

1 **Title: An age-dependent ovulatory strategy explains the evolution of dizygotic twinning in**
2 **humans**

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14

15

16 **Abstract**

17 Dizygotic twinning, the simultaneous birth of siblings when multiple ova are released, is an
18 evolutionary paradox. Twin bearing mothers often have elevated fitness; but despite twinning
19 being heritable, twin births only occur at low frequencies in human populations. We resolve this
20 paradox by showing that twinning and non-twinning are not competing strategies, instead
21 dizygotic twinning is the outcome of an adaptive conditional ovulatory strategy of switching

22 from single to double ovulation with increasing age. This conditional strategy when coupled with
23 the well-known decline in fertility as women age, maximizes reproductive success and explains
24 the increase and subsequent decrease in twinning rate with maternal age that is observed across
25 human populations. We show that the most successful ovulatory strategy would be to always
26 double ovulate as an insurance against early fetal loss, but to never bear twins. This finding
27 supports the hypothesis that twinning is a byproduct of selection for double ovulation rather than
28 twinning.

29

30 **Main**

31 The stable existence of alternative phenotypes in a single population is of interest because it
32 suggests a balance of evolutionary forces at play. Elucidating those forces, particularly when
33 they apply to humans, is an important focus of evolutionary biology ¹. For example, the tendency
34 to produce dizygotic twins, where the ovulation of two ova gives rise to the birth of siblings, is
35 heritable ² and varies within and among populations, its rate rising and then falling with
36 increasing maternal age ³. Here we show that a conditional strategy of switching from single to
37 double ovulation with increasing age explains why twinning rate rises and falls as females age,
38 and how switching from single to double ovulation with increasing age maximizes individual
39 reproductive success, thus explaining why dizygotic twinning persists in humans.

40 The evolutionary forces that account for twinning and the age-dependent change in its
41 rate are poorly understood. While the birthing of twins has fitness costs for both mothers and
42 offspring, mothers that produce twins often have greater fitness than mothers who have never
43 produced twins ⁴⁻⁸. We focus on how selection operates on the reproductive trait that makes
44 dizygotic twins possible, double ovulation. The ova insurance hypothesis ⁹ posits that twinning is

45 a maladaptive consequence of the ovulation of multiple ova, which serves as an adaptive counter
46 to poor prenatal offspring survival. Because prenatal mortality is known to dramatically increase
47 with maternal age ¹⁰⁻¹², we hypothesized that the age-dependent pattern of dizygotic twinning
48 observed in humans might be due to an adaptive ovulatory strategy of switching from single
49 ovulation to double ovulation with increasing age. This hypothesis makes two predictions. First,
50 an increasing rate of double ovulation coupled with a decreasing live birth rate should explain
51 the observed pattern of age-dependent twinning in humans. Second, the expected lifetime
52 reproductive success of women using this conditional strategy should exceed that of women who
53 always single or always double ovulate. We verified the first prediction by extending a simple
54 mathematical model that derives the twinning rate given the probabilities of double ovulation
55 and live birth. We asked whether a declining probability of live birth coupled with an increasing
56 probability of double ovulation with increasing maternal age could explain the pattern of age-
57 dependent twinning observed in human populations. To verify the second prediction, we used
58 postnatal and maternal survival rates for twins and singletons from a natural fertility population
59 and age-dependent prenatal survival rates at different stages of pregnancy to compare the
60 expected lifetime reproductive success of women who always single or double ovulate with that
61 of women who switch from single to double ovulating with increasing age.

62

63 **Results and Discussion**

64 With respect to the first prediction, only two parameters, the rate of double ovulation and
65 the live birth rate, are needed to predict the twinning rate. For a woman at age t , the twinning rate
66 (T_t) at birth is given by the formula $T_t = F_t p_t / (1 + F_t (1-p_t))$, where F_t is the double ovulation
67 rate and p_t is the probability of survival from fertilization to birth (see SI for derivation) ¹³. If the

68 observed change in twinning rate with age (T_t) is due to a conditional ovulatory strategy that
69 compensates for declining fertility, then a double ovulation rate (F_t) that increases with age and a
70 live birth rate (p_t) that decreases with age should produce age dependent twinning rates (T_t) that
71 closely match those observed in human populations. We used a cumulative normal function for
72 F_t so that the probability of double ovulation increases with age depending on the mean and
73 standard deviation of a normal distribution in age of switching from single to double ovulation.
74 We chose this function because it forms the basis of the environmental threshold model, the most
75 commonly used quantitative genetic model for conditional strategies¹⁴ (Fig. S1). Based on
76 studies of a natural fertility population¹⁰, we used a declining exponential function for the
77 probability of live birth (p_t), where p_t declines at a constant rate with female age from a value of
78 0.55 at age 18 (SI). We then derived age-dependent twinning rates (T_t) using combinations of
79 values for the mean and standard deviation of the cumulative normal distribution for age of
80 switching from single to double ovulation (F_t) and the annual rate of decline in probability of
81 live birth (p_t). We used *Microsoft Excel's* iterative model fitting function *Solver* to compare the
82 expected twinning rates (T_t) with those observed in nine data sets from human populations
83 unbiased by fertility treatments^{3,15-19}. *Solver* identified the combinations of values for the three
84 parameters (mean and standard deviation of the cumulative normal distribution for age of
85 switching from single to double ovulation, and the annual rate of decline in probability of live
86 birth) that maximized R^2 , we were able to determine what values of these parameters could best
87 explain the pattern of age-dependent twinning observed in each population.

88 Our results show that 90% or more of the variation in twinning rates in these populations
89 is explained by a shift from single ovulation to double ovulation with increasing age (Fig. 1;
90 Table 1), supporting the hypothesis that age-dependent twinning results from a conditional

91 ovulatory strategy. An increase in double ovulation rates, F_t , from near zero at menarche to over
92 50% prior to menopause (Fig. 1e), coupled with a constant decline in live birth rate, p_t , to less
93 than 10% as women approach menopause (Fig. 1f), readily explains the pattern of age-dependent
94 twinning (Fig. 1a-d). Because the decline in prenatal survival ensures that double ovulations
95 increasingly result in only singleton births or reproductive failure, the increased rate of double
96 ovulation does not translate into ever-increasing rates of twin births because as prenatal survival
97 rates decline it become increasingly unlikely that both offspring survive to birth. Hence, patterns
98 of age-dependent twinning are consistent with a conditional strategy that combines an age-
99 dependent switch to double ovulation with the well-established age-dependent decline in prenatal
100 viability ¹⁰⁻¹².

101 Our results also suggest that differences in age-dependent twinning rates amongst
102 populations can be explained by differences in the mean and standard deviation in age of
103 switching from single to double ovulation and the decline in probability of live birth per
104 conception with age. For example, the age-dependent twinning rates in a Nigerian population
105 (Fig. 1a), which has the steepest increase and subsequent decline in twinning rate with age,
106 requires an average age of switching to double ovulation of 33 years and an annual decline in
107 probability of live birth of 7% per year, compared with a switching age of 46 years for a
108 Japanese population, which has the lowest twinning rates (Fig. 1e; Table 1), and an annual
109 decline in probability of live birth of 11% (Fig. 1e, Table 1).

110 We used two complementary approaches, simulations and probabilistic modeling (see SI,
111 Figs. S3-S5, Tables S1 and S3) to evaluate the prediction that women playing a conditional
112 strategy of switching from single to double ovulation will have greater lifetime reproductive
113 success than women who always single or always double ovulate. Both approaches allowed us to

114 estimate the lifetime reproductive success of women switching from single to double ovulation at
115 different ages. By setting the age of switching to less than what we functionally defined as
116 menarche (age 18, based on the average age of first reproductive attempt in a natural fertility
117 populations) we could estimate the fitness of a strategy of always double ovulating. When the
118 switching age was set to greater than what we functionally defined as menopause (age 40, based
119 on the mean age of last birth in a natural fertility populations) we could estimate the fitness of
120 always single ovulating. Setting the switching age to ages between 18 and 40, allowed us to
121 estimate the fitness of conditional ovulatory strategies that switched from single to double
122 ovulation at different ages. We compared the success of the different strategies using the average
123 number of offspring surviving to age 15. The modeling allowed us to calculate the expected
124 number of zygotes per ovulatory cycle surviving to age 15, and the time between successive
125 cycles for different-aged single and double ovulating women (SI). From these data we estimated
126 age specific reproductive rates for women playing different ovulatory strategies. We treated the
127 survival of individual conceptions resulting from double ovulation as independent events,
128 assumed that each ovum was fertilized, and that women resumed ovulation only after complete
129 brood loss or weaning (SI).

130 These approaches required data on offspring survival rates between conception and birth,
131 maternal survival rates at the birthing of twins and singletons, singleton and twin survival rates
132 between birth and weaning and to reproductive age (assumed to be 15 yrs), and the time intervals
133 between successive ovulatory cycles. Such data are unavailable from any single population, so
134 we used multiple sources. Natural fertility populations in Bangladesh ¹⁰ and Gambia ⁵ provided
135 data for live birth rates per zygote at age 18 (0.55/conception), and maternal childbirth survival
136 rates and postnatal offspring survival rates for twin and singleton births (Table S1). We assumed

137 a decline in live birth rate of 11% which was the average decline rate estimated from our
138 analyses of observed twinning rates (Table 1). Data for determining prenatal survival rates at
139 different times between conception and birth for different aged women were based on an analysis
140 of the fates of over 1.2 million pregnancies in Denmark ²⁰ (Table S2, Fig.S2). Estimates of the
141 time intervals between successive ovulatory cycles were taken from the literature.²¹

142 Both simulations and modeling indicated that fitness was maximized when women
143 switched from single to double ovulation at approximately age 25 (Fig 2a, Fig 3a). This result
144 supports the hypothesis that the age-dependent conditional ovulatory strategy we have identified
145 as best explaining the observed age-dependent twinning rates is adaptive ¹. The modeling results
146 show why fitness is maximizes by switching from single to double ovulation with increasing age.
147 While at all ages the expected per capita number of offspring surviving to 15 per ovulatory cycle
148 was greater for a strategy of double ovulating than single ovulating (Fig 3b), this was especially
149 so in older women (91% greater at age 40 versus 26% greater at age 18). However, the lower
150 probability of livebirth per ovulatory cycle shortens the time between successive ovulations in
151 single ovulators, while in double ovulators the increased probability of at least one livebirth and
152 subsequent lactation, and lengthens the time between ovulations (Fig 3c). So, although the per
153 capita offspring per cycle was greater for double ovulations, this was more than compensated by
154 the increased number of ovulations of young single ovulators. Young double ovulators were also
155 more likely to birth twins whose poorer postnatal survival depressed fitness and whose birthing
156 incurred greater maternal risks (Fig. S6). Hence, double ovulating when young has fitness costs
157 in the investment of time in low-fitness high-risk pregnancies that produce twins, while double
158 ovulating when older has fitness benefits because twins are rarely produced. These differences in
159 the age-dependent reproductive effects of double and single ovulating results in reproductive

160 rates in young single ovulators that exceed those of young double ovulators, but in older women
161 the reverse is true (Fig. 3d). This age-dependent trade-off in reproductive rate fulfills an
162 important requirement for maintenance of a conditional strategy, and in the case of conditional
163 double ovulation, produces stabilizing selection on an optimal switching age between menarche
164 and menopause ²².

165 Our modeling indicates that the optimal switching age is sensitive to differences in
166 prenatal survival probabilities of embryos resulting from single versus double ovulation. For
167 example, our results are based on the assumption that prenatal probabilities of survival of
168 embryos resulting from single versus double ovulation are the same and independent (SI). While
169 this assumption is more likely to be valid early in pregnancy, later in development the survival of
170 individual twin fetuses are likely to be less than singletons ^{23,24} and when one of the twin fetuses
171 is lost, the probability of the second fetus being lost increases ²⁵, as do other adverse perinatal
172 outcomes ²⁶. As a result, the true optimum switching age is likely later than our analyses in
173 Figures 2 and 3 indicate, and more in line with the switching ages observed in human
174 populations (Fig. 1).

175 Finally, we asked whether twinning is a maladaptive byproduct of an otherwise adaptive
176 conditional ovulatory strategy ⁹. This hypothesis predicts that if women who double ovulate
177 throughout their lives could avoid birthing twins, for example via reabsorption of one fetus, then
178 their lifetime reproductive success should exceed that of women who switch from single to
179 double ovulation with increasing age, and therefore occasionally produce twins. We repeated the
180 simulations, but now women who double ovulated were only allowed to only give birth to
181 singletons even if they were expected to carry twins to term. Hence, they received the fertility
182 benefits of double ovulation without incurring the costs of twin births. In these simulations,

183 lifetime reproductive success was maximized at switching ages less than or equal to the age of
184 menarche (Fig. 2b). Since these women double ovulated during each ovulatory cycle, this result
185 supports the byproduct hypothesis 9.

186 Our results potentially shed light on why mothers who have produced twins often have
187 greater fitness than mothers who never do so 4,5,7,8. Follicle development and ovulation are
188 controlled by the hypothalamic-pituitary axis which is able to integrate an adaptive response to
189 cues associated with maternal condition and age 27. Mothers who produce twins often do so at
190 higher parities (independent of maternal age) 3, and often possess physical characteristics, such
191 as height and body mass indices, that potentially increase both the probability of double
192 ovulation, lifetime reproductive success and prenatal survival 5,28. In this study, we have only
193 attempted to explain the evolution of age-dependent double ovulation. However, if double
194 ovulation and prenatal survival are conditional on these factors, in addition to maternal age, then
195 it would not be surprising if women who have produced twins often have greater fitness than
196 those who have not.

197 Our findings indicate that the ultimate cause (*sensu* Mayr 29) of the pattern of age-
198 dependent twinning in human populations is natural selection favoring double ovulation with
199 increasing age in response to declining fertility. These results suggest that in human populations
200 in which increasing numbers of women delay first reproduction 30, a substantial fraction of
201 singleton births will result from double ovulation with the subsequent prenatal loss of one of the
202 siblings. For example, if the probability of double ovulation and probability of live birth per ova
203 for women at age 27 are 0.05 and 0.2 (Figure 1e, f), respectively, approximately 8% of all
204 singletons will have been produced following double ovulation. In contrast, at age 37, if the
205 probability of double ovulation and probability of live birth per ova are 0.4 and 0.05 (Fig. 1e, f),

206 respectively, the fraction of singletons produced by double ovulation rises to approximately 56%.
207 Alongside this, when reproduction is delayed, we also expect a population level increase in the
208 incidence of twin births, a phenomenon already seen in developed countries³¹.

209

210

211 **Materials and Methods**

212 **Estimating expected age-dependent twinning rates from the decline in of live birth rate and** 213 **increase in double ovulation rate**

214 Using the formula that calculates twinning rate as a function of the rates of live birth per
215 zygote and double ovulation, we used the *Solver* add-in in *Microsoft Excel* to determine the rates
216 of age-dependent decline in live birth per zygote and age-dependent increase in double ovulation
217 that provided the best fit to the observed age-dependent twinning rates (maximized the R^2 with
218 observed twinning rates) in large samples from populations with African, European and Asian
219 ancestries (Table 1). The models were fitted subject to several constraints. We fixed the
220 probability of live birth at age 18 (d_{18}) at 0.55 based on the best estimate of which we are aware
221 and coming from a natural fertility population in Bangladesh¹⁰. The probability of live birth per
222 zygote declines with maternal age^{10,12} and we assumed an exponential decline, where the annual
223 decline was constrained to be less than 0.99, and greater than 0.55 (no model approached either
224 boundary; see SI). Based on quantitative genetic models for conditional strategies^{22,32} (SI), we
225 assumed that the increase in probability of double ovulation per ovulatory cycle with maternal
226 age was best described by an increasing cumulative normal function, with mean (spm) and
227 standard deviation ($spSD$) constrained in our *Solver* searches to be greater than two years.

228 **Simulations**

229 The simulation model, which was written in the language R ³³, estimates lifetime
230 reproduction in a cohort of (nominally 1000) women by simulating ovulatory cycles from first
231 reproductive attempt until reproduction stops due to death or menopause (Table S1, Figs. S3 &
232 S4). Dependent on inputs governing the probability of prenatal loss, these cycles can result in
233 early loss, abortion, late fetal loss (miscarriage) or live birth (Table S2). The failure of a
234 pregnancy to proceed to term delays the commencement of cycling following the event by a
235 variable amount depending on when the pregnancy ends (Table S1). The simulation allows
236 women to either single or double ovulate based on her age at ovulation relative to a double
237 ovulation switch point that determines the age at which they switch from single to double
238 ovulation (*spm* in Table S1). We were able to simulate different conditional ovulatory strategies
239 by setting the ovulation switch point to values between age of menarche (age 18) and age of
240 menopause (age 40). Women could also be constrained to double or single ovulate throughout
241 their reproductive lives by setting the switch to ages less than 18 or greater than 40, respectively.
242 Depending on the number of ova released and the probabilities of surviving the prenatal period
243 (considered to be independent where there are two zygotes), either none, one or twin offspring
244 are born. Subject to inputs governing the probabilities of still birth, background adult death rate,
245 and maternal death in childbirth, successful live births occur (Table S1). Contingent on inputs
246 controlling postnatal mortality, children survive for periods of one month, one year, two years
247 (weaning) or to 15 years (Table S1). The duration of offspring survival influences the duration
248 of time that the female stops cycling (Table S1). Survival to 15 years is considered a successful
249 reproductive event for the mother and per capita number of offspring surviving to 15 years was
250 our measure of maternal fitness. Women are continually subject to the probability of death
251 including when pregnant and weaning (Table S1). When women died during childbirth, the

252 children they were birthing also died. The simulation allows for up to 20 parities; however a
253 woman's reproductive longevity is curtailed by declining ova quality (Table S2 and Fig. S2d).
254 Women older than the user-defined age at menopause, at the time that they are due to begin
255 cycling again after a pregnancy attempt or child bearing (Table S1), do not continue cycling, but
256 women that are not pregnant and younger than this age can cycle beyond that age.

257 The simulation assumes that women are not sperm limited and make no socially driven decisions
258 to delay or reduce the number of children they attempt to have, so successful pregnancy was only
259 a function of embryo survival to live birth. The simulation makes no provision for siblings,
260 grandparents or males assisting in the care of offspring. The estimates of the demographic
261 parameters used in the simulation come from multiple sources. The probability of live birth at
262 age 18 comes from a natural fertility population in Bangladesh¹⁰. The decline in probability of
263 live birth with increasing age was based on the decline in live birth probability needed to explain
264 the observed twinning rate averaged over all the populations summarised in Table 1. The
265 probabilities associated with different prenatal fates of zygotes were based on the ratio of
266 spontaneous abortions, stillbirths (late pregnancy losses) to live births in a study of over one
267 million pregnancies in Danish women of different ages (Table S2)²⁰, conditional on our
268 estimates of probability of live birth per zygote in women of different ages (Table 1). Postnatal
269 survival rates were based on those taken from a Gambian natural fertility population⁵. We
270 assumed prenatal survival probabilities to be the same for twins and singletons and independent
271 for zygotes produced by double ovulation (i.e. if the probability of survival per zygote is p , then
272 in double ovulations, the probability of both zygotes surviving is p^2 , one surviving is $2p(1-p)$ and
273 neither surviving is $(1-p)^2$). Other than parameters such as age of switching from single to
274 double ovulation and whether double ovulation could result in twin births which defined the

275 strategy, all ovulatory strategies had the same set of parameters of the simulated biological
276 background and so represented a comparison only of the differences that arise from the changes
277 in strategy.

278 In replicate simulations (Figs. S3 & S4 for further details), we estimated fitness by tallying the
279 number of offspring surviving to 15 produced by cohorts of 1000 women playing different
280 ovulatory strategies, each defined by the age at which women switched from single to double
281 ovulation. Simulations designated as ‘Twins not produced’ were identical to previously
282 described, except that whenever two offspring survived to birth, twin births were replaced with a
283 singleton birth. In each simulation we followed women from their first ovulation, through each
284 ovulatory cycle to either death or menopause and tabulated the number of offspring surviving to
285 age 15.

286

287 **Probabilistic model comparing fitness of single vs double ovulation strategies**

288 We have defined the fitness of a woman at age x as $\sum_{k=x}^M C(k)$ where $C(k)$ = number of
289 children conceived when the woman is age k that survive to age 15, and M is the age of
290 menopause. Our model estimates the expected value of this expression as

$$291 \quad F(x) = \sum_{k=x}^M N(k)S(k | x)$$

292 where $N(k)$ is the average number of offspring conceived to a woman age k that survive to age
293 15, and $S(k | x)$ is the probability that a woman alive at age x has not died before age k . We
294 determine $N(k)$ by

$$295 \quad N(k) = \frac{12V(k)}{T(k)}$$

296 where $V(k)$ is the expected number of offspring per ovulation that survive to age 15 when a
297 woman is age k , and $T(k)$ is the expected time between ovulations (in months) when a woman is
298 age k . $S(k | x)$ is determined by the recurrence relation

$$299 \quad S(x | x) = 1$$

$$300 \quad S(x + 1 | x) = R(x) \cdot asr$$

$$301 \quad S(x + 2 | x) = S(x + 1, x) \cdot R(x + 1) \cdot asr$$

$$302 \quad .$$

$$303 \quad .$$

$$304 \quad .$$

$$305 \quad S(k | x) = S(k - 1, x) \cdot R(k - 1) \cdot asr$$

306 where $R(t)$ is the probability a woman age t does not die in childbirth and asr is the annual
307 survival rate of the adult population. (See SI for details regarding the constructions of the
308 functions V , T , and R for single and double ovulators.)

309

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321 with the caveat that it cannot be used for further publications or distribution without the
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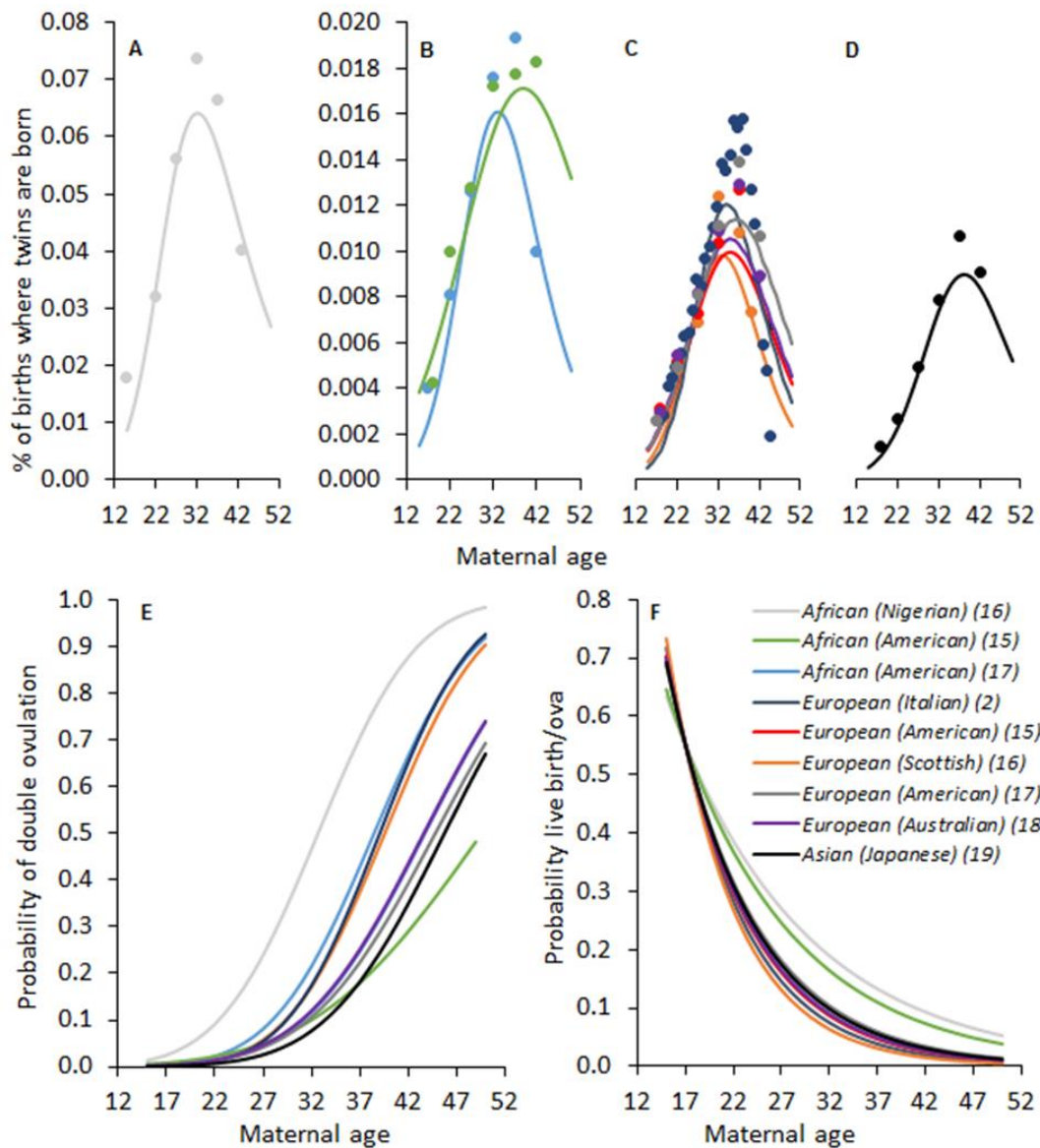
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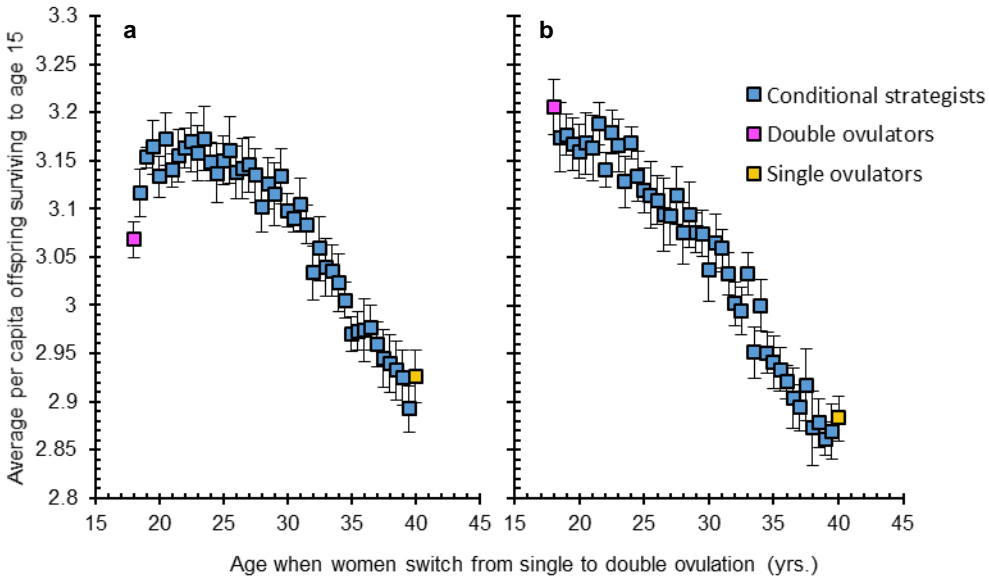
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397 **Fig. 1.** Declining prenatal survival and increasing double ovulation rates explain age-dependent
 398 twinning rates. **a-d**, Observed twinning rates (points) as a function of maternal age and those
 399 expected (lines) given **e**, increasing probability of double ovulation, and **f**, decreasing probability
 400 of live birth per zygote, both as a function of maternal age. Curves in **e** and **f** were chosen for
 401 their ability to minimize the squared deviations between the observed and expected twinning
 402 rates in **a-d** (See Table 1).

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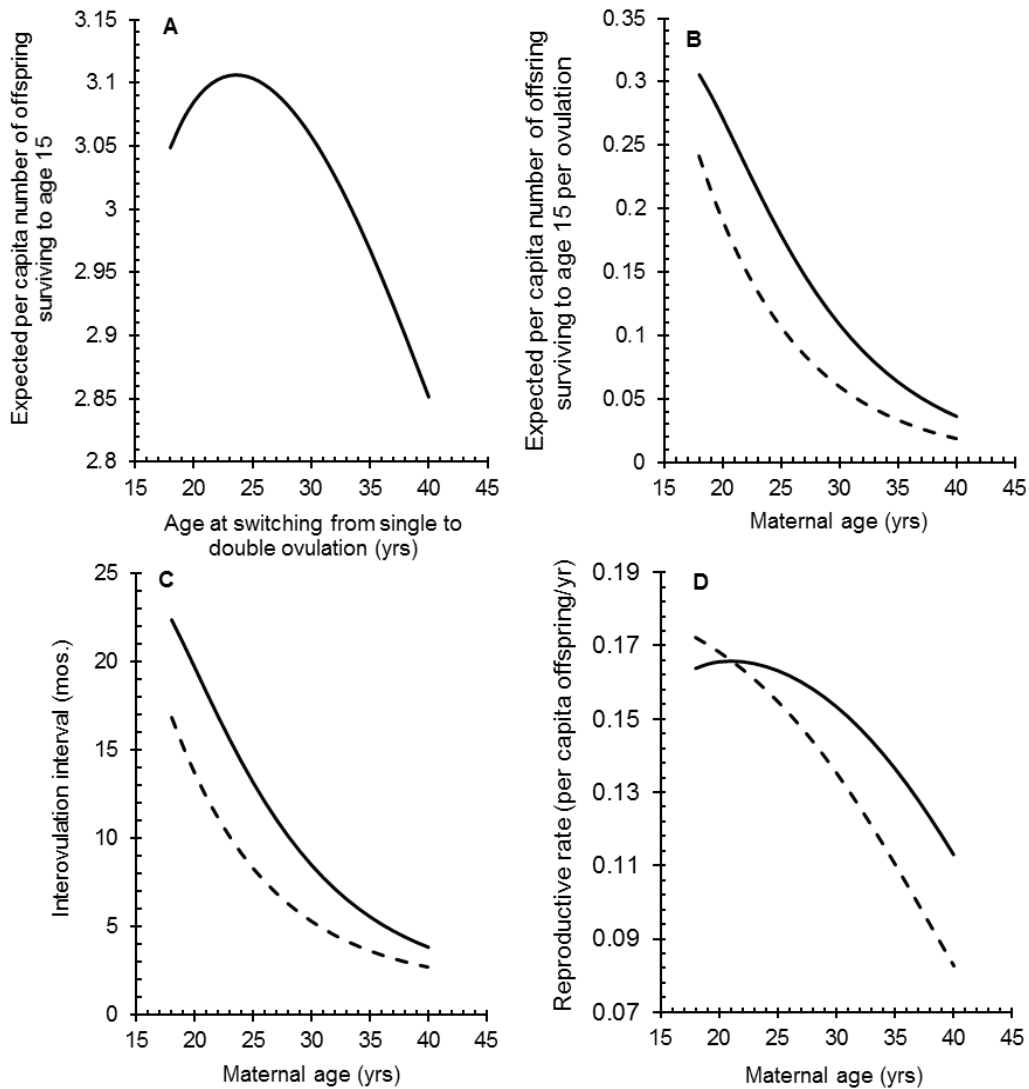


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406 **Fig. 2.** Average per capita numbers of offspring surviving to 15 years ($\pm 95\%$ CI, $n=10$) from
 407 simulations of the reproductive lives of 1000 women. When age of switch is 18 women always
 408 double ovulate throughout their reproductive lives; when it is 40 (age of menopause), they
 409 always single ovulate throughout their reproductive lives. When the switch age is between 18
 410 and 40, women are playing different conditional strategies defined by the switch age. **a,** Women
 411 that double ovulated could give birth to twins. **b,** Women that double ovulated carried only one
 412 offspring to term.

413



414

415 **Fig. 3.** Results of mathematical modeling of the reproductive characteristics of different
 416 ovulatory strategies. **a**, Expected lifetime reproductive success for women switching from single
 417 to double ovulation at different ages. **b**, Per capita number of offspring surviving to age 15 per
 418 ovulation for double (solid line) and single ovulators (dashed line) at different ages. **c**, Time
 419 between successive ovulations for double (solid line) and single ovulators (dashed line) at
 420 different ages. **d**, Expected annual reproductive rates for double (solid line) and single ovulators
 421 (dashed line) at different ages.

422

423 **Table 1. Estimates of the parameters that explain age-dependent twinning rates in nine**
 424 **human populations**

Population	n	<i>drb</i>	<i>dra</i>	<i>spm</i>	<i>spSD</i>	R ₂	study
African (Nigerian)	18,400	0.93	0.55	32.67	8.02	0.93	<i>16</i>
African (American)	22,100	0.92	0.55	49.62	13.76	0.96	<i>15</i>
African (American)	3,679	0.89	0.55	38.47	8.22	0.91	<i>17</i>
European (American)	21,809	0.89	0.55	44.80	10.27	0.97	<i>17</i>
European (Scottish)	49,000	0.87	0.55	39.56	7.98	0.90	<i>16</i>
European (American)	5,672,228	0.88	0.55	43.70	9.84	0.91	<i>15</i>
European (Italian)	1,817,736	0.88	0.55	39.05	7.53	0.99	<i>3</i>
European (Australian)	45,956	0.89	0.55	43.61	9.89	0.96	<i>18</i>
Asian (Japanese)	72,180	0.89	0.55	45.74	9.64	0.99	<i>19</i>
Mean ±	858,120.89	0.89	0.55	41.91	9.46	0.95	
SE	633136.269	0.007		1.664	0.636	0.012	

425 *drb* is the annual decline in prenatal survival rate per zygote with increasing maternal age; *dra* is
 426 the live birth rate per zygote at maternal age 18 yrs.; *spm* and *spSD* are the mean and standard
 427 deviation, respectively, of the cumulative normal function for the double ovulation rate with
 428 increasing maternal age; R₂ is fraction of variation in age-dependent twinning explained by these
 429 parameters (see Fig. 1).

430