Differential effects of early life adversity on male and female rhesus macaque lifespan

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Abstract

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Differential effects of early life adversity on male and female rhesus macaque lifespan

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Abstract

Early life adversity predicts shorter adult lifespan in several animal taxa. Yet, work on long-lived primate populations suggests the evolution of mechanisms that contribute to resiliency and long lives despite early life insults. Here, we tested associations between individual and cumulative early life adversity and lifespan on rhesus macaques at the Cayo Santiago Biological Field Station using 50 years of demographic data. We performed sex-specific survival analyses at different life stages to contrast short-term effects of adversity (i.e., infant survival) with long-term effects (i.e., adult survival). Rhesus macaques exposed to adversity at birth suffered a significant increase in mortality risk during infancy with both individual and cumulative adversities having the highest impact among affected females. However, when considering adult lifespan, affected males showed higher vulnerability to both individual and cumulative adversities early in life. Our study shows profound immediate effects of insults at birth on female infant cohorts and suggests that affected female adults are more robust (i.e., viability selection). In contrast, adult males who experienced harsh conditions early in life showed an increased mortality risk at older ages as expected from hypotheses of long-term effects of individual, as well as cumulative, adversity early in life. Our study reveals that mortality risk during infancy is mainly driven by the type of adversity, rather than their accumulation at birth. However, cumulative adversity seems to play a major role in adult survival. Our analysis suggests sex-specific selection pressures on life histories and highlights the need for studies addressing the effects of early life adversity across multiple life stages. This information is critical for planning life stage-specific strategies of conservation interventions.

Keywords. Cayo Santiago; early life adversity; life history evolution; rhesus macaques; survival analysis

Introduction

Adversity early in life is hypothesized to reduce fitness components, and thus influence the evolution of populations (Gluckman et al., 2008; Lindström, 1999). Emerging evidence now spans across several animal taxa (Snyder-Mackler et al., 2020) and includes associations between early life adversity and mortality in adult mammals (e.g., low social rank; maternal death; Gicquel et al., 2022; Tung et al., 2016) and birds (e.g., low temperature, high density; Berntsen & Bech, 2016; De Kogel, 1997), as well as associations between early life adversity and health-related stress responses later in life (e.g., glucocorticoids level; Grace & Anderson, 2018; Patterson et al., 2021; Rosenbaum et al., 2020). Multiple sources of early life adversity are also associated to the pace of reproduction (Belsky et al., 1991; Rickard et al., 2014) and consequent lifetime reproductive success (Descamps et al., 2008; Gicquel et al., 2022; Mumby et al., 2015; Pigeon & Pelletier, 2018; Sloboda et al., 2009). Yet, recent work on long-lived primate populations questioned the role of the early life environment on fitness components. Primate populations can evolve protective mechanisms that contribute to resiliency and long lives despite adverse conditions early in life (Morrison et al., 2023). Primate populations with multiple reproductive events can also evolve life history strategies to optimize reproductive schedules and compensate for shorter lifespans (Luevano et al., 2022; Weibel et al., 2020). Lastly, primate cohorts exposed to insults early in life can show significantly greater longevity due to viability selection during juvenile years (i.e., high-quality juveniles who survive insults; Morrison et al., 2023).

Here, we aim to contribute further to our understanding of how the early life environment affects the lifespan of a long-lived primate population. Exposure to individual insults early in life may affect a population through the increased mortality of vulnerable stages (e.g., developmental stages; Rosa et al., 2014; Zipple et al., 2020). If significant, such juvenile mortality can have profound effects on cohorts as it not only reduces population abundance but can also alter the distribution of phenotypes in the breeding population (e.g., age at maturity; Gosselin & Qian, 1997; Martin et al., 2018; Promislow & Harvey 1990; Stearns & Koella, 1986). For those individuals surviving developmental stages, early life adversity can have far-reaching consequences for adult health and survival by promoting disease and accelerated aging through stress-induced biological mechanisms (Patterson et al., 2023; Polsky et al., 2022) and physiological changes such as inflammation and disease risk (Kinnally et al., 2019; Nettle et al., 2017). Given the multiple ways in which early life adversity can influence eco-evolutionary process within populations, it is important to quantify and contrast its effects across different life stages. This would ultimately allow us to focus on critical life history periods for reversing such effects or planning life stage-specific strategies of conservation interventions.

Despite evidence of the role that early life adversity has on lifespan, understanding the link between adverse conditions early in life and survival in uncontrolled natural scenarios remains challenging. In such scenarios it is often not possible to disentangle underlaying mechanisms driving individual responses (e.g., resiliency, trade-offs). Data on social mammals is further limited to the non-dispersing sex. Studies on primate populations with social dispersal suffer from the limitation of being biased towards a single sex, which often results in hypotheses being tested only in females (Campos et al., 2020). Understanding the influence of the early life environment on male longevity is crucial to enhance our knowledge of evolutionary processes. If the male response to early life insults differs from that of females, sex-specific selection pressures on life histories are expected. However, if responses are similar, the contribution of males to eco-evolutionary processes within populations might have previously been understated (Campos et al., 2020).

In this study, we extend previous work on the effects of early life adversity on the lifespan of a long-lived primate population who showed that ecological sources of adversity early in life influence female reproduction (Luevano et al., 2022). We focus on multiple individual and cumulative sources of nutritional and psychosocial adversity on the rhesus macaque population at the Cayo Santiago Biological Field Station and carry out sex-specific survival analyses at different life stages to contrast the short-term effects of adversity (i.e., infant survival) with long-term effects (i.e., adult survival). Given that male dispersal is constrained to the island of Cayo Santiago, this population is ideal for testing sex-specific responses to early life adversity. Using 50 years of data, we define the early life environment for each monkey retrospectively based on individual and cohort traits. First, we evaluate the short-term effects of early life adversity by testing associations between the environment at birth and infant survival. We predict that short-term effects are negative and stronger, given the high vulnerability of developmental stages to insults at birth in altricial species (Tottenham, 2012). Second, we evaluate the long-term effects of early life adversity for those individuals surviving to adulthood by testing associations between the early life environment during juvenile stages and adult survival. We predict a significant but weaker negative association between early life adversity and adult lifespan, likely due to viability selection (Morrison et al. 2023). Finally, we predict that the accumulation of adversities will have a stronger negative effect on both short- and long-term survival, relative to individual adversity effects, because adverse conditions early in life likely act in aggregate to influence adult health and survival (Hatch, 2005; O'Rand, 1996).

Methods:

Study population

Cayo Santiago (CS) is a 15.2 ha island located 1 km off the southeastern coast of Puerto Rico (lat. 18°09’ N, long. 65°44’ W) that serves as biological field station for behavioral and noninvasive research of free-ranging rhesus macaques (*Macaca mulatta*). The field station was established in 1938 from 409 Indian-born monkeys being released onto the island and no new individuals have been introduced since (Kessler & Rawlins, 2016). The population is kept under naturalistic conditions allowing the natural occurrence of synchronized annual birth seasons, social groups, and social dispersal (Hernández-Pacheco et al., 2016a; Ruiz-Lambides et al., 2017). These rhesus macaques forage on natural vegetation, have ad libitum access to water, and ad libitum high protein monkey chow distributed daily at approximately 0.23 kg/animal/day. Veterinary intervention is restricted to the annual trapping season when yearlings are captured, marked for identification via ear notch and a unique three-character tattoo, tetanus vaccines are administered to 1- and 2-years old subjects, and physical samples are collected. During the trapping season, some individuals may be permanently removed from the island to control for population size (Hernández-Pacheco et al., 2016b). Regular visual censuses report on the date of birth, sex, maternal genealogy, social group membership, and date of death or permanent removal from the island for every individual in the population.

Adversity at birth and infant survival

To address the immediate effects of early life adversity on survival, we first evaluated four sources of adversity at birth: impending maternal death, maternal inexperience (primiparity), a major hurricane environment, and population density. We focused this analysis on infants (<1 year of age) as infancy is the highest vulnerable life stage during immaturity in this population (Blomquist 2013; Hoffman et al., 2010). Past one year of age, mean survival increases with values similar to those of adults (Hernández-Pacheco et al., 2013; Hernández-

Pacheco et al., 2016b). Impending maternal death was used as a proxy for poor maternal body condition at birth and was determined retrospectively following Zipple et al. (2020). Those individuals whose mother died within their first year of life were classified as experiencing impending maternal death at birth. Monkeys whose mother had an unknown fate due to being permanently removed from the population within their first year of life were not included in this analysis. Maternal inexperience was determined using the mother's reproductive history. Firstborn monkeys were classified as having an inexperienced (primiparous) mother. Cayo Santiago was affected by three major hurricanes (Category ≥ 3) throughout the span of our study period: Hugo (Category 3, windspeed: 201 km/h) on September 18, 1989, Georges (Category 3, windspeed: 185 km/h) on September 21, 1998, and Maria (Category 4, windspeed: 220 km/h) on September 20, 2017. Each hurricane event reduced tree canopy by 60-90% (Morcillo et. al., 2020; Luevano et al. 2022). Although ad libitum food was accessible 1 to 3 days after each hurricane event, the population is known to spend 50% of daily feeding time on natural vegetation (Marriott et al., 1989). Monkeys being born within a year after a hurricane event were classified as experiencing a hurricane environment at birth. Thus, we assumed exposure a year after the event had negligible effects on longevity. Finally, population density was defined as the total number of adult females (≥3 years of age) alive at the onset of the corresponding birth season. We used adult female abundance given the previously reported negative density dependent population dynamics driven by the annual number of adult females in the population (Hernández-Pacheco et al., 2013). We determined density at the onset of each birth season because Cayo Santiago monkeys exhibit reproductive synchrony with 73% of births occurring in a 3-month period (Hernández-Pacheco, et al., 2016a), and thus density at the onset of the birth season represents more accurately the experienced density of mothers post-conception as opposed to the density at birth due to the potential variation in density caused by culling events (permanent removal), especially late in the birth season (Luevano et. al., 2022). With this information, we assigned all individuals three binary variables describing whether they experienced impending maternal death, maternal inexperience, and hurricanes, as well as the numerical variable defining the number of adult females at the onset of the birth season. Our focal individuals included all monkeys born in Cayo Santiago between 1973 and 2018, with the exception of those whose mother had an unknown fate due to being permanently removed from the population within their first year of life (as described above). We monitored all individuals until death, removal, or the end of the study in 2022.

To evaluate whether each of these adversities at birth had an immediate effect on survival, we tracked each newborn over time and recorded the age at death or age at right censorship. Monkeys that survived to age one were treated as censored individuals who at least survived the infancy period. We used the Kaplan-Meier estimator and the log-rank test to estimate and compare survival functions followed by the Cox Proportional-Hazard Regression to estimate and compare hazard ratios. For the Kaplan-Meier estimator, we binarized density. For this, we evaluated the observed distribution of the annual number of adult females at the onset of each birth season. Individuals born in a year where the number of adult females was above the 3rd quartile of the distribution (≥ 349 adult females) were classified as experiencing high density (Tung et al., 2016). To test whether experiencing any of the four sources of adversity at birth increased mortality risk during infancy, we fitted mixed-effects Cox Proportional-Hazards models using each adversity as a fixed effect. In this analysis, adult female density was used as a numerical variable. To account for unobserved maternal effects, we included maternal ID as a random intercept. We tested correlations among fixed effects using phi-coefficients and pointbiserial correlations (Supporting Information Table S1, Table S2). Given no strong associations, we added all variables to a global model. Because some explanatory variables did not meet the proportional hazards assumption, i.e., the relation between the adversity effect and the time to death was not constant over time, we extended our Cox analysis using time-varying covariates by stratifying the variables into different age periods following visual inspection of the estimated coefficient across time (Zhang et al., 2018; Therneau et al., 2021). These new time-varying models met all assumptions for proportional hazards. We ran all models in R version 4.1.2 (R Core Team, 2021) using the packages *survival* (Therneau, 2021) and *coxme* (Therneau, 2022).

Cumulative adversity at birth and infant survival

To evaluate if the accumulation of adversities at birth was associated to infant survival, we constructed a cumulative adversity index defined as the total number of adversities an individual experienced at birth (Morrison et al., 2023; Tung et al., 2016; Zipple et al., 2019). For this analysis, we used the binarized definition for "high density" previously described. We fitted sex-specific mixed-effects Cox Proportional-Hazards models using the cumulative adversity index as a fixed effect and included maternal id as a random intercept. Monkeys that survived to age one were treated as censored individuals who at least survived the infancy period. Given that the model did not meet the proportional hazards assumption, we extended our analyses using time-varying covariates by stratifying the cumulative adversity index variable into different age periods following visual inspection of the estimated coefficient across time. These new time-varying models met all assumptions for proportional hazards.

Adversity early in life and adult survival

We extended our previous analysis to five sources of adversity early in life: competing younger sibling, maternal inexperience, maternal loss, major hurricanes, and population density.

We defined early life as the period from birth to the end of juvenile ages (< 3 years of age; Luevano et al., 2022). A competing younger sibling was identified as a sibling being born during the consecutive birth season after the focal individual's own birth season (i.e., one year apart, approximately). Maternal inexperience, and population density were defined as above. Maternal loss, however, was defined through maternal death or permanent removal during juvenile years, while experiencing a hurricane was determined by whether the individual experienced a major hurricane event during juvenile years. With this information, we assigned all individuals four binary variables describing whether they experienced a competing younger sibling, maternal inexperience, maternal loss, and hurricanes, and the numerical variable of the number of adult females at the onset of the birth season. Our focal individuals included all rhesus macaques born in Cayo Santiago between 1973 and 2018 that survived to adulthood. We monitored all individuals until death, removal, or the end of the study in 2022.

To evaluate whether early-life adversity was associated to adult survival, we tracked each adult individual (≥ 3 years of age) over time and recorded the age at death or age at right censorship (i.e., removal or end of study). We used the Kaplan-Meier estimator and the log-rank test to estimate and compare survival functions followed by a mixed-effects Cox Proportional-Hazard regression to estimate and compare hazard ratios. As described above, we estimated survival functions for adult monkeys experiencing each adversity relative to those who did not experience such adversity. To test whether experiencing any of the five sources of adversity early in life increased mortality risk during adulthood, we fitted sex-specific mixed-effects Cox Proportional-Hazards models using each adversity as a fixed effect and maternal ID as a random intercept. In this analysis, adult female density was used as a numerical variable. For those covariate effects that did not meet the proportional hazards assumption, we extended our Cox analysis using time-varying covariates as described above. These new models met all assumptions for proportional hazards.

Cumulative adversity early in life and adult survival

To evaluate whether the accumulation of adversities early in life was associated to adult survival, we constructed a cumulative adversity index as described above. For this analysis, we tracked each adult individual over time and recorded the age at death or age at censorship. We fitted sex-specific mixed-effects Cox Proportional-Hazards models using the index as a fixed effect and included maternal ID as a random intercept. Given that the index effect did not meet the proportional hazards assumption, we extended this analysis to time-varying covariates as described above. These new time-varying models met all assumptions for proportional hazards.

Results

Short-term effects of adversity at birth

The survival of male infants was significantly reduced for those who experienced impending maternal death and high density at birth ($p < 0.01$; Fig 1). Males experiencing impending maternal death who also died in the population had a median age at death of approximately 0.25 years (95% CI: 0.00, 9.63), or 3 months, in contrast to males who did not experience impending maternal death with a median age at death of 2.09 years (0.01, 21.37). Male infants experiencing impending maternal death were more than 7 times as likely to die relative to males that did not experience the adversity (HR= 7.42, 95% CI: 5.86, 9.34; n=4,435; Table 1; Fig 2). Males born into high density birth seasons who also died in the population had a median age at death of 0.89 years (0.01, 15.81), in contrast to males who did not experience high density at birth with a median age at death of 3.37 years (0.01, 21.83). Increments of one adult female to the population increased male infant mortality risk by 0.2% after approximately 0.19

years, or 2.30 months (HR= 1.002; 95% CI: 1.00, 1.004; Table 1; Fig 2). We found no associations between the survival of male infants and maternal inexperience or hurricane environments (Table 1). The survival of male infants was also associated to the accumulation of adversities at birth ($p < 0.001$, Fig 3). Male infants experiencing 1 adversity who also died in the population showed a median age at death of 1.13 years (0.01, 19.03), while those experiencing 2 or more adversities showed a median age at death of 0.56 years (0.01, 17.93). This is in contrast to male infants who did not experience any adversity at birth with a median age at death of 4.45 years (0.02, 22.03). Experiencing an additional adversity increased male infant mortality risk by 86% until approximately 0.94 years, or the 11th month of life (HR= 1.86; 95% CI: 1.65, 2.10; *n*=4,435; Table 1; Fig 2). After the 11th month of life, male infants experiencing an additional adversity showed a 55.8% reduction in mortality risk (HR= 0.44; 95% CI: 0.25, 0.79; Table 1).

The survival of female infants was associated to impending maternal death, maternal inexperience, and high density at birth ($p < 0.01$; Fig 1). Females experiencing impeding maternal death who also died in the population showed a median age at death of 0.35 years (95% CI: 0.01, 15.69), or approximately 4.2 months, in contrast to females who did not experience impeding maternal death with a median age at death of 2.08 years (0.01, 22.76). Female infants experiencing impending maternal death were more than 6 times as likely to die relative to females that did not experience the adversity (HR= 6.52; 95% CI: 5.10, 8.33, *n*=4,195; Table 1). Females having a primiparous mother who also died in the population showed a median age at death of 1.35 years (0.01, 22.79), in contrast to females who did not experience a primiparous mother with a median age at death of 1.98 years (0.01, 22.69). Female infants having a primiparous mother showed a 79% increase in the risk of dying until reaching approximately 0.77 years, or 9.2 months of age (HR= 1.79, 95% CI: 1.44, 2.23; Table 1). After 9.2 months of age, having a primiparous mother significantly reduced mortality risk by 65.4% (HR = 0.35, 95% CI: 0.18, 0.67; Table 1). Female infants born into high density birth seasons had a median age at death of 0.92 years (0.01, 19.94), in contrast to females who did not experience high density at birth with a median age at death of 3.32 years (0.01, 23.12). Increments in density at birth by one adult female increased the probability of dying by 0.50% after approximately 0.07 years, or 0.84 months of life (HR= 1.005, 95% CI: 1.00, 1.01; Table 1). We found no evidence of associations between the survival of female infants and major hurricane environments. The survival of female infants was also associated to the accumulation of adversities ($p < 0.001$, Fig 3). Female infants experiencing 1 adversity who also died in the population showed a median age at death of 1.17 years (0.01, 21.00), while those experiencing 2 or more adversities showed a median age at death of 0.59 years (0.01, 21.71), or approximately 7.1 months. This is in contrast to female infants who did not experience any adversity at birth with a median age at death of 4.03 years (0.02, 23.46). Females experiencing an additional adversity were twice as likely to die until approximately 0.94 years, or the 11th month of life relative to females who did not experience cumulative adversity (HR= 2.09; 95% CI: 1.85, 2.37; *n*=4,195; Table 1). After 11 months of age, experiencing an additional adversity significantly reduced female infant mortality risk by 58.8% (HR= 0.41; 95% CI: 0.24, 0.72; Table 1).

Long-term effects of early life adversity

The survival curve functions of male adults experiencing early life adversity were not significantly different to those from males who did not experience adversity early in life ($p > 0.05$, Fig 4). However, the mortality hazard was associated to major hurricanes. Male adults experiencing a major hurricane event early in life who also died in the population had a median age at death of 10.51 years (95% CI: 3.10, 22.82), in contrast to males who did not experience a major hurricane event t with a median age at death of 7.88 years (3.37, 22.88). Male adults who experienced a major hurricane event early in life showed a 37.1% reduction in mortality risk before reaching eight years of age (HR=0.63; 95% CI: 0.45, 0.88; *n*=2,142; Table 2; Fig 5), relative to males that did not experience a major hurricane event. After eight years of age, however, these male adults were twice as likely to die compared to males that did not experience this adversity (HR=2.25, 95% CI: 1.45, 3.49; Table 2; Fig 5). We found no associations between male adult survival and the presence of a competing younger sibling, maternal inexperience and loss, and high density (Table 2). Similarly, the survival curve functions of male adults experiencing early life cumulative adversity was not significantly different to males who did not experience adversities ($p > 0.05$, Fig 6). However, the hazard ratio of male adults was associated to the number of adversities they experienced early in life. Experiencing one additional adversity early in life reduced mortality risk by 13.4% until the 10th year of life (HR=0.87; 95% CI: 0.76, 0.98; *n*=2,142; Table 2) relative to males who did not experience early life adversity. After ten years of age, however, experiencing one additional adversity early in life significantly increased male adult mortality risk by 37.9% (HR= 1.38; 95% CI: 1.11, 1.71; Table 2).

Likewise for females, the survival curve functions of female adults experiencing early life adversity were not significantly different to that of females who did not experience an adversity ($p > 0.05$, Fig 4). However, the hazard ratio was associated to maternal loss (Table 2; Fig 5). Female adults who experienced maternal loss early in life showed a 77.2% reduction in mortality risk after 18 years of age (HR=0.23, 95% CI: 0.10, 0.52; *n*=2,229; Table 2; Fig 5). We found no associations between female adult survival and the presence of a competing younger sibling, maternal inexperience, major hurricanes, and population density (Table 2; Fig 5). The survival curve function of female adults experiencing early life cumulative adversity was not significantly different to females who did not experience adversity ($p > 0.05$, Fig 6). However, the mortality risk of female adults was associated to the number of adversities they experienced early in life (Table 2). Experiencing one additional adversity during early life reduced risk by 11.3% at every age (HR=0.89; 95% CI: 0.79, 0.99; *n*=2,229).

Discussion

Our analysis shows that early life adversity effects on survival are context specific. Rhesus macaques exposed to adversity at birth suffered a significant increase in risk of death during infancy with both individual and cumulative adversities having the highest impact among affected females. However, when we considered adults, males showed a higher sensitivity to both individual and cumulative adversity early in life. Our study shows how insults early in life can have profound immediate effects on the survival of females and suggests that affected females who managed to survive into adulthood are more robust (i.e., viability selection). Our study also reveals a delayed response for adult males who experience early life adversity in which negative consequences of adversity on adult survival appear only at older ages.

4.1 Short-term effects of adversity at birth

The survival of infants was significantly affected by impending maternal death. This is expected for altricial species such as rhesus macaques where maternal effects on infant survival are strong (Blomquist, 2013; Hoffman et al., 2010). During early life, mothers serve as the main source of nutrition, as well as the strongest social bond for offspring (Maestripieri & Hoffman 2012). However, we found a higher difference in risk of death among male infants experiencing impending maternal death, relative to males who did not experience it. In our population, maternal investment in male offspring is thought to be greater than in females due to the faster growth rate of male offspring and the relationship between the weight of male offspring and their future reproductive output (Bercovitch et al., 2000). Thus, the inability to fulfill the energetic demands of fast-growing male offspring given poor maternal condition could have led to a higher risk of death among affected male offspring. Our analysis also shows that female infants born to a primiparous mother experienced an increased risk of death during breastfeeding (infancy), relative to females who were born to an experienced mother. A recent study on captive rhesus macaques uncovered that daughters of primiparous mothers grew slower during juvenile ages, and these affected daughters later synthesized less available milk energy (milk energetic density by milk yield) compared to daughters of multiparous mothers (Pittet & Hinde, 2023). Although we did not measure intergenerational effect of primiparity, such related physiological and growth constraints may explain why having an inexperienced mother negatively affected female offspring. In contrast to Nuñez et al (2015), we did not observe a significant relationship between primiparity and infant male survival. Sex-biased investment during lactation varies with maternal life history in rhesus macaques (Bercovitch et al., 2000). Prior evidence suggests that milk quality in primiparous mothers is biased towards male offspring due to potential mechanisms of sex-specific regulation of anabolic and growth hormones or metabolic efficiency (Hinde, 2009). Producing a higher quality milk for male offspring suggests a flexible reproductive strategy of mothers to cope with high energetic demands of fast-growing offspring with higher reproductive output (Bercovitch, 2000; Hinde, 2007; Hinde, 2009; Landete-Castillejos et al., 2005; Robert & Braun, 2012; Trivers & Willard, 1973).

In contrast to maternal sources of early life adversity, infants being born in a hurricane environment exhibited no difference in risk of death, relative to those born in ordinary environments. This reflects prior survival analyses addressing the effects of ecological sources of early life adversity on lifespan in this population (Luevano et al., 2022). Hurricane induced changes in the annual demography of the Cayo Santiago rhesus macaques are mostly driven by suppressed female fertility (Morcillo et al., 2020). It could be the case that mothers who are able to successfully produce viable offspring during extreme climate environments possess a higher quality that can be passed on to their offspring (our subjects), buffering against mortality risk (Jenouvrier et al., 2015). However, infants who experienced increased density of adult females at birth showed a higher mortality risk. Although the risk of death was similar for males and females, the negative effects of increased density were observed earlier in affected female infants. In Cayo Santiago, high density of adult females can lead to increased competition for access to food (Bercovitch & Berard, 1993; Sterck et. al., 1997). In other rhesus macaque populations, increased aggressive interactions between female kin and non-kin due to increased density have been reported (Judge & De Waal, 1997). Variation in sex-specific infant susceptibility to high population density can be further explained by antagonistic encounters in environments with limited resources. In several macaque species, female infants are often more susceptible to mortality from adult female attacks than male infants (dispersing sex) as a potential mechanism to reduce future competition within the social group (toque macaques, Dittus, 1979; bonnet macaques, Silk et al., 1981). In our study population, adult females tended to threaten female infants more than male infants (Berman, 1980). Thus, increased aggression among females and their female infants during high female density years likely contributed to the observed negative density effect earlier in the life of females, in contrast to males.

The accumulation of adversity early in life also had negative effects on infant mortality risk. However, the mortality risk associated to cumulative adversity resulted higher among female infants. Yet, more than 50% of female infants were alive at 1 year of age regardless of the number of adversities they experienced (Figure 3). This is contrary to infants experiencing impending maternal death, and thus suggests that mortality risk during infancy is mainly driven by the type of adversity and not their accumulation at birth for both sexes. For these rhesus macaques, maternal investment remains the main driver of infant survival.

4.2 Long-term effects of early life adversity

Our analysis demonstrates that individual insults at birth strongly predict the survival of infants, but contrary to our predictions many of these effects do not translate into adulthood. Furthermore, we found that the male adult response to early life insults differed significantly from that of females, thus sex-specific selection pressures on life histories must be acting on this population. When addressing individual adversity effects, the survival of male adults was only associated to major hurricanes. Male adults experiencing a major hurricane early in life showed an initial reduction in mortality risk. However, risk increased at older ages. This response to extreme climates was unexpected given the absence of an association with infant mortality, as well as prior evidence of no immediate hurricane effects on Cayo Santiago female adult survival (Morcillo et al., 2020). It is possible that experiencing a hurricane event first-hand, as opposed to being born into the aftermath of it, may pose different stressful environments. However, recent work on the role of hurricanes on this rhesus macaque population suggest such extreme events play an important role on variability in individual life courses (Diaz et al., 2023). Here, we provide important evidence of the long-lasting effects that extreme climatic events early in life have on rhesus macaque males. In contrast, female adult survival was associated to maternal loss but such relation was positive. Affected female adults showed a significant reduction in mortality risk at very old ages, relative to unaffected ones. This finding supports prior evidence of the high resiliency of female adults in this population, including resilience to extreme climatic events. On the other hand, male adults with a higher accumulation of adversities early in life showed an initial reduction in mortality risk, followed by a significant increase in risk at older ages. In contrast, female adults with a higher accumulation of adversities showed a reduced mortality risk at any given age. Thus, our analysis on adult survival supports hypotheses on detrimental effects of cumulative adversity on male adult survival but this does not apply to females who showed a greater longevity when experiencing an additional adversity early in life. We argue that our findings in this primate population may be explained by one or a combination of the following processes: (1) viability selection (Douhard et al., 2014), (2) life history trade-offs (Stearns, 1989), and (3) social support and buffering effect (Cohen & Wills, 1985).

Viability selection and individual heterogeneity

Viability selection and individual heterogeneity likely play a major role in our population. Affected individuals surviving into adulthood may possess higher quality traits compared to those dying at immature ages (Douhard et al., 2014). Infant females showed high vulnerability to multiple adversities at birth, however adult females that experienced adversities or accumulated them showed a reduced risk. In contrast, male adults showed a higher sensitivity to both early life individual and cumulative adversity. Taken together, our findings strongly suggest that females experience greater viability selection than males, while maternal effects may be buffering male infant mortality in this primate population. Such observation contrast with prior studies suggesting that male mammals are under stronger viability selection, and thus only males are likely to retain the phenotypes with best fit at old ages (Gamelon et al., 2014; Morrison et al., 2023). Our study mirrors conclusions from a recent study in wild gorillas in which authors demonstrated that the link between early life adversity and increased risk later in life is not universal and that the resiliency of primates to early life adversity is indeed very high (Morrison et al., 2023). Our study contributes to this literature by showing that similar processes also occur in monkeys.

Life history trade-offs

Life history trade-offs can also play a critical role on adult survival in our primate population. Evidence of early life adversity effects on Cayo Santiago rhesus macaque female reproduction suggested that adversity-affected females ensure their future reproductive potential by allocating more energy to growth or maintenance processes at younger adult ages at the expense of reproduction (Luevano et al., 2022). This strategy among affected females may be driving the lack of negative associations between adversity early in life and female adult survival. Such lack of negative effects may result from adaptive physiological mechanisms acting during development that mainly favor survival-enhancing traits at the cost of reproduction-enhancing traits (Cooper & Kruuk, 2018; Metcalfe & Monaghan, 2001). On the other hand, trade-offs favoring reproduction may be occurring among affected males given the inverse relationship between testosterone and immune function (Muehlenbein & Bribiescas, 2005). It has been observed that increased levels of testosterone promote aspects of reproductive fitness yet reduces survival (John-Alder et al., 2009; Mills et al., 2009; Muller, 2017; Reed et al., 2006). Although still unexplored, our findings possibly reflect sex-specific life strategies of a promiscuous, sexually dimorphic, primate species: females may allocate more energy towards survival to ensure future reproduction while males penalize initial reproductive success to survive and may later invest more energy towards reproduction at the expense of long-term survival in response to early life adversity. The combined effects from environmental pressures (Watowich et al., 2022) and physiological constraints on male immune system may explain why we observed increased mortality rate at older ages in adversity-affected males.

Social support and the buffering effect

Social support is hypothesized to mediate glucocorticoid levels, and thus provide resources to better cope with stress and mitigate stress-induced physiological effects (Cohen & Wills 1985; Engh et al., 2006; Hennessy et al., 2009; Brent et al., 2011; Young et al., 2014). There is now evidence of the role of strong social bonds on increased male baboon longevity (Campos et al., 2020), and how social bonds may mitigate some negative early life adversity effects on adult female baboon lifespan (Lange et al., 2023). Morrison et al. (2021) found that cohesive social groups provided social support that potentially buffered against the effect of maternal loss in mountain gorillas. If social capital is passed on from mother to offspring, juveniles from well-integrated mothers could present a survival advantage, relative to those from poorly integrated mothers (Silk et al., 2009). Cayo Santiago rhesus macaques also show flexible behaviors that may alleviate stress. Following the most intense hurricane in the history of Cayo Santiago, changes in behavior involving an increase in affiliative social connections was observed as individuals became more tolerant of other monkeys and built new connections (Testard et al., 2021). In this way, social support may also be a fundamental mechanism that gregarious primates can adopt to cope with years of extreme ecological adversity such as major hurricanes and high density, potentially masking expected effects later in life.

Conclusions

Our study contributes to recent reports arguing that the link between early life adversity and increased risk later in life is not universal as primates can be highly resilient to early life adversity (Morrison et al., 2023). We provide further insight into factors that shape primate lifespans by demonstrating differential effects of early life adversity on male and female rhesus macaques at different life stages. Our findings suggest the presence of viability selection, life history trade-offs, and social support as underlaying mechanisms driving the observed short- and long-term effects of early life adversity. In this way, our analysis contributes new information on potential adaptive mechanisms that ameliorate the effects of harsh conditions early in life on lifespan. As the social environment is critical for primates, we also encourage future work to consider individual sociality as both early life adversity or enhancement and late life mediator. It is well-known that social status can bring forth forms of resources and competition (Sapolsky, 2005) and can thus influence glucocorticoid levels (Cavigelli & Caruso, 2015; Gesquiere et al., 2011; Rosenbaum et al., 2020; Sapolsky, 2005; Zhang, Cui, et al., 2018). Incorporating this would further our understanding of the observed differential effects of early life adversity in male and female primates. Other adaptive behaviors (e.g., foraging timing; Mainwaring et al., 2023) must also be addressed to fully understand how disadvantaged individuals may mitigate the adversity they experienced early in life. Finally, our study highlights the need for studies addressing the effects of early life adversity across multiple life stages. This will allow for informed conservation interventions targeting critical life history periods for ameliorating or reversing such effects.

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Table 1: Hazard ratio estimated from Cox regression models testing associations between adversity at birth and rhesus macaque infant survival.

	e^{β}	SE	95% CI
Males (*n*=4,435)			
Individual effects			
Impending maternal death	7.417	0.121	**5.857**, **9.394**
Maternal experience (primiparity)	1.207	0.001	0.970, 1.502
Major hurricane environment	0.951	0.195	0.649, 1.392
Population density ≤ 2.3 months	1.001	0.001	1.000, 1.003
Population density > 2.3 months	1.002	0.001	**1.000**, **1.004**
Cumulative effects			
Cumulative Adversity Index ≤ 11.3 months	1.859	0.061	**1.649**, **2.096**
Cumulative Adversity Index > 11.3 months	0.442	0.298	**0.246**, **0.794**
Females (*n*=4,195)			
Individual effects			
Impending maternal death	6.517	0.125	**5.101**, **8.327**
Maternal inexperience (primiparity) ≤ 9.2 months	1.791	0.112	**1.437**, **2.232**
Maternal inexperience (primiparity) > 9.2 months	0.346	0.337	**0.179**, **0.669**
Major hurricane environment	1.237	0.187	0.857, 1.784
Population density ≤ 0.84 month	0.999	0.001	0.997, 1.001
Population density > 0.84 month	1.005	0.001	**1.003**, **1.008**
Cumulative effects			
Cumulative Adversity Index ≤ 11.3 months	2.092	0.064	**1.845**, **2.373**
Cumulative Adversity Index > 11.3 months	0.412	0.286	**0.235**, **0.721**

Table 2: Hazard ratio estimated from Cox regression models testing associations between early life adversity and rhesus macaques adult survival.

	e^{β}	**SE**	**95% CI**
Males (*n*=2,142)			
Individual effects			
Maternal loss	1.076	0.111	0.865, 1.338
Maternal inexperience (primiparity)	0.947	0.104	0.773, 1.160
Competing sibling	0.933	0.087	0.787, 1.107
Population density	1.000	0.000	0.999, 1.001
Major hurricane environment 3-8 years	0.629	0.172	**0.449**, **0.881**
Major hurricane environment > 8 years	2.250	0.224	**1.450**, **3.490**
Cumulative effects			
Cumulative Adversity Index 3-10 years	0.866	0.064	**0.764**, **0.983**
Cumulative Adversity Index >10 years	1.379	0.111	**1.109, 1.714**
Females (*n*=2,229)			
Individual effects			
Maternal loss: 3-18 years	1.135	0.126	0.887, 1.452
Maternal loss: > 18 years	0.228	0.416	**0.101**, **0.515**
Maternal inexperience (primiparity)	0.846	0.109	0.683, 1.048
Competing sibling	0.908	0.091	0.759, 1.086
Population density	1.000	0.001	0.999, 1.001
Major hurricane environment	0.969	0.103	0.791, 1.187
Cumulative effects			
Cumulative Adversity Index	0.887	0.056	**0.794**, **0.991**

Note: Bold 95% CI indicate significance at 0.05 level.

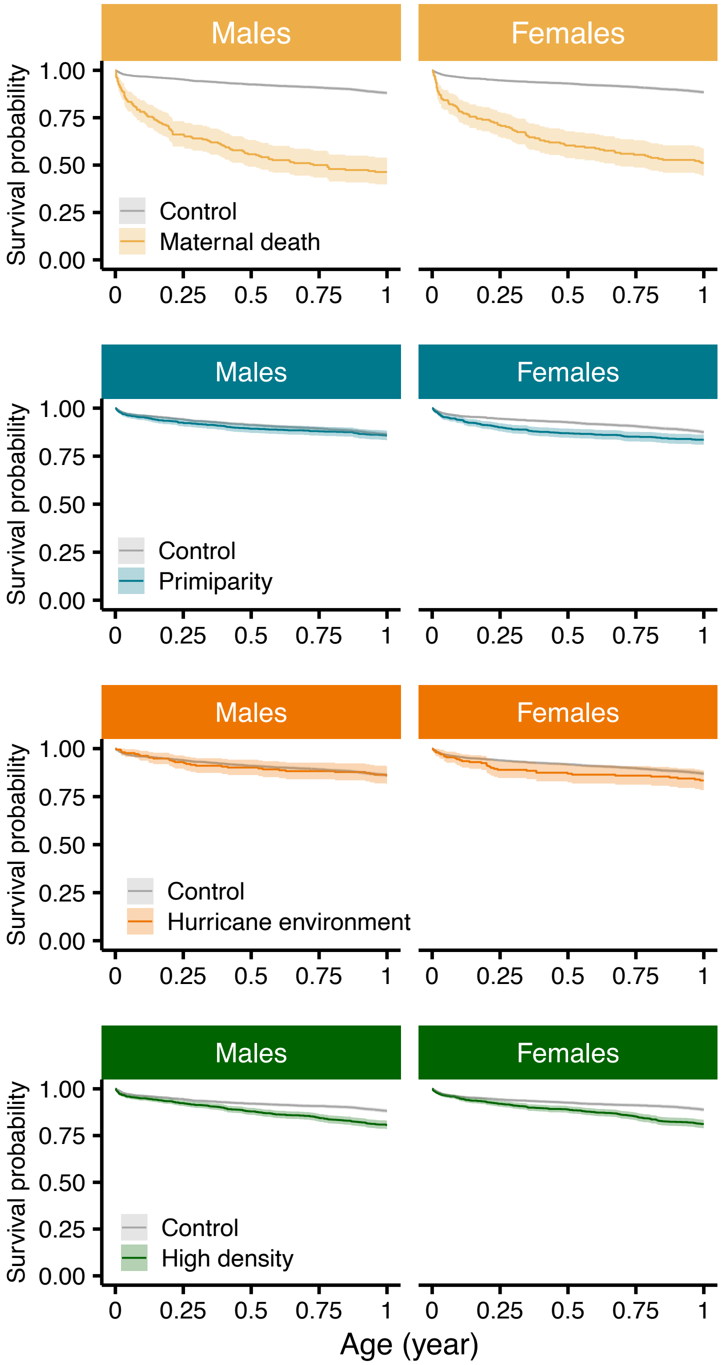

Figure 1: Survival curves for male (left) and female (right) rhesus macaques experiencing different sources of adversity at birth. Ribbons represent 95% confidence intervals.

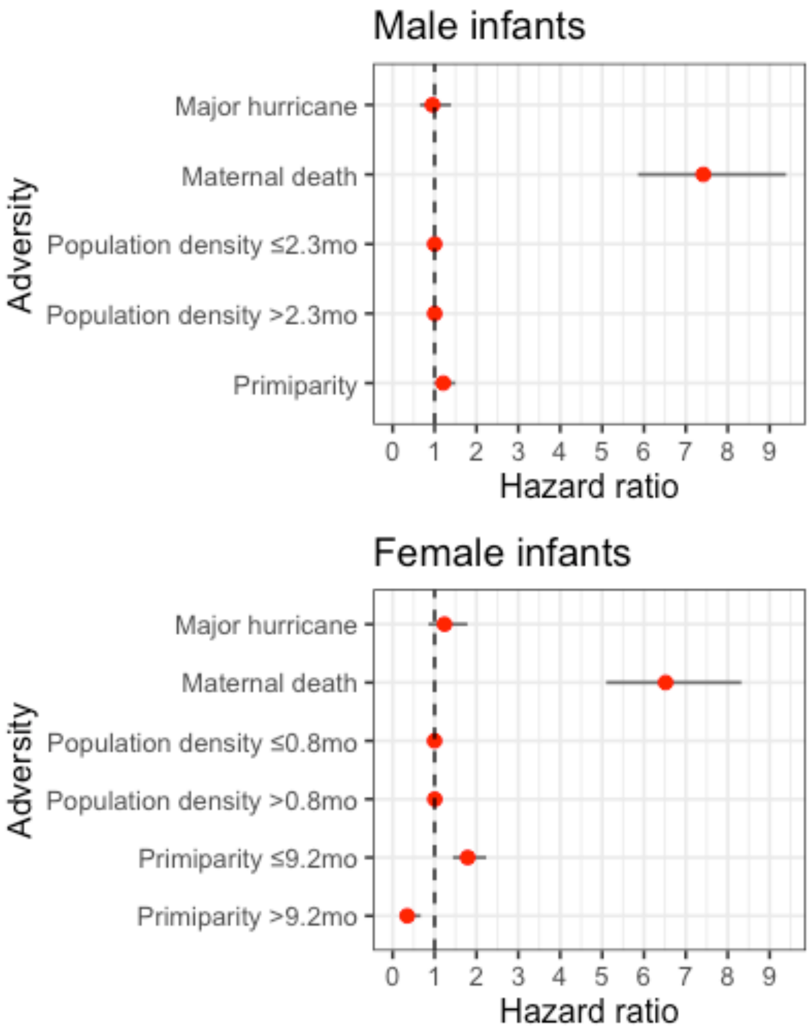

Figure 2: Hazard ratios for male (top) and female (bottom) infant rhesus macaques experiencing different sources of adversity at birth. Bars represent 95% confidence intervals.

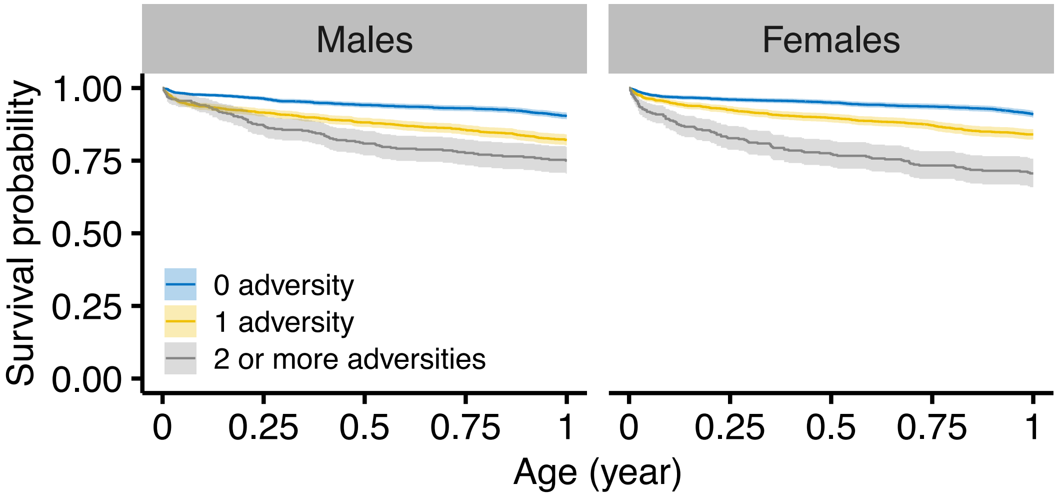

Figure 3: Survival curves for male (left) and female (right) rhesus macaques experiencing cumulative adversity at birth. Ribbons represent 95% confidence intervals.

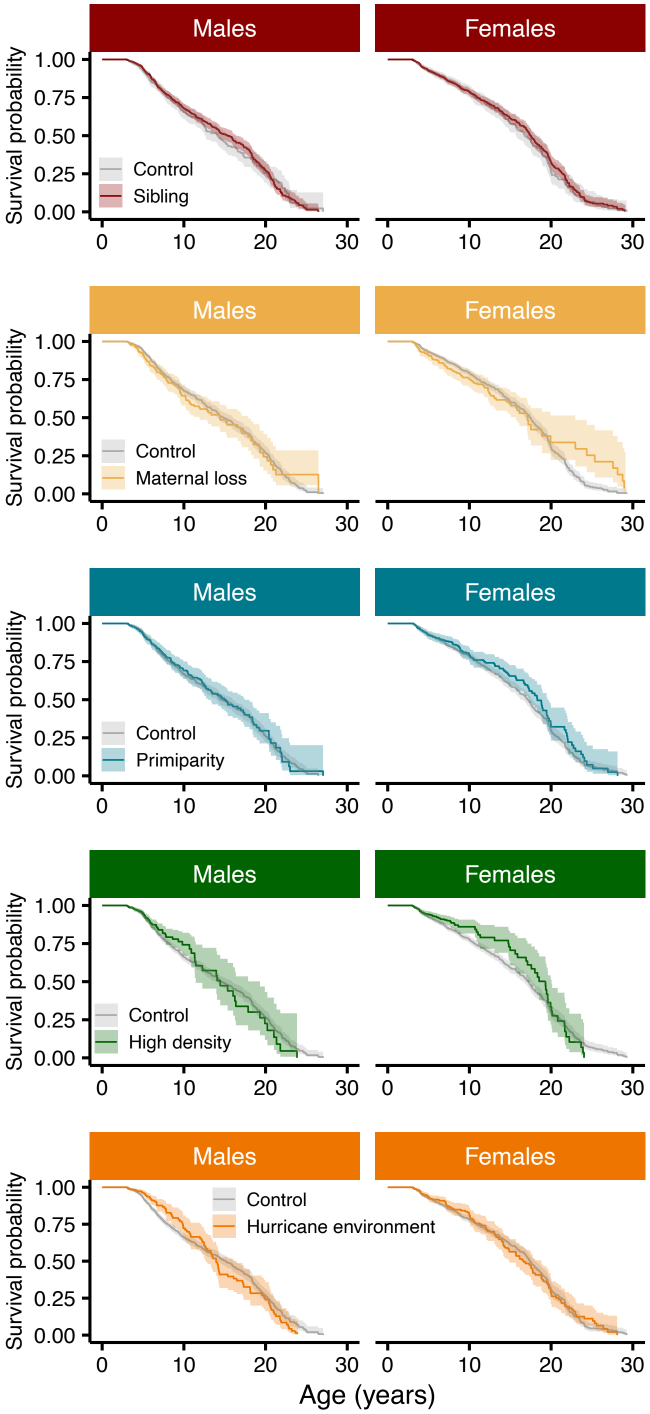

Fig 4: Survival curves for male (left) and female (right) adult rhesus macaques experiencing different sources of adversity early in life. Ribbons represent 95% confidence intervals.

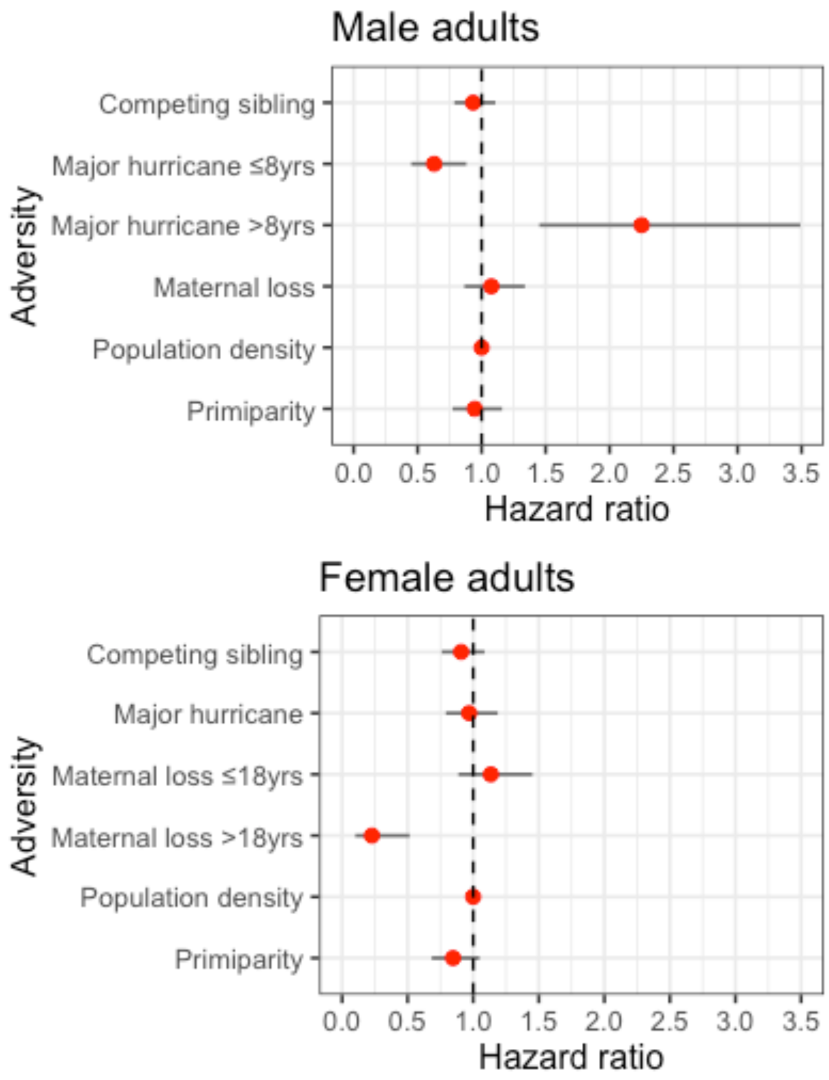

Figure 5: Hazard ratios for male (top) and female (bottom) adult rhesus macaques experiencing different sources of early life adversity. Bars represent 95% confidence intervals.

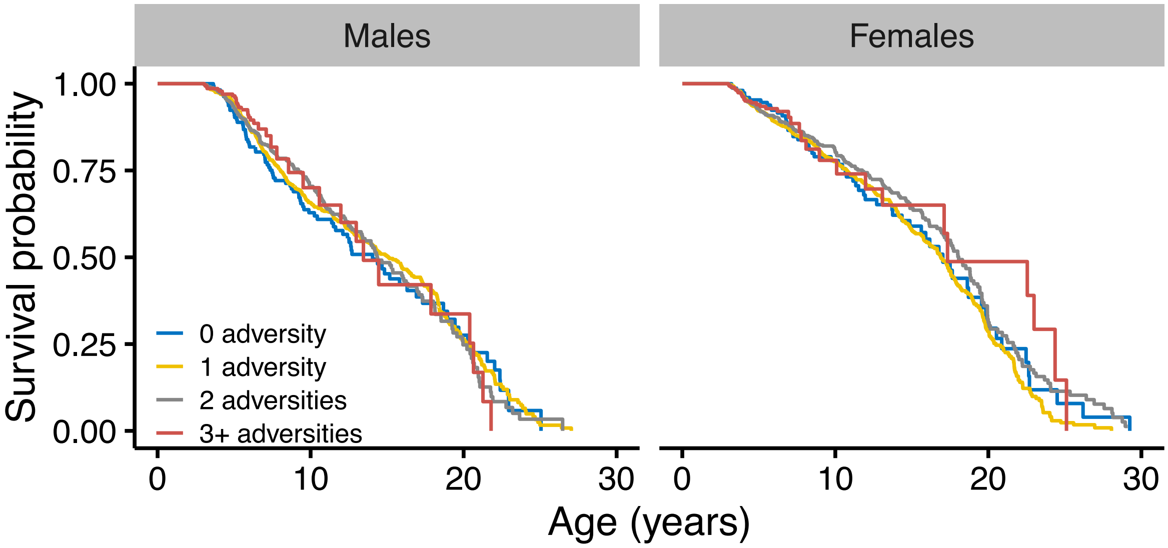

Figure 6: Survival curves for male (left) and female (right) adult rhesus macaques experiencing cumulative adversity early in life. For visual comparison, 95% confidence intervals are not shown.