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Authors

Zablocki-Thomas, Pauline

Rebout, Nancy

Karaskiewicz, Chloe

et al.

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Survival rates and mortality risks of *Plecturocebus cupreus* at the California National Primate Research Center

Pauline Zablocki-Thomas[1], **Nancy Rebout**[2], **Chloe L. Karaskiewicz**[1,3], **Karen L. Bales**[1,3,4]

[1]California National Primate Research Center, Davis CA

[2]FaunaStats, Schiltigheim, France

[3]Department of Psychology, University of California, Davis, United States of America

[4]Department of Neurobiology, Physiology, and Behavior, University of California, Davis, United States of America

Abstract

This article describes survivorship and explores factors affecting mortality risks in a captive colony of coppery titi monkeys (*Plecturocebus cupreus*) housed at the California National Primate Research Center (CNPRC), at UC Davis, in Davis, CA. We analyzed data collected on individuals since the colony's creation in the 1960s, with a sample of 600 animals with partially complete information (date of birth, age at death, body mass, parental lineage). We used three methods: (1) Kaplan-Meier regressions followed by a log-rank test to compare survival in male and female titi monkeys, (2) a breakpoint analysis to identify shifts in the survival curves and (3) Cox regressions to test the effect of body mass change, parental pair tenure, and parental age on mortality risk. We found that males tend to have a longer median lifespan than females (14.9y and 11.4y; $p = 0.094$) and that survival decreases earlier in males than in females during adulthood (9.8y and 16.2y). A body mass loss of 10% from adulthood to the time of death led to a 26% higher risk of dying ($p < 0.001$) as compared to an individual with stable body mass. We found no evidence of sociobiological factors on mortality risks (parental age, parental pair tenure), but an exploratory analysis suggested that a higher rate of offspring conceptions increases mortality risks. This description of factors influencing survival and mortality in titi monkeys is a first step toward understanding aging in this species in order to consider titi monkeys as a primate model for socioemotional aging.

Keywords

Survival; Kaplan-Meier regression; Bayesian breakpoint analysis; Cox regression; Hazard Ratio; Body mass loss

Corresponding Author: Pauline Zablocki-Thomas, Pauline.thomsa90@gmail.com, +1 (530) 760 6363, Address: California National Primate Research Center, 1 Shields Avenue, Davis CA, 95616, USA.

Conflicts of interest

We declare no conflict of interest.

Ethic statement

No animals were handled for the purpose of this article. We collected all the data already available in the colony database at the California National Primate Research Center.

1. Introduction

Non-human primates (NHPs) are our closest relatives and are essential for the understanding of our own evolution. Non-endangered species of NHPs bred in captive colonies or in zoos are a valuable resource that allow researchers to study individuals under controlled conditions and describe the biological processes of aging (Didier et al., 2016; Ross et al., 2012; Ross & Salmon, 2019; Tigges et al., 1988). In addition, having an extensive knowledge of their biology (from physiology or behavior to ecology) throughout the life of laboratory primates is crucial for their good health and well-being (Altschul et al., 2018; Gartner & Weiss, 2018; Tigges et al., 1988).

Several factors can impact aging and NHPs have already provided valuable information in this area (Didier et al., 2016). One factor affecting aging in primates is body mass. Body mass is affected by caloric restriction and is a source of potential applications for human health. Caloric restriction impacts Hazard Ratios (HR) and survival in several species (Colman et al., 2009; Mattison et al., 2017; Pifferi et al., 2019). A higher body mass index is also associated with a higher risk of inflammatory diseases (Obanda et al., 2014). Body mass is also an important measure of health in captive animals, and weight loss *without* caloric restriction is recognized as a marker of health decline in captive settings. For example, social stress is linked with loss of body mass and higher risk of mortality in female rhesus macaques (*Macaca mulatta*) (Hoffman et al., 2011), while lean body mass loss is a marker of senescence in both rhesus macaques and mouse lemurs (*Microcebus murinus*) (Colman et al., 2005; Hämäläinen et al., 2014). These relationships make changes in body mass a valuable measure for identifying changes in physical health (Lorenz & Mason, 1970).

In addition to physiological factors, social factors are also known to have an important impact on lifespan and health. The number and quality of social interactions impact health in both nonhuman primates (e.g., rhesus macaques) and humans (McCowan et al., 2016). In the wild, both higher social connectedness and higher levels of sociability are linked to longer lifespans. Among Western lowland gorillas (*Gorilla gorilla gorilla*), extraverted individuals live longer (Weiss et al., 2013); in female Amboseli baboons (*Papio cynocephalus*), stronger social connectedness predicts longer survival (Archie et al., 2014); in young female rhesus macaques, individuals with better social integration have a higher probability of survival than less integrated young females (Brent et al., 2014); and in chimpanzees (*Pan troglodytes*), male individuals with a less aggressive personality live longer (Altschul et al., 2018).

Finally, in species with parental care, parents are also likely to influence their offspring's survival in the long term (Conti et al., 2012), through the quality of the care they provide. In birds, experienced versus new parents may produce offspring of different quality in terms of both initial viability and later reproductive capacity (*Sula nebouxii:* Torres et al., 2011). In primates, early life stress has long-term health consequences which are mediated in part by epigenetic pathways (Conti et al., 2012; Fairbanks & McGuire, 1995; Kinnally, 2014). Variation in the quality of care may account for variation in early life stress for infants. Experience has an effect on both maternal and paternal parenting qualities, which appear to be mediated by hormonal changes (e.g., a father's prolactin increases with the number

of their mate's pregnancies) (Storey & Ziegler, 2016; Ziegler et al., 2000). A study in cotton-top tamarins (*Saguinus oedipus*) showed that parents' and helpers' prior experience had an effect on infants' early behavioral development, with infants climbing earlier and more often on their care givers (Washabaugh et al., 2002); however, parental experience did not affect infant survival. In monogamous mammals such as titi monkeys (*Plecturocebus cupreus*) or California mice (*Peromyscus californicus*), the experience of both parents is likely to be an important factor for infant survival, with a more important role of the father as the primary caregiver (Bales, 2017; Gubernick & Teferi, 2000). The role of the father is important in titi monkeys (Fragaszy et al., 1982), but good coordination between parents is also a factor to be considered (Mendoza & Mason, 1986), and we do not currently know if parents bonded for a longer duration will perform better than newly-bonded partners. Another possibility is that aging parents will have less success in infant care than younger parents will, because their own health is declining.

Finally, parents/fathers can also play an important role in their offspring's development through the transmission of epigenetic factors and non-social factors (Kinnally & Capitanio, 2015). Indeed, epigenetic factors (such as DNA methylation) are predictive of lifespan in vertebrates (Mayne et al., 2019). Telomere length, which is considered a good marker of aging, is inherited from the father (Njajou et al., 2007), and in mice, older fathers produce offspring with a shorter lifespan than younger fathers (Xie et al., 2018). In another primate species, the grey mouse lemur (*Microcebus murinus*), mother's age at conception but not father's was negatively associated with male offspring longevity, while clutch composition had no effect (Perret & Anzereay, 2022). In this case, the authors advocate that the highly seasonal biology of the mouse lemur is responsible for a high telomere stability (showing no shortening).

Titi monkeys are South American primates that form strong pair bonds and are used as a model for the study of social relationships, especially the biology of social bonding and parenting (Bales et al., 2017). Pair bonding is an important psychological construct demonstrated by a relatively small number of mammals (Kleiman, 1977), including humans, but by a much larger proportion of some other vertebrate groups (Bales et al., 2021). Pair bonding may be critical for healthy aging in humans and other species (House et al., 1988), suggesting that the titi monkey could become an emerging model species for the role of pair bonding in healthy socioemotional aging. However, we still know little about titi monkey aging and what factors may affect their mortality. Titi monkeys typically live in socially monogamous pairs with their subadult offspring in the wild and in captivity. This species exhibits maternal and paternal care, generally with higher investment by the father for non-nutritional care (Fragaszy et al., 1982; Karaskiewicz et al., 2021; Mendoza & Mason, 1986), and thus represents a good model in which to study the importance of parenting on survival.

One paper (Allman et al., 1998) has published data on survival in a captive colony of titi monkeys (*Callicebus sp.*), among other species, from a database provided by a zoo in Dallas (Kaemmerer & Stevens, 1997). They tested the hypothesis that the primary caregiver would benefit from a longer lifespan than the opposite sex in primates. Although this theory was confirmed in other primate species, the results were not significant for titi monkeys. In

addition, other than sex, no specific characteristics (i.e., physiological or sociobiological factors) of the individuals were investigated, and only a survival analysis was performed. Furthermore, the authors state that the lack of statistical significance in their results could be explained by their small sample (n = 163 females, n = 154 males).

The CNPRC possesses a unique colony of coppery titi monkeys (*Plecturocebus cupreus;* formerly known as *Callicebus cupreus*), which have been studied for several decades as a model for investigating various aspects of social relationships and their effects on health (Bales et al., 2017). The colony was established in 1970 (Lorenz & Mason, 1970), and the number of titi monkeys maintained in this facility since its inception has now reached 600 (as of October 15, 2021). We now possess sufficient data on lifespan, body mass throughout life, and parental history to study survival and mortality risks. Our objectives in the current paper were (1) to replicate the finding of Allman et al. (1998) on life expectancies in male and female titi monkeys with a larger sample of a different captive population; (2) to describe the pattern of the survival curves by using a breakpoint analysis; and (3) to estimate the effect of physiological and social factors (e.g., body mass change and parental age) on mortality risks. While we expected to find similar results as Allman and colleagues (1988) on the difference in life expectancies between male and female titi monkeys, we thought it possible that with this increased sample size, those trends might now be statistically significant. As male titi monkeys are the principal attachment figures and non-nutritive care providers in titi monkeys (Fragaszy et al., 1982; Mendoza & Mason, 1986), we hypothesized that they would live longer than females. Our intent with the breakpoint analysis was to find a timepoint in the life of titi monkeys where they show a change in the slope of their survival rates, which could be indicative of the onset of the aging process, as survival decrease seems to be steeper at older ages in longer-lived species and in primates (Colchero et al., 2021; Siler, 1979). By testing two different aspects of parental effects on survival (parental pair tenure and age of parents), we expected to see an effect of experience of the partners together on mortality risks, such that greater parental experience predicted lower risk of offspring mortality (Mendoza & Mason, 1986; Torres et al., 2011). Finally, we expected to find an effect of the age of the father on mortality risk in their offspring.

2. Methods

2.1. Subjects and data collection

We collected data from the CNPRC database on 600 individuals (271 females, 269 males, and 60 unsexed infants) with known, approximated, or unknown date of birth, and retrieved data on body mass for 453 individuals (for their entire life or since their arrival to the colony). Birth dates and death dates ranged from April 1, 1962 to October 15, 2021. Animals were typically housed in opposite sex pairs (full contact) with their unpaired offspring (until approximately 3 years of age). Individuals were sometimes housed in multi-male or multi-female groups, sibling groups, or single-parent and offspring groups.

Body mass records ranged from January 16, 1980 to April 27, 2021 and allowed us to determine an "*adult body mass*". Individuals in our sample had a median of 30 measurements (min = 1, max = 207) and individuals were weighted from 1 to 78 times per year ($M = 6.56$, $SD = 8.52$). To estimate adult body mass, we plotted average body

mass for each age in years for the entire colony and visually selected the age when body mass was stable (Figure 1). Using this method, we decided to consider adult body mass as the average body mass from 4 to 5 years. We confirmed this visual interpretation of body mass stabilization by a Generalized Additive Mixed Model (GAMM) analysis using the 'poptrend' package (Knape, 2016), which showed that body mass significantly increased until 3.56 years (Supplementary Figure S1). We considered body mass around the time of death to be the last body mass measurement in the body mass record, and body mass 1 year before death as the average body mass 6 to 18 months prior to death.

The "*body mass change*" was calculated as the difference between body mass around death and the adult body mass. The "*percentage of body mass change*" was calculated as the body mass change divided by the adult body mass and multiplied by 100. The "*Percentage of body mass change 6-18 month before death*" was calculated as the body mass difference between 6-18 months before death and body mass around death divided by body mass 6-18 months before death and multiplied by 100.

2.2. Data analysis

Natural date of death was unknown for 286 individuals, meaning that they were either still alive on October 15, 2021 (110 individuals), sent to another captive colony (103 individuals), euthanized for research purposes (24 individuals), or died in a virus outbreak in the colony (26 individuals: 20 due to a species-endemic adenovirus, 6 due to an outbreak of measles). We used right censoring in these cases, which allowed us to still collect information for the survival analysis from these individuals.

Natural causes of death were determined when an animal was found deceased (2 individuals) or when an animal was euthanized for severe health reasons in accordance with IACUC and veterinary recommendation (314 individuals). This classification is consistent with how previous work has handled clinical euthanasia in captive settings (Ha et al., 2000). Reported stillbirths were not included in the analysis (coded as missing data, 17 individuals), because it was not possible to identify a reliable date of birth.

2.2.1. Kaplan –Meier (KM) curves and log-rank test—

We visualized KM regressions with a dataset limited to individuals that survived beyond 31 days (193 females, 205 males) and compared them quantitatively using the log-rank test to test for a difference of survival between male and female titi monkeys. This first step allowed us to compare our analyses with the one previously described and to have visual information on the curves to help us build our Bayesian model for the following breakpoint analysis.

2.2.2. Breakpoint analysis—

In order to go further in our comparison of the survival curves, we used breakpoint analysis. Breakpoint analysis allowed us to identify changes in the slopes of the survival curves. Implementing breakpoint analysis requires continuous data. In order to turn survival information into continuous data we used the above-described survival analysis to precisely predict survival probability according to age for three different groups: all individuals, males only, and females only. We then used these data for the breakpoint analysis with a Bayesian approach. To do so, we had to specify the expected

model with the presence of breakpoints or plateaus to define different segments of the survival curves and to specify if these segments were joined or not.

We kept the model that gave us the best stability (good convergence evaluated by Rhat). The model we implemented implied one breakpoint and a joint slope for the two other segments separated by the breakpoint (cp1) (see details in the Supplementary materials).

These analyses were performed in R using the 'mcp' package (Lindeløv, 2020) with the latest version of Jags.

2.2.3. Cox regression—In order to test for the effect of body mass change and parental information on mortality risks, we used Cox regression models using the 'survival' R package. In the Cox regression with proportional risks, we tested 4 models: (1) with the effects of sex and the body mass change; (2) with the effects of sex and the percentage of body mass change; (3) with the effects of sex of the individual and the age of their parents; and (4) with the effects of sex of the individual and the age of their parents' pairing ("*pair tenure*"). We did not include the parental pair tenure and the age of the parents in the same model because they are confounded: younger individuals can only be involved in relatively more recent pairings, while older individuals may be in pairings of any duration. The number of individuals with available data are indicated in the results for each model.

We chose to present how the difference between the average body mass during adulthood (4-5 years, when the body mass stabilized in our population) and the body mass around death affected mortality risks, because body mass was measured at different time points across individuals and measured approximately every year. This means that body mass during adulthood is an averaged body mass over a specific period. In order to be sure that the choice of this period did not bias the outcomes of our models, we performed a Cox regression with percentage of body mass loss from the averaged body mass between 6 and 18 months before death as compared to body mass at death (Model 5, Supplementary Table 2).

We then checked the validity of our models by testing the proportionality of the risks. When proportionality of risk was not met (as was the case for paternal age in Model 3), Cox proportional models are not adequate (Cox, 1972), and we employed a weighted Cox regression using the R package 'coxphw' (Dunkler et al., 2018). In order to further investigate the effect of paternal age on survivorship, we conducted Kaplan-Meier regressions on survival data with different age groups for the fathers: young fathers (< 6y old), middle-aged fathers (> 6y and < 11y old), and old fathers (>11y old); and with fathers younger or older than the median survival for males (9.4y).

3. Results

In our colony, two males lived up to 29.6 and 28 years, but their date of birth was unknown or imprecise because they were wild-born and arrived as young individuals. Our oldest males with a precise date of birth lived 26.2 and 25.5 years (the second being currently alive). Our two oldest females lived 23.2 and 22.5 years (the second being currently alive).

Interestingly, the male that lived the longest in our colony was one of the first wild born individuals who arrived at the center in 1962.

3.1. Survival probability – Kaplan-Meier curves

The survival curves (Figure 3) showed a trend-level difference between male and female survival (log-rank test: $p = 0.094$). In the KM analysis without neonatal death, the median life span was 11.40 years (4160 days, 0.95 LCL - 0.95 UCL: 3345 - 5913 days) for females and 14.92 years (5447 days, 0.95LCL - 0.95UCL: 4453 - 7512 days) for males. The probability tables of survival per year are presented in the Supplemental Material (Supplementary Table S1). Across years, survival probability seems to decrease steadily, with the decrease becoming less steep after 10 years of age for both sexes.

With the inclusion of newborn deaths, the survival curves (Supplementary Figure S2) showed a significant difference between male and female survival (log-rank test: P=.024): Females had a median lifespan of 8.13 years (2968 days, 0.95LCL-0.95UCL: 2572 -4156 days) and males had a median lifespan of 11.84 years (4322 days, 0.95LCL-0.95UCL: 3318-6105 days). We can also note on this curve that there is a drop in survival probability around birth, which is representative of neonatal mortality (Supplementary Table S2).

4.2. Breakpoint analysis

Our breakpoint analysis (Figure 4) describes a time during adulthood when the slope in the survival curve changes. For males when all individuals are considered, this slope was smaller (less steep) after the breakpoint than before, meaning that survival probability starts decreasing more slowly at this time. Contrastingly, among females, the slope was bigger (more steep) and led to a faster decrease after the breakpoint. This breakpoint in the survival curve was estimated earlier at 3594 days (9.8 years) for males (Table 1); later for females at 5927 days (16.2 years) (Table 2), and when both sexes were combined, at 3577 days (Table 3). In summary, the slope of the survival curve is less steep (more horizontal) earlier in males than in females. Then, after the breakpoint (cp1), the slope decreases in males and increases in females.

After 16 years, 16 females were still alive and after 9 years, 57 males were still alive (Supplementary Table S1).

4.3. Mortality risks – Cox regressions

Body mass loss—In the Cox regression with proportional risks, sex was not significant, but body mass change and the percentage of body mass change were. In Model 1 the Hazard Ratio (HR) for a loss of 100g was 1.265, and in Model 2 the HR for a loss of 1% was 1.023, meaning a HR of 1.023^10 = 1.26 for a loss in body mass of 10% (in Table 4) and a HR for a loss of 20% was 1.023^20 = 1.58 (see explanation of this calculation in the supplementary materials). These two models converge to suggest that losing 100g or (~10% body mass) translates to a 26% increase in mortality likelihood compared to individuals with stable weight at a given time (t), and this likelihood increases to 58% for a loss of 20% adult body mass. We found similar results when we tested for the effect of the percentage of difference

between the body mass one year before death and the last body mass measurement before death (HR of 1.036 for a loss of 1%, results in Supplementary Table S3).

Parental age—The age of the parents did not significantly affect mortality risk for offspring (Table 5). We provide a survival analysis in the supplementary material with the relative age class of the father as a factor to illustrate survival curves according to the age of the father (Supplementary Figures S3 and S4). This additional analysis did not show significant results on survival curves according to the age of the father.

5. Discussion

Our analysis of survivorship on 50 years of data allowed us to estimate the median lifespan in the CNPRC titi monkey colony at 11.4 years for females and 14.9 years for males. Male and female titi monkeys do not significantly differ in their survival in this sample, although there is a tendency towards higher survivorship in males, as was found previously in a zoo population (Allman et al., 1998). A significant difference in survival between sexes would be consistent with an evolutionary theory that the primary caregiver of the offspring has a longer lifespan, although our data does not provide strong support for this hypothesis.

The survival curves drawn from our dataset seem very similar to those published previously in Allman et al. (1998), although Allman did not provide an estimate for the median lifespan (only graphical data). Our sample size was a little larger (Allman et al. had a sample of 163 females and 154 males), which made our power higher. In a supplementary analysis including more individuals (individuals that died before 31 days, for a sample size of 244 females and 243 males), the difference between males and female survival was significant. However, including neonatal deaths is less easily comparable with other survival studies (Nuss & Warneke, 2010).

One conclusion that we can draw from these results is that it seems reasonable to consider all titi monkeys among the “older” population when they reach ten years old. Physiological data are now needed to investigate the potential causes of the tendency for lower survivorship in females, and if females seem to be aging faster than males. The cost of reproduction in this species should be further investigated in order to see if gestating, birthing, lactating, and/or raising more offspring results in a higher mortality risk for females as it does in macaques (Hoffman et al., 2008). While we had access to information on the number of offspring conceived and raised by males and females, we did not present this data for two reasons. First, we suspected that these data were not as reliably recorded in the past as they are in the present, and second, we did not have enough information on the reproductive status of historical individuals (i.e., females treated with hormonal birth control, either sex modified with surgical contraceptive measures). However, we ran a supplementary analysis using a Cox regression with the average number of offspring conceived and raised per year during the reproductive period (when animals reached sexual maturity). These exploratory results seem to indicate that a higher number of offspring conceived increases mortality risk in females (See supplementary Materials).

Another well-known species of platyrrhine primate with biparental care used in laboratory studies is the marmoset (*Callithrix jacchus*). This species has become a desirable model for studying aging because its relatively short lifespan allows researchers to observe the same individuals across the lifespan (Rothwell et al., 2021). Like titi monkeys, but unlike many other primate species, marmoset fathers engage in high rates of paternal care, and research has shown that male survivorship is significantly longer than females in captivity (Nishijima et al., 2012). This captive longevity is specifically associated with a faster cognitive decline in females compared to males (Rothwell et al., 2022). In this species, females bear a high reproductive cost as they give birth to litters of twins and triplets, each weighing 20% of their body weight (Nishijima et al., 2012) and can become pregnant while nursing existing infants. They have short interbirth intervals, but benefit from the help of older offspring to take care of the infants. In contrast, titi monkey females only have one infant per birth, typically weighing less than 10% of their body weight and experience a period of postpartum anovulation while caring for their infant, resulting in almost year-long interbirth intervals (Valeggia et al., 1999). This lower reproductive cost for female titi monkeys might explain why their lifespan is not significantly shorter than that of males, and why the survival advantage of males is weaker compared to marmosets (Nishijima et al., 2012). Studies of Azara's owl monkeys (*Aotus azarae*), which are another species that exhibit biparental care, yield mixed results on sex differences in survival. One study found that males and females have the same life expectancy in both the wild and in captivity after reaching 2 years of age (Larson et al., 2016), while another found that male captive owl monkeys have a higher survival rate than females past sexual maturity and that mortality increases at a faster rate in females than in males (Allman, 1988). Reproductive cost for females likely differs across settings, with reduced costs being lower in captivity than in the wild due to contraception use reducing death related to early pregnancies (Larson et al., 2016) as well as managing, food supply, the overall number of conceptions, births, and infants reared. Finally, a study of captive Goeldi's monkeys (*Callimico goeldii*) identified the median life span as 5.5 years across individuals, but they did not compare survival between males and females, nor did they take into account the effect of reproduction on survival (Nuss & Warneke, 2010). Taken together, these studies suggest that the combined effects of the cost of reproduction for females and the evolutionary advantage of biparental (and sometimes alloparental) care may account for the shorter lifespan and lower survival rate of females compared to males in platyrrhine primates, as opposed to other primates where females generally live longer and primarily receive support in infant care from older related females (Thomas, 2013)

The Bayesian breakpoint analysis showed that in females, the decline in survivorship began to accelerate at 16.2 years, which is a typical pattern seen in mammals where survivorship decreases slowly from youth to adulthood and then more rapidly decreases at old age (Type I curve: Fernandez et al., 2006). In contrast, for males and the overall population, the analysis showed that the decline in survivorship slows down at older ages instead of accelerating (cp1 in Tables 1-3). The change in slope occurs later in females than in males, as indicated by the difference in cp1 estimation between males (9.8 years) and females (16.2 years). This analysis did not identify an age when survival probability declines faster, but rather an age when the decline of survival probability slows in males and for both sexes combined. In

statistical terms, the effect of age on survival becomes weaker after the breakpoint in these groups, suggesting that other factors may have a stronger influence on survival after that point than before. This study is the first to use a breakpoint analysis to describe survivorship in a nonhuman primate population, which is relevant to human studies that demonstrate a reduction of mortality at advanced ages (Kannisto et al., 1994). Further research could use this method to examine survival curves and patterns across species in greater detail to gain a better understanding of reduced mortality at older ages.

The last analysis we performed was the Cox regression, in order to investigate the effect of body mass changes on the risk of mortality, as well as the effects of parental age and parental pair tenure. Body mass loss was a good predictor of mortality risks, as individuals that lost 20% body weight were 70% more likely to die compared to individuals with stable weight. The UC-Davis criterion for humane euthanasia (loss of 20% of optimal body weight) seems to be empirically supported in our sample. Although it is also possible that this finding was driven by veterinary practice, only one individual was reported as euthanized specifically because of significant weight loss. A loss of body weight is likely to be associated with health issues that would lead to death, e.g. bone or muscle mass loss (Hämäläinen et al., 2014; Mattison et al., 2017), and we found that the percentage of body mass loss (relative to the average body mass) from 6 to 18 months before death as compared to body mass at death (Hazard Ratio = 1.030) did indeed increase mortality risks.

Surprisingly, with our weighted Hazard Regression Analysis parental age effects (Model 3), we did not find any effect of parental age on offspring mortality risks. Especially for the father, we expected that paternal age would influence the “quality” of the offspring and their mortality, potentially via epigenetic factors (Njajou et al., 2007; Xie et al., 2018). In a subsequent Kaplan-Meier regression with different age classes for fathers as a factor (younger fathers versus older fathers), we did not find any significant statistical difference between groups (see Supplements).

Similarly, our Cox regressions with parental pair tenure (Model 4) did not show a significant effect of parental pair tenure on mortality risk in offspring. One explanation for the absence of effects of parental pair bond tenure and paternal age could be an insufficient number of individuals with data on mortality and parental information. Indeed, some of the oldest individuals in our dataset had parents that were caught in the wild (without a known date of birth or pairing date) and a significant number of more recently-born individuals were right censored (still living, moved to another facility, or in very rare occasions euthanized for a research project; Supplementary Figure S3 and S4). Another alternative explanation for the absence of evident effects of these two sociobiological factors could be that parental pair tenure and age may have opposite effects on offspring mortality and thus their effects could be hidden in our models. Indeed, when pair tenure increases, parental care should be improved, but older parents could produce offspring of lower biological quality. This latter assertion could be tested in the future with titi monkeys by measuring telomere length in offspring.

There are several aspects of titi monkey sociality and captive housing that could explain the absence of significant results in the Cox regressions. First, the captive setting provides

expert husbandry and veterinary care, ameliorating health issues regardless of the social environment and mitigating any stress experienced during early life, leading to longer lifespans for all individuals in general. In a study of cotton-top tamarins, a cooperatively breeding primate species, researchers found no relationship between the experience of the parent and infant survival (Washabaugh et al., 2002), and they acknowledged that better husbandry practices have improved survival rates in first-breeding parents during the history of their colony. Second, in relation to the duration of the pair bond, the parity of the parents could be influential on an infant's early life, as a proxy of parental experience. However, these data were not reliably recorded in the past and often varied within pairs (i.e., the female had a previous partner and offspring while the male had never reproduced). Third, information on social relationship quality and number of prior pairings could be investigated in the future, as quality social bonds are predictive of increased survivability in a number of social species (House et al., 1988; Silk et al., 2003). Finally, a recent study also pointed out the importance of personality on lifespan longevity in captive chimpanzees (Altschul et al., 2018), which opens another perspective for our investigations on survival in captive titi monkeys.

In conclusion, this study provides an extended overview of the survivorship and the mortality risk in a colony of captive titi monkeys. We explored the effect of several biological (sex, body mass) and sociobiological factors (parental age and pair tenure), and suggest exploring physiological and epigenetic signs of aging in titi monkeys at least after ten years of age. This study also replicates a previous finding conducted in another captive colony of titi monkeys, wherein males tended to live longer than females. The break point analysis revealed an interesting pattern of survival across age and sex such that male aging progressed more slowly starting at an earlier age compared to female aging. Other sociobiological factors including parity, family structure, and personality should be investigated in future analyses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data sharing and Data accessibility

The data that support the findings of this study are available from the corresponding author upon reasonable request.

List of abbreviations

cp	change point
F	Female

HR	Hazard Ratios
KM	Kaplan-Meier
M	Male
NHP	Non-Human Primates

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Figure 1:
A titi monkey family at the CNPRC colony (from left to right): a 5-year-old female (mother), a 1-year-old male, a 12-year-old male (father), and a 2-year-old female. Photo by Alexander Baxter.

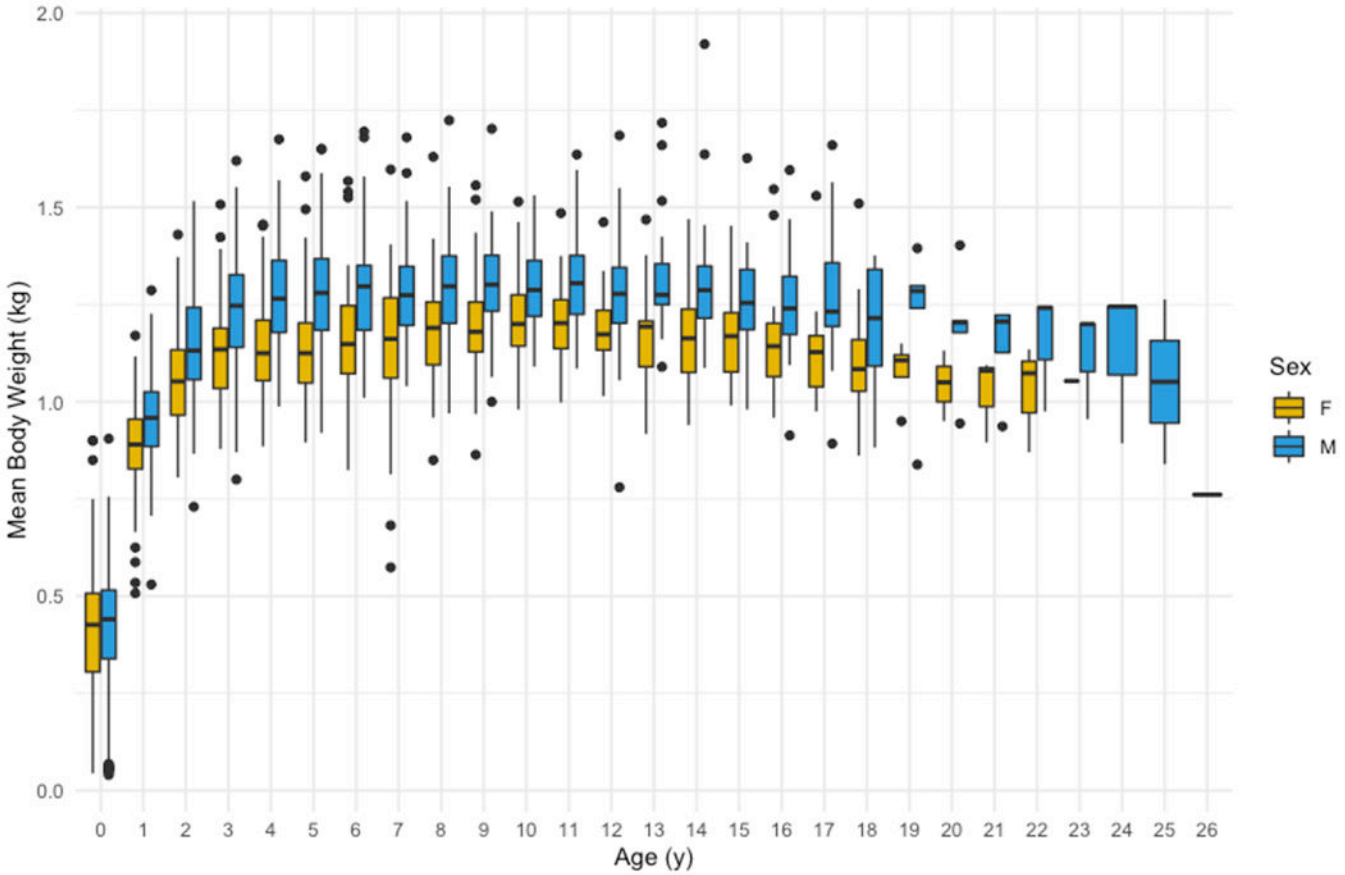


Figure 2:

Body mass per year. For each individual, we averaged their body mass per year and then drew boxplots as a function of age and sex. This graph, in addition to a GAMM analysis, allowed us to estimate the age range when titi monkeys stopped growing. At 4 years, Females = 1.14 kg (±0.11); Males = 1.28 kg (±0.14).

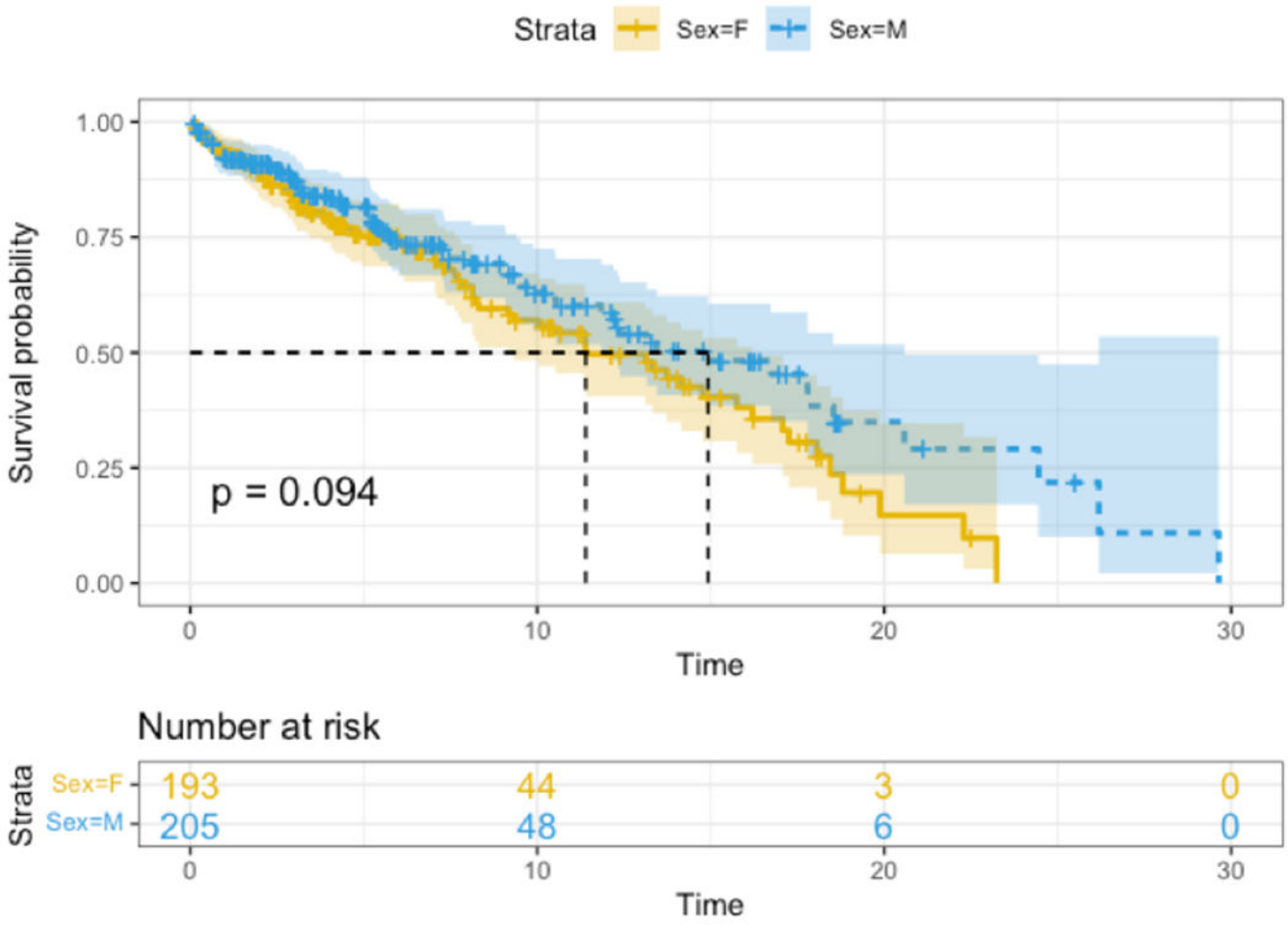
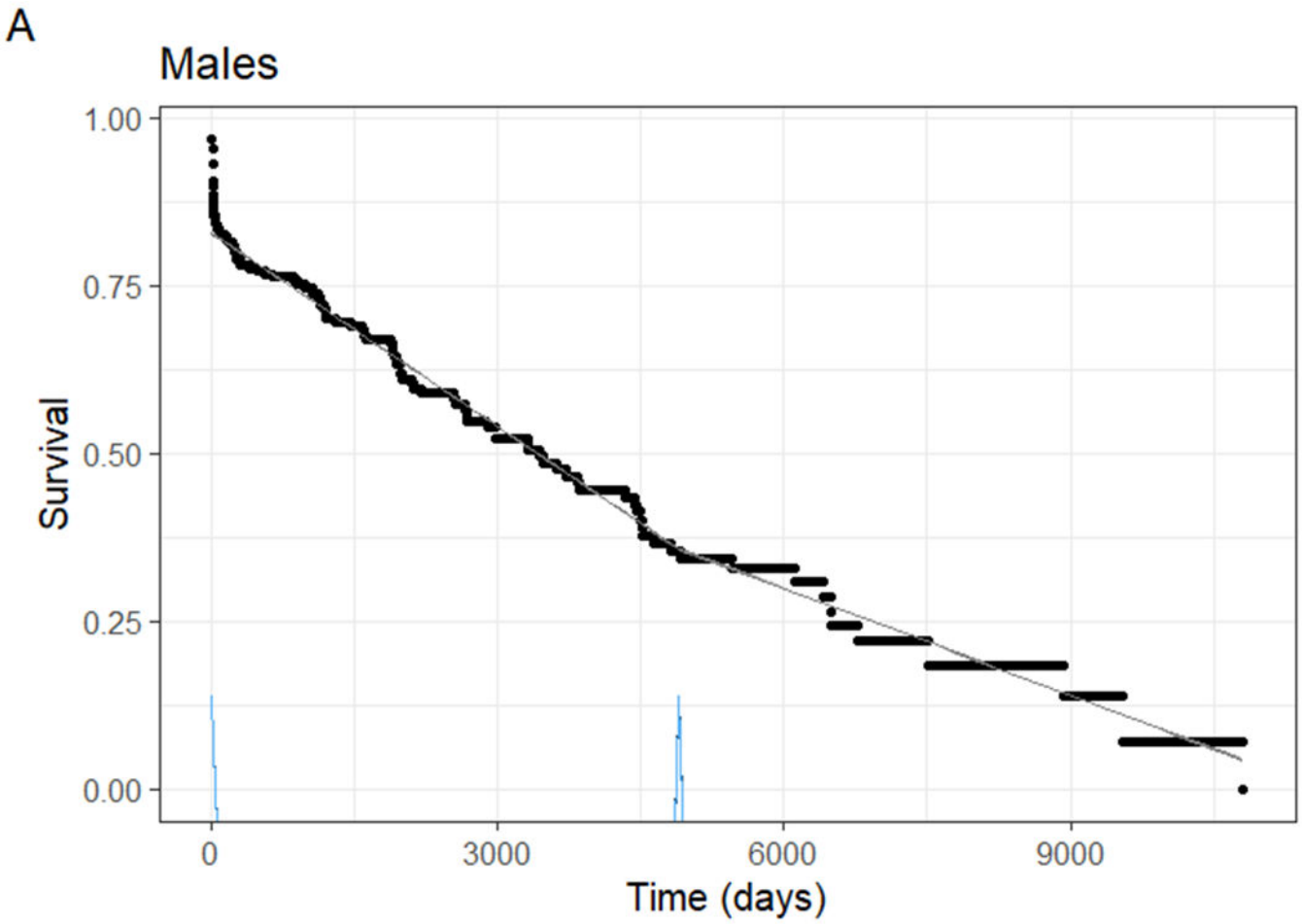
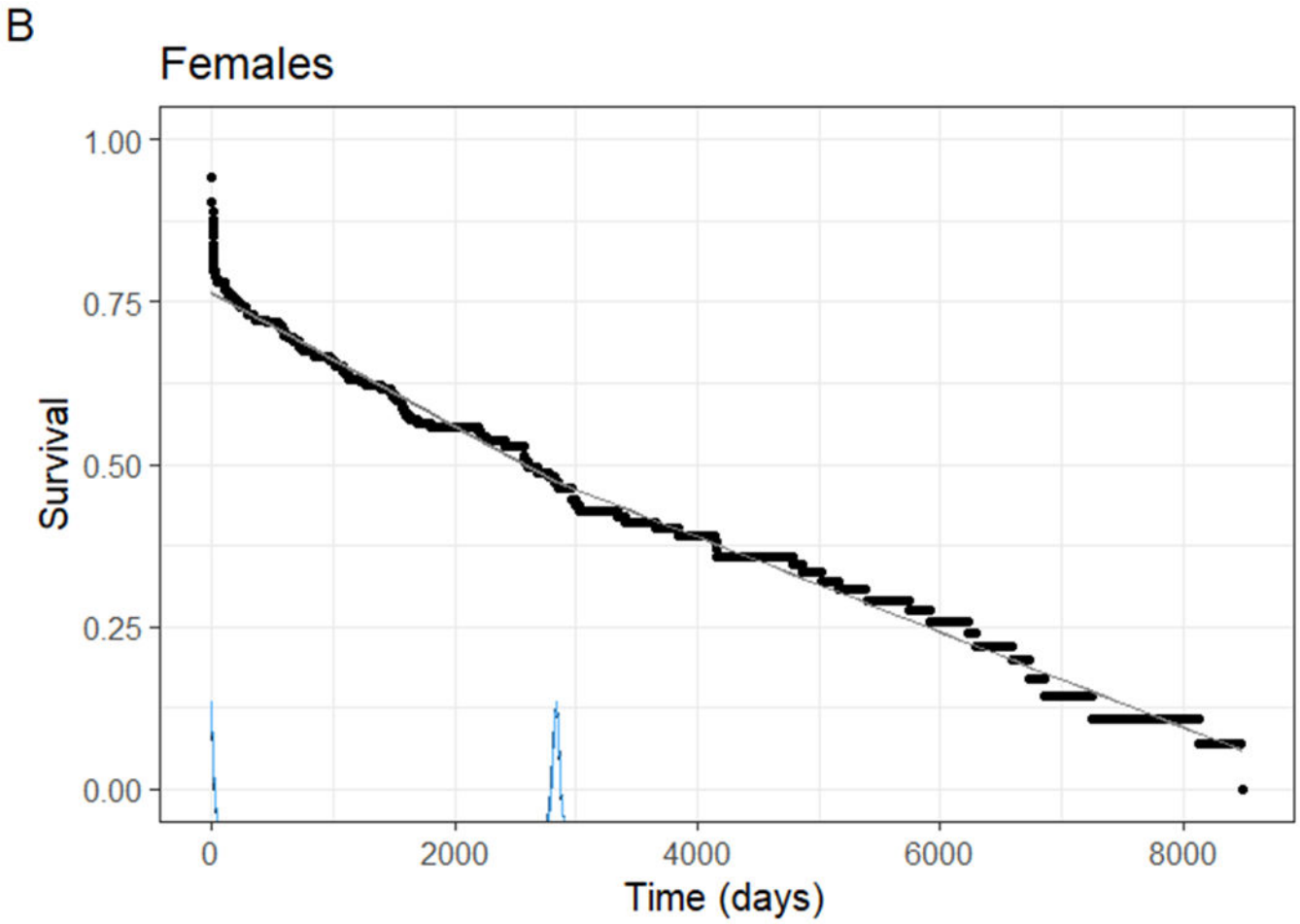


Figure 3:

Survival curves obtained from the Kaplan-Meier method featuring only individuals that survived beyond 31 days. Animals were right censored (vertical bars) when they were either: still alive on 10/15/21, sent to another captive colony, or euthanized for research purposes.





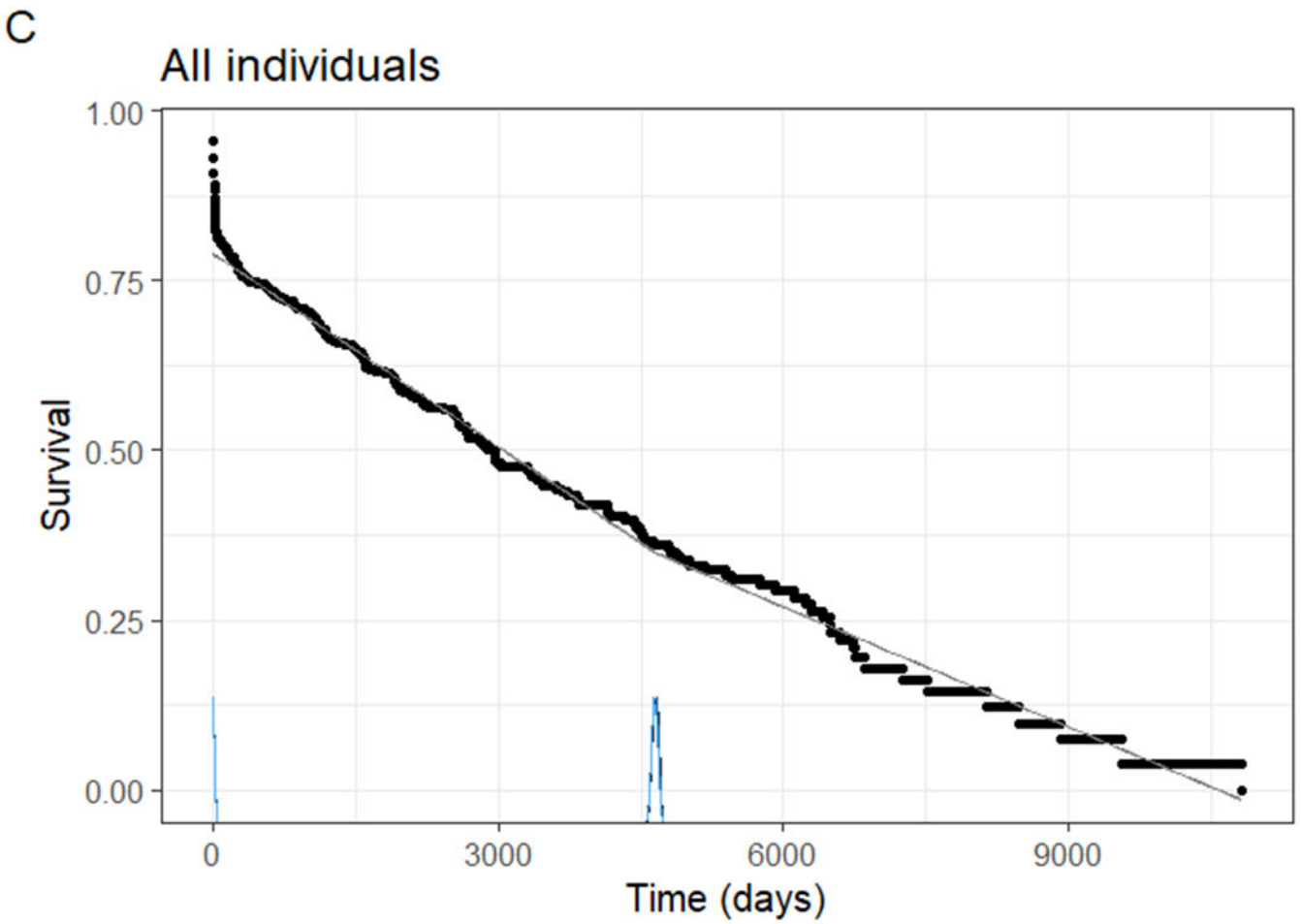


Figure 4:

Breakpoint analyses for (A) males, (B) females, and (C) all individuals with one breakpoint. The blue curve along the x-axes indicates the location and certainty around the change point (Lindeløv, 2020).

Table 1-3:

results of the breakpoint analysis using the mcp package. **Model 1**: for males only, **Model 2;** for females only; and **Model 3** for the entire population.

Table 1: males					
name	**mean**	**lower**	**upper**	**Rhat**	**n.eff**
Change point (cp1)	3594.060	3478.008	3707.789	1.036	243
int_1	0.973	0.971	0.974	1.143	232
Time_1 (slope)	−0.0000935	−0.0000942	−0.0000928	1.125	130
Time_2 (slope)	−0.0000771	−0.0000774	−0.0000769	1.001	892
sigma_1	0.022	0.022	0.022	1.000	5737
Table 2: females					
name	**mean**	**lower**	**upper**	**Rhat**	**n.eff**
Change point (cp1)	5927.510	5840.895	6024.990	1.003	2141
int_1	0.955	0.953	0.956	1.002	510
Time_1 (slope)	−0.000102	−0.000102	−0.000102	1.002	475
Time_2 (slope)	−0.000111	−0.000112	−0.000111	1.001	1429
sigma_1	0.021	0.021	0.021	1.000	6000
Table 3: all individuals					
name	**Mean**	**Lower**	**upper**	**Rhat**	**n.eff**
Change point (cp1)	3577.118	3474.065	3690.847	1.008	196
int_1	0.971	0.970	0.973	1.005	178
Time_1 (slope)	−0.000104	−0.000104	−0.000103	1.008	110
Time_2 (slope)	−0.000085	−0.000086	−0.000085	1.003	693
sigma_1	0.021	0.020	0.021	1.000	5302

Table 4:

Results of the Cox proportional and weighted Hazard Regression Analysis with survival as a dependent variable for Models 1 and 2. Here we removed all individuals without body mass records from 4y to 5y old in order to calculate body mass during adulthood. We tested for the risks proportionality of Model 1 with proportional risks first (Sex M: *chisq* = 1.57, df = 1, *p* = 0.211; Body mass change: *chisq* = 2.68, *df* = 1, *p* = 0.102; GLOBAL: *chisq* = 5.46, *df*=2, *p* = 0.065) and 2 (Sex M: *chisq* = 1.65, *df* = 1, *p* = 0.13; Percentage of body mass change: *chisq* = 0.199, *df* = 1, *p* = 0.071; GLOBAL: *chisq* = 6.45, *df* = 2, *p* = 0.040). As hazards were not proportional in Model 2, we present the results with a weighted Cox-regression.

Model 1	**Proportional risks**					
term	**N**	**estimate**	**std.error**	**Hazard Ratio**	**statistic**	**p.value**
Sex F	100					
Sex M	106	−0.248	0.265	0.780	−0.935	0.350
Body mass change	206	0.235	0.072	1.265	3.245	0.001
Model 2	**Weighted Hazard**					
	N	**coef**	**se(coef)**	**Hazard Ratio**	**z**	**p**
Sex F	100					
Sex M	106	−0.392	0.280	0.676	−1.401	0.161
Percentage of body mass change	206	0.022	0.010	1.023	2.344	0.019

Table 5:

Results of the Cox Proportional Hazard Regression Analysis with survival as a dependent variable for Models 3 and 4. We tested for the risk proportionality of Model 3 (Sex: *chisq* = 0.0138, *df* = 1, *p* = 0.91; Mother age: *chisq* = 0.1445, *df* = 1, *p* = 0.70; Father age: *chisq* = 2.4245, *df* = 1, *p* = 0.12; GLOBAL: *chisq* = 2.52, *df* = 3, *p* = 0.47) and Model 4 (Sex: *chisq* = 0.168, *df* = 1, *p* = 0.68; Parent Tenure: *chisq* = 0.13, *df* = 1, *p* = 0.19; GLOBAL: *chisq* = 2.286, *df* = 2, *p* = 0.32).

Model 3	**Proportional Hazard**					
term	**N**	**estimate**	**std.error**	**Hazard ratio**	**statistic**	**p.value**
Sex F	101					
Sex M	115	0.082	0.333	1.085	0.246	0.806
Mother age	215	0.017	0.046	1.017	0.360	0.719
Father age	215	−0.024	0.051	0.976	−0.467	0.640
Model 4	**Proportional risks**					
term	**N**	**estimate**	**sth.error**	**Hazard Ratio**	**statistic**	**p.value**
Sex F	100					
Sex M	114	0.169	0.307	1.184	0.551	0.582
Parent Tenure	214	0.056	0.058	1.057	0.964	0.335