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Post-reproductive survival in a polygamous society in rural Africa

Bodegom, D. van

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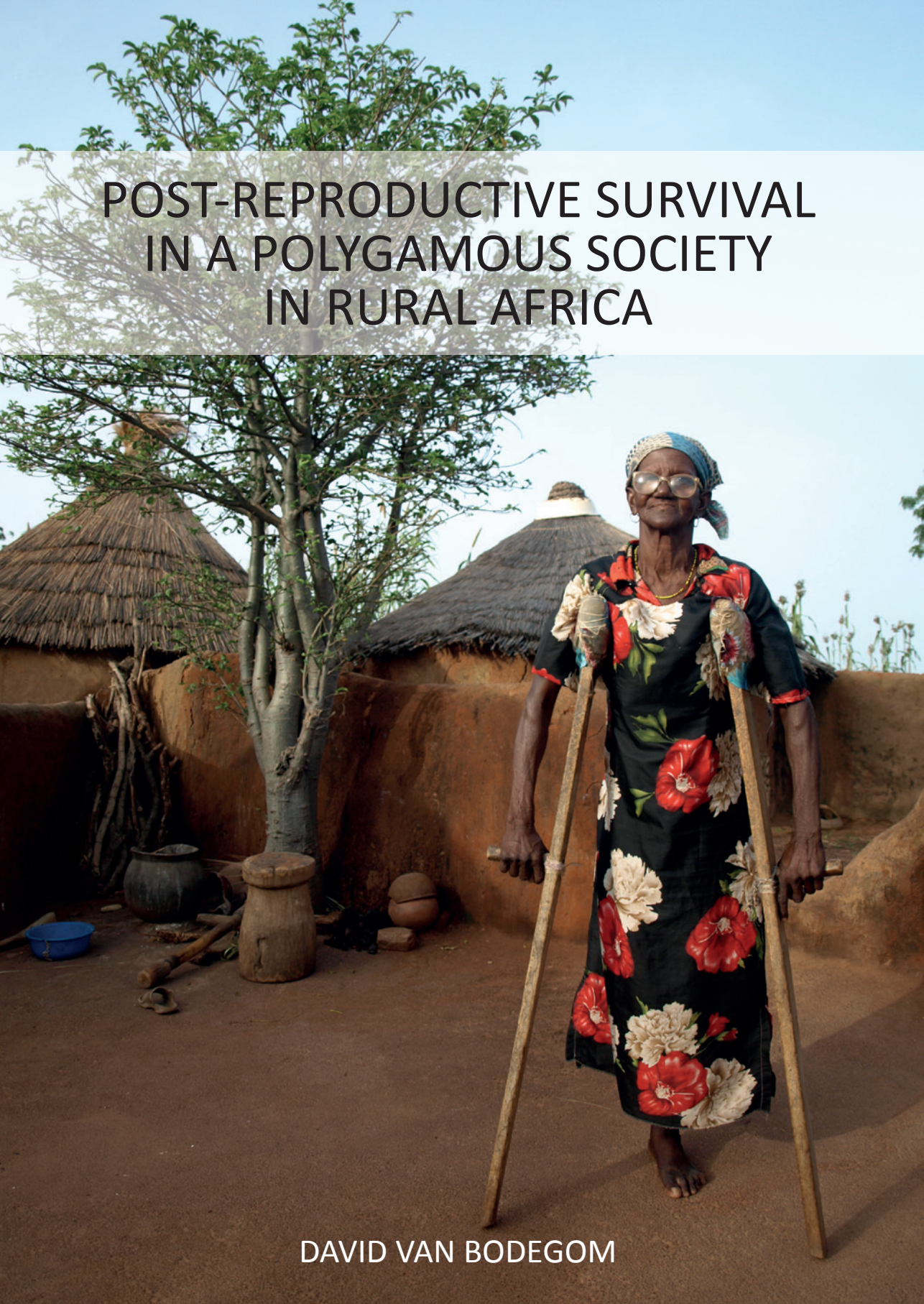

DAVID VAN BODEGOM

POST-REPRODUCTIVE SURVIVAL
IN A POLYGAMOUS SOCIETY IN RURAL AFRICA

Post-reproductive survival in a polygamous society in rural Africa
Proefschrift Leiden

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POST-REPRODUCTIVE SURVIVAL
IN A POLYGAMOUS SOCIETY IN RURAL AFRICA

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in 1978

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Promotor:	Prof. dr. R.G.J. Westendorp
Co-promotores:	Dr. J.J. Meij Dr. G.C.F. Thomése (Vrije Universiteit Amsterdam)
Overige leden:	Prof. dr. S. Daan (Rijksuniversiteit Groningen) Prof. dr. F.M. Helmerhorst Prof. dr. B.J. Zwaan (Wageningen University)

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Ik word aan 't oud zijn niet gewend.
De lichtelaaie die 'k heb gekend
zit nog te diep in mijne knoken
en blijft mij dag en nacht bestoken.

Willem Elsschot

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Chapter 1

General introduction

Introduction

Humans have a long post-reproductive life span. In this thesis we study this post-reproductive life span from an evolutionary perspective. Why did humans evolve such a long post-reproductive life span? What was the selective advantage of prolonged survival after the reproductive period?

It has long been thought that post-reproductive survival was beyond evolutionary control[1,2]. Because of the high external mortality from predators, infectious diseases and accidents in our evolutionary past, only few individuals would survive more than 50 years. Consequently, humans never evolved maintenance and repair mechanisms that would allow our bodies to reproduce after age 50 since most people would have passed away at that time. This reasoning was later amended with the principle of antagonistic pleiotrophy, which stated that the benefits of variants that lead to an advantage at young age greatly outweighed the benefits of variants that have their advantage at later ages because of the larger number on which they apply[3]. According to this line of thought, post-reproductive survival is largely a recent epiphenomenon resulting from our increased lifespan[4].

Others argue that our post-reproductive survival is not an epiphenomenon, but an adaptive trait with a selective advantage. In this reasoning, humans in past times also lived considerable years after reproductive age. Our historical life expectancy of around 40 years was mainly caused by high child mortality. Observations in present day hunter-gatherers also confirm that a significant number of people experience a post-reproductive life span[5]. Second, the orchestrated way in which menopause is regulated with distinct hormonal shifts, suggests that menopause, and therefore post-reproductive survival, could be an evolved mechanism rather than the consequence of accumulated damage.

A first adaptive explanation of our post reproductive survival was the 'mother' hypothesis, which suggests a selective advantage for older women as their presence would increase survival probabilities of their offspring[3]. The 'grandmother' hypothesis added the notion that help from older women may have had a selective advantage through increasing the reproductive success of their offspring[6-8]. Previous research has shown that the presence of post-reproductive women allows their children to reproduce earlier, more frequent and more successful, but the effects are not undisputed and context dependent[4,8]. It is

noteworthy that many currently available studies[7] originate from historical monogamous populations.
There are three arguments why historical populations are sometimes not optimal for the study of the evolution of our post-reproductive survival.

First, most historical studies, often based on church records, are from monogamous populations that live in nuclear three generational families. It is argued that this environment does not reflect our recent evolutionary past, during which we lived, as both y-chromosomal and anthropological studies indicate, in polygynous, extended families[9,10]. The selective advantages of post-reproductive survival could be very different in these populations compared to the historical populations.

Second, male longevity after age 50 has been recently suggested as an important selective advantage in our evolutionary past. In polygamous societies, men are able to reproduce up to high ages through the marriage of young fertile women[11]. This effect of older males in polygamous societies can also not be studied in the historical, monogamous populations, because monogamous men can no longer reproduce when their wife reaches the post-reproductive age. Although serial polygamy is sometimes practiced, this does not result in large numbers of offspring.

Third, in historical studies there is often no accurate measurement of socioeconomic status. This is essential, since richer households would have both better reproductive success and better survival of elderly persons, suggesting that the presence of long lived elders is responsible for the enhanced reproductive success. It is therefore possible that some of the previously found effects of post-reproductive women on subsequent generations are confounded by socioeconomic status.

To investigate whether our post-reproductive survival evolved as an adaptive mechanism it is essential to study the effect of post-reproductive kin members on reproduction and survival in an environment that resembles our evolutionary past. There is discussion during which time period in evolution our longevity evolved[12]. We studied the selective advantage of old age survival in both males and females in a large rural population of over 25,000 participants in northern Ghana who live in patrilocal, polygamous extended families and were prospectively followed for

reproduction and survival. We think this environment better resembles the evolutionary adaptive environment than most historical studies. We also collected extensive measures of other determinants of survival, most notably socioeconomic status and drinking source.

Aim of this thesis

In this thesis we study post-reproductive survival. We tested the hypothesis that males and females after age 50 are able to enhance their fitness either direct through continued reproduction or indirect through the improvement of the reproductive success of their offspring. We studied the effect of different kin members on offspring production and offspring survival in a prospective study in a polygamous African population. This environment could reflect our recent evolutionary past taking into account the anthropological and environmental determinants.

The Ghana study

All studies described in this thesis were conducted in the Garu-Tempane district in the Upper East Region of the Republic of Ghana[13]. The area has a semi-Saharan climate with an average maximum temperature of 32 ^{o}C throughout the year and only one rain season (June–August). The research area measures approximately 375 km^2 with approximately 25,000 participants living in around 40 villages. Figure 1 is a map of the research area that we created using GPS mapping of the compounds superimposed on existing hydrographic, altitude and road maps of the Centre for Remote Sensing and GIS (CERSGIS) of the Legon University in Accra, Ghana.

The participants in the research area live in extended families, with a median of fifteen persons per household. The head of the family, the landlord, is married to up to four wives. Approximately half of the landlords have more than one wife. The families live together in compounds; clay structures with thatched roofs, connected by clay walls. Figure 2 is an example of a compound. There are approximately 1,700 compounds in the research area. The people belong to several different tribes, the Bimoba (65%), Kusasi (25%) and several smaller tribes (Mamprusi, Busanga). A small group of more nomadic Fulani are living in the area as well. The vast majority of the people are farmers. The total agricultural process is done by hand. Migration is very low and amounts to less than 1% per year.

There is some additional seasonal migration of young men who move to the larger cities in Ghana to work in seasonal occupations. Illiteracy is very high, among adults it is almost complete and among children it is still very high (>50%). The average per capita income corrected for purchasing power parity of the Upper east region of Ghana in the year 2006 was US$ 304[14].

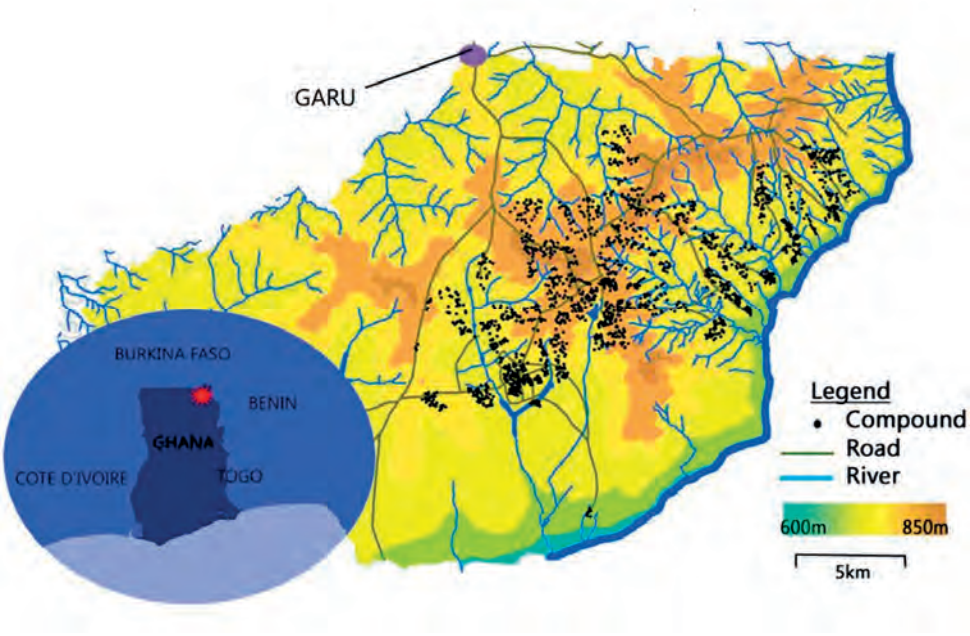

Figure 1. Map of the research area, the Garu-Tempane district in the Upper East Region of the Republic of Ghana. Map by Dr. L. May

Most people in the research area rely on traditional medical care, which is equally distributed throughout the area. There is no medical doctor working in the research area and the nearest hospital is at a 30 mile distance from the research area. Vaccination of children was introduced in the early nineties of the last century and at least 50% of the children under ten years have been vaccinated at least once. Birth control is virtually absent, although spacing of children by means of prolonged breastfeeding is sometimes practised by younger women. Most women want to have as many children as possible, since large families are highly regarded. In the past decades, clean drinking water from boreholes has been gradually introduced into the area.

Figure 2. Typical compound in the research area. Huts are made of mud with thatched roofs. In this patrilocal, polygamous population the landlord lives with his wives, sometimes accompanied by a (half-) brother or son and their wives. 48% of the households include a man who married more than one wife.

Table 1 summarizes the characteristics of the research area. In 2001, the research area was explored by the Department of Parasitology of the Leiden University Medical Centre that set up a database for parasitological research[13]. During eight years of follow-up from 2002-2010 we followed 28,994 participants for reproduction and survival. The area is undergoing the epidemiological transition[15]. For each member of the household, the father and mother were identified if they were living in the same household. From this we identified the grandparents. The socioeconomic status was assessed for all inhabited households in accordance with the Demographic and Health Survey (DHS) methods[16]. We defined poor and rich as the poorest 50% and the richest 50% divided by the median. Drinking water was assessed at household level, water from bore-holes was found to contain less pathogens and considered safe drinking water, water drawn from either open wells or from rivers were found to contain more pathogens en were considered unsafe drinking water[17].

Ethical approval was given by the Ethical Review Committee of the Ghana Health Service, the Medical Ethical Committee of the Leiden University Medical Centre in Leiden, the Netherlands and by the local chiefs and elders of the research area.

Table 1. Study characteristics

Participants (n)	28,994
Male (n (%))	13,323 (46%)
Female (n (%))	15,645 (54%)
Tribe	
Bimoba (%)	66%
Kusasi (%)	26%
Mamprusi (%)	2%
Fulani (%)	2%
Busanga (%)	2%
Other (%)	2%
Households (n)	1,703
Median number of inhabitants per compound (n)	15
Polygamous households (%)	48%
Mean value of household possessions in US$ (mean (SD))	1,063 (1,021)
Safe drinking water (%)	80%
Reproduction	
Numbers of newborns registered 2002-2010 (n)	3,645
Survival	
Follow up (calendar years)	2002-2010
Person years (n)	164,565
Mean follow up (years)	6.0
Deaths during followup (n)	1,344

Outline of this thesis

This chapter, **chapter one** provides a general introduction to the thesis.

Chapter two provides the theoretical background to the study, explaining the principles of life history theory. According to life history theory different physiological and behavioural characteristics of an organism's reproduction and survival are linked. Changes in one of the characteristics influences the other characteristics and only certain combinations lead to successful evolutionary strategies with high fitness. Post-reproductive lifespan is hypothesized to provide a selective advantage through investments in offspring that affect different life history characteristics; birth interval, total fertility, offspring growth and offspring survival among them. Life history theory is therefore important to understand the evolution of our longevity and the selective advantage of old age survival.

Chapter three provides a detailed description of the research area, the Garu Tempane district in the upper east region of Ghana. It provides the environmental, social and anthropological background of the area and the participants, most notably the Bimoba tribe to which most participants of this study belong. To come to an understanding and interpretation of the findings of the studies described in this thesis, this anthropological background is essential.

Chapter four describes the socioeconomic studies we undertook in the research area. Socio-economic status is a well known determinant of offspring survival and it was therefore important to measure it in the research area. Also, socioeconomic status could confound the relation of kin members and offspring survival. In richer households, children would have better survival but other kin members, e.g. post reproductive kin members, would also have better survival, creating the false impression that the presence of post-reproductive kin members improves offspring survival.

Life history theory predicts that maintenance trades off with fertility. In **chapter five** we test this prediction. We study the relation between offspring survival, reflecting the investments in maintenance, and the number of siblings, reflecting investments in fertility of the mother. We make use of the assumption of life history theory that these investment patterns are hereditary. By comparing co-wives in polygynous compounds we were able to maximally control for

differences in (micro) socioeconomic status. It is important to study the effect of the number of offspring on their survival in order to be able to study the effect that kin members have on offspring production and survival.

To elucidate the mechanism through which kin members and environmental factors influence offspring survival, we also studied the early growth patterns of the offspring in **chapter six**. The weights of offspring are not only determined by environmental determinants and in chapter six we also studied the genetic background of the weights of the children. We studied the CFTR gene, which causes cystic fibrosis in mutated form, the most common recessive genetic disease. It has been hypothesized that in our recent evolutionary past heterozygous carriers of CFTR mutations had a survival advantage. An understanding of the genetic component of the offspring weights is important to be able to asses the effect of kin members on offspring weight.

In **chapter seven** we describe our final analysis. Here, in a two sex model, we studied the selective advantage of old age survival for both males and females on survival and reproduction. We studied both the direct effect of continued reproduction and the indirect effect of the presence of elderly men and women on reproduction and child survival in the household.

In **chapter eight** we study the effects of the socioeconomic status on reproduction and survival in more detail. Socio-economic status can have large effects on these characteristics and these effects could be different in men and women. These differences are expected to be larger in a polygamous society. Since in this society it is custom that men pay a brideprice of four cows, rich men can afford to marry more wives and consequently it can be expected that they sire more offspring. For women, the effects of socioeconomic status on reproduction are expected to be less pronounced. We study these differences and the consequences for the reproductive prospects of sons and daughters in poor and rich households and investigate whether there are differences in the survival and nutritional status of sons and daughters in poor and rich compounds.

In **chapter nine** we discuss the grandmother hypothesis, which states that post-reproductive women improve the reproductive success of their children and the implications of this theory for the study of ageing. In this chapter we comment on

earlier studies and discuss the importance of environmental and anthropological determinants in the study of the grandmother effect. We also compare studies of the grandmother hypothesis in historical populations and studies in contemporary populations under adverse conditions.

In **chapter ten** we summarize the main conclusions and discuss the implications of the research described in this thesis. Also, we describe how evolution continues to shape our life histories, both for reproductive characteristics and (post reproductive) survival.

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Chapter 2

Regulation of human life-histories: the role of the inflammatory host response

D. van Bodegom*, L. May*, J.J. Meij, R.G.J. Westendorp

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* These authors contributed equally to this study

Abstract
Most species with a long life span have few offspring while species with a short life span have many offspring. This evolutionary trade-off between fertility and body maintenance, based on the theory of r/K-selection, is a central theme in the theory of life history regulation. This trade-off is not only found between various species but also between individuals within one species. There is accumulating evidence for this trade-off in humans. We hypothesize that the innate immune system is a critical factor skewing an individual into the direction of either a high fertility or better maintenance strategy. As over thousands of years human survival has been highly dependent on resistance to infectious diseases, genetic adaptations resulting in inflammatory responses were favored. An inflammatory host response is critical to fight infection necessary to survive up to reproductive age. An inflammatory host response is also negatively associated with fertility and can explain for the trade-off between fertility and body maintenance. After human reproductive age, these inflammatory responses contribute also to development of chronic degenerative diseases. These will especially become apparent in affluent societies where the majority of individuals reach old age. Identifying the inflammatory host response as a critical factor both in the regulation of human life-histories and in the occurrence of chronic diseases at old age implies means for intervention allowing individuals to live healthier for longer.

Introduction

The fitness of a species is determined by the capability of an organism to pass its genes to the next generations under defined environmental conditions. Fitness is therefore dependent on fertility *per se*, and maintenance, in order to survive up to reproductive age. Limited resources have to be divided between body maintenance and fertility. This can be described by the r/K-selection theory as proposed by MacArthur and Wilson[1]. The symbols r and K refer to two ends of a continuum, where a compensatory exchange occurs between investment in fertility (r-selection) and in body maintenance (K-selection). Both r- and K-strategies are adaptive survival strategies employed by species in different habitats. By means of natural selection, dependent upon environmental conditions, each species will be pushed to its own fitness optimum somewhere on this continuum between an extreme of r- or K-strategies. If extrinsic mortality is high, organisms tend to have their fitness optimum more at the r-side of the r/K continuum. In a more stable environment, organisms invest more in K at the cost of r. Support for this evolutionary trade-off between investment in body maintenance and fertility is pictured in figure 1 which shows the relation between body maintenance (life span) and fertility (number of offspring) of different mammals.

The r/K-selection theory also helps us to understand differences in the life-histories within one species and between individuals of one species[2,3]. Several experiments with the fruit fly *Drosophila melanogaster* support the existence of this trade-off between body maintenance and fertility within one species[4-6]. A selection regime favoring flies with prolonged fertility at later ages did result in populations with reduced fertility early in life and increased life span. Direct selection for longevity also produced long-lived populations with significantly reduced fertility[7]. A similar experimental trade-off has been found in the nematode *Caenorhabditis elegans*; a series of mutations in the insulin pathway are associated with an increase in life span of up to 200%, but at the cost of fertility[8,9].

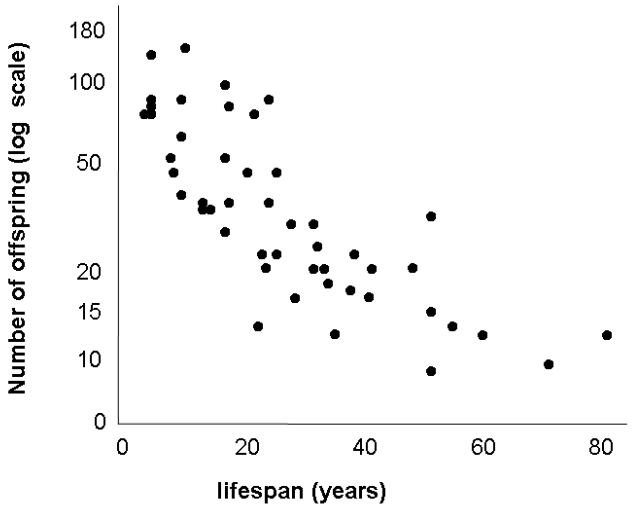

Figure 1. Life span and number of offspring in mammal species. Adapted from Holliday[80]

There is accumulating evidence that the evolutionary trade-off between body maintenance and fertility is also present in humans[10,11]. Earlier we have studied a historic data set, so as to investigate humans in an environment where evolutionary selection was still present. In the pedigrees of the British aristocracy who lived before 1700, we found that long lived women had fewer offspring, as shown in figure 2[12]. Several other studies have confirmed these findings in populations resembling the human 'natural habitat'. Korpelainen found the trade-off between reproductive success and longevity in women in a Finnish population between 1700 and 1899[13]. Thomas et al. found a trade-off in both sexes using data from 153 countries[14]. Some studies only found the trade-off to be present in women[15,16]. Other studies however, did not find evidence for the trade-off[17-21]. This could in part be explained by the fact that the populations under study resided in a modern affluent environment characterized by low mortality and fertility rates, i.e. having past the demographic transition. In line with this reasoning, Lycett et al demonstrated that the trade-off was stronger under poverty conditions[22]. We also showed that the trade-off disappeared when environmental conditions of the British aristocracy markedly improved after 1700 and initiated a demographic transition[12.] Similar trends over time were found by Korpelainen, who demonstrated that the trade-off in women[23] had disappeared upon further improvement of the environment[24].

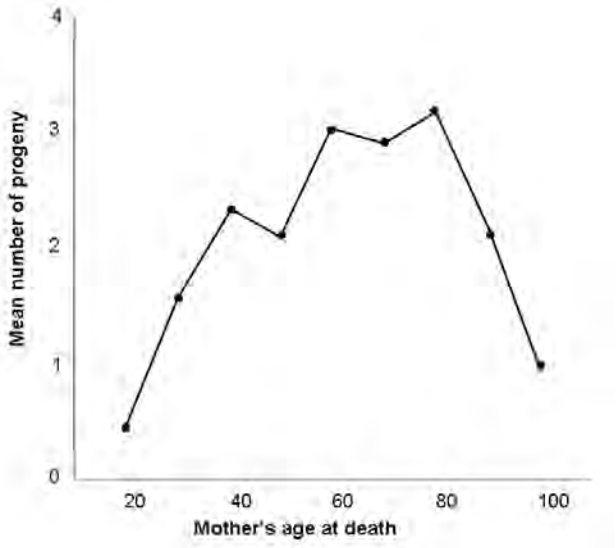

Figure 2. Progeny number for married aristocratic women from different birth cohorts as a function of age at death. Adapted from Westendorp et al.[12]

Nowadays, the demographic transition has taken place in most countries resulting in low fertility and low mortality rates under affluent conditions[25]. It is therefore not surprising that the r/K trade-off may not be found in contemporary populations. At present the population genome is not yet in evolutionary equilibrium with the dramatically improved environmental conditions in which we live. To understand which factors have contributed to the regulation of human life history, we first look at the r/K selection forces that have shaped our body under adverse conditions in our 'natural habitat'. From there we develop a line of thought in five steps to understand the consequences of this selection for our present day life.

Fundamentals

Human survival is strongly dependent on resistance to infectious diseases

The selections that took place during evolution of *Homo sapiens* in his natural habitat differ from other mammals, in that he constantly created new ways of living. First he eliminated the danger of cold with the mastery of fire some 100.000s of years ago. Additional contributions to the reduction of death from cold were the use of clothing, the transition from hunter/gatherer ways of living to agricultural civilization during the Neolithic period, and the construction of houses. Farming also managed to create a far more constant supply of food, reducing the selection of individuals withstanding hunger and shortage of food. The use of tools, superior intellect, the ability of speech and group cooperation reduced the number of deaths through predation. The result of expelling the major threats predation, hunger and cold is that selection pressure on infectious diseases became more prominent[26]. Resistance to infectious diseases (parasites, bacteria and viruses) became an even more important selection criterion when humans moved closer together. The developing farming societies were also able to feed a far greater population, leading to increased population sizes. The growing populations with a more sedentary life style were a perfect niche for different infectious diseases. In more recent history, with the rise of cities some thousands of years ago, the first epidemics occurred, sometimes killing as many as one third of a city population. This all has resulted in a predominant selection for resistance to infection to survive up to reproductive age, i.e. humans had to invest in K in order to maintain their fitness.

Resistance to infectious diseases is strongly dependent on an inflammatory host response

As, over the last thousands of years, *Homo sapiens* has developed in an environment with a high pathogenic burden, it can be hypothesized that selection has taken place on an inflammatory host response[27]. Evidence for genetic adaptations for resistance to infection is widely demonstrated and many of these adaptations have occurred in the innate immune system[28]. The innate immune system is the first line of defense and suffices for the overwhelming majority of invading pathogens[29]. Its components have evolved under high selective pressure in our ancient predecessors. The innate immune system is triggered by pathogens that are amongst others, identified by Toll-like receptors on antigen presenting cells[30]. Stimulation of these receptors results in a series of pro- and anti-inflammatory signals to adequately fight infection and to offset the immune

respons[31-33]. Survival up to reproductive age thus necessitates balancing of the pro- and anti-inflammatory responses. The elicited aspecific pro-inflammatory signals have a synergistic role in the inflammatory host response, mediated by cytokines such as TNFα. Cytokines also induce an adaptive, specific cell mediated immune response, able to attack a further number of pathogens that cannot efficiently be cleared by the innate, aspecific immune response alone. Anti-inflammatory cytokines regulate activation of the innate and adaptive immune response. They inhibit pro-inflammatory signals thus preventing collateral damage of a too abundant inflammatory host response. Moreover, these cytokines mediate recruitment of B cells, antibody responses, mast cells and eosinophils by cytokines like IL10. Not surprisingly, we have found the production and regulation of pro- and anti-inflammatory cytokines to be under tight genetic control, in line with the assumption that the inflammatory host response is submitted to evolutionary selection pressure[34].
Earlier we studied the production capacity of TNFα and IL10 in first-degree relatives of patients suffering from meningococcal infections and showed that the ratio of TNFα/IL10 was lower in cases in whom the infection was fatal. Our interpretation of these data is that subjects with an innate tendency towards anti-inflammatory signaling are at an increased risk of death through infection[35]. Many other studies now have demonstrated that pro-inflammatory signals are critical to protect against death from infection[36-38]. It is therefore likely that over the last thousands of years evolutionary selection favored genes that associate with an adequate inflammatory host response.

Pro-inflammatory signals are negatively associated with fertility
As humans have to be able to survive up to reproductive age, the immune system elicits pro-inflammatory signals in order to fight non-self antigens. However, protection against infection does not go well with fertility *per se*. Half of the fetus' antigens are from paternal origin, and are therefore considered non-self by the mother. These non-self antigens thus elicit a strong immunologic response resulting in pro-inflammatory signaling, local inflammation and rejection of the fetus. Successful reproduction necessitates an adequate immuno-tolerance to allow pregnancy to proceed. During pregnancy the mother physiologically enhances anti-inflammatory signaling, even though this makes her more susceptible to infection[39,40]. Several studies report increased pro-inflammatory signaling among women with spontaneous abortions and higher anti-inflammatory signaling

among women with reproductive success[41-43]. These studies support the hypothesis that pro-inflammatory signaling is negatively associated with fertility. In line, we have demonstrated that genetic variants that associate with increased pro-inflammatory signaling were enriched in married but infertile women[43,44]. We have concluded that investment in fertility and body maintenance is under tight genetic control, balancing between pro-inflammatory and anti-inflammatory signals. The pro-inflammatory signaling increases resistance to infections and is thus a component of K-selection, whereas selection for anti-inflammatory signaling increases fertility and can therefore be considered as a component of r-selection. Depending on the environment, and especially the risk of fatal infection, the balance between these various responses results in an optimal level of fitness, as shown in figure 3.

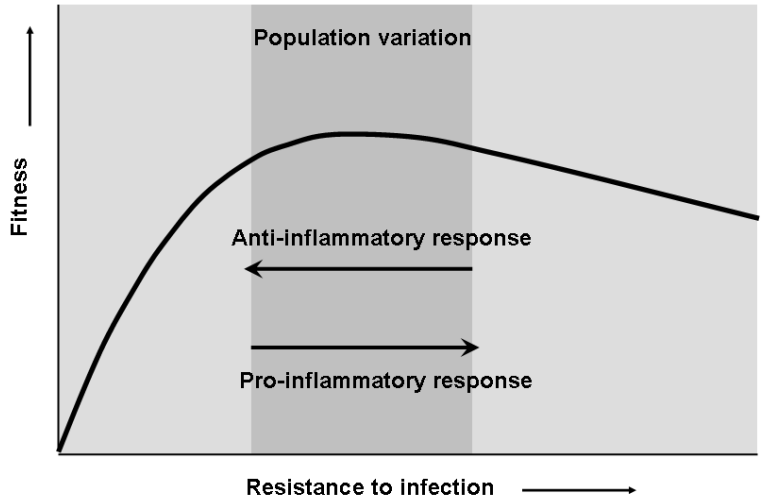

Figure 3. Schematic diagram showing fitness for different genes encoding pro- and anti-inflammatory signals. Adapted from Westendorp et al.[11]

Pro-inflammatory signaling promotes degenerative diseases after reproductive age

In our ancient, natural habitat not many individuals will have survived beyond 40 to 50 years. Not coincidental this is the age up to which we can bear offspring. In natural societies the durability of the body is optimized only to guarantee survival up to reproductive age and to raise one's offspring[45]. Figure 4 shows the decline of survival probabilities under adverse conditions. Mutations that have an effect after the age of 40 to 50 will neither be selected for nor against, for the sole reason that

most individuals did not have a post-reproductive life span. Events that occur after the reproductive period fall in the 'selection shadow', since these effects are not under an evolutionary selection pressure[46].

One may also consider that genes that have a beneficial effect early in life have detrimental effects later in life, as is proposed by the theory of antagonistic pleiotropy[47]. It says that chronic, degenerative diseases at later age are in fact the consequence of selection for genes that were beneficial at early age. Selection for a pro-inflammatory signaling that is protective in early life may in fact promote for what are generally called 'age related' or 'degenerative diseases', among which are atherosclerosis and the cardiovascular diseases, multiple sclerosis, rheumatoid arthritis, autoimmune thyroid diseases, osteoporosis and diabetes[48-51]. Dementia, may also become more likely as a consequence of inflammatory responses that were selected for because of their beneficial effects at child age[52,53]. This chronic inflammatory host response contributing to the occurrence of age related diseases has thus been referred to as 'inflammageing'[54].

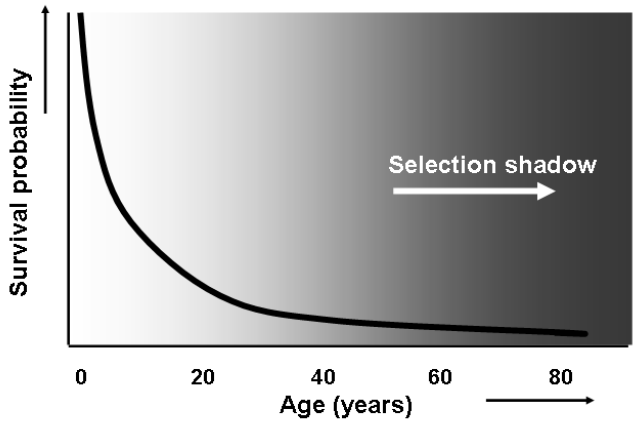

Figure 4. Human survival probabilities in our natural habitat. After reproductive age humans enter the selection shadow. Adapted from Kirkwood & Austad[81]

It is tempting to speculate that the chronic degenerative diseases in old age are part of our evolutionary shaped life history and do not directly result from our recent affluent life-style. Arguments for this reasoning can be found in the research of Magee et al., who demonstrated atherosclerosis in Egyptian mummies from

individuals who lived until their fifties or sixties[55]. Now the demographic transition has taken place, our life-expectancy has increased tremendously[56]. The simple fact that about half of our present life expectancy of 80 years takes place in what used to be the selection shadow, indicates that we are for a long time subjected to the deleterious effects of genes that encode for inflammatory responses[25].

Detrimental effects at late age get worse when humans improve their natural habitat
Our genome has evolutionary been shaped following environmental changes that occurred over millions of years. The improvement of our environment began slowly (see above) but accelerated during the last hundreds of years. Now we have almost dealt with death from infection. In developed countries clean drinking water, sanitation systems, improved hygiene, vaccination, antibiotics and improved medical care have changed human life-histories forever. We have converted our adverse natural habitat into a well protected environment. All these changes have resulted in a greatly reduced mortality risk from external causes and it is clear that a far larger proportion of recent birth cohorts will survive up to an age that can be considered as residing in the selection shadow. This is illustrated in figure 5. A larger proportion of the population is thus likely to suffer and die from chronic degenerative diseases. These radical demographic changes have not taken place everywhere at the same time, leaving large parts of the world still in environmental conditions resembling our natural habitat or in a transition phase. This brings us to what can be considered as the ultimate test of our hypothesis, i.e. that the inflammatory host response is the main regulator of the trade-off between maintenance of our bodies and fertility. What happens if immigrants, who were selected in order to survive under natural conditions, grow old in a protected environment? We assume that individuals who originated in an adverse environment are still under evolutionary pressure for inflammatory host responses when compared to individuals from protected environments. Quite often, immigrants to wealthy, affluent countries come from places with an adverse environmental condition where death from infection is still rampant. Thus still being selected for pro-inflammatory signaling, we expect them to suffer more from age related diseases when they live up to post reproductive age in the protected environment to which they have emigrated. Numerous studies have indeed reported that chronic degenerative diseases such as atherosclerosis[57-60], diabetes[61] and risk factors such as obesity and hypertension[62-64] are far more prevalent among

African Americans compared to Caucasian Americans. Other studies line up with the hypothesis that the excess of chronic diseases in immigrants has to be explained by a genetic predisposition[65-69]. Immigrants who are more heavily selected for an inflammatory response thus should also suffer from a reduced fertility (see above). Indeed several studies found pre-term deliveries and spontaneous abortions to be more common among African Americans than among Caucasians[70,71] and this finding appears to have a strong genetic explanation[72].

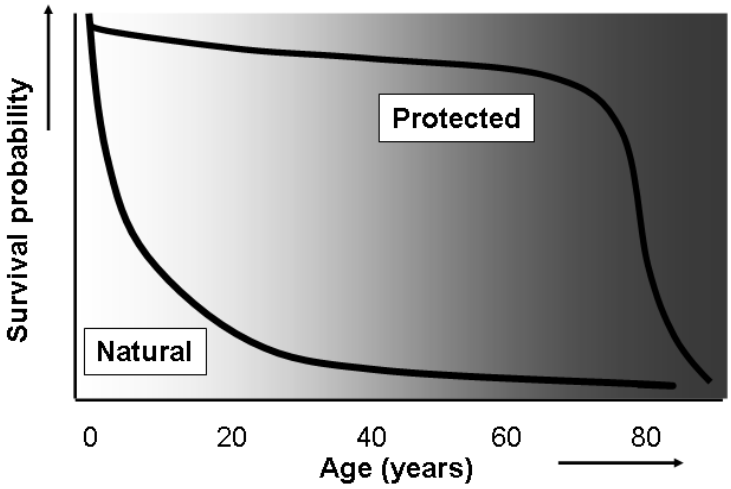

Figure 5. Survival probabilities in wild and domesticated populations. Adapted from Kirkwood & Austad[81]

Discussion

Organisms need to maintain their body up to reproductive age to show their reproductive success. Above we have reasoned that amongst other critical phenotypes man has strongly been selected for resistance to infection. As the necessary inflammatory responses come with a cost at fertility, investments in body maintenance are not maximized explaining why humans are still susceptible to fatal infection despite fierce evolutionary selection over thousands of years. As such it provides a biological mechanism for optimizing r/K strategies to maximize fitness under adverse conditions in our 'natural habitat'[73].

Health and disease after the reproductive age can best be understood from the theory of antagonistic pleiotropy which argues that the pro-inflammatory signaling that we have been selected for under adverse conditions negatively influences body maintenance at old age. As humans have increased their life span by improving the environment in which we live, a far greater proportion of people now reach older age and will suffer from late consequences of the inflammatory responses that were so beneficial at an early age. The costs of this selection for inflammatory responses are likely to be biggest among those who were born under conditions where death from infection was still present, but age under affluent conditions.

This line of reasoning is not only applicable to individuals but also to populations who have successfully improved their living conditions. A recent report from the WHO found that age-specific rates of many cardiovascular disease are currently higher among adults in sub-Saharan Africa than in industrialized countries[74]. Hence a fast transition from a natural to a protected environment leaves us with an ancient genome set for pro-inflammatory signals to be expressed in an environment where this is not a necessity and comes at a cost. The future of the developing countries is an emerging epidemic of chronic diseases[75,76] with cardiovascular diseases on top[77].

When concluding we emphasize three points. First, by no means have we wanted to suggest that inflammation is the only human phenotype that is under evolutionary selection, nor that it is the only factor that determines the occurrence of chronic degenerative diseases in old age. For instance humans were also selected for handling a shortage of food. We are set to store as much energy as possible during periods of abundance so as to increase our survival chances during the lean season. In the sedentary life-style of our protected environment with a plethora of foods this has lead to the epidemic of adipositas, which is nowadays one of the most threatening phenotypes from which we suffer[78].

Second, apart from evolutionary selection for specific genetic variants, it can be argued that differences in early phenotypic expression, i.e. plasticity, contribute also to the risk of chronic diseases at later age. A lucid example is the idea that fetal deprivation increases risk of mortality from cardiovascular diseases in old age[79]. The principle of plasticity can also be applied to the expression of the innate

immune system. Children who grew up in an environment with high infectious pressure have skewed their host response towards pro-inflammatory signaling and this may last a lifetime. Plasticity may thus contribute also to the increased risk of chronic degenerative diseases for those who moved from an adverse to an affluent environment.

Finally, man adapts genetically to its new environment. This Darwinian logic emphasizes that our population genome is on the change. In populations that have undergone a demographic transition, several birth cohorts have not been exposed to the fierce selection of resistance to infection. In stead of selective survival up to reproductive age, a period during which half of the original birth cohort may have died, under affluent conditions virtually all newborns will survive and pass their genotypes to the next generation. This includes individuals who have below average inflammatory responses and under adverse conditions would have suffered from fatal infection. These individuals can now escape selection pressure, are reproductively successful and may suffer less from chronic degenerative diseases as their genome encodes for less pro-inflammatory signaling. The population genome is likely to shift towards a predisposition for living healthier for longer.

Declarations

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Conflict of interest

There is no conflict of interest to disclose.

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Chapter 3

The Bimoba: the people of Yennu

J.J. Meij, D. van Bodegom, D. Baya Laar

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Introduction

In their book on Human Molecular Genetics Strachan & Read state that "Genetic research is of help in anthropological research"[1]. The other way around is true as well. To fully understand the epidemiological, demographic and genetic data, collected for our medical research, we needed the sociological, economical and anthropological background of the study population: the Bimoba.

The Bimoba tribe is scattered throughout the Upper East Region of Ghana, the western part of Togo and the southeast area of Burkina Faso. It is arguable whether the Bimoba are a tribe or not. Some mention them as a group only. Until now little has been written about them. We found one anthropological publication of sixteen pages describing the Bimoba in general and one unpublished essay[2,3]. Therefore, we collected data about the Bimoba, their history, their beliefs and their present situation alongside our medical research fieldwork in the southern part of the Garu-Tempane district; Upper East Region, Ghana.

The aim of this chapter is to provide a general description of the Bimoba as a whole and a more detailed description of the Bimoba clans living in the research area.

Methods

In 2003, during five months of fieldwork, we conducted several investigations in the Farfar area to obtain information about the Bimoba. We continued this research in 2004-2006 during four additional periods of field research (February 2004, July-August 2004, 2005 and 2006). For the data collection of this concise ethnography of the Bimoba people we used the Rapid Assessment Procedure as basic method[4]. In this procedure it is assumed that descriptive material on the local cultural systems is available. Since hardly any written material exists, we additionally investigated the economic system, kinship, religion, and social organization.

The information about history, traditions, and religion was collected during a series of structured and non-structured interviews with older men (some *Jaba* (shamans) among them) and women, as well as some Bimoba chiefs of the region. The information about housing, habits, work, and social structure was collected through participant observations in four randomly selected compounds and some additional interviews with the landlords of these compounds. Apart from this, group-interviews were held with Bimoba women from different villages to obtain information about daily life activities and habits. The demographic information, demographic characteristics are based on our (medical) demograph database. In this database all inhabitants of the research area are registered. A total update of this demographic database is carried out annually since 2001. To measure the health and medical situation we performed an indepth health survey among 2,000 inhabitants of three villages in the research area: (Bakinakoan (usually called Benakpezir), Zariboko and Tambalo). Finally, we interviewed several traditional healers about their work and practice.

We reviewed the available literature. As mentioned above, the total number of articles and publications is low and usually of poor scientific quality.
Although some books and articles acknowledge the existence of the Bimoba, no general description has been found yet. Unlike the neighbouring tribes like the Mamprusi[5], the Kokomba[6], and the Kusasi[7,8], the Bimoba are not known by way of sociological, anthropological, or historical study. On the rare occasions that the Bimoba are described, it is always short, or even just a footnote[9,10].

In 1990 the CUSO development organisation of Ghana asked Max Assimeng of Legon University to give a brief description of the Bimoba. CUSO missed

background information about the people they worked with and Assimeng drew a sixteen page sketch of the Bimoba[2]. He mentioned the existence of a few short unpublished essays about the marriage of the Bimoba[11], about the Koant, an initiation rite, and about some fragments of Bimoba history[12,13]. However, we could not trace these articles in the Upper East, nor in Accra or Legon. However, there are some anthropological publications about the neighbouring Moba tribe in Togo, which in its system and rituals has much in common with the Bimoba. Especially the monography of Juergen Zwerneman "*Studien zur Kultur der Moba (Nord Togo*)" is comprehensive[14].

A brief introduction to Bimoba history

The origin of the Bimoba people is not clear. According to oral history the Bimoba originate from the east and the west of Africa. Assimeng states that the Bimoba came from Burkina Faso, but he also describes other possibilities[15]. All written sources are clear about the fact that the Bimoba tribe is a combination of different smaller groups, although the combination of clans is different in every source (Bims, Moba and Daggams[2] or Moba, Basaalis, Gurmas, and Kokombas[16]).

The Moba, closely related to the Bimoba, migrated from Sudan to the west of Africa and it is clear that some clans of the Bimoba (the Naniik, Kpikpira and Nabakib clans) were sub-groups of the Moba. There is no clear indication when the Moba or Bimoba actually came to the west, but oral history claims that they did so in the aftermath of fights at the end of the Shilluk reign, 1500 AD[17]. They all settled along the route from Sudan to Ghana. The Bimoba settled at the end of the line and claim that they have migrated from the Sudan separately and seem to originate from nomad traders. Some other clans (Tambiouk, Maab, Bakpang and Tont) came, according to oral history, from the area that is presently known as south Togo and the Southern regions of Ghana (Ashanti and Dagomba land).
Although the Moba have some form of tribe structure, there is no such structure in the Bimoba group. They belong to the acephalous tribes[18]. In contrast with the surrounding tribes (Mamprusi (south), Kusasi (west), and Moshi (north) and Chekosi (east)), there are no kings, chiefs or big men among the Bimoba. The clan and clan group (see table 1) are the focus point of the members of the tribe. History varies from clan to clan. The only common history they share is the history of their first chief, Turinwe. Allthough Turinwe is connected to only four clans, all clans accept the story of his migration as the first fact of Bimoba history.

Table 1. Clans of the Bimoba

Clan group of Baakpang	Baakpang
	Tont
	Nayalib
Clan group of Turinwe	Nabagib
	Kpikpira
	Mauk
	Tanbiuung
	Naniig
Clan group of Kanyakib	Kanyakib
	Sisiak
	Miir
	Kollimasi
Individual clans	Kpanbolik
	Njaanu

When they settled in East Ghana and West Togo, they occupied the least fertile and most remote parts of this region, mainly in the area they still live in. This indicates that they were not able or did not want to rival the existing kingdoms at large. As a result of this the Bimoba are a group with limited power. Up till now only a few Bimoba men from the more developed area of Nakpanduri (Northern Region) have entered the government at a senior level.
On the whole, the Upper East Region has been neglected for al long time. Compared to the south of Ghana, the region is still poor and less developed. The Gross Domestic Product of the Upper East Region is US$ 304 per capita per year, against 2150 for the whole of Ghana[19,20].

As in many cases, it is arguable whether the Bimoba are a tribe. People also form groups (with its own history and habits) out of political reasons and this could also be the case with the Bimoba. We regard the Bimoba as an ethnic group with significant tribe elements, for four reasons. First, the group is a well known,

although not well documented, group of people. Second, genealogic analysis shows endogamic relations within the group. Third, the structure of the clans forms an important and leading element in the social organisation of the group, and fourth, the people regard themselves as Bimoba and refer to the Bimoba as their tribe.

Demography

There is no exact figure of the size of the Bimoba Tribe. Most of the written sources estimate the total population of the Bimoba around 300,000. The Bimoba clans are spread throughout the upper west of Togo, the Upper East Region and the north-eastern tip of the Northern Region of Ghana. Approximately 17,000 Bimoba are living in our research area, which measures approximately 400 square kilometres. This area is inhabited by 25,000 individuals (Bimoba (66%), Kusasi (24%), Mamprusi (4%), Fulani (2%), Busanga (2%) and some smaller numbers of other groups).

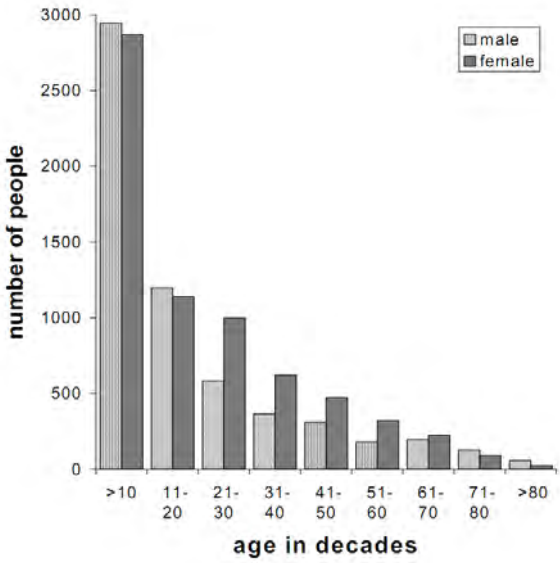

Figure 1. Age distribution of Bimoba in research area

Figure 1 shows the total age distribution of the Bimoba population, based on our own observations from 2003. 50 percent of all Bimoba is 12 years or younger (Ghana national: 33%), 2.3% of the population is 70 years or older. The life expectancy at birth is 55 years (Ghana National: 57.5 male, 59.5 female). These

figures are quite different from the national data, but are in line with the underdeveloped status of the area. The situation in the Upper East Region is more like the situation in Burkina Faso than in Ghana[21]. Only the life expectancy, which is much better than expected, is almost similar to the south of Ghana.

As stated before, the Bimoba do not have an integrated tribe structure. There is no paramount chief or Bimoba king. The total group consists of more than twenty different clans. Each clan has its own geographical focal point throughout the Bimoba region. Table 1 shows the clan and clan group structure of the Bimoba. Bimoba can only marry outside their clan. Marrying outside the tribe is permitted, but rarely seen. By marrying, the wife is accepted in the clan of the man. She then regards herself and her kin as member of her husbands clan. If the husband dies, the widow can remarry, but by doing so she might loose all her rights of possession and custody. Only when she remarries within the clan or clan group of her late husband, she will remain in her right. In 2004 we performed a detailed genealogical evaluation of two clans in a typical Bimoba village. Despite the paucity of male variation, but likely because of the social ban on marrying within clans, we found the inbreeding co-efficient to be low[22].

Like many groups in the region, the Bimoba people are living in family compounds. Although extended family and clan are the main basis for social setting, most of the Bimoba are living in a semi-nuclear family compound under guidance of an adult man (the landlord). On average a compound is inhabited by fifteen persons, but the largest compound we found had 214 inhabitants, the smallest only one. Polygamy is widespread (figure 2). Bimoba men can take up to four women, depending on their financial means. Bimoba families are still large. The average number of delivered offspring in post-menopausal women is eight[23].

Bimoba are patrifocal and therefore, children always remain under custody of the father. Many women do have their first delivery before their official marriage and many of them with another man than their future husband. Casual sex before marriage is common and the children born out of these contacts are not frowned upon. The children are usually raised by the mother although at any time the father can demand that his child returns to his custody.

The work on the compound and at the farm is divided between men and women. The women on the compound divide their work between each other. If some of the women are farming or have gone to the market, the other women of the compound take care of the children, which includes (breast)feeding. All members of the family, including the children, are part of the compound labour force, especially during ploughing, sowing, and harvesting time.

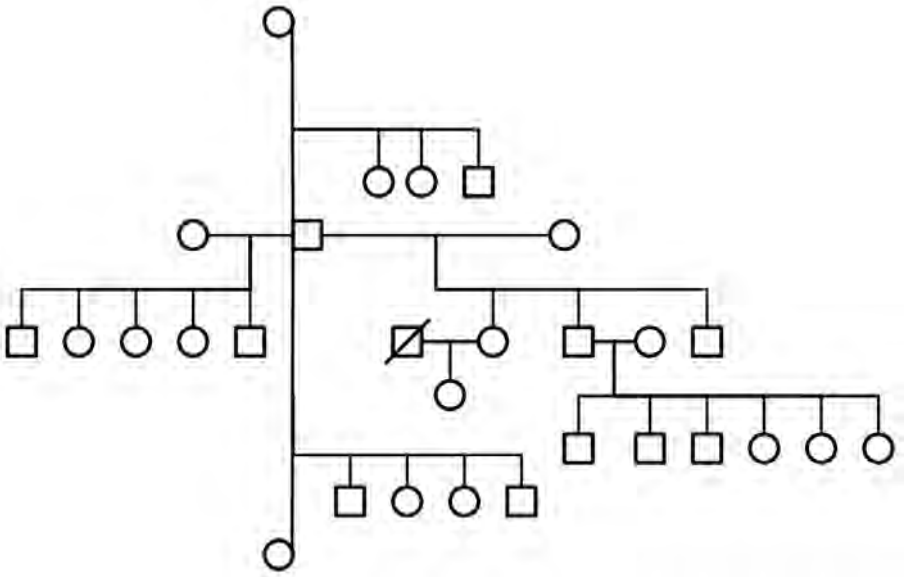

Figure 2. Typical compound pedigree of a Bimoba family

Political situation and power

The Bimoba tribe is one of the smallest ethnic groups in Ghana. Comprising only 0.6% of the nation's population and having no chief or kingdom, they lack any formal power. In Ghana there are - basically three different power systems. First, there is a governmental system with a democratic structure throughout the country. Second, there is the rural chieftainship. Each region has a chief, appointed

by the government and an informal tribal chief. These chiefs are assembled in the 'district house of chiefs'. The chiefs are highly respected mediators between the people and the government, but lack official power. Third, many tribes still have their tribe-chief or king. The tribe-chiefs and kings can settle disputes and deal with tribe and family matters. The Bimoba have some tribal chiefs but the chief of the (Bimoba) Farfar district is a member of the Mamprusi tribe for twenty years now, although the Mamprusi tribe form less than 3% of the population.
The regional chieftainship of the Northern Region caused recurring tribal wars in the last century. Several wars were fought between the Konkombas and the Bimoba. These wars have cost thousands of lives. The original sporadic fighting has become more frequent, more intense and wider in scope since the 1980s, with destruction of life and property. By official counts, the Konkomba-Bimoba wars of 1984, 1986, and 1989 left 60 people dead, with several hundreds displaced. This tribal fight was part of a larger series of tribal fights. Most of these wars were fought in the Northern Region (Gonja-Nawuri war of 1992; the Konkomba and allies against the Gonjas in 1992; the Konkombas and Mossis in 1993. Finally, the 1994/95 Guinea fowl war in which modern weapons were widely used, resulted in at least 2,000 people killed, 200,000 internally displaced and 441 villages completely destroyed[24]. These fights were mainly induced by the introduction of a district council and the changing political structure (the power of the traditional leaders weakened). Clashes are rare now but the Bimoba-Konkomba relationship is still a matter of concern.

The Bimoba of the Upper East region escaped most of these atrocities but seem to be more and more aware of their situation nowadays. Some are interested in the chieftainship, but did not reclaim it yet. At present the Bimoba are living in relative peace with the surrounding ethnic groups and do not pay a lot of attention to the relative powerless chiefs of the region.

Religion
Yennu is the God of all Bimoba. Yennu is a complex referring to all different elements of the power of God. The name Yennu is used to describe 'God', it means 'sun', as well as the various places in a compound dedicated to Yennu (as one of our informants put it 'everybody has his Yennu but there is only one God almighty'). Yennu is also the name for the pile of sand that sort of marks the 'center' of any N'Yennu (the *personal* God, possessed by an individual). This pile of

sand is also referred to as Yennu and should therefore be regarded as part of any Yennu, or as an informant put it: 'the pile alone should be enough.' Yennu is extremely important in daily Bimoba life and his might is everywhere. The influence of religion cannot easily be overestimated.
The Bimoba religion is purely individual. There are no churches or weekly gatherings. Nevertheless, Yennu and all elements of the religion are completely integrated in normal life. Besides the important and ever present Yennu, ancestors play a major role in daily life. The ancestors are – although deceased - still living on the compound and they guide the Bimoba through their life. They are in close contact with Yennu and every living spirit (Mier) and body (Gbanant) is not only of the living 'owner', but also theirs.

To please the ancestors, rituals and sacrifices are made. These sacrifices are made on the Patir (plural: patra), a clay construction annex to the inside wall of the ritual hut (Nakouk). The patir is a place of worship for the whole compound, men and women, although women do not enter the Nakouk.
Besides the communal Patir, every man or woman can put up his or her own small altar, called 'Mier'. The Mier of a woman is set up in her own hut, the Mier of a man is usually set up inside or next to the Nakouk.

Apart from the individual shrines/altars, the Tingban is the shrine of the whole farm or the whole village. Tingban is usually a pile of stones or a tree (Baobab mostly) on a place, selected by the Jaba, the religious shaman. The village Tingban consists of four shrines (one main shrine, two sub-shrines, and one shrine for Tinnj Yennu (the earth God). Bimoba visit their Tingban in case of problems (sickness, strong winds, long drought, insects, etc.).

To communicate with Yennu a Bimoba can pray to the ancestors or see his Jaba. The Jaba is a senior member of the Bimoba who possesses supernatural powers. He is a mediator between the people and Yennu. All the individual arrangements of N'Yennu are the concern of the Jaba.

Traditions and rituals

Based on our interviews, we found only a few tribe festivals and rites, most of them being rites of passage. The festival of Danjuor, where the history of Turinwe is told and the coming of Turinwe to the region is celebrated. This used to be the biggest and most colourful festival of the Bimoba. It had not been held for some decades, but in January 2004 the festival was reintroduced. The Danjuor festival includes music, dance, and one-day coming together of all Bimoba. The Danjuor festival of 2004 was visited by over 2,500 people.

In the Bimoba tribe four rites of passage are of great importance: the Koant, the Ba Wanu (a ritual to establish Jaba's), the wedding, and the funeral.

Koant

In the Koant ritual a secret language is learned and a new name is given to a member of the tribe undergoing the ritual. Each member of the Bimoba has different names. Apart from the first and family name, many have a Christian or Muslim name, mostly used when going to school or going 'Kumasi' (far away). Besides these names, Bimoba can obtain a ritual Bimoba name. These names (Konjit, Konduuk, Dinwaak and Tanjon for women, Duut, Laar, Kombat, Lambon, Konlan and Bombom for men) are given to them during a lengthy initiation process. This ritual is regarded to be holy and secret. Unlike other tribes, any Bimoba, man or woman, can request a Koant. The ritual is not compulsory and nowadays hardly performed, but still many initiated (Koantjies) are living in the area. Before entering the Koant process, the Konatji (the one undergoing the Koant) requests permission of the most senior Koant-member. After consulting the parents of the Koantji, the date of entering is fixed. The whole Koant process takes three months for men and four months for women. It gives the Koantjie a highly regarded status and the possibility to speak with other Koantjies in their own, secret language.

Ba Wanu

The Ba Wanu initiation, which most Bimoba undergo, establishes whether you are a Jaba (shaman) or not. The initiation takes twelve hours or even more. The Ba Wanu initiation is requested by a person's Mier (which literally means nose but actually means a man's spirit). Usually this happens when uncommon things happen to life such as death, drought, or heavy flooding. There is no fixed age for married males to undergo the Ba Wanu initiation and, although it is possible to do

the Ba Wanu at any age if you are not married, the vast majority of the unmarried men do not undergo the Ba Wanu under the age of 40. Women do not undergo the initiation if they are not married and if married they only do the Ba Wanu at the age of 45. The actual initiation is usually done by a Jaba, selected by another Jaba. The complicating factor is, that if a wrong Jaba is chosen to perform the initiation, the person initiated can either die or go mad. The owner of the Mier is made to faint for some time. In this period of unconsciousness the man can see whether he is a Jaba or not. If he is a Jaba, he will see two dwarfs (a man and a woman) on the rooftop of the nakouk. The attendees of the ritual will listen to his recollections after he comes back to his senses. If the attendees are satisfied with the answer (in fact the right description of the dwarfs on top of the nakouk) they can decide that the man is a Jaba. This implies that every Jaba has undergone the Ba Wanu initiation, but not every person who has undergone the Ba Wanu initiation is a Jaba. The person known to be a Jaba is then trained by an older Jaba. This training includes the interpretation of the message from the dwarfs to the people who come to him for consultation.

Women do not undergo this fainting process but they can be a Jaba if their mier want them to be. There are only a few female Jabas in the Bimoba community. Although female Jabas can not perform the Ba Wanu for another person, they can advise other people.

Marriage

The Bimoba regard marriage to be an important ritual, but the actual wedding is low profile. The original ritual (Pochianu) has faded out almost completely. Nowadays the groom seeks the permission of the father of his wife to be. This permission is obtained by intermediaries. Up till now there is no fixed bride price, and only small gifts are send to the father after agreement (cola nuts, guinea fowl, some local gin). The wedding ritual itself is performed by a simple visit to the parents of the bride. After this visit the groom sends more cola nuts, tobacco, two bottles of gin, a jerry can of local beer, and two guinea fowls. Influenced by the Kusasi culture, an additional bride price of four cows is set in most cases. This part of the bride price can be delivered during the first years of the marriage. Although not original Bimoba, this additional pricing has become widespread. Reciprocal wedding arrangements are known, but now fading out. There is no other ritual in the Bimoba culture in celebrating a wedding, but due to the introduction of world

religions, some seek the blessing of the church. This is –due to the low percentage of Christians and Muslims- still very rare.

Funerals

Funerals are the most important social activity among the Bimoba. Each funeral is attended by hundreds of people and the funerals are more a social event than a sad gathering of mourners. Most of the funerals consist of two consecutive parts, the Kumian (Fresh Funeral) and the Kukoan (final funeral rite). Kumian and Kukoan are only performed for natural deaths. In cases of Kubir (bad death) a different ritual is performed. The funeral of a male Bimoba takes three days, for a female it takes four days. During the first day, the funeral is announced in the early morning by firing carbide grenades, three for a male, four for a female. As soon as possible the corps is placed in a round grave close to the compound, naked in a sitting (foetal) position. The grave is covered and the water bucket of the deceased is put on the grave, broken into pieces, to mark the end of his life. At sunset some clans perform specific funeral rituals. The following two or three days the family and close friends stay together to remember the deceased and are visited frequently by relatives and friends.
The Kukoan (final funeral rite) is performed some time later, during the (next) dry season. Again the social gathering of the clan and friends is the central part of the final rites. They are famous for the social side effects; sex, alcohol use, and dancing.

Balance of power

As in most groups, rituals play a role in balancing society (as well as religion does). In the Bimoba tribe two rituals are important in keeping that balance: The Koant (name giving) and the Bawa Nu (appointing of Jabas). Through the Koant, the adults have learned a new and secret language in which they can communicate among each other at any time and place they want. This gives the group an elevated position over the rest of the tribe who cannot understand the language.

During the ritual of the Ba Wanu, the new Jaba's are selected. Although it is said that the Ba Wanu has to see the dwarfs during his absences, the attendees of the ritual decide whether the candidate saw the right dwarfs or right things. So in fact the clan (or at least those attending the Ba Wanu) decides who is a new Jaba and consequently one of the new informal leaders: if they do not want a certain candidate, they can easily say that he just did not see the right things. This

balancing power is seen more often and is quite influential. It maintains the balance in the community without harassment of those who were rejected as being a new leader. In Africa this pattern is seen for instance in the Mwari Cult in Zimbabwe[25].

Leadership and organization

In contrast to most of the surrounding tribes, the Bimoba do not have their own chief or general leader. As stated before, they belong to the acephalous tribes, tribes without rulers[18]. The clan is regarded to be the most important organizational structure. Apart from this clan leadership, Bimoba accept the ruling of non-Bimoba chiefs. In our research area, one of the regional chiefs (the chief of Zariboko) is a Mamprusi and he is in charge of the whole area, including the Bimoba living there. The *Bawku naba* (chief of the whole Bawku district) is a Kusasi. Due to the strong clan structure and the close-knit clan network, the mutual assistance system is extremely strong. As part of this system, the Nnoboa, the Bimoba have a norm of assisting the clan with the building of huts, farming, and sharing wealth.

All the land in the Farfar area is owned by three families. The boundaries are based on family history. The oldest man of the clan is the caretaker of the land and decides who can live or cultivate the different parts of the property.
Not all the land is cultivated yet, and not al the cultivated land is cultivated by the owner. Landowners share uncultivated land with clan members as part of the Nnoboa. This is done at no cost, but the land has to be returned to the owner when needed. Since the boundaries are only based on this oral agreement and only marked with small trees or crop, many conflicts occur.

Housing

Figure 3 shows a plan of a Bimoba compound. Bimoba housing is extremely simple. Each compound consists of a number of round huts placed in a circle. The compound is located in the middle of the property (farmland). All huts are made of clay and the roofs are made of reed and straw. The huts have no windows. Due to its vulnerable structure the average life span of a normal hut is up to four years. Over the past decade rectangular shaped huts with corrugated iron roofing were introduced. Many farmers combine one or two of these modern huts with a series of traditional huts.

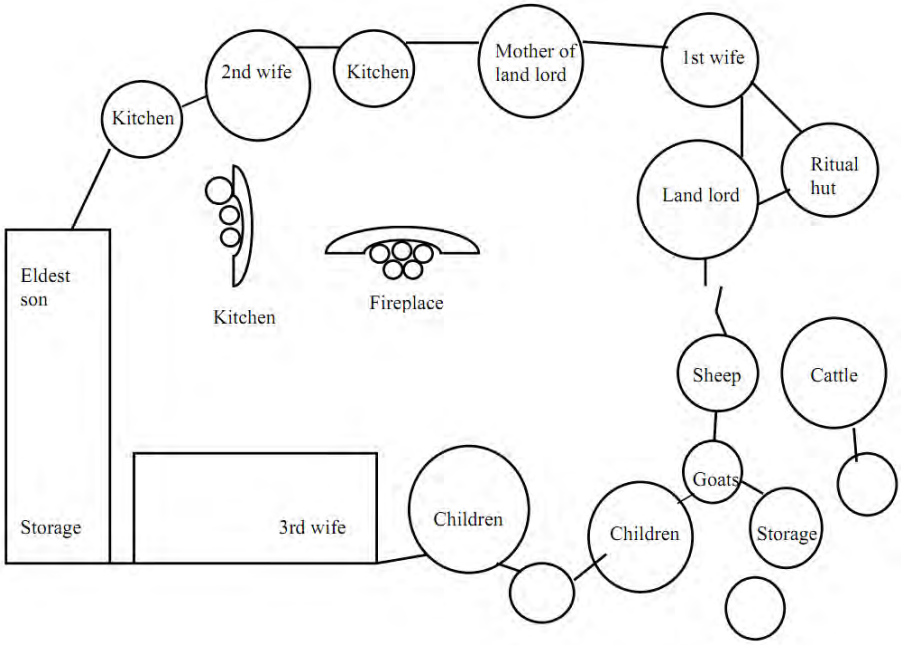

Figure 3. Bimoba compound

There is one hut for every adult (starting at the age of thirteen). There are separate huts for the children who sleep together until they reach puberty. There is a hut for storing food and a patra (ritual hut). All huts are linked by a wall. The wall and huts seal off the compound from the outside world. In front of the compound, some huts are placed for the animals and birds. Kitchens are placed in the centre of the compound, one for each woman living on the compound and sometimes a common kitchen for brewing beer. Some corners between the huts are separated by a small wall and used as a shower.
Three villages have access to electricity although the vast majority of the houses is not connected. If connected, the electricity is mainly used for illumination.

Economy
The Bimoba in the Upper East Region are almost all subsistence agriculturists. Only a small percentage of the population is involved in petty commodity or informal trade activities. Every family farms predominantly for its own use and

survival. The estimated average income is below the international standard of one US$per day (poverty scale United Nations).

Investments in tools or machines are rare. The average farmland that is used by one family is about ten acres, but the actual size of the possessed land varies considerably. Most of the families own land around the compound and acres further away. Often, the land is hired out to other Bimoba (as part of the Nnoboa).

There is one sowing season with two harvesting periods. During the sowing season, May-June, millet (early and normal millet), round beans, maize, corn, and groundnuts are sowed. Apart from these; tomatoes, green pepper, and cotton are produced on a smaller scale. Harvesting of early millet is as early as July; the other products are harvested in late September and October.
The total farming is done by hand. In the whole Bimoba region, no tractor was found during our visits, but according to local informers, one tractor is available, owned by a Mamprusi. Some 40% of the farmers make use of bull oxes for the ploughing of the land. The others plough by hand. The ploughing with bull oxes is done by men; the hand ploughing is equally divided between men and women. Sowing is almost exclusively done by women.
Fertilizers are used, but not by all farmers. Many farmers lack the money to invest in fertilizers and insecticides. Bad harvests are common and famine occurs in some parts of our research area too. In years of famine, many farmers lack the money for clothing, schooling and healthcare. In these years, people are barely surviving and the actual situation does not differ a lot from the situation some 50 years ago. In her study "Tribes of the Northern Territories of the Gold Coast" Manoukian describes the farming north of the escarpment which closely mimics the present situation[26].

The almost absence of a market economy in the region explains why the traditional mutual assistance (the nnoboa) is still functioning and because of this, the chances to survive periods of drought and famine are higher than expected based on their socioeconomic status. We observed the strength of the system during a period of drought in 2003-2004, when the more market oriented Kusasi tribe suffered far more from the disaster. Due to the Nnoboa and the strong clan ties, most of the Bimoba escaped the famine by sharing the scarce foodresources.

Education

Illiteracy is still very high among the Bimoba in the Upper East Region. Based on a survey in three villages in our research area (n=960) we estimate that about 5% of the population over 15 year old is able to read and/or write. Since we did not test their ability to write or read, the actual percentage may even be lower. About 25% of the present population of children between 4 and 15 years visit school. Since many children do not attend school regularly, this is an overestimation. In the research area several primary schools (25 in total) and several junior secondary schools are available. Education at senior secondary level or higher is available in Tempane or Bawku. Garu, the nearest central market village, has some small schools for vocational training, but only a few Bimoba go there. Most schools are established and run by the government. There is no monthly school fee for primary schools, but the monthly fee for secondary school is 60,000 cedi (approximately € 5). Although all women mention the importance of good education, they admit that farming is more important and that most children prefer working on the land instead of going to school. Apart from this, the landlords often lack the money to pay for the school uniform and the school fee.

The Bimoba tribe has its own language: Moar. The classification of the language is: Niger-Congo, Atlantic–Congo, Volta–Congo, Central, Northern, Oti-Volta, Guma, Moba. The language is related to the Moba, Togo, but not inherently intelligible with it[27]. The Summer Language Institute's catalogue of languages of the world (14th edition, 2004) estimates the number of Moar speakers at 76,000. Most of the Bimoba speak different varieties of Moar.

The language has been described in the mid-sixties[28]. Some missionaries wrote a language course, but Moar is still mainly an oral language. Recently some schoolbooks have been written to teach the language. We found two books in Moar: one private publication by the Canadian missionary society containing some clan stories (not dated, but most likely around 1990) and the Bimoba Bible (new testament 1986, old testament 2004) .

Health care. Traditional/non-traditional

Table 2 shows the distribution of the Body Mass Index (BMI) of a small representative survey in three villages and of rural and urban Ghana[29,30]. Data are expressed on the scale of chronic energy deficiency[31] and referred to standard WHO BMI rates[32]. We observed that almost one third of the Bimoba living in this

area suffer from chronic energy deficiency. For comparison, the corresponding figure for rural Ghana is 19.1%[30]. This high percentage of chronic energy deficiency in the region shows that the region is still in a pre- or early-transitional stadium of development.

The vaccination rate is increasing (especially due to mass vaccination programs), but from an (inter)national point of view still low. We have estimated that only about 50% of the children under ten years of age are fully vaccinated against common child diseases. Many families cannot afford the vaccination of all their children. In the Farfar area there are no hospitals. More recently some primary health posts/clinics have been set up. These posts provide for very basic mother and childcare. Only the clinic in Garu, approximately 25 kilometres from Farfar, provides some medical care, but a medical doctor is absent. Most of the Bimoba rely on traditional healers. They can be found throughout the region and treat all possible diseases. The Bimoba also use traditional birth attendants. Traditional healthcare is more readily available and cheaper than modern healthcare.

The Ghana Health Service has reported on the following outbreaks of infectious diseases[29]: meningitis 1984, 1991, 1996, 2002; measles (but mass vaccination is carried out now and then); yellow fever (1996/97); cholera (1991, 1995 and 1998); anthrax (yearly); malaria (100.000 cases reported each year in the Bawku East district).

Apart from this, morbidity of other water/environment related diseases like schistosomiasis, soil-transmitted helminthes is high.
Although AIDS/HIV is not considered to be a big problem (estimated prevalence of infection is <1%), the risk of introducing the infection to the region is high. The regional health care authorities also observed a high micronutrient deficiency among the under five (Vit A 65%, Iodine 85%) over the last five years.

Table 2. BMI of Bimoba adults (age >20) in research villages, whole population, rural and urban Ghana

	Bimoba	Rural Ghana	Urban Ghana
	n=140	n=5,788 [31]	n=3,427 [31]
Mean BMI (SD)	19.4 (2.0)	20.7 (n.g)	22.5 (n.g)
<16	6.4%	1.7%	0.8%
16-16.9	7.9%	3.4%	2.0%
17-18.4	17.6%	14.0%	8.7%
18.5-24.9	67.6%	74.7%	68.6%
25-29.9	0%	4.8%	13.6%
30-39.9	0%	1.3%	5.6%
>40	0%	0.1%	0.6%

BMI-ranges "<16", "16-16.9", "17-18.4" are also referred to as Grade III, II, I of Chronic Energy Deficiency; BMI 25-30: overweight, BMI >30: obesity[31,32]

Birth control, family planning

Bimoba women are proud of a large kinship. Young women with large numbers of children are highly regarded and respected. Most of the Bimoba women deliver their first child before turning eighteen, sometimes at a much younger age (13 or 14). On average, Bimoba women deliver eight children during their life[23]. Although infant mortality is on the decrease, it is still high and all respondents during our interviews mention this as one of the main reasons for producing many children. Birth control is virtually absent and although mostly younger women know the existence of oral contraceptives, ac-devices, and condoms, they are hardly used. They report that this is the result of their husband's wish. Spacing technique during breastfeeding is used by few women, as many of the respondents complained about the ineffectiveness of the technique.

Conclusion

The Bimoba people are a relatively small tribe of West Africa. Their economy is based on subsistence agriculture. Bimoba live in nuclear family compounds. They are less developed and less organised than mainstream Ghana or mainstream Africa[33,34] and the surrounding tribes such as Mamprusi, Kusasi, or Dagomba's. This marginalized position is caused by long lasting neglect of the region by the

central government but also by the strong family and clan structure, the weak acephalous structure and their scattered existence throughout the Northern Region, Upper East Region of Ghana and the Western region of Togo. Because of this combination of factors, the Bimoba people were not able to acquire enough power to put themselves in an advanced position. Since the focus on family and clan is still strong, the total socioeconomic status is still low and since most of the Bimoba cannot read or write, rapid changes are not to be expected and are not likely to be successful when introduced centrally. All landlords act individually with the guidance of one or more Jaba's. Therefore (health) education, development and improvement of the social status has to be introduced and organized at a grass root level. Once the cooperation of the landlords and local (informal) leaders has been achieved, projects for improvement of the local conditions can be implemented more successfully.

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Chapter 4

Socio-economic status by rapid appraisal is highly correlated to mortality risks in rural Africa

D. van Bodegom, L. May, M. Kuningas, R. Kaptijn, F. Thomése, J.J. Meij, J. Amankwa, R.G.J. Westendorp

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Abstract

Socio-economic status is an important determinant of health and survival in rural Africa and necessitates a practical and valid instrument to implement in health studies. Our objective was to investigate the validity of the rapid appraisal method to assess socioeconomic status and its ability to identify individuals at risk.

Among 1,573 households in rural northern Ghana, we calculated the Demographic Health Survey (DHS) wealth index and conducted two rapid appraisal methods: self-reported wealth and interviewer- reported wealth. In addition we followed the 25,184 participants from these households for survival with a mean follow up of 3.9 years, during which 885 participants died.

The DHS wealth index was moderately correlated to self-reported wealth (Spearman Rho 0.59, $p<0.001$) and interviewer- reported wealth (Spearman Rho 0.75, $p<0.001$). Mortality risks were significantly higher for people with lower self-reported wealth compared to average (HR 1.30 [95%CI 1.11–1.51]) and lower interviewer reported wealth (HR 1.40 [95%CI 1.21–1.62]). Mortality risks were lower for people with higher self-reported wealth (HR 0.81 [95%CI 0.32–2.03]) and higher interviewer-reported wealth (HR 0.84 [95%CI 0.58–1.21]). Similar discriminative mortality risks were assessed when using tertiles of the DHS wealth index ($p_{trend} <0.001$).

Introduction

Socio-economic status (SES) is a difficult concept, both to define and to measure. Here, we interpret SES as a hierarchical position that determines someone's access to human or material resources. SES largely influences health and survival in both developing and developed countries[1]. In developed countries SES is mostly measured as a combination of education, income and occupation[2,3]. In developing countries however, especially in rural areas, most people have little education and income tends to be fluctuant depending both on the season and on the year and is not easily expressed in numbers. Also, the SES in developing countries is largely dependent upon a relative, social position in the community, clan or extended family and this is not always reflected in property[4]. In an attempt to measure SES in resource poor countries, long questionnaires of housing, household items, expenses, income, land use or food intake were constructed[5]. These long property questionnaires, however, were impractical because they were very time-consuming. Expenditure surveys are another method to estimate the socioeconomic status. However, in many rural areas the largest part of the economy is based on the exchange of goods and labor. Expenditure is difficult to measure in these settings. Most countries and institutions now use the Demographic and Health Survey (DHS) wealth index as a practical, valid and comparable method to assess the SES.

The DHS wealth index has some limitations. First, the DHS questionnaire was never developed to measure SES in the first place. All items that are used to construct the DHS wealth index were included in the DHS to assess different health aspects. The availability of a television or radio was included to measure the exposure to mass media health campaigns, the availability of a motorcycle or car to measure the ability to reach a nearby clinic in an emergency. From these possessions, it was later thought possible to construct a wealth index. Because of this historical origin, obvious possessions such as live stock were not included in the original DHS asset list. However, this was also noted by the DHS institution, who proposed an extension of the property assets in 2004[6]. A second limitation to the DHS wealth index is its practical implication. The use of country specific item lists with principal component analysis to weigh the different items allows the wealth index to be employed in different countries and allows a reasonable cross-country comparison. This is practical for public health officers and health policy makers. However, for the clinician-researcher who wants to estimate the SES differences in his study population in a rural resource-poor community, it is less

practical. For medical research in resource-poor countries it is crucial to asses the SES differences of the study population, because these differences have a large effect on health outcomes. However, because of the high workload in medical hospitals in these resource-poor countries it is not always possible to visit the participants at home, or to question all the participants on their possessions.
For the clinician-researcher, the rapid appraisal method could be a practical method to asses the differences in SES. The rapid appraisal method is an anthropological method which uses qualitative measures of SES and is designed to rank or stratify participants in wealth categories. Different rapid appraisal methods have been developed. Here we study two rapid appraisals. The first is the self-reported wealth, in which one asks the participant whether he/she regards his/her wealth to be below average, average or above average. The second rapid appraisal is the interviewer-reported wealth, which is more suited for fieldwork, where interviewers visit the participants at home. Based on the interviewers' observations here, the interviewer is asked to rank the household as below average, average or above average. Rapid appraisals, however, have always been looked upon as 'quick and dirty' estimates, while the longer property questionnaires were regarded as more valid and scientific[7]. Development workers have used the rapid appraisals extensively but validation studies are few in number and have not reached the established academic journals[8].
As questions remain on the validity and on the ability of the rapid appraisal method for health studies to identify individuals at risk, we conducted a comparative study in a rural area in northern Ghana comparing the DHS wealth index with two rapid appraisal methods: self-reported wealth and interviewer-reported wealth. To this end we have followed 25,184 participants from 2002 to 2007 and calculated mortality risks to see whether the rapid appraisal methods are able to identify individuals at risk.

Methods

Study area

The study was conducted in the Garu-Tempane district which is situated in the Upper East Region of the Republic of Ghana[9]. This region is far less developed than the southern part of Ghana, in socioeconomic aspect as well as in agricultural means. The Upper East Region, therefore, more resembles the neighboring countries of Burkina Faso and Togo. The area has a semi-Saharan climate with an average maximum temperature of 32 ^{o}C throughout the year and only one rain

season (June–August). The research area measures approximately 375 km^2 with approximately 25,000 participants living in around 40 villages. Most people in the research area rely on traditional medical care, which is equally distributed throughout the area. There is no medical doctor working in the research area and the nearest hospital is 40 kilometer away.

Study population

People in the research area live in polygamous extended families, with an average of 12 persons per household. The families live together in compounds; clay structures with thatched roofs, connected by clay walls. There are some 1,500 compounds in the research area. The people belong to several different tribes, mainly Bimoba, Kusasi and Mamprusi. A small group of more nomadic Fulani are living in the area as well. The vast majority of the people are farmers. The total agricultural process is done by hand. The average per capita income corrected for purchasing power parity of the whole of Ghana in the year 2008 was US$1,513 [10]. In the research area no formal estimation of the per capita income has ever been performed, but because of the agricultural aspect and exchange nature of the economy this seems not very indicative either. The area as a whole however, is much less developed than the rest of Ghana.

Socio-economic study

In 2007 we designed a DHS type questionnaire to asses the SES of the study participants using a free listing technique whereby we asked people from different villages of the research area, both male and female, in focus group discussions to list the household items of most value. These self-listed property questionnaires are reported to be highly correlated to longer property questionnaires[11]. The resulting list of valuable items was comparable to part of the Core Welfare Indications Questionnaire (CWIQ) from the World Bank and to the extended DHS asset list, adapted to our region[5]. Table 1 shows the different items, including mainly domestic livestock and different valuable household items comprising motorbikes, bicycles and iron roofing. From these assets a DHS wealth index was calculated. This was done as explained in paragraph 2.2 of the DHS wealth index comparative report[6]. Using SPSS factor analysis, the indicator variables were first standardized by calculating z-scores. Second, the factor coefficient scores or factor loadings are calculated. The DHS wealth index is the sum of the indicator values

multiplied by the loadings. This index is itself a standardised score with a mean of zero and a standard deviation of one.
As a rapid appraisal we asked the landlord or another senior person of the compound to rate the wealth status of their compound as below average, average or above average as compared to the other households in the research area. We also asked the interviewers to rate the wealth status of the compound as below average, average or above average. The interviewers worked in pairs of two and discussed their rating of the household to find consensus. All interviewers are born in the area, have many years of training and experience with the fieldwork and were explicitly trained for the DHS wealth index and rapid appraisal methods in 2007.

Survival study
In September 2002 we started with a database of all the inhabitants of the area, set up by the department of Parasitology of the Leiden University Medical Centre[12]. All compounds and inhabitants were registered and each compound was plotted on a map by means of GPS-handheld systems[9].
From 2002 through 2007 we have annually visited all compounds in the research area from June to August to update demographic data including migration, new-borns and mortality.

Statistical analysis
The correlation between the DHS wealth index and the rapid appraisal methods was calculated using Spearman's correlation coefficient. The correlation between self-reported wealth and interviewer-reported wealth was calculated with a linear weighted kappa. We used a Cox proportional hazard model with robust standard errors clustered on compound to calculate age and sex adjusted hazard ratios and plotted Kaplan-Meier survival plots. We tested for proportionality of hazards and found no evidence that the assumption of proportionality of hazards was violated. We used robust standard errors clustered on compound because mortality is an individual measurement and the wealth status is a measurement on the compound level. By using robust standard errors of the compound level however, we take into account that two dead children from one compound share more (genetic and environmental) determinants than just SES. Otherwise, our estimate of the importance of SES for mortality risks would be inflated. To plot the Kaplan-Meier plots, we divided the DHS wealth index in tertiles, to compare the DHS method to

the rapid appraisal methods which also uses three categories. However, the p for trend for the DHS wealth index was estimated using the continuous measurement. Because of the different ages of entry in the study we used left-censoring. Using this method we were able to calculate cumulative survival probabilities for all ages using our follow-up data from 2002 to 2007. Because the mortality risks as plotted by the Kaplan-Meier curves are age specific, this also corrects for any differences in age in the different wealth categories. All calculations were performed with SPSS 14.0 (SPSS Inc., Chicago, USA) with the exception of the hazard ratios, Kaplan-Meier plots and weighed kappa analysis which were calculated and plotted with Stata 9.0 (StataCorp LP, Texas USA).

Results

Socio-economic status

Table 1 shows the characteristics of the study population and results of the DHS wealth index and rapid appraisal methods. There was a correlation between the DHS wealth index and both self-reported wealth (Spearman Rho 0.59, $p<0.001$) and interviewer-reported wealth (Spearman Rho 0.75, $p<0.001$) figure 1). Self-reported wealth and interviewer-reported wealth were also correlated with 74% agreement (weighed kappa 0.56, $p<0.0001$).

Table 1. Characteristics of the study population

Participants (n)	25,184	
Male (n)	11,788 (46%)	
Female (n)	13,650 (54%)	
Mean follow up (years)	3.9	
Compounds (n)	1,573	
Participants per compound (n)[1]	12 (1-153)	
DHS wealth index[1]		
Number of male cattle	1 (0-16)	
Number of female cattle	0 (0-30)	
Number of goats	3 (0-40)	
Number of sheep	2 (0-60)	
Number of pigs	2 (0-20)	
Number of donkeys	0 (0-9)	
Number of motorbikes	0 (0-9)	
Number of bicycles	2 (0-27)	
Compounds with iron roofing (%)	61%	
Compounds with electricity (%)	15%	
Compounds using fertilizer last season (%)	68%	
Rapid appraisal	**Compounds**	**Participants**
Self-reported wealth (n)	1,549 (94%)	24,719 (97%)
Below average (n)	1,104 (71%)	14,928 (60%)
Average (n)	436 (28%)	9,560 (39%)
Above average (n)	9 (1%)	231 (1%)
Interviewer-reported wealth (n)	1,548 (94%)	24,696 (97%)
Below average (n)	870 (56%)	10,432 (42%)
Average (n)	618 (40%)	12,462 (51%)
Above average (n)	60 (4%)	1,802 (7%)

[1]Data presented as medians with minimum and maximum.

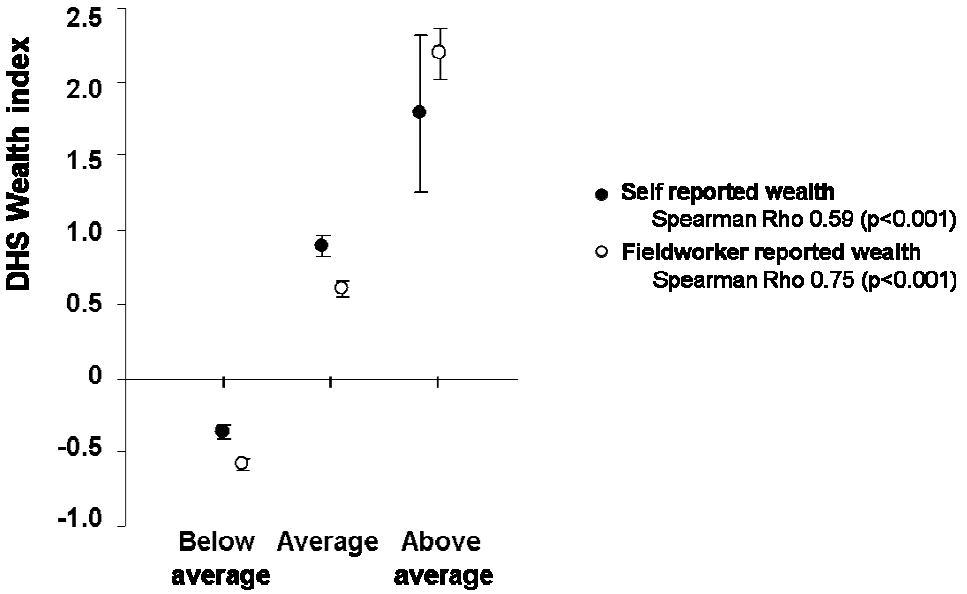


Figure 1. Correlation between rapid appraisal methods (self-reported wealth and interviewer-reported wealth) and DHS wealth index. Data are represented as means with 95% confidence interval.

Mortality risks

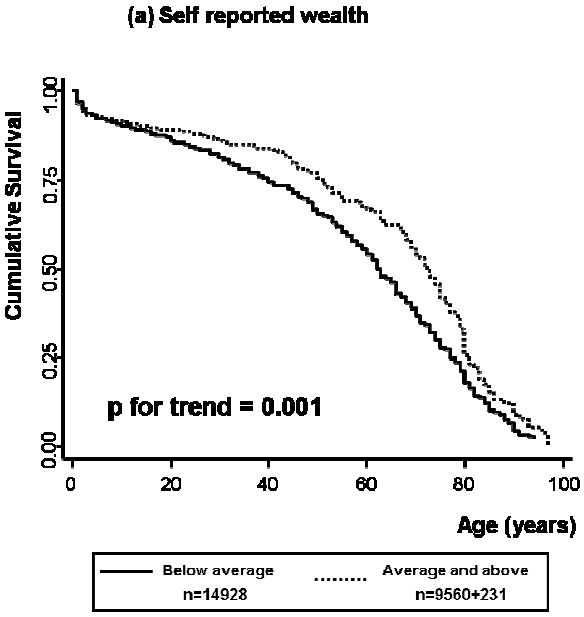
To assess whether the rapid appraisal method is able to identify individuals at risk we calculated mortality risks for the different wealth groups. The mean follow-up period was 3.9 years, during which 885 (3.5%) participants had died. We found significantly higher mortality risks for people with lower self-reported wealth (HR 1.30 [95%CI 1.11–1.51]) and lower interviewer-reported wealth (HR 1.40 [95%CI 1.21–1.62]) as compared to average (table 2). Mortality risks were also lower for people with higher wealth status compared to average for self-reported wealth (HR 0.81 [95%CI 0.32–2.03]) and interviewer-reported wealth (HR 0.84 [95%CI 0.58–1.21]). Going from lower to higher wealth status mortality risks decrease both with self-reported wealth (p_{trend}=0.001) and interviewer-reported wealth (p_{trend}<0.001). Similar patterns were observed for males and females separately (table 2). To compare the rapid appraisals with the DHS wealth index we divided the DHS wealth index in tertiles. We found a similar relation of lower wealth with higher mortality risks (HR 1.22 [95%CI 1.02-1.45]) and of higher wealth with lower

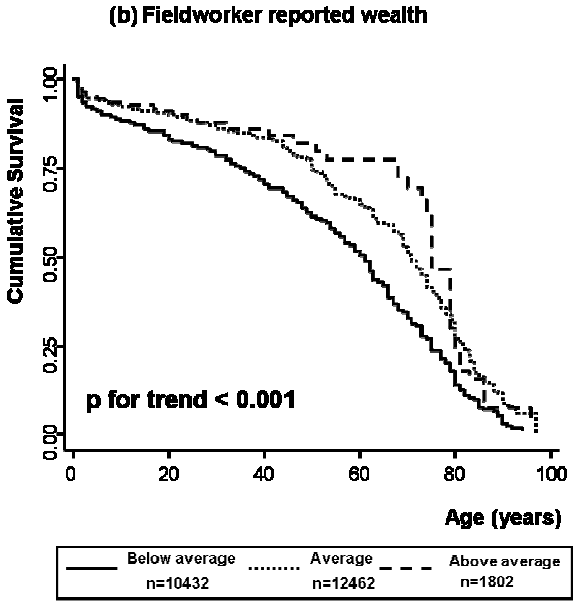
mortality risks (HR 0.88 [95%CI 0.73-1.06]). Going from lower to higher DHS wealth index, mortality risks decrease (p_{trend} <0.001).
Figure 2a and 2b show the corresponding cumulative survival probabilities of the different wealth categories for both self-reported wealth and interviewer-reported wealth. Figure 2c shows the survival probabilities for the different tertiles of the DHS wealth index.

Table 2. Mortality risks for different wealth categories

	Below average HR (95%CI)	**Average** (ref)	**Above average** HR (95%CI)	**p for trend**
Self-reported wealth				
All	1.30 (1.11-1.51)	1	0.81 (0.32-2.03)	0.001
Males	1.32 (1.09-1.60)	1	0.93 (0.27-3.19)	0.005
Females	1.26 (1.02-1.55)	1	0.62 (0.15-2.60)	0.029
Interviewer-reported wealth				
All	1.40 (1.21-1.62)	1	0.84 (0.58-1.21)	<0.001
Males	1.51 (1.25-1.82)	1	0.93 (0.62-1.41)	<0.001
Females	1.26 (1.03-1.54)	1	0.74 (0.47-1.18)	0.004
Tertiles of DHS wealth index				
All	1.22 (1.02-1.45)	1	0.88 (0.73-1.06)	<0.001
Males	1.40 (1.13-1.73)	1	0.98 (0.77-1.23)	0.001
Females	1.03 (0.81-1.30)	1	0.83 (0.64-1.06)	0.068

Cox proportional hazard model adjusted and stratified for sex. Data presented as hazard ratios (HR) with 95% confidence intervals (CI). Different wealth categories as reported by the rapid appraisal methods and wealth index divided in tertiles for the DHS wealth index. P for trend estimated for the DHS wealth index using the continuous measurement (see Methods section).


(a) Self reported wealth
Cumulative Survival
0.00
0.25
0.50
0.75
1.00
p for trend = 0.001
0
20
40
60
80
100
Age (years)
Below average
n=14928
Average and above
n=9560+231


(b) Fieldworker reported wealth
Cumulative Survival
0.00
0.25
0.50
0.75
1.00
p for trend < 0.001
0
20
40
60
80
100
Age (years)
Below average
n=10432
Average
n=12462
Above average
n=1802

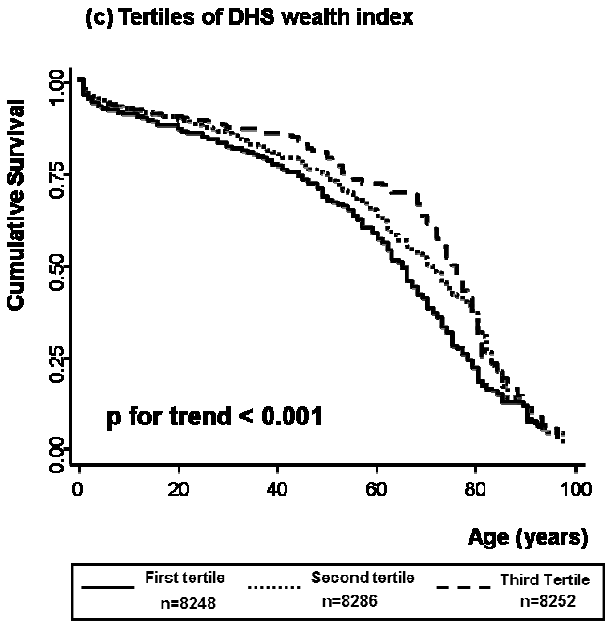


Figure 2. Survival probabilities dependent on various estimates of SES. (a) Self-reported wealth (b) Interviewer-reported wealth and (c) Tertiles of DHS wealth index. Estimates based on annual surveys between 2002–2007, analyzed with left censored Cox proportional regression with robust standard errors clustered on compound adjusted for sex. P for trend estimated for the DHS wealth index using the continuous measurement.

Discussion

In a rural community in northern Ghana we compared the DHS wealth index with two rapid appraisal methods to estimate wealth and to identify individuals at risk. The rapid appraisal methods are very practical to include in health studies in resource-poor environments. Questions remained on their validity however. We conclude that rapid appraisal can be used as a practical method to assess SES in health studies in rural Africa. The rapid appraisals are correlated with the DHS wealth index but more practical; it takes only a minute to rate the wealth status of a compound as below average or above average. The rapid appraisal methods also identify individuals at higher risk of mortality, even a little better then the DHS wealth index. One of the strengths of the rapid appraisal is that it could measure relative wealth, derived from the social status of the household members in the community. This position in family or clan structures is of utmost importance in the rural areas of developing countries and is not always reflected in their property[4]. Therefore, the rapid appraisal method is not only more practical but could indeed be more accurate to identify individuals at risk.

One of the complications of this study was that participants could be inclined to rate their household as below average. This could have happened because the participant might think this would make them more eligible to developmental programs in the area. Also, some participants may have refused cooperation because they were anxious that extra tax measures would be imposed upon them. The interviewers explained to all participants in their own language the reason of our visit and explicitly stated that neither developmental help nor extra taxes would be assigned to them based on their answers. We have also asked the interviewers to give their objective estimate of the household wealth and this resulted in more households being categorized in the above average category. All in all, we reason that if these biases would have occurred, it would have diminished the association with mortality risks and the real effect could therefore only be stronger than reported here. Both rapid appraisal methods are suitable for the measurement of SES, but from this experience the interviewer-reported wealth could be more satisfactory in some studies.

One problem of our study was that the interviewer-reported wealth was estimated after the interviewers had gone through the asset list with the participants. Therefore, the possessions could have influenced the ranking of the interviewer. The correlation between the interviewer-reported wealth and the DHS wealth index could therefore be inflated. We tried to train the fieldworkers to make an unbiased estimation based on their own impression. As the fieldworkers estimates differ from both the property estimates and the self-reported wealth estimates we think this was clearly understood by the fieldworkers. Also, we see a similar correlation of the self-reported wealth with the DHS wealth index and because the participant is already aware of his possessions, his ranking is not influenced by the previous collection of the DHS wealth index. Because many indicator variables are visible to the interviewer when he visits a compound (iron roofing, electricity, bicycles, motorbikes, livestock around the compound) we think that when the fieldworker reported wealth would have been taken before the DHS wealth index, a similar correlation would have been found. However it should be acknowledged that this is one of the limitations of this study.

Another limitation could be that our list of valuable items is limited. However, in this poor rural environment no other common items of value have been found and even the land is common property. Because we have asked the participants

themselves to list all items of value in the area during the preparation of the questionnaire, a technique known as free listing, we are fairly confident that we have covered the items of reasonable value. Previously, it was also shown that a short list created with this technique is equally valid as the longer property questionnaires[11].

One final limitation of the rapid appraisal method is that it is not able to identify the poorest decile or poorest quartile, while the DHS, as a continuous measurement, is able to do so.

The use of average benchmarks requires that participants or fieldworkers are aware of which area they are comparing over. It should therefore be noted that the rapid appraisal methods are probably best suited for populations that are not too large and where the socioeconomic status is not clustered and evenly spread across the research area. Therefore, rural areas in developing countries seem best suited to this method.

This study shows that rapid appraisal, consisting of only one question and easily incorporated in health studies, is moderately correlated to the DHS wealth index and can identify individuals at risk. This applies to both rapid appraisal methods: self-reported wealth and interviewer-reported wealth.

Declarations

Ethical approval

This study is part of the study "Role of innate immunity into the trade-off between reproductive success and early survival in the Upper East Region of Ghana", for which ethical approval has been given by the Ethical Review Committee of the Ghana Health Service under number GHS-ERC-03/3/06 and also by the Medical Ethical Committee of the Leiden University Medical Centre in Leiden, the Netherlands.

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Conflict of interest

None declared.

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Chapter 5

Quality-quantity tradeoff of human offspring under adverse environmental conditions

J.J. Meij*, D. van Bodegom*, J.B. Ziem, J. Amankwa,
A.M. Polderman, T.B.L. Kirkwood, A.J.M. de Craen, B. J. Zwaan,
R.G.J. Westendorp

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* These authors contributed equally to this study

Abstract

A central paradigm in life history theory is the tradeoff between offspring number and quality. Several studies have investigated this tradeoff in humans, but data are inconclusive, perhaps because prosperous sociocultural factors mask the tradeoff. Therefore, we studied 2,461 offspring groups in an area under adverse conditions in Northern Ghana with high fertility and mortality rates. In a linear mixed model controlling for differences in age and tribe of the mother and socioeconomic status, each additional child in the offspring group resulted in a 2.3% (95%CI 1.9%-2.6%, $p<0.001$) lower proportional survival of the offspring. Furthermore, we made use of the polygamous population structure and compared offspring of co-wives in 388 households, thus controlling for variation in resources between compounds. Here, offspring survival decreased 2.8% (95%CI 2.3%-4.0%, $p<0.001$) for each increase in offspring number. We interpret these data as an apparent quality-quantity tradeoff in human offspring.

Introduction

Life history theory predicts that during evolution resource acquisition is maximized and that adaptation to the prevailing environmental conditions is realized by differential resource allocation. For any plant or animal species, reproduction is a costly process, and many resources are allocated to reproduction, at the expenses of other processes such as growth and maintenance.
For reproduction a further division of resources can be predicted; reproductive investment in quality and quantity of offspring. For different species or different populations of the same species, the precise balance between quality and quantity of offspring will depend on the selective forces operating, such as the shape of the reproductive effort curve, the presence of parent offspring conflicts and the availability of resources in the environment[1,2].

The tradeoff between quality and quantity of offspring is well known in plants, for example in seed number and size[3,4]. Also, both between and within animal species, a strong negative association between number and survival of offspring is found[5-7]. Most evidence of animal studies comes from birds. Here, increasing clutch size was found to be related to lower offspring survival[8], a finding also reproduced in experimental studies in diverse species[9-13] including non-human primates[14]. As early as Becker there has been an interest in the tradeoff in humans[15]. To date, the evidence for the tradeoff in humans, however, is inconclusive. The study of these biological principles in humans, besides being of general interest, can also lead us to better understand different health care issues[16].

Several studies have investigated the tradeoff between quality and quantity of offspring in both historical and contemporary human populations. These studies largely differ in their assessment of quality. From a biological or evolutionary point of view the best measurement of quality would be the number of surviving offspring that are capable of successful reproduction. In contemporary societies this is difficult to study because socio-cultural factors such as birth planning and high survival chances may mask the predicted tradeoff[17]. Some studies have therefore investigated cultural or sociological features such as school results, job success or socioeconomic status as a measure of quality[18.19]. Several of these studies find evidence for a quality-quantity tradeoff as defined above. Because survival can be difficult to assess, some have also chosen to measure the health of the offspring as a proxy for survival (probabilities) and found some evidence for the

tradeoff[20,21]. Different historical studies have also assessed the tradeoff in humans, using survival as a measure of quality, and found contrasting results[14,22-25]. Historical studies always rely on written records which are only generated in societies with a certain level of civilization. It is possible that in these civilizations, the tradeoff is difficult to find, because resources are not scarce enough. Three studies, however, have investigated the tradeoff in present day pre-transitional, natural fertility populations under resource-poor conditions using the survival of offspring as a measurement of offspring quality. A small study among 167 women of the Dogon of Mali showed evidence for the tradeoff with decreasing offspring survival with an increasing number of offspring[26]. Several larger studies however, among 491 women of the !Kung of Botswana[27], among 324 women of the Ache of Paraguay[28] and among the Kipsigis in Kenya[9], found no evidence for the quality-quantity tradeoff. Instead they found that with an increasing number of offspring, the number of offspring that survive also increased. The absence in these studies of a clear quality-quantity tradeoff, however, could be explained by confounding by socioeconomic status, whereby women with higher status have larger families that also experience higher offspring survival because of better environmental conditions.

In this study we investigate the relation between the number of offspring and proportional offspring survival in a large cohort of 2,461 women of a rural community in northern Ghana, an environment we think resembles our recent evolutionary past. This allowed us to circumvent some of the problems encountered in other studies. First, because of the scarcity of resources in the research area, it is expected that the tradeoff is maximally apparent. Second, we also assessed the socioeconomic status, and were therefore able to control for this common confounding factor in our analysis. Third, the polygamous structure of the research population allowed us to compare 388 pairs of co-wives within their compound in a pair wise analysis, further controlling for differences in (micro) socioeconomic status.

Materials and methods

Research area

The study was conducted in the remote Garu-Tempane district in the Upper East region of Ghana, a densely populated agricultural area. In 2001, the research area was explored by the Department of Parasitology of the Leiden University Medical

Centre which set up a database for parasitological research[30]. In this database name, sex, estimated age, tribe, and location of the compound were registered. We started our study by using this database and added detailed demographic information about fertility and child mortality.

The Garu-Tempane district is inhabited by several tribes; mostly Bimoba (66%) and Kusasi (24%). Compared to the south of Ghana, the whole of the Upper East region, and especially the Garu-Tempane district, is underdeveloped. The estimated gross domestic product per capita is less than US$ 100 in this region, while the gross domestic product per capita for the whole of Ghana is US$ 2,700[31]. The region has a semi-Saharan climate with an average maximum temperature of 32 ^{o}C throughout the year with one annual rain season from June to August. The research area around the village of Garu measures approximately 375 km^2 with an estimated density of 66 inhabitants per km^2. Most of the people are farmers and the agricultural process is entirely done by manual labour. There are some schools in the area, but illiteracy among adults above 30 is estimated to be around 90%. Recently, some small health clinics have been set up in the area, but these are not fully in service yet. Vaccination of children was introduced in the early 1990s. In 2003, about 50% of the children under ten years had been vaccinated at least once for either measles, polio, or diphtheria.
As estimated from our annual surveys from 2003 to 2007, migration is very low and amounts to less than 1% per year. There is some additional seasonal migration of young men who move to the larger cities in Ghana to work in seasonal occupations. All individuals live in extended family compounds. Each compound consists of a number of separate huts linked by a surrounding wall. The oldest man in the compound is head of the family (land lord) and takes care of up to four wives. Within the compound the individual women have their own hut, but activities such as farming and child care are a shared responsibility. Although food preparation and cleaning are private activities, food at the compound is shared during communal meals. All children share the same hut, and the custom of formula-feeding infants is absent.

In the study area, most women begin sexual activity around the age of sixteen, and most give birth before the age of twenty. Birth control is virtually absent, although spacing of children by means of prolonged breastfeeding is sometimes practised by

younger women. Most women want to have as many children as possible, since large families are highly regarded.

Subjects and methods

All villages and compounds were mapped with the Global Positioning System in 2001 and 2002. Since there are no civil registries, all villages and compounds within the study area were registered and assigned a unique identification number. The name, sex, age, and tribe of each individual were registered. In total 24,801 individuals were registered in the original database, living in 2,350 compounds, including 4,016 women aged 25 years and over.

In 2003 we revisited all compounds in the research area. During these fieldvisits the database was updated and all women of 25 years and older who were present at their compound (n=2,479) were invited to participate in the present survey of which 2,461 women agreed to participate. As most women are illiterate, witnessed oral informed consent was obtained by a local translator. Nineteen women refused co-operation. Both the Ethical Review Committee of the Ghana Health Service and the Medical Ethical Committee of the Leiden University Medical Centre in Leiden, the Netherlands, approved this study.

Demographic characteristics

If the age of a woman was unknown, it was calculated as the average from three independent estimations by local and Dutch researchers in 2003. Data on the number and survival status of all births were retrieved in line with the Ghana Demographic and Health Surveys (DHS), an internationally representative household survey for monitoring and impact evaluation of indicators in the areas of population, health, and nutrition[32,33]. To obtain the most accurate information, we set up compound interviews under supervision of local co-workers, assisted by translators, in which all women who were present in the compound participated. During these interviews the women discussed with each other the number of offspring they had had, including the number of offspring who had died and the number of offspring who were still alive at the time of the interview. These interviews increased the accuracy of the information considerably, and we did not encounter any hesitation to openly discuss these matters. Based on the number of offspring and the number of offspring still alive, we calculated the proportional

survival of the offspring for each mother as the number of surviving offspring divided by the total number of offspring.

Village interviews

To obtain information on reproductive strategies of women we set up a series of village interviews. Five groups of twenty women, all coming from different villages, were interviewed by two female co-workers. During these interviews information was obtained about the desired number of offspring, reproduction, spacing strategies, and the use of contraceptives.

Socio-economic study

In 2007 we designed a questionnaire to asses the socioeconomic status of the study participants using a free listing technique whereby we asked people from different villages of the research area, both male and female, in focus group discussions to list the household items of most value[34]. These self-listed property questionnaires are reported to be highly correlated to longer property questionnaires[35] The resulting list of valuable items was comparable to the Core Welfare Indications Questionnaire (CWIQ) from the World Bank or the DHS, adapted to our region[36,37]. The valuable items included mainly domestic livestock and different valuable household items such as motorbikes, bicycles, and iron roofing. The value of the different items was also discussed in focus group discussions and consensus was found on the value of all different items. The total value of the compound property was calculated by taking the sum of the number of the items possessed by the compound, multiplied by the value of these items.

Statistical analysis

Proportional survival for the different offspring groups was calculated using a linear regression model. To correct for possible confounding factors, we also performed multivariate linear regression analyses, adjusted for age of the mother, tribe of the mother and socioeconomic status. In the same way we also calculated the number of offspring alive for different numbers of offspring. Especially the correction for age is important because older women have not only more offspring but as offspring is of higher age they had more accumulated risk of dying. We also performed a restricted analysis of people of the Bimoba tribe only to further minimize the influence of tribe on the proportional survival, and a restricted

analysis to women above 45 years, who were considered 'post-menopausal'. We estimated the menopausal age in this area to be around 40 years.

We modelled our data using three different regression models. First we used a linear model described by the function $y(x)=a+bx$, secondly a quadratic model $y(x)=a+bx+cx^2$ and lastly a plateau model $y(x)=a+b*\arctan(cx)$.

We made use of the unique polygamous structure of the research population and compared offspring groups of co-wives in 388 households who share the same environmental conditions. To do this, we selected pairs of co-wives with the smallest difference in age from compounds with at least two co-wives with a maximum of ten years difference. The mean offspring survival in the smallest offspring group was calculated. We then used regression to calculate the difference in offspring survival dependent on the difference in number of offspring within the pair of co-wives. A pair-wise analysis was also applied using a linear mixed model, clustered on compound, in which we included all 2,443 women with at least one delivery, adjusted for age of the mother, tribe of the mother and socioeconomic status. All calculations were performed with SPSS version 14.0.

Results

We interviewed 2,461 women on their past fertility histories. Table 1 shows the demographic characteristics of these women. We found 18 (0.7%) women who reported to have had no offspring, whereas seven women (0.3%) reported having had fifteen offspring. Proportional offspring survival decreased with an increasing number of offspring, reducing from around 90% among offspring groups of less than four to around 50% among offspring groups of more than twelve. The distribution of the number of offspring in Bimoba women was similar to the distribution in the whole population suggesting that the maternal fertility pattern between tribes is not different. The mean number of offspring was 6.3 (SE 0.05) for all women and 7.7 (SE 0.07) for women aged 45 years and over. The socioeconomic status of the households of these women differed slightly, with a trend of decreasing socioeconomic status in the women with an increasing number of offspring. The number of offspring decreased with increasing wealth from 6.35 (SE 0.10) in the lowest wealth quintile to 5.98 (SE 0.10) in the highest wealth quintile (p for trend = 0.007). The proportional survival of offspring increased with increasing

wealth from 0.74 (SE 0.01) in the lowest quintile to 0.78 (SE 0.01) in the highest quintile (p for trend = 0.009).

Table 1. Demographic and fertility characteristics of the 2,461 women included in the study

Number of offspring	Number of women (n)	Proportional survival (SE)	Mean age (St. dev.)	Percentage of postmeno-pausal women	Percentage of Bimoba women	SES in US$ (St. dev.)
0	18	-	41.8 (14)	44.4	70.6	1,898 (1,753)
1	56	0.95 (0.03)	28.3 (9)	7.1	60.7	2,027 (1,703)
2	120	0.92 (0.02)	30.0 (10)	8.3	62.5	1,917 (1,219)
3	196	0.87 (0.02)	31.0 (10)	9.2	65.1	1,982 (1,757)
4	220	0.86 (0.01)	35.0 (12)	17.3	61.4	1,629 (1,450)
5	344	0.83 (0.01)	40.4 (14)	30.5	64.2	1,590 (1,374)
6	362	0.81 (0.01)	43.0 (13)	40.5	65.8	1,622 (1,379)
7	387	0.74 (0.01)	48.5 (14)	58.1	65.4	1,747 (1,460)
8	253	0.69 (0.01)	48.7 (14)	58.5	70.8	1,762 (1,537)
9	238	0.65 (0.01)	53.4 (14)	75.2	69.7	1,803 (1,631)
10	165	0.59 (0.02)	54.6 (12)	81.2	73.2	1,559 (1,258)
11	58	0.56 (0.03)	57.7 (12)	86.2	67.2	1,458 (1,643)
12	22	0.51 (0.04)	63.0 (16)	86.4	68.2	1,820 (1,214)
13	12	0.48 (0.06)	59.5 (17)	81.3	91.7	1,568 (553)
14	3	0.57 (0.12)	58.3 (16)	66.7	66.7	987 (399)
15	7	0.40 (0.08)	66.6 (19)	100	71.4	1,878 (1,520)

SES = socioeconomic status. An age of 45 years and over was considered post-menopausal.

The observation of declining proportional survival with an increasing number of offspring, however, has to be adjusted for various potentially confounding variables. Using multivariate regression we adjusted for these factors using several models. Table 2 shows the different analyses of the relationship between number and proportional survival of the offspring for the 2,443 women who had had at least one delivery. In the unadjusted analysis the proportional survival of offspring decreased 4.0% (95%CI 3.7%-4.3%, $p<0.001$) for each additional child. However, as

among older women the number and the age of offspring will be higher, adjusting for age of the mother is critical to adjust for the different accumulated mortality risks of the offspring. Because different tribes could have different fertility patterns and different survival probabilities, an adjustment for tribe is also necessary. Finally, we adjusted for socioeconomic status, because wealthier families have both higher proportional survival, more wives per compound and less offspring per wife. To further minimize the effect of tribe and age, we also performed two restricted analyses. All models show that even after correcting for the various confounders, and when performing the restricted analyses, the association between the number of offspring and proportional survival persisted.

Table 2. Different analyses of the relation between number of offspring and proportional survival of offspring. Reported values are percentages with 95% confidence intervals

Model	n	Decrease in proportional survival for each increase in offspring number (95%CI)	p
1 Unadjusted	2,443	4.0% (3.7%-4.3%)	<0.001
2 Adjusted for age	2,443	2.4% (2.1%-2.8%)	<0.001
3 Adjusted for age, SES	2,443	2.3% (2.0%-2.7%)	<0.001
4 Adjusted for age, SES, tribe	2,443	2.3% (1.9%-2.6%)	<0.001
5 Model 3 restricted to the Bimoba tribe	1,623	2.5% (2.1%-2.9%)	<0.001
6 Model 4 restricted to post-menopausal	957	2.3% (1.6%-2.9%)	<0.001

SES = socioeconomic status. An age of 45 years and over was considered post-menopausal.

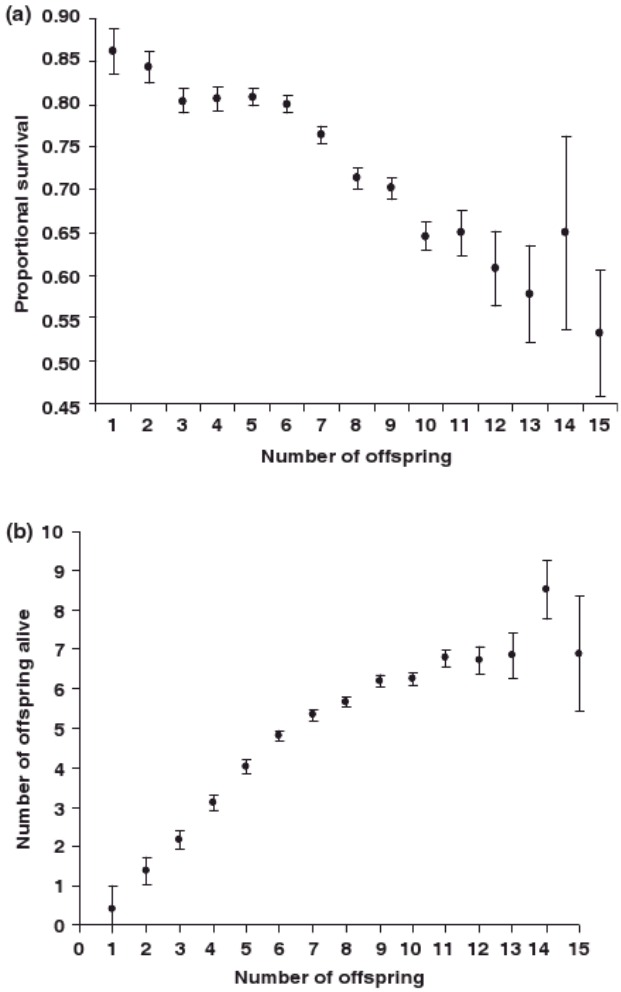

Figure 1. Relation between quality and quantity of offspring
(a) Proportional offspring survival dependent on the number of offspring. Data presented as means with standard error from linear regression models, adjusted for age of the mother, tribe of the mother and socioeconomic status. (b) Relation between number of offspring and number of offspring alive. Estimates from a linear regression model adjusted for age of the mother, tribe of the mother and socioeconomic status.

Using the regression models, we could plot the adjusted proportional survival for the groups with different numbers of offspring. Figure 1a is a graphical representation of the regression model adjusted for age of the mother, tribe of the mother and socioeconomic status. Here, each additional child resulted in a 2.3% (95%CI 1.9%-2.7%, $p<0.001$) lower proportional survival of the offspring.
Figure 1b shows the relation between the number of offspring and the number of offspring alive for all 2,461 women, as obtained from the same regression model. Going from lower offspring numbers to higher offspring numbers, the number of offspring alive reached a plateau around seven life offspring. These data show that with an increasing number of offspring the reproductive succes is maximized at about seven offspring alive.

When fitting the observed fertility patterns using regression, we found that a quadratic model ($r2=0.49$, $p<0.001$) described our data better than a linear model ($r2=0.44$, $p<0.001$). A quadratic model has often been used in animal species and assumes that at higher clutch sizes almost no offspring will survive. This may not apply to humans who increase the number of offspring with sequential births. Therefore, a plateau model was fitted and it was found that this described the data equally well as the quadratic model ($r2=0.49$, $p=<0.001$). The three different models are depicted in figure 2.

To further study the quality-quantity tradeoff we made use of the polygamous structure of the population. We compared different offspring groups from pairs of co-wives of the same compound or household, who share the same environmental conditions. A graphical representation of a compound is shown in figure 3a, the critical observation being that all children of various women within the compound share the same resources. All children are collectively raised, food at the compound is shared during communal meals and all children share the same hut. In this way we made use of an experiment by nature, studying two offspring groups with a different family background but sharing the same environment.

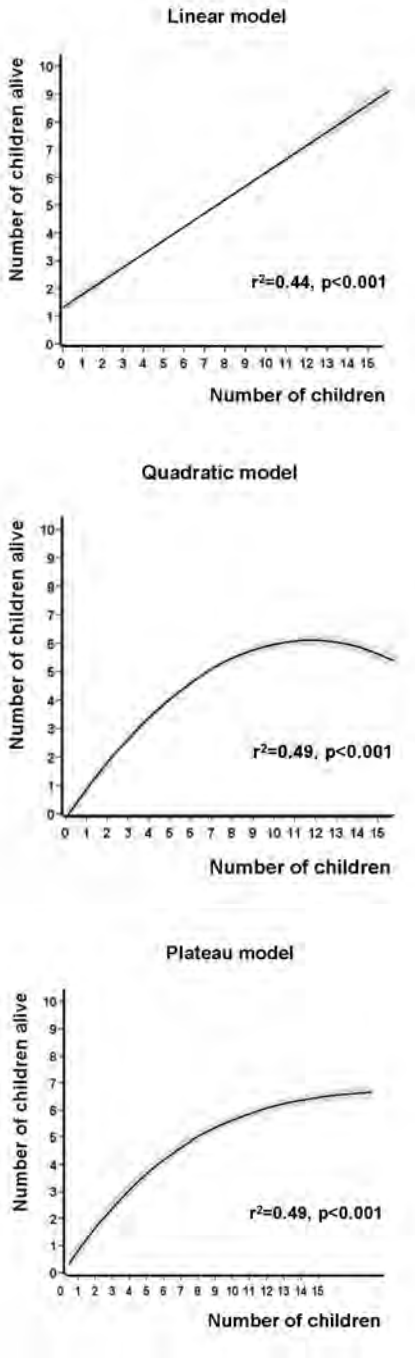

Figure 2. Different models of the relation between number of offspring and number of offspring alive. Grey area indicates 95% confidence interval.

Within compounds we have selected pairs of co-wives within an age band of ten years at a maximum; the mean difference in age between co-wives was 3.9 years (SE 0.11). Figure 3b shows the differences in offspring survival comparing the offspring groups of pairs of co-wives within one compound. The offspring group with the larger number is compared to the one with the smallest number, categorized as +1, +2, +3, etc. based on the number of extra offspring when compared to the offspring group with the smallest number. The figure shows that within pairs of co-wives of the same compound, proportional offspring survival is significantly lower among the larger offspring groups (p for trend <0.001).

The pair-wise analysis within compounds can also be employed in a linear mixed model including all women with at least one offspring. When adjusted for age of the mother and tribe of the mother and clustered on compound we calculated a 2.8% (95%CI 2.3%–4.0%, p<0.001) decrease in proportional offspring survival for each increase in offspring number.

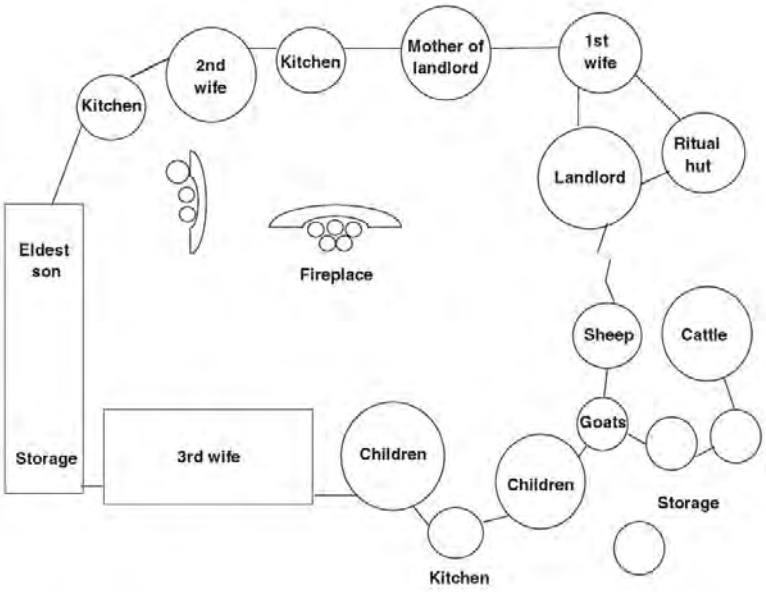

Figure 3. Pair-wise analysis of co-wives within one compound.
a) Typical example of a Bimoba Compound. The land lord and his three wives live in separate huts. First, second and third wife denote the order of marriage and not esteem or position. All women have their private kitchen but the food is shared. All children over four years of age live in the same hut, separated from their mother. Upon puberty children obtain their individual hut.

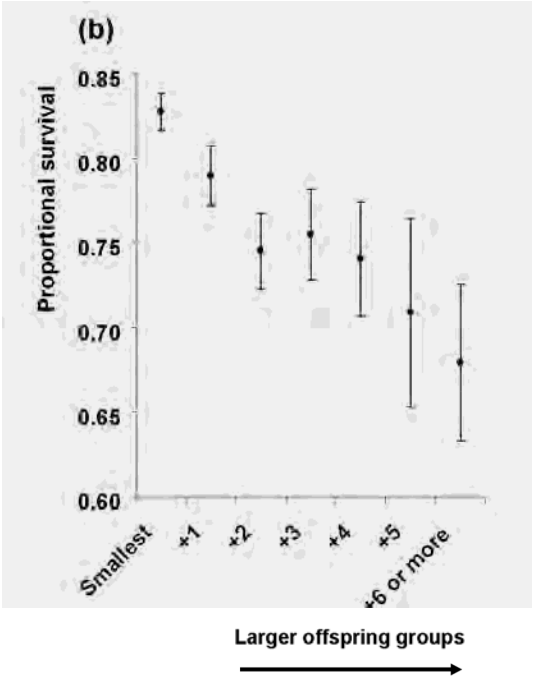

Figure 3. Pair-wise analysis of co-wives within one compound.
b) Offspring survival within polygamous compounds, comparing offspring groups of 388 pairs of co-wives within an ageband of ten years. Data present the difference in offspring survival (means with standard errors) among women with the largest offspring group when compared to the co-wife with the smallest number of offspring, categorized as +1, +2, +3 etc.

However, several alternative explanations for the outcomes of our study need to be considered. First, the observed association between the number and survival of offspring might better be explained by differences in social position within the compound. An observation of this kind was made among the Kipsigis in Kenya, where women with more inherited land had higher esteem and better offspring survival[29]. Also in our research area, larger families are regarded as a marker of esteem. As the wife with the highest social status would be expected not only to have more offspring but also to have better living conditions, it can thus be expected that their numerous offspring would have a higher proportional survival. We have observed the opposite: within large families survival of offspring was lowest. If anything, the observed survival cost would be an underestimation of the effect. It is therefore unlikely that our observed association is caused by differences in social status. Second, another possible confounding variable was identified

when studying polygyny among the Dogon. Child mortality in polygynous households was higher than in monogamous households[38]. Since we still found evidence for the tradeoff when comparing pairs of co-wives, all living in polygynous compounds, it can not account for the observed association. Third, early mortality, especially neonatal mortality, is far less likely among breast-fed infants when compared to formula-fed infants[39,40]. As the habit of formula-feeding in our research area is virtually absent, this is unlikely to have influenced our results. Fourth, our results might have been biased because of vertical transmission of the HIV virus. In this reasoning, women with more offspring would have had more sexual contact and would have been more likely to have contracted the HIV virus. Vertical transmission to the child would have consequentially lowered offspring survival, creating the association between number of offspring and offspring survival. However, the sero-prevelance of HIV in the region of the research area is very low. According to the 2003 Ghana Demographic and Health Survey, the sero-prevalence of HIV among pregnant women in the whole region is 0.8% and among sexually active men it is 2.2%[33,40]. It is therefore unlikely that mother to child transmission of the HIV virus can explain for the present data. Finally, the higher proportional offspring survival among women who had a smaller number of offspring could be the result of survival-based family planning. This would be the case if a mother would become pregnant earlier when one of her offspring has died. While this is a phenomenon seen in other societies[40,41], we do not think that this explains the findings presented here. All interviewed women expressed the wish to have as many offspring as possible, independent of the individual survival of the offspring. Therefore, the effect of survival-based family planning is likely to be limited. In line with this reasoning, we found the number of offspring alive being maximized at around seven. Also, only 40% of the under fifteen mortality is between birth and the age of two, the estimated average breastfeeding time. Therefore, only in a minority of the deaths, the birth interval would be reduced by shortening the lactation period. However, when children die at a young age, duration of lactation can be reduced and birth intervals could be shorter which may partly account for our findings. We think, however, that the impact of this effect is small and cannot fully account for the relation we have found.

It is allways possible that external, unmeasured, determinants or factors also influence the observed relation between number of offspring and proportional survival of offspring. Parents might consider economic, social or cultural

determinants, even unconsciously, in family planning matters[42]. Different life history tradeoffs could also be at play, for example the tradeoff between parental care and fecundity, as some studies in birds have also shown[43].

When we modelled our data using three different models, a quadratic model fitted our data better then a linear model. Such a quadratic relationship between offspring number and offspring alive is found in different animal studies, for example in birds, from which an optimum clutch size can be inferred. A plateau model however, fitted the data as well as the quadratic model and we would propose this model as an alternative model to describe the human situation. This model reflects the human fertility patterns since human children are not born simultaneously, but at average intervals of two to three years. Since children are at greatest survival risk in the first five years, additional newborns mainly influence the survival chances of their youngest sib. A quadratic model, in contrast, implies that at higher numbers of offspring, the additional offspring also diminish the survival chances of their older sibs. In the human situation, with sequential births, this seems unlikely. It appears that environmental constraints limit the number of offspring alive to a maximum of about seven. One could question why the observed mean number of offspring is lower than the optimum number of offspring as inferred from the models. We hypothesize that a higher number of offspring goes with a cost of reproduction to the mother. With the declining return with increasing numbers of offspring, the effort for the mother could be too great. The risk from child birth or the weakness from subsequent pregnancies could result in the death of the mother which would also put the younger children at risk. The best strategy could therefore be to limit the number of offspring to around seven, when the returns of increasing numbers of offspring diminish strongly and no longer outweigh the risks and costs of reproduction.

We further studied the tradeoff making use of the polygamous family structure of the research population. Hereby, we were able to compare offspring groups from co-wives of one compound who share exactly the same socioeconomic environment. Even when comparing these offspring groups, larger offspring groups had lower proportional survival than the smaller offspring groups of the same compound. Because the environmental conditions are the same for all offspring in the compound, an additive biological mechanism seems to be at play.

Different explanations are possible for this residual difference within one compound. A first possibility is that there is still a difference in the resources available to the offspring. In this reasoning the children from smaller offspring groups would still have better access to care and resources. We think that this could partly explain for the residual differences. However, we think that we have maximally controlled for the (micro) socioeconomic differences using the polygamous structure of this population and question whether the effect is large enough to account for the observed survival differences. A second explanation for the residual differences in proportional survival could be persisting differences not in the children but in the mothers. These persisting differences could be quality differences of the mother which are caused by a non-shared environmental determinant or by other life history characteristics. A second possibility is that next to environmental factors genetic factors also play a role in the tradeoff. These genetic factors could influence both the fertility of the mother, i.e. the offspring number and also offspring survival. Others have also found that certain women carry a fertile fenotype, independent of their health-status[44,45]. One could think of genetic factors that account for efficient food storage, which would not only give children a higher survival chance but also allow mothers to quickly rebuild resources after giving birth. This would allow them to have shorter birth intervals and therefore more children. Another possible genetic mechanism that could influence both the quality and the quantity of offspring is the innate immune system[46]. Accumulating evidence exists on the role of the innate immune system on both survival and fertility. As over thousands of years human survival has been highly dependent on resistance to infectious diseases, genetic adaptations resulting in inflammatory responses were favored. An inflammatory host response is critical to fight infection necessary to survive up to reproductive age. An inflammatory host response however, is also negatively associated with fertility because immunotolerance for the paternal antigens of the fetus is required for pregnancy to proceed successfully. It has been shown that sub-fertile women with concurrent abortions have higher pro-inflammatory markers[47]. One could hypothesize on the existence of an 'anti-inflammatory' and therefore vulnerable but fertile fenotype, and a 'pro-inflammatory' and therefore resistant but less fertile fenotype. Earlier we have provided evidence that specific inflammatory signaling cytokines associated with survival to infectious diseases[48,49] are negatively associated with[47,50,51]. Since the innate immune system is highly genetically determined, these characteristics would cross generations and could lead fertile – but vulnerable –

mothers to give birth to vulnerable – but fertile - offspring. These genetic mechanisms, however, are hypothetically only and are presented here as an alternative explanation to the environmental explanations of the residual differences within co-wives of one compound. The biological mechanisms behind the quality-quantity tradeoff have yet to be fully unraveled. Note also that life history tradeoffs are often presumed to be resource allocation tradeoffs, while hard empirical evidence that these tradeoffs are actually resource allocating tradeoffs is scarce.

One of the strengths of our study is that we studied the tradeoff under adverse conditions. This is reinforced as we based our inference on the fertility histories of the women, i.e. making use of data that reflect the environmental past of the last 80 years, which was even more adverse. Another strong point is that we were able to control for socioeconomic differences, which can easily mask the quality-quantity tradeoff as wealthier women could have both less offspring and higher proportional offspring survival. A stratified analysis of the tradeoff in different wealth categories showed that with increasing wealth the effect of the tradeoff reduces. This could explain why other studies did not show evidence for the tradeoff because they studied contemporary data, that are likely to originate from a less adverse environment. Finally, we could make use of the unique polygamous family structure in the area. Thus, we were able to compare offspring groups from co-wives from the same compound, who share the same socioeconomic environment, allowing us to maximally control for (micro) socioeconomic differences.

An important consideration is the observational nature of the study. In animal studies, more experimental methods have been used, sometimes giving strong arguments for the existence of a quality-quantity tradeoff. In humans, however, it is not possible to experimentally alter the number of offspring. In any observational study, there is always the problem of unmeasured factors. This should also be noted in this study. However, we tried in two ways to overcome this limitation. First we corrected for socioeconomic status, an important determinant of quality differences. Second we used the polygynous familystructure to compare co-wives of one compound and in this way matched women on as many unmeasured factors as posssible. With both different approaches we still found a negative relation between number of offspring and

proportional survival. It is however always possible that other non-shared environmental or heritable factors influence the 'quality' of the mother.

Alltogether, our data show a strong negative association between number of offspring and survival of offspring in humans. This is in line with findings from studies in plants and animals. We interpret our data as consistent with a quality-quantity tradeoff in humans under adverse conditions. Despite the general validity of the theory, the biological mechanism that accounts for this tradeoff has yet to be unraveled.

Declarations

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Conflict of interest

We have no conflict of interest.

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Chapter 6

Common CFTR gene variants influence body composition and survival in rural Ghana

M. Kuningas, D. van Bodegom, L. May, J.J. Meij, P.E. Slagboom, R.G.J. Westendorp

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Abstract

Various studies in mice have found support for the hypothesis that heterozygous carriers of *CFTR* mutations have an increased resistance to fatal infection compared to both homozygous mutation carriers and non-carriers, while in humans such evidence is scarce. In this study, we assessed the *CFTR* heterozygotes survival advantage hypothesis in a contemporary rural population that lives under adverse environmental conditions in the Upper-East region of Ghana. We genotyped 30 SNPs throughout the *CFTR* gene in 4,230 participant and tested their influence on survival and on body composition in the population at large. With a sliding-window haplotype analysis, we identified a set of six common haplotypes that influenced survival probabilities (global $p=6.00x10^{-05}$). Individual haplotype analyses revealed two haplotypes of specific interest. One of these haplotypes was enriched (p=0.003) whereas the other was depleted (p=0.041) among people of old age (≥65 years) compared to young study participants (≤5 years). In addition, children (n=474) carrying the latter haplotype had lower body weight ($p_{trend}=0.020$) and height ($p_{trend}=0.010$) compared to non-carriers. For all these analyses, similar associations for heterozygous and homozygous *CFTR* haplotype carriers were observed, revealing an additive effect of haplotype alleles. In conclusion, we identified common haplotypes in the *CFTR* gene that influence survival and body composition in the population at large with no evidence for heterozygote advantage.

Introduction

The cystic fibrosis transmembrane conductance regulator (CFTR) gene contains a variety of mutations which all contribute to the development of cystic fibrosis (CF). In order to explain the high frequency of CF in various populations, it has been hypothesized that in our recent evolutionary past heterozygous carriers of *CFTR* mutations have had a survival advantage compared to both homozygous mutation carriers and non-carriers[1]. Proposed mechanisms that would lead to such advantage are an increased resistance to cholera, typhoid fever, or tuberculosis[2-7]. Several studies with mouse models have provided support for this hypothesis, where it has been shown that heterozygous *CFTR* mutation carriers are more resistant to cholera-induced diarrhea, and against bacteria that use CFTR for entering cells[2,5]. In case of humans however, support for this hypothesis is generally lacking[3,8]. Therefore, the aim of this study was to assess the *CFTR* heterozygotes advantage hypothesis in a contemporary rural population that lives under adverse environmental conditions in the Garu-Tempane district, a densely populated agricultural area in southeast of the Upper-East region of Ghana[9,10]. This region is highly endemic for malaria, typhoid fever, diarrheal diseases and intestinal helminth infections, whereas hospitals and medical services are only marginally available. As there is evidence that the mutation spectrum for CF in African populations is different than in European populations[11-13], we selected common variants from the *CFTR* gene and tested their influence on survival as well as on body composition in the population at large.

Materials and methods

Research area and study population

This study was conducted in the Garu-Tempane district, a densely populated agricultural area in the southeast of the Upper-East region of Ghana, which is inhabited by several tribes, mostly Bimoba (67%) and Kusasi (27%)[9]. The area is highly endemic for malaria, typhoid fever, meningococcal disease and intestinal helminth infections. Hospitals and medical services are only marginally available in the area. Vaccination of children was introduced in the early 1990s, but coverage amongst children is highly variable. It is estimated that about 50% of the children under the age of ten years have been vaccinated at least once against either measles, poliomyelitis, or diphtheria-tetanus-pertussis[9]. The region and study population have been described in more detail elsewhere[9,10]. The Medical Ethical Committee of the Ghana Health Service in Ghana, as well as the Medical Ethical

Committee of the Leiden University Medical Center in the Netherlands approved the study. Witness observed oral informed consent was obtained from all participants.

The measurement of body composition and socioeconomic status (SES)
Weight (kg) and height (cm) was measured in 2007 for 474 children who were equal to or younger than five years of age. In 2007 a DHS-type questionnaire was designed to assess the SES of the study participants using a free listing technique, whereby we asked people, both male and female, from different villages in the research area in focus group discussions to list the household items of most value[10]. The resulting list of valuable items was comparable to part of the core welfare indications questionnaire (CWIQ) from the World Bank and to the extended DHS asset list, adapted to our region.

SNP selection and genotyping
We selected 37 SNPs from the *CFTR* gene region covering 204.3 kbp (chr7:116897317-117101642) from the HapMap database release #21 (www.hapmap.org) using the Yoruba in Ibadan, Nigeria (Yoruba) data. The Haploview's program Tagger[14] was used to derive a set of tag SNPs from the whole gene region such that each common SNP (5%) in that set was captured with r^2 0.8. All SNPs were genotyped using mass spectrometry (Sequenom Inc, San Diego, CA, USA), according to the manufacturer's instructions. Altogether 4,336 participants were genotyped for 37 SNPs in the *CFTR* gene. Genotyping failed for 7 SNPs as determined by more than 20% missing individuals. From the 4,336 participants 106 (2.44%) were excluded due to >50% missing genotypes, leaving 4,230 participants for further analyses.

Statistical analysis
The program Haploview[14] was used to estimate allele frequencies, Hardy–Weinberg equilibrium and pair-wise linkage disequilibrium (LD) between the SNPs. Sliding window haplotype analysis was performed with the program Haplo.Stats (version 1.4.0)[15]. In this analysis, using a range of n.slide values, the region with the strongest association will consistently have low p-values for locus subsets containing the associated haplotypes. The global p-value measures significance of the entire set of haplotypes for the locus subset. Haplo.stats was also used to calculate and compare allele frequencies between young and old study

participants. Haplotypes and haplotype frequencies per individual were calculated using the program SNPHAP(http://wwwgene.cimr.cam.ac.uk/clayton/software). The prevalence of *CFTR* haplotype alleles in elderly compared to young was analyzed using logistic regression. For analyses with body weight and height, these variables were first converted into age-adjusted z-scores ([individual level-mean level]/SD), in order to provide comparable estimates for haplotype effects. The cross-sectional associations between *CFTR* haplotypes and body weight and height were performed using linear regression. The linear and logistic regression analyses were performed using STATA version 9 (StataCorp LP, TX, USA) statistical software. In all these analyses the posterior probabilities of pairs of haplotypes per participant, as estimated by SNPHAP, were used as weights. All analyses were adjusted for sex, SES and tribe. No evidence for population stratification or structure was detected when conducting non parametric clustering of genotypes for 147 SNP genotyped in controls (children ≤5 years of age) and cases (elderly ≥65 years of age) using the AWClust algorithm (http://awclust.sourceforge.net/).

Table 1. Characteristics of the study population

N	4,230
Women (n, %)	2,888 (68%)
Elderly (≥65 years, n %)	819 (19%)
Children (≤5 years, n %)	936 (22%)
Children ≤5 years measured (n, %)	474 (11%)
Weight (mean, SD)	13.5 (1.84)
Height (mean, SD)	94.7 (7.04)

Results

Altogether 30 single nucleotide polymorphisms (SNPs) in the *CFTR* gene were genotyped in 4,230 participants (supplementary table 1). From these participants 936 (22%) were children five years of age or younger (age range 0-5) and 819 (19%) were 65 years of age or older (age range 65-97) (table 1). To assess whether genetic variants in the *CFTR* gene influence survival in adverse environmental conditions, we compared allele frequencies between these young and old study participants. As linkage disequilibrium (LD) within the *CFTR* gene is not strong, we used a sliding window haplotype analysis approach. With a window length of four SNPs, strong associations for haplotype frequency differences between young and old study participants were observed for two locations in the *CFTR* gene: in the middle (global $p=6.00x10^{-05}$) and in the 3' end of the gene (global p-value of $8.20x10^{-4}$) (figure 1). However, only one very rare haplotype (population frequency 0.05%) contributed to the association in the 3' end of the gene, and therefore it was not investigated further.

In the middle of the *CFTR* gene, the rs213952, rs10281281, rs17140174 and rs3808185 SNPs constitute the window that associated with allele frequency differences between young and old study participants. These SNPs, give rise to six common haplotypes (frequency ≥5%) (figure 2). From the individual haplotypes, haplotype 1 (frequency 26%) was depleted in participants of old age (p=0.041) whereas haplotype 5 (frequency 13%) was enriched (p=0.003) (figure 2). In addition, an additive effect of haplotype alleles for lower ($p_{trend}=0.06$) and higher ($p_{trend}=0.004$) chances to reach an old age was observed for carriers of haplotype 1 and haplotype 5, respectively (table 2). Hence, no evidence for advantage or disadvantage for the heterozygous haplotype carriers over homozygotes was observed.

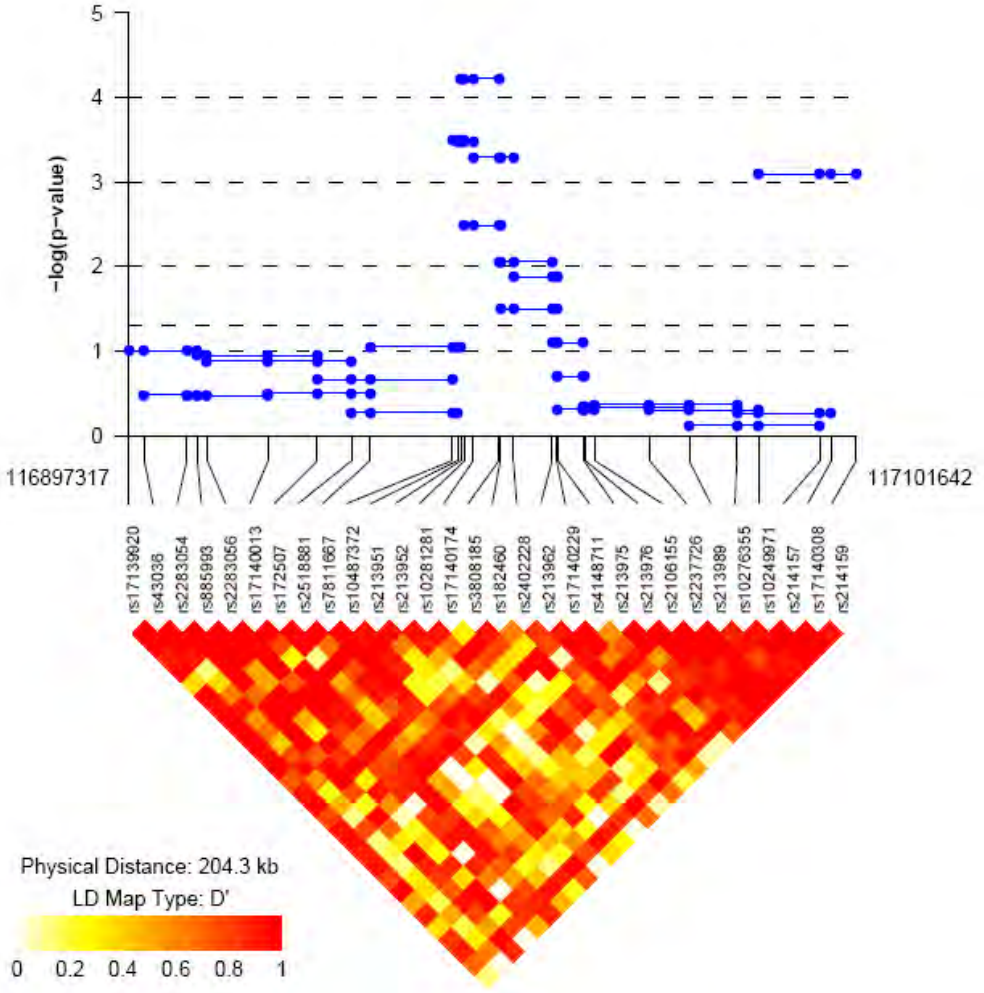

Figure 1. The genetic structure of CFTR gene and –log p-values for the global association of CFTR haplotype frequency differences between young (≤5 years, n=936) and old ((≥65 years, n=819) study participants, as assessed by sliding window haplotype analysis. Analysis was adjusted for sex, socioeconomic status and tribe.

Table 2. The prevalence of *CFTR* haplotypes in the group of old (≥65 years) study participants compared to young (≤5 years)

	Young versus old			
	0- copies	1-copy	2-copies	P_{trend}
	OR (95%CI)	OR (95%CI)	OR (95%CI)	
Haplotype 1	1 (reference)	0.91 (0.75-1.10)	0.69 (0.47-1.01)	0.06
Haplotype 2	1 (reference)	1.16 (0.96-1.41)	1.06 (0.66-1.71)	0.22
Haplotype 3	1 (reference)	1.15 (0.94-1.40)	0.85 (0.49-1.48)	0.47
Haplotype 4	1 (reference)	0.93 (0.76-1.14)	0.54 (0.27-1.08)	0.13
Haplotype 5	1 (reference)	1.26 (1.02-1.55)*	2.20 (1.07-4.52)*	**0.004**
Haplotype 6	1 (reference)	1.07 (0.81-1.40)	1.14 (0.12-10.5)	0.65

OR = odds ratio; CI = confidence interval; *-p<0.05. Odds ratios were calculated using sex, socioeconomic status and tribe adjusted logistic regression.

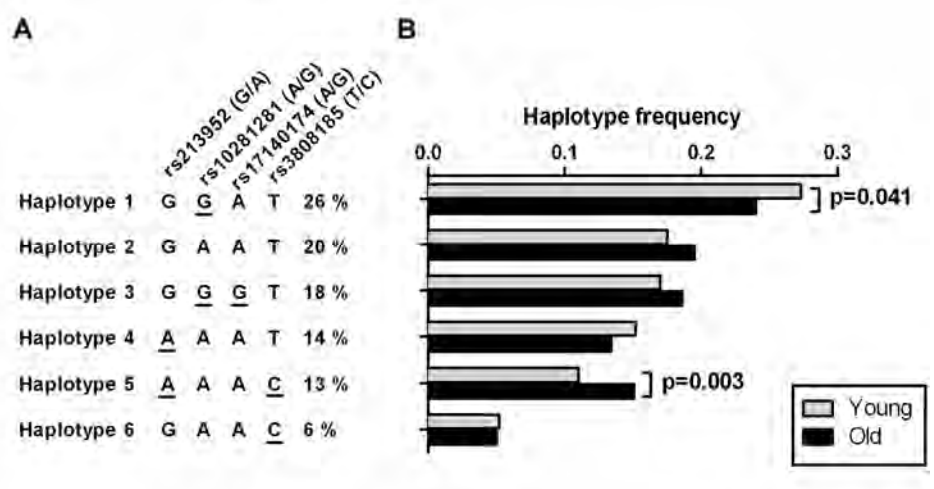

Figure 2. CFTR haplotypes and their frequencies in the general population (n=4230) (A), and in the young (≤5 years, n=936) and old (≥65 years, n=819) study participants (B). Underlining denotes the minor allele. Differences in haplotype frequencies between young and old were analyzed using sex, socioeconomic status and tribe adjusted Haplo.stats.

In addition to survival, we also assessed the influence of *CFTR* haplotypes on weight and height in 474 children who were equal to or younger than five years of

age (mean age 3.42 years, SD 0.61). Carriers of haplotype 1 had lower weight (p_{trend}=0.020) and height (p_{trend}=0.010), whereas children carrying haplotype 5 had only marginal differences in weight (p_{trend}=0.11) and height (p_{trend}=0.43) compared to non-carriers (figure 3; supplementary table 2). Besides these associations a beneficial influences on body composition were observed for haplotype 4 (frequency 14%). Carriers of this haplotype had higher weight (p_{trend}=0.013) and height (p_{trend}=0.12) compared to non-carriers (figure 3; supplementary table 2), even though they had similar survival probabilities. For all these analyses similar associations were observed for boys and girls, and for children from compounds with different socioeconomic status (data not shown).

All these analyses were repeated using the four individual SNPs: rs213952, rs10281281, rs17140174 and rs3808185. These analyses revealed associations with two of these SNPs (rs10281281 and rs3808185), which however were not as strong as in combination within a haplotype (supplementary tables 3 and 4).

Discussion

In this study we identified common *CFTR* haplotypes that influence body composition in children and survival in the population at large. In all our analyses we observed an additive effect of haplotype alleles and no selective advantage for heterozygous carriers over both, homozygous mutation carriers and non-carriers. This observation is in accordance with the few other studies that have been conducted[3,7]. Therefore, it has been hypothesized that other mechanisms, such as a past selective event or random genetic drift, would explain for the high frequency of CF in European populations. Interestingly, the prevalence of CF and its causal mutations are different in populations of different origin, and do not coincide with locations in the world where the proposed selective agents, such as cholera and typhoid fever have the highest prevalence[16]. In Africa the prevalence of CF is low and the mutation spectrum for CF in African populations has been shown to be different than in European populations[11-13]. One reason for the lower prevalence of CF in Africa could be that the affected individuals die in early childhood either due to the lack of proper diagnosis and/or medical care. This might also be the case in our research area.

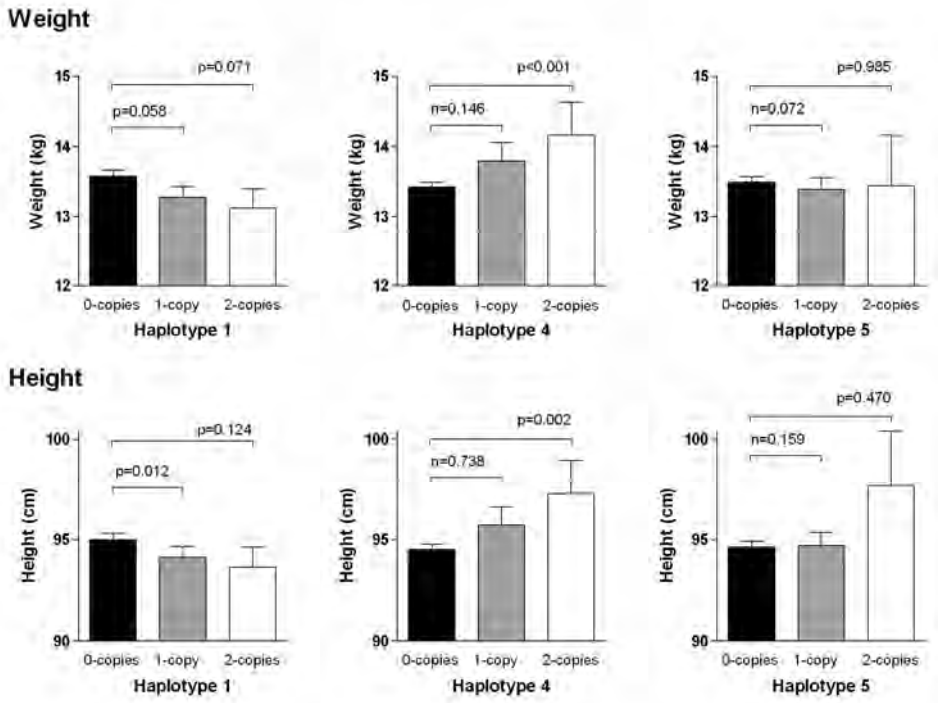

Figure 3. The influence of CFTR haplotypes on weight and height in children equal to or younger than five years of age (n=474). Linear regression adjusted for sex, socioeconomic status and tribe.

On the other hand, the lack of evidence for selective advantage for heterozygous carriers over both, homozygous mutation carriers and non-carriers in our study could rely on our selection of common variants in the *CFTR* gene, instead of mutations that have been associated with CF. It could be that the common variants contribute to mild functional differences of the CFTR protein, leading to additive effects. In case of *CFTR* mutations, such effects would be observed for the heterozygous carriers, whereas homozygous carriers would suffer CF.

Previously, it has been observed that children with untreated or poorly controlled CF have poor growth, reflected by lower weight and height[17,18]. Also in this study, genetic variants in the *CFTR* gene influenced body composition. Carriers of haplotype 1 had lower weight and height and this haplotype was depleted in people of old age. This detrimental effect could be because of pancreatic insufficiency that leads to malnutrition[19,20]. However, the mechanisms that lead to the enrichment of haplotype 5 still need to be elucidated, since carriers of this

haplotype had no differences in body compositions compared to non-carriers. The opposite was true for carriers of haplotype 4, who had better body compositions but no survival advantage. It is known that variation in the *CFTR* gene influences multiple phenotypes and it might be that some variants are more detrimental to some phenotypes than to others. In addition, the phenotypic influences of *CFTR* variants can be affected by other genes, as recently, several modifier genes for CF have been identified[21,22].

The strengths of this study are the large population size and the thorough evaluation of common variants in the *CFTR* gene, which through linkage disequilibrium capture the information for functional variants that were not genotyped. The limitations include the lack of data on body composition for grown-ups, on the prevalence of diseases, and on the specific mortality causes. Therefore, we could not directly assess the influence of *CFTR* variants on health. In addition, considering the number of tests performed, it cannot be excluded that some of the observed associations were due to chance. Nevertheless, we identified common haplotypes in the *CFTR* gene that influence survival and body composition in the population at large.

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Supplementary table 1. Genotyped *CFTR* SNPs

#	Name	Position	Alleles	MAF
1	rs17139920	promoter	G:A	0.377
2	rs43036	promoter	C:T	0.428
3	rs2283054	Intron 1	G:A	0.049
4	rs885993	Intron 1	C:T	0.076
5	rs2283056	Intron 1	A:G	0.182
6	rs17140013	Intron 3	T:G	0.075
7	rs172507	Intron 3	T:A	0.264
8	rs2518881	Intron 4	G:A	0.291
9	rs7811667	Intron 7	A:G	0.049
10	rs10487372	Intron 11	C:T	0.139
11	rs213951	Intron 11	A:G	0.208
12	rs213952	Intron 11	G:A	0.282
13	rs10281281	Intron 11	A:G	0.475
14	rs17140174	Intron 11	A:G	0.211
15	rs3808185	Intron 11	T:C	0.227
16	rs182460	Intron 11	A:G	0.075
17	rs2402228	Intron 11	A:T	0.169
18	rs213962	Intron 12	C:G	0.065
19	rs17140229	Intron 12	T:C	0.408
20	rs4148711	Intron 13	A:T	0.243
21	rs213975	Intron 15	C:T	0.096
22	rs213976	Intron 15	G:T	0.079
23	rs2106155	Intron 15	A:C	0.062
24	rs2237726	Intron 21	C:T	0.234
25	rs213989	Intron 21	C:A	0.215
26	rs10276355	Intron 22	C:G	0.024
27	rs10249971	Intron 23	A:T	0.085
28	rs214157	Intron 24	G:A	0.115
29	rs17140308	3' UTR	A:G	0.224
30	rs214159	3' UTR	A:C	0.407

MAF = minor allele frequency.

Supplementary table 2. The influence of *CFTR* haplotypes on weight and height in children equal to or younger than five years of age (n=474)

	Haplotype alleles			
	0-copies	1-copy	2-copies	
z-scores	Mean (SE)	Difference (SE)	Difference (SE)	P_{trend}
Haplotype 1				
Weight	reference	-0.15 (0.08)	-0.29 (0.16)	**0.020**
Height	reference	-0.19 (0.08)*	-0.18 (0.12)	**0.010**
Haplotype 2				
Weight	reference	0.15 (0.08)	-0.04 (0.20)	0.28
Height	reference	0.14 (0.08)	0.07 (0.19)	0.16
Haplotype 3				
Weight	reference	-0.01 (0.09)	0.07 (0.20)	0.89
Height	reference	-0.08 (0.09)	0.16 (0.15)	0.92
Haplotype 4				
Weight	reference	0.13 (0.09)	0.42 (0.12)*	**0.013**
Height	reference	0.03 (0.08)	0.43 (0.14)*	0.12
Haplotype 5				
Weight	reference	-0.16 (0.09)	0.01 (0.34)	0.11
Height	reference	-0.12 (0.08)	0.34 (0.47)	0.43
Haplotype 6				
Weight	reference	0.07 (0.14)	-0.09 (0.09)	0.64
Height	reference	0.06 (0.11)	0.64 (0.31)	0.56

Linear regression adjusted for sex, socioeconomic status and tribe; *p-value <0.05 in comparison to people carrying 0-copies of the respective haplotype.

Supplementary table 3. The prevalence of *CFTR* SNPs in the group of old (≥65 years) study participants compared to young (≤5 years)

	Young versus old			
	0- copies OR (95%CI)	1-copy OR (95%CI)	2-copies OR (95%CI)	P_{trend}
rs213952 (G/A)	1 (reference)	0.98 (0.80-1.20)	0.98 (0.66-1.44)	0.848
rs10281281 (A/G)	1 (reference)	0.92 (0.73-1.17)	0.72 (0.54-0.96)*	**0.030**
rs17140174 (A/G)	1 (reference)	1.15 (0.93-1.41)	0.91 (0.58-1.41)	0.536
rs3808185 (T/C)	1 (reference)	1.24 (1.01-1.53)*	1.46 (0.96-2.23)	**0.014**

Logistic regression adjusted for sex, SES and tribe.

Supplementary table 4. The influence of *CFTR* SNPs on weight and height in children equal to or younger than five years of age (n=474)

	Haplotype alleles			
	0-copies	1-copy	2-copies	
z-scores	Mean (SE)	Difference (SE)	Difference (SE)	P_{trend}
rs213952 (G/A)				
Weight	reference	-0.002 (0.09)	0.20 (0.17)	0.422
Height	reference	-0.07 (0.08)	0.28 (0.16)	0.468
rs10281281 (A/G)				
Weight	reference	-0.22 (0.10)*	-0.19 (0.12)	0.122
Height	reference	-0.28 (0.10)*	-0.19 (0.11)	0.090
rs17140174 (A/G)				
Weight	reference	-0.003 (0.09)	0.04 (0.18)	0.890
Height	reference	-0.07 (0.09)	0.14 (0.17)	0.960
rs3808185 (T/C)				
Weight	reference	-0.11 (0.09)	0.03 (0.20)	0.470
Height	reference	-0.07 (0.09)	0.10 (0.19)	0.837

Linear regression adjusted for sex, socioeconomic status and tribe; *p-value <0.05 in comparison to people carrying 0-copies of the respective haplotype.

Chapter 7

Selection for longevity in a polygamous society in rural Africa

D. van Bodegom, L. May, H.J. Meij, E.E. Treffers, J.B. Ziem,
F. Thomése, B.J. Zwaan, R.G.J. Westendorp

Submitted for publication

Abstract

Human longevity was long thought to be non-adaptive, resulting from better environmental conditions. Later, a selective advantage of grandmothers has been suggested. Recently, it was put forward that continued reproductive success of older men in polygamous societies provides an evolutionary explanation for the length of our lifespan. Here, we tested these hypotheses simultaneously by prospectively following 28,994 individuals of a polygamous culture in rural Africa, where the conditions likely mimic our evolutionary past. Presence of post-reproductive women increased the number of newborns by some 2.7%. However, 18.4% of offspring was sired by fathers aged 50 and above. These results suggest that length of our lifespan may have evolved predominantly through selection for longevity of men, rather than through selection favouring post-reproductive survival in women.

Longevity is often considered to be non-adaptive and the result of recent environmental improvements[1,2]. In historical times, however, human life expectancy of around 40 years was mainly determined by high child mortality but a significant number of people lived to old age; a notion that is confirmed by observations among present day hunter-gatherers[3]. A first adaptive explanation of our longevity was the 'mother' hypothesis, which suggests a selective advantage for older women as their presence would increase survival probabilities of their offspring[4]. The 'grandmother' hypothesis added the notion that help from older women may have had a selective advantage through increasing the reproductive success of their offspring[5,6]. Previous research has found that the presence of post-reproductive women allows their children to reproduce earlier, more frequently and more successfully, but the effects are context dependent and not undisputed[7-9]. It is noteworthy that currently available studies originate mostly from historical populations with nuclear families and largely from monogamous populations[7].

Recently, it has been suggested that, in polygamous populations, older men could also have played an important role in the evolution of longevity through continued reproduction up to high age[10,11]. Both Y-chromosomal and anthropological studies indicate that during our evolutionary past, in which our longevity evolved, the human species predominantly lived in polygamous populations[12,13].

Here we present the outcome of a prospective analysis in a large polygamous, patrilineal African population from the upper east region in Ghana. The people here are subsistence agriculturalists. Child mortality has recently started to decline but remains high and the corresponding population structure is dominated by children with relatively few older people[14-20]. From 2002 onwards, we have followed life history characteristics of 28,994 individuals, comprising 1,703 extended families in separate households. We were able, in a full kin analysis of

two sexes, to compare the effect of older women and older men on offspring survival and reproduction and to adjust for socioeconomic status, anthropological, and environmental factors to a degree that has often been impossible in historical studies. The characteristics of the population under study are summarized in supplementary table 1.

Table 1. Hazard ratios for mortality up to reproductive age

	HR (95%CI)	p
Presence of kin members		
Mother (present vs absent)	0.67 (0.53-0.85)	**0.002**
Father (present vs absent)	0.81 (0.61-1.07)	0.13
Paternal grandmother (present vs absent)	0.99 (0.76-1.29)	0.93
Paternal grandfather (present vs absent)	0.92 (0.67-1.26)	0.58
Number of siblings (effect per sibling)	1.00 (0.98-1.02)	0.85
Number of adults (effect per adult)	1.00 (0.98-1.02)	0.74
Environmental determinants		
Socio-economic status (rich vs poor)	0.77 (0.61-0.96)	**0.02**
Drinking water (safe vs unsafe)	0.66 (0.52-0.84)	**0.001**

Results from multiple Cox regression analysis of 16,332 children, clustered on household, corrected for tribe, sex and all other variables in the model. Estimates express the hazard ratio for mortality up to age 18 years dependent on the presence of kin and environmental determinants during an eight year prospective follow-up during which 471 died. HR = hazard ratio; CI = confidence interval.

First, we studied the survival probabilities of offspring. To this end we have followed 16,632 children up to reproductive age (≤18 years) during an eight-year prospective follow-up, in which we observed 471 deaths. Figure 1 shows Kaplan-Meier survival plots dependent on kin members. The presence of the mother was associated with a 33% lower mortality risk (HR 0.67, p=0.002) pointing to increased survival probabilities. In contrast, the presence of the grandmother was not associated with a mortality difference (HR 0.99, p=0.93). Presence or absence of fathers and grandfathers did not affect offspring survival. Table 1 shows hazard ratios (HR) for mortality dependent on the presence of kin members and environmental determinants, as derived from multiple Cox regression. Children in

rich households had significantly lower mortality when compared to poor households (HR 0.77, p=0.02) and children with access to safe drinking water also had a reduced mortality risk (HR 0.66, p=0.001).

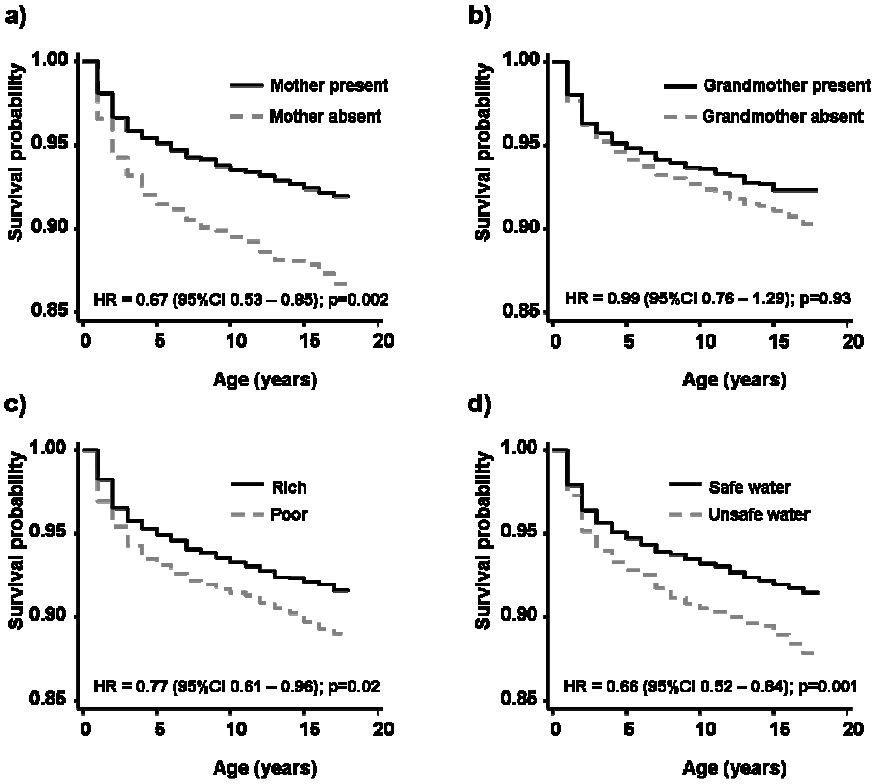

Figure 1. Survival probabilities dependent on the presence of kin and environmental determinants. a) mother, b) grandmother, c) socio-economic status, d) drinking water. Hazard rates (HR) with 95% confidence intervals (95%CI) from multivariate Cox proportional hazards model, adjusted for all other variables in the model (table 1).

Next, we studied the reproductive success of households. Table 2 shows the number of newborns dependent on the presence of kin members and environmental determinants as derived from multiple regression analysis. In line with their polygamous culture, for each additional woman aged 18 to 50 years, we observed an extra 0.42 number of newborns during the eight year observation period ($p<0.001$). Reproductive success was not higher when there were, next to

the landlord, additional men in the household. Counter intuitively, there was a lower number of newborns when men over 50 were around (Table 2). In this patrilineal society older men, most often the landlord, monopolize resources and women, and it is them who delay the marriage and reproductive success of the younger men in their household. In line, we observed young men up to 50 years to have an average number of 5.1 newborns when an older men was absent, while they had only 3.7 newborns when an older man was present in the household. Oral history taking has identified a plausible mechanism that explains these observations; not before the 'old man' dies, the younger son inherits his livestock and is able to marry a (next) wife.

Table 2. Number of newborns in households

	Extra newborns (SE)	p	Explained variance
Effect for each additional kin member present			
Parental generation			
for each additional woman (18-49 years)	0.42 (0.02)	**<0.001**	11,7%
for each additional man (18-49 years)*	0.02 (0.03)	0.55	1,0%
Grandparental generation			
for each additional woman 50 years and above	0.13 (0.05)	**0.007**	2,7%
for each additional man 50 years and above	-0.22 (0.07)	**0.001**	6,7%
Environmental determinants			
Socio-economic status (rich vs poor)	0.72 (0.10)	**<0.001**	1,8%
Drinking water (safe vs unsafe)	0.14 (0.12)	0.24	0,0%

Results from multivariable linear regression analysis, corrected for tribe and all other variables in the model. Estimates indicate the extra number of newborns observed in an average household dependent on the presence of kin and environmental determinants during an eight year follow-up period in 1,703 households during which a total of 3,645 newborns were registered. * 92% of compounds have at least one man 18-49 years present. SE = standard error.

Since women are no longer able to reproduce after age 50 because of the onset of menopause, any selection for longevity in women must be by increasing the fertility or the survival probabilities of her kin in the household. We found the presence of post-reproductive women to give rise to an additional increase in the number of newborns in the household. For each extra woman aged 50 and above, the number of newborns additionally increased with 0.13 during the eight year

observation period (table 2, p=0.007), indicating a selective advantage for post-reproductive survival in women. Analysis of variance showed the presence of post-reproductive women to increase the number of newborns by 2.7%. One could hypothesize on the nature of the effect of older women on household reproduction. One possible explanation is that elderly women allow fertile women to reproduce with shorter birth intervals because they assist with supplementary feeding or lighten the burden of child care, as has been suggested earlier[21]. Apart from accidental observations during our surveys we do not have quantitative data to test this hypothesis.

Finally, to assess the effect of continued reproduction on the selection for longevity, we calculated the fertility rates and the cumulative survival probabilities up to different ages, as shown in figure 2a and 2b. The polygamous culture of the population resulted in a higher fertility rate for men than women. Since it is customary that older men sequentially marry young fertile women, men are able to continue reproduction up to old age. By multiplication of sex-specific survival probabilities (l_x) and fertility rates (m_x), we have calculated the reproductive probability of men and women of different ages based on our prospective observations over eight years. These estimates are shown in figure 2c. At younger ages, reproductive probability is somewhat higher in women than in men. After age 35, however, reproductive probability is considerably higher in men. Since they continue to reproduce up to higher age, men have positive reproductive probabilities after age 50.

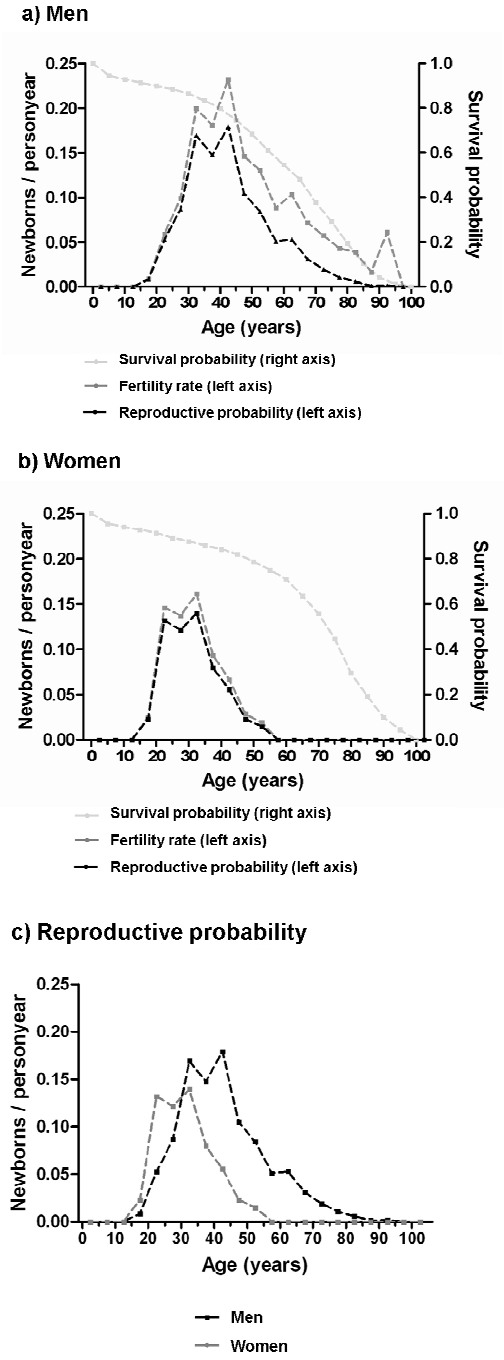

Figure 2. Selection for longevity, observed during an eight year prospective follow-up. Fertility rate, survival probability and reproductive probability for a) men and b) women of different ages and c) reproductive probability for men and women of different ages.

The net result of the continued reproduction of older men is shown in figure 3. Cumulated over an eight-year follow-up period, including a total of 3,645 newborns, 18.4% of this offspring were sired by fathers aged 50 and above, with whom they share 50% of their genome. In an additional analysis we found that children born to fathers aged 50 and above had similar survival probabilities up to reproductive age as did children born from younger fathers (HR 1.14 [95%CI 0.87 – 1.51], p=0.35). As older women increased the number of newborns with only 2.7% (see above) with whom they share 25% of their genome, these data suggest that the selective advantage of the continued reproduction of older men is far larger than the selective advantage of post-reproductive survival of women.

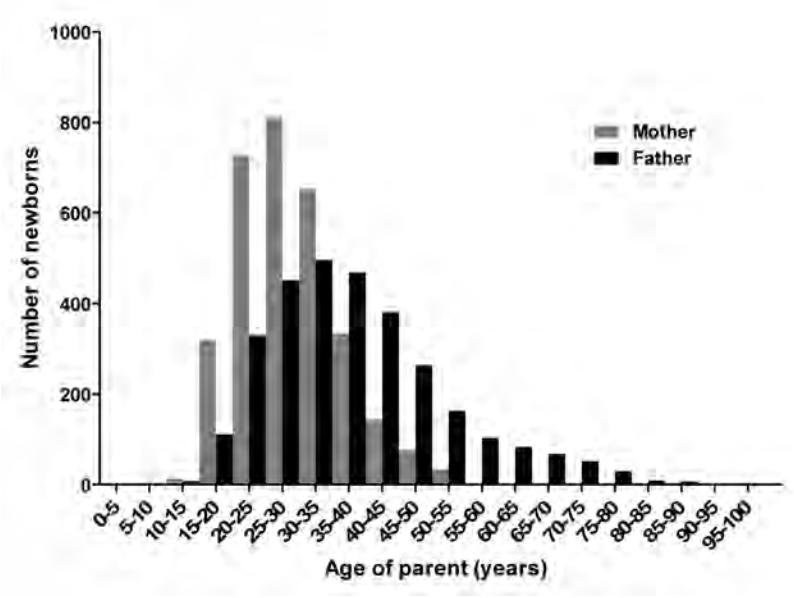

Figure 3. Number of newborns of parents from different ages. Of all 3,645 newborns observed during the eight year follow-up, 18.4% were sired by fathers aged 50 and above.

It needs to be considered that in this patrilineal society, virtually all grandparents in the household are paternal grandparents. Previous research has shown different effects of maternal and paternal grandparents on offspring survival[7,22]. It is possible that depending on the social structure, paternal or maternal grandparents

may have larger effects on selection in different populations. In this light it would be interesting to also assess the selective advantages of longevity in matrilineal populations.

An important consideration is that in this polygamous, patrilineal society, some men never find a partner and consequently will not reproduce. There is both outmigration of men to the south of Ghana and inward migration of women from as far as neighboring Togo. We do not have follow-up of the males that have permanently left the research area. Outward migration is limited to an average 2% per year. For estimating reproductive probability and selective advantages, only reproducing males are important and those are all included in the present study.

Outcomes of recent collaborative studies into the genetic underpinning of human longevity have not identified particular loci with strong effects[23]. There are likely many genes involved and these are probably spread across many different chromosomes, and not just restricted to sex-chromosomes only. Long-lived fathers would therefore pass on their genetic disposition for longevity equally to their daughters and sons. Consequentially, women are long-lived because of the selection for longevity in men via continued successful reproduction into old age. The residual question is why most comparisons show that women live even longer than men. It needs to be emphasized however, that best estimates for male and female longevity come from present day societies that enjoy dramatically improved environmental conditions[24]. In our evolutionary past, the average lifespan of women, taking into account the risk of for instance childbirth, could have been markedly different. Furthermore, female longevity under present affluent conditions has a myriad of biological underpinnings, including the non-adaptive, cultural or epiphenomenal.

The contribution of kin members to reproductive success of men and women is highly dependent on the environmental conditions, the population structure and cultural aspects. Therefore, the data presented here are by no means applicable to all populations. However, since a polygamous society with extended families is most likely to resemble the population structure of our evolutionary past, the data presented here suggests that longevity has primarily evolved through the effect of continued reproduction of men after age 50, more than through effects of post-reproductive survival in women.

Supporting material

This study was conducted in the Garu-Tempane district in the Upper East region of Ghana and has been described in more detail elsewhere[14-20]. The people are patriarchal, patrilineal and patrilocal and live in extended families of which 48% are polygamous (Supplementary figure 1). Since the elderly live with their oldest son, 99% of the grandparents are paternal grandparents. During eight years of follow-up from 2002-2010 we followed 28,994 participants for reproduction and survival. The area is currently undergoing the epidemiological transition[15]. For each member of the household, the father and mother were identified if they were living in the same household. The socioeconomic status was assessed for all inhabited households in accordance with the Demographic and Health Survey (DHS) methods[17]. We defined poor and rich as divided by the median. Drinking water from bore-holes was considered safe drinking water, water drawn from wells or rivers was considered unsafe[14]. Informed consent was obtained after the nature and possible consequences of the studies were explained. Ethical approval was given by the Ghana Health Service, the Leiden University Medical Centre in Leiden, The Netherlands and by the local chiefs and elders of the research area.

Reproductive probabilities were calculated as the multiplication of the age specific fertility rates (m_x) and the cumulative survival probabilities (l_x)[2]. For the reproduction analysis we used a multiple linear regression analysis, adjusted for

tribe and all other variables in the model. For the survival analysis we used a multiple left-censored Cox regression analysis adjusted for sex and tribe and all other variables in the model. The left-censored plots represent age-specific survival probabilities based on eight year follow-up. All analyses were performed with Stata 11.0 (StataCorp LP, Texas USA).

Supplementary table 1. Characteristics of the study population

Participants (n)	28,994
Male (n (%))	13,323 (46%)
Female (n (%))	15,645 (54%)
Tribe	
Bimoba (%)	66%
Kusasi (%)	26%
Mamprusi (%)	2%
Fulani (%)	2%
Busanga (%)	2%
Other (%)	2%
Households (n)	1,703
Polygamous households (%)	48%
Mean value of household possessions in US$ (mean (SD))	1,063 (1,021)
Safe drinking water (%)	80%
Numbers of newborns registered 2002-2010 (n)	3,645
Presence of kin members in household	
Men 19-49 years (median (IQR))	2 (1-3)
Women 19-49 years (median (IQR))	3 (2-5)
Men >49 years (median (IQR))	1 (0-1)
Women >49 years (median (IQR))	1 (0-2)
Survival analysis	
Offspring ≤ 18 years (n)	16,632
Follow up (calendar years)	2002-2010
Person years (years)	91,256
Mean follow up (years)	5.5
Deaths during follow up (n)	471
Presence of kin members with offspring	
Mother (%)	77%
Father (%)	71%
Paternal grandmother (%)	29%
Paternal grandfather (%)	13%
Maternal grandmother (%)	1%
Maternal grandfather (%)	1%
Number of siblings ≤18 years (median (IQR))	12 (8-17)
Number of adults > 18 years (median (IQR))	9 (6-13)

IQR = interquartile range; SD = standard deviation,

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Chapter 8

Socio-economic status determines sex dependent survival of human offspring

D. van Bodegom, M.P. Rozing, L. May, H.J. Meij, F. Thomése, B.J. Zwaan, R.G.J. Westendorp

Submitted for publication

Abstract

In polygamous societies, rich men have high reproductive prospects through the marriage of multiple wives. Evolutionary, rich households would therefore benefit more from sons. In a polygamous African society, men had three times higher fertility rates than women in rich households. As hypothesized, sons had both higher survival and better nutritional status here.

In polygamous societies, richer men can afford to marry multiple wives and consequently increase their reproductive success. From an evolutionary perspective rich households would therefore benefit more from sons. To test this hypothesis we have first studied the effects of socioeconomic status on fertility rate of men and women in a polygamous society of 28,994 individuals in the Upper East Region of Ghana. Second we investigated the sex differences in offspring survival and offspring weight in poor and rich households. The main characteristics and methods are summarized in the supplementary information and table. General fertility and mortality patterns have previously been described in more detail[1].

Figure 1a shows the age specific fertility rates in poor and rich households. The people in the research area are polygamous and the man must pay a bride price of four cows to arrange a marriage. Consequently, richer men are able to increase their number of offspring. From the area under the curve, we found that in poor households men can expect 5.5 offspring and women can expect 3.1 offspring. In rich households men had much higher reproductive prospects; they can expect 9.2 offspring, while women can expect only 3.5 offspring.

Studies have shown a strong heritability of socioeconomic status in pre-transitional societies[2]. This seems applicable to this population also, since income is generated largely through agriculture and sons inherit the land of their fathers. If offspring inherits the socioeconomic status from their parents and rich men have better reproductive prospects, one could hypothesize that rich households would benefit more from sons, which would create an opportunity for selection on sex specific survival dependent on socioeconomic status. We tested this and compared the offspring survival and weights of offspring in poor and rich households.

First, we studied survival of 16,632 offspring up to reproductive age (≤18 years) (figure 1b). In poor households sons had much higher mortality risk compared to

daughters (hazard ratio 1.45 [95%CI 1.08-1.95]; p=0.01) In rich households, however, mortality risk of sons was similar to that of daughters (hazard ratio 1.05 [95%CI 0.82-1.34]; p=0.71). These ratio's were significantly different (p for interaction = 0.028).

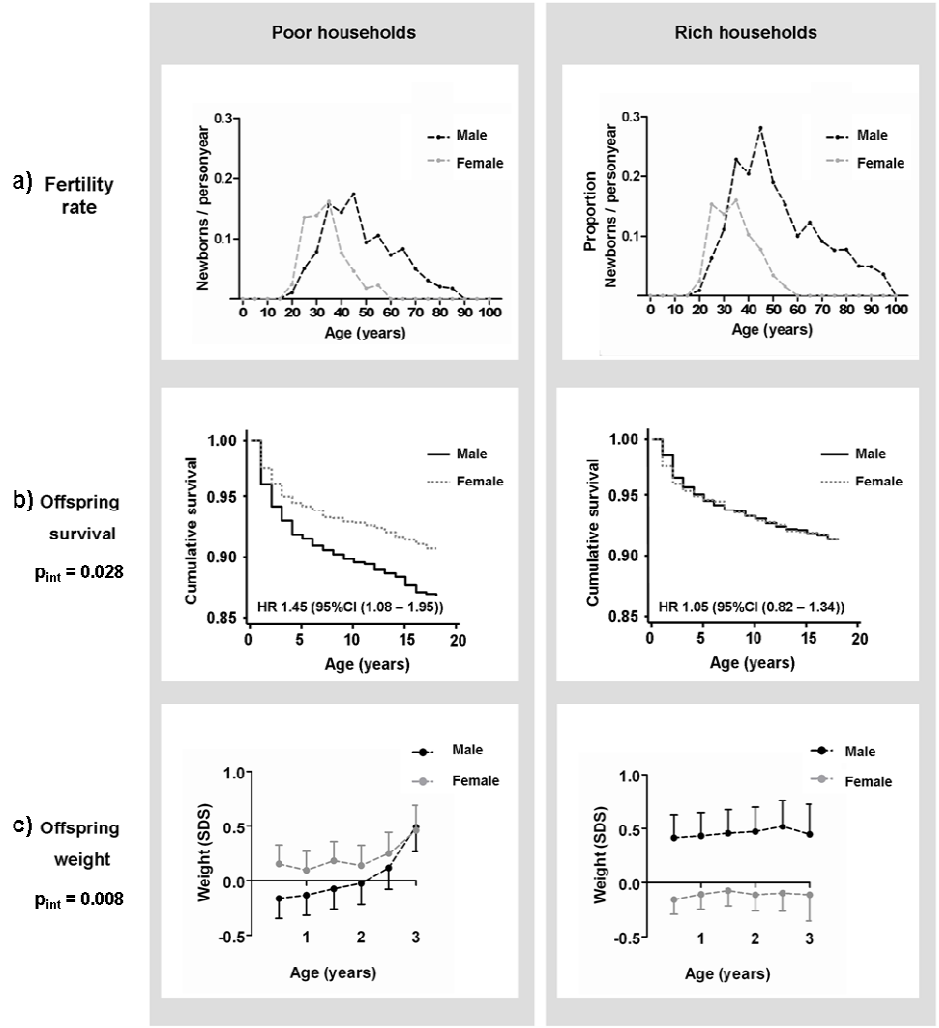

Figure 1. Fertility rate, offspring survival and offspring weight in poor and rich households. Error bars indicate standard errors.

Second, we analyzed the weights of offspring using repeated measurements from growth charts of the local health clinics. In an analysis of 9,842 age and sex standardized measurements among 1,470 offspring up to the age of three years, in poor households, daughters had higher weights while in rich households sons had higher weights (figure 1c). These differences in sex specific weight gain were significantly different (p for interaction = 0.008).

There are two possible explanations for the marked sex specific effects of socioeconomic status on life course characteristics. First, they could be a reflection of higher intrinsic vulnerability of sons to poor conditions. Men have higher mortality risks throughout life in almost all countries[3].

Second, our observations are also in line with differences in parental investment as hypothesized by Trivers and Willard[4]. According to their hypothesis parents invest more in offspring of that sex that has the best reproductive prospects. Although Trivers-Willard effects have been found in different mammal species, it is highly debated whether these effects are present in humans[5]. The observed sex differences in weight could reflect differences in parental nursing habits; sex differences in breastfeeding have previously been observed in Poland and the Caribbean[6,7].

Whether the sex differences that we have observed in our study reflect the higher vulnerability of sons to poor conditions, or reflect a sex specific parental investment as proposed by Trivers and Willard, the net result is the same; sons are better off in richer households which maximizes the reproductive prospects of households in this polygamous society.

Supplementary information

This study was conducted in the Garu-Tempane district in the Upper East region of Ghana. General fertility and mortality patterns have been described elsewhere[8]. The people are patriarchal, patrilinial and patrilocal and live in extended families of which 48% are polygamous. During eight years of follow-up from 2002-2010 we followed 28,994 participants for reproduction and survival. The area is currently undergoing an epidemiological transition[9]. The socioeconomic status was assessed for all inhabited households in accordance with the Demographic and Health Survey (DHS) methods[1]. We defined poor and rich as the poorest 50% and the richest 50% divided by the median. Drinking water was assessed on household level, water from bore-holes was considered safe drinking water, water drawn from either open wells or from rivers was considered unsafe drinking water[10]. The survival analysis includes all offspring up to reproductive age (≤18 years) and used a multivariable left-censored Cox regression analysis adjusted for sex, tribe and drinking source. We found no evidence that the assumption of proportionality of hazards was violated. The left-censored plots represent age-specific survival probabilities rather than a prospective eighteen year follow-up. The weights of the offspring were obtained from growth charts of local health clinics in 2008. The clinics use hanging scales to measure the weight and use growth charts from the Ghana Health Service, adapted from the World Health Organisation. We standardized the weights on age and sex and used a linear mixed model adjusted for tribe, drinking source and the month and year of measurement, as weights fluctuated dependent on the season. All analyses were performed with Stata 11.0 (StataCorp LP, Texas USA). This research was supported by the Netherlands Foundation for the advancements of Tropical Research (WOTRO) the Netherlands Organization for Scientific Research (NWO), the EU funded Network of Excellence LifeSpan, an unrestricted grant of the Board of the Leiden University Medical Center and the Association Dioraphte. None of these organizations had any role in the design, analysis, interpretation, or report of the study. Ethical approval was given by the Ethical Review Committee of the Ghana Health Service, the Medical Ethical Committee of the Leiden University Medical Centre in Leiden, the Netherlands and by the local chiefs and elders of the research area.

Supplementary table 1. Characteristics of the study population

Participants (n)	28,994
Male (%)	46%
Female (%)	54%
Tribe	
Bimoba (%)	66%
Kusasi (%)	26%
Other (%)	8%
Households (n)	1,703
Polygamous households (%)	48%
Value of household possessions in US$ (mean (SD))	1,063 (1,021)
Safe drinking water (%)	80%
Reproduction	
Numbers of newborns registered 2002-2010 (n)	3645
socioeconomic status available (n)	3511
Offspring survival	
Offspring ≤18 years (n)	16,632
Follow up (calenderyears)	2002-2010
Person years (n)	91,256
Mean follow up (years)	5.5
Deaths during followup (n)	471
Weights of offspring	
Offspring ≤3 years with growth chart (n)	1,470
Weight measurements (n)	9,842
Average number of measurements per child (n)	7

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Chapter 9

When grandmothers matter

D. van Bodegom, M. Rozing, L. May, M. Kuningas, F. Thomése, J.J. Meij, R.G.J. Westendorp

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In a recent issue of Gerontology, Herndon discussed the grandmother hypothesis and its implications for studies on cognitive ageing[1]. According to this hypothesis the long post-reproductive life span in human females is an adaptive mechanism that evolved to maximize female fitness by investing resources in the care of their grandchildren rather than by continuing to reproduce themselves. From this Herndon deduces that special cognitive robustness to be maintained until after the age of menopause must have co-evolved because grandmothers can only exert the beneficial effect if their cognitive abilities remain intact. He therefore pleas to compare cognitive ageing in humans with other primates, especially chimpanzees, because they lack a long post-reproductive life span and would therefore not have evolved this cognitive robustness. Here, we question the important role of grandmothers in our evolutionary past, first because of the different family structures during this time and second because of the low number of females that actually lived to experience a post-reproductive lifespan. We also show that in a population that reflects our evolutionary past, grandmothers do not have an important role for child survival. Finally we react on the implications for the study of cognitive ageing as put forward by Herndon.

From an evolutionary perspective the long post-reproductive period in human females is a puzzle. Since the length of the reproductive period is a variable trait with a genetic basis[2] with obvious consequences for reproductive success, why did human females evolve such a long post-reproductive period? One of the theories put forward to explain this phenomenon is the grandmother hypothesis[3-3]. In this theory the human species evolved a post-reproductive life span as an adaptive mechanism because women who stop reproducing around 50 can assist their children to raise the grandchildren. Ultimately, this strategy would result in a larger number of grand-offspring than continuing to reproduce themselves. In support of the grandmother hypothesis, numerous studies have found a positive effect of grandmothers on offspring survival, which were summarized in a recent review[6].

Our first remark concerns the nature and family structure of the populations of our evolutionary past. Both anthropological and genetic y-chromosomal analyses indicate that the human species until recently lived in polygynous extended families in which one man lives together with multiple wives and a large group of kin[7,8]. In these populations with polygynous extended families, the wives can

divide the task of childcare with the other kin members and an important role for grandmothers is less likely to be expected. Most studies that have found an effect of grandmothers were conducted in historic populations dating from 1600 to the present. We think that these populations are very different from the populations that constitute our evolutionary past up to recent cultural changes. The study populations were already developed enough to leave written historical records of child survival and genealogical information. These societies are mostly Christian, monogamous agricultural societies. It is possible that in these populations, with three generational nuclear families, composed of man, wife, grandparents and children, grandmothers have a larger influence[9], because there is only one wife to take care of all children and household tasks, who would greatly benefit from an assisting grandmother.

Some studies were conducted in populations with a polygynous extended family structure. These studies found contrasting results for the effects of both maternal and paternal grandmothers[6]. We studied a large polygynous extended family population of 26,170 individuals in the north of Ghana for five years, which is described in more detail elsewhere[10,11]. We investigated the effect of different kin members on child survival up to reproductive age (eighteen years). The results in figure 1 show that, the presence of grandmothers did not have a significant effect on the survival of children in this population. Also when we stratified the grandmothers into those below 65 years and those above 65 years, we saw similar patterns. As expected, the mother did have a large effect on the survival of the children. Children whose mother was present during all five years had a 30% survival benefit compared to children of whom the mother was not present during all five years of follow-up. This is a further indication that in polygynous extended family populations, the role of grandmothers on child survival is probably limited and the role of grandmothers in evolution seems to be limited to recent times. Given the remarkably contrasting results, especially in matrilocal and patrilocal societies, we stress the importance of anthropological differences in tribal, clan and family structures. Which kin members influence child survival seems by a large extent determined by cultural factors.

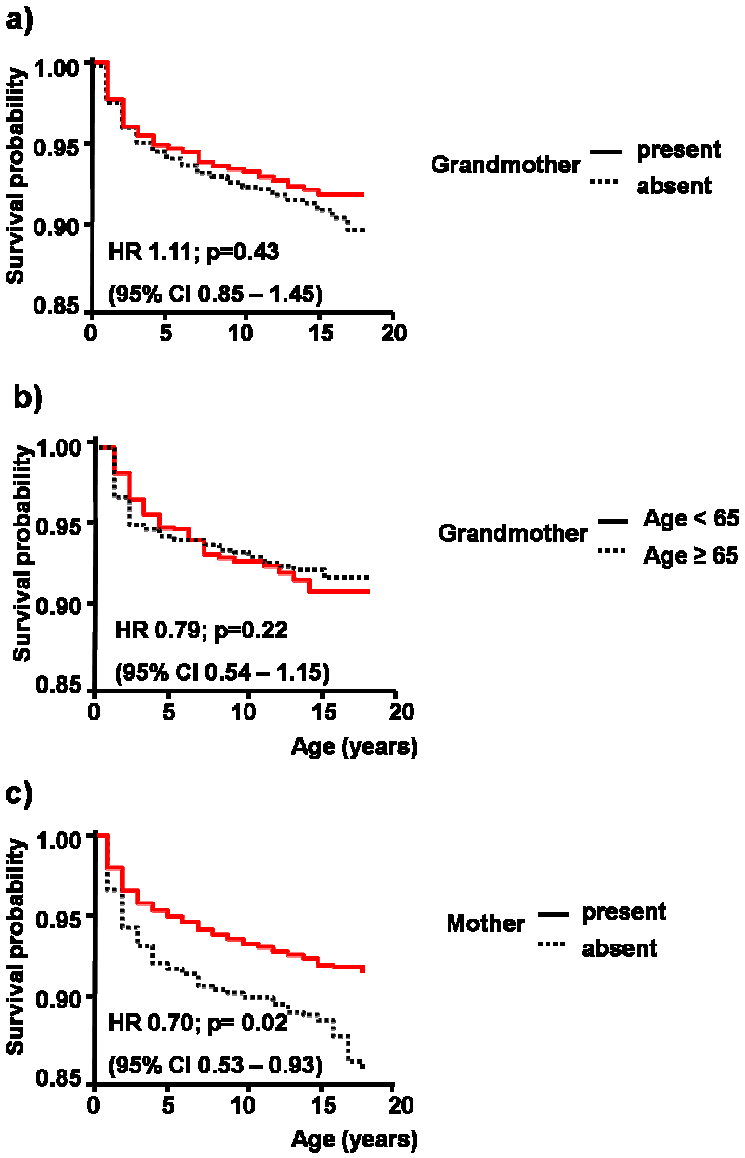

Figure 1. Survival probabilities for children up to eighteen years dependent on the presence of different kinmembers. a) grandmothers; b) grandmothers above 65 years and below 65 years; c) mothers. Left-censored Kaplan Meier plots, hazard ratios (HR) derived from multivariate Cox regression analysis, adjusted for sex, all other kinmembers, socioeconomic status and tribe. All analyses were performed with Stata 9.0, Statacorp, USA.

A second remark to the role of grandmothers in our evolutionary past is that in earlier civilizations, with high extrinsic mortality, only very few individuals would live long enough to experience a post-reproductive life span beyond the age of 50[12,13]. Variants that yield an increase in female fertility at younger ages would be preferentially selected over variants that result in a fitness benefit at old age, when only a few individuals are left to experience this advantage[14]. The post-reproductive life span in this reasoning is not so much an evolutionary puzzle but a recent epiphenomenon of our increased life span. Some argue that these few old individuals could have had a very important function in the community, by transferring special knowledge or skills. This theory is however dependent on group selection which can execute only a small selective advantage, because of the low amount of shared genetic material on a community level.

We would like to make two remarks on the implications for the study of cognitive ageing as put forward by Herndon. Many characteristics of the human species as we know it today, evolved during a long period of evolution. A recent role of grandmothers, as has been found in some populations cannot have given rise to the co-evolution of maintenance of cognitive robustness until after the age of menopause as Herndon implies. The evolution of our brain which separates us from other primates, evolved during a long period of evolution. It is possible that the presence of grandmothers has an advantage for children nowadays, but we think that this effect is too recent to have given rise to a co-evolved maintenance of cognitive robustness until after the age of menopause. Instead the existence of age-associated diseases, such as Alzheimer, cancer and cardiovascular diseases, in our view strongly argues against selection for robustness at higher age. This is in line with the classic theory of ageing as put forward by Medawar which indicates that selective pressure decreases very rapidly after the time of reproduction and rearing of offspring which is therefore called the selection shadow[14].

As a second reaction to the implications, we also think that human life history does not stand out very differently from other primate species. During our evolution in the past 10.000 generations, with the exception of the last ten, the median life span of humans was probably not 80 years as noted in figure 1 of Herndons paper, but much lower, around 40 years[15]. Human life history in this case would be very similar to the life history of chimpanzees or rhesus monkeys, because most humans would also not live long enough to experience a post reproductive life span.

Concluding, we question the important role of grandmothers in our evolutionary past up to recent times, which was characterized by polygynous extended families. In line with this reasoning, we also do not find an effect of grandmothers in a polygynous extended family population. Consequentially we question whether humans developed special cognitive robustness to be maintained until after the age of menopause which is also inconsistent with current theories of ageing. Also, we question whether human life history is very different from other primate life histories. Although it is possible that the study of the chimpanzee brain can teach us many things about cognitive ageing, we do not think that the role of grandmothers in our evolution provides us with good reasons to believe this.

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Chapter 10

General discussion

Discussion

In this thesis we studied post-reproductive survival from an evolutionary perspective. We tested the hypothesis that men and women after age 50 are able to contribute to their fitness either direct by continued reproduction or indirect through improving the reproductive success of subsequent generations. In a prospective full kin analysis in the Upper East Region in Ghana, we studied the effect of different kin members on offspring production, survival and early growth patterns in a polygamous population that lives in an environment that could reflect our recent evolutionary past.

Main conclusions

Chapter two describes a theoretical framework for the study. In this chapter we set out the principles of life history theory and apply this theory from the field of evolutionary biology to humans. Life history theory postulates that different physiological and behavioural characteristics of an organism's reproduction and survival are linked. There is growing evidence that a trade-off between maintenance and longevity is equally applicable to humans. We further hypothesized a mechanism that could underline this trade-off. Human survival has been strongly dependent on resistance to infectious diseases during our evolution. Resistance to infectious diseases is strongly dependent on an inflammatory host response. Pro-inflammatory signals, however, are negatively associated with fertility, since immunotolerance for the paternal antigens of the foetus is essential for normal pregnancy. In this way we hypothesize that the immune response could be the underlying mechanism for the trade-off between maintenance and fertility. We also note that humans are genetically still optimized for an environment with scarcity and infectious diseases and that our thriftiness and strong immune response evolved in an environment that has dramatically changed. In our new environment a predisposition for thriftiness could lead to obesitas and strong immune responses to many chronic diseases, most notably atherosclerosis. Life history theory and evolutionary theory can help us to better understand these epidemics of chronic diseases which are now starting to affect the rapidly changing developing countries to an even greater degree. These observations warrant a shift in focus of traditional healthcare in developing countries from mother- and childcare and acute medicine to the prevention and management of chronic diseases.

Chapter three provides a description of the research area, the Garu Tempane district in the upper east region of Ghana. It provides the environmental, social and anthropological background of the area and the participants, most notably the Bimoba tribe to which most participants of this study belong. This anthropological background is essential to interpret the findings of the studies described in this thesis.

In **chapter four** we studied the socioeconomic status of the participants, which was essential to study of the effect of different kin members on offspring survival, since socioeconomic status would confound the relation between kin members and offspring survival. In richer households, children would have better survival, but other kin members, e.g. grandmothers, would also have better survival, creating the impression that the presence of grandmothers improves offspring survival. Traditional socioeconomic assessments use a composite measure of education level, job status, income and savings. This could not be applied in this pre-transitional research area and we had to develop another method. We made use of an anthropological method of the 1970's: the rapid appraisal method, consisting of an interviewer- perceived wealth status and a self-perceived wealth status. We compared these methods to a more traditional measurement of socioeconomic status, the DHS wealth index, based on the possession of valuable items. We conclude that rapid appraisal can be used as a practical method to assess socioeconomic status in health studies in rural Africa. The rapid appraisals are correlated with the DHS wealth index but are more practical; it takes only a minute to rate the wealth status of a compound as average, below average or above average. The rapid appraisal methods also identify individuals at higher risk of mortality. Individuals that were ranked as below average wealth had a 30% higher mortality risk compared to average, while those that were ranked as above average wealth had a 20% reduction in mortality risk compared to average. One of the strengths of the rapid appraisal is that it could measure relative wealth, derived from the social status of the household members in the community. This position in family or clan structures is of utmost importance in the rural areas of developing countries and is not always reflected in their property. Therefore, the rapid appraisal method is not only more practical but could indeed be more accurate to identify individuals at risk. These findings could also be of benefit to health policy makers or non governmental organisations that need a quick and reliable method to identify individuals at risk of mortality.

In **chapter five** we studied the effect of the number of offspring on offspring survival. Before studying the effect of kin members on offspring survival, it is important to quantify this effect. A trade-off between the quantity and quality of offspring is a central paradigm in life history theory. In birds for example larger litter sizes are associated with lower survival. In chapter five we investigated this trade-off in humans. Several studies have investigated this trade-off in humans, but data are inconclusive, perhaps because prosperous sociocultural factors masked the trade-off. With our previous assessment of socioeconomic status, we were able to better study the trade-off. We found a 2.3% decrease in proportional survival of offspring with each increasing number of offspring. We also made use of the polygamous population structure and compared co-wives within one compound. In this way, we were able to maximally control for (micro) environmental differences. The tradeoff was still found even when the environment was the same, thereby providing additional arguments that genetic or biological mechanisms could be at the basis of the observed tradeoff. The effect remained significant after adjustment for socioeconomic status. The present data set from an adverse contemporary environment provided robust arguments for quantity to be traded off against quality in humans, a central paradigm in life history theory, an effect well known in different plant and animal species. Despite the ultimate explanation of the theory, the proximal explanation that accounts for this trade-off has yet to be fully unravelled.

Next to mortality, we also studied the nutritional status of the children by taking extensive biometrical measurements of the offspring, described in **chapter six**, through which we were able to detect smaller differences in nutritional status of the offspring as an intermediate phenotype. The weights of offspring however, are not only determined by environmental determinants and we investigated whether genetic variants also determined the weights of the children. We identified genetic variants in the CFTR gene, which causes cystic fibrosis in mutated form, that influence body composition in children and survival in the population at large. Using a sliding window technique we identified a haplotype which was depleted among people of old age (≥65 years) compared to young study participants (≤5 years). In addition, offspring carrying this haplotype had lower body weight and height compared to non-carriers. This shows that in an environment where the availability of food is critical, next to environmental factors, genetic variants influence body composition. This is in line with evolutionary theory, which

predicts that in environments that have strong selective pressures (e.g. with periodic food scarcity) genetic variants that provide small advantages can quickly spread in a population. A possible mechanism in which this genetic variation plays a role could be the ability to metabolise and store the scarce food supply, whose availability is highly dependent on the season, as additional analyses later showed.

In **chapter seven,** we describe our final analysis, combining all findings from previous chapters. Here we studied the selection advantage of survival past age 50 for men and women. In a full kin analysis, using a two-sex model, we assessed both the direct effect of continued reproduction in men and the indirect effect of the presence of older men and women on the reproduction and offspring survival in the household. We observed selection for longevity in men; of all 3,645 observed newborns, 18.4% were born of fathers aged 50 and above. We also observed selection for post-reproductive survival in women; the presence of women aged 50 and above increase the total number of offspring in the household with 2.7%. We also observed that the presence of older men suppressed the total number of newborns in households by 6.7%. Offspring survival up to reproductive age was not affected by the presence of either older women or older men. Our results suggest that human longevity evolved predominantly through a direct effect for longevity in older men, more than through the indirect effects of post-reproductive survival in older women, as earlier suggested.

In **chapter eight** we study the effects of socioeconomic status on survival and reproduction. Since in this society it is custom that men pay a brideprice of four cows, rich men can afford to marry more wives and consequently sire more children. For women, the effects of socioeconomic status on reproduction are less pronounced. We found that in rich households men had three times higher reproductive prospects compared to women. In poor households, the reproductive prospects of men was comparable to that of women. Evolutionary, rich households would therefore benefit more from male offspring. In line with this, we found that male to female survival probabilities were higher in rich compounds when compared to poor compounds. We also found that male offspring weights were higher in rich households while female offspring weights were higher in poor households. These observations could reflect a higher vulnerability of male offspring to adverse conditions. However, they are also in line with differences in parental investment as hypothesized by Trivers and Willard. Irrespective of the

underlying mechanism however, the differential survival of male and female offspring dependent on socioeconomic status maximizes reproductive success of the households in this polygamous society.

In **chapter nine** we comment on other studies on the effect of grandmothers on offspring survival. We conclude that the environment in which you study these effects is crucially important. Here we stress the difference between historical studies and contemporary studies in adverse environments. Many historical studies, often based on church records, are from monogamous Christian farming populations. It is possible that in these populations grandmothers have a larger influence, because there is only one mother to take care of all the children and household tasks, who would greatly benefit from an assisting grandmother. This environment does not reflect our recent evolutionary past since both y-chromosomal and anthropological studies indicate that we lived in polygynous, extended families. Also, in historical populations, there is often no accurate measurement of socioeconomic status. This is essential, since richer households would have both better reproductive success and better survival of elderly persons, suggesting that the presence of long lived elders is responsible for the enhanced reproductive success. Also, we suggest that dependent on the environment, not only grandmothers but also other kin-members contribute to offspring survival.

Addition to previous research

We were able to study post-reproductive survival in an environment that resembles our evolutionary past more than studies in modern monogamous environments[1,2]. This is important when post-reproductive survival is an adaptive trait, the selective advantages can only be studied in an environment that resembles the environment where post-reproductive survival has evolved. We were also able to measure different environmental determinants, that would otherwise confound our results, most notably drinking source and socioeconomic status This was often not possible in previous studies which were mostly conducted in historical, Christian farming communities[3]. In this population we could therefore for the first time study both the direct selective advantage of old age survival in males through continued reproduction with younger females and the indirect effect of older women and men in the extended families of the research area.

In this study, we were able to confirm that post-reproductive survival in females indeed has a selective advantage. However, in this population, the advantage was not through increased survival of offspring as found by others, but through increased reproduction of their household. Also, we found that grandfathers, through continued reproduction up to high age created a large selective pressure for old age survival. This direct effect was much larger than the indirect effect of post-reproductive survival in women which points to a more important role of men in the evolution of longevity than previously thought. This also translates to a selection for post-reproductive survival in women since both sons and daughters of long-lived men inherited the genes that made possible their longevity.

Limitations

During our studies we noticed that the population was undergoing the demographic transition[4]. Observed mortality levels were lower than expected from the population distribution. This low mortality resulted in lower power to pick up determinants of child mortality. The demographic transition could also change the role different kin members have in offspring survival. Since the area was only at the start of the demographic transition we think the cultural patterns might not have changed dramatically, child mortality was over 5% and our analyses did show large effects on child mortality of both socioeconomic status, drinking source and the presence of the mother. Our large data set and long prospective follow-up allowed us to pick up these effects with considerable certainty and therefore the demographic transition did not inflate the outcomes of our study.

Our annual follow-up could have resulted in an underestimation of child mortality since we did not register children that were born and died between two field visits. Although this limited the power of the study, it did not create bias, since we have no reason to believe that the children that we did not register were a selected group.

Since there was no civil register in the research area, not all people were aware of their age. Also, since old age is highly regarded, participants could have been inclined to overestimate their age. If age was unknown, we estimated the age, as the average of several individual observations of both local and Dutch fieldworkers.

Although this study provided further insights in the evolution of our longevity, residual questions remain. The existence of menopause per se can not be explained from the effect of older men. It is possible that the age difference of co-wives within the polygamous household could play a role in this, but other socio-cultural factors could also play a role. If men preferably have children with their younger wives, there could never be a selective advantage to counteract wear and tear of the reproductive system, resulting in menopause. Although we have no formal anthropological observations, we have noticed that it is custom in the research area that men have less sexual intercourse with their older wives compared to their younger wives.

Another limitation to this study is that we have no data on the activities of elderly men and women which could give an indication of the mechanisms through which e.g. grandmothers increase the reproduction of the household. Previous research in the Hadza has shown that grandmothers make a large contribution to the household food supply[5]. Assistance in childcare however has been repeatedly observed in many different societies in anthropological studies[3]. Further studies of the investment patterns could give further insight in the possible role of different kin members in offspring production, survival and health in this population which would provide further arguments for the selective advantages of post-reproductive survival of both male and females.

This study was conducted in a polygamous society in rural Ghana. Therefore it is questionable to what extend these results could be extrapolated to other times, places and other cultures. In the last part of this discussion, we will discuss some key differences between our study population and others. These differences point out that there is no general pattern for the role that kin members have in child care and as such also invites to continued research of the role of kin members on reproduction and offspring survival in other societies.

Extrapolation of study results

How can the results of this study be extrapolated to other populations? The role of elderly people differs considerably in different societies. In this part, we discuss four major distinctions that could partly determine the role that elderly play in child care. First, we discuss patrilocal versus matrilocal societies, which determines whether maternal or paternal grandmothers live with the (grand)children.

Second, we consider the differences between polygamous and monogamous populations. Third, we discuss the differences between people living in nuclear families and in extended families and finally we consider the shift from pre-transitional societies to post-transitional societies. Here, we also discuss future implications of the results in this study.

Patriarchal versus matriarchal

The rural society in the research area is classic patriarchal, which means it is patrilocal, patrifocal and patrilinear. In patrilocal societies women move into the household of the men. In patrilinear societies inheritance is through the male line and in patrifocal societies the men is the head of the household and has authority over women and children. These differences could also determine which kinmembers are involved in child rearing. The most important consideration here is the patrilocality, since this determines to a large part which kin members assist in child rearing.

In patrilocal societies men continue to live in the house of their elders or in a house very close to this and women move into the household of the man after marriage. The result of this pattern is that in patrilocal societies the grandparents that live with the children are paternal grandparents. In matrilocal societies on the other hand, men move into the household of the women and almost all grandparents will be maternal grandmothers. Different studies have found that maternal grandparents and paternal grandparents have different effects on offspring survival[3]. A study of 19th century Krummhorn in Germany found that paternal grandmothers had a negative impact on child survival while maternal grandmothers had a positive effect on child survival[6].

Different mechanisms have been proposed to explain the different effects of maternal and paternal grandmothers. Since women in general have a larger role in child care than men, it has been proposed that grandmothers could be more inclined to assist their own daughters with child rearing in matrilocal societies than their daughters-in-law in patrilocal societies[7]. This could explain why maternal grandmothers in matrilocal societies would be more inclined to assist in child care than paternal grandmothers in patrilocal societies.

Because of the polygamous nature of the research population, reproduction is almost twice as high in men, as was shown in chapter seven. In this population, paternal grandmothers that live with their son, could therefore exert their influence on twice as many children compared to maternal grandmothers who live with their daughter. From an evolutionary perspective, it could therefore be more beneficial for a grandmother to live with their son, although the dilution of the resources that could be directed to the children should be taken into account. With twice the number of children, a quality quantity trade-off in the attention and resources that could be directed to the individual children could be expected.

Socio-biologists explain the higher tendency of maternal grandmothers to assist in child care with the principle of paternity uncertainty. Mothers are always more certain children are theirs while fathers can never be certain. A grandmother can therefore be certain that the children of her daughter and son-in-law carry her genes while the children of her son and daughter-in-law could be from her son, but she can not be completely certain.The extent and effect of paternity uncertainty has been highly debated. A review found that paternity uncertainty rates differed between 1% and 10% in populations worldwide[8].

It is important to note that in the research population, even when a large percentage of the offspring would be from other men, because of the much larger number of offspring of men, grandmothers could still exert their influence on a larger number of genocopies when they live with their son as paternal grandmothers compared to when they would live with their daughter. Second, in a separate analysis, we have cross-checked the DNA of the newborns with their fathers and found the number of false paternities in the research area to be below 5%.

Polygamous versus monogamous

In polygamous populations older men continue successful reproduction up to high age through the marriage of younger fertile women[9,10]. In monogamous societies, men are not able to continue reproduction when their wife is post-menopausal. Since in general men and women are of similar age, monogamy in practice also makes men post-reproductive around age 50.

Since, in polygamous societies, men that live to 80 have more offspring compared to men that live to 50 and this continued reproduction of elderly men results in a selection on longevity. Longevity has a known genetic component and since both sons and daughters inherit the genes that allowed the men to live long, this selection for longevity in men also results in long lived women. In monogamous populations this selective pressure is no longer present and as a result there is less selection on longevity in monogamous populations. Some older men continue reproduction in monogamous societies also, through the (re)marriage of younger women. However, the percentage of children born to men older than 50 years in the Netherlands in 2006 was only 1.0%, compared to 18.4% in the polygamous society in Ghana[11].

Nuclear versus extended family

In nuclear families, a man and woman live together with their children and, up to recent times, grandparents often co-resided or lived close to these families. In this situation, an extra pair of experienced hands from a grandmother or grandfather to assist in child care could be most welcome. The grandparents could be expected to plat a large role in child care in societies where people live in nuclear families. Previous research in Finland, Canada and other societies with nuclear families has shown that the presence of post-reproductive women here allows their children to reproduce earlier, more frequent and more successful[3,12].

In societies where people live in extended families, larger kin groups live together and in these households many different kin members, can assist in child care. It has been found that other kin members, older siblings, co-wives, aunts, also assist in child care in different populations[3]. In extended families the role of the grandparent is more easily substituted by other kin members when compared to nuclear families where they are the only other adults around are the grandparents. Whether people live in nuclear or extended families will therefore be of great importance to who will assist in child care.

Pre-transitional versus post-transitional

To understand how evolution shaped human life histories and our long post-reproductive life span in particular, it is essential to study this in the environment where this long reproductive life span evolved. Only in this environment, with these population structures, it is possible to measure the selective advantage that

shaped our life history. Our life histories evolved in societies that were pre-transitional; societies that had not experienced the demographic transition and where reproduction and mortality were both high and death was largely due to infectious diseases

There are two reasons why the findings in pre-transitional societies are of interest to contemporary societies. First, life history traits that have evolved in the past still exert a large influence on many aspects of life. Even though the contemporary post-transitional societies look remarkably different from pre-transitional societies, gestation still takes nine months, litter size is in general limited to a single child and the fertile period for women is still from around 18 to 49 years. These life history traits, that evolved long ago are therefore still of key importance today. There is however, a second reason to compare our findings in the light of contemporary societies. Contemporary societies are not the end product of evolution, selection still takes place and has seen a large shift as to which (genetic) traits are selected in today's post-transitional societies. The traits that are selected for today will influence subsequent generations. Considering how these selective pressures have changed and what traits are selected for today is important if we want to consider what the results of this study could learn us about the future of our life histories.

In the transition from pre-transitional to post-transitional societies, first mortality reduced dramatically, largely due to a control of infectious diseases by preventive measures. Second, reproduction declined. Increased child survival reduced the need to give birth to many offspring and many other cultural factors reduced the number of desired children which was also made increasingly controllable through contraceptive methods.

Contraceptive methods made possible the restriction of the number of offspring, while fertility assisting techniques made possible the reproduction of less fertile couples. The result is that in contemporary post-transitional societies there is less variation in the number of offspring. Most couples will have two children and there is only limited variation in the number of offspring. Low fertile couples can have children with the aid of fertility assisting techniques and high fertile couples can limit the number of offspring through contraception. This is remarkably different from the situation in pre-transitional societies where a small group of

highly fertile women produced a large proportion of the next generation. More fertile people had more offspring in the past and the result was a high selection on fertility in pre-transitional societies that is no longer present in post-transitional societies. This selection could partly explain the increasing number of couples experiencing fertility problems, which is often only attributed to the higher age at which couples start reproducing.

Contraception made possible, not only the restriction of the number of offspring, but also the timing of reproduction. As a consequence women have children much later in post-transitional societies compared to pre-transitional societies. In the Netherlands, the mean age a mother delivers her first child was 29.4 years in 2009[13]. Since reproduction becomes increasingly difficult with advancing age, some women that postpone their reproduction, will not have the desired number of offspring. The result is that the next generations will become enriched with individuals capable of reproducing at higher ages since there is selection of those individuals that have the (genetic) capability of reproduction at higher ages, while those that were unable do not contribute genes to the gene pool of the next generation. This is partly counteracted by fertility assisting techniques, but this is only partly able to counteract this effect as many couples are still left without children or without the desired number of children. The result of this is that there is selection for late fertility, through which future generations could easier have children at later ages.

In many post-transitional societies women are engaged in professional work and the raising of children is shared with either professional child care or other family members. Grandparents in particular are increasingly involved in child care now that more women have entered the labor market. In the Netherlands it was found that child care support from grandparents increases the probability that the parents have additional children[14]. This strikingly mimics the findings in the Ghanaian population described in this study. This finding that in a post-transitional society, grandparents could also increase the reproductive success is interesting from two perspectives.

First, it could indicate that ancient, evolved behavioral patterns are still influencing the way we raise children today. Many physiological but also behavioral traits can still be related to traits that have evolved in history of our evolution. In this light

many research has focused on differences in male and female behavior and physiology that can be understood by the different roles they had in our evolutionary past. Everybody is aware that grandmothers spoil their grand children the world over. Few might however realize that –next to the fact that their grandmother is probably the nicest grandmother on earth- grandmothers could actually display this behavior because it has been selected for in the past. Grandmothers that felt spoiling grandchildren was something desirable, had more surviving grandchildren than those who did not and this grand offspring carried the 'spoil-your-grandchildren-gene' with them. Economical reasons might also partly underlie the common observation that grandmothers enhance the reproductive success of their families. By taking care of the children, grandmothers alleviate the mothers and allow them to take up other (paid) labor. The enhanced family income could also make it possible for the family to have more children.

Second, the finding that also in contemporary post-transitional societies grandmothers can increase the reproductive success has important implications for the future of our life histories. If grandparents that assist in child care have more grandchildren than those that do not assist in child care or are not able to assist, there is selection for those individuals that both live long and are stay healthy enough to assist in child care. Both these factors are partly genetically determined and will be enriched in the gene pool of the next generation. In the future, more and more people will therefore live longer lives and longer healthy lives, and in this way a spiral could start. Longer healthy lives would again make possible prolonged assistance in child care. If this would lead to more offspring, the next generation would again have more individuals with healthy long lives that can assist in child care, and this reasoning can go on for generation after generation *ad infinitum*.

The conclusion is that as long as people are both healthy and active, there will be selection for long healthy lives. The prerequisite is that elderly people continue to invest in their (grand)children.

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Nederlandse samenvatting

Post-reproductieve levensduur in een polygame samenleving in Afrika

Introductie

Met een levensverwachting van bijna 80 jaar behoren mensen tot de langst levende zoogdieren. Vanuit evolutionair perspectief is dit een vraagstuk, te meer omdat mensen na hun 50e nog maar zelden nakomelingen verwekken. In dit proefschrift onderzoeken we deze lange post-reproductieve levensduur.

Lange tijd is gedacht dat onze lange post-reproductieve levensduur een bijverschijnsel is van de recent toegenomen levensverwachting in een verbeterde leefomgeving. Dit is onjuist: de lage levensverwachting in vroeger tijden werd voornamelijk veroorzaakt door een hoge kindersterfte. Een groot deel van de mensen die de eerste jaren overleefden, maakte ook een post-reproductieve levensfase door. Waarnemingen in huidige jager-verzamelaar samenlevingen bevestigen dat: ook hier kennen een aanzienlijk aantal mensen een post-reproductieve levensfase[1]. De laatste decennia zijn er een aantal adaptieve theorien over onze post-reproductieve levensduur naar voren gebracht, die stellen dat de lange post-reproductieve levensduur een selectievoordeel met zich meebracht en zodoende het resultaat is van selectie.

Een eerste adaptieve theorie was de moeder-hypothese, die veronderstelde dat de post-reproductieve levensduur een voordeel bood omdat moeders zo langer voor hun nakomelingen konden zorgen. Vrouwen met een post-reproductieve levensduur zouden dan een groter reproductief succes hebben dan vrouwen zonder een post-reproductieve levensduur. Later werd deze theorie uitgebreid tot de grootmoeder-hypothese. Vrouwen met een post-reproductieve levensduur zouden niet alleen beter voor hun jonge kinderen kunnen zorgen, maar ook hun oudere kinderen kunnen helpen bij de zorg voor de kleinkinderen. Eerder onderzoek heeft aanwijzingen gevonden dat de aanwezigheid van post-reproductieve vrouwen hun kinderen in staat stelde eerder, vaker en succesvoller te reproduceren[2]. Deze studies zijn echter sterk contextafhankelijk en zijn bijna allemaal gebaseerd op waarnemingen in historische monogame populaties[3].

De beschikbare studies naar de (groot)moederhypothese hebben drie grote bezwaren. Ten eerste zijn de meeste studies gebaseerd op kerkregisters, afkomstig van monogame christelijke landbouwgemeenschappen. Veel van de boerenfamilies

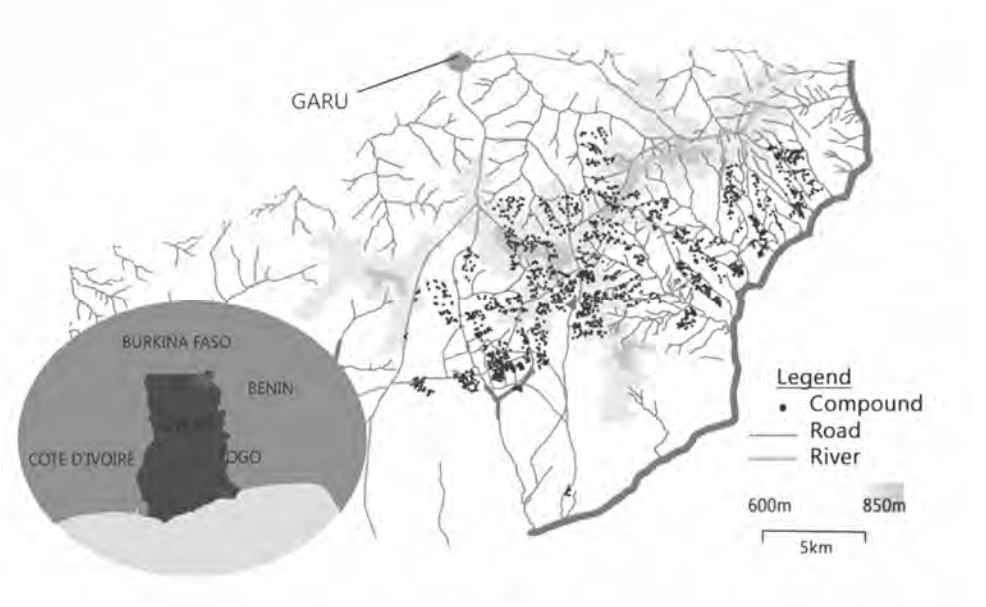
in deze gemeenschappen bestaan uit een kerngezin van drie generaties. Hierin zijn de kinderen afhankelijk van vader, moeder en grootouders. Deze situatie weerspiegelt waarschijnlijk niet de situatie waarin onze langlevendheid geëvolueerd is. Uit genetische en antropologische studies is bekend dat de mens gedurende een groot deel van zijn recente evolutionaire verleden in polygame samenlevingen woonde in grotere *extended families*. Eventuele selectievoordelen van post-reproductieve overleving zouden moeten worden onderzocht in de omgeving waarin deze post-reproductieve levensduur is geëvolueerd: een polygame samenleving met *extended families*. Een tweede bezwaar van de beschikbare studies is dat bijna alle studies alleen de bijdrage van post-reproductieve vrouwen bestuderen terwijl er recente onderzoeken zijn die suggereren dat mannen boven de vijftig een belangrijkere rol hebben gespeeld bij de evolutie van onze post-reproductieve levensduur. In polygame samenlevingen zijn mannen in staat tot op hoge leeftijd te reproduceren door te trouwen met jonge vruchtbare vrouwen. Dit effect van oudere mannen kan niet worden bestudeerd in de historische, monogame populaties. In de derde plaats is er in veel studies, in het bijzonder de historische, geen nauwkeurige meting van de sociaal-economische status. Dit is essentieel, omdat rijkere huishoudens zowel een beter reproductief succes kennen als een betere overleving van ouderen. Dit kan de valse suggestie wekken dat de aanwezigheid van ouderen zelf verantwoordelijk is voor het reproductief succes. Het is dus mogelijk dat sommige van de eerder gevonden effecten van de post-reproductieve vrouwen op latere generaties vertekend zijn door samenlevingsspecifieke kenmerken of de sociaal-economische status.

Doel van dit proefschrift

In dit proefschrift onderzoeken we het selectievoordeel van post-reproductieve overleving. Wij bestudeerden hiervoor gedurende acht jaar een polygame samenleving in het noorden van Ghana en onderzochten de hypothese dat de aanwezigheid van zowel mannen als vrouwen na de leeftijd van vijftig jaar effect had op de reproductie in hun huishouden en de overleving van de kinderen. We gebruikten hiervoor een familie-analyse en waren in staat om te corrigeren voor vertekenende variabelen als sociaal-economische status, drinkwater en stamverbanden.

De studie in Ghana

Alle studies beschreven in dit proefschrift werden uitgevoerd in het Garu-Tempane district, gelegen in de Upper East Region van Ghana. Het gebied heeft een Sahel-klimaat met een gemiddelde maximumtemperatuur van 32 ^{o}C gedurende het jaar en een regenseizoen van juni tot augustus. Het onderzoeksgebied meet ongeveer 375 km^2 met 28.994 deelnemers woonachtig in 40 dorpen. Figuur 1 is een kaart van het onderzoeksgebied, verkegen met behulp van GPS-waarnemingen geprojecteerd over bestaande hydrografische, hoogte- en wegenkaarten van het Centre for Remote Sensing en GIS (CERSGIS) van de Legon Universiteit in Accra, Ghana.



Figuur 1. Kaart van het onderzoeksgebied.in het Garu-Tempane district in the Upper East Region van Ghana. Kaart van dr. L. May

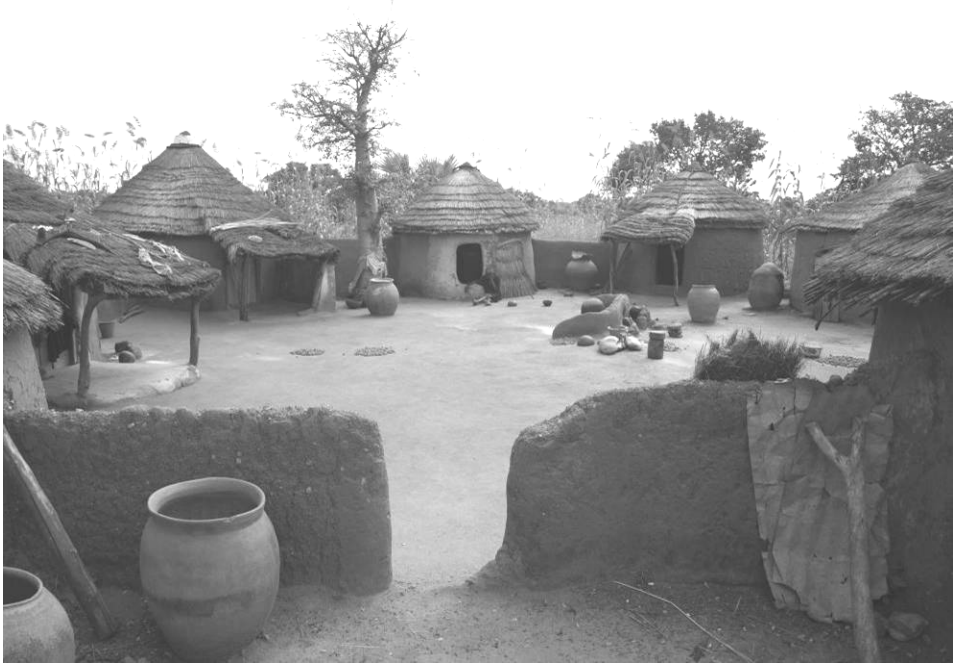
De deelnemers aan het onderzoeksgebied leven in grote *extended families* met gemiddeld twaalf personen per huishouden. De samenleving is patrilocaal, patrifocaal, patrilineair en polygaam. Het hoofd van de familie, de *landlord,* is getrouwd met ten hoogste vier vrouwen. Ongeveer de helft van de *landlords* heeft meer dan één vrouw. De gezinnen wonen samen in *compounds,* kringen van lemen hutjes met rieten daken die een binnenplaats omsluiten. Er zijn in totaal ruim 1700 *compounds* in het onderzoeksgebied. Een voorbeeld van een compound is te zien in figuur 2.

De mensen behoren tot verschillende stammen: Bimoba (65%), Kusasi (25%) en een aantal kleinere stammen zoals Mamprusi en Busanga. Een groep nomadische Fulani woont ook in het gebied. De overgrote meerderheid van de mensen zijn zelfvoorzienende landbouwers. De migratie is laag en bedraagt minder dan 1% per jaar, wel is er tijdelijke migratie van jonge mannen naar de grotere steden in Ghana om te werken in seizoensgebonden beroepen. Analfabetisme is wijdverbreid, bij volwassenen bijna compleet en bij kinderen is het nog steeds zeer hoog (>50%). In het onderzoeksgebied is geen formele schatting van het inkomen per hoofd uitgevoerd, maar het gebied als geheel is veel minder ontwikkeld dan de rest van Ghana. Het inkomen per hoofd van de bevolking in de Upper East Region is 304 US$per jaar[6].

De meeste mensen in het onderzoeksgebied zijn aangewezen op traditionele medische zorg. Er is geen arts werkzaam in het onderzoeksgebied en het dichtstbijzijnde ziekenhuis ligt op 40 kilometer afstand. Vaccinatie van kinderen werd in de vroege jaren '90 van de vorige eeuw ingevoerd. Geboortebeperking is slechts zeer beperkt aanwezig, de meeste vrouwen prefereren een groot aantal kinderen, omdat grote gezinnen in hoog aanzien staan. In de afgelopen decennia is schoon drinkwater uit *boreholes* geleidelijk ingevoerd in het gebied.

Overzicht van dit proefschrift

Hoofdstuk één is een algemene inleiding op het proefschrift. **Hoofdstuk twee** bevat een theoretische inleiding, waarin de beginselen van de *life history theory* uiteengezet worden. Volgens de *life history theory* zijn verschillende fysiologische en gedragskenmerken van de overleving en de voortplanting van een organisme met elkaar verbonden. Wijzigingen in een van deze kenmerken beïnvloedt de andere kenmerken en alleen bepaalde combinaties leiden tot een succesvolle evolutionaire strategie met een hoge fitness. Kortlevende en langlevende organismen hebben daardoor zeer uiteenlopende levenslopen. Langlevende dieren zijn over het algemeen groter, reproduceren pas op latere leeftijd, hebben een kleiner aantal nakomelingen per worp, een langere zoogtijd en langere intervallen tussen de geboortes.



Figuur 2. Voorbeeld van een *compound*. In deze kring van lemen hutten met daken van stro woont de *landlord* met zijn vrouwen en zijn *extended family*. In deze patrilocale, polygame samenleving heeft de helft van de *landlords* meer dan één vrouw.

Post-reproductieve levensduur wordt verondersteld om een selectievoordeel te bieden door middel van investeringen in het nageslacht die invloed hebben op verschillende kenmerken van de *life history theory* zoals geboorte-interval, totale vruchtbaarheid, groei en de overleving van nakomelingen. *Life history theory* is daarom belangrijk om onze levensverwachting op een evolutionaire manier te bestuderen en het selectievoordeel van onze post-reproductieve levensduur te bestuderen.

Hoofdstuk drie geeft een gedetailleerde beschrijving van het onderzoeksgebied en de Bimoba, de voornaamste stam in het gebied, in het bijzonder. Het beschrijft de geografische, sociale en antropologische achtergrond van het gebied en de deelnemers. Om te komen tot een begrip en interpretatie van de bevindingen van de studies beschreven in dit proefschrift is deze achtergrond van essentieel belang.

Hoofdstuk vier beschrijft de sociaal-economische studies die we in het onderzoeksgebied ondernomen hebben. De sociaal-economische status is een belangrijke determinant van de overleving van kinderen. Het is echter ook een belangrijke determinant van de overleving op hoge leeftijd. Hierdoor zou de sociaal-economische status de relatie tussen post-reproductieve levensduur en de overleving van kinderen kunnen vertekenen. In rijkere huishoudens hebben niet alleen kinderen een betere overlevingskans, maar ook post-reproductieve familieleden. Dat zou ten onrechte de indruk kunnen wekken dat de aanwezigheid van post-reproductieve familieleden de overleving van kinderen verbetert.

Traditioneel wordt sociaal-economische status gemeten als een samengestelde maat van opleidingsniveau, beroepsstatus, inkomen en spaartegoeden. In het onderzoeksgebied zijn alle deelnemers echter landbouwers, is het inkomen afhankelijk van de oogst waardoor het zowel per seizoen als per jaar verschilt, en zijn spaartegoeden zeldzaam. We moesten dus een andere methode ontwikkelen om de sociaal-economische status in het onderzoeksgebied in kaart te brengen.

Tijdens een eerste bezoek lijken alle deelnemers in het onderzoeksgebied arm. Bij nadere beschouwing zijn er echter grote verschillen in sociaal-economische status, groter zelfs dan in veel westerse landen. Op basis van antropologische methoden hebben we een nieuwe methode om de sociaal-economische status te meten ontwikkeld: een *rapid appraisal* methode, bestaande uit een zelf-ervaren rijkdomsstatus en een door de interviewer ervaren rijkdomsstatus. Bij deze methode vroegen wij de deelnemers of ze zich in vergelijking met de mensen die om hen heen woonden gemiddeld, bovengemiddeld of ondergemiddeld rijk vonden. We vergeleken deze methoden met een meer traditionele maat van sociaal-economische status, de *DHS (Demographic and Health Survey) wealth* index. Alle drie methoden bleken een sterke voorspeller van de sterfterisico's; mensen uit arme gezinnen hadden een veel hogere sterftekans. Een belangrijke bevinding was dat het met de *rapid appraisal* methode, waarbij maar één vraag hoeft te worden gesteld, hetzelfde werd bereikt als met de veel uitgebreidere vragenlijst. Deze bevinding kan grote implicaties hebben omdat zo op eenvoudige wijze een risicostratificatie kan worden gemaakt voor zowel gezondheidsinterventies als populatiestudies.

In **hoofdstuk vijf** testen we de voorspelling van de *Life history theory* dat er in het lichaam een balans bestaat tussen investeringen in herstel en investeringen in vruchtbaarheid. Bij veel zoogdieren is deze relatie al vaker gevonden, maar bij mensen was nog onduidelijk of een dergelijke balans ook bestond. We bestuderen de relatie tussen de overleving van kinderen, als gevolg van de investeringen in herstel, en het aantal broers en zussen, als afschatter van de investeringen in vruchtbaarheid. Wij maakten gebruik van de aanname van de *life history theory* dat deze investeringspatronen erfelijk zijn. Door het vergelijken van vrouwen in polygame huwelijken waren we in staat om maximaal te controleren voor verschillen in (micro)sociaal-economische status. Wij hebben vastgesteld dat het aantal nakomelingen een belangrijke determinant is van de overleving van nakomelingen. Hoe meer kinderen er in huishoudens waren, hoe lager de percentuele overleving in die huishoudens was. Omdat dit verband ook tussen vrouwen in hetzelfde huishouden bestond, kon dat niet alleen worden verklaard door een verdeling van de beschikbare voorzieningen over de kinderen. Dit maakt aannemelijk dat er inderdaad ook biologische mechanismen aan ten grondslag liggen, zoals voorspeld door de *life history theory* en zoals eerder aangetoond bij verschillende diersoorten.

Op zoek naar het mechanisme waardoor post-reproductieve familieleden de overleving van kinderen zouden kunnen beïnvloeden hebben we de vroege groeipatronen van de kinderen in kaart gebracht in **hoofdstuk zes.** De gewichten van de kinderen zijn echter niet alleen bepaald door omgevingsfactoren maar ook door genetische factoren. In hoofdstuk zes hebben we het CFTR-gen bestudeerd, dat in gemuteerde vorm taaislijmziekte veroorzaakt, de meest voorkomende recessief erfelijke ziekte. Er wordt verondersteld dat in ons recente evolutionaire verleden heterozygote dragers van CFTR-mutaties een overlevingsvoordeel hadden. We hebben genetische varianten van het CFTR-gen geïdentificeerd die verantwoordelijk zijn voor zowel lengte als gewicht van de kinderen.

Nadat we in voorgaande hoofdstukken alle afzonderlijke determinanten van kindersterfte in kaart hebben gebracht bespreken we in **hoofdstuk zeven** onze afsluitende analyse. Hier bestuderen we het effect van verschillende familieleden op het aantal nakomelingen en de overleving van de kinderen in een familieanalyse, gecorrigeerd voor de sociaal-economische status, stam en omgevingsdeterminanten. We identificeren hier voor het eerst in een prospectieve

studie de selectievoordelen van overleving na het 50e jaar bij zowel mannen als vrouwen. Post-reproductieve vrouwen hadden geen invloed op de overleving van de kleinkinderen, maar in huishoudens met een post-reproductieve vrouw werden wel 2,3% meer kinderen geboren. Mannen ouder dan 50 jaar hadden eveneens geen invloed op de overleving van kinderen, maar in deze polygame samenleving verwekten zij nog 18,4% van hun nakomelingen na hun 50e levensjaar.
Evolutionair gezien biedt dit een selectievoordeel voor een levensduur langer dan 50 jaar, de leeftijd waarop bij vrouwen de post-reproductieve periode begint. Deze twee selectievoordelen, in een populatie die een afspiegeling zou kunnen zijn van ons recente evolutionaire verleden, zouden verantwoordelijk kunnen zijn voor de evolutie van onze post-reproductieve levensduur. Deze bevindingen suggereren dat onze lange levensduur primair is geëvolueerd door het selectievoordeel van mannen die op hoge leeftijd reproduceren, en in veel mindere mate door het selectievoordeel van het effect van post-reproductieve vrouwen op (klein)kinderen.

In **hoofdstuk acht** bespreken we het effect van de sociaal-economische status op de reproductie van mannen en vrouwen en de overleving van mannelijke en vrouwelijke nakomelingen.
In deze polygame samenleving moeten mannen een bruidsprijs van vier koeien betalen om te trouwen. Hierdoor kunnen rijke mannen zich meer vrouwen veroorloven en zo ook meer nageslacht verwekken. Voor vrouwen heeft de sociaal-economische status veel minder invloed op het aantal nakomelingen dat zij krijgen. Hierdoor hebben mannen in rijke huishoudens ruim twee keer zoveel nakomelingen als vrouwen in rijke huishoudens. In arme huishoudens is dat verschil veel kleiner. Evolutionair gezien zouden rijke huishoudens dus meer profiteren van zonen, omdat zij waarschijnlijk meer nageslacht zullen verwekken dan dochters. In overeenkomst hiermee vonden wij inderdaad dat mannenlijk nageslacht beter af was in rijke huishoudens. Niet alleen hadden zij hier een veel betere overleving, ook hadden ze hogere gewichten gedurende de eerste drie jaar. Deze observaties zouden verklaard kunnen worden door de kwetsbaarheid van mannen voor slechte omstandigheden. Ze zijn echter ook in overeenkomst met verschillen in investeringen van de ouders, zoals voorspeld door Trivers en Willard. Onafhankelijk van het achterliggende mechanisme, leiden de hier gevonden verschillen in overleving echter in elk geval tot een maximalisatie van het reproductief succes van het huishouden in deze polygame samenleving.

Hoofdstuk negen is een discussie over de grootmoederhypothese en de implicaties daarvan voor de studie van veroudering. De grootmoeder hypothese stelt dat de post-reproductieve levensfase is geëvolueerd omdat vrouwen het reproductieve succes van hun kinderen verhogen. In dit hoofdstuk geven we commentaar op eerdere studies en bespreken het belang van antropologische en omgevingsfactoren in de studie van het 'grootmoedereffect'. We geven ook commentaar op historische studies naar de grootmoederhypothese en studies bij hedendaagse populaties in een moderne omgeving. We zetten bovendien vraagtekens bij de extrapolatie van bevindingen naar andere samenlevingen en andere tijden.

In **hoofdstuk tien** vatten we de voornaamste conclusies samen en bespreken we de implicaties van het onderzoek beschreven in dit proefschrift.

Conclusie

In dit proefschrift hebben we het selectievoordeel van een post-reproductieve levensduur onderzocht in een polygame samenleving in Ghana. Wij hebben het effect bestudeerd van de aanwezigheid van mannen en vrouwen boven de vijftig in het huishouden op het aantal nakomelingen en de overleving van de nakomelingen.

De aanwezigheid van een vrouw boven de vijftig vermeerderde het aantal nakomelingen met 2,3% maar had geen invloed op de overleving van die nakomelingen. De aanwezigheid van een man boven de vijftig was evenmin van invloed op de overleving van de kinderen. In deze polygame samenleving konden mannen echter tot op hoge leeftijd kinderen verwekken en 18,4% van de kinderen werd verwekt door mannen ouder dan 50 jaar. Dit betekent dat mannen die tot 80 oud worden gemiddeld meer nakomelingen hebben dan mannen die tot 50 jaar oud worden. Er is dus een belangrijk selectievoordeel voor langlevendheid bij mannen.

Dit werpt een heel nieuw licht op de oorspong van onze lange (post-reproductieve) levensduur. Hoewel vaak gedacht is dat post-reproductieve levensduur vooral een voordeel bood bij vrouwen, vinden wij aanwijzingen dat het selectievoordeel van de reproductie tot op hoge leeftijd van mannen na hun 50^{e} groter is dan het selectievoordeel van post-reproductieve levensduur bij vrouwen. Het grote

selectievoordeel van langlevendheid bij mannen kan enkel worden gerealiseerd in samenlevingen waar mannen nog kinderen kunnen verwekken bij hun veel jongere echtgenoten. Dit is vaak het geval in polygame samenlevingen. De selectiedruk van oude mannen die kinderen verwekken in polygame samenlevingen kan alleen maar een rol gespeeld hebben in de evolutie van onze langlevendheid als mensen gedurende hun recente evolutionaire verleden in polygame samenlevingen woonden. Een eerste indicatie hiervoor komt uit antropologische inventarisaties, die laten zien dat de meerderheid van de samenlevingen die wij kennen inderdaad polygaam is[7]. Deze samenlevingen bestaan echter uit veel minder individuen dan de monogame samenlevingen die nu weidverspreid zijn, maar dit is het resultaat van relatief recente expansie. Naast deze antropologische observaties laat ook genetisch onderzoek zien dat wij in ons recente evolutionaire verleden in polygame samenlevingen woonden. Mannen krijgen het Y-chromosoom van hun vader, maar hun mitochondriaal DNA van hun moeder. Rekening houdend met verschillen in structuur en mutatiesnelheid, is de huidige variatie in het mitochondriaal DNA veel groter dan in het Y-chromosoom[8]. Dit geeft aan dat de huidige populatie mannen afkomstig is van een veel kleiner aantal vaders dan moeders en dat wij gedurende een groot deel van ons recente evolutioniare verleden voornamelijk in polygame samenlevingen woonden. Aangezien onze langlevendheid gedurende deze tijd is geëvolueerd zijn de bevindingen in deze studie een sterke indicatie dat wij onze langlevendheid meer te danken hebben aan de reproductie op hoge leeftijd van onze voorvaders dan van voordelen van de post-reproductieve levensduur van onze voormoeders.

Dit roept echter direct een andere vraag op. Als de lange post-reproductieve levensduur te danken is aan een selectievoordeel in mannen, waarom leven vrouwen nu dan zelfs langer dan mannen? De verschillen in levensduur tussen mannen en vrouwen waren vroeger anders dan nu, aangezien veel meer vrouwen in het kraambed stierven dan tegenwoordig. Aan de huidige verschillen in levensduur kunnen heel verschillende mechanismen ten grondslag liggen; biologische die verband houden met zwangerschap en bevalling evenals meer recente culturele en maatschappelijke verschillen.

De bevindingen zetten ook aan tot nadenken over de toekomst van onze levensverwachting. In de meeste westerse samenlevingen verwekken mannen na hun vijftigste weinig nakomelingen meer. Grootouders spelen echter wel in

toenemende mate een rol in de zorg voor kleinkinderen. Een studie in Amsterdam concludeerde bij voorbeeld dat ouders met een opa of oma die oppast eerder kinderen krijgen[9].

Mensen leven tegenwoordig langer en ook langer in goede gezondheid. Hierdoor is het mogelijk dat zij ook tot op hogere leeftijd actief blijven en een deel van de zorg van de kleinkinderen van de ouders overnemen. Als grootouders die voor de kleinkinderen zorgen meer kleinkinderen krijgen dan zij die dat niet doen is er dus selectie voor die individuen die zowel lang leven als gezond genoeg blijven om voor de kinderen te zorgen. Aangezien beide kenmerken deels genetisch bepaald zijn zullen zij dus in de genenpool van de volgende generatie verrijken. In de toekomst zullen daardoor meer en meer mensen langer en gezonder leven.

Bovenstaande selectie zal blijven bestaan zolang mensen tot op hoge leeftijd gezond en maatschappelijk actief blijven. Hiervoor zijn twee dingen noodzakelijk. In de eerste plaats moeten ouderen zelf actief blijven en in de tweede plaats moet de maatschappij ze ook die plek gunnen. *Ageism,* leeftijdsdiscriminatie, is echter uitgebreid gedocumenteerd: Ouderen worden uit de arbeidsmarkt verstoten en de mogelijkheid om zich te ontplooien wordt hun ontzegd.

Vanuit een *life history* perspectief zijn er conflicterende belangen voor jongere en oudere individuen. Uiteindelijk maakt iedereen echter beide levensfasen door en het is daarom in het belang van iedereen dat we een maatschappij ontwikkelen waarin mensen in alle levensfasen een zinvol en plezierig leven kunnen leiden.

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* These authors contributed equally to this study

Curriculum vitae

Curriculum vitae

David van Bodegom was born on the 30th of January 1978 in Zuidhorn, the Netherlands. From 1990 to 1996 he attended the Rotterdam Montessori Lyceum and completed his VWO studies. At age eighteen, he moved to Leiden, where he studied Ancient history and in 2000 graduated (cum laude) on a study on Greek sacrifices. After this, he started his medical training, which resulted in his master degree in 2004 (cum laude) and his medical degree in 2007. From 2004 onwards he became involved in the Ghana research project of the department of Gerontology & Geriatrics of the Leiden University Medical Centre. First as a student and later as a Phd student, he travelled extensively between the Netherlands and the research area in Ghana. Since 2009, he is a member of the scientific staff of the Leyden Academy on Vitality and Ageing, which aims to improve the quality of life of older people. Here, his main responsibilities include the research programme of the academy and the international post-graduate master Vitality and Ageing, which trains medical doctors to become pioneers in the field of ageing. Since 2010, he is appointed assistant professor of medicine at the Leiden University Medical Centre.

Since 2007 David volunteers as a medical doctor at the *Kruispost* in Amsterdam, a health clinic where he provides basic medical care to people who can not find help elsewhere. In his spare time he enjoys writing columns and fiction.