

## LETTER

# Severe intergenerational reproductive conflict and the evolution of menopause

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### Abstract

Human menopause is ubiquitous among women and is uninfluenced by modernity. In addition, it remains an evolutionary puzzle: studies have largely failed to account for diminishing selection on reproduction beyond 50 years. Using a 200-year dataset on pre-industrial Finns, we show that an important component is between-generation reproductive conflict among unrelated women. Simultaneous reproduction by successive generations of in-laws was associated with declines in offspring survivorship of up to 66%. An inclusive fitness model revealed that incorporation of the fitness consequences of simultaneous intergenerational reproduction between in-laws, with those of grandmothing and risks of dying in childbirth, were sufficient to generate selection against continued reproduction beyond 51 years. Decomposition of model estimates suggested that the former two were most influential in generating selection against continued reproduction. We propose that menopause evolved, in part, because of age-specific increases in opportunities for intergenerational cooperation and reproductive competition under ecological scarcity.

### Keywords

Cooperation, ecological constraints, grandmother hypothesis, inclusive fitness, kin selection, mother hypothesis, reproductive conflict hypothesis, reproductive skew, restraint, suppression.

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## INTRODUCTION

Hunter-gatherers live in extended family-groups wherein reproduction is monopolised by a minority of group members and non-breeders contribute to rearing the offspring of breeders (Hrady 2009). In combination, such features are unusual in the animal kingdom, but are common to all cooperative breeding societies (Wilson 1971; Emlen 1995; Russell 2004). Yet, among cooperative breeders, humans are atypical because a significant proportion of non-breeding helpers comprise post-menopausal women. While it remains unclear whether menopause arose following the evolution of prolonged lifespan or before, a key question is why there is a dramatic mismatch between age-specific survival and fertility in women. The Mother (Williams 1957) and Grandmother (Hawkes *et al.* 1998) Hypotheses suggest that the answer lies in the direct costs of late-life reproduction or in the indirect benefits of increasing the reproductive success of existing offspring, respectively. Calculations have suggested that menopause could evolve if almost certain maternal death ensued from childbirth late in life (Pavard *et al.* 2008), particularly in conjunction with beneficial grandmother effects (Shanley *et al.* 2007). However, such extreme risks of childbirth seem improbable, given that the probability of dying seldom exceeds 3% before menopause in populations lacking modern medicine (Cant *et al.* 2009; Lahdenperä *et al.* 2011a). Consequently, although inclusive fitness theory (Hamilton 1964) has been successful in accounting for the evolution of sterile workers in social insects (Abbot *et al.* 2011) and non-sterile helpers in cooperative

breeding vertebrates (Cornwallis *et al.* 2009), whether it can account for the evolution of human menopause is contentious (Hill & Hurtado 1991; Rogers 1993; Cant *et al.* 2009).

Previous inclusive fitness calculations, however, have ignored inevitable age-specific increases in reproductive overlap between generations of women. Cant & Johnstone (2008) showed using game-theoretic modeling that reproductive conflict between mother and adult offspring could select against late-life reproduction, potentially leading to selection against increasing ages of fertility in line with increases in longevity (hereafter the Reproductive Conflict Hypothesis). Simultaneous reproduction between mothers and daughters was unlikely to generate selection against continued reproduction in the elder generation because mothers and daughters will often be equally related to the offspring of the elder-generation mother ( $R = 0.5$ ), whereas mothers from the elder generation will always be half as related to her daughter's offspring as her own ( $R = 0.25$  vs.  $0.5$ ). By contrast, while mothers-in-laws will be more related to their own offspring than those of their daughter-in-law ( $R = 0.5$  vs.  $\sim 0.25$ ), daughters-in-law will be unrelated to the offspring of mothers-in-law ( $R = 0.5$  to own offspring vs.  $0$  to mother-in-law's offspring). Thus, daughters-in-law will be under greater selection to 'win' any conflict over reproduction between the two parties; potentially selecting against continued reproduction in the elder generation (Cant & Johnstone 2008).

Reproductive conflict between successive female generations is universal in cooperative animal societies; resulting in temporal or

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irreparable sterility in insect and mammal species (Wilson 1971; Russell 2004). In addition, intergenerational reproductive overlap between females is typically low in cooperative breeders, including humans (Cant *et al.* 2009; Mace & Alvergne 2012). Although the beneficial effects of non-breeding (particularly maternal) grandmothers are well documented (Volland *et al.* 2005; Sear & Mace 2008), there is suggestive evidence that grandoffspring nutriment acquisition and survivorship decrease when maternal grandmothers reproduce (Sear *et al.* 2000). Whether mother–daughter or in-law pairings interact depends on the dispersal system. The majority of contemporary human societies show philopatry by both sexes (Alvarez 2004), although where it is biased, it tends to favour sons (Marlowe 2004). In general, therefore, cooperation or conflict could arise between both mother–daughter and in-law reproductive pairings, although interactions among the latter might be expected to be more common. Either way, co-residence is not required for cooperative or conflictual interactions to be realised (Mace & Alvergne 2012); we have shown previously that non-breeding maternal and paternal grandmothers can have similarly beneficial effects on their offspring, provided they live in the same parish (Lahdenperä *et al.* 2004). However, whether co-breeding between successive generations is conflictual, whether any costs contribute to selection against reproduction late in life and the importance of such costs relative to other inclusive fitness components, are largely unknown (Mace & Alvergne 2012).

Using an individual-based multi-generational dataset of pre-industrial Finns, we test: (1) whether intergenerational reproductive conflict exists; (2) whether the consequences of intergenerational reproductive overlap, when added to the direct fitness consequences of late-life reproduction (Mother Hypothesis) and the indirect benefits of grandmothers (Grandmother Hypothesis), are sufficient to account for reduced selection on personal reproduction around 50 years; and (3) the relative importance of the three hypotheses outlined above for selecting against late-life reproduction. In each case, we consider the effects separately under matri- and patri-locality. We first show that simultaneous reproduction by in-laws from successive generations is associated with dramatic reductions in offspring survivorship, although this was not true of mother–offspring pairings. Second, using an inclusive fitness model, we illustrate that reduced offspring survival associated with simultaneous reproduction by in-laws might be integral to selection against reproduction beyond menopause age. Finally, decomposition analyses reveal that such effects, in conjunction with the indirect benefits of grandmothers, primarily account for waning selection on late-life reproduction, whereas the direct costs associated with dying in childbirth had marginal effects. We acknowledge that the conditions experienced by pre-industrial Finns are unlikely to resemble those of our hominin ancestors. Nevertheless, the basic assumption that family-resources are limiting is true of all pre-modern societies (Fogel 1994), and our data offers a rare opportunity to measure the necessary parameters to investigate selection pressures on age-specific reproduction using people living in natural fertility/mortality conditions (Korpelainen 2003).

## MATERIAL AND METHODS

The Lutheran Church has been obliged to submit accurate registers of all births, inter-parish movements, marriages and deaths in Fin-

land since the 17th century. Our data contains survival and reproductive details for three generations from five geographically distinct agrarian communities (Soininen 1974). We collected data from a sample of 653 women born during 1702–1823 who delivered 4703 offspring during 1732–1863 and of which 1736 delivered 9164 grandoffspring during 1757–1908. During the study period, the population was strictly monogamous with divorce outlawed and re-marriage possible only after the death of a spouse. In addition, these time periods pre-dated modern contraceptive and health care systems in Finland (Saarivirta *et al.* 2010). Statistical analyses were conducted using SAS (release 9.2, 2002–2008; SAS Institute Inc., Cary, NC, USA).

## Consequences of reproductive overlap for offspring survival to adulthood

Intergenerational reproductive overlap was defined from both the first- and second-generation-mother's point of view. In the case of the former, overlap was defined to occur when a first-generation woman of reproductive age (< 54 years) gave birth within 2 years of the birth of a grandchild. In the case of the latter, overlap was defined if a second-generation woman of reproductive age (> 16 years) gave birth within 2 years of their mother (or mother-in-law). Our rationale for this 2-year cut-off either side of a birth is that this will encapsulate most completely periods when mothers are in greatest conflict over resources. Mothers-to-be need to gain sufficient resources to conceive and nurture gestating offspring (Lumey 1992; Jasienska 2009; Roseboom *et al.* 2011), while postpartum mothers need to provide substantial resources to suckling offspring (Butte & King 2005; Kramer 2005) until other helpers can help provision offspring following weaning (Sear & Mace 2008; Hrdy 2009). The youngest woman with a reproductively active offspring was 36, while the oldest reproducing woman in the population was 52; thus analyses were restricted to include those births delivered during periods in which reproductive overlap (as defined) was conceivable (i.e. when first-generation mothers were 34–54 years). The survival analysis of offspring born to first-generation mothers was conducted on 613 offspring born to 209 mothers, whereas that of second-generation mothers was conducted on 824 offspring born to 342 mothers.

The consequences of simultaneous intergenerational reproduction for offspring survivorship to age 15 years were then investigated using two Cox proportional hazards models (one each for offspring of first- and second-generation mothers). The mortality hazards were proportional for the overlap variable in both cases (first generation  $\chi_1^2 = 0.070$ ,  $P = 0.79$ ; second-generation  $\chi_1^2 = 0.65$ ,  $P = 0.42$ ). We analysed survival to 15 years, because although competition will have the strongest impact on offspring survival during the first 2 years of life when mothers require substantial resources to support lactation, such competition might impose both immediate and delayed mortality costs on offspring (Lummaa 2003; Roseboom *et al.* 2011). A single analysis of offspring survival to age 15 years for each generation avoids multiple testing, and ensures the incorporation of the entire developmental period over which evolutionary implications of reproductive overlap can be manifest (Courtiol *et al.* 2012). Both analyses controlled for offspring sex, birth order and maternal age, as well as the number of years between births of focal children and those of their nearest 'competitor' from the other generation and the number of years (of the 15

possible) that offspring and the competitor spent in-conflict (see Supporting Information for further details). All of these terms were retained, irrespective of significance, to control most effectively for any confounding influences that they might have on the effect sizes of terms of interest. Finally, we controlled for potential effects of maternal presence, living area, social class and birth cohort (see Supporting Information), although in these cases, terms were dropped when they failed to have significant model explanatory power.

### Inclusive fitness consequences of reproductive overlap

Whether the consequences of intergenerational reproductive overlap contribute to stabilising selection around a particular mean age at last reproduction (mALR) was determined using a fully parameterised age-structured inclusive fitness model (see Supporting Information for full details). Assuming a stable population age-structure, we utilised a powerful method, derived by Goodman *et al.* (1974), to give the expectation that offspring encountered living mothers, reproductive or non-reproductive grandmothers, or reproductive older siblings. Combining this information with the observed effects of these kin on offspring survival, we simulated the age-functions of survival corresponding to different kin effects under either matri- and patri-local female dispersal at maturity (c.f. Shanley & Kirkwood 2001; Shanley *et al.* 2007). We repeated this for a range of female fertility phenotypes, each representing the effect of a rare mutant allele that changes the mALR (precisely defined below). Assuming that this mutant occurs only in heterozygote form at a single locus otherwise fixed for the 'wild-type' mALR, standard theory gives the strength of selection as the difference in population growth rate between the homozygote and heterozygote genotypes (Charlesworth 1994). To calculate inclusive fitness, we modified this approach by correcting the population growth rate of each mALR mutant for the relatedness-weighted interactions of its female carriers with kin from either the older or younger generations (Hamilton 1964; Oli 2003; Rousset 2004). Our results use this calculation to estimate the strength of selection on different mALRs by the difference in inclusive fitness between the naturally observed and mutant phenotypes.

We constructed age-specific fertility functions in which the mALR was incrementally increased at 5-year intervals between 36 and 66 years, with 41 being the mALR for married women surviving to 50 in our current data (ca. menopause age) and 66 being close to the mean age at death for the same women (i.e. 68 years, Lahdenperä *et al.* 2004). We do not presuppose a scenario in which ancestral women continued to bear into their sixties, but rather investigate the role of reproductive conflict in selecting against genetic variants that code for increasing ages at last birth. For each fertility function, we calculated the corresponding stable age-function of survivorship for mothers (from 16 years) and their offspring (to 15 years). Maternal survival probability to the following year was calculated as a function of age-specific fertility and probability of surviving childbirth (Lahdenperä *et al.* 2011a). Offspring survival probability was calculated using: (1) the probability, and survival consequences, of having a living mother (Lahdenperä *et al.* 2011a) and/or grandmother (Lahdenperä *et al.* 2004) and (2) the probability, and consequences, of being born to a co-breeding mother of a given identity. Thus, in effect, the model incorporates the basic ingredients of the Mother and Grandmother Hypotheses (see Intro-

duction), and adds to this the essence of the Reproductive Conflict Hypothesis (Cant & Johnstone 2008).

First, we model the inclusive fitness gains from incrementally delaying ages at last reproduction by 5 years without the effects of overlapping reproduction between generations. In effect, this investigates the combined roles of the Mother and Grandmother Hypotheses on the selection for increasing ages at last reproduction. Second, we add the offspring survival consequences of being born in-overlap with offspring from a given mother of another generation. Our models are fully parameterised using statistically generated data from our study population, including: actual and statistically projected age-specific probabilities of childbirth-related death for mothers (Lahdenperä *et al.* 2011a); the age-specific consequences of maternal death for offspring survival from birth to 15 years (Lahdenperä *et al.* 2011a); and age-specific grandmothing effects on offspring survival (Lahdenperä *et al.* 2004). Our models consider effects under both patri- and matri-locality (i.e. differing relatedness of co-breeding females to offspring produced by each party), and account for the fact that the relatedness of mother-offspring is double that of grandmother-grandchildren (see Supporting Information).

### Decomposing the effects

The inclusive fitness model above elucidates whether intergenerational reproductive conflict might play a role in selecting against late-life reproduction, but does not consider its importance relative to those factors proposed in competing hypotheses. To address this shortcoming, we investigated how the Mother, Grandmother and Reproductive Conflict Hypotheses each contributed to the selection against delayed menopause, by considering the effect of each individually in the model. We considered the relative importance of the competing hypotheses in terms of the change to inclusive fitness between mALRs of 41 and 46 years, as this is the 5-year increment over which the parameters relevant to all three hypotheses can be directly observed and the probability of breeding begins to diminish dramatically. We first calculated the increment to inclusive fitness by last reproducing at 46 instead of 41 years, in the absence of any potential costs of dying in childbirth (Mother Hypothesis), helpful grandmother effects (Grandmother Hypothesis) or being in reproductive competition (Reproductive Conflict Hypothesis). We then added each cost of continued reproduction separately under both patri- and matri-locality, with the former involving co-breeding between female in-laws and paternal grandmothing effects and the latter involving mother-daughter co-breeding and maternal grandmother effects.

In the inclusive fitness model above, the difference in population structure between matri- and patri-locality affects relatedness values (i.e. between mother-offspring vs. in-laws) and thereby also the fertility phenotypes that interact between generations. For example, with matri-local dispersal, females and their mothers both carry the age at menopause mutation on which we model selection, and therefore under matri- but not patri-locality both female generations exhibit delayed reproduction. To show the relative importance of the differences in intergenerational relatedness/phenotypes vs. the effects of reproductive overlap on offspring survival, we swapped the effects on offspring survival associated with matri- and patri-local female dispersal between dispersal scenarios. In other words, the observed effects of intergenerational reproductive overlap under

patri-locality (i.e. co-breeding by in-laws) were associated with the co-breeding female relatedness values and fertility phenotypes associated with matri-locality, and *vice versa*. Again, we focused on how these differences affected the difference in inclusive fitness between mALRs of 41 and 46 years. Obviously, reproductive outcomes and relatedness asymmetries between co-breeding women are likely to be linked, but our intention here is to investigate more generally the role of relatedness asymmetries vs. conflict outcomes in generating any differences in estimated inclusive fitness associated with continued reproduction.

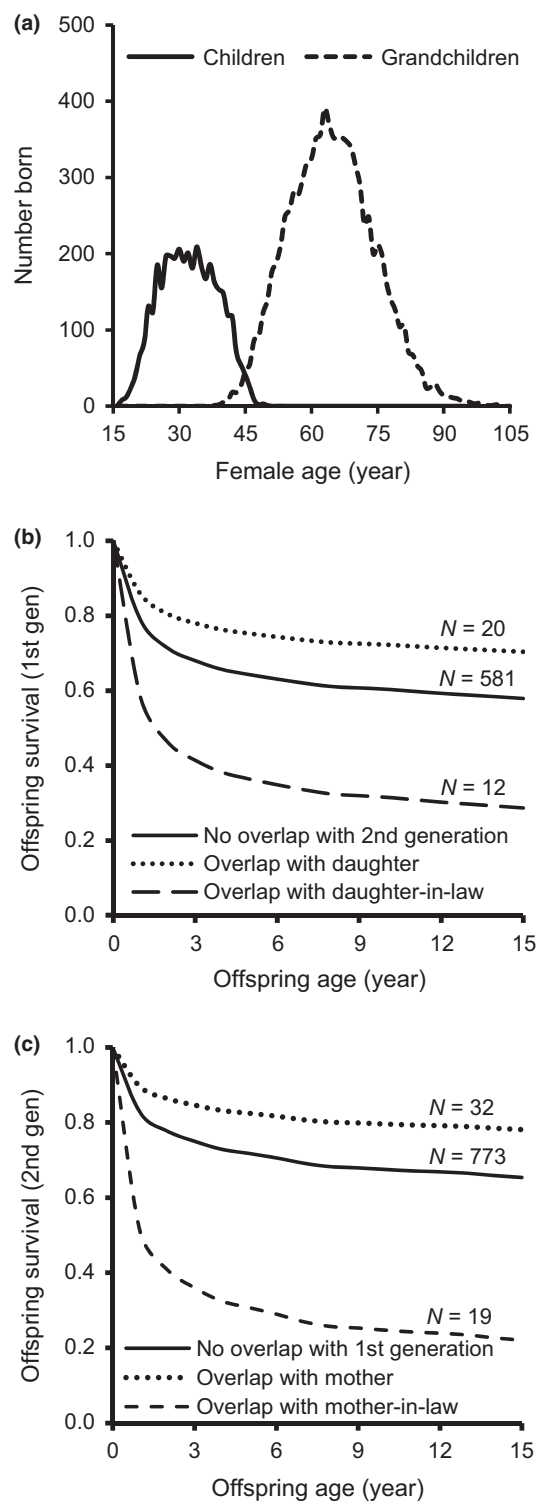
## RESULTS

### Consequences of reproductive overlap for offspring survival to adulthood

The demography of pre-industrial Finland reflected natural fertility and mortality, with mothers in our current data giving birth to an average of  $6.9 \pm 0.12$  (SE) offspring, with 54% of offspring surviving to reproduce. The earliest reproducing women in our population was 16 years (mean  $\pm$  SD =  $25.4 \pm 4.6$ ) and the latest was 52 (mean  $\pm$  SD =  $39.7 \pm 5.0$ ). Reproductive overlap between generations was rare in pre-industrial Finland, with 6.6% of 556 mothers (reproducing at least twice) delivering a child within 2 years of their first grandchild (Fig. 1a). Overall, offspring survivorship was significantly influenced when two mothers from successive generations gave birth simultaneously (Cox Regression: offspring of older-generation mothers  $\chi^2_2 = 8.45$ ,  $P = 0.015$  (Fig. 1b, Table S1a); offspring of younger-generation mothers  $\chi^2_2 = 13.31$ ,  $P = 0.0013$  (Fig. 1c, Table S1b). Further comparisons revealed that differences were statistically non-significant between mother–daughter pairs, but highly significant when in-laws overlapped reproductively with one another. The survival of offspring from second generation mothers was not affected significantly by being born simultaneously with offspring from their mother's mother ( $\chi^2_1 = 0.51$ ,  $P = 0.48$ ;  $\beta = -0.21 \pm 0.29$  (SE)), nor was the survival of offspring from first generation mothers significantly altered by being born simultaneously with offspring from their mother's daughter (i.e. from their older sister) ( $\chi^2_1 = 2.36$ ,  $P = 0.12$ ;  $\beta = -0.52 \pm 0.34$  (SE)), although in the latter case there was a possible statistical trend for increased survivorship when born simultaneously. By contrast, offspring of older-generation mothers suffered a 50% reduction in survivorship to age 15 if born alongside offspring produced by younger-generation daughters-in-law ( $\chi^2_1 = 4.81$ ,  $P = 0.028$ ;  $\beta = 0.79 \pm 0.36$  (SE)), and offspring born to younger-generation mothers had a 66% survivorship reduction if born alongside offspring from older-generation mothers-in-law ( $\chi^2_1 = 11.36$ ,  $P = 0.0008$ ;  $\beta = 1.01 \pm 0.30$  (SE)). These results suggest that inter-generational reproductive conflict is low among related mothers and daughters, but is substantial between unrelated in-laws.

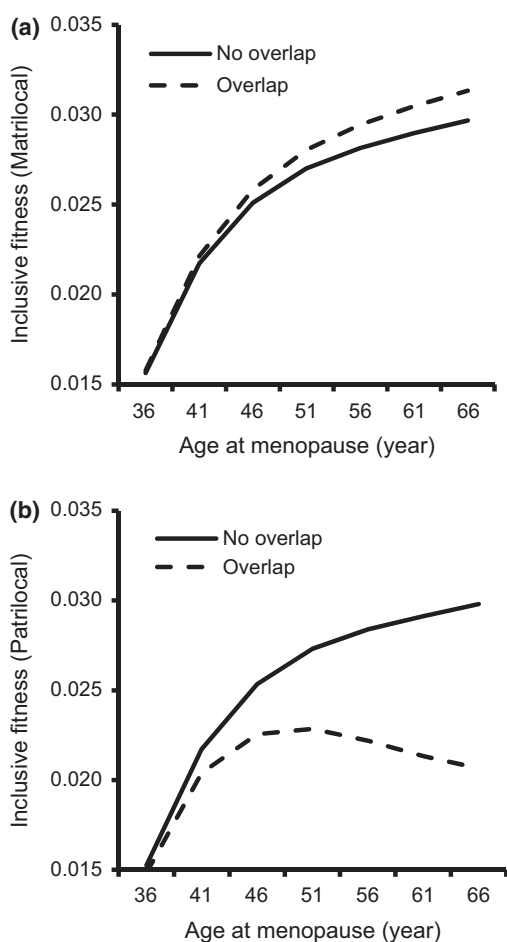
### Inclusive fitness consequences of reproductive overlap

We found little evidence to suggest that selection should act against advancing mean age at last reproduction (mALR) based solely on the risks of dying in childbirth and indirect fitness gains through grandmothing. With the exclusion of offspring survival consequences of reproductive overlap, inclusive fitness rose by 30, 14, 7, 4, 3 and 2% with each 5-year increment to mALR from age 36 to



**Figure 1** Degree of intergenerational reproductive overlap and consequences for offspring survival to maturity (15 years). (a) Age-specific fertility distribution illustrating the ages over which mothers and offspring overlap in their reproductive periods [ $n = 556$  (grand)mothers, 4091 offspring and 8730 grand-offspring]. Reproductive overlap significantly reduced the survival of offspring from: (b) first-generation mothers ( $n = 613$  offspring); and (c) second-generation mothers when the reproductive overlap occurred between unrelated women (mothers-in-law and daughters-in-law), but had less effect when mothers and daughters reproduced simultaneously ( $n = 824$  offspring). Figures show predicted relationships from Cox regressions. Gen refers to generation.





**Figure 2** Covariation of inclusive fitness with mean female age at last reproduction (mALR). Figures show inclusive fitness advantages of continued reproduction when: (a) females breed in their natal group (matrilocal); and (b) females transfer to breed in their mate's natal group (patrilocal). In each, the solid line excludes any consequences of simultaneous intergenerational reproductive overlap, while the dashed line models its inclusion. The consequences of reproductive overlap are only significant in the case of females dispersing into their mate's natal group generating co-breeding between female in-laws: the inclusive fitness returns from delayed mALR diminish rapidly and indicate stabilising selection around a mALR of age 51 (b).

66 years (Fig. 2a, b; solid line). Thus, the strength of selection for delayed mALR waned considerably with increasing age, but remained positive throughout, in the absence of reproductive competition between overlapping female generations.

The relationship between inclusive fitness and mALR was largely unaffected by introducing the offspring survival consequences of reproductive overlap between mothers and their biological daughters; leading to a maximum of a 5% increase in inclusive fitness gained from a 5-year delay in mALR between ages 61 and 66 (Fig. 2a). By contrast, reproductive overlap between female in-laws had significant detrimental effects on the inclusive fitness gains from delayed mALR (Fig. 2b). Inclusive fitness increased by 27% and 9% as mALR increased from age 36 to 41 years and from age 41 to 46, respectively. However, postponing mALR from age 46 to 51 increased inclusive fitness by only 1%, and further delays after age 51 resulted in up to 4% reductions in inclusive fitness with extensions in mALR.

Under patrilocality, large inclusive fitness differences arose between situations where offspring survival consequences of reproductive overlap were (vs. were not) considered, especially for the highest ages of mALR (Fig. 2b). For example, the inclusive fitness linked to mALR fell by 7% after including the effects of reproductive competition at 41 years (the actual mALR in pre-industrial Finland), by 20% after including the effects at age 51 (the approximate age of menopause), and by 37% after including the effects at age 66 (2 years short of the mean lifespan of women surviving to menopause Lahdenperä *et al.* 2004). Thus, the addition of reproductive conflict among in-laws led to substantially reduced selection for reproduction beyond age 46 years, and to selection against reproduction after the age of 51.

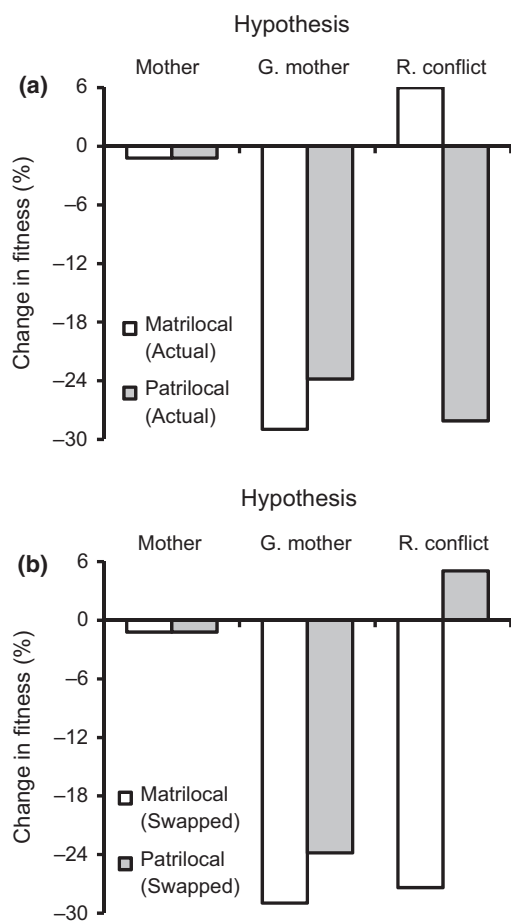
### Decomposing the effects

Delaying the last age at reproduction to 46 rather than 41 years led to an overall positive inclusive fitness increment through the production of more offspring (Fig. 2a, b). However, the value of this increment was reduced by 55% under patri-locality and 23% under matri-locality, following the combined inclusion of the effects of reproductive overlap, reduced grandmothering benefits and increased risks of death in childbirth (Fig. 3a). Decomposition of this combined effect under patri-locality, wherein the combined effects appear sufficiently strong to select against continued reproduction beyond menopaual age (i.e. 51 years; Fig. 2b vs. 2a), revealed that reproductive conflict, reduced grandmothering effects and increases in the risks of dying in childbirth explained approximately 51, 43 and 2%, respectively, of the reduction in the increment to inclusive fitness generated from delaying reproduction to 46 years (Fig. 3a). Thus, reproductive conflict between in-laws and grandmothering effects had similarly strong effects on selecting against late-life reproduction, with the risks and consequences of dying in childbirth having lesser effects.

Swapping the statistically observed effects of intergenerational reproductive overlap between the genetic relatedness values under patri- versus matri-locality (and *vice versa*), revealed that the key component contributing to reduced inclusive fitness by co-breeding in-laws was the observed effect on offspring survival. In other words, asymmetries in the actual relatedness values between co-breeding women had relatively minor effects on inclusive fitness calculations. Thus, if offspring survival outcomes resulting from mother–daughter reproductive pairings were similar to those of in-law reproductive pairings, substantial reductions in inclusive fitness would ensue (Fig. 3b).

### DISCUSSION

The classical theory of life-history evolution suggests that natural selection should favour individuals whose reproductive and somatic functions senesce simultaneously, as is the case in human males (Williams 1957; Charlesworth 1994). That women show menopause, an inevitable loss of reproductive capacity around age 50, and yet live for decades thereafter, is thus an evolutionary enigma. Menopause cannot be explained entirely by the extension of lifespan resulting from modern improvement to medicine and sanitation because in hunter–gatherers, living in the absence of each, ~60% of women who survive to reproductive age (15 years) reach menopaual age and many inevitably survive well beyond (Gurven &



**Figure 3** Decomposition of changes to inclusive fitness accrued from delaying last reproduction from 41 to 46 years. Marginal percentage effects of costs of dying in childbirth (Mother Hypothesis); loss of grandmothing (Grandmother Hypothesis); and intergenerational reproductive overlap (Reproductive Conflict Hypothesis) under patri- and matri-locality with: (a) true relatedness between co-breeding women under each dispersal system; and (b) relatedness values between co-breeding swapped between the two dispersal systems. Note that in all cases the white and grey bars in (a) are effectively reversed in (b), indicating that the behavioural outcomes are more relevant to calculations of inclusive fitness outcomes than the asymmetries in relatedness values *per se* (m. = mother, g. = grand, r. = reproductive). The results were not changed qualitatively when decomposition models included extreme probabilities of death in childbirth (Shanley *et al.* 2007) (see Fig. S5 for further details).

Kaplan 2007). The enigma is further deepened by findings suggesting directional selection on increasing reproductive lifespan in women (Helle *et al.* 2005; Byars *et al.* 2010) and an age at menopause which is both variable and heritable (Peccei 2001). A likely explanation for the maintenance of human female menopause over evolutionary time-scale is thus stabilising selection (Hawkes *et al.* 1998; Cant *et al.* 2009): the question is what are the stabilising forces?

Previous attempts to account for the evolution of menopause around age 50, based on the elevated risks of dying in childbirth and/or the benefits of grandmothing, have largely failed (Mayer 1984; Hill & Hurtado 1991; Rogers 1993). One possible exception was presented by Shanley *et al.* (2007), who concluded that given sufficiently large benefits of grandmothing and risks of dying in childbirth, menopause could be selected around 55–60 years.

However, fitness was calculated as the population growth rate rather than as increments to inclusive fitness; doing so ignores relatedness asymmetries between one's offspring ( $R = 0.5$ ) vs. grandoffspring ( $R = 0.25$ ), leading to an overestimation of the fitness benefits of grandmothing (Hamilton 1964; Rousset 2004). In addition, values used for maternal mortality risk in childbirth were extreme, such that breeding beyond age 54 almost guaranteed maternal death. Across populations, the risk of dying in childbirth seldom exceeds 2% at age 40 years and we have estimated, even using exponentially increasing mortality functions from the mean age at last reproduction (~38 years), that it would have been unlikely to have exceeded 2.4% by the age of 70 years in Finland (Lahdenperä *et al.* 2011a). While this might be construed unrealistically low, it is important to bear in mind that non-linear changes to age-specific mortality functions in late life might themselves be an inevitable consequence of selection against late-life reproduction (Cant *et al.* 2009). Notwithstanding, our inclusive fitness models based on calculated projections of age-specific increases in mortality risk from childbirth (Lahdenperä *et al.* 2011a) and measured grandparenting benefits (Lahdenperä *et al.* 2004) were insufficient to select against continued reproduction late in life.

Recently, using game-theoretic modelling, Cant & Johnstone (2008) illustrated that stabilizing selection resulting in menopause could be driven by competition between successive generations of reproductively mature women over limiting resources. Their model predicted that the severity of such competition should be greatest between co-breeding in-laws; leading to selection for reproductive quiescence in the older generation (see Introduction). Our results confirm that intergenerational conflict between in-laws can be intense, with overlapping reproduction being associated with substantial reductions in the survival of offspring from mothers of both generations. The addition of such effects to an inclusive fitness model containing the direct fitness costs of age-specific elevations of death in childbirth and indirect fitness benefits of grandmothing, led to significant reductions in inclusive fitness increments arising from reproducing at 46 and overall declines from age 51. Nevertheless, decomposition of age-specific changes to inclusive fitness associated with delaying reproduction revealed that both reproductive conflict between in-laws and loss of grandmothing benefits similarly contributed to the observed reductions, with elevated risks of dying in childbirth having more marginal effects. While it might be argued that the low explanatory power of the Mother Hypothesis in our analyses was due to unrealistically low probabilities of death in childbirth (but see Cant *et al.* 2009), decomposition analyses using extreme risks of death in childbirth from Shanley *et al.* (2007) failed to alter our conclusions qualitatively (see Fig. S5). Thus, the evidence from this study would suggest that reproductive conflict between in-laws constitutes a salient missing piece of the evolutionary puzzle of menopause, rather than the entire solution. Our results suggest that multiple pressures combine to select against continued reproduction and that the indirect benefits of grandmothing (Hawkes *et al.* 1998) in conjunction with the inclusive fitness costs of co-breeding with offspring (Cant & Johnstone 2008) are primarily, and similarly, influential.

The pre-industrial Finns on which this study was based were characterised by monogamy, only slight differences in spousal age (males < 1 year older at first birth), philopatry by both sexes and male-biased primogeniture (Lahdenperä *et al.* 2011b). Thus, mothers would have the opportunity to compete and/or cooperate with

biological daughters and in-laws, as is the case in most human societies (Alvarez 2004; Marlowe 2004). Further studies are required to test the generality of our findings across societies varying in each of these social characters as well as the magnitude of grandmaternal benefits and costs of co-breeding. Cant & Johnstone (2008) proposed that reproductive conflict would be integral to the evolution of menopause, and then offered one example of a likely form that this conflict might take (i.e. intergenerational conflict between in-laws). Nevertheless, other forms of conflict might be viable (Mace & Alvergne 2012). For example, in societies wherein polygyny is common and men are older than their spouses, we might expect a reduced role for intergenerational conflict between in-laws and an increased role of intragenerational conflict between unrelated co-wives of vastly differing ages. Inter-female conflict rather than cooperation often characterises non-sororal women breeding with the same man in polygynous human societies, whereas this is less true of sororal women (Chisholm & Burbank 1991). Given that resources are almost always limiting, but have a profound effect on reproductive success, we should not be surprised if women attempt to reduce the reproductive output of, particularly unrelated, female competitors (West *et al.* 2006). Indeed, we found evidence to suggest that it is the degree of conflict, rather than relatedness asymmetries *per se*, which primarily govern inclusive fitness reductions associated with co-breeding, and so it follows that any comparable form of female conflict, irrespective of the partaking individuals, could similarly contribute to selection against continued reproduction in age-structured populations.

Finally we found no evidence for reproductive conflict between mother–daughter pairings; hence little evidence that menopause should be selected through simultaneous intergenerational reproduction in purely matri-local societies. Indeed, we found a possible statistical trend for a benefit to mothers of overlapping reproduction with daughters, suggesting that daughters might benefit by helping to rear younger siblings. Our study therefore raises the intriguing question of why women have not been selected to maintain plasticity in their ability to conceive late in life. One explanation is that the fitness accrued through grandmothering, although lower, is more predictable than that gained through late-life reproduction when conflict or death in child-birth might arise unpredictably (Cockburn & Russell 2011; Rubenstein 2011). Menopause might be selected if lifespan can be more prolonged and indirect benefits of grandmothering can be increased, by shutting down energetically costly systems that are seldom used beneficially (Jasienska 2009). This restraint hypothesis predicts a negative relationship between age at menopausal onset and indirect fitness accrued through grandmothering. Another possibility is that in our evolutionary past, menopause evolved as a signal advertising a lack of reproductive intent. It is noteworthy that, in some social insect species, being born with reproductive potential leads to maiming or death (Beekman & Ratnieks 2003), whereas in cooperative birds, mothers are commonly evicted from their territory by sons attempting to facilitate immigration by unrelated females (Russell 2004). This suppression hypothesis predicts that women are more accepted into families following menopause, being so is advantageous and that during our evolutionary past, the costs of eviction from the group were terminal. Future studies are required to elucidate the merits of these hypotheses, but evidence here showing that grandmaternal benefits and reproductive conflict were the primary forces selecting against continued reproduction, provides some tentative support. Irrespective of the competing parties, we emphasise that the

full appreciation of Hamilton's rule, including the inclusive fitness costs of competing with other group members will provide a significant advance in our understanding of the evolution of menopause and of human life-histories in general.

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## AUTHORSHIP

ML, AFR and VL conceived and designed the experiments. ML and VL performed the experiments. ML, DOSG and AFR analysed the data. ML, DOSG and AFR wrote the paper with contributions from VL.

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