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Grace Cayless March 30, 2025

Effects of Respiratory Outbreaks During Early Life on Lifespan and Survival Probabilities in Wild Eastern Chimpanzees (*Pan troglodytes*) in Gombe National Park, Tanzania

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Abstract

Effects of Respiratory Outbreaks During Early Life on Lifespan and Survival Probabilities in Wild Eastern Chimpanzees (*Pan troglodytes*) in Gombe National Park, Tanzania
By Grace Cayless

Early life adversity (ELA) has been linked to poor health and behavioral outcomes in many long-lived social mammals, including humans. Currently, the long-term effects of cumulative adversity have only been studied in two primate species, with conflicting results – in female baboons, cumulative ELA predicted a shortened lifespan, while the experience of 3+ sources of ELA was correlated with a 70% reduction in later-life mortality risk for mountain gorillas. Chimpanzees, like humans, exhibit lengthy, defined stages of development, during which they face various sources and magnitudes of adversity while forming complex relationships with conspecifics. This makes them quality models for investigating how ELA influences health and survival outcomes. Health adversity has not been addressed in previous primate studies of ELA, but respiratory outbreaks are known to create severe energetic stress in wild chimpanzees. Therefore, exposure to respiratory outbreaks during development is a potentially significant source of early life adversity. Here, 'exposure' refers to being present in a community during a respiratory outbreak, rather than confirmed infection with a specific pathogen. To explore this further, I utilized long-term field data collected on wild chimpanzees living in Gombe National Park, Tanzania to evaluate the impact of exposure to respiratory outbreak during critical developmental windows on lifespan and survival probabilities. I found that experiencing fatal outbreaks in-utero significantly reduced the likelihood of surviving to age 10. However, post-birth exposure to fatal outbreaks in the first five and 10 years of life decreases the risk of death with age, seemingly creating a protective effect. Furthermore, I found that the highest counts of cumulative exposures in the first 10 years of life are associated with a decreased risk of death with age. Overall, my findings suggest that different mechanisms mediate the consequences of in-utero and post-birth respiratory outbreak exposures, such that in-utero exposures have a detrimental impact, while post-birth exposures may bolster immune development. Future research should focus on evaluating the impact of specific pathogens, maternal health, and the timing of exposure during these developmental windows.

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Overview

Early life adversity (ELA) has been linked to poor health and behavioral outcomes, such as reduced lifespan, in a range of long-lived social mammals, including humans (Felitti et al., 1998; reviewed in Dettmer & Chusyd, 2023). For example, events of physical or psychological abuse during childhood have been shown to result in increased risk of substance abuse (Mersky & Topitzes, 2010), while experiencing neighborhood violence was found to accelerate epigenetic aging (Jovanovic et al., 2016). However, the mechanisms behind these outcomes remain unclear, and isolating the unique and interacting contributions of multiple adversities in humans can be ethically and logistically challenging. Therefore, studies of ELA in wild primates have begun to yield valuable insights into these linkages.

At present, ELA has only been examined in two nonhuman primate (hereafter: primate) species – baboons and mountain gorillas – with conflicting results. For baboons, potential sources of adversity were defined as drought in the first year of life, high group density, low maternal dominance rank, low maternal social connectedness, maternal loss before age four, and the presence of a competing sibling. Female baboons who experienced multiple adversities had significantly shorter lifespans, which impacted their reproductive success; they were also more socially isolated from other females in adulthood (Tung et al., 2016). In contrast, a study of wild mountain gorillas found that cumulative early life adversity did not predict reduced lifespans. Sources of adversity were defined as paternal or maternal loss, group instability, infanticide of a group member, having few age-mates, and the presence of a competing sibling. Experiencing more than three of these adversities led to a 70% *reduction* in risk of death, suggesting that gorillas may be more resilient to ELA (Morrison et al., 2023). This is potentially due to their high-resource, low-competition environments, as well as their cohesive family units (Morrison et

al., 2021). In humans, close familial/friendly relationships have been shown to reduce the effects of stress on children (Chen et al., 2017). Ultimately, this contrast emphasizes how species-specific contexts, such as social structure and ecological stability, can shape resilience.

As humans' closest living relatives, chimpanzees can shed further light on the evolution of development and resilience. Like humans, chimpanzees exhibit lengthy, defined stages of infancy, juvenility, and adolescence, during which they navigate a variety of sources and magnitudes of adversity. Infants are cared for primarily by mothers who make a significant energetic investment, providing the sole source of nutrition for the first three to five years, followed by further care and socialization throughout juvenility (Goodall, 1986; Stanton et al., 2014). Due to the primacy of this relationship, a significant source of adversity is maternal loss, which causes reductions in lifespan even for young chimpanzees who have already been weaned and are thus nutritionally independent (Stanton et al., 2020). Beyond maternal loss, other sources of adversity have yet to be identified and investigated in wild chimpanzees.

Respiratory Disease as a Potential Source of Adversity

One potentially important source of adversity is exposure to respiratory disease outbreaks. In this context, 'exposure' refers to being present in a community during a respiratory outbreak, rather than confirmed infection with a specific pathogen. Respiratory illness significantly contributes to wild chimpanzee mortality at most field sites (Williams et al., 2008; Emery Thompson et al., 2018), and abnormal respiratory symptoms were found to have the highest monthly prevalence of all clinical signs in a wild population (Lonsdorf et al., 2018). Studies of respiratory disease in wild populations have found that outbreaks are a significant source of energetic stress for chimpanzees (González et al., 2020). Biomarkers of immune function and energy balance, such as cortisol, neopterin, and C-peptide, have demonstrated the

energetic costs of respiratory outbreaks, providing insights into the physiological impacts of these events (Emery Thompson et al., 2008; Wu et al., 2018; Behringer et al., 2020). Given this high level of morbidity and mortality, and the potential energetic costs, exposure to respiratory outbreaks may be a significant form of early adversity. Multiple exposures may compromise the developing immune system, increasing susceptibility to long-term health risks.

The hypothalamic-pituitary-adrenal (HPA) axis is a neuroendocrine system that regulates the body's physiological response to stress (Danese & McEwen, 2011) via hormonal secretions such as cortisol. Higher levels of cortisol indicate increased stress; chronic activation of the HPA axis may result in dysregulation across cardiovascular, immune, and neuroendocrine systems (Sapolsky, 2002). During a respiratory outbreak in Taï National Forest (Ivory Coast), urinary cortisol was found to increase 10-fold in symptomatic chimpanzees, and diurnal cortisol slopes were flattened (Behringer et al., 2020). This finding indicates that a) disease outbreaks produce physiological stress, and b) cortisol may mediate infection via its impacts on the immune system. Therefore, chronic HPA axis activation (such as that produced by ELA (Herman et al., 2016)) may impair immune responses, increasing the risk of mortality during later-life health challenges.

Neopterin functions as a marker of innate immune activation, and is released when macrophages are triggered in the early immune response. Elevated neopterin levels are correlated with disease severity and mortality risk in humans (Denz et al., 1990) and chimpanzees (Wu et al., 2018). Studying the aforementioned respiratory outbreak at Taï, Behringer et al. (2020) also found that cortisol was positively correlated with neopterin levels, reinforcing the link between stress and immune activation. Investigation of a different respiratory outbreak at Taï revealed that individuals who died from respiratory illness had significantly higher pre- and mid-outbreak

neopterin levels (Wu et al., 2018); this suggests that when the immune system is already challenged, its response to respiratory infection is compromised. This underscores the potential role of early immune stressors, such as those created by exposure to disease outbreaks, in increasing mortality risk later in life.

Finally, C-peptide of insulin has been used to provide indications of energy balance (Sherry & Ellison, 2007). As insulin is produced in the pancreas, the C-peptide molecule is released into the blood in equal amounts. Because insulin regulates the uptake and storage of glucose, and provides a signal of energy balance to the brain, measurements of C-peptide can provide assessments of this equilibrium. In the Kanyawara community of Kibale National Park (Uganda), the energy balance of male chimpanzees was shown to be severely and negatively impacted by a respiratory outbreak, despite favorable feeding conditions (Emery Thompson et al., 2008). This suggests that even when energy costs are offset by food intake, activation of the immune system is demanding enough to produce a negative energy balance.

Like humans, chimpanzees engage in a stronger, nonspecific early response to bacterial and viral stimulation than Asian and African monkeys (Hawash et al., 2021). Species with larger body sizes, slow life histories (Xu et al., 2024), and high sociality (Kappeler et al., 2015) experience an increase in pathogen exposure over their lifetimes. According to life history theory, this higher pathogenic burden would result in a greater allocation of energy towards maintenance and repair processes, rather than growth and reproduction (Behringer et al., 2019; Negrey et al., 2021). When an individual is exposed to early life adversity, the costs of this consistently high energetic investment may become compounding, restricting the ability to maintain energy balance and immune function. Ultimately, this could result in an impaired immune response, which may increase mortality risk and contribute to a reduced lifespan.

Critical Periods for Exposure

In-utero

For humans, exposure to pathogens in-utero can have especially strong consequences, potentially resulting in increased susceptibility to later-life health challenges. During pregnancy, viral clearance mechanisms are sub-optimal and often generate widespread inflammation, delaying recover from viral infection (Oseghale et al., 2022). This prolonged inflammation can increase disease severity and cause maternal and fetal health problems. Studies in humans have shown that exposure to influenza, RSV, and COVID-19 in-utero increases the risk of low birthweight, preterm birth, and short gestation lengths (Dorélien et al., 2019; Trinh et al., 2024).

In chimpanzees, an evaluation of risk factors for respiratory illness in a wild population revealed that infants who died of suspected respiratory disease had mothers who exhibited respiratory signs at the same time (Emery Thompson et al., 2018). This suggests that the negative consequences of pathogen exposure may result from both direct physiological impacts on the infant as well as indirect impacts via maternal health complications and suboptimal care from a sick mother.

In addition to these direct physiological impacts of infection, maternal stress plays a significant role in shaping offspring outcomes. Human studies have shown that both social (e.g., loss of a partner or close relative: Class et al., 2011) and environmental (e.g., natural disasters: Glynn et al., 2001) stressors can lead to lower birthweight and shorter gestational lengths. Pandemic-related stress has been shown to result in an impaired mother-infant bond, leading to alterations in infants' ability to manage emotions and behavior (Provenzi et al., 2021). Furthermore, infants whose mothers reported higher levels of distress during the COVID-19

pandemic had smaller white matter and left amygdalar volumes, reinforcing that maternal stress may lead to alterations in social and emotional development (Weiner et al., 2024).

Pregnant chimpanzees without clinical signs of illness display moderately elevated levels of neopterin, indicating a heightened immune response (Negrey et al., 2021). Cortisol levels also peak during late pregnancy in chimpanzees (Smith et al., 1999); this coincides with an increased probability of malaria parasite detection (De Nys et al., 2014) and gastrointestinal parasite shedding (Phillips et al., 2020) towards the end of pregnancy. Cortisol elevation is potentially related to immune impairment, which would result in increased susceptibility to malarial and gastrointestinal parasite infections. Overall, the increased level of energetic stress during pregnancy likely results in both an elevated risk of infection and more serious consequences if infection should occur.

Infancy and Juvenility/Adolescence

In human infants, immune function is especially weak at birth, making them vulnerable to viral and bacterial infections (Simon et al., 2015). This reduced functioning is likely due to the need to tolerate maternal antigens and cope with the energetic stress of development. Throughout infancy and adolescence, the immune system gradually matures; by early adulthood it is typically more robust, and individuals experience fewer infections. Studies of neopterin levels in humans have reflected this pattern; young children have especially high concentrations that decline throughout development until around age 20 (Fuchs et al., 1992; Winkler et al., 2003). These levels reflect a highly active immune system, reacting to more frequent exposures to new pathogens; with age and exposure, the immune response becomes more refined. This relationship has also been identified in bonobos, as neopterin levels were seen to decline after birth and stabilize between four and five years (Behringer et al., 2017).

Human studies have found that early life respiratory infection and subsequent immune system activation may result in structural damage to the lungs and altered immune development, changes which last into adulthood (Achten et al., 2021). Furthermore, early exposure to lower respiratory tract infection was associated with a nearly doubled risk of premature adult death from respiratory disease (Allinson et al., 2023). This suggests that, like in-utero exposures, disease outbreaks experienced during infancy can result in negative health outcomes in adulthood.

Importantly, pathogen exposure also shapes the immune system's development and memory, impacting future responses to subsequent infections (Tregoning & Schwarze, 2010; Simon et al., 2015). An immune system that is never challenged will not hold this reservoir of information, and is thus more vulnerable to severe infections later on. This is typically addressed with vaccination in humans, wherein weakened or inactive pathogenic agents stimulate immunity, allowing for infants and adolescents to be exposed without severe risk (Laupèze et al., 2021).

In wild primate populations, vaccines are not employed; the development of immunological memory relies on natural exposure to pathogens. This would suggest the need for balance between complete absence of exposure (and subsequent lack of immunological memory) and too many exposures (which may overwhelm the immune system). In other words, a certain degree or number of exposures may build immunity and resilience, potentially extending longevity. Evidence of this need for immunocompetence has been found in comparisons of neopterin levels between wild and zoo-living chimpanzees; in the wild, individuals had consistently elevated neopterin concentrations, indicating a permanently challenged immune system (Behringer et al., 2019).

Purpose and Objectives

Certain developmental periods have been shown to be critical for downstream development and health in humans (Ben-Shlomo & Kuh, 2002) and other wild primates (Dettmer & Chusyd, 2023). In previous studies of cumulative adversity in baboons and mountain gorillas, poor health as a source of adversity has not been addressed (Tung et al., 2016; Morrison et al., 2023). However, respiratory outbreaks have a clear impact on energetic stress levels in wild chimpanzees (Emery Thompson et al., 2008; Wu et al., 2018; Behringer et al., 2020). Therefore, exposure to respiratory outbreak during development is a potentially significant source of early life adversity. To examine this, I focused on exposures to respiratory outbreaks in the in-utero, infancy, and juvenile/adolescent periods in a wild chimpanzee population in Gombe National Park, Tanzania.

I formulated two predictions for the developmental periods of interest: 1) exposure to respiratory outbreak in-utero will have a strong negative impact on lifespan and survival probabilities with age; and 2) both excessive and minimal cumulative exposures in infancy (birth to age five) and early adolescence (birth to age ten) will have a negative impact on lifespan and survival probabilities.

This work will provide a foundation for further research into the mechanisms through which early life respiratory outbreak exposure influences immune function, health, and longevity, and contribute to a deeper understanding of how early life adversity impacts long-term health and survival.

Methods

This study focused on the Kasekela and Mitumba communities in Gombe National Park, located in western Tanzania. Opportunistic and standardized behavioral and health data has been

collected on these groups since the 1960s (Kasekela) and 1990s (Mitumba). For the periods of interest (1966-2024), the population size of Kasekela ranged from 39-62; the Mitumba community ranged from 20-31 (Wilson et al., 2020; Gombe PI consortium, unpublished data).

Demographic Data and Study Subjects

Chimpanzees live in multimale, multifemale communities with flexible fission-fusion grouping patterns to cope with variation in food availability (Furuichi et al., 2009). Average gestation length is 228 days (Wallis, 1997). Although there is variation in weaning patterns, infants usually become nutritionally independent around age five (Lonsdorf et al., 2020). There is a lengthy post-weaning period of dependence on the mother, and this period of juvenility and early adolescence is associated with significant social re-orientation, as well as the learning of valuable skills such as foraging and tool use (Reddy et al., 2022). Males are the philopatric sex, while females typically emigrate around ages 10-15 (Walker et al., 2018). The average life expectancy for wild chimpanzees is 30 years for males, and 35 years for females (Wood et al., 2017).

The Kasekela and Mitumba chimpanzees are habituated and individually recognizable to observers, allowing for detailed demographic records to be kept on each animal. The base demographic dataset has information on birth and death events, as well as community membership, for 370 individuals. Birthdates are assigned as the midpoint of the last observation of a mother without an infant and the first observation with an infant. Departure dates (when an individual exits the community) are assigned based on the last date an individual was observed; they are considered dead when strong evidence (such as observable poor health prior to disappearance) is available; they are considered “permanently disappeared” when there is

uncertainty as to whether the individual died or could have emigrated (which applies only to females as the dispersing sex).

Due to chimpanzees' fission-fusion social system, and the observational nature of our data, there is occasionally uncertainty about individual birthdates, and thus age at departure. To combat this and ensure accurate calculations of each developmental window, I removed 122 individuals whose dataset entry date and estimated birthdate differed by more than 6 months, resulting in a N = 248 subjects. Additionally, I removed nine individuals born in Kasekela before 1966 and 13 born in Mitumba before 1996, as this preceded the beginning of standardized data collection; 1 individual born in the unhabituated Kalande community was also removed.

For nine individuals classified as permanently disappeared without evidence of death, I applied probabilistic criteria to decide whether to include them as dead or right-censor them (i.e., declare their survival time unknown because they were still alive when the observational period ended). I classified three young males who disappeared before the age of five as dead; males are philopatric, so it is highly unlikely that they had emigrated to a different community, especially at such a young age. Three young individuals were removed entirely due to uncertainty surrounding their identities. I right-censored the remaining six females because they disappeared around ages 9-11, meaning they likely emigrated to a different community. All other individuals who were alive at the end of the study period were right-censored. The final dataset was comprised of 222 individuals.

Outbreak Periods

Given that the primary variable of interest was exposure to outbreak throughout development, I had to define the periods of respiratory outbreaks for both KK and MT. Health data at Gombe primarily consists of observations of clinical signs; respiratory illness was

indicated by coughing, runny nose, and sneezing. Unlike human epidemiological studies, we are typically unable to confirm outbreaks and diagnoses in real time at Gombe; even in retrospect, we can rarely identify the specific pathogen associated with a given outbreak. Therefore, I focus here on incidence of clinical signs to define the beginning and end of outbreaks (Wolf et al. 2019a, b).

A combination of field notes and weekly/monthly health charts were utilized to construct weekly counts of respiratory symptoms. Clusters were defined as starting when two or more individuals exhibited the same clinical signs, and ending when no individuals were exhibiting signs. Previous studies of respiratory illness at Gombe have defined "outbreak" as at least 20% of the population showing clinical signs, and at least one individual dying (Williams et al., 2008). Based on these criteria, 10 outbreaks were identified. However, I also noted several periods in which over 20% of the population exhibited respiratory symptoms, but no deaths attributable to respiratory illness occurred. Given the potential significance of such high case counts, I created a 'major outbreak' category (describing nonfatal outbreaks that had incidence over 20%, thus aligning with existing criteria) as well as a 'minor outbreak' category (incidence above 10%, but below 20%), allowing for exploration of outbreaks with a lower, but still potentially significant, level of population impact).

I overlaid the start and end dates for each outbreak period with dates of the three developmental periods of interest for each individual: in-utero (from conception to birth, calculated as the birthdate minus 228 days), birthdate to date age five, and birthdate to date age 10. This comparison of timeframes allowed me to determine which outbreaks an individual was present during.

Analyses

To examine whether early life outbreak exposure predicted survival outcomes, I utilized a combination of Cox proportional hazards models (Cox, 1972) and categorical analyses (Fisher's exact tests and chi-square tests (Agresti, 1992)). The Cox proportional hazards model is used to analyze the relationship between time to an event (in this case, death) and predictor variables (outbreak); it estimates the effect of these variables on the hazard of the event occurring. A key assumption of this model is the hazard ratios between different groups remain constant over time. I used the cox.zph() function in the R "survival" package to confirm that all models run in this study met the proportional hazards assumption. Separate Cox models were fitted to assess each developmental stage and exposure category, as outlined below.

I. In-utero

I assessed in-utero exposure to fatal and nonfatal outbreaks; the nonfatal category combined major and minor outbreaks. For the fatal outbreak model, I included all individuals meeting the initial inclusion criteria (e.g., birthdate known within six months, etc.), resulting in a sample of 222 individuals. For the nonfatal outbreak model, individuals had been exposed to a fatal outbreak were excluded from the dataset, leaving a sample of 202.

II. Birth to age five

For this period, the range of total outbreak exposures was 0 to 6. To account for this wider range, as well as for overlap in fatal and nonfatal outbreaks, I assessed the impacts of minor, major, and fatal outbreaks separately. This analysis included only individuals from the initial dataset who had survived to age five (N = 111). I chose this threshold because a) infant mortality is high (Hill et al., 2001), and b) to minimize the confounding effect of longer-lived individuals simply accumulating more outbreak exposures.

III. Birth to age 10

From birth to age 10, the range of possible outbreak exposure counts was 0 to 10 (see Figure S1); as before, I evaluated the impacts of minor, major, and fatal outbreaks separately. Additionally, I created a variable comparing ≤3, 4-6, and 7+ outbreaks, based on examination of the distribution for total possible exposures (see Figure S1); this was done to address the 'excessive' and 'minimal' levels of exposure described in my second prediction. These models were fit with both the 'survived to five' dataset, as well as a more restricted 'survived to 10' dataset (N = 81). The restrictive dataset served to minimize the aforementioned confounding effect produced by longer-lived individuals.

I generated Kaplan-Meier survival curves (Kaplan & Meier, 1958) to visualize differences in survival probabilities across exposure levels. In addition to the Cox models, Fisher's exact tests and chi-square tests were utilized to assess the categorical outcome of survival to age 10 (the age which individuals begin social orientation in their own groups (males) or emigrate (females)). Fisher's exact test was used when expected cell counts were too low for a chi-square test. For these tests, we manually censored the datasets so as to exclude individuals who were alive at the end of the study period but born after May 2014 (and would thus not yet have reached age 10).

Results

Outbreak Periods

Examination of the weekly respiratory symptom counts revealed a total of 37 outbreaks. Of these, 28 occurred in the Kasekela (KK) community, and nine in the Mitumba (MT) community (Figure 1). Using the aforementioned incidence criteria, I identified nine fatal, 21 major, and seven minor outbreaks (see Figure 1; Table 1).

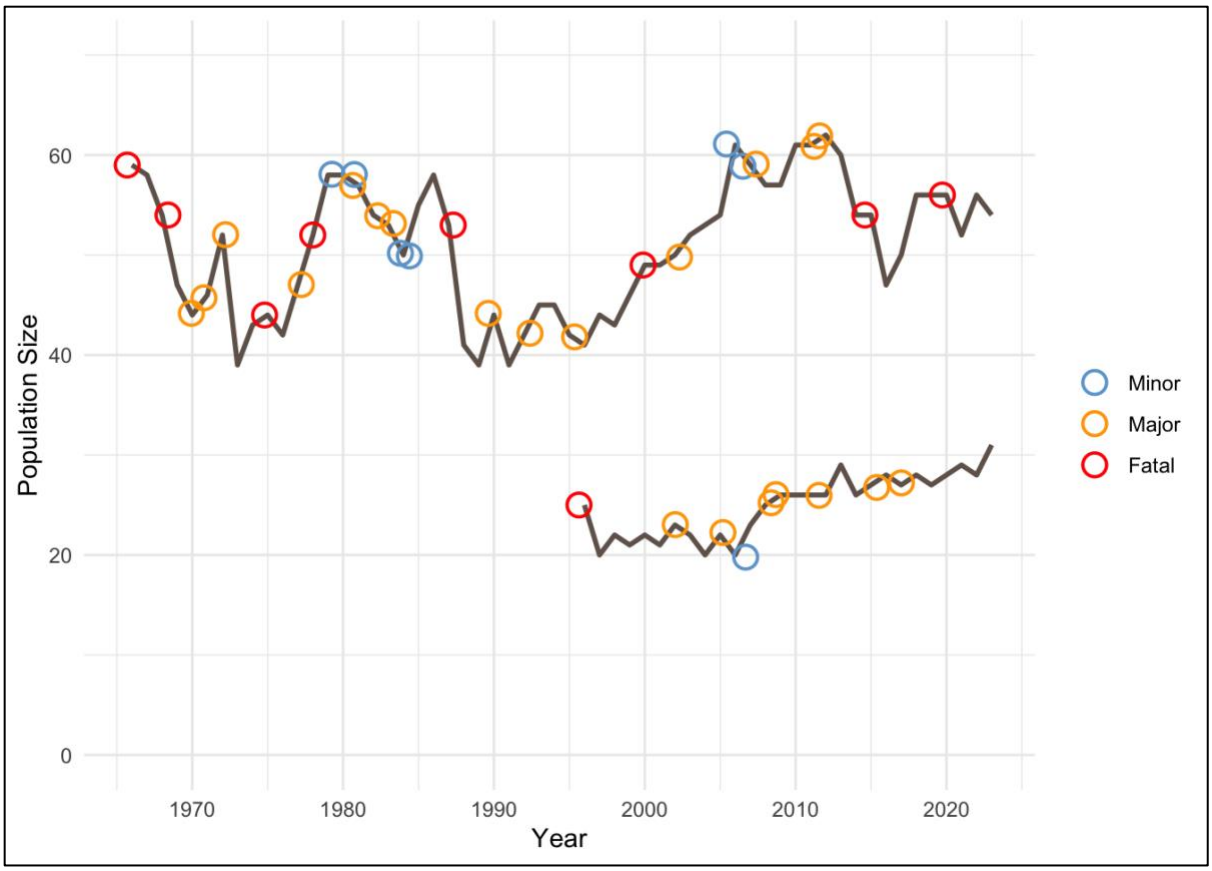

Figure 1. Population Sizes and Outbreaks from 1996 to 2024 in the Kasekela and Mitumba Communities. Population sizes for 1996-2024 for Kasekela (upper) and Mitumba (lower). Years when outbreaks occurred are circle in blue (minor), orange (major), or red (fatal). Nine fatal, 21 major, and seven minor outbreaks were identified.

Table 1. List of Outbreaks from 1996 to 2024 in the Kasekela and Mitumba Communities. List of outbreak years, including the community affected, start month, case counts and percentage of community affected.

Year	Community	Start Month	Case Count	% Affected	Outbreak Type
1966	KK	September	12	20.3	Fatal
1968	KK	January	31	57.4	Fatal
1970	KK	October	14	31.8	Major
1971	KK	February	22	47.8	Major
1972	KK	May	19	36.5	Major
1975	KK	February	25	56.8	Fatal
1977	KK	October	22	46.8	Major
1978	KK	August	15	28.8	Fatal
1980	KK	March	8	13.8	Minor
1980	KK	May	6	10.3	Minor
1981	KK	June	31	54.4	Major
1982	KK	August	20	37	Major
1983	KK	September	20	37.7	Major
1984	KK	May	6	12	Minor
1984	KK	June	6	12	Minor
1987	KK	May	16	30.2	Fatal
1990	KK	March	24	54.5	Major
1992	KK	March	13	31	Major
1995	KK	May	18	42.9	Major
1996	MT	March	21	84	Fatal
2000	KK	February	34	69.4	Fatal
2002	KK	September	24	48	Major
2002	MT	September	5	21.7	Major
2005	MT	February	5	22.7	Major
2006	MT	March	3	15	Minor
2006	KK	June	10	16.4	Minor
2007	KK	March	7	11.9	Minor
2007	KK	August	15	25.4	Major
2008	MT	December	11	44	Major
2009	MT	October	20	76.9	Major
2011	KK	October	54	88.5	Major
2012	MT	June	6	23.1	Major
2012	KK	June	17	27.4	Major
2015	KK	March	23	42.6	Fatal
2015	MT	December	6	22.2	Major
2017	MT	May	17	63	Major
2020	KK	February	27	48.2	Fatal

In-utero

There were no significant associations between either outbreak category (0 vs. 1 fatal outbreak, or 0 vs. 1+ nonfatal outbreaks) and risk of death with age (see Table 2). However, it was notable that fatal outbreaks were correlated with an increased risk of death (HR > 1), while nonfatal outbreaks were correlated with decreased risk (HR < 1).

Visual inspection of the Kaplan-Meier survival curves for fatal in-utero outbreaks (Figure 2) suggested that a difference may exist in the first 10 years of life. A Fisher's exact test confirmed this, revealing that the likelihood of surviving to age 10 is significantly reduced for individuals who experienced a fatal outbreak in-utero (odds ratio of 0.265, $p = 0.038$). A chi-square test comparing nonfatal outbreaks with survival to age 10 did not yield a significant result ($x^2 = 1.36$, $df = 1$, $p = 0.244$), providing further evidence that nonfatal outbreaks in-utero do not impact risk of death (also see Figure 3).

Table 2. No Associations for Exposure to Fatal or Nonfatal Outbreaks In-Utero and Risk of Death with Age. Results of separate Cox proportional hazards models examining the effects of fatal and nonfatal outbreaks in-utero. Results for fatal outbreaks are from a model fitted with the all-inclusive dataset (N = 222), while results for nonfatal outbreaks are from a model fitted with the dataset in which fatal exposures were removed (N = 202).

Exposure Type	β	HR	SE (β)	z	p
Fatal Outbreak (0 vs. 1)	0.378	1.459	0.274	1.378	0.168
Nonfatal Outbreak (0 vs. 1+)	-0.321	0.725	0.205	-1.569	0.117

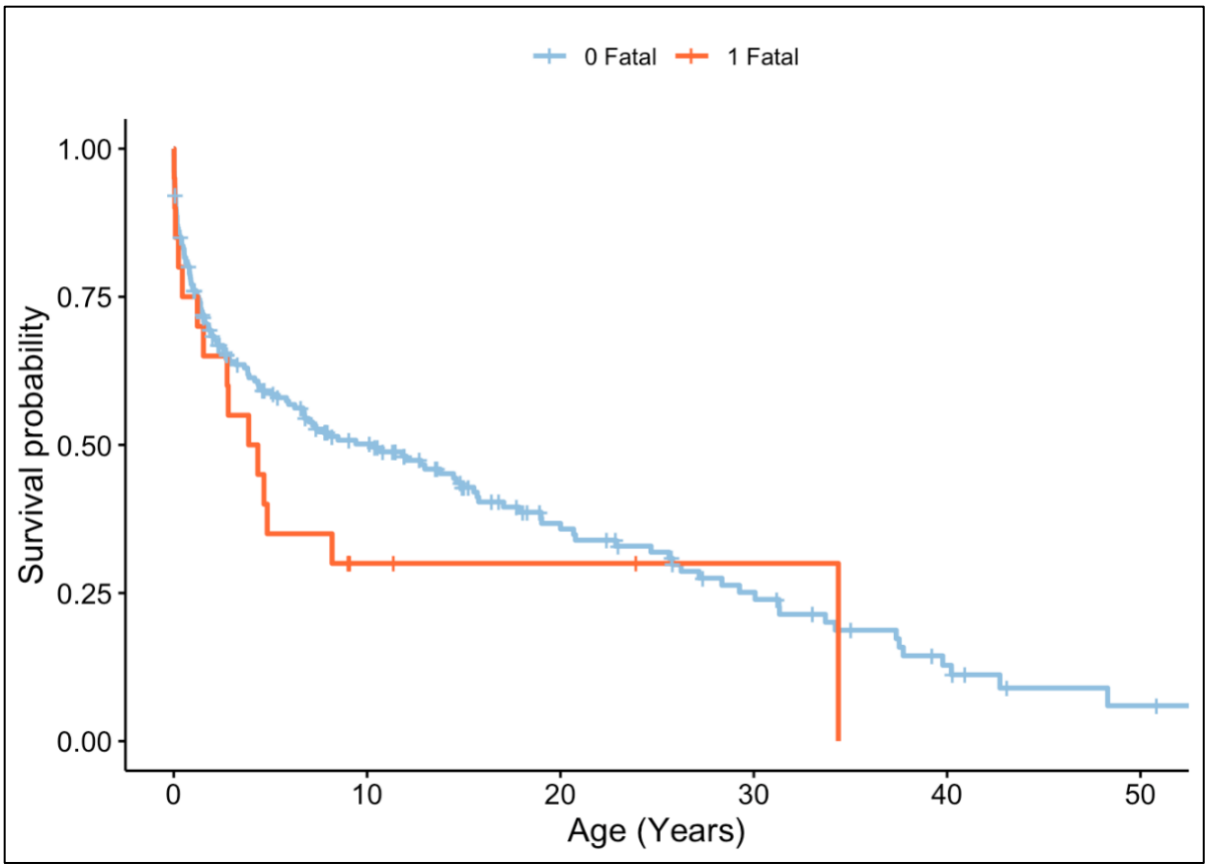

Figure 2. No Association for Risk of Death with Age for Individuals Exposed to 0 vs. 1 Fatal Outbreaks In-utero. Survival curves comparing the effect of exposure to fatal outbreak in-utero on hazard ratios ($p = 0.168$; $N = 222$). Visual inspection of years 0-10 reveals a marked difference in survival probability.

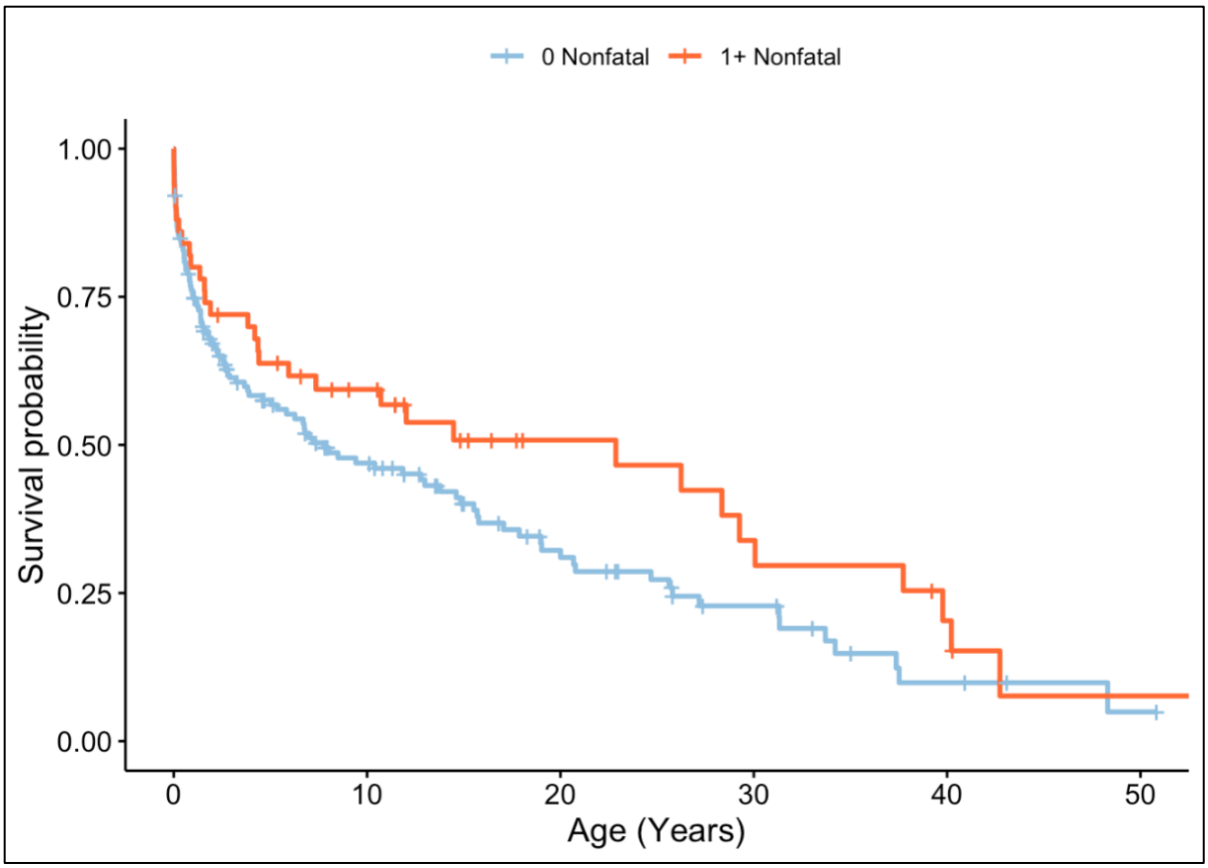

Figure 3. No Association for Risk of Death with Age for Individuals Exposed to 0 vs. 1+ Nonfatal Outbreaks In-utero. Survival curves comparing the effect of exposure to nonfatal outbreaks in-utero on hazard ratios (p = 0.117; N = 202).

Birth to Age Five

There were no associations between minor, major, or fatal outbreak exposures and risk of death (see Table 3). Visual inspection of the Kaplan-Meier survival curves for fatal outbreak exposure revealed a potential difference following age 15 (see Figure 4), with exposed individuals exhibiting decreased risk with age. Unlike the results of in-utero exposure, experiencing 1+ fatal outbreaks in the first five years is correlated with a decreased risk of death (HR < 1).

Table 3. No Associations for Exposure to Minor, Major, or Fatal Outbreaks from Birth to Age Five. Results of separate Cox proportional hazards models examining the effects of minor, major, and fatal outbreaks from birth to age five. All results are from a model fitted with a dataset restricted to individuals who survived to age five (N = 111).

Exposure Type	β	HR	SE (β)	z	p
Fatal Outbreak (0 vs. 1+)	-0.419	0.658	0.283	-1.481	0.139
Major Outbreaks (0-3)	-0.017	0.983	0.149	-0.112	0.91
Minor Outbreaks (0-2)	0.0545	1.056	0.150	0.362	0.717

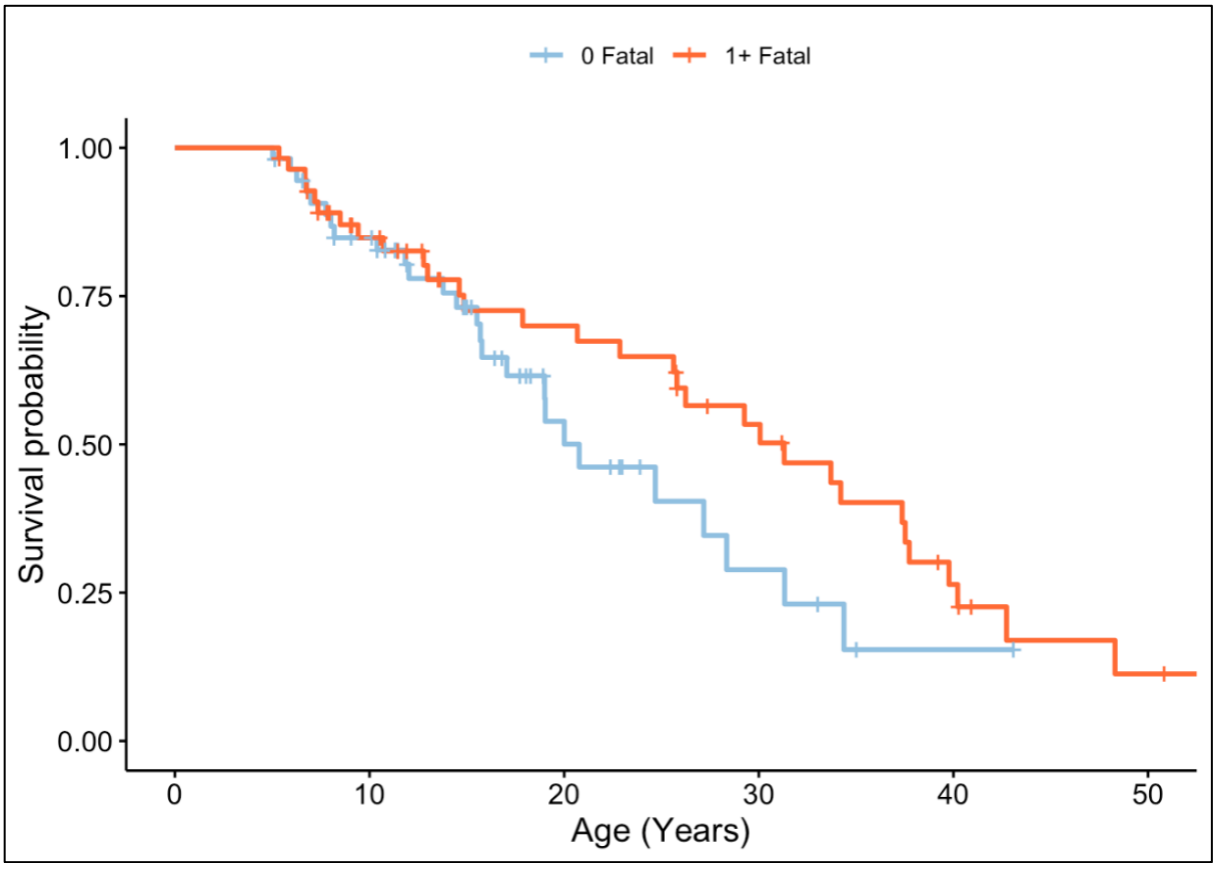

Figure 4. No Association for Risk of Death with Age for Individuals Exposed to 0 vs. 1+ Fatal Outbreaks from Birth to Age Five. Survival curves comparing the effect of exposure to fatal outbreaks from birth to age five (p = 0.139; N = 111). Visual inspection indicates a potential difference after age 15, with exposure to fatal outbreak decreasing the risk of death.

Birth to Age 10

I. Survival to Age Five Dataset

Utilizing the 'survived to age five' sample, I examined the impacts of exposure to minor, major, and fatal outbreaks from birth to age 10, as well as cumulative exposures to ≤3, 4-6, or 7+ outbreaks (see Table 4). Fatal outbreaks were associated with decreased risk of death with age ($p = 0.0217$; Figure 5). Experiencing 7+ total outbreaks was also associated with decreased risk of death with age ($p = 0.054$; Figure 6). Major and minor outbreak exposures were not associated with risk of death.

Table 4. Exposure to Fatal Outbreaks and 7+ Cumulative Exposures from Birth to Age 10 Decreases Risk of Death; No Association for Exposure to Minor, Major, or More Than Three Outbreaks. Results of separate Cox proportional hazards models examining the effects of minor, major, fatal, and total outbreak exposures from birth to age 10. Exposure to more fatal outbreaks was significant at $p < 0.05$. Exposure to 7+ total outbreaks was significant at $p > 0.10$. All results are from a model fitted with a dataset restricted to individuals who survived to age five (N = 111). For total exposures, the reference group is ≤3; the first value in the table represents the results of the model for the 4-6 group; the second value is the results for the 7+ group.

Exposure Type	β	HR	SE (β)	z	p
Fatal Outbreaks (0-2)	-0.453	0.636	0.198	-2.295	*0.0217* *
Major Outbreaks (0-5)	-0.184	0.832	0.137	-1.339	0.181
Minor Outbreaks (0-2, 4)	-0.050	0.951	0.111	-0.45	0.653
Total (≤3 vs. 4-6 vs. 7+)	-0.238, -0.754	0.788, 0.471	0.309, 0.392	-0.769, -1.923	0.4417, *0.054* (†)

* $p < 0.05$
† $p < 0.10$

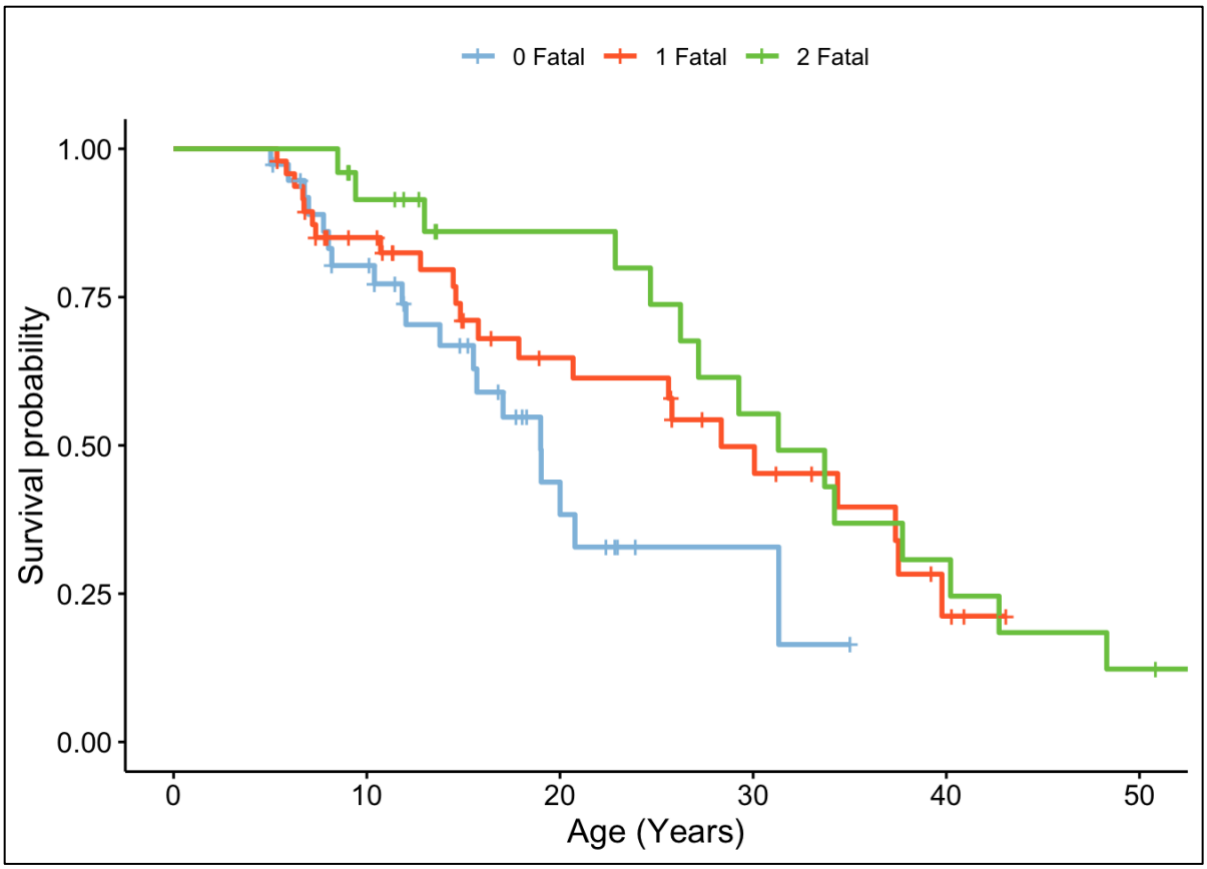

Figure 5. Exposure to More Fatal Outbreaks from Birth to Age 10 Decreases Risk of Death (Survived to Age Five Dataset). Survival curves comparing the effects of exposure to 0, 1, and 2 fatal outbreaks from birth to age 10 (p = *0.0217*); fitted with the dataset restricted to individuals who had survived to age five (N = 111).

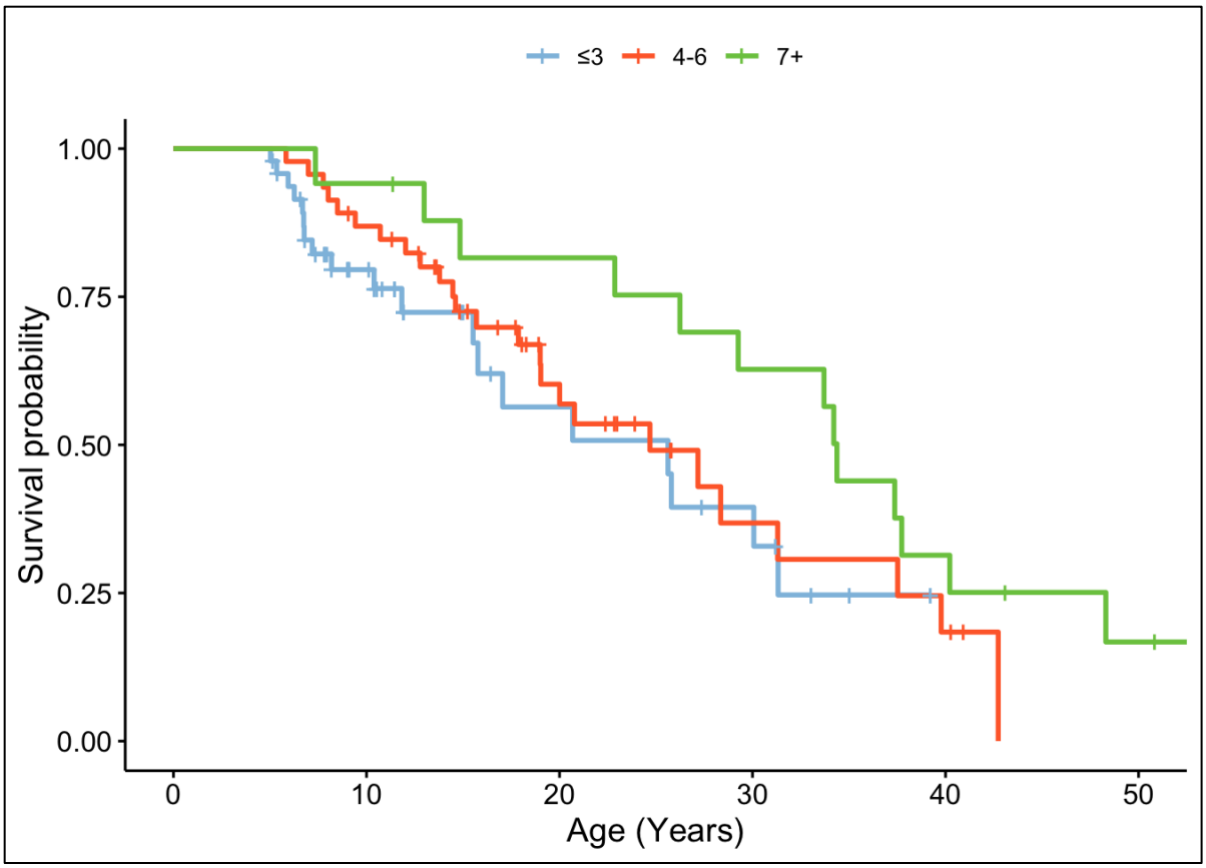

Figure 6. Exposure to 7+ Outbreaks from Birth to Age 10 Decreases Risk of Death (Survived to Age Five Dataset). Survival curves comparing exposures to ≤3, 4-6, and 7+ outbreaks from birth to age 10 ($p = 0.054$); fitted with the dataset restricted to individuals who had survived to age 5 (N = 111).

II. Survival to Age 10 Dataset

The 'survived to age 10' sample was utilized in order to account for the opportunity for longer-lived individuals to naturally accrue more outbreak exposures. Here, experiencing more fatal outbreaks was significant at the $p < 0.10$ level ($p = 0.052$), and associated with decreased risk of death with age (Figure 7). Unlike the results from models utilizing the survival to age five dataset, experiencing 7+ outbreaks did not yield a significant association, but the same trend of decreased risk of death with age is visible in the Kaplan-Meier survival curves (Figure 8). There was no association for minor or major outbreaks and risk of death (Table 5).

Table 5. Exposure to Fatal Outbreaks from Birth to Age 10 Decreases Risk of Death; No Association for Exposure to Minor, Major, or More Than Three Outbreaks. Results of separate Cox proportional hazards models examining the effects of minor, major, fatal, and total outbreak exposures from birth to age 10. to more fatal outbreaks was significant at $p < 0.10$. Unlike the results of the survived to age five dataset, experiencing 7+ outbreaks was not associated with risk of death. All results are from a model fitted with a dataset restricted to individuals who had survived to age 10 (N = 81). For total exposures, the reference group is ≤3; the first value in the table represents the results of the model for the 4-6 group; the second value is the results for the 7+ group.

Exposure Type	β	HR	SE (β)	z	p
Fatal Outbreaks (0-2)	-0.465	0.628	0.240	-1.94	*0.052* †
Major Outbreaks (0-5)	-0.0066	0.993	0.180	-0.037	0.971
Minor Outbreaks (0-2, 4)	-0.052	0.949	0.131	-0.401	0.689
Total (≤3 vs. 4-6 vs. 7+)	-0.031, -0.538	0.969, 0.584	0.397, 0.456	-0.078, -1.18	0.938, 0.238

† $p < 0.10$

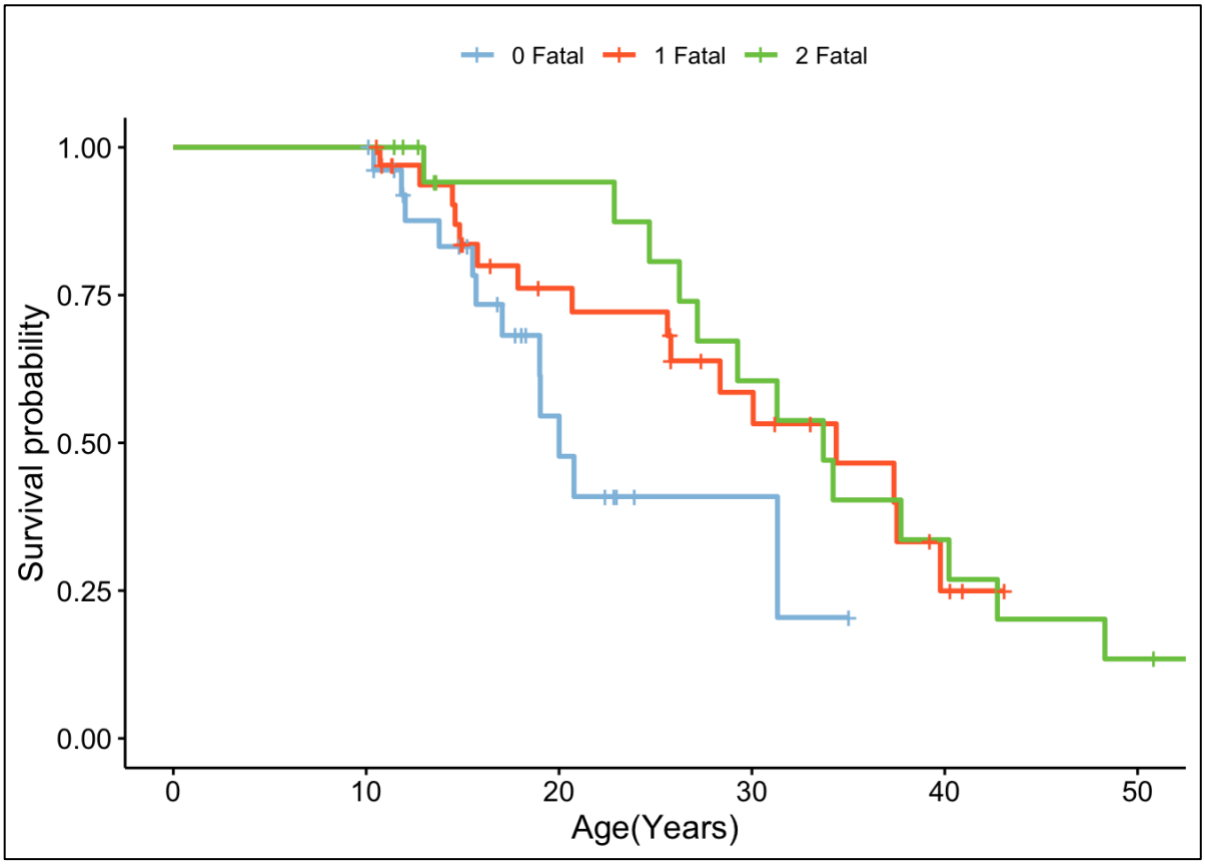

Figure 7. Exposure to More Fatal Outbreaks from Birth to Age 10 Decreases Risk of Death. Survival curves comparing the effects of exposure to 0, 1, and 2 fatal outbreaks from birth to age 10 ($p = 0.052$); fitted with the dataset restricted to individuals who had survived to age 10 (N = 81).

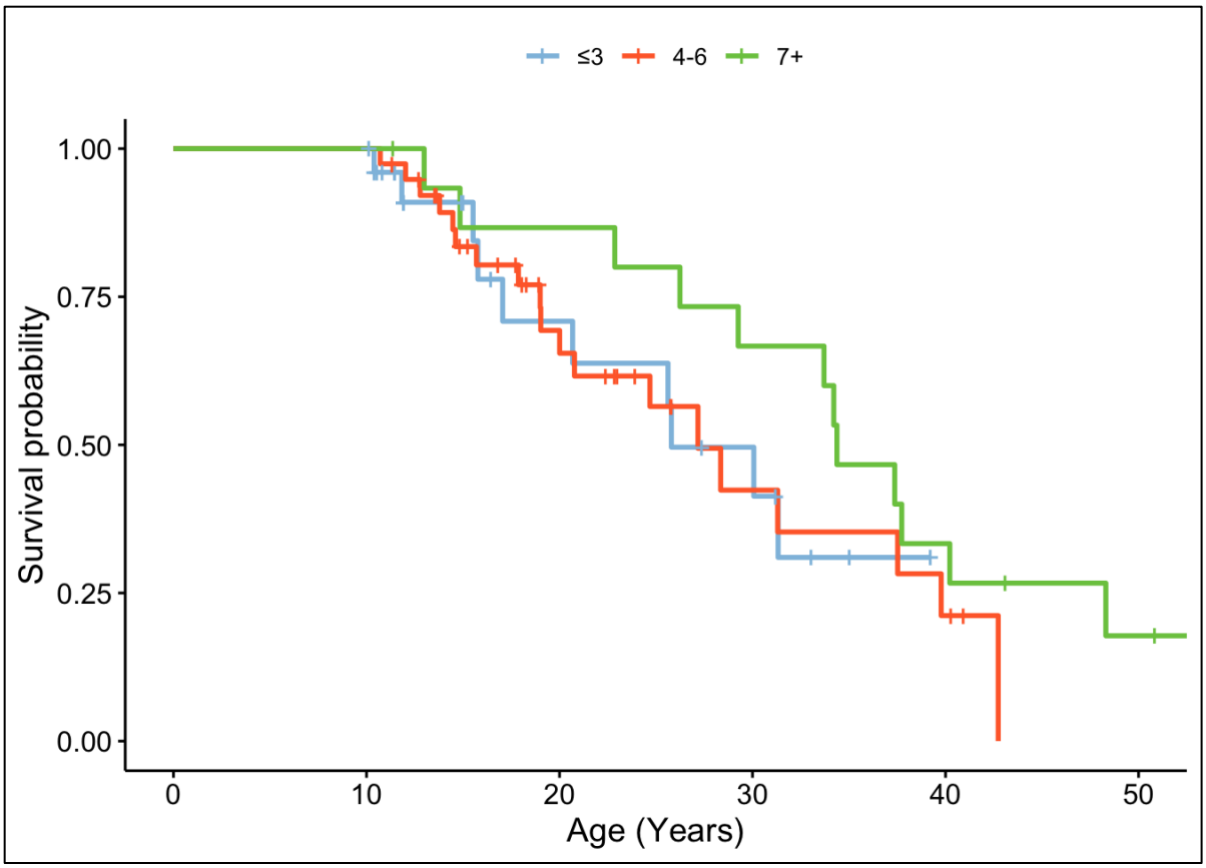

Figure 8. No Association for Risk of Death with Age for Individuals Exposed to ≤3, 4-6, or 7+ Outbreaks from Birth to Age 10 (Survived to Age 10 Dataset). Survival curves comparing exposures to ≤3, 4-6, and 7+ outbreaks from birth to age 10 (p = 0.938, 0.238); fitted with the dataset restricted to individuals who had survived to age 10 (N = 81).

Discussion

The results of this study provide insights into the potential impacts of experiencing respiratory disease outbreaks in early life in wild chimpanzees. While previous research on primates has focused on social and ecological stressors as sources of ELA (Tung et al., 2016; Morrison et al., 2023), this study expands the scope by investigating disease outbreaks as a stressor with potential long-term health consequences.

Outbreak Periods

The identification of 37 respiratory outbreaks highlights the recurrent nature of epidemic respiratory illness in wild chimpanzee populations. Given that respiratory illness is a significant contributor to mortality in the wild (Williams et al., 2008), and studies of biomarkers during

outbreaks have found several indicators of energetic stress (Emery Thompson et al., 2008; Behringer et al., 2020; Negrey et al., 2021), respiratory outbreaks may function as a source of adversity. Furthermore, differentiating between types of outbreaks (as fatal, major, and minor) allows for a wider framework with which to assess the potential impacts of respiratory illness. Fatal outbreaks seem to occur more infrequently than nonfatal outbreaks – on average, there was an interval of 6.65 years between fatal outbreaks, but only 2.96 years between major outbreaks.

In-utero Exposure

The prediction that outbreaks in-utero would have a strong, negative impact on risk of death was partially supported. A Fisher's exact test demonstrated that experiencing fatal outbreaks significantly and negatively affected the probability of surviving to age 10; however, experiencing nonfatal outbreaks did not affect this probability. Notably, a key limitation in this study is the inability to confirm whether or not a mother exhibited signs of illness during an outbreak, as chimpanzees will often leave the group when they are ill to avoid social rejection and/or competition (Goodall, 1986b). As such, this study measured only whether an individual was alive in the community at the time of a respiratory outbreak. The existing human literature predicts significant consequences for in-utero outbreak exposure, regardless of whether it is in the form of maternal infection (Dauby et al., 2012) or outbreak-induced stress (Provenzi et al., 2021). The Fisher's exact test, which demonstrated that individuals exposed to fatal outbreaks in-utero were less likely to reach age 10, is more in line with these findings and suggests that being in-utero during fatal outbreaks has important consequences in the context of reaching adulthood. Furthermore, the distinction between fatal and nonfatal outbreaks appears justified in the context of in-utero exposures, as fatal outbreaks had hazard ratios consistent with an increased risk of

death (HR > 1) while nonfatal outbreaks had hazard ratios consistent with decreased risk (HR < 1).

Another limitation in these analyses is that all Cox models are based on live birth. In humans, maternal infection can have a dramatic effect on the intrauterine environment, resulting in miscarriage (Goldenberg et al., 2005). This impact may be especially strong in the first trimester, during which major structural development is taking place; miscarriages as a result of maternal infection often occur in the first trimester (Dorélien et al., 2019). It's possible that a similar effect could exist for chimpanzees; however, at this point, we are unable to know whether exposure to an outbreak might result in miscarriage. Future research should attempt to clarify the role of maternal health for in-utero outbreak exposures. Additionally, examining the timing of exposure during pregnancy may help clarify these relationships – several studies on maternal illness in humans have found that the trimester in which a mother is infected (Kwok et al., 2022; Piekos et al., 2022) or exposed to stress (Mulder et al., 2002) is important when evaluating infant outcomes.

Exposures Throughout Infancy

The prediction that outbreaks within the first five years of life would reduce lifespan and increase risk of death with age, especially for excessive and minimal exposure counts, was not supported. Most striking was that fatal outbreaks during the birth to age five period were not associated with risk of death, despite exposure to fatal outbreaks in-utero being associated with reduced survival in the first 10 years of life. These results may not be entirely unexpected, as they might align with theories about immune system development. Studies on human children have found that although the infant immune response is generally weaker (Simon et al., 2015; Heinonen et al., 2019), viral infection in the first two years of life is extremely common, and is

often asymptomatic or doesn't require medical attention (Teoh et al., 2024). Additionally, despite increased vulnerability to infection, there is evidence that increased exposure ultimately results in a more robust immune system (Strachan, 1989).

Visual inspection of the Kaplan-Meier curves for exposure to fatal outbreaks would seem to support these ideas, as the protective effect of 1+ fatal outbreaks seems most noticeable after age 15. Fatal outbreaks may have impacts for fitness beyond survival to adulthood – living longer means reproducing more (Charnov & Berrigan, 1993). Again, this contrasts with the in-utero results, reinforcing the idea that fatal outbreaks in-utero are potentially more dangerous than those that take place once the immune system has begun to develop. The models for major and minor outbreaks indicate only a weak or negligible protective effect for exposure to nonfatal outbreaks for the birth to age five period. More detailed research on when outbreaks occur during this developmental period, as well as whether there are interaction effects with outbreak exposures in other stages of development, will be required in order to better understand the impact of respiratory disease exposure in infancy.

Exposures from Birth Through Juvenility/Adolescence

The prediction that both excessive and minimal outbreak exposures in the first 10 years of life would increase risk of death was similarly unsupported. Fatal outbreaks from birth to age 10 were associated with decreased risk (significant at the $p < 0.05$ level for the 'survived to age five' dataset, and at the $p < 0.10$ level for the 'survived to age 10' dataset). Furthermore, there was a trend shown in decreased risk of death with age for individuals who experienced the 'excessive' level of outbreak exposures (defined as the 7+ group); this was significant in the survived to age five dataset, but not for the survived to age 10 dataset, likely due to the smaller sample size. As previously discussed, this finding isn't necessarily unexpected due to human

studies emphasizing the importance of pathogen exposure for building a robust immune response (Strachan, 1989). The trend in 'excessive' levels of outbreak exposure within the first 10 years of life decreasing risk of death indicates that further research is needed to understand how these developmental windows interact with immune competence and longevity.

The observed difference in the impacts of exposure to fatal outbreaks – wherein in-utero exposures increased risk of death, while exposures throughout the first five and 10 years of life decreased risk – is intriguing and will require further investigation. The most likely explanation for this discrepancy is that the effects of exposure during these developmental windows are mediated by distinct mechanisms. While in-utero, a fetus relies on the mother's immune system; pathogen exposure can trigger a significant immunoinflammatory response, which can disrupt fetal development and alter the intrauterine environment (Prabhudas et al., 2021; Trinh et al., 2024). This increase in inflammation is commonly proposed as the mechanism through which respiratory viruses such as RSV, COVID-19, and influenza create severe consequences for human fetuses (Dorélien et al., 2019; Trinh et al., 2024). On the other hand, exposure to fatal outbreaks after birth may have a protective effect due to immune priming. Because the immune system is still developing, exposure to pathogens may enhance future responses to infection (Yu et al., 2018; Simon et al., 2015). Therefore, experiencing a fatal outbreak could allow an individual to develop stronger immunity, potentially reducing the risk or severity of disease in later life.

Across all models, fatal outbreaks seemed to exert comparatively stronger effects than nonfatal outbreaks when considering survival outcomes. This effect appears detrimental in the context of in-utero exposure, but protective when it occurs post-birth. Nonfatal outbreaks seem to make less of an impact, possibly because they occur more frequently and are therefore less

likely to have strong, lasting effects on exposed or unexposed individuals. Although the nonfatal outbreak categories applied in this study (‘major’ and ‘minor’) were based on percentage thresholds, further studies could implement categories based on measures of outbreak intensity, such as symptom severity or duration, data on which were not available in this dataset. Future investigations should emphasize capturing pathogen data (for example, via fecal: Negrey et al., 2022; Blinkova et al., 2010 or saliva sampling: Dunay et al., 2023) in order to better understand how fatal and nonfatal outbreaks differ, and clarify the mechanisms through which respiratory infection impacts individuals.

These results are also interesting in the context of examining how early life adversity shapes populations. A common theme in these discussions is whether this shaping takes the form of mortality selection or scarring (Klemp & Weisdorf, 2012). Mortality selection refers to a process through which individuals who are exposed to ELA and make it to later life are more robust, and thus experience lower relative mortality compared to unexposed individuals. Conversely, scarring is the idea that ELA causes lasting damage, so exposed individuals live to adulthood but experience greater frailty at older ages and higher relative mortality later in life. As shown in Figure 2, experiencing fatal outbreaks in-utero is detrimental in the context of reaching maturity; however, the individuals who survived to age 10 exhibited no increase in risk of death compared to unexposed individuals, which seems to align with mortality selection. On the other hand, scarring might be observed for individuals who are not exposed to fatal outbreaks in the first five or 10 years of life. Unlike in-utero exposures, fatal outbreaks during these periods do not have an impact on reaching adulthood; however, a seemingly protective effect appears around age 15, and exposed individuals appear to live longer and have a reduced risk of death as they age (see Figures 4, 5, and 7). It could be that those who are exposed to, and survive fatal

outbreaks are more robust than those who are unexposed; this is similar to the effects of cumulative ELA in gorillas, where exposed individuals are more robust.

As research on early life adversity in chimpanzees expands past maternal loss, it will be important to examine interaction effects with other adverse conditions. For example, future studies of respiratory illness as an adverse source would benefit from implementing data on factors such as social networks and maternal rank data. Social network analyses have shown that chimpanzees who are centralized within their social groups are more likely to show clinical signs (Sandel et al., 2021). Maternal rank is a key factor in how social a female chimpanzee, and therefore her offspring, are (Kahlenberg et al., 2008). "Core-ranging" females (those who are higher-ranking and forage within the core of a community's territory, as opposed to the periphery) are central within social networks, as they frequently associate with family members and other female-offspring units (Goodall, 1986a; Rushmore et al., 2013). Together, this suggests that maternal rank and gregariousness are important predictors when examining exposure to respiratory outbreak.

Overall, this study examined respiratory illness as a form of early life adversity in chimpanzees. Although survival analyses largely revealed a lack of association between different forms of exposure and risk of death, chi-square/Fisher's exact tests and visual inspection of Kaplan-Meier curves point to differing effects at different life stages. Given that early immune development is a key aspect of later-life health and mortality, early and repeated exposure to respiratory pathogens may be vital in ensuring a well-developed immune system. This has intriguing implications for future studies on respiratory illness as a source of adversity, as experiencing 'adversity' in this context may mean not having exposure to respiratory outbreaks as an adolescent; scarring in adult populations might be observed for individuals not exposed to

fatal outbreaks. Ultimately, this work underscores the need for further research exploring the nuances of respiratory outbreak in wild chimpanzees. Elucidating the impact of timing, specific pathogens, and maternal health will be vital in forming a deeper understanding of the individual and population-level impacts of early life disease exposure.

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Supplementary Figures

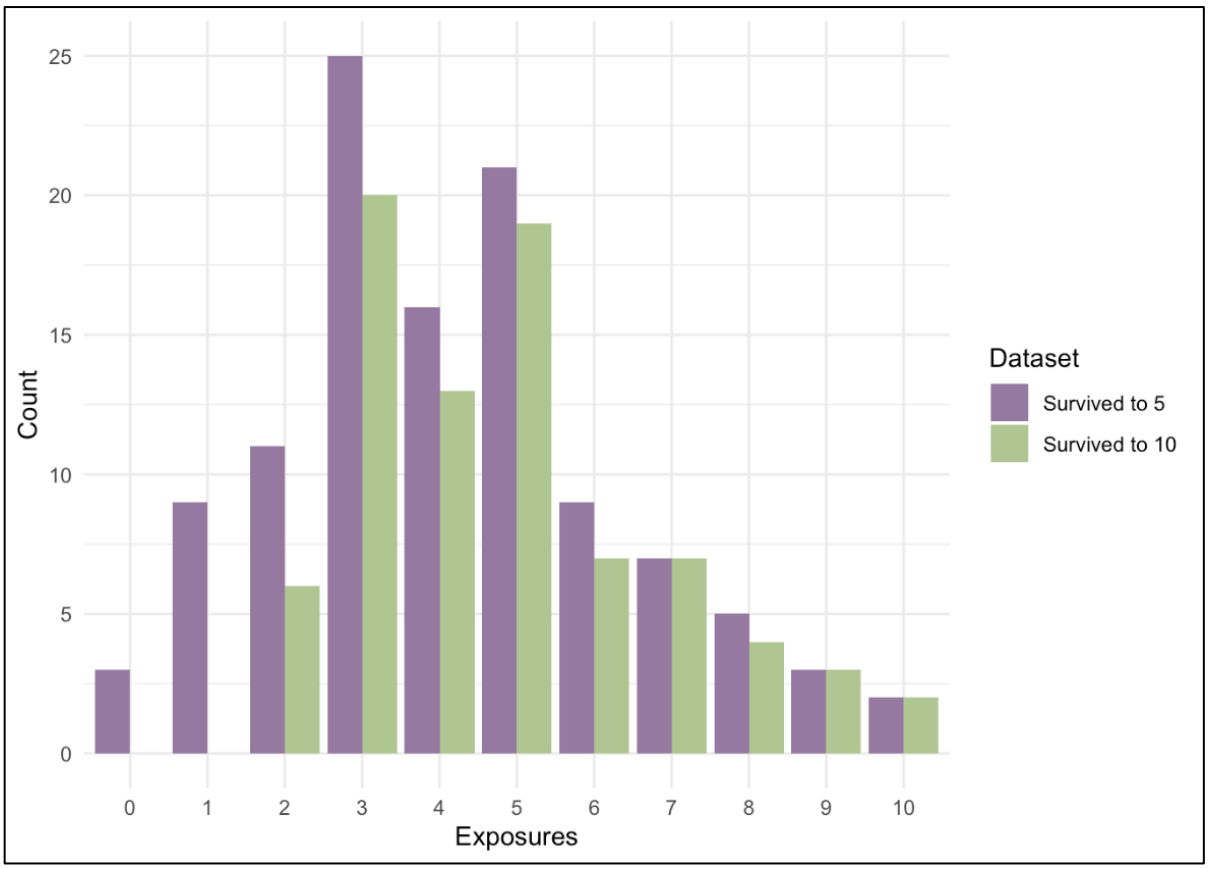

Figure S1. Total Outbreaks from Birth to Age 10 in Wild Eastern Chimpanzees (*Pan* troglodytes) in Gombe National Park, Tanzania Range from 0 to 10. I compared the distributions for total outbreak counts from birth to age 10 for the 'survived to age five' dataset (purple; N = 111) and 'survived to age 10' dataset (green; N = 81). This revealed a mode of three for both datasets, informing my decision to split the total outbreaks variable into groups of ≤3, 4-6, or 7+ total exposures.