorithm confirmed that gut microbiome taxonomic features exhibit a clock-like association with age and that our estimates of microbial aging were consistent with well-known patterns of sex-specific senescence in humans and other primates (Lemaître et al., 2020). Interestingly, females not only lived longer lives, but also exhibited a slower rate of microbial aging than males after maturity. As discussed in Lemaître et al. (2020),

this may be attributed to the interaction between local environments and sex-specific costs of sexual selection - e.g. from the time of maturity until their death, male-male competition is shaped by density-dependent resource access to cycling females while female competition is largely shaped by densisty-independent resource access to food (Levy et al., 2020). This is supported by the impact of season on the rate of female microbial aging: females are microbially young-for-age during the wet season, when food is more diverse and plentiful. However, this does not diminish the relevance of the gut microbiome as a biomarker as aging, and instead reinforces the idea that these host-associated ecological communities reflect a wide range of individual-specific, age-related changes in their host.

Community compositional change over time was characterized by the importance of several key taxa. Specifically, when we removed the phylum Firmicutes from our machine learning model, our ability to predict age dropped significantly. This is in congruence with the findings by Claesson et al. (2011), where the relative abundance of Firmicutes dropped by nearly 10% between the healthy young adults and the elderly subjects. Further, the removal of phylum Bacteroidetes, Proteobacteria, or Actinobacteria from our model had similar comparisons between the healthy human adults and elderly subjects (Claesson et al., 2011).

This research has several interesting future directions. First, I observed heteroskedasticity in the relationship between host age and microbiome age. Specifically, as hosts aged variation in microbial age estimates increased. Initially, I hypothesized that an increase in chronological age is often associated with the breakdown of physiological processes (e.g. aging), and thus the increase in microbial variation with increased age may be due to a breakdown of processes governing gut microbial composition or stability. However, this change also corresponds with decreasing sample sizes at very old age. This warrants further investigation: is this heteroskedasticity due to biological phenomena, or statistical artifact? This

question could be investigated in a few ways. The most obvious solution would be to increase collections for animals that are extremely old, but this is likely less than feasible since wild animals that make it to higher chronological ages disappear for a myriad of reasons. Confirmation of these results in a well-characterized captive animal model of aging may be another solution. Using the data we already have available, looking for non-linear relationships between host age and microbiome stability may also result in a more flexible and biologically accurate model of host aging.

Second, this microbiome aging clock is based on taxonomic data. Given that the gut microbiome is known to exhibit high levels of functional redundancies, I had to leverage this unprecedented dataset in order to find a distinct signature of aging. However, reliance on taxonomic designations in microbes that transfer genes horizontally make this research especially difficult to compare to microbiome aging studies in other organisms. The use of shotgun metagenomics and other functional assays will be an important next step in not only understanding how host biological functioning changes with age, but also how baboon biological aging compares to biological aging in other organisms.

Third, creating microbiome aging clocks for other species or microbiome aging clocks including data from multiple species may be a useful step forward in understanding aging across primates, or even other mammals. Projects that aid in the collaboration between field-based primate study camps such as the Primate Microbiome Project (`https://www.primatemicrobiome.org/`) have protocols for sequencing based on the Earth Microbiome Project (Gilbert et al., 2014) and are a good step towards developing a systematic understanding of variation in the aging microbiome across all primates. Grouping primates based on life history and demographic similarities may confirm that specific pressures on sexual selection impact primate aging uniquely.

4.2 The gut microbiome is a useful biomarker of host biological aging

Understanding that the gut microbiome changes with age is important, but do these changes predict important developmental milestones for hosts? My thesis provides a first answer to this question. To do this, I applied my microbiome aging clock to understand (1) which individuals have young- or old-for-age microbiomes, or faster or slower paces of aging relative to the population, and (2) whether this variation predicts the timing of maturation or death. With respect to the first question, the most pervasive effect was that of rank: I found that animals who were low-ranked exhibit faster rates of microbial aging relative to high-ranked peers. As rank is closely tied to access to resources (Levy et al., 2020), this result provides further support that increase access to resources is associated with changes to health or fitness outcomes (Herd et al., 2018).

With respect to the second question, I found that animals who were microbially old for age attained adult rank earlier and females experiencing faster paces of aging attained menarche earlier. These effects were apparent for models examining microbial metrics of aging across lifespan as well as prior to the milestone of interest, implying that the gut microbiome may indeed play a role in preparing the host for their next developmental stage. In congruence with the result that low-ranked animals exhibit faster rates of aging, I speculate that low-ranked animals develop faster in order to compensate for the energetic consequences of being low-ranked (e.g. low rates of nutrient acquisition could be related to longer inter-birth intervals) (Gesquiere et al., 2018).

Across life, there are well-known points of developmental transition, such as the weaning and the shift to solid foods or the process of puberty. Transitions outside of these periods are less well-studied due to inter-individual variation in aging and development, but, due to the gut's role in host physical functioning, the gut microbiome may provide one mechanism in which we can detect these periods. While

we tested microbial metrics over life and prior to the milestone of interest, a future line of research may include understanding the gut's role in preparing the host for their next developmental stage. One way to test this would be through testing for inflection points that might indicate a change in the rate of microbiome aging. This could be examined using piecewise regressions to estimate the age at which the slope of the microbial aging metric might change in an individual. With more sequencing resources, it might also be valuable to expand the work in Chapter 2 by examining how microbial functional changes with age would be an important next step. First and foremost, are there functional changes with age outside of weaning? For example, is there an increased incidence of anti- or pro-inflammatory pathways with age (Sanada et al., 2018; Wang et al., 2020)? As age-related wear in dentition reduces hosts' abilities to mechanically break down tough foods, do microbiomes become more efficient at breaking down diverse nutrients, or rely on other microbe-microbe mechanisms to ensure communities remain functioning? While many unanswered questions remain, my findings in Chapter 2 demonstrate that, even at the taxonomic level, the gut microbiome is a useful, noninvasive biomarker of host aging.

4.3 Early life adversity leaves a lasting impact on the microbiome

In Chapter 3, I turned my attention to whether there are long-term impacts of early life adversity on the baboon gut microbiome. In both free-living and host associated communities, events early in the formation of the community have consequences for subsequent community assembly and dynamics (Ghosh et al., 2014; Lennon and Jones, 2011; Livermore and Jones, 2015; Macpherson et al., 2017; Smith et al., 2013; Voreades et al., 2014). For instance, in the human gut microbiome, a handful of studies show that malnutrition or birth style (vaginal vs cae-

sarean) influence microbiome composition (Bäckhed et al. 2005; Cong et al. 2016; Dominguez-Bello et al. 2010). However, few studies have been able to comprehensively test whether events that occur in early life influence variation in the gut microbiome across the life span using longitudinal data. I hypothesized that early life adversity would be linked to consistent differences in microbiome composition and stability across hosts. To test this hypothesis, I tested whether early life experiences, including the six individual sources and their cumulative effects, were linked to predictable differences in gut microbial community composition, abundances of individual microbes, and microbiome community stability, both in early life as the adversity is occurring, and in adulthood.

Using types of early life adversity explored in Tung et al. (2016), I found that there were compositional differences in animals that experienced specific types of early life adversities as compared to those who did not experience any early life adversity. Specifically, the presence of a competing sibling or having a low-ranking mother significantly changed the composition of the microbiome, especially after the juvenile period has passed. The presence of both of these adversities was most important later in life. The birth of a competing sibling indicates a shorter interbirth interval and thus a short period of reliance on the mother's milk, which may impact the animal's long term development negatively. Similarly, a low-ranked mother may have fewer resources to share with her offspring, causing limitations on a developing infant that are only apparent after maturity. Similarly, I calculated microbial stability and found that specific types of early life adversity were correlated decreased stability only after the juvenile period or over lifespan. There, high group size or the presence of a drought in early life decreased gut microbial stability in adulthood. Together, these results may provide indirect support for the developmental constraints hypothesis, where animals that experienced poor environmental conditions early in life may have health consequences later in life (Lea

et al., 2015).

This work could be carried forward in a number of ways. First and simplest, is smoothing out the age class analysis by using sliding windows instead of discrete time blocks. While my results show that there are some impacts of early life adversity later in life, these effects appear and disappear between the age class windows, causing concern that they might be artifacts, despite a number of quality controls and conservative reporting. Like Chapter 2 and 3, this work would be complemented by additional metagenomic or shotgun sequencing and data from other wild animal models or experimental studies. Specifically, there were a number of important ASVs that were shared between adversities and it may be fruitful to further investigate the functional aspects that are shared between the adversities. This is especially important as the adversities studied in the Amboseli population likely cause both nutritional and psychosocial limitations, and an understanding of the functional changes associated with each adversity may help tease apart their specific impacts on the host. Studies in other model systems with well-defined types of early life adversities will also complement our understanding of the functional impact of adverse events on not only the microbiome but also host health over lifespan.

4.4 Concluding remarks

In sum, my research provides the first prospective, longitudinal study of gut microbiome dynamics and their links to aging and developmental outcomes in any wild vertebrate. By determining factors that impact the composition and stability of the gut microbiome, my results not only contribute to the field of evolutionary biology by testing the correlation between microbiome composition and markers of Darwinian fitness, but also reveal what constitutes a healthy microbiome across

life. This in turn can be used to inform microbiome interventions that aim to improve host health.

APPENDIX A

CHAPTER 2 SUPPLEMENTARY MATERIALS

Following the typical structure of a Supplementary File, this appendix includes text describing supplementary methods and results, followed by supplementary figures, then supplementary tables.

A.1 Supplementary methods and results

A.1.1 Estimating the impact of chronological age on microbial features using a linear mixed modelling approach.

Features modeled with a Gaussian error distribution.

A total of 1619 features were examined using a Gaussian error distribution, but 179 of the models failed to converge or had other fit problems. Here, we show the results for the remaining 1440 features. Of those 1440 features, 757 of the 1619 features modeled with a Gaussian distribution exhibited significant linear or quadratic relationships with age after correcting for multiple tests via Benjamini-Hochberg procedure (Figure 2.2 shows the linear coefficient for the 50 taxa with the strongest relationships as well as 11 significant community metrics, Figure A.2 shows the quadratic coefficient; FDR threshold = 0.05). A subset of successfully completed models are included in Table A.2, with the entire table available in the Supplementary Excel Sheet.

Features modeled with a binomial error distribution.

A total of 7,956 features were examined using a binomial error distribution, but 1,166 of the models failed to converge or had other fit problems. Here, we show the results for the remaining 6,790 features. Of those 6,790 features, 3381 of the features exhibited significant linear relationship with age, 2,506 had a significant quadratic relationship with age after correcting for multiple tests via Benjamini-Hochberg procedure (FDR threshold = 0.05). A subset of successfully completed models are included in Table A.3, with the entire table available in Supplementary Excel.

A.1.2 Creating and assessing age-predictive machine learning models: Introduction to the Approaches

We tested three supervised machine learning algorithms in the process of creating our microbiome aging clock: elastic net regression, random forest regression, and Gaussian process regression (Breiman, 2001; Rasmussen and Williams, 2005; Zou and Hastie, 2005). Below we summarize the strengths and weaknesses of each machine learning algorithm.

Elastic net regression is a regression algorithm that produces a linear model. It improves upon the predictions from simple linear regressions by incorporating coefficient penalties from the L1 regularization (LASSO regression) and L2 regularization (ridge regression) (Zou and Hastie, 2005). Elastic net regression is infrequently used in microbiome studies, but has produced promising results in epigenetic aging clocks due to its flexibility in choosing which features to keep and which to remove (Anderson et al., 2021; Binder et al., 2018; Chen et al., 2016a; Horvath, 2013; Marioni et al., 2015). However, elastic net regressions produce linear relationships between the input chronological age and the predicted age, which may not accurately affect the true relationship between chronological age and the microbiome.

Random forest is an ensemble learning method that creates a number of parallel decision trees, each producing its own prediction (Breiman, 2001). The prediction is then averaged among all trees to create the final estimate. A key advantage of random forest over elastic net regression is that it does not assume a linear relationship between the predicted estimate and the input chronological age, but the model may be biased by correlated features. Random forest is commonly used in microbiome research, including other microbiome clocks (Bosch et al., 2017; Chen et al., 2019; Metcalf et al., 2016; Saulnier et al., 2011; Subramanian et al., 2014; Thaiss et al., 2016).

Gaussian process regression is a nonparametric, Bayesian approach that infers a probability distribution over all the potential functions that fit the data (Rasmussen and Williams, 2005). Like random forests, Gaussian process regressions do not assume a linear relationship between chronological age and predicted age, but has the additional advantage of kernel customization. As such, Gaussian process regressions may be able to better handle heteroskedasticity in the data (an issue in our clock; see below). As an increase in chronological age is often associated with the breakdown of physiological processes (e.g. aging), heteroskedasticity in microbial age estimates may indicate a breakdown of the host's processes that regulate the gut microbiome.

A.1.3 Creating and assessing age-predictive machine learning models: Methods and optimization of machine learning algorithms

Prior to running each algorithm, all features were center log ratio transformed within sample. We then chose a ratio of training to test dataset. To do this, I first compared the model fit of different ratios of training to test sets. These included the following training:test splits: 50:50, 60:40, 75:25, 80:20, and 90:10. In order to balance model performance and the risk of overfitting, we chose an 80:20 data

split.

In order to calculate a microbial age estimate for every sample and estimate generalization error, we used a nested cross-validation framework. Each of the algorithms chosen has its own internal cross-validation where a subset of the training data is held apart and used to internally validate the model. We added an additional, external layer of cross-validation with our 80:20 training:test data split. We classified samples into five different test sets where individual was as evenly represented as possible in all training and test sets. As the number of samples varied between individuals, we randomly assigned each sample a test set without replacement if an individual's sample count was less than five, or with replacement if an individual's sample count was greater than five. For each model run, four of the test datasets were treated altogether as training data and the fifth set was the validation test set.

Elastic net regressions were run in R using function cv.glmnet() from package glmnet (Friedman et al., 2010). The two main parameters for this model are λ, which is the penalty from the LASSO regression that penalizes extra predictors by shrinking coefficients to zero, and α, the parameter that balances between minimizing between the residual sum of squares and minimizing the magnitude of the coefficients. cv.glmnet() automatically fits 100 values of λ by default and names the λ that produces the minimum cross-validated error "lambda.min". We used lambda.min as our value of λ. For α, we manually ran the model with 200 values of alpha (from 0 to 1 in increasing increments of 0.005) and picked a value of alpha that would minimize the mean absolute error and maximize the adjusted R^2 (Figure A.4).

Random forest regressions were conducted in Python 3 using scikit-learn (Pedregosa et al., 2011; Van Rossum and Drake, 2009). The main parameter here was the number of decision trees being used, and defaults to 100. Too many trees

could result in overfitting so in order to minimize overfitting and optimize R^2, we ran a series of Random forest regressions with different numbers of trees: we increased the number of trees in increments of 50, stopping at 400 because of minimal changes in R^2 relative to 200 trees.

Gaussian process regressions were also conducted in Python 3 using scikit-learn (Pedregosa et al., 2011; Van Rossum and Drake, 2009). In both the non-heteroskedastic-kernel model and heteroskedastic-kernel model, the main parameters we use to modify the kernel function include the scale and bounds. These parameters moderate the level of overfitting in the algorithm: the scale parameter specifies a starting point for which the algorithm optimizes within the confines of the bounds parameters. As with the parameters for the other models, we incrementally changed both the scale parameter within a wide range of bounds and checked the output model's R^2 and median error. Ultimately, we kept a wide range of bounds (1 to 100) and set the scale parameter to the median euclidian distance of the dataset as calculated in R using function vegdist() from R package vegan (Dixon, 2003).

Due to the heteroskedasticity exhibited by the models above (Figure A.5), we modified the Gaussian process regression's kernel function further to account for the variance within the dataset. Specifically, we multiplied the variance in the training data by the radial basis function, which distributed the higher variance in later life more evenly across lifespan.

A.1.4 Creating and assessing age-predictive machine learning models: Comparison of machine learning algorithms

To assess model accuracy, we used the predicted age estimates from all 5 runs of the nested cross-validation procedure to assess model fit and accuracy. As in Horvath (2013), we regressed the sample's chronological age (age_c) against the

model's predicted microbial age (age_m) and determining the (1) R^2 correlation coefficient between age_c and age_m with either a linear fit, (2) Pearson's correlation coefficient, and (3) the median error, or the median absolute difference between age_c and age_m (Table A.4 and Figure A.6). Across algorithms, we observed that males always aged faster than females, which is consistent with well-known patterns of sex-specific senescence in humans and other primates (Lemaître et al., 2020). The Gaussian Process Regression with the heteroskedastic kernel was the best model for every metric assessed - it maximized R^2 and Pearson's R to 0.488 and 0.698 (respectively) while minimizing median error. It also was the only model with which we were able to alleviate any heteroskedasticity.

A.2 Supplementary Figures and Tables

TABLE A.1

A SUB-SET OF THE 9,575 MICROBIOME FEATURES USED IN ANALYSES.

Feature	**Feature Category**	**ASV DNA Sequence**
ASV Richness	Alpha Diversity	NA
ASV Shannon's H	Alpha Diversity	NA
ASV Simpson's Diversity	Alpha Diversity	NA
Hill Number (q=1)	Alpha Diversity	NA
Hill Number (q=2)	Alpha Diversity	NA
Compositional PC1	Composition	NA
Compositional PC2	Composition	NA
Compositional PC3	Composition	NA
Compositional PC4	Composition	NA
Compositional PC5	Composition	NA
Archaea $>$ Euryarchaeota	Phylum	NA
Archaea $>$ Euryarchaeota $>$ Halobacteriales $>$ Halococcaceae	Family	NA
Archaea $>$ Euryarchaeota $>$ Halobacteriales $>$ Halococcaceae $>$ Halalkalicoccus	Genus	NA
ASV 1	ASV	*Full ASV Sequence*

NOTE: A total of 9,575 features were used to characterize the gut microbiome. To be included, features must have been present in three or more samples. Features were grouped into the following categories: ASVs (n = 8493), genus (747), family (290), phyla (30), compositional principal components (10), and alpha diversity (5). For ASVs, the Feature column corresponds to their "ASV ID", which is a short identifier. The "ASV DNA Sequence" column is the ASV's specific sequence. Table is truncated due to length constraints; see supplementary excel file.

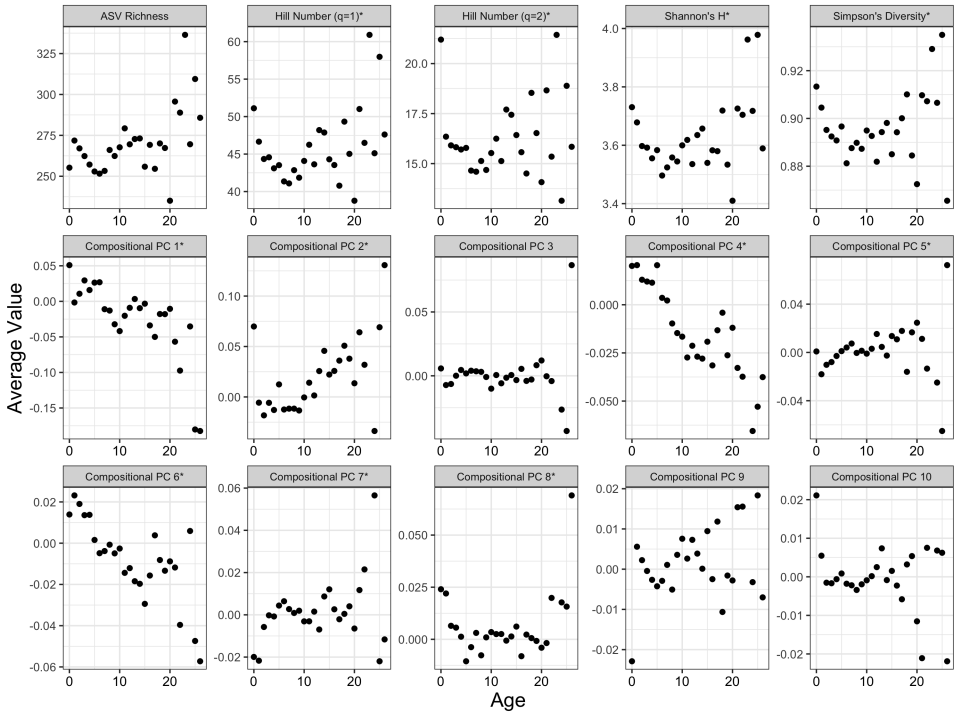

Figure A.1. Relationship between all community metrics and age. Metrics that were significantly predicted by age are indicated with a * after their label.

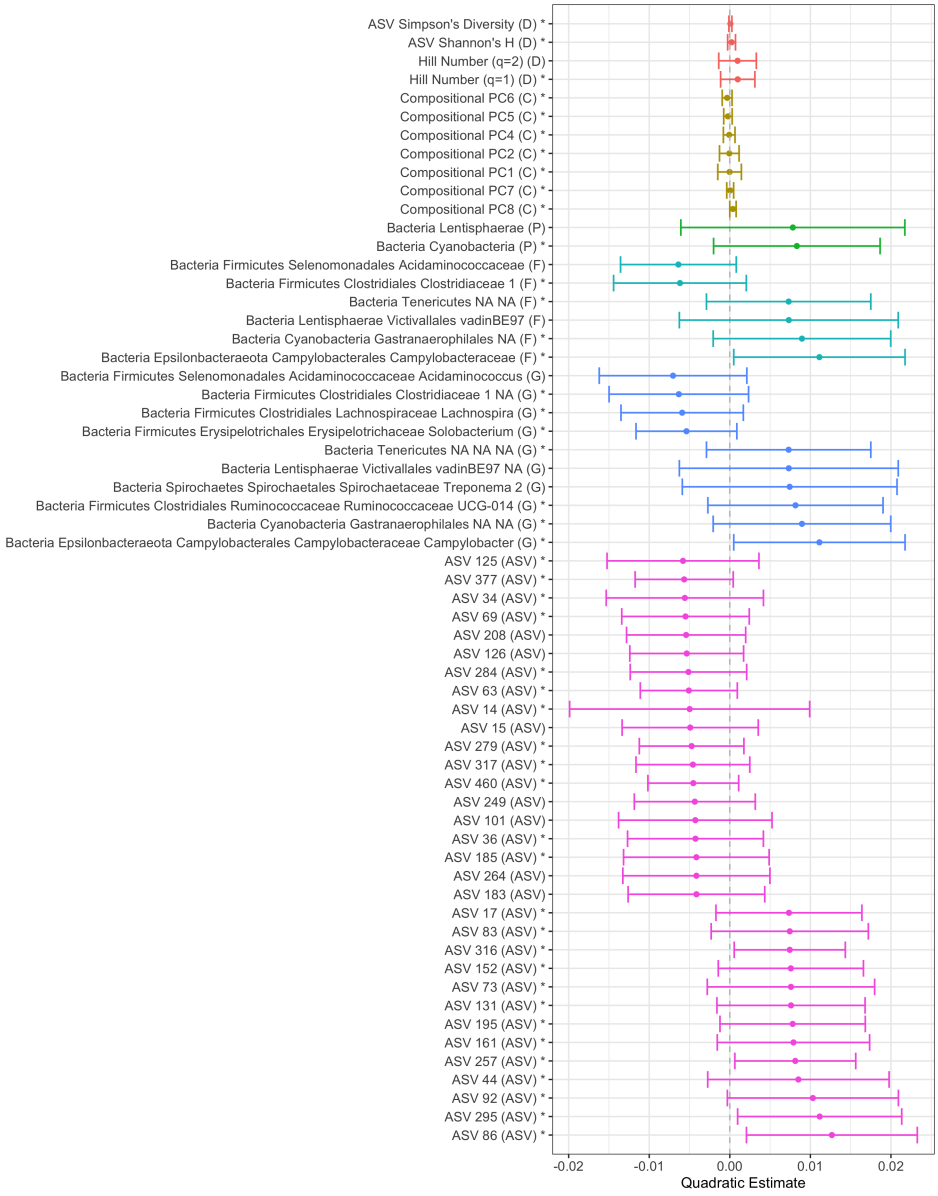

Figure A.2. Taxa with the highest quadratic associations with age. Plot shows the size of the quadratic estimate for taxa that had significant associations with age. Points are colored by category of feature.

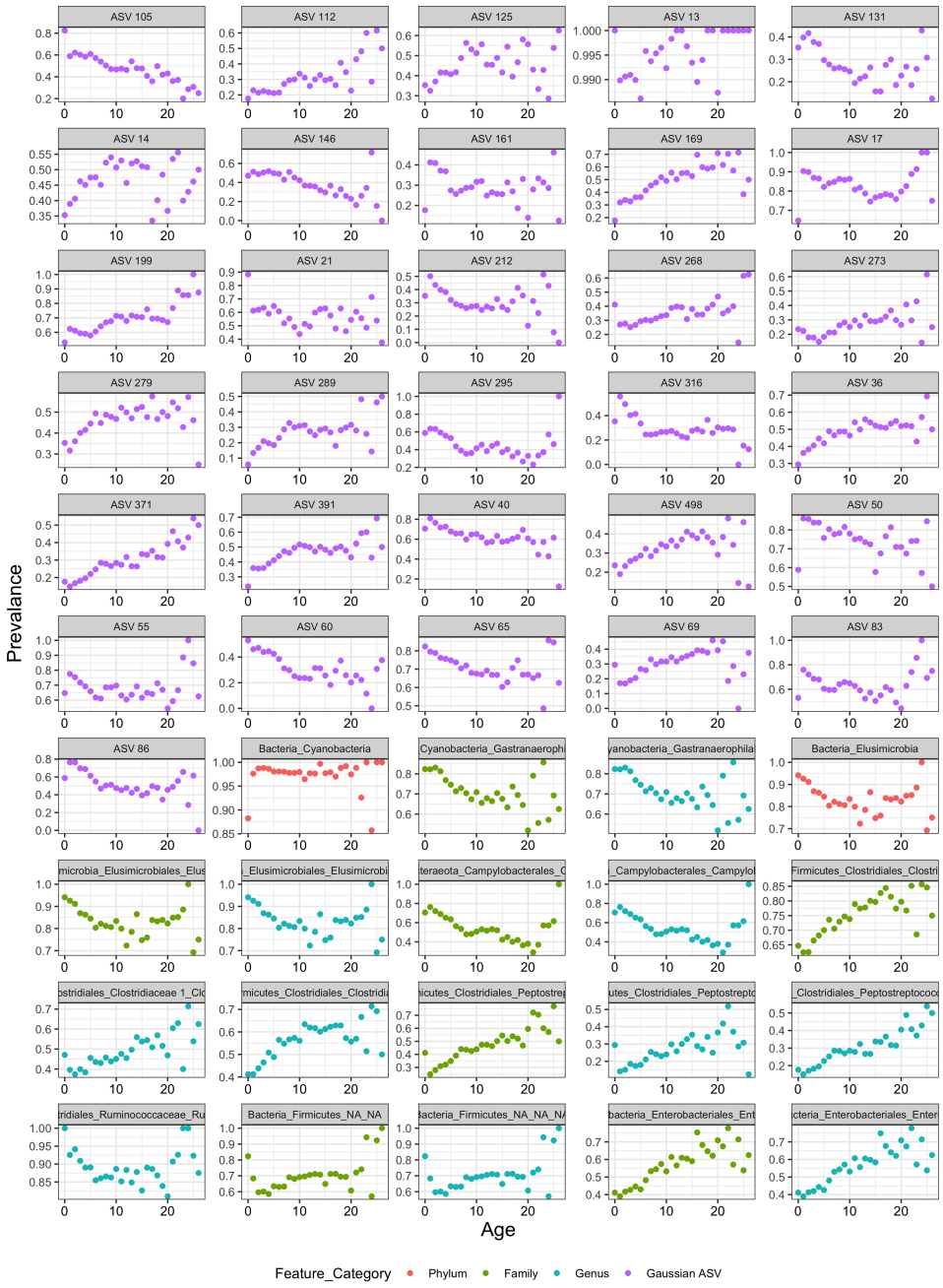

Figure A.3. Relationship between the top 50 features modeled with a Gaussian error distribution and age.

TABLE A.2

RESULTS FROM A SERIES OF LINEAR MIXED MODELS TESTING WHETHER HOST AGE PREDICTS MICROBIOME FEATURES MODELED USING A GAUSSIAN ERROR DISTRIBUTION.

Feature	**Feature Category**	**Variable Type**	**Coefficient**	**SE**	**Adjusted P-value**
ASV Richness	Alpha Diversity	Linear	-0.00097	6.00E-04	0.20404
ASV Richness	Alpha Diversity	Quadratic	0.00011	6.00E-04	0.17916
ASV Shannon's H	Alpha Diversity	Linear	-0.0016	0.00049	0.00397
ASV Shannon's H	Alpha Diversity	Quadratic	0.00022	0.00049	0.00085
Compositional PC1	Composition	Linear	-0.00807	0.00146	0
Compositional PC1	Composition	Quadratic	-3.00E-05	0.00146	0.89176
Compositional PC2	Composition	Linear	-0.00481	0.00122	0.00039
Compositional PC2	Composition	Quadratic	-6.00E-05	0.00122	0.73072
Archaea > Euryarchaeota	Phylum	Linear	-0.0148	0.0092	0.20711
Archaea > Euryarchaeota	Phylum	Quadratic	0.00184	0.0092	0.06623
Archaea > Thaumarchaeota	Phylum	Linear	-0.00407	0.00105	0.00051
Archaea > Thaumarchaeota	Phylum	Quadratic	0.00027	0.00105	0.12038

NOTE: Model results from a series of linear mixed models testing the whether age is predictive of microbial features. Features included here were only those that were present in 25% or more of samples that could be assessed using a Gaussian error distribution. Table is truncated due to length constraints; see supplementary excel file.

TABLE A.3

RESULTS FROM A SERIES OF LINEAR MIXED MODELS TESTING WHETHER HOST AGE PREDICTS THE PRESENCE OF MICROBIOME FEATURES MODELED USING A BINOMIAL ERROR DISTRIBUTION.

ASV ID	Related Genus	Variable Type	Coefficient	SE	Adjusted P-value
ASV 10699	Bacteria > Tenericutes > Mollicutes RF39 > NA > NA	Linear	-94395.12	34.38	0
ASV 10699	Bacteria > Tenericutes > Mollicutes RF39 > NA > NA	Quadratic	-8741.02	10.82	0
ASV 21757	Bacteria > Proteobacteria > Sphingomonadales > Sphingomonadaceae > Qipengyuania	Linear	-74684.56	55529.35	0.30959
ASV 21757	Bacteria > Proteobacteria > Sphingomonadales > Sphingomonadaceae > Qipengyuania	Quadratic	-7474.96	5553.64	0.37038
ASV 4720	Bacteria > Bacteroidetes > NA > NA > NA	Linear	-37456.51	0.13	0
ASV 4720	Bacteria > Bacteroidetes > NA > NA > NA	Quadratic	-5756.86	0.13	0

NOTE: Model results from a series of linear mixed models testing the whether age is predictive of microbial features. Features included here were only those that were present in under 25% of samples and could be assessed using a binomial error distribution. Table is truncated due to length constraints; see supplementary excel file.

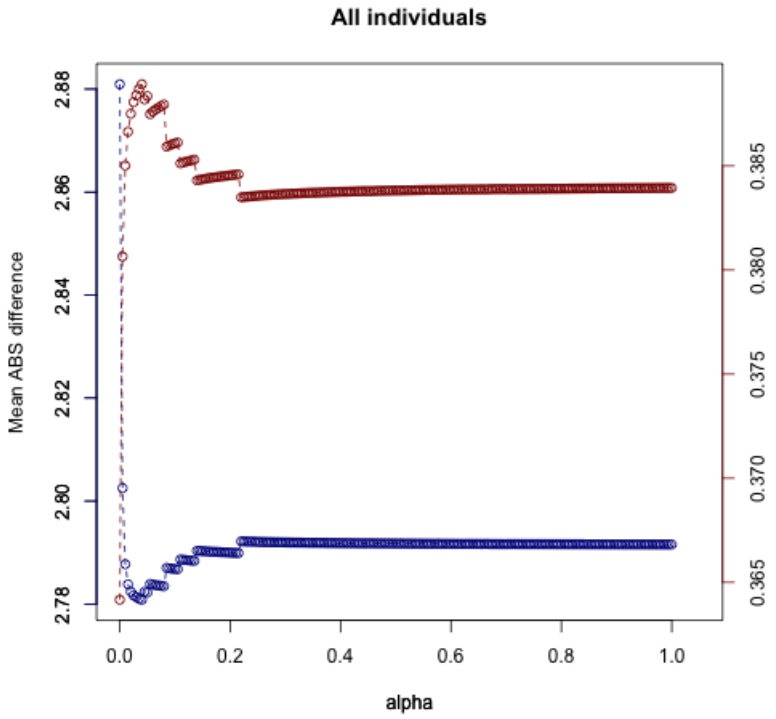

Figure A.4. Approach for optimizing the alpha parameter in elastic net regressions. For different values of alpha (x-axis), I calculated the mean absolute error in predicted host age (blue; left-hand y-axis), and adjusted R^2 for the relationship between true and predicted age (red; right-hand y-axis). All other parameters were held constant.

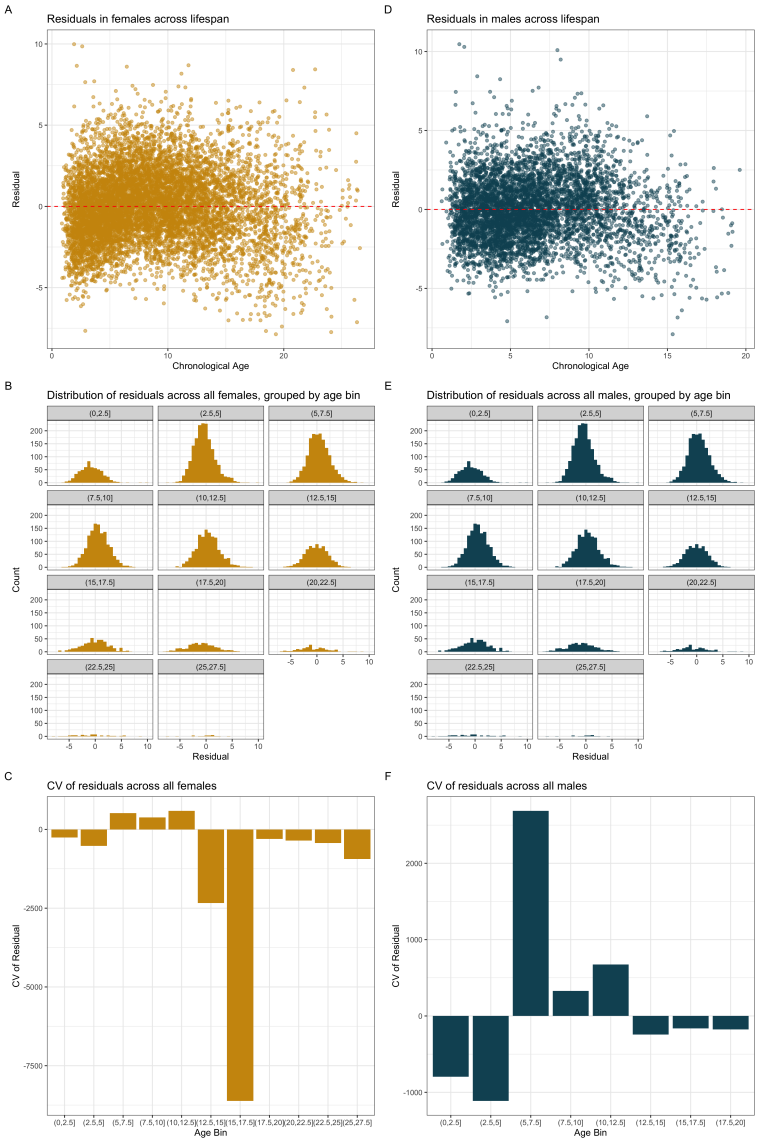

Figure A.5. Variance in residuals across lifespans in the Gaussian process regression prior to correction. Plots show chronological age relative to the residuals of the age_m produced by a Gaussian process regression with a radial basis function kernel. Females are in yellow, and males are in blue. (A) shows a scatter plot of age_c and the residuals of age_m. As a host gets older, the spread of the residuals gets wider. (B) shows the distributions of the residuals at different age subsets. The distribution flattens around 12.5 in females and 10 in males. (C) shows the coefficient of variation of the residuals is especially high at the around 12.5 in females and 10 in males.

TABLE A.4

SUMMARY METRICS FOR EACH MACHINE LEARNING ALGORITHM: ELASTIC NET REGRESSION, RANDOM FOREST, AND GAUSSIAN PROCESS REGRESSION

Algorithm	**Subset**	**Adjusted R^2**	**Pearson's R**	**Median Error**
Elastic Net Regression	All	0.417	0.645	2.195
Elastic Net Regression	Females	0.414	0.644	2.386
Elastic Net Regression	Males	0.457	0.676	1.931
Random Forests Regression	All	0.291	0.539	2.533
Random Forest Regression	Females	0.272	0.522	2.832
Random Forest Regression	Males	0.338	0.581	2.14
Gaussian Process Regression	All	0.433	0.658	2.001
Gaussian Process Regression	Females	0.428	0.655	2.214
Gaussian Process Regression	Males	0.457	0.676	1.724
Gaussian Process Regression with heteroskedastic kernel	All	0.488	0.698	1.962
Gaussian Process Regression with heteroskedastic kernel	Females	0.489	0.699	2.15
Gaussian Process Regression with heteroskedastic kernel	Males	0.5	0.707	1.706

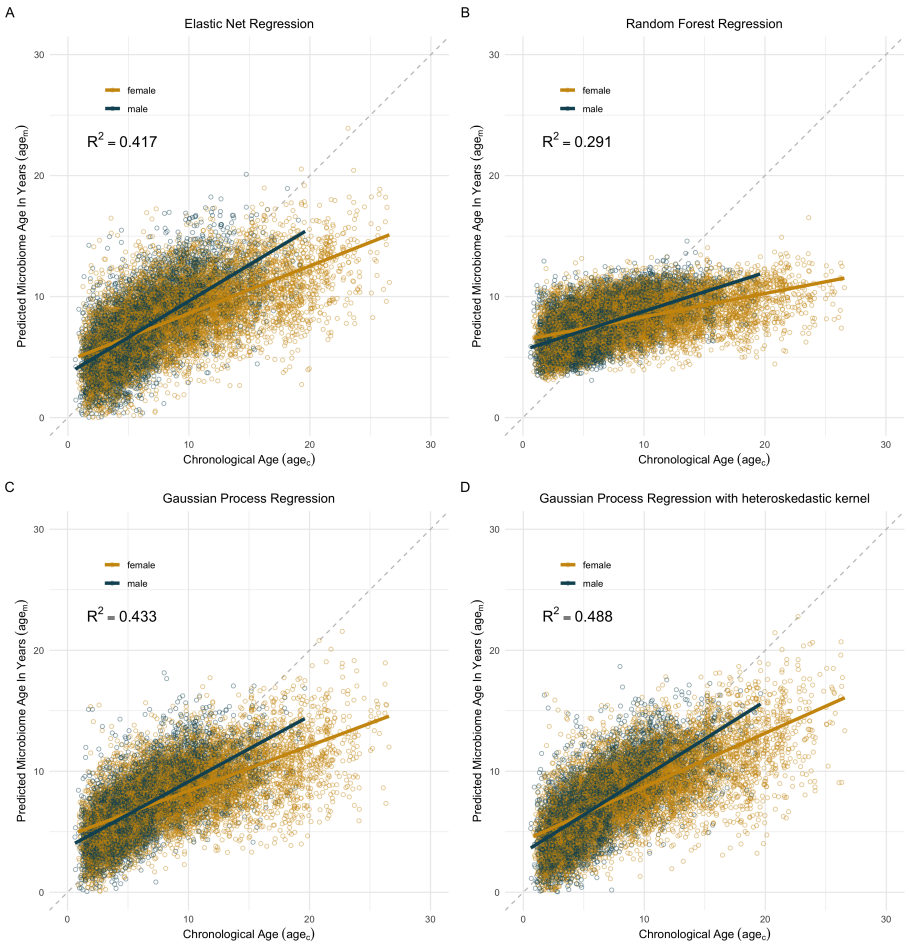

Figure A.6. Microbiome clocks of aging from an ensemble of machine learning algorithms. Plots show predicted host ages (age_m) relative to the host's true, chronological age (age_c) at the time of sample collection. Points are colored by sex with yellow indicating a female sample and blue indicating a male sample. Grey dashed line indicates a 1-to-1 relationship between age_c and age_m. Plot A is the output from an elastic net regression and plot B is the output of a Random Forest regression. Plots C and D show the estimates from Gaussian process regression, but the kernel input for model in plot D was customized to account for heteroskedasticity in the data.

TABLE A.5

RESULTS FROM LINEAR MIXED MODELS SUBSET TO EACH SEX AND TESTING FOR SEX-SPECIFIC DIFFERENCES IN AGE_M

Sex	Subset	Predictor	n samples	Estimate	SE	p-value
Females	Prior Maturity	Intercept	1980	2.829	0.180	$<$0.001
Females	Prior Maturity	Chronological Age	1980	0.710	0.057	$<$0.001
Females	Post Maturity	Intercept	6265	5.131	0.075	$<$0.001
Females	Post Maturity	Chronological Age	6265	0.378	0.006	$<$0.001
Females	Lifespan	Intercept	8245	4.201	0.051	$<$0.001
Females	Lifespan	Chronological Age	8245	0.449	0.005	$<$0.001
Males	Prior Maturity	Intercept	2382	3.086	0.144	$<$0.001
Males	Prior Maturity	Chronological Age	2382	0.623	0.039	$<$0.001
Males	Post Maturity	Intercept	2849	4.251	0.073	$<$0.001
Males	Post Maturity	Chronological Age	2849	0.533	0.006	$<$0.001
Males	Lifespan	Intercept	5231	3.231	0.064	$<$0.001
Males	Lifespan	Chronological Age	5231	0.631	0.009	$<$0.001

NOTE: Data were subset to three timeframes – prior to maturity, post maturity, and over the entire lifespan. In each of those subsets, age_m was our response variable, as predicted by the variables in the predictor column.

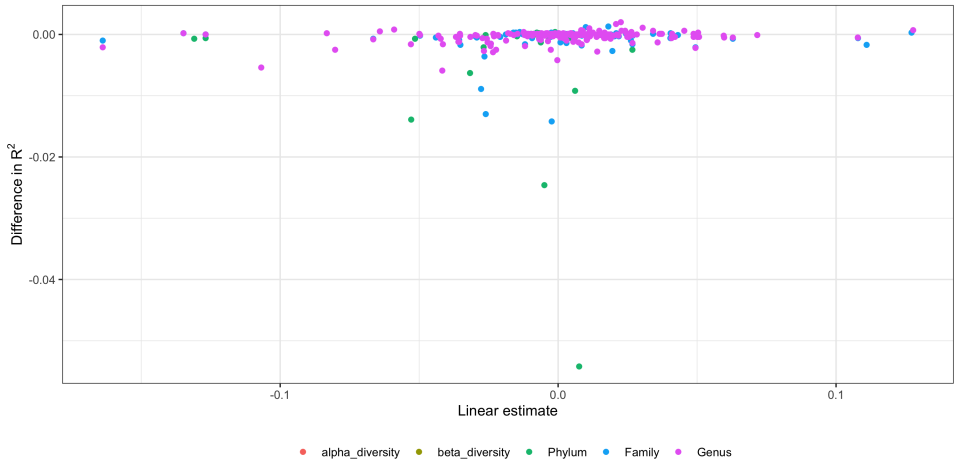

Figure A.7. Correlating the results from the linear mixed model analysis of features and the leave-one-out version of the machine learning algorithm. X-axis shows the difference in R^2 from the algorithm without missing features to algorithms with selected missing features. Y-axis shows the linear coefficient for age produced when age is regressed on the feature of interest. Points represent all non-ASV features.

TABLE A.6

SELECTED RESULTS FROM GAUSSIAN PROCESS REGRESSION

LEAVE ONE OUT ANALYSIS

Missing Feature	**Feature Type**	**R^2**	**Pearson's R**	**Median Error (years)**	**Difference in R^2**
None	All	0.47774	0.69133	1.98586	-0
Bacteria > Firmicutes	Phylum	0.42357	0.65099	2.10845	-0.0542
Bacteria > Bacteroidetes	Phylum	0.45318	0.67334	2.03185	-0.0246
Bacteria > Firmicutes > Clostridiales > Ruminococcaceae	Family	0.46355	0.68099	2.03044	-0.0142
Bacteria > Epsilonbacteraeota	Phylum	0.46386	0.68122	2.03770	-0.0139
Bacteria > Bacteroidetes > Bacteroidales > Prevotellaceae	Family	0.46470	0.68183	1.98056	-0.013
Bacteria > Proteobacteria	Phylum	0.46855	0.68465	1.99950	-0.0092
Bacteria > Firmicutes > Selenomonadales > Veillonellaceae	Family	0.46888	0.68489	1.98232	-0.0089
Bacteria > Actinobacteria	Phylum	0.47147	0.68678	2.00864	-0.0063
Bacteria > Bacteroidetes > Bacteroidales > Prevotellaceae > NA	Genus	0.47185	0.68706	1.99841	-0.0059

NOTE: Microbiome features important to machine learning model. All 1080 non-ASV features were tested in this analysis. Table is truncated due to length constraints; see supplementary excel file.

TABLE A.7

DESCRIPTION OF PREDICTOR VARIABLES FOR LINEAR MIXED MODELS AND COX PROPORTIONAL HAZARDS MODELS

Variable	**Type of effect**	**Description of effect**	**Justification of effect**	**Relevant microbial metric**
Individual ID	random	Identity of the host.	Individual idosynchrasies have been shown to be an important contributor to a host's gut microbiome.	Age acceleration only
Hydrological year	random	Seasons in Amboseli consist of a short, intense wet season starting in November and an prolonged dry season. Hydrological year thus ranges from November to October.	Amboseli is a highly variable seasonal environment and resource availability varies dramatically from hydrological year to hydrological year.	Age acceleration only
Social group at time of collection	random	Host's social group on the date of collection. Census data regarding group membership are recorded for each study group several times a week. Census data include all births, deaths, immigrations and emigrations, and allow us to know group membership and size with considerable accuracy.	Increased sociality and cohabitation have been shown to be important determinants of the gut microbiome.	Age acceleration only

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Chronological age	fixed	Host's chronological age. The age of most individuals (all females and 67% of males in this dataset) is known through direct observation as the baboons are followed from birth.	Included due to machine learning algorithm's performance at higher chronological ages: as chronological age increased, microbial age estimates were consistently lower (compressed relative to chronological age).	Age acceleration only
Average maximum temperature during sampling month	fixed	An average of the maximum temperature for the month of collection. ABRP collects the daily minimum and maximum temperature using a min/max thermometer located in its research camp.	Average temperatures may impact the types of forage available which may alter gut microbiome composition.	Age acceleration only
Total rainfall during sampling month	fixed	Total rainfall during the month of collection. ABRP collects daily rainfall using a rain gauge located in its research camp.	Total rainfall may impact the types of forage available which may alter gut microbiome composition.	Age acceleration only
Season (wet)	fixed	Whether the collection month was part of the wet or dry season based on hydrological patterns in Amboseli.	Amboseli is a highly variable seasonal environment and resource availability varies dramatically between the wet and dry season.	Age acceleration only
Loss of mother before age 4	fixed	Source of early life adversity: whether an animal's mother died prior to the animal turning 4. While baboons are weaned and nutritionally independent by the age of 1.5 years, they remain socially dependent on their mothers much longer.	Mothers provide the primary source for both nutrition until weaned and sociality after weaning, both of which may impact the gut microbiome depending on the age of loss.	Both

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Sibling born within 1.5 years of focal individual	fixed	Source of early life adversity: whether an animal's mother had another infant before the animal turned 1.5 years of age, which represents the lowest quartile of surviving interbirth intervals in this population.	Mothers provide the primary source of nutrition for infants until weaning, which occurs approximately at 1.5 years of age. However, a competing sibling may cause the mother to avert resources away from the focal animal towards their new, more vulnerable sibling.	Both
Born during a drought year	fixed	Source of early life adversity: whether the animal was born in a drought year. ABRP defines drought years as those with less than 200 mm of rainfall (approximately the bottom 15% of years).	Drought limits the amount of preferred foods available in the environment. Animals born during a drought year maybe impacted by low nutritional availability to their mother both while pregnant and lactating.	Both
Highest quartile group size at time of birth	fixed	Source of early life adversity: whether the animal was born into a group in the highest quartile. This corresponds to groups with 38 or more adult animals present. Census data regarding group membership are recorded for each study group several times a week. Census data include all births, deaths, immigrations and emigrations, and allow us to know group membership and size with considerable accuracy.	High group size at birth may impact nutritional resource availability.	Both

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Low maternal social connectedness at birth	fixed	Source of early life adversity: whether the animal was born to a mother in the lowest quartile of social connectedness. Maternal social connectedness is measured as the frequency with which the subjectâ€™s mother was a grooming partner with other adult female populations in her social group, relative to all other adult females in the population that year. This value is then normalized relative to these rates for all other females alive in the population during that same year, as well as standardized and adjusted for observer effort.	Social isolation is linked to lower survival in adult females and lower offspring survival (Silk et al. 2003; Archie et al. 2014). Additionally, animals born to socially isolated mothers may not interact with other group members as often.	Both
Low maternal rank at birth	fixed	Source of early life adversity: Whether an animal was born to a mother with the lower quartile rank. Low dominance rank is defined as a social status in the bottom quartile of all ranks. Dominance ranks measured on a monthly basis, using the dyadic aggressive interactions recorded over the previous month. These records are then compiled into a pairwise interaction matrix and arranged in such a way that rank is a parsimonious measure of wins and losses between low and high ranked animals.	Animals born to low ranked mothers may experience increased competition for resources. Females additionally inherit their mother's rank, so this effect will persist and impact her own offspring.	Both

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Cumulative early life adversity	fixed	The sum of the described adverse early life events that happened to an animal. These include	Increased early life adversity may have an additive effect on the health and fitness of an individual animal.	Both
Rank (ordinal for males, proportional for females)	fixed	Social dominance rank is measured as each animal's ordinal rank in the dominance hierarchy. Dominance ranks measured on a monthly basis, using the dyadic aggressive interactions recorded over the previous month. These records are then compiled into a pairwise interaction matrix and arranged in such a way that rank is a parsimonious measure of wins and losses between low and high ranked animals. In cases were rank impacts access to density dependent resources, ordinal rank can be scaled by group size to produce proportional rank.	Social dominance rank impacts access to other animals and resources.	Both
Number of adult females in group at time of collection	fixed	The count of adult females present in the group at the time of collection.	A measure of group density for density dependent resources.	Both

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Dyadic social connectedness in females	fixed	A measure of the strength of an animal's top 3 female bonds. This is assessed based on grooming interactions. Grooming is the most common form of physical contact in baboons and is correlated with microbiome composition. Grooming interactions are recorded through representative interaction sampling, where observers move through the group at random, recording all observed instances of grooming.	Animals that are more socially connected may interact with other animals more.	Both
Number of maternal sisters in group	fixed	The number of maternal half-sisters in an animal's social group. Census data regarding group membership are recorded for each study group several times a week. Census data include all births, deaths, immigrations and emigrations, and allow us to know group membership and size with considerable accuracy.	The number of maternal half-sisters in a group indicate an animal's social network and potentially the mother's experience successfully raising offspring.	Both
Hybridization score	fixed	A measure estimating the proportion of an individual's genetic ancestry attributable to Anubis (closer to 1) or yellow (closer to 0) baboon ancestry based on genotypes at 14 microsatellite loci.	Animals with increased Anubis ancestry are more likely to mature at earlier ages.	Both

TABLE A.7 CONTINUED FROM PREVIOUS PAGE

Variable	Type of effect	Description of effect	Justification of effect	Relevant microbial metric
Number of excess cycling females in group	fixed	The difference between the number of cycling females and the number of mature males within an animal's social group. Census data regarding group membership are recorded for each study group several times a week. Census data include all births, deaths, immigrations and emigrations, and allow us to know group membership and size with considerable accuracy. Sexual maturity in males is characterized by fully enlarged testicles. Sexual maturity in females occurs at menarche. Reproductive state is observable in yellow baboons by the state of a female's sexual skin, and is assessed during each day's census.	A direct estimate of the intensity of sexual competition a male will encounter as an adult. An important predictor of male maturation.	Both

TABLE A.8

DESCRIPTION OF DEVELOPMENTAL MILESTONES

Milestone	**Sex**	**Description of event**	**Description of censored animals**
Age of first rank attainment	F	The age at which an individual consistently began to outrank at least one other adult of the same sex in agonistic interactions. Animals were excluded if their rank date was not known to be accurate within a few days.	Animals that matured prior to the assessment of juvenile female ranks (started in $\sim$1998) or that did not attain their first rank by Jan 2021 were censored.
Age of menarche	F	Menarche is assessed by near daily visual inspection of the sexual skin for evidence of the first sexual swelling. Animals were excluded if they died prior to maturation or their maturity date was not known to be accurate within a few days.	Animals that did not mature by Jan 2021, dispersed, or were part of a group dropped from observation were censored.
Age of first live birth	F	Age at which a female had her first live offspring. Animals were excluded if they died prior to successfully giving birth.	Animals that did not give birth by Jan 2021, dispersed, or were part of a group dropped from observation were censored.
Age of testicular enlargement	M	Testicular enlargement is assessed by systematic visual inspection of the scrotal sac each month, starting from when a male has reached four until his testes are enlarged. During this time, the scrotum will shift from appearing like a concave flap of skin to rapidly enlarging until completely convex and pendulous at puberty. Animals were excluded if they died prior to maturation or if their maturity date was not known to be accurate within a few days.	Animals that did not mature by Jan 2021, dispersed, or were part of a group dropped from observation were censored.

TABLE A.8 CONTINUED FROM PREVIOUS PAGE

Milestone	Sex	Description of event	Description of censored animals
Age of dispersal from natal group	M	The age at which an individual leaves their natal group, without returning, permanently. Animals were exluded if they died prior to maturation or if their dispersal could not be confirmed with high confidence.	Animals that did not disperse by Jan 2021, dispersed, or were part of a group dropped from observation were censored.
Age of adult rank attainment	M	The age at which an individual consistently began to outrank at least one other adult of the same sex in agonistic interactions. Animals were excluded if they died prior to maturation or if their rank date was not known to be accurate within a few days.	Animals that did not attain their adult rank by Jan 2021, dispersed, or were part of a group dropped from observation were censored.
Juvenile survival	Both	Assessing whether an animal died prior to age 4.	Animals that did not die by the age of 4, dispersed, or were part of a group dropped from observation were censored.
Adult survival	F	Assessing adult female longevity. Animals that died prior to age 4 were excluded from this analysis.	Adult animals that did not die by Jan 2021, dispersed, or were part of a group dropped from observation were censored.

TABLE A.9

SAMPLE SIZES FOR SOCIO-ENVIRONMENTAL PREDICTORS OF MICROBIAL AGING

Metric	Timeframe	Male Samples	Males	Female Samples	Females
Age Acceleration	Juvenile	2347	169	1912	178
Age Acceleration	Adult	2204	99	4543	132
Age Acceleration	Lifespan	4355	168	6743	192
Pace of Aging	Juvenile	2362	161	1956	161
Pace of Aging	Adult	2839	110	6235	140
Pace of Aging	Lifespan	4881	161	7197	188

TABLE A.10

SAMPLE SIZES FOR DEVELOPMENTAL MILESTONES

Milestone	Subset	Hybrid Score Included	n Samples	n Individuals	Missing Data	Censored	Events
Female Rank Attainment	Prior	Y	2346	147	28	25	94
Female Rank Attainment	Prior	N	2346	147	20	27	100
Female Rank Attainment	Lifespan	Y	4270	147	28	25	94
Female Rank Attainment	Lifespan	N	4270	147	20	27	100
Menarche	Prior	Y	2961	139	0	0	139
Menarche	Prior	N	2961	139	0	0	139
Menarche	Lifespan	Y	5707	155	16	0	139
Menarche	Lifespan	N	5707	155	7	0	148
First Live Birth	Prior	Y	4371	164	41	0	123
First Live Birth	Prior	N	4371	164	33	0	131
First Live Birth	Lifespan	Y	6053	164	41	0	123
First Live Birth	Lifespan	N	6053	164	33	0	131
Testicular Enlargement	Prior	Y	4419	142	20	0	122
Testicular Enlargement	Prior	N	4419	142	16	0	126
Testicular Enlargement	Lifespan	Y	4436	153	31	0	122

TABLE A.10 CONTINUED FROM PREVIOUS PAGE

Milestone	Subset	Hybrid Score Included	n Samples	n Individuals	Missing Data	Censored	Events
Testicular Enlargement	Lifespan	N	4436	153	27	0	126
Dispersal	Prior	Y	4442	148	37	0	111
Dispersal	Prior	N	4442	148	35	0	113
Dispersal	Lifespan	Y	4455	157	46	0	111
Dispersal	Lifespan	N	4455	157	44	0	113
Male Rank Attainment	Prior	Y	3918	121	43	0	78
Male Rank Attainment	Prior	N	3918	121	41	0	80
Male Rank Attainment	Lifespan	Y	3937	121	43	0	78
Male Rank Attainment	Lifespan	N	3937	121	41	0	80

TABLE A.11

SAMPLE SIZES FOR JUVENILE AND ADULT SURVIVAL MODELS

Timeframe	Subset	n Samples	n Individuals	Missing Data	Censored	Events
Juvenile	All Animals	3039	310	19	267	24
Juvenile	Males	1417	151	9	132	10
Juvenile	Females	1622	159	10	135	14
Adult Female	Lifespan with Hybrid Score	8127	211	49	84	78

TABLE A.12

SOCIO-ENVIRONMENTAL PREDICTORS OF AGE ACCELERATION PRIOR TO MATURITY

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	2.682	1.267	0.034	
Females	Individual sources	Chronological age	-0.236	0.061	0	All model estimates are compressed compared to chronological age
Females	Individual sources	Average maximum temperature during sampling month	0.007	0.038	0.864	
Females	Individual sources	Total rainfall during sampling month	0.001	0.002	0.589	
Females	Individual sources	Season (wet)	-0.112	0.145	0.44	
Females	Individual sources	Loss of mother before age 4	-0.36	0.182	0.05	Females that lose their mother are microbially young for age prior to maturity.
Females	Individual sources	Sibling born within 1.5 years of focal individual	0.209	0.186	0.264	
Females	Individual sources	Born during a drought year	0.187	0.22	0.397	
Females	Individual sources	Highest quartile group size at time of birth	0.424	0.244	0.085	
Females	Individual sources	Low maternal social connectedness at birth	-0.182	0.178	0.309	

TABLE A.12 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Low maternal rank at birth*	0.422	0.199	0.035	Females born to lower ranked mothers are microbially young for age prior to maturity.
Females	Individual sources	Number of adult females in group at time of collection	0.002	0.016	0.893	
Females	Cumulative adversity	Intercept	2.59	1.27	0.042	
Females	Cumulative adversity	Chronological age	-0.255	0.061	0	All model estimates are compressed compared to chronological age
Females	Cumulative adversity	Average maximum temperature during sampling month	0.01	0.038	0.794	
Females	Cumulative adversity	Total rainfall during sampling month	0.001	0.002	0.653	
Females	Cumulative adversity	Season (wet)	-0.117	0.145	0.42	
Females	Cumulative adversity	Cumulative adversity	-0.116	0.086	0.181	
Females	Cumulative adversity	Number of adult females in group at time of collection	0.01	0.016	0.532	
Males	Individual sources	Intercept	4.117	1.071	0	
Males	Individual sources	Chronological age	-0.366	0.042	0	All model estimates are compressed compared to chronological age
Males	Individual sources	Average maximum temperature during sampling month	-0.029	0.033	0.372	
Males	Individual sources	Total rainfall during sampling month	0.001	0.001	0.303	

TABLE A.12 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Individual sources	Season (wet)	-0.011	0.128	0.932	
Males	Individual sources	Loss of mother before age 4	0.104	0.159	0.515	
Males	Individual sources	Sibling born within 1.5 years of focal individual	0.004	0.159	0.979	
Males	Individual sources	Born during a drought year	-0.378	0.188	0.045	Males born during a drought are microbially young for age prior to maturity.
Males	Individual sources	Highest quartile group size at time of birth	0.278	0.207	0.181	
Males	Individual sources	Low maternal social connectedness at birth	-0.263	0.157	0.096	
Males	Individual sources	Low maternal rank at birth*	0.13	0.162	0.425	
Males	Individual sources	Number of adult females in group at time of collection	NA	NA	NA	
Males	Cumulative adversity	Intercept	4.044	1.071	0	
Males	Cumulative adversity	Chronological age	-0.355	0.042	0	All model estimates are compressed compared to chronological age
Males	Cumulative adversity	Average maximum temperature during sampling month	-0.029	0.033	0.372	
Males	Cumulative adversity	Total rainfall during sampling month	0.001	0.001	0.338	
Males	Cumulative adversity	Season (wet)	-0.006	0.128	0.96	

TABLE A.12 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Cumulative adversity	Cumulative adversity	-0.048	0.071	0.497	
Males	Cumulative adversity	Number of adult females in group at time of collection	NA	NA	NA	

NOTE: This table shows the fixed effects of four different linear mixed models where age acceleration was the response variable. Data was subset to only samples taken prior to the median age of maturation and to either males or females. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable - positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.13

RANDOM EFFECTS FOR AGE ACCELERATION MODELS PRIOR TO MATURITY

Sex	Type of adversity	Random effect	Variance	SD	n
Females	Individual Sources	Individual ID	0.428	0.655	178
Females	Individual Sources	Hydrological year	0.213	0.462	14
Females	Individual Sources	Social group at time of collection	0.051	0.226	12
Females	Cumulative adversity	Individual ID	0.471	0.686	178
Females	Cumulative adversity	Hydrological year	0.225	0.474	14
Females	Cumulative adversity	Social group at time of collection	0.059	0.242	12
Males	Individual Sources	Individual ID	0.26	0.51	169
Males	Individual Sources	Hydrological year	0.102	0.32	14
Males	Individual Sources	Social group at time of collection	0.05	0.224	12
Males	Cumulative adversity	Individual ID	0.273	0.522	169
Males	Cumulative adversity	Hydrological year	0.097	0.312	14
Males	Cumulative adversity	Social group at time of collection	0.055	0.234	12

TABLE A.14

SOCIO-ENVIRONMENTAL PREDICTORS OF PACE OF AGING PRIOR TO MATURITY

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	0.778	0.042	0	
Females	Individual sources	Loss of mother before age 4	-0.041	0.029	0.168	
Females	Individual sources	Sibling born within 1.5 years of focal individual	0.049	0.031	0.121	
Females	Individual sources	Born during a drought year	0.046	0.032	0.156	
Females	Individual sources	Highest quartile group size at time of birth	0.049	0.034	0.154	
Females	Individual sources	Low maternal social connectedness at birth	-0.014	0.029	0.62	
Females	Individual sources	Low maternal rank at birth*	0.088	0.031	0.005	Females born to a lower ranked mother have a slower pace of aging prior to maturity.
Females	Individual sources	Average number of adult females in group at time of collection	-0.002	0.002	0.41	
Females	Cumulative adversity	Intercept	0.781	0.04	0	
Females	Cumulative adversity	Cumulative adversity	-0.011	0.013	0.391	
Females	Cumulative adversity	Average number of adult females in group at time of collection	-0.001	0.002	0.508	

TABLE A.14 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Individual sources	Intercept	0.623	0.01	0	
Males	Individual sources	Loss of mother before age 4	0.028	0.016	0.091	
Males	Individual sources	Sibling born within 1.5 years of focal individual	0.002	0.016	0.9	
Males	Individual sources	Born during a drought year	0.04	0.017	0.018	Males born during a drought have a faster pace of aging prior to maturity.
Males	Individual sources	Highest quartile group size at time of birth	-0.008	0.017	0.65	
Males	Individual sources	Low maternal social connectedness at birth	0.016	0.014	0.276	
Males	Individual sources	Low maternal rank at birth*	-0.008	0.015	0.601	
Males	Individual sources	Average number of adult females in group at time of collection	NA	NA	NA	
Males	Cumulative adversity	Intercept	0.624	0.01	0	
Males	Cumulative adversity	Cumulative adversity	0.013	0.006	0.036	Males with higher cumulative early life adversity have a faster pace of aging prior to maturity.
Males	Cumulative adversity	Average number of adult females in group at time of collection	NA	NA	NA	

NOTE: This table shows the fixed effects of four different linear models where pace of aging was the response variable. Data was subset to only samples taken prior to the median age of maturation and to either males or females. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable - positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.15

SOCIO-ENVIRONMENTAL PREDICTORS OF AGE ACCELERATION POST MATURITY

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	2.682	1.267	0.034	
Females	Individual sources	Chronological age	-0.236	0.061	0	All model estimates are compressed compared to chronological age
Females	Individual sources	Average maximum temperature during sampling month	0.007	0.038	0.864	
Females	Individual sources	Total rainfall during sampling month	0.001	0.002	0.589	
Females	Individual sources	Season (wet)	-0.112	0.145	0.44	
Females	Individual sources	Loss of mother before age 4	-0.36	0.182	0.05	Females that lose their mother are microbially young for age prior to maturity.
Females	Individual sources	Sibling born within 1.5 years of focal individual	0.209	0.186	0.264	
Females	Individual sources	Born during a drought year	0.187	0.22	0.397	
Females	Individual sources	Highest quartile group size at time of birth	0.424	0.244	0.085	
Females	Individual sources	Low maternal social connectedness at birth	-0.182	0.178	0.309	

TABLE A.15 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Low maternal rank at birth*	0.422	0.199	0.035	Females born to lower ranked mothers are microbially young for age prior to maturity.
Females	Individual sources	Number of adult females in group at time of collection	0.002	0.016	0.893	
Females	Cumulative adversity	Intercept	2.59	1.27	0.042	
Females	Cumulative adversity	Chronological age	-0.255	0.061	0	All model estimates are compressed compared to chronological age
Females	Cumulative adversity	Average maximum temperature during sampling month	0.01	0.038	0.794	
Females	Cumulative adversity	Total rainfall during sampling month	0.001	0.002	0.653	
Females	Cumulative adversity	Season (wet)	-0.117	0.145	0.42	
Females	Cumulative adversity	Cumulative adversity	-0.116	0.086	0.181	
Females	Cumulative adversity	Number of adult females in group at time of collection	0.01	0.016	0.532	
Males	Individual sources	Intercept	4.117	1.071	0	
Males	Individual sources	Chronological age	-0.366	0.042	0	All model estimates are compressed compared to chronological age
Males	Individual sources	Average maximum temperature during sampling month	-0.029	0.033	0.372	
Males	Individual sources	Total rainfall during sampling month	0.001	0.001	0.303	

TABLE A.15 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Individual sources	Season (wet)	-0.011	0.128	0.932	
Males	Individual sources	Loss of mother before age 4	0.104	0.159	0.515	
Males	Individual sources	Sibling born within 1.5 years of focal individual	0.004	0.159	0.979	
Males	Individual sources	Born during a drought year	-0.378	0.188	0.045	Males born during a drought are microbially young for age prior to maturity.
Males	Individual sources	Highest quartile group size at time of birth	0.278	0.207	0.181	
Males	Individual sources	Low maternal social connectedness at birth	-0.263	0.157	0.096	
Males	Individual sources	Low maternal rank at birth*	0.13	0.162	0.425	
Males	Individual sources	Number of adult females in group at time of collection	NA	NA	NA	
Males	Cumulative adversity	Intercept	4.044	1.071	0	
Males	Cumulative adversity	Chronological age	-0.355	0.042	0	All model estimates are compressed compared to chronological age
Males	Cumulative adversity	Average maximum temperature during sampling month	-0.029	0.033	0.372	
Males	Cumulative adversity	Total rainfall during sampling month	0.001	0.001	0.338	
Males	Cumulative adversity	Season (wet)	-0.006	0.128	0.96	

TABLE A.15 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Cumulative adversity	Cumulative adversity	-0.048	0.071	0.497	
Males	Cumulative adversity	Number of adult females in group at time of collection	NA	NA	NA	

NOTE: This table shows the fixed effects of four different linear mixed models where age acceleration was the response variable. Data was subset to only samples taken post the median age of maturation and to either males or females. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable - positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.16

RANDOM EFFECTS FOR POST MATURITY AGE ACCELERATION MODELS

Sex	Type of adversity	Random effect	Variance	SD	n
Females	Individual Sources	Individual ID	0.515	0.718	132
Females	Individual Sources	Hydrological year	0.13	0.36	14
Females	Individual Sources	Social group at time of collection	0.039	0.197	8
Females	Cumulative adversity	Individual ID	0.497	0.705	132
Females	Cumulative adversity	Hydrological year	0.128	0.358	14
Females	Cumulative adversity	Social group at time of collection	0.052	0.227	8
Males	Individual Sources	Individual ID	0.352	0.593	99
Males	Individual Sources	Hydrological year	0.056	0.237	14
Males	Individual Sources	Social group at time of collection	0.075	0.274	7
Males	Cumulative adversity	Individual ID	0.384	0.62	99
Males	Cumulative adversity	Hydrological year	0.057	0.238	14
Males	Cumulative adversity	Social group at time of collection	0.085	0.291	7

NOTE: This table shows the random effects of four different linear mixed models where age acceleration was the response variable. Data was subset to only samples taken post the median age of maturation and to either males or females. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.17

SOCIO-ENVIRONMENTAL PREDICTORS OF PACE OF AGING POST MATURITY

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	0.437	0.02	0	
Females	Individual sources	Loss of mother before age 4	0.014	0.009	0.108	
Females	Individual sources	Sibling born within 1.5 years of focal individual	-0.005	0.009	0.568	
Females	Individual sources	Born during a drought year	0	0.011	0.969	
Females	Individual sources	Highest quartile group size at time of birth	-0.004	0.01	0.697	
Females	Individual sources	Low maternal social connectedness at birth	0	0.008	0.97	
Females	Individual sources	Low maternal rank at birth*	0.003	0.009	0.759	
Females	Individual sources	Average rank (ordinal for males*, proportional for females)	-0.033	0.018	0.07	Lower ranked animals have a faster pace of aging after maturity.
Females	Individual sources	Average number of adult females in group at time of collection	-0.001	0.001	0.377	
Females	Individual sources	Average dyadic social connectedness in females	-0.009	0.006	0.108	
Females	Cumulative adversity	intercept	0.44	0.02	0	
Females	Cumulative adversity	Cumulative adversity	0.001	0.004	0.853	

TABLE A.17 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Cumulative adversity	Average rank (ordinal for males*, proportional for females)	-0.032	0.017	0.057	Lower ranked animals have a faster pace of aging after maturity.
Females	Cumulative adversity	Average number of adult females in group at time of collection	-0.001	0.001	0.195	
Females	Cumulative adversity	Average dyadic social connectedness in females	-0.009	0.006	0.109	
Males	Individual sources	Intercept	0.619	0.02	0	
Males	Individual sources	Loss of mother before age 4	-0.02	0.018	0.254	
Males	Individual sources	Sibling born within 1.5 years of focal individual	-0.05	0.02	0.012	Males with a competing sibling have a slower pace of aging after maturity.
Males	Individual sources	Born during a drought year	-0.066	0.03	0.031	Males born during a drought have a slower pace of aging after maturity.
Males	Individual sources	Highest quartile group size at time of birth	-0.056	0.032	0.082	
Males	Individual sources	Low maternal social connectedness at birth	0.007	0.019	0.731	
Males	Individual sources	Low maternal rank at birth*	0.017	0.018	0.344	
Males	Individual sources	Average rank (ordinal for males*, proportional for females)	-0.003	0.001	0.05	Lower ranked males have a faster pace of aging after maturity.

TABLE A.17 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Individual sources	Average number of adult females in group at time of collection	NA	NA	NA	
Males	Individual sources	Average dyadic social connectedness in females	NA	NA	NA	
Males	Cumulative adversity	intercept	0.626	0.017	0	
Males	Cumulative adversity	Cumulative adversity	-0.022	0.009	0.014	Males with higher cumulative adversity have a slower pace of aging after maturity.
Males	Cumulative adversity	Average rank (ordinal for males*, proportional for females)	-0.002	0.001	0.071	Lower ranked animals have a faster pace of aging after maturity.
Males	Cumulative adversity	Average number of adult females in group at time of collection	NA	NA	NA	
Males	Cumulative adversity	Average dyadic social connectedness in females	NA	NA	NA	

NOTE: The fixed effects of four different linear models where pace of aging was the response variable, with data subset to samples post median age of maturation in either males or females. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable: positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.18

SOCIO-ENVIRONMENTAL PREDICTORS OF AGE ACCELERATION OVER LIFESPAN

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	3.39	0.7	0	
Females	Individual sources	Chronological age	0.449	0.012	0.001	All model estimates are compressed compared to chronological age
Females	Individual sources	Average maximum temperature during sampling month	-0.004	0.021	0.857	
Females	Individual sources	Total rainfall during sampling month	0.001	0.001	0.282	
Females	Individual sources	Season (wet)	-0.18	0.078	0.021	Female samples from the wet season are young for age over life.
Females	Individual sources	Loss of mother before age 4	-0.036	0.16	0.823	
Females	Individual sources	Sibling born within 1.5 years of focal individual	0.265	0.166	0.113	
Females	Individual sources	Born during a drought year	-0.183	0.189	0.333	
Females	Individual sources	Highest quartile group size at time of birth	0.062	0.217	0.776	
Females	Individual sources	Low maternal social connectedness at birth	-0.116	0.148	0.436	
Females	Individual sources	Low maternal rank at birth*	-0.16	0.171	0.35	

TABLE A.18 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Rank (ordinal for males*, proportional for females)	1.745	0.206	0.001	Low ranked females are microbially young for age over life.
Females	Individual sources	Number of adult females in group at time of collection	-0.007	0.009	0.415	
Females	Cumulative adversity	Intercept	3.388	0.703	0	
Females	Cumulative adversity	Chronological age	0.449	0.011	0.001	All model estimates are compressed compared to chronological age
Females	Cumulative adversity	Average maximum temperature during sampling month	-0.004	0.021	0.846	
Females	Cumulative adversity	Total rainfall during sampling month	0.001	0.001	0.287	
Females	Cumulative adversity	Season (wet)	-0.178	0.078	0.022	Female samples from the wet season are young for age over life.
Females	Cumulative adversity	Cumulative adversity	0.011	0.074	0.885	
Females	Cumulative adversity	Rank (ordinal for males*, proportional for females)	1.723	0.199	0.001	Low ranked females are microbially young for age over life.
Females	Cumulative adversity	Number of adult females in group at time of collection	-0.006	0.01	0.506	
Males	Individual sources	Intercept	3.811	0.814	0	

TABLE A.18 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Individual sources	Chronological age	0.596	0.02	0.001	All model estimates are compressed compared to chronological age
Males	Individual sources	Average maximum temperature during sampling month	0.001	0.024	0.957	
Males	Individual sources	Total rainfall during sampling month	0.002	0.001	0.088	
Males	Individual sources	Season (wet)	-0.103	0.091	0.259	
Males	Individual sources	Loss of mother before age 4	0.092	0.137	0.502	
Males	Individual sources	Sibling born within 1.5 years of focal individual	-0.032	0.142	0.823	
Males	Individual sources	Born during a drought year	-0.451	0.193	0.021	Males born during a drought are microbially young for age over life.
Males	Individual sources	Highest quartile group size at time of birth	0.471	0.22	0.033	Males born into high density groups are microbially old for age over life.
Males	Individual sources	Low maternal social connectedness at birth	-0.395	0.143	0.006	Males born to socially isolated mothers are microbially young for age over life.
Males	Individual sources	Low maternal rank at birth*	0.102	0.144	0.477	
Males	Individual sources	Rank (ordinal for males*, proportional for females)	0.033	0.009	0	Low ranked males are microbially young for age over life.

TABLE A.18 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Cumulative adversity	Intercept	3.589	0.812	0	
Males	Cumulative adversity	Chronological age	0.612	0.019	0.001	All model estimates are compressed compared to chronological age
Males	Cumulative adversity	Average maximum temperature during sampling month	0.002	0.024	0.948	
Males	Cumulative adversity	Total rainfall during sampling month	0.002	0.001	0.085	
Males	Cumulative adversity	Season (wet)	-0.103	0.091	0.259	
Males	Cumulative adversity	Cumulative adversity	-0.062	0.065	0.345	
Males	Cumulative adversity	Rank (ordinal for males*, proportional for females)	0.027	0.008	0.001	Low ranked males are microbially young for age over life.

NOTE: This table shows the fixed effects of four different linear models where age acceleration was the response variable. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable - positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.19

RANDOM EFFECTS FOR AGE ACCELERATION MODELS OVER LIFESPAN

Sex	Type of adversity	Random effect	Variance	SD	n
Females	Individual Sources	Individual ID	0.504	0.71	192
Females	Individual Sources	Hydrological year	0.101	0.318	14
Females	Individual Sources	Social group at time of collection	0.009	0.096	8
Females	Cumulative adversity	Individual ID	0.489	0.699	192
Females	Cumulative adversity	Hydrological year	0.1	0.316	14
Females	Cumulative adversity	Social group at time of collection	0.026	0.16	8
Males	Individual Sources	Individual ID	0.25	0.5	168
Males	Individual Sources	Hydrological year	0.091	0.301	14
Males	Individual Sources	Social group at time of collection	0.089	0.298	7
Males	Cumulative adversity	Individual ID	0.273	0.522	168
Males	Cumulative adversity	Hydrological year	0.081	0.284	14
Males	Cumulative adversity	Social group at time of collection	0.1	0.316	7

NOTE: This table shows the random effects of four different linear mixed models where age acceleration was the response variable. Data was subset to only samples taken post the median age of maturation and to either males or females. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.20

SOCIO-ENVIRONMENTAL PREDICTORS OF PACE OF AGING OVER LIFESPAN

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Individual sources	Intercept	0.667	0.043	0	
Females	Individual sources	Loss of mother before age 4	0.036	0.022	0.1	
Females	Individual sources	Sibling born within 1.5 years of focal individual	-0.01	0.023	0.682	
Females	Individual sources	Born during a drought year	-0.012	0.024	0.614	
Females	Individual sources	Highest quartile group size at time of birth	0.008	0.026	0.743	
Females	Individual sources	Low maternal social connectedness at birth	-0.005	0.021	0.813	
Females	Individual sources	Low maternal rank at birth*	0.015	0.023	0.529	
Females	Individual sources	Average rank (ordinal for males*, proportional for females)	-0.181	0.044	0	Lower ranked females have a faster pace of aging than higher ranked females.
Females	Individual sources	Average number of adult females in group at time of collection	-0.001	0.002	0.706	
Females	Cumulative adversity	Intercept	0.664	0.042	0	
Females	Cumulative adversity	Cumulative adversity	0.004	0.01	0.69	

TABLE A.20 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Females	Cumulative adversity	Average rank (ordinal for males*, proportional for females)	-0.172	0.042	0	Lower ranked females have a faster pace of aging than higher ranked females.
Females	Cumulative adversity	Average number of adult females in group at time of collection	-0.001	0.002	0.547	
Males	Individual sources	Intercept	0.681	0.014	0	
Males	Individual sources	Loss of mother before age 4	-0.007	0.014	0.628	
Males	Individual sources	Sibling born within 1.5 years of focal individual	-0.023	0.015	0.126	
Males	Individual sources	Born during a drought year	0.02	0.016	0.198	
Males	Individual sources	Highest quartile group size at time of birth	-0.016	0.019	0.418	
Males	Individual sources	Low maternal social connectedness at birth	-0.002	0.013	0.891	
Males	Individual sources	Low maternal rank at birth*	-0.001	0.013	0.955	
Males	Individual sources	Average rank (ordinal for males*, proportional for females)	0	0.001	0.766	
Males	Individual sources	Average number of adult females in group at time of collection	NA	NA	NA	
Males	Cumulative adversity	Intercept	0.677	0.012	0	
Males	Cumulative adversity	Cumulative adversity	-0.002	0.006	0.714	

TABLE A.20 CONTINUED FROM PREVIOUS PAGE

Sex	Type of adversity	Variable	Estimate	SE	p-value	Interpretation
Males	Cumulative adversity	Average rank (ordinal for males*, proportional for females)	0	0.001	0.589	
Males	Cumulative adversity	Average number of adult females in group at time of collection	NA	NA	NA	

NOTE: This table shows the fixed effects of four different linear models where pace of aging was the response variable. A * indicates that this variable's coefficient was multiplied by -1 in order to make the direction of the effect more easily interpretable - positive coefficients always indicate higher values in high-ranking animals/lower values in low-ranking animals. Type of adversity indicates whether the model included the all the individual sources of adversity vs. only including cumulative adversity.

TABLE A.21

PREDICTING AGE AT RANK ATTAINMENT IN FEMALES, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.37	1.447	1.049 - 1.996	0.024	Animals who look old for age will attain the milestone sooner.
Prior	Pace of aging prior to milestone	-2.516	0.081	0.001 - 9.816	0.304	
Prior	Mean chronological age of samples	-0.381	0.683	0.468 - 0.997	0.048	Animals with a higher mean chronological age will attain the milestone later.
Prior	Mother in same group during approximate timing of milestone	-0.297	0.743	0.435 - 1.268	0.276	
Prior	Average number of maternal sisters in group prior to milestone	0.115	1.122	0.955 - 1.319	0.162	Animals with a higher number of maternal sisters in group will attain the milestone sooner.
Prior	Low maternal rank at birth	-1.329	0.265	0.143 - 0.489	0	Animals born to mothers with lower ranks will attain the milestone later.

TABLE A.21 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Average number of adult females in group prior to milestone	0.055	1.056	1.015 - 1.1	0.008	Animals in groups with more adult females will attain the milestone sooner.
Prior	Average rainfall prior to milestone	0	1	0.996 - 1.004	0.981	
Prior	Hybridization score	-0.673	0.51	0.199 - 1.31	0.162	
Lifespan	Lifetime age acceleration	0.335	1.398	1.035 - 1.887	0.029	Animals who look old for age will attain the milestone sooner.
Lifespan	Lifetime pace of aging	-0.728	0.483	0.053 - 4.409	0.519	
Lifespan	Mean chronological age of samples	-0.27	0.764	0.659 - 0.885	0	Animals with a higher mean chronological age will attain the milestone later.
Lifespan	Mother in same group during approximate timing of milestone	-0.146	0.864	0.501 - 1.489	0.598	
Lifespan	Average number of maternal sisters in group over life	0.098	1.103	0.938 - 1.297	0.236	
Lifespan	Low maternal rank at birth	-1.436	0.238	0.127 - 0.446	0	Animals born to mothers with lower ranks will attain the milestone later.

TABLE A.21 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Average number of adult females in group over life	0.032	1.032	0.99 - 1.077	0.141	
Lifespan	Average rainfall over life	-0.002	0.998	0.993 - 1.003	0.351	
Lifespan	Hybridization score	-0.708	0.492	0.181 - 1.338	0.165	

NOTE: Cox proportional model results showing the predictors of rank attainment in females, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.22

PREDICTING AGE AT RANK ATTAINMENT IN FEMALES, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	-0.011	0.989	0.74 - 1.323	0.942	
Prior	Pace of aging prior to milestone	4.582	97.695	1.272 - 7501.289	0.039	Animals with a faster pace of aging will attain the milestone sooner.
Prior	Mean chronological age of samples	-0.086	0.918	0.681 - 1.237	0.573	
Prior	Mother in same group during approximate timing of milestone	-0.32	0.726	0.477 - 1.104	0.134	
Prior	Average number of maternal sisters in group prior to milestone	0.131	1.14	0.997 - 1.303	0.056	
Prior	Low maternal rank at birth	-0.319	0.727	0.458 - 1.154	0.176	
Prior	Average number of adult females in group prior to milestone	0.024	1.024	0.991 - 1.058	0.149	
Prior	Average rainfall prior to milestone	-0.001	0.999	0.996 - 1.002	0.581	
Lifespan	Lifetime age acceleration	0.204	1.226	0.929 - 1.619	0.149	

TABLE A.22 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Lifetime pace of aging	-0.744	0.475	0.052 - 4.318	0.509	
Lifespan	Mean chronological age of samples	-0.246	0.782	0.677 - 0.902	0.001	Animals with a higher mean chronological age will attain the milestone later.
Lifespan	Mother in same group during approximate timing of milestone	-0.077	0.925	0.549 - 1.56	0.771	
Lifespan	Average number of maternal sisters in group over life	0.086	1.089	0.927 - 1.28	0.299	
Lifespan	Low maternal rank at birth	-1.422	0.241	0.133 - 0.437	0	Animals born to mothers with lower ranks will attain the milestone later.
Lifespan	Average number of adult females in group over life	0.02	1.02	0.984 - 1.057	0.274	
Lifespan	Average rainfall over life	-0.001	0.999	0.994 - 1.004	0.673	

NOTE: Cox proportional model results showing the predictors of rank attainment in females, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.23

PREDICTING AGE AT MENARCHE, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	-0.009	0.991	0.742 - 1.323	0.95	
Prior	Pace of aging prior to milestone	4.475	87.808	1.11 - 6948.926	0.045	Animals with a faster pace of aging will attain the milestone sooner.
Prior	Mean chronological age of samples	-0.057	0.945	0.703 - 1.269	0.706	
Prior	Mother in same group during approximate timing of milestone	-0.328	0.72	0.474 - 1.095	0.125	
Prior	Average number of maternal sisters in group prior to milestone	0.148	1.16	1.011 - 1.33	0.034	Animals with a higher number of maternal sisters in group will attain the milestone sooner.
Prior	Low maternal rank at birth	-0.343	0.71	0.445 - 1.131	0.149	
Prior	Average number of adult females in group prior to milestone	0.022	1.022	0.989 - 1.056	0.195	
Prior	Average rainfall prior to milestone	-0.001	0.999	0.996 - 1.002	0.589	

TABLE A.23 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Hybridization score	0.482	1.62	0.748 - 3.505	0.221	
Lifespan	Lifetime age acceleration	0.24	1.271	0.982 - 1.644	0.069	
Lifespan	Lifetime pace of aging	-0.806	0.447	0.083 - 2.4	0.347	
Lifespan	Mean chronological age of samples	-0.061	0.941	0.84 - 1.054	0.294	
Lifespan	Mother in same group during approximate timing of milestone	-0.378	0.685	0.448 - 1.048	0.082	
Lifespan	Average number of maternal sisters in group over life	0.126	1.134	0.987 - 1.303	0.076	
Lifespan	Low maternal rank at birth	-0.253	0.777	0.497 - 1.214	0.268	
Lifespan	Average number of adult females in group over life	0.022	1.022	0.988 - 1.057	0.209	
Lifespan	Average rainfall over life	-0.003	0.997	0.993 - 1.002	0.214	
Lifespan	Hybridization score	0.423	1.527	0.703 - 3.314	0.285	

NOTE: Cox proportional model results showing the predictors of menarche in females, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.24

PREDICTING AGE AT MENARCHE, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	-0.011	0.989	0.74 - 1.323	0.942	
Prior	Pace of aging prior to milestone	4.582	97.695	1.272 - 7501.289	0.039	Animals with a faster pace of aging will attain the milestone sooner.
Prior	Mean chronological age of samples	-0.086	0.918	0.681 - 1.237	0.573	
Prior	Mother in same group during approximate timing of milestone	-0.32	0.726	0.477 - 1.104	0.134	
Prior	Average number of maternal sisters in group prior to milestone	0.131	1.14	0.997 - 1.303	0.056	
Prior	Low maternal rank at birth	-0.319	0.727	0.458 - 1.154	0.176	
Prior	Average number of adult females in group prior to milestone	0.024	1.024	0.991 - 1.058	0.149	
Prior	Average rainfall prior to milestone	-0.001	0.999	0.996 - 1.002	0.581	
Lifespan	Lifetime age acceleration	0.189	1.208	0.947 - 1.54	0.128	

TABLE A.24 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Lifetime pace of aging	-0.934	0.393	0.077 - 2.016	0.263	
Lifespan	Mean chronological age of samples	-0.084	0.92	0.825 - 1.025	0.13	
Lifespan	Mother in same group during approximate timing of milestone	-0.33	0.719	0.479 - 1.08	0.112	
Lifespan	Average number of maternal sisters in group over life	0.115	1.122	0.983 - 1.28	0.088	Animals with more maternal half-sisters will attain this milestone sooner.
Lifespan	Low maternal rank at birth	-0.249	0.78	0.515 - 1.181	0.241	
Lifespan	Average number of adult females in group over life	0.016	1.016	0.985 - 1.049	0.313	
Lifespan	Average rainfall over life	-0.002	0.998	0.994 - 1.002	0.397	

NOTE: Cox proportional model results showing the predictors of menarche in females, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.25

PREDICTING AGE AT FIRST LIVE BIRTH, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.115	1.122	0.841 - 1.497	0.434	
Prior	Pace of aging prior to milestone	-0.182	0.834	0.084 - 8.244	0.876	
Prior	Mean chronological age of samples	-0.227	0.797	0.614 - 1.036	0.09	
Prior	Mother in same group during approximate timing of milestone	-0.112	0.894	0.604 - 1.324	0.576	
Prior	Average number of maternal sisters in group prior to milestone	0.07	1.073	0.915 - 1.258	0.388	
Prior	Low maternal rank at birth	-0.15	0.861	0.536 - 1.383	0.536	
Prior	Average number of adult females in group prior to milestone	-0.007	0.993	0.959 - 1.027	0.679	
Prior	Average rainfall prior to milestone	-0.007	0.993	0.988 - 0.998	0.005	Animals that experience higher rainfall prior to the milestone will attain the milestone later.

TABLE A.25 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Hybridization score	0.949	2.584	1.143 - 5.841	0.023	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.
Lifespan	Lifetime age acceleration	0.023	1.024	0.786 - 1.334	0.862	
Lifespan	Lifetime pace of aging	-1.679	0.187	0.032 - 1.095	0.063	
Lifespan	Mean chronological age of samples	-0.089	0.915	0.802 - 1.045	0.19	
Lifespan	Mother in same group during approximate timing of milestone	-0.099	0.906	0.604 - 1.358	0.632	
Lifespan	Average number of maternal sisters in group over life	0.057	1.058	0.904 - 1.24	0.482	
Lifespan	Low maternal rank at birth	-0.169	0.845	0.522 - 1.366	0.492	
Lifespan	Average number of adult females in group over life	-0.008	0.992	0.957 - 1.028	0.646	
Lifespan	Average rainfall over life	-0.007	0.993	0.988 - 0.999	0.011	Animals that experience higher rainfall over life will attain the milestone later.
Lifespan	Hybridization score	0.994	2.701	1.187 - 6.148	0.018	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.

NOTE: Cox proportional model results showing the predictors of first live birth in females, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.26

PREDICTING AGE AT FIRST LIVE BIRTH, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.068	1.07	0.822 - 1.393	0.614	
Prior	Pace of aging prior to milestone	-0.255	0.775	0.088 - 6.801	0.818	
Prior	Mean chronological age of samples	-0.317	0.728	0.571 - 0.928	0.01	Animals with a higher mean chronological age will attain the milestone later.
Prior	Mother in same group during approximate timing of milestone	-0.074	0.928	0.635 - 1.357	0.701	
Prior	Average number of maternal sisters in group prior to milestone	0.05	1.051	0.905 - 1.221	0.516	
Prior	Low maternal rank at birth	-0.185	0.831	0.53 - 1.304	0.421	
Prior	Average number of adult females in group prior to milestone	-0.003	0.997	0.965 - 1.029	0.841	
Prior	Average rainfall prior to milestone	-0.007	0.993	0.989 - 0.998	0.008	Animals that experience increased rainfall will attain the milestone later.

TABLE A.26 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Lifetime age acceleration	-0.006	0.994	0.774 - 1.275	0.961	
Lifespan	Lifetime pace of aging	-1.713	0.18	0.034 - 0.961	0.045	Animals with a faster pace of aging will attain the milestone later.
Lifespan	Mean chronological age of samples	-0.13	0.878	0.774 - 0.996	0.043	Animals with a higher mean chronological age will attain the milestone later.
Lifespan	Mother in same group during approximate timing of milestone	-0.071	0.931	0.628 - 1.38	0.723	
Lifespan	Average number of maternal sisters in group over life	0.043	1.044	0.897 - 1.214	0.581	
Lifespan	Low maternal rankat birth	-0.179	0.836	0.532 - 1.316	0.44	
Lifespan	Average number of adult females in group over life	-0.006	0.994	0.962 - 1.028	0.726	
Lifespan	Average rainfall over life	-0.005	0.995	0.99 - 1	0.035	Animals that experience increased rainfall will attain the milestone later.

NOTE: Cox proportional model results showing the predictors of first live birth in females, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.27

PREDICTING AGE AT TESTICULAR ENLARGEMENT, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.163	1.177	0.896 - 1.548	0.242	
Prior	Pace of aging prior to milestone	-1.101	0.333	0.02 - 5.584	0.444	
Prior	Mean chronological age of samples	0.152	1.165	1.019 - 1.331	0.025	Animals with a higher mean chronological age will attain the milestone sooner.
Prior	Mother in same group during approximate timing of milestone	0.091	1.096	0.711 - 1.688	0.679	
Prior	Average number of maternal sisters in group prior to milestone	-0.205	0.814	0.668 - 0.993	0.043	Animals with a higher number of maternal sisters in group will attain the milestone later.
Prior	Low maternal rank at birth	0.124	1.132	0.711 - 1.802	0.603	
Prior	Average number of excess cycling females in group prior to milestone	0.135	1.145	1.003 - 1.307	0.046	Animals in groups with excess cycling females will attain the milestone sooner.

TABLE A.27 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Average rainfall prior to milestone	0.002	1.002	0.998 - 1.006	0.411	
Prior	Hybridization score	0.779	2.179	1.032 - 4.6	0.041	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.
Lifespan	Lifetime age acceleration	0.171	1.187	0.901 - 1.564	0.223	
Lifespan	Lifetime pace of aging	-1.056	0.348	0.027 - 4.433	0.416	
Lifespan	Mean chronological age of samples	0.147	1.158	1.013 - 1.325	0.032	Animals with a higher mean chronological age will attain the milestone sooner.
Lifespan	Mother in same group during approximate timing of milestone	0.093	1.097	0.713 - 1.689	0.674	
Lifespan	Average number of maternal sisters in group over life	-0.208	0.812	0.665 - 0.991	0.041	Animals with a higher number of maternal sisters in group will attain the milestone later.
Lifespan	Low maternal rank at birth	0.125	1.134	0.712 - 1.805	0.597	
Lifespan	Average number of excess cycling females in group over life	0.134	1.143	1.003 - 1.304	0.045	Animals in groups with excess cycling females will attain the milestone sooner.

TABLE A.27 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Average rainfall over life	0.002	1.002	0.998 - 1.006	0.384	
Lifespan	Hybridization score	0.786	2.195	1.041 - 4.627	0.039	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.

NOTE: Cox proportional model results showing the predictors of testicular enlargement in males, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.28

PREDICTING AGE AT TESTICULAR ENLARGEMENT, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.105	1.111	0.888 - 1.391	0.358	
Prior	Pace of aging prior to milestone	-1.262	0.283	0.017 - 4.701	0.379	
Prior	Mean chronological age of samples	0.196	1.216	1.071 - 1.381	0.003	Animals with a higher mean chronological age will attain the milestone sooner.
Prior	Mother in same group during approximate timing of milestone	0.134	1.143	0.75 - 1.743	0.534	
Prior	Average number of maternal sisters in group prior to milestone	-0.148	0.863	0.717 - 1.037	0.116	
Prior	Low maternal rank at birth	0.021	1.021	0.646 - 1.614	0.929	
Prior	Average number of excess cycling females in group prior to milestone	0.103	1.109	0.975 - 1.261	0.115	
Prior	Average rainfall prior to milestone	0.002	1.002	0.998 - 1.006	0.402	

TABLE A.28 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Lifetime age acceleration	0.106	1.112	0.888 - 1.392	0.356	
Lifespan	Lifetime pace of aging	-1.155	0.315	0.025 - 3.976	0.372	
Lifespan	Mean chronological age of samples	0.195	1.215	1.069 - 1.38	0.003	
Lifespan	Mother in same group during approximate timing of milestone	0.135	1.145	0.752 - 1.744	0.528	
Lifespan	Average number of maternal sisters in group over life	-0.149	0.862	0.716 - 1.037	0.114	
Lifespan	Low maternal rank at birth	0.02	1.02	0.646 - 1.613	0.931	
Lifespan	Average number of excess cycling females in group over life	0.103	1.109	0.975 - 1.26	0.115	
Lifespan	Average rainfall over life	0.002	1.002	0.998 - 1.006	0.392	

NOTE: Cox proportional model results showing the predictors of testicular enlargement in males, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.29

PREDICTING AGE AT NATAL DISPERSAL IN MALES, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.072	1.074	0.794 - 1.453	0.642	
Prior	Pace of aging prior to milestone	-4.038	0.018	0 - 0.776	0.037	Animals with a faster pace of aging will attain the milestone later.
Prior	Mean chronological age of samples	-0.017	0.983	0.873 - 1.107	0.779	
Prior	Mother in same group during approximate timing of milestone	0.448	1.565	0.959 - 2.554	0.073	
Prior	Average number of maternal sisters in group prior to milestone	0.01	1.01	0.834 - 1.224	0.916	
Prior	Low maternal rank at birth	-0.383	0.682	0.414 - 1.123	0.133	
Prior	Average number of excess cycling females in group prior to milestone	0.163	1.177	1.021 - 1.357	0.024	Animals in groups with more reproductively available females will attain the milestone sooner.
Prior	Average rainfall prior to milestone	-0.002	0.998	0.994 - 1.003	0.481	

TABLE A.29 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Hybridization score	1.115	3.05	1.352 - 6.881	0.007	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.
Lifespan	Lifetime age acceleration	0.058	1.06	0.784 - 1.434	0.704	
Lifespan	Lifetime pace of aging	-3.6	0.027	0.001 - 0.823	0.038	Animals with a faster pace of aging will attain the milestone later.
Lifespan	Mean chronological age of samples	-0.013	0.987	0.875 - 1.114	0.833	
Lifespan	Mother in same group during approximate timing of milestone	0.463	1.588	0.968 - 2.605	0.067	
Lifespan	Average number of maternal sisters in group over life	0.006	1.006	0.83 - 1.22	0.95	
Lifespan	Low maternal rank at birth	-0.396	0.673	0.41 - 1.107	0.119	
Lifespan	Average number of excess cycling females in group over life	0.166	1.18	1.024 - 1.361	0.022	Animals in groups with more reproductively available females will attain the milestone sooner.
Lifespan	Average rainfall over life	-0.002	0.998	0.994 - 1.003	0.474	

TABLE A.29 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Hybridization score	1.129	3.092	1.367 - 6.997	0.007	Animals with a higher hybrid score (more anubis) will attain the milestone sooner.

NOTE: Cox proportional model results showing the predictors of natal dispersal in males, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.30

PREDICTING AGE AT NATAL DISPERSAL IN MALES, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.03	1.03	0.771 - 1.376	0.842	
Prior	Pace of aging prior to milestone	-3.047	0.048	0.001 - 1.856	0.103	
Prior	Mean chronological age of samples	0.006	1.006	0.892 - 1.134	0.927	
Prior	Mother in same group during approximate timing of milestone	0.495	1.64	1.015 - 2.65	0.043	Animals in groups with their mother present will attain the milestone sooner.
Prior	Average number of maternal sisters in group prior to milestone	0.058	1.06	0.878 - 1.279	0.546	
Prior	Low maternal rank at birth	-0.42	0.657	0.402 - 1.072	0.093	
Prior	Average number of excess cycling females in group prior to milestone	0.137	1.147	1 - 1.315	0.049	Animals in groups with more reproductive females will attain the milestone sooner.
Prior	Average rainfall prior to milestone	-0.001	0.999	0.995 - 1.004	0.709	

TABLE A.30 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Lifetime age acceleration	0.021	1.022	0.765 - 1.365	0.885	
Lifespan	Lifetime pace of aging	-2.681	0.068	0.003 - 1.814	0.109	
Lifespan	Mean chronological age of samples	0.01	1.01	0.895 - 1.14	0.869	
Lifespan	Mother in same group during approximate timing of milestone	0.506	1.659	1.022 - 2.693	0.041	Animals in groups with their mother present will attain the milestone sooner.
Lifespan	Average number of maternal sisters in group over life	0.055	1.056	0.874 - 1.276	0.571	
Lifespan	Low maternal rank at birth	-0.429	0.651	0.399 - 1.062	0.086	
Lifespan	Average number of excess cycling females in group over life	0.139	1.149	1.002 - 1.318	0.047	Animals in groups with more reproductive females will attain the milestone sooner.
Lifespan	Average rainfall over life	-0.001	0.999	0.995 - 1.004	0.707	

NOTE: Cox proportional model results showing the predictors of natal dispersal in males, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.31

PREDICTING AGE AT FIRST RANK ATTAINMENT IN MALES, WITH HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.406	1.501	1.051 - 2.142	0.025	Animals that are microbially old for age will attain the milestone sooner.
Prior	Pace of aging prior to milestone	-3.527	0.029	0 - 2.527	0.121	
Prior	Mean chronological age of samples	-0.052	0.95	0.822 - 1.097	0.484	
Prior	Mother in same group during approximate timing of milestone	-0.168	0.846	0.467 - 1.53	0.579	
Prior	Average number of maternal sisters in group prior to milestone	-0.29	0.748	0.592 - 0.945	0.015	Animals with a higher number of maternal sisters in group will attain the milestone later.
Prior	Low maternal rank at birth	-0.866	0.421	0.219 - 0.807	0.009	Animals born to lower ranking mothers will attain the milestone later.
Prior	Average number of excess cycling females in group prior to milestone	0.162	1.176	0.971 - 1.425	0.097	

TABLE A.31 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Average rainfall prior to milestone	-0.002	0.998	0.99 - 1.007	0.7	
Prior	Hybridization score	2.057	7.82	2.953 - 20.71	0	Animals with higher hybrid scores (more anubis) will attain the milestone sooner.
Lifespan	Lifetime age acceleration	0.448	1.565	1.086 - 2.256	0.016	Animals that are microbially old for age will attain the milestone sooner.
Lifespan	Lifetime pace of aging	-3.162	0.042	0.001 - 1.939	0.105	
Lifespan	Mean chronological age of samples	-0.064	0.938	0.812 - 1.083	0.383	
Lifespan	Mother in same group during approximate timing of milestone	-0.17	0.844	0.469 - 1.52	0.571	
Lifespan	Average number of maternal sisters in group over life	-0.286	0.751	0.595 - 0.947	0.015	Animals with a higher number of maternal sisters in group will attain the milestone later.
Lifespan	Low maternal rank at birth	-0.927	0.396	0.206 - 0.761	0.005	Animals born to lower ranking mothers will attain the milestone later.
Lifespan	Average number of excess cycling females in group over life	0.168	1.183	0.977 - 1.432	0.085	

TABLE A.31 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifespan	Average rainfall over life	-0.001	0.999	0.991 - 1.008	0.852	
Lifespan	Hybridization score	2.119	8.324	3.125 - 22.175	0	Animals with higher hybrid scores (more anubis) will attain the milestone sooner.

NOTE: Cox proportional model results showing the predictors of rank attainment in males, including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.32

PREDICTING AGE AT FIRST RANK ATTAINMENT IN MALES, WITHOUT HYBRID SCORE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Age acceleration averaged prior to milestone	0.186	1.2	0.918 - 1.579	0.18	
Prior	Pace of aging prior to milestone	-2.05	0.129	0.002 - 7.213	0.319	
Prior	Mean chronological age of samples	0.062	1.06	0.928 - 1.221	0.374	
Prior	Mother in same group during approximate timing of milestone	0.044	1.04	0.616 - 1.772	0.872	
Prior	Average number of maternal sisters in group prior to milestone	-0.14	0.87	0.703 - 1.075	0.197	
Prior	Low maternal rank at birth	-0.828	0.437	0.222 - 0.861	0.017	Animals born to lower ranking mothers will attain the milestone later.
Prior	Average number of excess cycling females in group prior to milestone	0.086	1.09	0.91 - 1.305	0.349	

TABLE A.32 CONTINUED FROM PREVIOUS PAGE

Timeframe	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Prior	Average rainfall prior to milestone	0	1	0.993 - 1.007	0.992	
Lifespan	Lifetime age acceleration	0.191	1.21	0.925 - 1.584	0.165	
Lifespan	Lifetime pace of aging	-1.721	0.179	0.006 - 5.33	0.32	
Lifespan	Mean chronological age of samples	0.061	1.063	0.93 - 1.215	0.369	
Lifespan	Mother in same group during approximate timing of milestone	0.047	1.048	0.617 - 1.78	0.862	
Lifespan	Average number of maternal sisters in group over life	-0.137	0.872	0.706 - 1.078	0.205	
Lifespan	Low maternal rank at birth	-0.846	0.429	0.217 - 0.848	0.015	Animals born to lower ranking mothers will attain the milestone later.
Lifespan	Average number of excess cycling females in group over life	0.088	1.092	0.913 - 1.307	0.336	
Lifespan	Average rainfall over life	0	1	0.994 - 1.007	0.937	

NOTE: Cox proportional model results showing the predictors of rank attainment in males, not including hybrid score as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.33

PREDICTING JUVENILE SURVIVAL WITH SOURCES OF EARLY LIFE ADVERSITY

Subset	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
All Animals	Age acceleration prior age 4	0.371	1.449	0.92 - 2.282	0.109	
All Animals	Pace of aging prior age 4	0.382	1.465	0.079 - 27.01	0.797	
All Animals	Mean chronological age of samples	-2.747	0.064	0.027 - 0.155	0	Animals with a higher mean chronological age will die later.
All Animals	Loss of mother before age 4	0.157	1.17	0.405 - 3.382	0.771	
All Animals	Sibiling born within 1.5 years of focal individual	-0.201	0.818	0.289 - 2.313	0.705	
All Animals	Born during a drought year	0.044	1.045	0.349 - 3.135	0.937	
All Animals	Highest quartile group size at time of birth	-0.996	0.369	0.084 - 1.625	0.188	
All Animals	Low maternal social connectedness at birth	0.625	1.869	0.715 - 4.89	0.202	
All Animals	Low maternal rank at birth	-0.671	0.511	0.144 - 1.818	0.3	
All Animals	Sex = M	-0.553	0.575	0.239 - 1.387	0.218	

TABLE A.33 CONTINUED FROM PREVIOUS PAGE

Subset	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Females Only	Age acceleration prior age 4	0.421	1.523	0.791 - 2.935	0.208	
Females Only	Pace of aging prior age 4	-0.145	0.865	0.033 - 22.728	0.931	
Females Only	Mean chronological age of samples	-3.77	0.023	0.005 - 0.115	0	Animals with a higher mean chronological age will die later.
Females Only	Loss of mother before age 4	0.291	1.338	0.36 - 4.965	0.664	
Females Only	Sibiling born within 1.5 years of focal individual	-0.501	0.606	0.15 - 2.449	0.482	
Females Only	Born during a drought year	-1.187	0.305	0.038 - 2.479	0.267	
Females Only	Highest quartile group size at time of birth	-1.914	0.147	0.012 - 1.874	0.14	
Females Only	Low maternal social connectedness at birth	0.844	2.325	0.596 - 9.076	0.225	
Females Only	Low maternal rank at birth	-2.147	0.117	0.008 - 1.647	0.112	
Males Only	Age acceleration prior age 4	0.359	1.432	0.519 - 3.952	0.488	
Males Only	Pace of aging prior age 4	-1.95	0.142	0 - 91.128	0.554	

TABLE A.33 CONTINUED FROM PREVIOUS PAGE

Subset	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Males Only	Mean chronological age of samples	-2.265	0.104	0.028 - 0.383	0.001	Animals with a higher mean chronological age will die later.
Males Only	Loss of mother before age 4	0.084	1.088	0.117 - 10.101	0.941	
Males Only	Sibiling born within 1.5 years of focal individual	-0.075	0.928	0.174 - 4.956	0.93	
Males Only	Born during a drought year	0.941	2.563	0.487 - 13.478	0.266	
Males Only	Highest quartile group size at time of birth	-0.589	0.555	0.066 - 4.648	0.587	
Males Only	Low maternal social connectedness at birth	0.348	1.417	0.317 - 6.323	0.648	
Males Only	Low maternal rank at birth	0.326	1.386	0.298 - 6.456	0.678	

NOTE: Cox proportional model results showing the predictors of juvenile survival, including individual sources of adversity as predictors. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.34

PREDICTING JUVENILE SURVIVAL WITH CUMULATIVE ADVERSITY

Subset	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
All Animals	Age acceleration prior age 4	0.302	1.352	0.896 - 2.04	0.151	
All Animals	Pace of aging prior age 4	0.881	2.413	0.146 - 39.911	0.538	
All Animals	Mean chronological age of samples	-2.602	0.074	0.032 - 0.173	0	Animals with a higher mean chronological age will die later.
All Animals	Cumulative number of adverse events in early life	-0.148	0.863	0.601 - 1.239	0.424	
All Animals	Sex = M	-0.467	0.627	0.268 - 1.464	0.28	
Females Only	Age acceleration prior age 4	0.163	1.177	0.685 - 2.023	0.556	
Females Only	Pace of aging prior age 4	1.319	3.738	0.199 - 70.048	0.378	
Females Only	Mean chronological age of samples	-3.233	0.039	0.01 - 0.157	0	Animals with a higher mean chronological age will die later.
Females Only	Cumulative number of adverse events in early life	-0.454	0.635	0.372 - 1.085	0.097	

TABLE A.34 CONTINUED FROM PREVIOUS PAGE

Subset	Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Males Only	Age acceleration prior age 4	0.256	1.291	0.512 - 3.259	0.588	
Males Only	Pace of aging prior age 4	-1.371	0.254	0 - 129.428	0.666	
Males Only	Mean chronological age of samples	-2.355	0.095	0.027 - 0.329	0	Animals with a higher mean chronological age will die later.
Males Only	Cumulative number of adverse events in early life	0.222	1.248	0.696 - 2.238	0.457	

NOTE: Cox proportional model results showing the predictors of juvenile survival, not including individual sources of adversity as predictors. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.35

PREDICTING ADULT FEMALE SURVIVAL WITH SOURCES OF EARLY LIFE ADVERSITY

Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Lifetime age acceleration	-0.025	0.975	0.717 - 1.326	0.873	
Lifetime pace of aging	0.505	1.658	0.152 - 18.039	0.678	
Mean chronological age of samples	-0.1	0.905	0.836 - 0.98	0.014	Animals with a higher mean chronological age will die later.
Loss of mother before age 4	1.086	2.963	1.646 - 5.331	0	Adult females that lose their mother prior to age 4 die sooner.
Sibiling born within 1.5 years of focal individual	-0.144	0.865	0.446 - 1.68	0.67	
Born during a drought year	-0.029	0.972	0.478 - 1.973	0.936	
Highest quartile group size at time of birth	0.367	1.444	0.617 - 3.376	0.397	
Low maternal social connectedness at birth	0.076	1.079	0.627 - 1.859	0.783	
Low maternal rank at birth	0.709	2.033	1.082 - 3.818	0.027	
Average social connectedness to other adult females over life	0.239	1.271	0.757 - 2.132	0.365	
Average social connectedness to adult males over life	-0.241	0.786	0.528 - 1.169	0.234	

TABLE A.35 CONTINUED FROM PREVIOUS PAGE

Predictor	Coefficient	Hazard Ratio	95% CI	p-value	Interpretation
Average proportional rank over life	0.751	2.119	0.548 - 8.201	0.277	

NOTE: Cox proportional model results showing the predictors of adult female survival, including individual sources of adversity as predictors. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

TABLE A.36

PREDICTING ADULT FEMALE SURVIVAL WITH CUMULATIVE ADVERSITY

Predictor	**Coefficient**	**Hazard Ratio**	**95% CI**	**p-value**	**Interpretation**
Lifetime age acceleration	-0.092	0.912	0.668 - 1.245	0.562	
Lifetime pace of aging	1.249	3.489	0.356 - 34.209	0.283	
Mean chronological age of samples	-0.078	0.925	0.86 - 0.995	0.037	Animals with a higher mean chronological age will die later.
Cumulative number of adverse events in early life	0.345	1.412	1.063 - 1.876	0.017	Adult females with higher cumulative early life adversity die sooner.
Average social connectedness to other adult females over life	0.15	1.162	0.712 - 1.894	0.548	
Average social connectedness to adult males over life	-0.19	0.827	0.564 - 1.212	0.33	
Average proportional rank over life	0.545	1.724	0.475 - 6.252	0.407	

NOTE: Cox proportional model results showing the predictors of adult female survival, including cumulative adversity as a predictor. Predictors were averaged over the timeframe of interest: either prior to the population average age of the milestone or over the lifespan.

APPENDIX B

CHAPTER 3 SUPPLEMENTARY MATERIALS

TABLE B.1

SAMPLE SIZES FOR ALL CHAPTER 3 MODELS

Age Category	**Sex**	**Individuals**	**Samples**
(0,30)	All	431	12298
(0,30)	Females	234	7321
(0,30)	Males	197	4977
(0-4]	All	375	2999
(0-4]	Females	195	1587
(0-4]	Males	180	1412
(4-7]	All	276	3753
(4-7]	Females	144	1914
(4-7]	Males	132	1839
(7-10]	All	179	2350
(7-10]	Females	92	1326
(7-10]	Males	87	1024
(10-13]	All	102	1679
(10-13]	Females	72	1168
(10-13]	Males	30	511

TABLE B.1 CONTINUED FROM PREVIOUS PAGE

Age Category	Sex	Individuals	Samples
(13-16]	All	62	844
(13-16]	Females	48	679
(13-16]	Males	14	165
(16-19]	All	31	417
(16-19]	Females	27	392
(16-19]	Males	4	25
(19-27]	All	19	256
(19-27]	Females	18	255
(19-27]	Males	1	1

NOTE: Sample sizes for all models. Linear models only used data from all individuals across life course, and other subsets were specific to PERMANOVA analyses.

TABLE B.2

PERMANOVAS TESTING THE EFFECTS OF INDIVIDUAL TYPES OF ADVERSITY ON BRAY-CURTIS DISSIMILARITIES.

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Both	Quantity	DNA extraction plate	1.065	0.017	0.006	0.048
Lifespan (0,30)	Both	Quantity	Season at the time of collection	1.427	0	0.114	0.456
Lifespan (0,30)	Both	Quantity	Hydrological year at the time of collection	1.06	0.001	0.237	0.605
Lifespan (0,30)	Both	Quantity	Social group at time of collection	2.722	0.002	0.001	0.002
Lifespan (0,30)	Both	Quantity	Sex	1.773	0	0.043	0.149
Lifespan (0,30)	Both	Quantity	Chronological age at time of collection	2.118	0	0.012	0.096
Lifespan (0,30)	Both	Quantity	Total quantity of adversity experienced	1.211	0	0.218	0.359
Lifespan (0,30)	Both	Quantity	Individual identity	1.311	0.045	0.001	0.001
Lifespan (0,30)	Both	Type	DNA extraction plate	1.065	0.017	0.013	0.072

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Both	Type	Season at the time of collection	1.427	0	0.121	0.484
Lifespan (0,30)	Both	Type	Hydrological year at the time of collection	1.06	0.001	0.247	0.588
Lifespan (0,30)	Both	Type	Social group at time of collection	2.722	0.002	0.001	0.002
Lifespan (0,30)	Both	Type	Sex	1.773	0	0.042	0.147
Lifespan (0,30)	Both	Type	Chronological age at time of collection	2.118	0	0.014	0.112
Lifespan (0,30)	Both	Type	Loss of mother prior to age 4	1.168	0	0.206	0.516
Lifespan (0,30)	Both	Type	Presence of a competing sibling	2.26	0	0.012	0.032
Lifespan (0,30)	Both	Type	Drought in early life	1.602	0	0.057	0.456
Lifespan (0,30)	Both	Type	Highest quartile group size	0.967	0	0.422	0.744
Lifespan (0,30)	Both	Type	Lowest quartile maternal social connectedness	1.587	0	0.061	0.181
Lifespan (0,30)	Both	Type	Lowest quartile maternal rank	2.483	0	0.003	0.016

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Both	Type	Individual identity	1.306	0.044	0.001	0.001
Lifespan (0,30)	Females	Quantity	DNA extraction plate	1.094	0.03	0.001	0.008
Lifespan (0,30)	Females	Quantity	Season at the time of collection	1.635	0	0.053	0.212
Lifespan (0,30)	Females	Quantity	Hydrological year at the time of collection	1.08	0.002	0.21	0.56
Lifespan (0,30)	Females	Quantity	Social group at time of collection	2.755	0.004	0.001	0.002
Lifespan (0,30)	Females	Quantity	Chronological age at time of collection	2.958	0	0.001	0.008
Lifespan (0,30)	Females	Quantity	Total quantity of adversity experienced	1.002	0	0.423	0.677
Lifespan (0,30)	Females	Quantity	Individual identity	1.296	0.04	0.001	0.004
Lifespan (0,30)	Females	Type	DNA extraction plate	1.094	0.03	0.001	0.008
Lifespan (0,30)	Females	Type	Season at the time of collection	1.635	0	0.054	0.216
Lifespan (0,30)	Females	Type	Hydrological year at the time of collection	1.08	0.002	0.231	0.616

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Females	Type	Social group at time of collection	2.755	0.004	0.001	0.003
Lifespan (0,30)	Females	Type	Chronological age at time of collection	2.958	0	0.003	0.024
Lifespan (0,30)	Females	Type	Loss of mother prior to age 4	1.415	0	0.107	0.523
Lifespan (0,30)	Females	Type	Presence of a competing sibling	2.124	0	0.015	0.045
Lifespan (0,30)	Females	Type	Drought in early life	1.44	0	0.125	0.726
Lifespan (0,30)	Females	Type	Highest quartile group size	1.123	0	0.304	0.426
Lifespan (0,30)	Females	Type	Lowest quartile maternal social connectedness	2.079	0	0.016	0.128
Lifespan (0,30)	Females	Type	Lowest quartile maternal rank	1.318	0	0.158	0.546
Lifespan (0,30)	Females	Type	Individual identity	1.287	0.039	0.001	0.008
Lifespan (0,30)	Males	Quantity	DNA extraction plate	0.99	0.04	0.675	0.675
Lifespan (0,30)	Males	Quantity	Season at the time of collection	0.617	0	0.911	0.911

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Males	Quantity	Hydrological year at the time of collection	1.193	0.003	0.049	0.147
Lifespan (0,30)	Males	Quantity	Social group at time of collection	1.313	0.003	0.005	0.018
Lifespan (0,30)	Males	Quantity	Chronological age at time of collection	1.59	0	0.071	0.426
Lifespan (0,30)	Males	Quantity	Total quantity of adversity experienced	1.075	0	0.312	0.547
Lifespan (0,30)	Males	Quantity	Individual identity	1.288	0.05	0.001	0.003
Lifespan (0,30)	Males	Type	DNA extraction plate	0.99	0.04	0.667	0.667
Lifespan (0,30)	Males	Type	Season at the time of collection	0.617	0	0.922	0.922
Lifespan (0,30)	Males	Type	Hydrological year at the time of collection	1.192	0.003	0.04	0.12
Lifespan (0,30)	Males	Type	Social group at time of collection	1.313	0.003	0.003	0.014
Lifespan (0,30)	Males	Type	Chronological age at time of collection	1.59	0	0.066	0.396
Lifespan (0,30)	Males	Type	Loss of mother prior to age 4	1.386	0	0.131	0.262

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
Lifespan (0,30)	Males	Type	Presence of a competing sibling	3.08	0.001	0.001	0.006
Lifespan (0,30)	Males	Type	Drought in early life	1.055	0	0.353	0.706
Lifespan (0,30)	Males	Type	Highest quartile group size	0.98	0	0.466	0.713
Lifespan (0,30)	Males	Type	Lowest quartile maternal social connectedness	1.233	0	0.198	0.604
Lifespan (0,30)	Males	Type	Lowest quartile maternal rank	3.177	0.001	0.002	0.005
Lifespan (0,30)	Males	Type	Individual identity	1.27	0.048	0.001	0.006
(0 - 4]	Both	Quantity	DNA extraction plate	1.03	0.069	0.151	0.179
(0 - 4]	Both	Quantity	Season at the time of collection	0.894	0	0.525	0.7
(0 - 4]	Both	Quantity	Hydrological year at the time of collection	1.004	0.004	0.468	0.605
(0 - 4]	Both	Quantity	Social group at time of collection	1.535	0.006	0.001	0.002
(0 - 4]	Both	Quantity	Sex	2.047	0.001	0.018	0.126
(0 - 4]	Both	Quantity	Chronological age at time of collection	1.309	0	0.179	0.544
(0 - 4]	Both	Quantity	Total quantity of adversity experienced	1.327	0	0.156	0.359
(0 - 4]	Both	Quantity	Individual identity	1.094	0.133	0.001	0.001

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(0 - 4]	Both	Type	DNA extraction plate	1.03	0.069	0.116	0.155
(0 - 4]	Both	Type	Season at the time of collection	0.894	0	0.53	0.707
(0 - 4]	Both	Type	Hydrological year at the time of collection	1.004	0.004	0.466	0.588
(0 - 4]	Both	Type	Social group at time of collection	1.535	0.006	0.001	0.002
(0 - 4]	Both	Type	Sex	2.047	0.001	0.017	0.119
(0 - 4]	Both	Type	Chronological age at time of collection	1.309	0	0.153	0.504
(0 - 4]	Both	Type	Loss of mother prior to age 4	1.142	0	0.258	0.516
(0 - 4]	Both	Type	Presence of a competing sibling	0.756	0	0.74	0.74
(0 - 4]	Both	Type	Drought in early life	0.607	0	0.92	0.92
(0 - 4]	Both	Type	Highest quartile group size	0.696	0	0.825	0.825
(0 - 4]	Both	Type	Lowest quartile maternal social connectedness	1.594	0.001	0.067	0.181
(0 - 4]	Both	Type	Lowest quartile maternal rank	1.031	0	0.388	0.443
(0 - 4]	Both	Type	Individual identity	1.097	0.131	0.001	0.001
(4 - 7]	Both	Quantity	DNA extraction plate	1.009	0.054	0.332	0.332
(4 - 7]	Both	Quantity	Season at the time of collection	0.982	0	0.447	0.7
(4 - 7]	Both	Quantity	Hydrological year at the time of collection	1.01	0.003	0.429	0.605
(4 - 7]	Both	Quantity	Social group at time of collection	1.863	0.005	0.001	0.002

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(4 - 7]	Both	Quantity	Sex	1.107	0	0.311	0.435
(4 - 7]	Both	Quantity	Chronological age at time of collection	0.661	0	0.886	0.886
(4 - 7]	Both	Quantity	Total quantity of adversity experienced	0.682	0	0.849	0.849
(4 - 7]	Both	Quantity	Individual identity	1.117	0.079	0.001	0.001
(4 - 7]	Both	Type	DNA extraction plate	1.009	0.054	0.376	0.376
(4 - 7]	Both	Type	Season at the time of collection	0.982	0	0.452	0.707
(4 - 7]	Both	Type	Hydrological year at the time of collection	1.01	0.003	0.432	0.588
(4 - 7]	Both	Type	Social group at time of collection	1.863	0.005	0.001	0.002
(4 - 7]	Both	Type	Sex	1.107	0	0.3	0.42
(4 - 7]	Both	Type	Chronological age at time of collection	0.661	0	0.864	0.864
(4 - 7]	Both	Type	Loss of mother prior to age 4	0.619	0	0.934	0.934
(4 - 7]	Both	Type	Presence of a competing sibling	1.256	0	0.17	0.272
(4 - 7]	Both	Type	Drought in early life	0.917	0	0.482	0.851
(4 - 7]	Both	Type	Highest quartile group size	1.255	0	0.172	0.647
(4 - 7]	Both	Type	Lowest quartile maternal social connectedness	1.054	0	0.352	0.563
(4 - 7]	Both	Type	Lowest quartile maternal rank	1.349	0	0.15	0.3
(4 - 7]	Both	Type	Individual identity	1.116	0.078	0.001	0.001

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(7 - 10]	Both	Quantity	DNA extraction plate	1.055	0.087	0.025	0.076
(7 - 10]	Both	Quantity	Season at the time of collection	0.682	0	0.818	0.935
(7 - 10]	Both	Quantity	Hydrological year at the time of collection	1.138	0.006	0.1	0.605
(7 - 10]	Both	Quantity	Social group at time of collection	1.17	0.005	0.074	0.085
(7 - 10]	Both	Quantity	Sex	1.414	0.001	0.128	0.224
(7 - 10]	Both	Quantity	Chronological age at time of collection	0.918	0	0.509	0.679
(7 - 10]	Both	Quantity	Total quantity of adversity experienced	1.125	0	0.269	0.359
(7 - 10]	Both	Quantity	Individual identity	1.147	0.084	0.001	0.001
(7 - 10]	Both	Type	DNA extraction plate	1.055	0.087	0.033	0.072
(7 - 10]	Both	Type	Season at the time of collection	0.682	0	0.828	0.946
(7 - 10]	Both	Type	Hydrological year at the time of collection	1.138	0.006	0.117	0.588
(7 - 10]	Both	Type	Social group at time of collection	1.17	0.005	0.076	0.087
(7 - 10]	Both	Type	Sex	1.414	0.001	0.131	0.229
(7 - 10]	Both	Type	Chronological age at time of collection	0.918	0	0.522	0.696
(7 - 10]	Both	Type	Loss of mother prior to age 4	0.675	0	0.86	0.934
(7 - 10]	Both	Type	Presence of a competing sibling	2.503	0.001	0.007	0.032
(7 - 10]	Both	Type	Drought in early life	0.857	0	0.593	0.851

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(7 - 10]	Both	Type	Highest quartile group size	1.246	0.001	0.185	0.647
(7 - 10]	Both	Type	Lowest quartile maternal social connectedness	1.157	0	0.25	0.5
(7 - 10]	Both	Type	Lowest quartile maternal rank	1.579	0.001	0.079	0.211
(7 - 10]	Both	Type	Individual identity	1.14	0.081	0.001	0.001
(10 - 13]	Both	Quantity	DNA extraction plate	1.055	0.124	0.029	0.076
(10 - 13]	Both	Quantity	Season at the time of collection	0.591	0	0.947	0.947
(10 - 13]	Both	Quantity	Hydrological year at the time of collection	0.977	0.007	0.549	0.605
(10 - 13]	Both	Quantity	Social group at time of collection	1.2	0.008	0.043	0.057
(10 - 13]	Both	Quantity	Sex	0.894	0.001	0.543	0.543
(10 - 13]	Both	Quantity	Chronological age at time of collection	1.139	0.001	0.279	0.558
(10 - 13]	Both	Quantity	Total quantity of adversity experienced	1.42	0.001	0.103	0.359
(10 - 13]	Both	Quantity	Individual identity	1.174	0.068	0.001	0.001
(10 - 13]	Both	Type	DNA extraction plate	1.055	0.124	0.036	0.072
(10 - 13]	Both	Type	Season at the time of collection	0.591	0	0.949	0.949
(10 - 13]	Both	Type	Hydrological year at the time of collection	0.977	0.007	0.555	0.588
(10 - 13]	Both	Type	Social group at time of collection	1.2	0.008	0.047	0.063
(10 - 13]	Both	Type	Sex	0.894	0.001	0.545	0.545

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(10 - 13]	Both	Type	Chronological age at time of collection	1.139	0.001	0.298	0.596
(10 - 13]	Both	Type	Loss of mother prior to age 4	1.984	0.001	0.02	0.16
(10 - 13]	Both	Type	Presence of a competing sibling	1.635	0.001	0.043	0.086
(10 - 13]	Both	Type	Drought in early life	1.313	0.001	0.152	0.608
(10 - 13]	Both	Type	Highest quartile group size	0.871	0.001	0.576	0.758
(10 - 13]	Both	Type	Lowest quartile maternal social connectedness	0.967	0.001	0.434	0.579
(10 - 13]	Both	Type	Lowest quartile maternal rank	0.828	0	0.63	0.63
(10 - 13]	Both	Type	Individual identity	1.171	0.064	0.001	0.001
(13 - 16]	Both	Quantity	DNA extraction plate	1.059	0.233	0.038	0.076
(13 - 16]	Both	Quantity	Season at the time of collection	1.781	0.002	0.029	0.232
(13 - 16]	Both	Quantity	Hydrological year at the time of collection	1.059	0.016	0.271	0.605
(13 - 16]	Both	Quantity	Social group at time of collection	1.597	0.02	0.001	0.002
(13 - 16]	Both	Quantity	Sex	1.611	0.002	0.064	0.149
(13 - 16]	Both	Quantity	Chronological age at time of collection	0.95	0.001	0.485	0.679
(13 - 16]	Both	Quantity	Total quantity of adversity experienced	0.751	0.001	0.738	0.843
(13 - 16]	Both	Quantity	Individual identity	1.196	0.078	0.001	0.001
(13 - 16]	Both	Type	DNA extraction plate	1.059	0.233	0.033	0.072

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(13 - 16]	Both	Type	Season at the time of collection	1.781	0.002	0.041	0.328
(13 - 16]	Both	Type	Hydrological year at the time of collection	1.059	0.016	0.263	0.588
(13 - 16]	Both	Type	Social group at time of collection	1.597	0.02	0.001	0.002
(13 - 16]	Both	Type	Sex	1.611	0.002	0.077	0.18
(13 - 16]	Both	Type	Chronological age at time of collection	0.95	0.001	0.464	0.696
(13 - 16]	Both	Type	Loss of mother prior to age 4	0.659	0.001	0.879	0.934
(13 - 16]	Both	Type	Presence of a competing sibling	0.781	0.001	0.737	0.74
(13 - 16]	Both	Type	Drought in early life	0.829	0.001	0.638	0.851
(13 - 16]	Both	Type	Highest quartile group size	0.975	0.001	0.425	0.744
(13 - 16]	Both	Type	Lowest quartile maternal social connectedness	0.724	0.001	0.79	0.816
(13 - 16]	Both	Type	Lowest quartile maternal rank	2.507	0.003	0.004	0.016
(13 - 16]	Both	Type	Individual identity	1.2	0.071	0.001	0.001
(16 - 19]	Both	Quantity	DNA extraction plate	1.044	0.402	0.157	0.179
(16 - 19]	Both	Quantity	Season at the time of collection	1.121	0.003	0.296	0.602
(16 - 19]	Both	Quantity	Hydrological year at the time of collection	0.967	0.023	0.605	0.605
(16 - 19]	Both	Quantity	Social group at time of collection	1.466	0.031	0.001	0.002
(16 - 19]	Both	Quantity	Sex	0.941	0.002	0.521	0.543

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(16 - 19]	Both	Quantity	Chronological age at time of collection	0.72	0.002	0.802	0.886
(16 - 19]	Both	Quantity	Total quantity of adversity experienced	1.226	0.003	0.197	0.359
(16 - 19]	Both	Quantity	Individual identity	1.053	0.052	0.251	0.287
(16 - 19]	Both	Type	DNA extraction plate	1.044	0.402	0.148	0.169
(16 - 19]	Both	Type	Season at the time of collection	1.121	0.003	0.299	0.6
(16 - 19]	Both	Type	Hydrological year at the time of collection	0.967	0.023	0.588	0.588
(16 - 19]	Both	Type	Social group at time of collection	1.466	0.031	0.001	0.002
(16 - 19]	Both	Type	Sex	0.941	0.002	0.489	0.545
(16 - 19]	Both	Type	Chronological age at time of collection	0.72	0.002	0.8	0.864
(16 - 19]	Both	Type	Loss of mother prior to age 4	0.658	0.002	0.863	0.934
(16 - 19]	Both	Type	Presence of a competing sibling	0.809	0.002	0.691	0.74
(16 - 19]	Both	Type	Drought in early life	0.986	0.002	0.441	0.851
(16 - 19]	Both	Type	Highest quartile group size	0.827	0.002	0.65	0.758
(16 - 19]	Both	Type	Lowest quartile maternal social connectedness	1.551	0.004	0.068	0.181
(16 - 19]	Both	Type	Lowest quartile maternal rank	1.14	0.003	0.304	0.405
(16 - 19]	Both	Type	Individual identity	1.086	0.041	0.174	0.199
(19 - 30]	Both	Quantity	DNA extraction plate	1.059	0.521	0.141	0.179

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(19 - 30]	Both	Quantity	Season at the time of collection	1.11	0.004	0.301	0.602
(19 - 30]	Both	Quantity	Hydrological year at the time of collection	0.993	0.03	0.501	0.605
(19 - 30]	Both	Quantity	Social group at time of collection	1.241	0.023	0.088	0.088
(19 - 30]	Both	Quantity	Chronological age at time of collection	1.238	0.005	0.204	0.544
(19 - 30]	Both	Quantity	Total quantity of adversity experienced	1.181	0.004	0.248	0.359
(19 - 30]	Both	Quantity	Individual identity	0.992	0.038	0.516	0.516
(19 - 30]	Both	Type	DNA extraction plate	1.059	0.521	0.096	0.154
(19 - 30]	Both	Type	Season at the time of collection	1.11	0.004	0.3	0.6
(19 - 30]	Both	Type	Hydrological year at the time of collection	0.993	0.03	0.523	0.588
(19 - 30]	Both	Type	Social group at time of collection	1.241	0.023	0.087	0.087
(19 - 30]	Both	Type	Chronological age at time of collection	1.238	0.005	0.189	0.504
(19 - 30]	Both	Type	Loss of mother prior to age 4	1.26	0.005	0.185	0.516
(19 - 30]	Both	Type	Presence of a competing sibling	2.117	0.008	0.009	0.032
(19 - 30]	Both	Type	Drought in early life	0.749	0.003	0.746	0.853
(19 - 30]	Both	Type	Lowest quartile maternal social connectedness	0.717	0.003	0.816	0.816
(19 - 30]	Both	Type	Lowest quartile maternal rank	1.147	0.004	0.256	0.405
(19 - 30]	Both	Type	Individual identity	0.851	0.019	0.859	0.859

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(0 - 4]	Females	Quantity	DNA extraction plate	1.024	0.13	0.211	0.231
(0 - 4]	Females	Quantity	Season at the time of collection	0.764	0	0.75	0.75
(0 - 4]	Females	Quantity	Hydrological year at the time of collection	0.933	0.008	0.71	0.728
(0 - 4]	Females	Quantity	Social group at time of collection	1.168	0.007	0.075	0.085
(0 - 4]	Females	Quantity	Chronological age at time of collection	0.978	0.001	0.421	0.674
(0 - 4]	Females	Quantity	Total quantity of adversity experienced	1.411	0.001	0.116	0.494
(0 - 4]	Females	Quantity	Individual identity	1.063	0.125	0.033	0.044
(0 - 4]	Females	Type	DNA extraction plate	1.024	0.13	0.188	0.227
(0 - 4]	Females	Type	Season at the time of collection	0.764	0	0.726	0.726
(0 - 4]	Females	Type	Hydrological year at the time of collection	0.933	0.008	0.748	0.757
(0 - 4]	Females	Type	Social group at time of collection	1.168	0.007	0.094	0.094
(0 - 4]	Females	Type	Chronological age at time of collection	0.978	0.001	0.436	0.698
(0 - 4]	Females	Type	Loss of mother prior to age 4	1.07	0.001	0.325	0.523
(0 - 4]	Females	Type	Presence of a competing sibling	0.993	0.001	0.441	0.588
(0 - 4]	Females	Type	Drought in early life	1.085	0.001	0.333	0.726
(0 - 4]	Females	Type	Highest quartile group size	1.177	0.001	0.242	0.424
(0 - 4]	Females	Type	Lowest quartile maternal social connectedness	1.698	0.001	0.051	0.204

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(0 - 4]	Females	Type	Lowest quartile maternal rank	1.057	0.001	0.369	0.546
(0 - 4]	Females	Type	Individual identity	1.061	0.121	0.025	0.033
(4 - 7]	Females	Quantity	DNA extraction plate	1.065	0.11	0.012	0.048
(4 - 7]	Females	Quantity	Season at the time of collection	2.057	0.001	0.009	0.072
(4 - 7]	Females	Quantity	Hydrological year at the time of collection	1.183	0.007	0.045	0.36
(4 - 7]	Females	Quantity	Social group at time of collection	1.473	0.008	0.001	0.002
(4 - 7]	Females	Quantity	Chronological age at time of collection	0.638	0	0.923	0.923
(4 - 7]	Females	Quantity	Total quantity of adversity experienced	0.759	0	0.742	0.742
(4 - 7]	Females	Quantity	Individual identity	1.092	0.077	0.006	0.012
(4 - 7]	Females	Type	DNA extraction plate	1.065	0.11	0.01	0.04
(4 - 7]	Females	Type	Season at the time of collection	2.057	0.001	0.017	0.136
(4 - 7]	Females	Type	Hydrological year at the time of collection	1.183	0.007	0.045	0.36
(4 - 7]	Females	Type	Social group at time of collection	1.473	0.008	0.002	0.003
(4 - 7]	Females	Type	Chronological age at time of collection	0.638	0	0.896	0.896
(4 - 7]	Females	Type	Loss of mother prior to age 4	1.166	0.001	0.226	0.523
(4 - 7]	Females	Type	Presence of a competing sibling	1.08	0.001	0.337	0.539
(4 - 7]	Females	Type	Drought in early life	1.034	0.001	0.359	0.726

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(4 - 7]	Females	Type	Highest quartile group size	1.296	0.001	0.147	0.359
(4 - 7]	Females	Type	Lowest quartile maternal social connectedness	0.663	0	0.868	0.868
(4 - 7]	Females	Type	Lowest quartile maternal rank	0.947	0	0.478	0.546
(4 - 7]	Females	Type	Individual identity	1.092	0.075	0.004	0.008
(7 - 10]	Females	Quantity	DNA extraction plate	1.023	0.149	0.197	0.231
(7 - 10]	Females	Quantity	Season at the time of collection	1.009	0.001	0.382	0.509
(7 - 10]	Females	Quantity	Hydrological year at the time of collection	0.92	0.006	0.728	0.728
(7 - 10]	Females	Quantity	Social group at time of collection	1.248	0.01	0.019	0.025
(7 - 10]	Females	Quantity	Chronological age at time of collection	1.265	0.001	0.202	0.504
(7 - 10]	Females	Quantity	Total quantity of adversity experienced	1.398	0.001	0.138	0.494
(7 - 10]	Females	Quantity	Individual identity	1.131	0.072	0.002	0.005
(7 - 10]	Females	Type	DNA extraction plate	1.023	0.149	0.219	0.227
(7 - 10]	Females	Type	Season at the time of collection	1.009	0.001	0.396	0.528
(7 - 10]	Females	Type	Hydrological year at the time of collection	0.92	0.006	0.757	0.757
(7 - 10]	Females	Type	Social group at time of collection	1.248	0.01	0.017	0.023
(7 - 10]	Females	Type	Chronological age at time of collection	1.265	0.001	0.168	0.434
(7 - 10]	Females	Type	Loss of mother prior to age 4	1.089	0.001	0.327	0.523

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(7 - 10]	Females	Type	Presence of a competing sibling	1.513	0.001	0.08	0.16
(7 - 10]	Females	Type	Drought in early life	0.823	0.001	0.658	0.869
(7 - 10]	Females	Type	Highest quartile group size	1.546	0.001	0.074	0.359
(7 - 10]	Females	Type	Lowest quartile maternal social connectedness	1.107	0.001	0.289	0.771
(7 - 10]	Females	Type	Lowest quartile maternal rank	1.01	0.001	0.401	0.546
(7 - 10]	Females	Type	Individual identity	1.131	0.067	0.003	0.008
(10 - 13]	Females	Quantity	DNA extraction plate	1.055	0.176	0.042	0.112
(10 - 13]	Females	Quantity	Season at the time of collection	0.807	0.001	0.677	0.75
(10 - 13]	Females	Quantity	Hydrological year at the time of collection	1.089	0.012	0.182	0.56
(10 - 13]	Females	Quantity	Social group at time of collection	1.395	0.012	0.002	0.003
(10 - 13]	Females	Quantity	Chronological age at time of collection	1.205	0.001	0.252	0.504
(10 - 13]	Females	Quantity	Total quantity of adversity experienced	0.797	0.001	0.672	0.742
(10 - 13]	Females	Quantity	Individual identity	1.109	0.061	0.017	0.027
(10 - 13]	Females	Type	DNA extraction plate	1.055	0.176	0.041	0.109
(10 - 13]	Females	Type	Season at the time of collection	0.807	0.001	0.667	0.726
(10 - 13]	Females	Type	Hydrological year at the time of collection	1.089	0.012	0.19	0.616
(10 - 13]	Females	Type	Social group at time of collection	1.395	0.012	0.002	0.003

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(10 - 13]	Females	Type	Chronological age at time of collection	1.205	0.001	0.217	0.434
(10 - 13]	Females	Type	Loss of mother prior to age 4	0.958	0.001	0.446	0.595
(10 - 13]	Females	Type	Presence of a competing sibling	2.011	0.002	0.017	0.045
(10 - 13]	Females	Type	Drought in early life	0.978	0.001	0.454	0.726
(10 - 13]	Females	Type	Highest quartile group size	1.016	0.001	0.378	0.441
(10 - 13]	Females	Type	Lowest quartile maternal social connectedness	0.668	0.001	0.853	0.868
(10 - 13]	Females	Type	Lowest quartile maternal rank	0.828	0.001	0.641	0.641
(10 - 13]	Females	Type	Individual identity	1.108	0.056	0.023	0.033
(13 - 16]	Females	Quantity	DNA extraction plate	1.029	0.275	0.209	0.231
(13 - 16]	Females	Quantity	Season at the time of collection	1.439	0.002	0.114	0.304
(13 - 16]	Females	Quantity	Hydrological year at the time of collection	0.961	0.018	0.609	0.728
(13 - 16]	Females	Quantity	Social group at time of collection	1.679	0.026	0.001	0.002
(13 - 16]	Females	Quantity	Chronological age at time of collection	0.872	0.001	0.59	0.787
(13 - 16]	Females	Quantity	Total quantity of adversity experienced	0.788	0.001	0.683	0.742
(13 - 16]	Females	Quantity	Individual identity	1.215	0.07	0.001	0.004
(13 - 16]	Females	Type	DNA extraction plate	1.029	0.275	0.198	0.227
(13 - 16]	Females	Type	Season at the time of collection	1.439	0.002	0.112	0.299

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(13 - 16]	Females	Type	Hydrological year at the time of collection	0.961	0.018	0.621	0.757
(13 - 16]	Females	Type	Social group at time of collection	1.679	0.026	0.001	0.003
(13 - 16]	Females	Type	Chronological age at time of collection	0.872	0.001	0.56	0.747
(13 - 16]	Females	Type	Loss of mother prior to age 4	0.775	0.001	0.725	0.725
(13 - 16]	Females	Type	Presence of a competing sibling	0.685	0.001	0.846	0.846
(13 - 16]	Females	Type	Drought in early life	0.605	0.001	0.924	0.924
(13 - 16]	Females	Type	Highest quartile group size	1.308	0.002	0.154	0.359
(13 - 16]	Females	Type	Lowest quartile maternal social connectedness	0.804	0.001	0.688	0.868
(13 - 16]	Females	Type	Lowest quartile maternal rank	2.408	0.003	0.005	0.04
(13 - 16]	Females	Type	Individual identity	1.223	0.061	0.002	0.008
(16 - 19]	Females	Quantity	DNA extraction plate	1.031	0.411	0.231	0.231
(16 - 19]	Females	Quantity	Season at the time of collection	1.17	0.003	0.242	0.469
(16 - 19]	Females	Quantity	Hydrological year at the time of collection	0.963	0.024	0.611	0.728
(16 - 19]	Females	Quantity	Social group at time of collection	1.544	0.035	0.001	0.002
(16 - 19]	Females	Quantity	Chronological age at time of collection	0.689	0.002	0.838	0.923
(16 - 19]	Females	Quantity	Total quantity of adversity experienced	1.192	0.003	0.221	0.494
(16 - 19]	Females	Quantity	Individual identity	1.03	0.044	0.344	0.393

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(16 - 19]	Females	Type	DNA extraction plate	1.031	0.411	0.227	0.227
(16 - 19]	Females	Type	Season at the time of collection	1.17	0.003	0.265	0.475
(16 - 19]	Females	Type	Hydrological year at the time of collection	0.963	0.024	0.596	0.757
(16 - 19]	Females	Type	Social group at time of collection	1.544	0.035	0.002	0.003
(16 - 19]	Females	Type	Chronological age at time of collection	0.689	0.002	0.843	0.896
(16 - 19]	Females	Type	Loss of mother prior to age 4	0.774	0.002	0.698	0.725
(16 - 19]	Females	Type	Presence of a competing sibling	0.811	0.002	0.652	0.745
(16 - 19]	Females	Type	Drought in early life	0.972	0.002	0.446	0.726
(16 - 19]	Females	Type	Highest quartile group size	0.891	0.002	0.548	0.548
(16 - 19]	Females	Type	Lowest quartile maternal social connectedness	1.014	0.003	0.41	0.82
(16 - 19]	Females	Type	Lowest quartile maternal rank	0.968	0.002	0.45	0.546
(16 - 19]	Females	Type	Individual identity	1.106	0.033	0.149	0.17
(19 - 30]	Females	Quantity	DNA extraction plate	1.063	0.52	0.11	0.22
(19 - 30]	Females	Quantity	Season at the time of collection	1.11	0.004	0.293	0.469
(19 - 30]	Females	Quantity	Hydrological year at the time of collection	0.993	0.03	0.514	0.728
(19 - 30]	Females	Quantity	Social group at time of collection	1.241	0.024	0.085	0.085
(19 - 30]	Females	Quantity	Chronological age at time of collection	1.238	0.005	0.188	0.504

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(19 - 30]	Females	Quantity	Total quantity of adversity experienced	1.181	0.004	0.247	0.494
(19 - 30]	Females	Quantity	Individual identity	0.992	0.038	0.509	0.509
(19 - 30]	Females	Type	DNA extraction plate	1.063	0.52	0.11	0.22
(19 - 30]	Females	Type	Season at the time of collection	1.11	0.004	0.297	0.475
(19 - 30]	Females	Type	Hydrological year at the time of collection	0.993	0.03	0.482	0.757
(19 - 30]	Females	Type	Social group at time of collection	1.241	0.024	0.09	0.094
(19 - 30]	Females	Type	Chronological age at time of collection	1.238	0.005	0.2	0.434
(19 - 30]	Females	Type	Loss of mother prior to age 4	1.26	0.005	0.212	0.523
(19 - 30]	Females	Type	Presence of a competing sibling	2.117	0.008	0.013	0.045
(19 - 30]	Females	Type	Drought in early life	0.749	0.003	0.76	0.869
(19 - 30]	Females	Type	Lowest quartile maternal social connectedness	0.717	0.003	0.807	0.868
(19 - 30]	Females	Type	Lowest quartile maternal rank	1.147	0.004	0.279	0.546
(19 - 30]	Females	Type	Individual identity	0.851	0.019	0.866	0.866
(0 - 4]	Males	Quantity	DNA extraction plate	1.067	0.148	0.016	0.075
(0 - 4]	Males	Quantity	Season at the time of collection	1.16	0.001	0.253	0.506
(0 - 4]	Males	Quantity	Hydrological year at the time of collection	1.226	0.011	0.023	0.138
(0 - 4]	Males	Quantity	Social group at time of collection	1.339	0.009	0.009	0.018

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(0 - 4]	Males	Quantity	Chronological age at time of collection	1.157	0.001	0.23	0.46
(0 - 4]	Males	Quantity	Total quantity of adversity experienced	1.03	0.001	0.352	0.547
(0 - 4]	Males	Quantity	Individual identity	1.095	0.134	0.004	0.006
(0 - 4]	Males	Type	DNA extraction plate	1.067	0.148	0.008	0.048
(0 - 4]	Males	Type	Season at the time of collection	1.16	0.001	0.269	0.538
(0 - 4]	Males	Type	Hydrological year at the time of collection	1.226	0.011	0.017	0.102
(0 - 4]	Males	Type	Social group at time of collection	1.339	0.009	0.006	0.014
(0 - 4]	Males	Type	Chronological age at time of collection	1.157	0.001	0.263	0.526
(0 - 4]	Males	Type	Loss of mother prior to age 4	1.372	0.001	0.105	0.262
(0 - 4]	Males	Type	Presence of a competing sibling	0.962	0.001	0.442	0.442
(0 - 4]	Males	Type	Drought in early life	0.631	0	0.895	0.895
(0 - 4]	Males	Type	Highest quartile group size	0.773	0.001	0.713	0.713
(0 - 4]	Males	Type	Lowest quartile maternal social connectedness	1.124	0.001	0.287	0.604
(0 - 4]	Males	Type	Lowest quartile maternal rank	0.897	0.001	0.552	0.552
(0 - 4]	Males	Type	Individual identity	1.099	0.131	0.004	0.008
(4 - 7]	Males	Quantity	DNA extraction plate	1.017	0.11	0.243	0.292
(4 - 7]	Males	Quantity	Season at the time of collection	0.769	0	0.732	0.911

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(4 - 7]	Males	Quantity	Hydrological year at the time of collection	1.05	0.007	0.317	0.476
(4 - 7]	Males	Quantity	Social group at time of collection	1.325	0.007	0.008	0.018
(4 - 7]	Males	Quantity	Chronological age at time of collection	0.579	0	0.957	0.994
(4 - 7]	Males	Quantity	Total quantity of adversity experienced	0.809	0	0.657	0.788
(4 - 7]	Males	Quantity	Individual identity	1.118	0.076	0.001	0.003
(4 - 7]	Males	Type	DNA extraction plate	1.017	0.11	0.256	0.307
(4 - 7]	Males	Type	Season at the time of collection	0.769	0	0.744	0.922
(4 - 7]	Males	Type	Hydrological year at the time of collection	1.05	0.007	0.256	0.463
(4 - 7]	Males	Type	Social group at time of collection	1.325	0.007	0.007	0.014
(4 - 7]	Males	Type	Chronological age at time of collection	0.579	0	0.953	0.996
(4 - 7]	Males	Type	Loss of mother prior to age 4	0.683	0	0.845	0.994
(4 - 7]	Males	Type	Presence of a competing sibling	1.448	0.001	0.11	0.22
(4 - 7]	Males	Type	Drought in early life	0.658	0	0.874	0.895
(4 - 7]	Males	Type	Highest quartile group size	0.879	0	0.578	0.713
(4 - 7]	Males	Type	Lowest quartile maternal social connectedness	1.095	0.001	0.302	0.604
(4 - 7]	Males	Type	Lowest quartile maternal rank	1.625	0.001	0.059	0.098
(4 - 7]	Males	Type	Individual identity	1.118	0.073	0.002	0.006

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(7 - 10]	Males	Quantity	DNA extraction plate	1.036	0.176	0.123	0.246
(7 - 10]	Males	Quantity	Season at the time of collection	1.213	0.001	0.218	0.506
(7 - 10]	Males	Quantity	Hydrological year at the time of collection	1.052	0.012	0.301	0.476
(7 - 10]	Males	Quantity	Social group at time of collection	1.066	0.01	0.258	0.31
(7 - 10]	Males	Quantity	Chronological age at time of collection	1.262	0.001	0.187	0.46
(7 - 10]	Males	Quantity	Total quantity of adversity experienced	1.038	0.001	0.365	0.547
(7 - 10]	Males	Quantity	Individual identity	1.147	0.09	0.003	0.006
(7 - 10]	Males	Type	DNA extraction plate	1.036	0.176	0.121	0.242
(7 - 10]	Males	Type	Season at the time of collection	1.213	0.001	0.228	0.538
(7 - 10]	Males	Type	Hydrological year at the time of collection	1.052	0.012	0.321	0.463
(7 - 10]	Males	Type	Social group at time of collection	1.066	0.01	0.241	0.289
(7 - 10]	Males	Type	Chronological age at time of collection	1.262	0.001	0.177	0.526
(7 - 10]	Males	Type	Loss of mother prior to age 4	1.668	0.002	0.048	0.262
(7 - 10]	Males	Type	Presence of a competing sibling	2.684	0.003	0.004	0.012
(7 - 10]	Males	Type	Drought in early life	1.205	0.001	0.234	0.706
(7 - 10]	Males	Type	Highest quartile group size	0.799	0.001	0.68	0.713
(7 - 10]	Males	Type	Lowest quartile maternal social connectedness	0.759	0.001	0.742	0.89

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(7 - 10]	Males	Type	Lowest quartile maternal rank	2.904	0.003	0.001	0.005
(7 - 10]	Males	Type	Individual identity	1.105	0.082	0.019	0.028
(10 - 13]	Males	Quantity	DNA extraction plate	1.073	0.343	0.025	0.075
(10 - 13]	Males	Quantity	Season at the time of collection	0.716	0.001	0.809	0.911
(10 - 13]	Males	Quantity	Hydrological year at the time of collection	0.718	0.01	0.987	0.987
(10 - 13]	Males	Quantity	Social group at time of collection	1.186	0.025	0.062	0.093
(10 - 13]	Males	Quantity	Chronological age at time of collection	0.474	0.001	0.994	0.994
(10 - 13]	Males	Quantity	Total quantity of adversity experienced	1.085	0.002	0.312	0.547
(10 - 13]	Males	Quantity	Individual identity	1.031	0.047	0.325	0.39
(10 - 13]	Males	Type	DNA extraction plate	1.073	0.343	0.039	0.117
(10 - 13]	Males	Type	Season at the time of collection	0.716	0.001	0.81	0.922
(10 - 13]	Males	Type	Hydrological year at the time of collection	0.718	0.01	0.994	0.994
(10 - 13]	Males	Type	Social group at time of collection	1.186	0.025	0.062	0.093
(10 - 13]	Males	Type	Chronological age at time of collection	0.474	0.001	0.996	0.996
(10 - 13]	Males	Type	Loss of mother prior to age 4	1.172	0.002	0.271	0.407
(10 - 13]	Males	Type	Presence of a competing sibling	1.204	0.002	0.211	0.316
(10 - 13]	Males	Type	Highest quartile group size	1.092	0.002	0.349	0.713

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(10 - 13]	Males	Type	Lowest quartile maternal social connectedness	0.601	0.001	0.939	0.939
(10 - 13]	Males	Type	Lowest quartile maternal rank	1.378	0.003	0.142	0.178
(10 - 13]	Males	Type	Individual identity	1.019	0.039	0.41	0.492
(13 - 30]	Males	Quantity	DNA extraction plate	1.057	0.584	0.216	0.292
(13 - 30]	Males	Quantity	Season at the time of collection	1.236	0.006	0.239	0.506
(13 - 30]	Males	Quantity	Hydrological year at the time of collection	1.035	0.032	0.401	0.481
(13 - 30]	Males	Quantity	Social group at time of collection	1.025	0.042	0.404	0.404
(13 - 30]	Males	Quantity	Chronological age at time of collection	0.608	0.003	0.898	0.994
(13 - 30]	Males	Quantity	Total quantity of adversity experienced	0.43	0.002	0.995	0.995
(13 - 30]	Males	Quantity	Individual identity	0.953	0.024	0.59	0.59
(13 - 30]	Males	Type	DNA extraction plate	1.057	0.584	0.187	0.28
(13 - 30]	Males	Type	Season at the time of collection	1.236	0.006	0.223	0.538
(13 - 30]	Males	Type	Hydrological year at the time of collection	1.035	0.032	0.386	0.463
(13 - 30]	Males	Type	Social group at time of collection	1.025	0.042	0.415	0.415
(13 - 30]	Males	Type	Chronological age at time of collection	0.608	0.003	0.877	0.996
(13 - 30]	Males	Type	Loss of mother prior to age 4	0.43	0.002	0.994	0.994
(13 - 30]	Males	Type	Presence of a competing sibling	0.996	0.005	0.425	0.442

TABLE B.2 CONTINUED FROM PREVIOUS PAGE

Age Class	Sex	Model Version	Variable	F	R^2	P-value	Adjusted P-value
(13 - 30]	Males	Type	Lowest quartile maternal social connectedness	1.013	0.005	0.407	0.61
(13 - 30]	Males	Type	Individual identity	0.919	0.014	0.597	0.597

NOTE: PERMANOVAs testing the effects of individual types of adversity on Bray-Curtis dissimilarities. PERMANOVAs were run on lifespan and age class subsets of the data. In addition to the variables below, models also included plate, season, hydrological year, sex (if both sex model), individual identity, chronological age, and social group. Models were run for 999 permutations, and p-values were corrected for multiple tests using the Benjamini-Hochberg procedure.

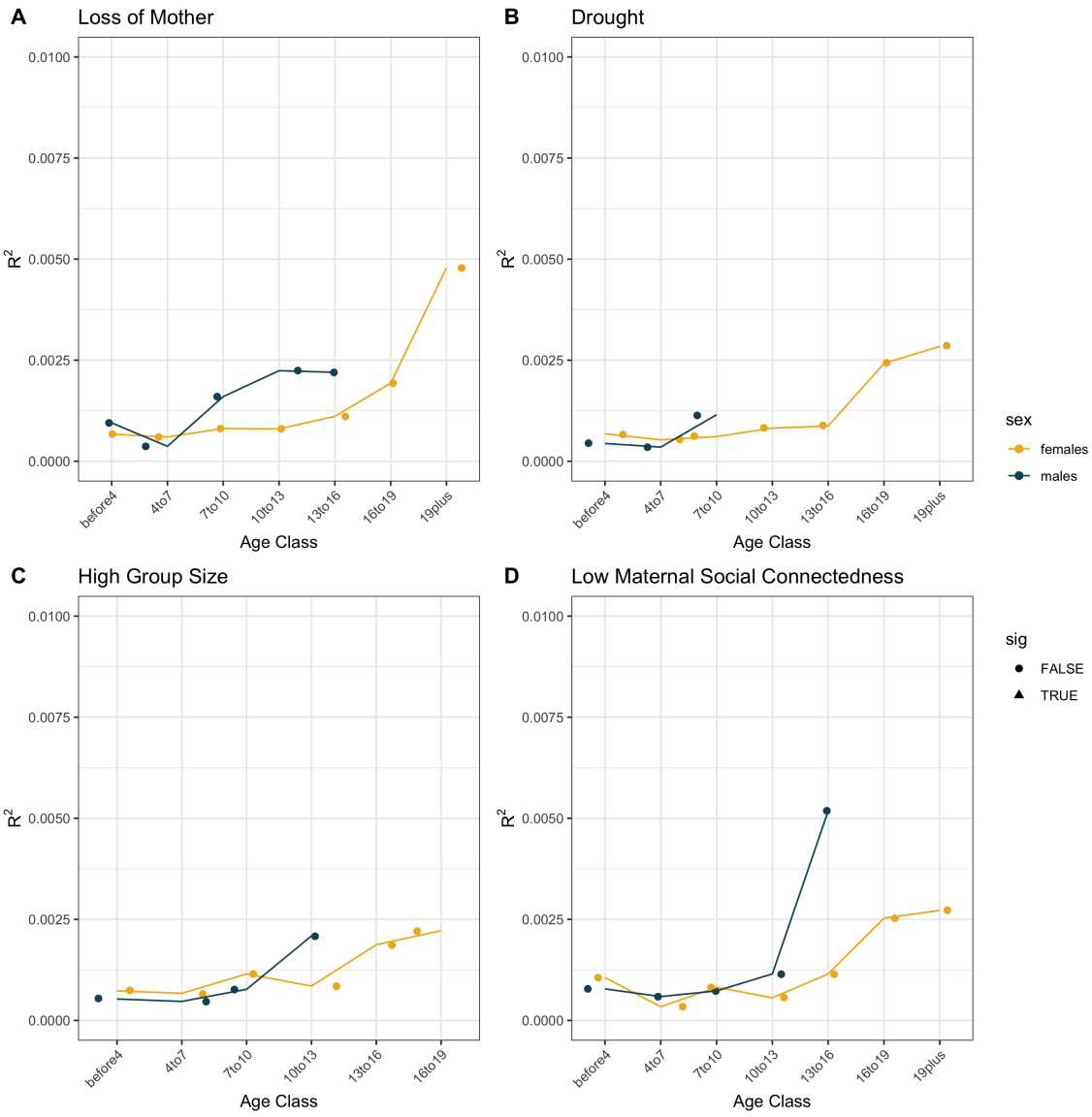

Figure B.1. Change in microbial variation (R^2) between age classes in quantity and type of early life adversity in both sexes. Colors indicate the sex subset in the model, with yellow representing females and blue representing males. Point shape indicates whether the relationship was significant after adjusting for multiple tests using the Benjamini-Hochberg procedure. Cumulative adversity, competing sibling, and low maternal rank are visualized in Figure 3.2.

TABLE B.3

SELECTED FEATURES MODELED PREDICTED BY CUMULATIVE ADVERSITY AND MODELED WITH A BINOMIAL ERROR DISTRIBUTION

Feature	**Related Genus**	**Coefficient**	**SE**	**Adjusted P-value**
ASV 5372	Bacteria > Firmicutes > Clostridiales > Ruminococcaceae > Faecalibacterium	-92.148	1057.583	1
ASV 8009	Bacteria > Firmicutes > Clostridiales > Ruminococcaceae > Faecalibacterium	-92.148	1057.583	1
ASV 4770	Bacteria > Firmicutes > Clostridiales > Clostridiaceae 1 > NA	-89.671	613864.701	1
ASV 5911	Bacteria > Bacteroidetes > Bacteroidales > Prevotellaceae > Prevotella 7	-77.371	65.296	0.657
ASV 4859	Bacteria > Firmicutes > Clostridiales > Lachnospiraceae > NA	-76.621	1726.285	1
ASV 14361	NA > NA > NA > NA > NA	-75.353	0.004	0
ASV 16179	Bacteria > Firmicutes > Clostridiales > Ruminococcaceae > [Eubacterium] coprostanoligenes group	-71.623	457711.66	1
ASV 4226	Bacteria > Firmicutes > Clostridiales > Clostridiales vadinBB60 group > NA	-69.608	591678.242	1

NOTE: A total of 7,956 features were examined using a binomial error distribution, but 944 of the models failed to converge or had other fit problems. Here, we show the selected results for the remaining 7,012 features. Of those 7,012 features, 1,683 of the features exhibited significant relationships with cumulative adversity after correcting for multiple tests via Benjamini-Hochberg procedure (FDR threshold = 0.05). Table is truncated due to length constraints; see supplementary excel file.

TABLE B.4

22 FAMILIES REPRESENTED IN THE TOP 30 ASVS PREDICTED A TYPE OF EARLY LIFE ADVERSITY

Type of Adversity	Families with positive estimates	Families with negative estimates
Drought in early life	Actinomycetaceae, Nocardioidaceae, Prevotellaceae (3), Rhodobacteraceae, Ruminococcaceae, Sporolactobacillaceae, Uncharacterized Family (7)	Beijerinckiaceae, Blastocatellaceae, Chitinophagaceae, Clostridiaceae 1, Lachnospiraceae (2), Moraxellaceae, Nocardioidaceae, Peptococcaceae, Prevotellaceae (3), Uncharacterized Family (3)
High group density	Acidaminococcaceae, Lachnospiraceae (4), Lactobacillaceae, Prevotellaceae, Rhizobiaceae, Ruminococcaceae (2), Uncharacterized Family (5)	Acetobacteraceae, Bifidobacteriaceae, Burkholderiaceae, Chloroflexaceae, Clostridiaceae 1, Desulfovibrionaceae, Lachnospiraceae (2), Moraxellaceae, Nocardioidaceae, Prevotellaceae (3), Ruminococcaceae, Uncharacterized Family
Loss of mother before age 4	Acidaminococcaceae, Chitinophagaceae, Family XI_2II, Lachnospiraceae (4), Prevotellaceae, Rhizobiaceae, Ruminococcaceae (3), Sporolactobacillaceae, Uncharacterized Family, Veillonellaceae	Lachnospiraceae, Longimicrobiaceae, Nocardioidaceae, Prevotellaceae (4), Pseudomonadaceae, Ruminococcaceae (2), Uncharacterized Family (5)
Low Maternal Rank	Bifidobacteriaceae, Burkholderiaceae, Chitinophagaceae, Lachnospiraceae, Nocardioidaceae, Prevotellaceae (5), Ruminococcaceae, Uncharacterized Family (4)	Acetobacteraceae, Actinomycetaceae, Chitinophagaceae, Family XI_2, Lachnospiraceae (5), Nitrosococcaceae, Prevotellaceae (2), Sphingomonadaceae, Uncharacterized Family (2)
Low Maternal Social Connectedness	Anaerolineaceae, Lachnospiraceae (2), Methanobacteriaceae, Nostocaceae, Prevotellaceae, Rikenellaceae, Ruminococcaceae (3), Sphingomonadaceae, Uncharacterized Family (4)	Chloroflexaceae, Cyanobiaceae, Lachnospiraceae (2), Micromonosporaceae, Moraxellaceae, Prevotellaceae (4), Ruminococcaceae, Uncharacterized Family (3), Veillonellaceae

TABLE B.4 CONTINUED FROM PREVIOUS PAGE

Type of Adversity	Families with positive estimates	Families with negative estimates
Presence of competing sibling	Acidaminococcaceae, Actinomycetaceae, Clostridiaceae 1, Erysipelotrichaceae, Family XI_2II (2), Lachnospiraceae (3), Methanobacteriaceae, Nostocaceae, Prevotellaceae, Rhizobiaceae, Uncharacterized Family (2)	Bacillaceae, Beijerinckiaceae, Burkholderiaceae, Chthoniobacteraceae, Lachnospiraceae (4), Microbacteriaceae, Peptostreptococcaceae, Prevotellaceae (2), Uncharacterized Family (3)

NOTE: The 22 families represented in the top 30 ASVs predicted a type of early life adversity. These families had the the largest absolute estimates for each type of adversity. Families with more than one ASV include the number of ASVs represented in parentheses.

TABLE B.5

LINEAR PREDICTORS OF STABILITY IN BRAY-CURTIS DISSIMILARITY

Time period	Model Version	Variable	Estimate	SE	P-value
Juvenile	Quantity	Intercept	0.13609	0.08894	0.12747
Juvenile	Quantity	Total quantity of adversity experienced	-3.2e-4	0.01351	0.98126
Juvenile	Quantity	Mean chronological age	0.13526	0.03007	1e-5
Juvenile	Quantity	Number of samples	-0.00192	4.7e-4	7e-5
Juvenile	Quantity	Sex, male	0.00437	0.0238	0.85452
Juvenile	Type	Intercept	0.14666	0.09237	0.11384
Juvenile	Type	Lost mother prior to age 4	-0.01614	0.03051	0.59727
Juvenile	Type	Competing sibling born within 1.5 years	-0.03238	0.03014	0.28392
Juvenile	Type	Experienced a drought in early life	-0.02718	0.03435	0.42969
Juvenile	Type	Experienced high group size in early life	0.05136	0.03678	0.16404
Juvenile	Type	Had a socially isolated mother	-0.01411	0.02816	0.61694
Juvenile	Type	Had a low ranked mother	0.03072	0.02996	0.30633
Juvenile	Type	Mean chronological age	0.12943	0.03116	5e-5
Juvenile	Type	Number of samples	-0.00164	5e-4	0.00122

TABLE B.5 CONTINUED FROM PREVIOUS PAGE

Time period	Model Version	Variable	Estimate	SE	P-value
Juvenile	Type	Sex, male	0.00126	0.02382	0.95796
Adult	Quantity	Intercept	0.54029	0.02913	0
Adult	Quantity	Total quantity of adversity experienced	0.00936	0.00914	0.30629
Adult	Quantity	Mean chronological age	-0.01219	0.00277	2e-5
Adult	Quantity	Number of samples	-0.00231	3.3e-4	0
Adult	Quantity	Sex, male	-0.02739	0.01691	0.10655
Adult	Type	Intercept	0.52767	0.02866	0
Adult	Type	Lost mother prior to age 4	-0.025	0.01964	0.20437
Adult	Type	Competing sibling born within 1.5 years	-0.0121	0.02049	0.55538
Adult	Type	Experienced a drought in early life	0.08363	0.02359	4.7e-4
Adult	Type	Experienced high group size in early life	0.02838	0.02579	0.27219
Adult	Type	Had a socially isolated mother	6.5e-4	0.01903	0.97284
Adult	Type	Had a low ranked mother	0.0132	0.01979	0.5054
Adult	Type	Mean chronological age	-0.0127	0.00277	1e-5
Adult	Type	Number of samples	-0.00196	3.4e-4	0
Adult	Type	Sex, male	-0.02467	0.01664	0.13947
Lifespan	Quantity	Intercept	0.3476	0.00576	0

TABLE B.5 CONTINUED FROM PREVIOUS PAGE

Time period	Model Version	Variable	Estimate	SE	P-value
Lifespan	Quantity	Total quantity of adversity experienced	0.00247	0.00203	0.22514
Lifespan	Quantity	Mean chronological age	-0.00195	5.5e-4	5.2e-4
Lifespan	Quantity	Number of samples	-0.00115	7e-5	0
Lifespan	Quantity	Sex, male	5.6e-4	0.00371	0.87923
Lifespan	Type	Intercept	0.34342	0.00561	0
Lifespan	Type	Lost mother prior to age 4	-0.00782	0.00431	0.0706
Lifespan	Type	Competing sibling born within 1.5 years	7.6e-4	0.00439	0.86315
Lifespan	Type	Experienced a drought in early life	0.01226	0.00504	0.01572
Lifespan	Type	Experienced high group size in early life	0.01898	0.00562	8.5e-4
Lifespan	Type	Had a socially isolated mother	-0.00114	0.00415	0.78318
Lifespan	Type	Had a low ranked mother	0.00117	0.00433	0.78761
Lifespan	Type	Mean chronological age	-0.00189	5.5e-4	6.5e-4
Lifespan	Type	Number of samples	-0.00107	8e-5	0
Lifespan	Type	Sex, male	0.0012	0.00361	0.73959

NOTE: Stability, or the coefficient of variation in Bray-Curtis dissimilarity across an individual's samples, was calculated across three time periods of interest. We then tested if type or quantity of early life adversity impacted CV using linear models.

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