



ORGANISMAL BIOLOGY

Early life adversity and adult social relationships have independent effects on survival in a wild primate

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Adverse conditions in early life can have negative consequences for adult health and survival in humans and other animals. What variables mediate the relationship between early adversity and adult survival? Adult social environments represent one candidate: Early life adversity is linked to social adversity in adulthood, and social adversity in adulthood predicts survival outcomes. However, no study has prospectively linked early life adversity, adult social behavior, and adult survival to measure the extent to which adult social behavior mediates this relationship. We do so in a wild baboon population in Amboseli, Kenya. We find weak mediation and largely independent effects of early adversity and adult sociality on survival. Furthermore, strong social bonds and high social status in adulthood can buffer some negative effects of early adversity. These results support the idea that affiliative social behavior is subject to natural selection through its positive relationship with survival, and they highlight possible targets for intervention to improve human health and well-being.

INTRODUCTION

In humans and other animals, harsh conditions in early life can have profound effects on adult health and survival (1–5). In the first comprehensive study of the effects of cumulative early life adversity on adult survival, Brown and colleagues (6) reported that people with six or more adverse childhood experiences (ACEs) had average life spans nearly 20 years shorter than those with no ACEs. A more recent study found that people who experienced more than three sources of socioenvironmental adversity before age 18 faced a 9.5-year reduction in quality-adjusted adult life expectancy (1).

If adverse experiences in early life predict reduced adult survival, the effects of early life adversity must be mediated through conditions that occur in adulthood. Identifying these conditions is challenging; early life adversity is known to affect many behavioral and physiological processes (3), from components of the immune system (4, 5, 7) to mental health (8), but few studies have explicitly quantified the effects of candidate mediators proposed to link early adversity and adult survival.

Adult social environments are one such candidate. Many studies have demonstrated links between early life adversity and social adversity in adulthood, including both low adult socioeconomic status and challenges in forming strong, supportive adult social relationships (9–11). At the same time, low socioeconomic status and social isolation are widely linked to poor health and to all-cause mortality (12–15). Thus, it is possible that the effects of early life adversity on

survival are strongly mediated by the adult social environment. For example, if early life adversity negatively influences adult social environments, perhaps by promoting poor mental or physical health in adulthood, then these effects may, in turn, partly or largely account for the effects of early life adversity on adult survival. Such a chain of events would support a version of the “health selection” hypothesis, in which poor health arising, in this example, from early life adversity, contributes to both adverse social environments and poor survival in adulthood (16).

Alternatively, the effects of early life adversity on survival may be only weakly mediated, or not mediated at all, by the adult social environment, even if the adult social environment strongly predicts adult survival (12–15, 17). In this scenario, early life adversity and the adult social environment are linked to survival through partially or entirely independent pathways, supporting the idea that both early life and adult environments are suitable targets of interventions to improve adult survival. This alternative implies that the adult social environment could also function as a source of resilience against the harm caused by early adversity, in a type of “social buffering” process in which social advantage ameliorates some of the costs of early life insults (18–20). Such an outcome would help narrow the scope of investigation about the relative importance of health selection versus “social causation” in explaining the link between social environments and survival (social causation occurs when social environments in adulthood play a direct, causal role in determining survival) (13, 21). While both health selection and social causation are increasingly recognized as playing a role in adult health and survival, their relative importance at different stages of the life course and for different causes of mortality is still under investigation [e.g., (22–25)].

Understanding the extent to which early life adversity and adult social environments involve independent pathways to survival is important to both evolutionary biologists and social scientists. Identifying the forces that drive variation in survival helps identify the traits targeted by natural selection, shedding light on the evolutionary underpinnings of early life effects and sociality. At the same time, understanding the causes of variation in health and mortality

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can inform investment in public health interventions and policy. To date, no study in either animals or humans has sought to prospectively link early life adversity, adult social behavior, and survival in an integrated analysis. Therefore, it is unknown if adult social relationships play an important mediating role in linking early life to survival or if their effects on survival are largely independent of the effects of early life adversity on survival.

The best approach for determining whether adult social environments mediate the effects of early life adversity is to link prospectively collected data on early life adversity to prospectively collected information on the adult social environment and survival in the

same individuals (24, 26). Existing data typically do not permit such analyses in human populations, but appropriate data are sometimes available for wild animal populations that have been under continuous observation for many years (12). Furthermore, the social determinants of health in many social mammal species resemble those described in humans, making wild animal models a useful tool for dissecting the relationships among early life adversity, adult social behavior, and life span. For example, in several non-human mammals, early life adversity is linked to low adult social status or weak adult social relationships (27–30). Similarly, low social status or weak social relationships are associated with higher mortality rates in a range of social mammal species (12).

In this study, we use a mediation analysis framework to examine the relationships among early life adversity, adult social behavior, and survival in an established wild animal model: the baboons studied by the Amboseli Baboon Research Project in the Amboseli ecosystem, Kenya (31, 32). Previous research on female baboons in Amboseli has laid substantial groundwork for the present analysis. First, we have shown that cumulative early life adversity predicts reduced adult female life span (27, 33), as well as a moderate degree of social isolation in adulthood (17, 27). Second, we have demonstrated that weak social bonds predict reduced life span in female baboons, a result that has also been reported in other wild mammals, including other baboons (12, 34–36). Third, we have investigated the capacity of social bonds to mediate the effects of early life adversity on an important physiological measure, glucocorticoid (GC) concentrations (34). In that analysis, we found evidence for only modest mediation, probably, in part, because the relationship between early life adversity and adult social bonds, while detectable, is itself modest. Here, we ask whether social bonds mediate the much stronger relationship between early adversity and survival, an outcome that directly contributes to lifetime reproductive success and that integrates many dimensions of health (not only those reflected in GC levels). Together, these differences raise the possibility that social bonds have greater potential to mediate the effects of early adversity than we detected previously (12, 36).

The previous research described above positions our study system as an excellent one in which to ask whether adult social environments mediate the relationship between early adversity and survival and to determine whether adult social relationships can buffer the effects of early life adversity. We focus on adult females rather than males because male baboons disperse from their natal social groups when they mature, making it difficult to distinguish male dispersal from death (37). Furthermore, we focus on adult female social bonds as candidate mediators and exclude adult social status as a potential mediator for two reasons: (i) Previous studies in this population find no effects of female social status on survival (34, 35), and (ii) preliminary analyses using our mediation framework ruled out social status as a potential mediator of early life adversity and demonstrated that social status is not influenced by cumulative early life adversity (see Materials and Methods). However, in our test of the social buffering hypothesis, we consider both adult social bonds and adult social status as possible moderators of the relationship between early life and survival.

Mediation and moderation frameworks

Mediation models

Our mediation analysis framework is based on structural equation models that examine the links between early life, adult social

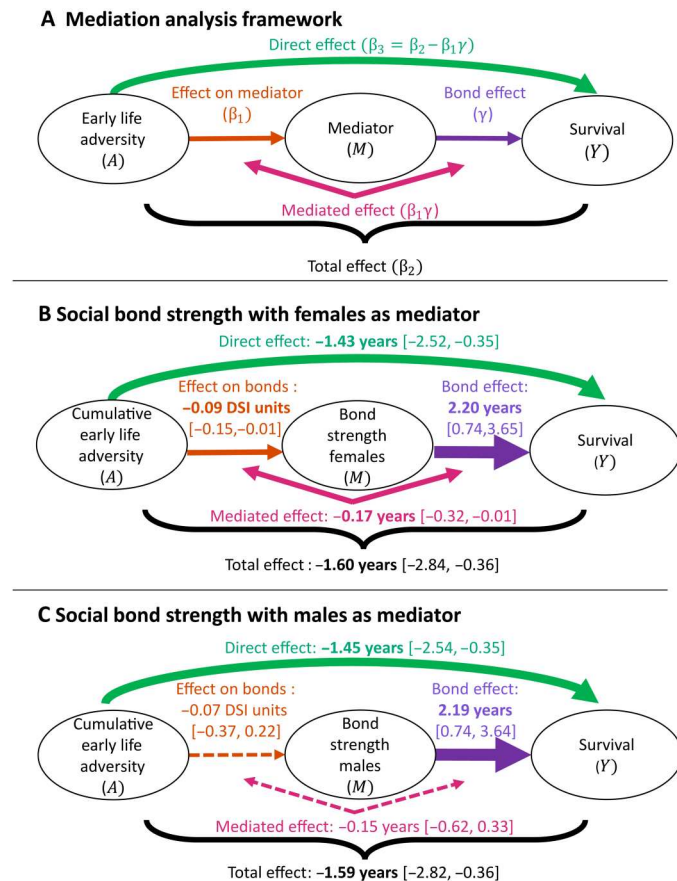


Fig. 1. Mediation analysis framework and results. (A) The mediation analysis models the links between early life adversity (A_1), adult mediator phenotypes (M_1 , social bond strength with females or males), and survival (Y_1). Mediation models produce estimates of (i) the direct effect of early life adversity on survival outside of the pathway that includes the mediator (β_3 , green arrow), (ii) the mediated effect of early life adversity on survival through the pathway that includes the mediator ($\beta_1\gamma$, pink arrow), (iii) the effect of early life adversity on the mediator (β_1 , orange arrow), (iv) the effect of the mediator on survival independent of early adversity (γ , purple arrow, the bond effect), and (v) the total effects on survival (β_2 , black bracket). Note that the expressions $\beta_1\gamma$ and ($\beta_3 = \beta_2 - \beta_1\gamma$) in (A) hold exactly only when all models (between A , M , and Y) are linear. Here, we use these merely as notations (instead of mathematical equations) to label the qualitative relationship between total, mediated, direct, and bond effects. (B) Results from our mediation model using social bond strength with adult females as the mediator. (C) Results from our mediation model using social bond strength with adult males as the mediator. Solid lines indicate effects for which 95% credible interval did not overlap zero; dashed lines indicate effects for which 95% credible interval did overlap zero.

phenotypes, and survival (Fig. 1A) (38–40). The 199 females in this study were observed from birth and all survived to at least 4 years old, approximately the earliest age of reproductive maturation (average age at menarche = 4.73 ± 0.56 years). We evaluated predictors of survival beginning at age of 4 years (see fig. S1 for age distributions at death and censoring). For each female, we evaluated her exposure to six different adverse socioenvironmental conditions in early life: (i) drought in the first year of life, (ii) large group size at birth, (iii) low maternal social status at birth, (iv) low maternal social connectedness during the first 2 years of life, (v) the presence of a close-in-age younger sibling, and (vi) maternal loss before 4 years of age (Table 1) (26, 33, 34).

We constructed two sets of mediation models (see Materials and Methods), each with a different mediator variable (*M*), linking the treatment (early life adversity, *A*) to survival (*Y*, measured by the hazard ratio, λ ; Fig. 1A). The two mediators that we examined were quantitative measures of social bond strength with other adult females and with adult males (see the “Potential mediators and moderators” section below). Because both of these variables are known to be linked to adult survival (35), either could act as a mediator of early life adversity. We considered a female’s social bonds with other adult females separately from her social bonds with adult males because same-sex and opposite-sex social

relationships have different relationships with early adversity and with survival and are not well correlated (17, 27, 34, 35). We note that social bonds to other females are, a priori, more likely to act as a mediator than social bonds with males, as early adversity has not shown a strong relationship to social bonds with males in previous analyses (17, 27, 34). However, we evaluated both forms of social bonds for completeness, as both predict survival, and to parallel our tests for social buffering below.

The mediation analysis enables us to break down the total effect of early life adversity on survival (β_2 , black arrow in Fig. 1A) into direct (β_3) and mediated ($\beta_1\gamma$) effects. The direct effect (β_3) of early life adversity on survival is the pathway connecting these variables independent of the mediator (green arrow in Fig. 1A). The mediated (or indirect) effect ($\beta_1\gamma$) is the pathway connecting early life adversity and survival that runs through the mediator variable, in our case, measures of social bond strength (pink arrows in Fig. 1A). The mediation framework also assesses the effect of early adversity on the mediator (β_1 , orange arrow in Fig. 1A) and the effect of the mediator on survival independent of early adversity, hereafter the “bond effect” (γ , purple arrow in Fig. 1A).

For each of our candidate mediators, we estimated the links between early life adversity (*A*), social bond strength (*M*), and survival (*Y*, measured by the hazard ratio λ) by fitting three equations as proposed by Zeng and colleagues (41) (for more details, see Materials and Methods). The first equation evaluates the effect of early life adversity on observed values for the mediator, conditional on covariates, *C*, and random effects, r_i (orange arrow in Fig. 1A; see Supplementary Text for more information)

$$M_{it} = M_i(t) = \beta_0(t) + A_i\beta_1(t) + \theta_1C_{it}^M + r_i + \varepsilon_{it} \tag{1}$$

where *i* is individual and *t* is age class. Here, β_1 represents the effect of early adversity on social bond strength. The second equation models the total effect of early life adversity on survival (e.g., the change in hazard rate related to early adversity; β_2 , black arrow in Fig. 1A), which does not differentiate between direct and mediated effects

$$\lambda(t|X_i, A_i) = \lambda_0(t)\exp(\tilde{\beta}_2A_i + \theta_2C_{it}^S + \tilde{r}) \tag{2}$$

The third equation is similar to Eq. 2 but incorporates estimates of the mediator based on the parameters previously fit for Eq. 1. It allows us to estimate the value of the effect of the mediator on survival given an estimate of the mediator $f\{\alpha, M_i(t)\}$

$$\lambda(t|X_i, A_i, M_{it}) = \lambda_0(t)\exp(\tilde{\beta}_3A_i + f\{\alpha, M_i(t)\} + \theta_3C_{it}^S + \tilde{r}) \tag{3A}$$

where the mediator component $f\{\alpha, M_i(t)\}$ equals

$$f\{\alpha, M_i(t)\} = \int_0^{t_{\max}} \alpha(u)M_i(u)du \tag{3B}$$

where t_{\max} is the maximum lagged time (here 3 years) and $\alpha(u)$ is a time varying constant. Equation 3B estimates the mediator for the previous 3 years of life based on values for the covariates, early life adversity, and the effect sizes estimated in Eq. 1 (i.e., Eq. 3B is fit on the basis of estimated values of the mediator, not directly on observed data). We designate this value the “3-year mediator value,” where each year corresponds to a female age class, starting on her birthday and ending 1 day before her subsequent birthday. We also

Table 1. Sources of early life adversity and the number of females that experienced each source.			
Source of adversity	Description	N of females who experienced adversity	N of females who did not experience adversity
Drought	<200 mm of rainfall during the first year of life	28	171
Large group size	Group size in the top quartile (>33 adults) at the subject’s birth, indicating high social density	32	167
Close-in-age younger sibling	Younger sibling born less than 1.5 years after the subject’s birth	40	159
Maternal loss	Mother dies during the first 4 years of the subject’s life	38	161
Low maternal social status	Mother’s proportional dominance rank in the lowest quartile at the subject’s birth	46	153
Low maternal social connectedness	Mother’s social connectedness in the lowest quartile during the subject’s first 2 years of life	54	145

considered models where the mediator was estimated on the basis of the same year of life as survival ("1-year mediator models"), and results are consistent with 3-year mediator models (tables S1 and S2).

Note that the effects β_2 and β_3 in Fig. 1A are not numerically identical to the coefficients β_2 and β_3 in Eqs. 2 and 3, respectively. While they are analogous to β_2 and β_3 in terms of the effects that they represent, they differ because of the nonlinear hazard scale and complex functional model adopted in the analysis [i.e., in practice, we analyze a decomposition of a functional form fit to the social relationship data rather than the estimated social bond values directly; see (41)]. Similarly, the bond effect γ does not directly correspond to a specific model parameter. Instead, β_2 , β_3 , and γ are calculated from functions involving all parameters in Eqs. 1 to 3 [see Materials and Methods and derivations by Zeng and colleagues (41)].

First, we modeled the effects of cumulative early adversity on both mediators (social bond strength with females and social bond strength with males) and on survival. We measured cumulative early adversity as a continuous variable representing the sum of the six individual sources of adversity for each subject. No individual had a cumulative adversity score greater than four (mean = 1.196 \pm 0.936 SD). Second, we built multivariate models to assess the effect of each individual source of adversity on each mediator and on survival while holding the other sources of adversity at zero. In these models of individual sources of adversity, each measure of adversity was modeled as a categorical variable (a value of one for subjects that experience the adverse event and zero for those that did not).

Moderation models

To test the social buffering hypothesis, which posits that adult social relationships act as a source of resilience in the face of early adversity, we next treated three adult social phenotypes (social bond strength with females, social bond strength with males, and social status) as potential moderators instead of mediators of early life adversity. In contrast to the mediation models, the moderation models test whether the social phenotypes influence the strength and

direction of the effect of early life adversity on survival without making causal assumptions about the pathways involved. Moderation is captured by the interaction between the exposure A_i and mediator $M_i(t)$ with the interaction term $A_i g\{\eta, M_i(t)\}$ in the following model, which again incorporates estimates of the mediator from Eq. 1

$$\lambda(t|X_i, A_i, M_{it}) = \lambda_0(t) \exp(\xi A_i + f\{\alpha, M_i(t)\} + A_i g\{\eta, M_i(t)\} + \theta C_{it}^S + \tilde{r})$$
 (4)

Therefore, this approach allows us to estimate how the effects of early adversity on survival vary across different values for social bonds or social status in adulthood.

Potential mediators and moderators
Mediators

We measured each female's social bond strength with females, i.e., the strength of her social bonds with her top three female partners in each year of her life, and each female's social bond strength with males, the strength of her social bonds with her top three male partners in each year of her life, as two distinct potential mediators (M) of the effects of early life adversity on survival. We used grooming relationships to assess social bond strength because grooming is the most prominent affiliative behavior in baboons and many other primates (42–45). These mediators were represented in Eqs. 2 and 3 as estimates over 3-year periods (Eq. 3B) based on the values of their covariates and the parameters fit in Eq. 1. We also estimated mediators over shorter, 1-year periods, as reported in tables S1 and S2; because all analyses based on shorter periods produced qualitatively similar results, we focus on the 3-year estimates here.

Moderators

We considered adult social bond strength with females, adult bond strength with males, and adult social status as potential moderators. We assessed social bond strength using the same method described above (based on grooming relationships calculated as trajectories as in Eq. 1). We assessed social status using observations of wins and

Table 2. Mediation results from models in which social bond strength with females was the mediator. Total, direct, mediated, and bond effects are measured in years. The effect on the mediator is measured in social bond strength units (i.e., DSI units; 1 SD in social bonds with females = 0.59 DSI units). Bolded effects are those for which the 95% credible intervals (shown in brackets after each effect size estimate) did not overlap zero.

	Total effect (β_2 , years)	Direct effect (β_3 , years)	Mediated effect ($\beta_1\gamma$, years)	Effect on mediator (β_1 , DSI units)	Bond effect (γ , years)
Drought	−2.70 [−4.96, −0.44]	−2.26 [−4.04, −0.48]	−0.44 [−0.85, −0.03]	−0.21 [−0.38, −0.03]	2.19 [0.56, 3.82]
Large group size	−1.60 [−4.02, 0.83]	−1.38 [−2.89, 0.13]	−0.22 [−0.44, 0.01]	−0.11 [−0.22, 0.01]	2.39 [0.61, 4.17]
Close-in-age younger sibling	−0.90 [−5.45, 3.65]	−0.59 [−1.99, 0.81]	−0.31 [−0.66, 0.04]	−0.15 [−0.28, −0.03]	2.29 [0.75, 3.83]
Maternal loss	−3.30 [−5.79, −0.81]	−2.67 [−4.77, −0.57]	−0.63 [−1.20, −0.06]	−0.26 [−0.47, −0.04]	2.60 [0.79, 4.40]
Low maternal social connectedness	0.10 [−2.07, 2.27]	0.15 [−1.31, 1.62]	−0.05 [−0.27, 0.17]	−0.05 [−0.15, 0.06]	2.60 [0.87, 4.34]
Low maternal social status	−1.80 [−4.37, 0.78]	−1.36 [−2.90, 0.19]	−0.44 [−0.93, 0.05]	−0.14 [−0.25, −0.03]	2.49 [0.66, 4.32]
Cumulative adversity	−1.60 [−2.84, −0.36]	−1.43 [−2.52, −0.35]	−0.17 [−0.32, −0.01]	−0.09 [−0.16, −0.01]	2.20 [0.74, 3.65]

losses in dyadic agonistic interactions between adult female study subjects. A female dominance matrix was created for each month based on these win/loss outcomes, and female ordinal dominance ranks were assigned by minimizing entries below the diagonal (46, 47). We then scaled these ordinal rankings by group size and assigned to each female a “proportional dominance rank” (48), calculated as $[1 - (\text{ordinal rank} - 1)/(\text{number adult females} - 1)]$. A female’s proportional dominance rank represents the proportion of adult females that she dominates. We first calculated annual means for social status for each subject. We then estimated their social status trajectories over 3-year periods, given covariates and parameter estimates for an analog of Eq. 1, where M_{it} was redefined as annual mean proportional dominance rank instead of annual social bond strength (see also Materials and Methods).

RESULTS

Cumulative early adversity and survival: Mediated effects are weak, and direct effects are strong

As expected, we found a strong total effect (β_2) of cumulative early adversity on adult female survival, recapitulating previous work (Tables 2 and 3; black brackets in Fig. 1, B and C; black points with 95% credible intervals in Fig. 2) (27, 33). Approximately 90% of the total effect (1.43 of 1.60 years of lost life per additional exposure and 1.45 of 1.59 years, for the models considering social bond strength with females and social bond strength with males, respectively) was explained by the direct effect (β_3) of cumulative early adversity on survival, outside of the pathways that included social bonds with either sex (Tables 2 and 3; green arrows in Fig. 1, B and C; green points with 95% credible intervals in Fig. 2). Thus, the lives of females who experience four sources of early life adversity are predicted to be 6.4 years shorter than those of females that experience none, on average. Of these 6 years, ~5.6 years would be explained by the effects of early adversity on survival, independent of mediation by social bonds. Results were similar if we estimated mediation effects over shorter, 1-year periods instead of 3-year periods (tables S1 and S2).

We also found substantial effects of both mediators (γ) on survival, independent of effects of early life adversity. A one-unit increase in social bond strength with either adult females or adult males predicted a 2.2-year improvement in survival, independent of the effects of early adversity. Here, one unit represents approximately 1.7 SDs for social bond strength with females and 1.4 SD for social bond strength with males (Tables 2 and 3; purple arrows in Fig. 1; purple points with 95% credible intervals in Fig. 2; see tables S1 and S2 for results with mediators estimated over shorter, 1-year periods). While the effects of social bonds on survival broadly recapitulate previous findings in this population (34, 35), this analysis demonstrates that these effects remain strong after controlling for levels of early adversity.

Notably, despite the fact that cumulative early adversity significantly predicted weaker social bonds with females (β_1 , orange arrows in Fig. 1) and that stronger social bonds with both sexes predicted higher survival, mediated effects were weak in all of our models of cumulative adversity. Specifically, the pathway through social bonds with females explained only 2.04 months (10.6%) of the 1.60-year reduction in life span for each additional source of adversity (the mediated effect, $\beta_1\gamma$, pink bracket in Fig. 1B; pink points with 95% credible intervals in Fig. 2). This result may stem from the fact that the effect of cumulative early adversity on social bonds, while detectable, is relatively weak: Early adversity is associated with a 0.09-unit decrease in social bonds with females, which is small compared to the 1-unit increase in social bonds with females necessary to produce a 2.2-year improvement in life span via the bond effect. Consistent with the lack of a significant relationship between early adversity and social bonds with males (orange arrow in Fig. 1C), social bonds with males did not detectably mediate the relationship between cumulative early adversity and survival (Figs. 1C and 2 and Table 3 show values with 95% credible intervals).

Together, our results indicate that early adversity and social bonds both appear to have direct, independent links to survival that are of similar magnitudes. Consequently, a female baboon who experienced higher-than-average (1 SD above the mean) cumulative early life adversity, adult social bond strength with

Table 3. Mediation results from models in which social bond strength with males was the mediator. Total, direct, mediated, and bond effect are measured in years. The effect on the mediator is measured in social bond strength units (i.e., DSI units; 1 SD in social bond strength with males = 0.70 DSI units). Bolded effects are those where the 95% credible intervals did not overlap zero.					
	Total effect (β_2 , years)	Direct effect (β_3 , years)	Mediated effect ($\beta_1\gamma$, years)	Effect on mediator (β_1 , DSI units)	Bond effect (γ , years)
Drought	−2.70 [−4.96, −0.44]	−2.33 [−4.17, −0.50]	−0.37 [−0.71, −0.02]	−0.16 [−0.29, −0.02]	2.40 [0.62, 4.17]
Large group size	−1.60 [−4.01, 0.82]	−1.53 [−3.20, 0.15]	−0.07 [−2.07, 1.93]	−0.04 [−0.92, 0.84]	2.39 [0.61, 4.17]
Close-in-age younger sibling	−0.89 [−5.33, 3.55]	−0.69 [−2.08, 0.70]	−0.20 [−1.60, 1.20]	−0.11 [−0.61, 0.39]	2.29 [0.75, 3.84]
Maternal loss	−3.30 [−5.78, −0.81]	−3.21 [−5.73, −0.68]	−0.09 [−2.56, 2.38]	−0.06 [−1.95, 1.84]	2.20 [0.67, 3.73]
Low maternal social connectedness	0.11 [−1.90, 2.12]	0.37 [−1.26, 1.99]	−0.26 [−0.66, 0.15]	−0.15 [−0.32, 0.02]	2.20 [0.73, 3.66]
Low maternal social status	−1.80 [−4.38, 0.78]	−1.16 [−2.70, 0.38]	−0.64 [−1.35, 0.07]	−0.25 [−0.44, −0.06]	2.30 [0.61, 3.99]
Cumulative adversity	−1.59 [−2.82, −0.36]	−1.45 [−2.54, −0.35]	−0.15 [−0.62, 0.33]	−0.07 [−0.37, 0.22]	2.19 [0.74, 3.64]

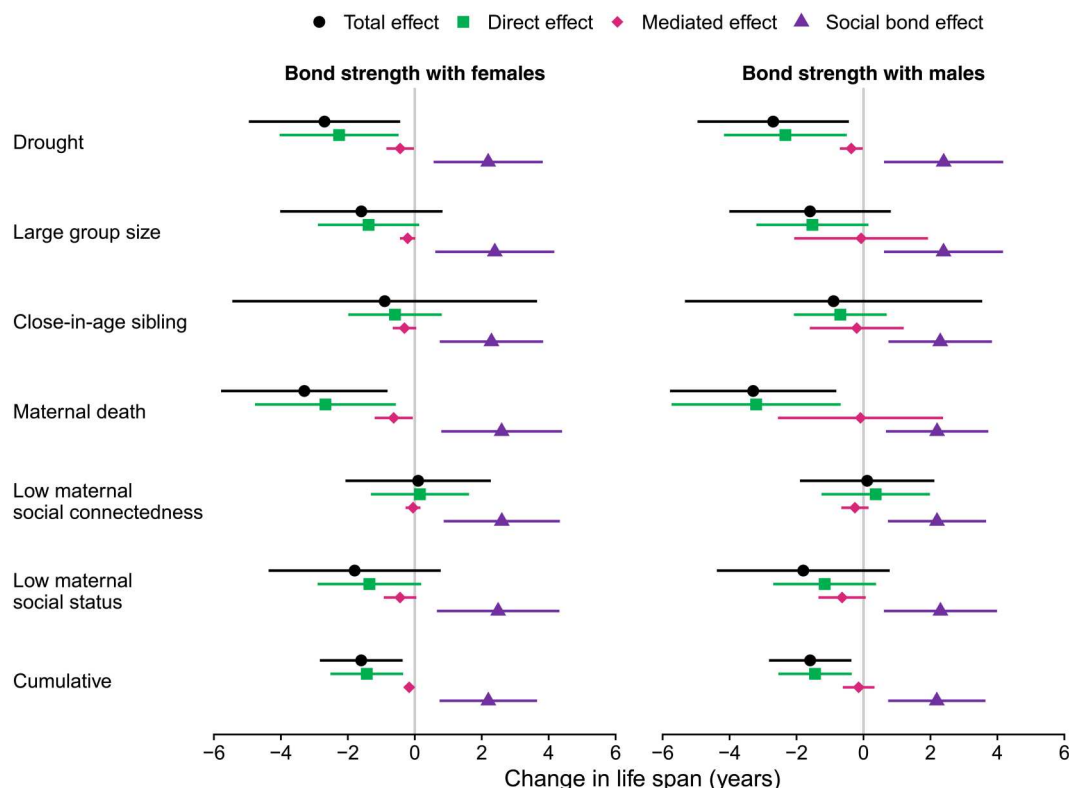


Fig. 2. Effects of early adversity on survival. (Left) Results of models in which social bond strength with females was the mediator. (Right) Results of models in which social bond strength with males was the mediator. Symbols and lines show effect sizes and 95% credible intervals for the total, direct, mediated, and social bond effects on survival. Effects are colored as in Fig. 1.

females, and adult social bond strength with males would be predicted to experience a 1.35-year reduction in life span attributable to her early life environment, a 1.29-year improvement in life span attributable to her social bonds with other females in adulthood, and a 1.29-year improvement in life span attributable to her social bonds with males in adulthood. In other words, both early adversity (likely via a route through poor adult health) and adult social behavior are (nonredundantly) important in determining survival in adulthood.

We next considered whether the weak mediation that we observed, despite effects of early adversity on social bonds and of social bonds on survival, might result from a mismatch in the timing of these effects. To explore this possibility, we designed a simulation analysis in which we modeled social bonds at different periods of adulthood as a series of distinct mediators. That is, we defined two mediators corresponding to bonds in early and late adulthood, respectively, which can differ in strength. Their effects on survival (designated γ_1 and γ_2) are each fixed, and the two effects are constrained to sum to a constant value (e.g., if γ_1 is large in a given simulation run, then γ_2 must be small; see the "Simulation to explore the weak mediated effect" section in Supplementary Text). That is, in our simulations, we fixed the values of both the effect of early adversity on each mediator ("Effect on mediator"; orange arrow in Fig. 1A) and the effect of each mediator on survival ("Bond effect"; purple arrow in Fig. 1A). We then assigned early life effects on the mediators and the mediators' effects on survival in all possible combinations of early and late timing of effects.

Although the component parts of the mediated effect were kept constant in the simulations, our simulation indicates that the magnitude of the overall mediated effect (pink arrows in Fig. 1A) depended on the timing of these effects. Mediated effects were largest when the timing of early life effects and mediator effects were matched, i.e., when either (i) early adversity affected early-adulthood social bonds and early-adulthood social bonds affected survival or (ii) early adversity affected later-adulthood social bonds and later-adulthood social bonds affected survival (see the "Simulation to explore the weak mediated effect" section in Supplementary Text; fig. S5). In contrast, mediated effects were weakest when the timing of early life and mediator effects were mismatched, i.e., when either (i) early adversity affected early-adulthood social bonds but only later-adulthood social bonds affected survival or (ii) early adversity affected later-adulthood social bonds but only early-adulthood social bonds affected survival. The results of this simulation support the idea that the timing of these effects during the life course could play a role in determining the strength of the mediated effect. They further suggest that, in the Amboseli baboons, the timing of early life effects on adult social bonds may be mismatched with the timing of social bond effects on survival.

Social bonds do not mediate the effects of individual sources of early adversity

Similar to the effects of cumulative early adversity, individual sources of adversity acted outside the pathway that includes social bonds, with little evidence for mediated effects in our 3-year

mediator models (Tables 2 and 3 for estimated effects and 95% credible intervals; also Fig. 2). More than 81% of the effects of individual sources of adversity were attributable to direct effects (87% if only considering significant direct effects). Among the six individual sources of early adversity, maternal loss and drought exerted the strongest and most consistent effects on both adult female survival and social bond strength with adult females (Tables 2 and 3 and Fig. 2). Drought, but not maternal loss, was also linked to weaker social bonds with adult males. In contrast to the effects of maternal loss on social isolation from adult females, maternal loss did not predict social bond strength with adult males: The estimated effect size was near zero [0.06 dyadic sociality index (DSI) units; Table 3]. Consistent with our main results, the effects of individual sources of adversity on survival were also not detectably mediated by measures of social bonds with either sex based on 1-year intervals (tables S1 and S2).

Moderating effects: Social bonds buffer the effects of some sources of early adversity

Neither social status nor social bond strength with either sex moderated the link between cumulative early adversity and survival

Table 4. Moderation results from models in which social bond strength with females, social bond strength with males, and female social status were the moderators. Values represent the magnitude of the interaction effects measured in log hazard ratio (HR). Bolded effects (those for which the 95% CI did not overlap zero) show that the effects of maternal loss on survival were moderated by all three phenotypes and that the effects of low maternal social connectedness were moderated by adult social relationships with males and female social status. A negative interaction effect indicates that increased adult social bond strength or higher social status acts as a buffer to reduce the negative effects of early adversity on survival. A positive interaction effect value means that adult social bond strength or higher social status acts as an amplifier to increase the negative effects of early adversity on survival.			
	Social bonds w/ females (log HR)	Social bonds w/ males (log HR)	Social status (log HR)
Drought	−0.19 [−0.41, 0.03]	−0.13 [−0.33, 0.06]	−0.07 [−0.29, 0.15]
Large group size	0.19 [−0.06, 0.44]	−0.12 [−0.27, 0.02]	−0.19 [−0.40, 0.02]
Close-in-age younger sibling	0.13 [−0.38, 0.64]	0.00 [−0.33, 0.33]	0.25 [−0.19, 0.69]
Maternal loss	−0.26 [−0.39, −0.13]	−0.21 [−0.30, −0.12]	−0.18 [−0.33, −0.04]
Low maternal social connectedness	0.11 [−0.03, 0.26]	−0.15 [−0.24, −0.06]	−0.19 [−0.37, −0.01]
Low maternal social status	0.02 [−0.15, 0.18]	0.04 [−0.04, 0.13]	−0.02 [−0.19, 0.16]
Cumulative adversity	−0.02 [−0.05, 0.01]	−0.03 [−0.05, 0.00]	0.02 [−0.02, 0.06]

(Table 4 and Fig. 3A; results were similar when we used moderator trajectories estimated over a shorter, 1-year period; table S3). However, social bond strength with males and social bond strength with females both moderated the link between one individual source of adversity, maternal loss, and survival. Specifically, stronger social bonds with either females or with males during adulthood buffered the negative effect of maternal loss on survival (and, conversely, weaker social bonds amplified the negative effect of maternal loss on survival; Table 4; table S3; and Fig. 3, A and B). In other words, survival was disproportionately lower for females who lost their mother early in life and were more socially isolated in adulthood (and, conversely, survival was disproportionately higher for females who lost their mother but formed strong social relationships in adulthood, with either sex; Fig. 3, A and B). Females who lost their mother early in life but maintained strong social relationships with other females (1 SD above the mean) experienced a 10% reduction in hazard ratios relative to females who lost their mothers and had average social bond strength to other females. In contrast, females who lost their mothers and had weak social relationships with females (1 SD below the mean) had 16% higher hazard ratios than females who lost their mothers and had average social bond strength to other females (Fig. 3B). The effect was stronger for bonds with males, where females who lost their mothers in early life but maintained strong social bonds with males (1 SD above the mean) had an 18% lower hazard ratio, while those who had weak social bonds with males (1 SD below the mean) had a 16% higher hazard ratio, compared to the effects of maternal loss for females with average social bond strength (Fig. 3B). In addition, another individual source of early adversity, low maternal social connectedness, was buffered by strong adult social bonds with males but not by adult social bonds with females (Fig. 3A).

Female social status also moderated the effects of early life maternal loss and low maternal social connectedness on survival (Fig. 3A and Table 4; note that this effect was not detectable when moderator trajectories were estimated over a shorter, 1-year period; table S3). Specifically, survival was disproportionately lower for low-ranking females who lost their mothers early in life or had a socially isolated mother and disproportionately higher for high-ranking females who lost their mothers early in life or had a socially isolated mother (Fig. 3, A and B). Females who lost their mother early in life but were of high social status in adulthood (1SD above the mean) had a 1% lower hazard ratio compared to females who lost their mother but were of average social status. In contrast, females who lost their mother early in life but were of low social status in adulthood (1SD below the mean) had 9% higher hazard ratios compared to the effects of maternal loss for females with average social status.

DISCUSSION

Previous work has debated the relative importance of early adversity and adult social relationships in determining adult mortality risk in humans (22, 24, 25, 49). Our results shed light on this debate by providing an example of a wild animal model in which both early life experiences and adult social relationships are important and act independently on survival, with effects of similar magnitude. In addition, our moderation analysis indicates that at least for some sources of adversity, social relationships in adulthood may act as sources of resilience, allowing individuals to buffer the negative

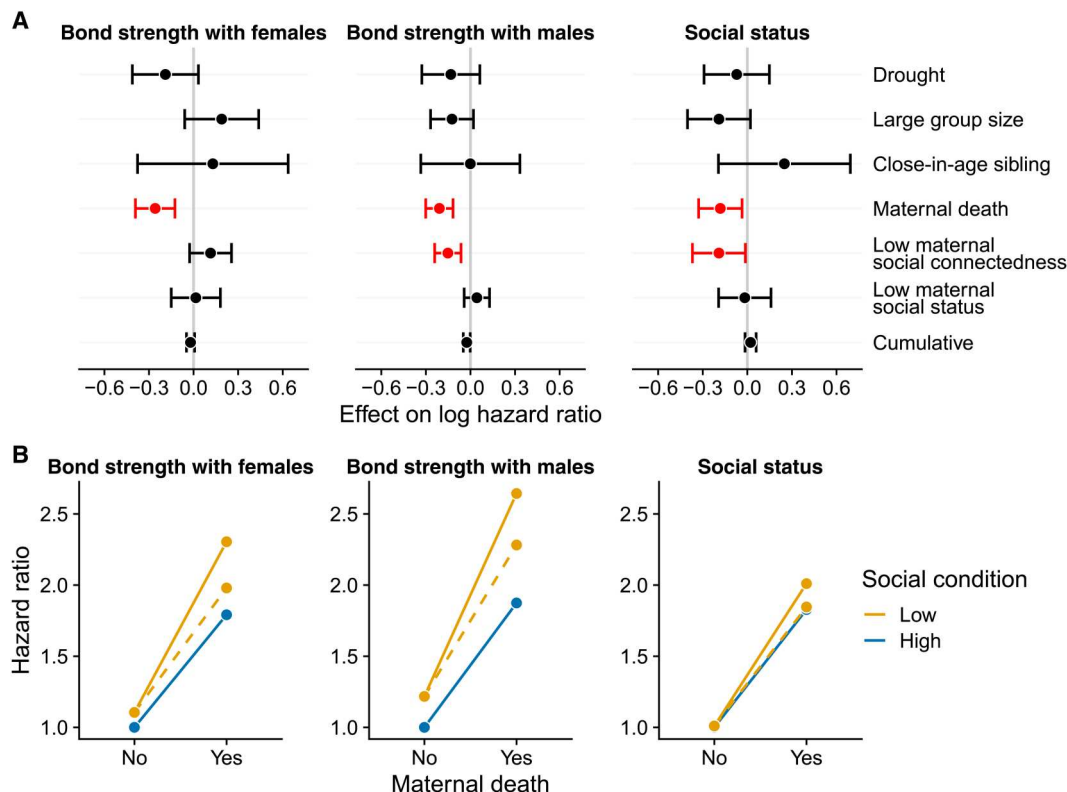


Fig. 3. Moderating effects of adult social conditions. (A) Moderating effects of social bond strength with females, social bond strength with males, and social status on the relationship between early adversity and survival (log of the hazard ratio). A negative value on the x axis means that greater social bond strength or higher social status reduces the negative effects of early adversity on survival. Effects colored in red are those whose credible intervals do not overlap zero: Strong social bonds with females buffer the effects of maternal death. Strong social bonds with males buffer the effects of both maternal death and low maternal social connectedness. High social status buffers the effects of both maternal death and low maternal social connectedness. (B) The effects of social bond strength with females, social bond strength with males, and social status on the relationship between maternal death and survival (measured as the hazard ratio). The yellow dashed lines represent the expected effect of maternal death on the hazard ratio for adult females in the absence of moderating effects. The blue solid lines show a disproportionately lower hazard ratio for females who have maternal loss but who have strong social bonds (1 SD above the mean) or whose social status is 1 SD above the mean. The yellow solid lines show a disproportionately higher hazard ratio for females who have maternal loss and have social bond strength or social status 1 SD below the mean.

effects of poor early life experiences. Below, we consider several implications of these results, including the puzzle of weak mediation despite significant links between treatment and putative mediator and between putative mediator and outcome.

The puzzle of weak mediation

We observed strong effects of both early adversity and adult behavior on survival and effects of early adversity on at least one aspect of the adult social environment, with little or no mediation. One potential explanation for the lack of mediation is that an assumption of the mediation analysis was violated, thus producing spurious results. The most likely violated assumption is that of sequential unconfoundedness: i.e., if an unmeasured confounder in our system affects both the mediator and survival (50, 51). For example, individuals with better phenotypic or somatic quality (resulting from either genetic or environmental differences that were not included in our analysis) may experience both stronger social bonds and better survival, independent of early adversity. In this case, phenotypic/somatic quality would be an unmeasured confounder [see discussion of sequential unconfoundedness in (52)]. To examine the potential for a confounding variable to affect our analyses, we conducted sensitivity analyses that assess how the mediated effect

estimates vary as a function of the extent of the correlation between an unmeasured confounding variable and the mediator and between that same variable and survival. Our sensitivity analyses demonstrate that our results are relatively robust to the assumption of sequential unconfoundedness (see the “Sensitivity analysis for sequential unconfoundedness” section in Supplementary Text; figs. S3 and S4). As a consequence, it is likely that we are correctly estimating a small mediation size in this study.

A second, more likely, explanation is that the effects of cumulative early life adversity on social bonds in adulthood, albeit detectable, are too modest to support strong mediation. Rosenbaum and colleagues (17) found similar results for individual sources of adversity and for a categorical three-level measure of cumulative adversity, when analyzing GC levels as an outcome. In contrast, here, we analyzed survival as the outcome of interest, where the link with early adversity is stronger than for GCs, and used the continuous score for early adversity from the work of Tung and colleagues (27), which first reported the link between early adversity and adult social relationships. Nevertheless, we find similar results: While a mediating pathway can be identified, it accounts for only a small fraction of the overall relationship between early adversity and survival. Both findings likely stem from the observation that

cumulative early adversity has only modest effects on social bond strength with females and consistently no detectable relationship on social bond strength with males. Consequently, social bonds are unlikely to strongly mediate the comparatively quite strong connection between early adversity and adult survival.

In addition, our causal mediation pathway may be shaped by a mismatch in the timing of the effects of early adversity on social bonds and of social bonds on survival, as suggested by our simulation model. For example, let us assume that social bonds at different periods of adulthood are distinct mediators. In that case, if (i) early life adversity primarily affects early-adulthood social bonds and (ii) survival is most strongly affected by early-adulthood social bonds, then (iii) the matched timing of these effects can give rise to a strong mediating effect of social bonds. However, if (i) early life adversity primarily affects early-adulthood social bonds but (ii) survival is most strongly affected by late-adulthood social bonds, then (iii) the mismatched timing of these effects leads to a weak mediation effect. Previous work in birds and humans has shown that such mismatched timing can occur (10, 53, 54). For example, in a survey of American adults, Nurius and colleagues (10) show that social relationships in young adulthood are not linked to health but that older adults with stronger social connections are in better health. Yang and colleagues (54) also identified variability in the effects of social integration on several health biomarkers between American adolescents and adults. Understanding how the effects of early adversity depend on life stage is therefore an important future avenue of research.

Two additional explanations are consistent with our observation of independent effects of social bonds and early adversity, combined with weak mediation. First, social bonds may be one of a larger set of mediators that all weakly mediate the link between early life environments and survival. Second, an as-yet unidentified variable could act as a strong mediator of early life adversity without involving social bonds. For example, the biological embedding hypothesis predicts that GCs, produced by the hypothalamic-pituitary-adrenal (HPA) axis and involved in regulating multiple physiological processes, link early adversity and life span (55, 56). In our study population, early life adversity predicts elevated concentrations of GC metabolites in fecal samples in adulthood (17). Furthermore, elevated fecal GC (fGC) concentrations in adulthood are associated with a shortened life span (57). At the same time, social bonds in adulthood are only modestly correlated with fGC concentrations (17), pointing to fGCs as a possible mediator of early life adversity that bypasses the pathway through social bonds. However, fGC concentrations, like social bonds, also appear to be weak mediators of the early life adversity-survival relationship in the Amboseli baboons (41). This observation suggests that the HPA axis function may be one of many mediators as opposed to the dominant pathway through which early life effects on life span manifest.

The evolutionary significance of sources of variance in survival

The independent effects of cumulative early life adversity and social bonds on female baboon survival are considerable. For each additional source of early adversity, life span is decreased by approximately 1.4 years, independent of social bond strength. Similarly, a 1 SD decrease in social bond strength with either sex predicts 2.2 years of decreased life span, independent of early adversity. Notably, life span explains >80% of the variation in lifetime

reproductive success (27, 33, 58), and females who experience early life adversity do not accelerate reproduction to compensate for the reduction in life span (33). Consequently, the combined effects of cumulative early life adversity and adult social isolation on survival have major consequences for lifetime reproductive success for female baboons.

These large effects on fitness indicate that phenotypes that allow individuals to survive in the face of multiple sources of adversity, which include features of the physical, social, and maternal environment, are likely to be favored by natural selection (59–61). Features of the social and maternal environment can be under direct natural selection. For example, our results suggest that selection should favor low adult mortality partly because maternal mortality directly decreases offspring survival in adulthood (in addition to other effects, such as the increase in the number of reproductive opportunities that comes with longer life spans). In contrast, features of the physical environment (e.g., drought) cannot be under direct natural selection. However, adverse physical environments impose natural selection that acts on individual responses to environmental adversity. Work in humans has identified many genetic variants that influence the response to environmental stressors (e.g., pathogens and chemical stimuli), and some of these variants also carry genetic signatures of selection (62, 63). Thus, we expect natural selection to favor genotypes that confer resilience to early life adversity even if the resulting phenotypes have lower fitness than phenotypes produced by the same genotypes under advantageous early life conditions (59–61).

Adult social relationships also have strong effects on adult survival that are independent of early adversity, supporting the idea that adult social behavior may be directly targeted by natural selection. Previous work on the links between social bonds and fitness did not control for early life experience (34, 35), limiting the ability to disentangle direct and indirect effects of adult behavior on fitness (12, 64). Our results suggest that adult social behaviors that maintain social bonds should be under strong selection. Because social behavior is almost always partially heritable, including in our study population [e.g., (65–67)], these behaviors have the potential to evolve via natural selection. Furthermore, our findings suggest that indirect genetic effects, in which the genotypes of social partners affect behavior, could play an important role in social selection and evolution (68, 69). Indirect genetic effects are unique because they illustrate that the environment itself can evolve and, as a result, create feedback loops that amplify or constrain evolutionary change, even in the absence of direct selection. However, selection on sociality is also likely to be limited by tradeoffs (70, 71). For example, tradeoffs may occur between the time allocated to sociality versus to other activities that are important for maintenance, such as foraging. In addition, sociality itself imposes costs, including potential increases in pathogen transmission, intraspecific competition, and social stress. Last, the mechanisms that link adult social relationships to survival remain unclear, making it difficult to definitively identify potentially important targets of selection in addition to social bonds themselves.

Individual sources of early adversity

We found strong effects of two individual sources of adversity on adult social bond strength and survival: maternal loss and drought. Consistent with previous findings (17, 27, 33, 41, 72), females whose mothers died when they were young had weaker

social bonds with other females and reduced survival compared to females who did not experience early maternal loss, although they exhibited no differences in social relationships with males. In non-human primates, maternal loss during the juvenile period compromises the learning of social and foraging skills (73–76). In our study system in particular, losing a mother early in life is associated with shorter adult life spans, weaker adult social bonds with females, compromised patterns of adult rank acquisition (77), elevated GC concentrations in adulthood (17, 40, 41), and relatively poor survival of offspring (72, 78). Maternal loss also has negative consequences for adult phenotypes and fitness in other mammal species (28, 78–82) including humans (83, 84). Therefore, maternal loss during development represents a strong source of early adversity across taxa, especially in species where mothers are essential for the development of crucial skills.

In addition to maternal loss, drought emerged as an important source of early life adversity in this analysis. Females who experienced drought in their first year of life had weaker social bonds with both females and males and also experienced reduced survival relative to females born in nondrought years via both mediated and direct effects (Tables 2 and 3). Drought threatens food availability, which, in turn, hinders growth and development, especially but not only during the crucial first year of life (85–89). In addition, individuals born during droughts may have fewer opportunities to learn foraging skills during younger years when adults are more tolerant of them during foraging (75, 90). Consistent with our results, experiencing droughts in early life negatively affects health in humans (91–96).

Notably, two previous analyses in our study system found that drought did not predict adult survival independently of other sources of early adversity (27, 33). The difference between the previous studies and this one may be attributable to using somewhat different subsets of the long-term data because of different data requirements for each analysis. For instance, the current analysis includes a larger representation of females who were born during a particularly severe drought in 2008–2009, a 2-year consecutive period in which annual rainfall was less than 200 mm (97). This drought inflicted substantial mortality on wildlife and livestock throughout the Amboseli ecosystem and surrounding areas (98, 99). Therefore, it represented an extreme climatic event in the early lives of these individuals, which may have driven the strong effects of drought not detected in previous analyses (27, 33).

Moderating effects of adult behavior

Our analyses indicate that strong social bonds in adulthood may buffer the negative consequences of adverse early life events. Social buffering has also been suggested as a mechanism to counteract the negative effects of early life adversity in other mammals (19, 100) and humans (84). For example, mountain gorillas who lose their mothers tend to strengthen their social bonds with other group members; perhaps as a consequence, they suffer no detectable survival costs from maternal loss (100). Social bonds with males may be a particularly important buffer as, unlike social bonds with females, they are not weakened by maternal loss (17).

Conclusions and future directions

By linking prospective data on early life adversity with data on social bonds and survival in adulthood, we confirmed the far-reaching effects of early life adversity, which contributes directly to both

compromised adult social relationships and adult survival, and also confirmed a direct influence of adult social relationships on survival. Together, these results provide indirect support for both social causation and health selection. Furthermore, for at least some sources of early adversity, strong adult social bonds can reduce the negative effects of early life adversity. In addition, our findings argue that responses to early adversity, sources of early adversity, and adult social behavior are all likely targets of natural selection. Future work should explore how variations in the timing of early life effects and in the timing of the effects of adult phenotypes affect connections between early adversity, mediators, and survival in other species. Future work should also examine other potential mediators (e.g., phenotypic quality, immune response, and GC levels) of the relationship between early adversity and life span.

MATERIALS AND METHODS

Study subjects

We used longitudinal data on 199 wild adult female baboons [*Papio cynocephalus*, with some natural admixture from the closely related species *Papio anubis* (101, 102)] from the Amboseli ecosystem in Kenya collected between 1983 and 2019. Subjects are habituated to and individually recognized by experienced observers who collect demographic and behavioral data 6 days a week, year-round, following one to two social groups (“study groups”) per day. Birth and death dates for all study subjects are accurate to within a few days’ error. Two original study groups (studied beginning in 1971 and 1980, respectively) experienced multiple permanent fissions and fusions over the years, resulting in a total of 19 different social groups that persisted for varying lengths of time. Female baboons remain in their natal social group throughout their lives (except for group fissions or fusions), and thus, any disappearance of a female in our dataset was considered a death. Of the 199 females in the study, 74 had died by the end of the study, and the rest were considered censored in survival analyses. To be included in the study, females had to meet the following criteria: (i) They survived to at least 4 years of age (most females reach menarche between 4 and 5 years of age) (103); (ii) they had available data on exposure to all six sources of early adversity in the infant and juvenile period; and (iii) they were members of study groups that foraged entirely on naturally occurring foods (17, 27, 33). The research in this study was approved by the Institutional Animal Care and Use Committee at Duke University (no. A044-21-02) and adhered to the laws and guidelines of the Kenyan government.

Measuring early life adversity

We created an index of cumulative early life adversity by considering six conditions that represent socioenvironmental adversity experienced during the first 4 years of life: drought in the first year of life, large group size at birth, low maternal social status at birth, low maternal social connectedness in the first 2 years of life, a close-in-age younger sibling, and maternal loss before age four (Table 1) (27, 33). Drought years were those in which less than 200 mm of rain fell. Large group sizes were considered as those in the highest quartile of the group size (number of adults) distribution. Low maternal social status was assigned when the mother’s proportional dominance rank in the month of her offspring’s birth was in the lowest quartile of dominance ranks. Proportional dominance rank ranges from 0 (lowest-ranking female) to 1 (highest-ranking female) and indicates

the proportion of adult females in a study subject's social group that she dominated in agonistic interactions (48). Low maternal social connectedness was assigned when the mother's social connectedness to other females was in the lowest quartile of the distribution of social connectedness values during our study subjects' first 2 years of life. Following previous work on early life adversity in this population (27, 33), social connectedness was measured as the relative frequency of the mother's grooming interactions with other adult females in her social group, adjusted for observer effort (see the "Measuring social bond strength" section for information about observer effort). Close-in-age younger siblings were those born within 1.5 years of the subject's birth, approximately the shortest quartile of observed interbirth intervals in the Amboseli baboons (27). A subject was considered to experience maternal loss if her mother died within her first 4 years of life (i.e., before the earliest age of sexual maturation for females in this population).

Each subject's cumulative adversity index was calculated as the sum of exposures to these six sources of adversity. In our dataset, 48 females experienced zero sources of adversity, 84 experienced one, 50 experienced two, 14 experienced three, 3 experienced four, and none experienced five or six.

Measuring social bond strength

We measured an adult female's social relationships by assessing the strength of social bonds with her top three male or female social partners separately, in each year of her life, measured relative to the social bonds of all other females in the population with males or females respectively, as described by Rosenbaum and colleagues (17). Briefly, grooming interactions are recorded during all hours of observation using representative interaction sampling in which observers record all the interactions that they see while conducting 10-min focal follows on a randomized set of individuals. From these data, we calculated the number of grooming interactions with each partner per day of co-residence in the same group, for each year of life for each female subject starting on her birthday. Calculating interaction rates from such data is complicated by the fact that the number of observers remains constant over time, while social group sizes vary, so that higher numbers of grooming interactions per pair of animals (per dyad) will generally be observed in smaller groups compared to larger groups. We corrected for this variation in observer effort by regressing daily rates of grooming interactions per dyad against observer effort, where observer effort was calculated as the number of focal samples on adult females collected during each observer day, divided by the mean number of adult females in the group during those days, divided by the number of days that each dyad was co-resident (17, 35). We z-scored the corrected rates within years to control for temporal variation in sociality in the population.

Each subject's social bond strength with females and with males was taken as the average of the subject's three most frequent adult female grooming partners and adult male grooming partners, respectively, to calculate a DSI. A positive value for social bond strength indicates that a female had relatively strong social bonds with her top three partners compared to the population average. A negative value for social bond strength means the subject had relatively weak social bonds with her top three partners.

Random effects and covariates

Previous work has demonstrated that several environmental and demographic variables not discussed above (i.e., presence of maternal relatives, group size, social status, percent of prior year with young infant, percent of prior year cycling, and rainfall) explain variation in social bond strength and/or survival (17, 34, 35, 43). To control for these effects, we included them as covariates in our mediation and moderation analyses (for details, see the Supplementary Materials). We also included social group and hydrological year as random effects in all models to control for group-to-group and interannual variation (17). Age was not included as a covariate, although social bonds vary with age, because age effects are captured by our functional principal components analysis (FPCA) approach to modeling the mediator (see below). Because our baboon study population represents an admixed population (yellow baboon ancestry is dominant, but all individuals exhibit some degree of admixture with anubis baboons), we also ran separate analyses that included a covariate measure of individual admixture, a "genetic hybrid score" that represents the proportion of each individual's genome estimated to be from *P. anubis* ancestry [see the Supplementary Materials and (104, 105)]. Results that incorporated hybrid score (tables S4 and S5) were similar to those of the full model (Tables 2 and 3).

In preliminary analyses, we considered social status as a third potential mediator of the effects of early adversity on survival. However, as previously reported (34, 35), we found no effects of social status (again measured as proportional dominance rank) on female survival (table S6). In addition, we found no effect of cumulative early adversity on female social status, and no mediating effects of female social status on the relationship between early life adversity and survival (table S6). As a consequence, we focus on social bond strength as the primary mediating variable in the main text, but report models for social status as a mediator in the Supplementary Materials.

One individual source of early adversity strongly predicted proportional dominance rank: Low maternal dominance rank predicted low proportional rank for the study subject in adulthood (table S6), which is expected, as rank is matrilineally inherited in this species (106). The correlation between maternal dominance rank and adult social status is ~ 0.7 in our dataset. In light of this relationship, we controlled for proportional rank by including it as a covariate when estimating the effect of early life adversity on the mediator. We also note that adult social status acted as neither a mediator nor a moderator of cumulative early adversity or low maternal dominance rank in our analyses, suggesting that the correlation between maternal dominance rank and adult social status does not affect our interpretation of our results.

Mediation analysis implementation

We fit two models in each of our mediation analyses (41). The first model captures the relationship between early adversity and the mediator. The second model characterizes the relationship between early adversity, the mediator, and survival. Models were implemented using the R packages *survival* and *flexsurv*. The reproducible code is available at <https://zenodo.org/record/7808802#.ZDB7euzMI-Q>.

The first model: The relationship between early adversity and the mediator

Our first model applies to the observed mediator trajectory M_{ij} and the measure of early adversity A_i , where i indexes individual and j indexes time. This model corresponds to Eq. 1. Because the observed mediator values are noisy and potentially measured imprecisely, we consider them, after adjusting for covariates and random effects, as realizations of an underlying smooth process $[M_i(t_{ij})]$ with random noise. Specifically, we modeled the trajectory of the mediator M_{ij} as a combination of covariate effects $C_{ij}\beta_m$, a baboon-specific random effect that consists of a social group random effect $r_{\text{social group}}^m$ and a hydrological year random effect r_{hydro}^m (note, $r_{\text{social group}}^m + r_{\text{hydro}}^m$ is equivalent to r_i in Eq. 1), an underlying smooth process $M_i(t_{ij})$, and an error term ε_{ij}

$$M_{ij} = C_{ij}\beta_m + r_{\text{social group}}^m + r_{\text{hydro}}^m + M_i(t_{ij}) + \varepsilon_{ij}, \varepsilon_{ij} \sim N(0, \sigma_m^2) \quad (5)$$

Because $M_i(t_{ij})$ is of infinite dimension mathematically, we performed dimension reduction to improve the statistical power of our analysis. Specifically, we used a FPCA method to decompose the smooth process as the linear combination of the fewest possible functional principal components (40, 41, 107–109). We began by examining the correlation between any two time points in the mediator process (e.g., between the values of the mediator at ages 4 and age 8, between the values of the mediator at ages 4 and 9, and so on) to produce a correlation structure between mediator values at different time points, which we then expressed as principal components or eigenfunctions

$$\text{Cov}[M_i(t_1), M_i(t_2)] = \sum_{k=1}^{\infty} \lambda_k \psi_k(t_1) \psi_k(t_2), \lambda_1 \geq \lambda_2 \geq \dots \geq 0 \quad (6)$$

where λ_k is the explained variance of the orthogonal normal principal components $\psi_k(t)$. We ordered the principal components by the amount of variance that they explained to reflect the fact that principal components that explain more variance (larger λ_k) are more important in expressing the smooth process. We then used the first K principal components, where K is the number of components necessary to collectively explain at least 90% of the variance ($\sum_{k=1}^K \lambda_k / \sum_{k=1}^{\infty} \lambda_k \geq 90\%$).

In the next step, we represent the smooth process of each subject's mediator process as a linear combination of the K principal components

$$M_i(t) = \sum_{k=1}^K \xi_{ik} \psi_k(t) \quad (7)$$

where ξ_{ik} is the principal score for individual i on the k th principal component or eigenfunction. The variance of ξ_{ik} corresponds to the explained variance of principal component, λ_k . We can efficiently express the smooth process and trajectory with a small number of principal components (K is never greater than 4 in our work), capturing the dominant sources of variance in our sample. Therefore, coupled with the FPCA, we posit the following model of the

mediator

$$M_{ij} = C_{ij}^m \beta_m + r_{\text{social group}}^m + r_{\text{hydro}}^m + \sum_{k=1}^K \xi_{ik} \psi_k(t) + \varepsilon_{ij}, \varepsilon_{ij} \sim N(0, \sigma_m^2) \quad (8)$$

which corresponds to Eq. 1. Furthermore, we assume that the differences in trajectories caused by early adversity are captured by the differences in the principal scores. Therefore, we use the following specification for the principal scores, with different means for each level of adversity in the cumulative model or with different means for the group that experienced each early adversity and for the group that did not experience early adversity in the models of individual sources of adversity,

$$\xi_{ik} = A_i(\tau_1^k - \tau_0^k) + \tau_0^k + \eta_{ik}, \eta_{ik} \sim N(0, \lambda_k), \lambda_1 \geq \lambda_2 \geq \dots \geq \lambda_K \geq 0 \quad (9)$$

where τ_1^k denotes the mean of the k th principal score for the subjects in the adversity group, while τ_0^k represents that for the non-adversity group (for cumulative adversity, τ_1^k denotes the k th principal score for a higher level of adversity relative to τ_0^k , the score for one level lower). We fit Eq. 8 simultaneously with Eq. 9. Hence, instead of estimating the effect of adversity on the trajectories directly, which is a high-dimensional problem, we estimate its effect on the first K principal scores $\xi_{i1}, \xi_{i2}, \dots, \xi_{iK}$.

The effect of early adversity parameterized with different means for the principal scores is not directly interpretable. Therefore, we estimated the effect of early adversity on the mediator as the difference in the mean of the trajectories for the adversity group versus the non-adversity groups (for the cumulative adversity measure, it was the difference in means comparing two adjacent levels of adversity, e.g., for a cumulative score of 3 versus 2). On the basis of Eqs. 8 and 9, we can express the conditional expectation of the mediator process M_{ij} at time point t_{ij} as follows

$$E(M_{ij} | C_{ij}, A_i) = \beta_m C_{ij} + r_{\text{social group}}^m + r_{\text{hydro}}^m + \sum_{k=1}^K [A_i(\tau_1^k - \tau_0^k) + \tau_0^k] \psi_k(t_{ij}) \quad (10)$$

which corresponds to Eq. 1. Next, we express the effect of early adversity on social bond strength using

$$b_1(t) = \sum_{k=1}^K (\tau_1^k - \tau_0^k) \psi_k(t) \quad (11)$$

The effect on the mediator is also time-indexed because we are estimating the effect of adversity on the mediator trajectory across the life span. Integrating $b_1(t)$ over time gives an estimation of parameter β_1 (the β coefficient associated with the effect on the mediator) in Eq. 1

$$\beta_1 : \frac{1}{T} \int_0^T b_1(t) dt \quad (12)$$

The second model: The relationship between early adversity, the mediator, and survival

Our second model estimated direct and mediated effects on the survival outcomes. We adopted a Cox model for the hazard rate $\lambda(t)$. Specifically, we used the following model

$$\begin{aligned} \lambda[t | C_{it}, A_i, M_i(t)] \\ = \lambda_0(t) \exp(\tilde{\beta}_3 A_i + f\{\alpha, M_i(t)\} + \theta_3 C_{it}^S + r_{\text{social group}}^y \\ + r_{\text{hydro}}^y) \end{aligned} \quad (13)$$

where (i) $f\{\alpha, M_i(t)\}$ is the function of the mediator process up to time point t with parameter α characterizing the effect of the mediator process on the hazard rate [note that $M_i(t)$ is replaced by its estimated value $\hat{M}_i(t_{ij})$ from Eq. 8 in practice] and (ii) $\lambda_0(t)$ is the baseline hazard rate, which we specify as following a Gompertz distribution (110, 111)

$$\lambda_0(t) = a \exp(bt) \quad (14)$$

We consider two specifications of f in our case: (i) a model using estimated trajectories of 3-year mediator values that assumes the hazard rate depends on the mediator history in the previous 3 years, $f\{\alpha, M_i(t)\} = \int_{t-3}^t \alpha(s) M_i(s) ds$, and (ii) a model using estimated trajectories of 1-year mediator values that assumes the hazard rate depends on the current mediator value assessed in the year in which survival is assessed, $f\{\alpha, M_i(t)\} = \alpha M_i(t)$. For the 3-year model, we specify $\alpha(t)$ as a linear combination of the spline basis $\alpha(t) = s(t)' \rho$, $s(t) = [1, t, (t - k_1)^2, (t - k_2)^2, \dots, (t - k_L)^2]$ (109), which allows a flexible modeling of how the past mediator affects the survival.

Following the notation in the causal mediation analysis literature (112, 113), let $S_{z,z'}(t)$ denote the survival function when the subject's early adversity status is z and the mediator trajectory counterfactually takes the value as if the subject has early adversity status z' . The adversity status z can be ordinal (for cumulative adversities) or binary ($z = 0$ for the non-adversity group and $z = 1$ for the adversity group) to estimate the total, direct, and mediated effects. For example, if $z = 0$ and $z' = 1$, then $S_{z,z'}(t)$ is the survival function for baboons who did not experience early adversity but whose mediator values are counterfactually calculated as if they did experience early adversity. This strategy is standard in causal mediation research; it allows us to decompose the total effect into the mediated effect and the indirect effect (41, 113–115). On the basis of the model for hazard rate, we can calculate the $S_{z,z'}(t)$ up to time t by integrating the hazard function. Specifically, it takes the following form

$$S_{z,z'}(t) = \exp[-\Lambda_{z,z'}(t)] \quad (15)$$

$$\begin{aligned} \Lambda_{z,z'}(t) = \frac{1}{N} \sum_i^N \sum_j^T \lambda_0(t_{ij}) \exp(\alpha z + \theta_3 C_{ij}^S + f\{\alpha, C_{ij}^S \beta_m \\ + \sum_{k=1}^K \tau_z^k \psi_k(t_{ij})\} s)(t_{ij} - t_{ij-1}) \end{aligned} \quad (16)$$

where $\Lambda_{z,z'}(t)$ is the cumulative hazard function. Once we obtain

$S_{z,z'}(t)$, we can calculate the total effect, direct effect, and mediated effect on the scale of years

$$\text{total effect} = \beta_2 = \int_0^T \{S_{1,1}(u) - S_{0,0}(u)\} du \quad (17A)$$

$$\text{direct effect} = \beta_3 = \int_0^T \{S_{1,0}(u) - S_{0,0}(u)\} du \quad (17B)$$

$$\text{mediated effect} = \beta_1 \gamma = \int_0^T \{S_{1,1}(u) - S_{1,0}(u)\} du \quad (17C)$$

To estimate the effect of the mediator on survival (while controlling for the effects of early adversity on the mediator), we followed similar steps. We calculated the mediator trajectory for a one-unit change in social bond strength while fixing the value of early adversity exposure to one (a value that corresponds to experiencing exactly one source of adversity in the cumulative adversity model or to experiencing adversity in the models for each individual source of adversity). This approach allows us to estimate the consequences of the unit change in the mediator, irrespective of the underlying reason why it might change (i.e., whether because of the effects of early adversity or some other reason), because it controls for the effects of early adversity that act independently of the mediator. Thus, the isolation effect describes how one-unit change in social bond strength affects survival in years, where a one-unit change represents approximately 1.7 SD for social bond strength with females and 1.4 SD for social bond strength with males (1 SD in social bond strength with females = 0.59 social bond strength units and 1 SD in social bond strength with males = 0.70 units).

Causal assumptions

To interpret the above models as causal, three assumptions are required. The first is the assumption of unconfoundedness. In our case, we assume that early adversity is randomly assigned to the subjects in the study. It also assumes that no unmeasured confounding variables cause variation in both early adversity and the mediator or cause variation in both early adversity and survival time, a result that follows if exposure to early adversity is largely determined by natural events that are independent of the subject's individual traits, which is most likely true in our case.

The second is the assumption of sequential unconfoundedness, which states that no unmeasured confounding variables cause variation in both the mediator and survival, besides the observed covariates C and the past history of the mediator M (50, 51, 116). This assumption will be violated if an unmeasured variable (for instance, phenotypic or somatic quality, resulting from either genetic or environmental differences that were not included in our analysis) enhances or reduces both the mediator and survival.

We controlled for confounders as much as possible by including covariates when modeling the mediators and survival, but the sequential unconfoundedness assumption is essentially untestable because it invokes the possibility of an unknown and therefore unidentified covariate (52). To estimate the potential effect of one or more unidentified covariates, we performed a sensitivity analysis (for details, see the "Sensitivity analysis for sequential unconfoundedness" section in Supplementary Text). Specifically, we assumed

the existence of an unmeasured confounder between the mediator and survival that violates the sequential unconfoundedness assumption (117, 118). In our simulation, the correlation between the unmeasured confounder and the mediator or outcome quantifies the degree of violation of the assumption. For a set of prespecified correlation values, we repeated the mediation analysis and examined the sensitivity of the results to the degree of violation of the sequential unconfoundedness assumption. We found that under various degrees of violation of the assumption, the mediated effect was not significant (figs. S3 and S4). Therefore, our conclusions are robust to the untestable assumption. Details of the sensitivity analysis can be found in Supplementary Text and the work of Zeng and colleagues (41).

The third assumption that we impose is independent censoring, i.e., we assume that the time at which a subject drops out of the study before death is random with respect to characteristics of the subject or its experience of early adversity. This assumption is likely to hold in our study because female baboons are censored in only two circumstances in our study: Either they survived to the end of the period of data collection, or the social group in which they lived was dropped for logistical reasons.

Moderation analysis implementation

For the moderation analysis, we modified Eq. 13 by incorporating an interaction term between A and M in the hazard function for survival, as follows

$$\lambda(t | C_{it}^S, A_i, M_{it}) = \lambda_0(t) \exp\{\xi A_i + f\{\alpha, M_i(t)\} + A_i g\{\eta, M_i(t)\} + \theta_3 C_{it}^S + r_{\text{group}}^S + r_{\text{hyrdo}}^S\} \quad (18)$$

Adding this interaction term, $A_i g\{\eta, M_i(t)\}$, in the hazard function allows us to test for the interaction between early adversity and social behavior predicted by the social buffering hypothesis. Therefore, this approach allows us to estimate how the effects of early adversity on survival vary across different levels of the moderator. Similar to the survival model in the mediation analysis, we imposed two specifications for the interaction term $A_i g\{\eta, M_i(t)\}$: (i) a 3-year model $g\{\eta, M_i(t)\} = \int_{t-3}^t \eta(s) M_i(s) ds$ and (ii) a 1-year model $g\{\eta, M_i(t)\} = \eta M_{it}$. For the 3-year model, we use $\int_0^T \eta(s) ds$ as the summary for the moderation effect. When $\eta < 0$, the model indicates that a higher value for the moderator buffers the negative effects of early adversity. When $\eta > 0$, the model implies that the moderator amplifies these negative effects.

Supplementary Materials

This PDF file includes:

Supplementary Text
Figs. S1 to S5
Tables S1 to S6

[View/request a protocol for this paper from Bio-protocol.](#)

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