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**Age & Fertility:**  
*Can women wait until  
their early thirties to try for  
a first birth?*

## **Age and fertility:**

**Can women wait until their early thirties to try for a first birth?**

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# *First birth postponed versus foregone*

- **progressive postponement of age at family formation**
- **if start of childbearing is postponed too long, it might be impossible for couples to reach their reproductive goals**
- **can we wait until the early 30s?**

## *Age and (in)fertility*

- **increased interest in studies on the relationship between biological ageing and probability of conception**
- Weinstein M, Wood J & Chang MC (1993) **Age patterns of fecundability**. In R. Gray (ed.) Biomedical and demographic determinants of reproduction. Oxford: Clarendon Press.

# ***Coital frequency across the life course***

- if coital frequency decreases with age
- any analysis which fails to take this into account would yield an apparent, but artefactual, decline in fecundability with age (Weinstein et al 1993)

# *Coital frequency across the life course*

- (study of) pattern is not so simple
- “marriage duration, women’s age and husband’s age will always increase together at the exact same rate; *these effects are completely confounded for longitudinal data* on a single couple”
- Brewis A & Meyer M (2004) Marital coitus across the life course. *Journal of Biosocial Science* 37, 499-518.

## *Age and fertility*

- in order to correctly estimate the age effect on the biological capacity to conceive, it is crucial to adequately adjust for sexual behaviour
- limit of past studies: lack of data on pattern of sexual behavior within a menstrual cycle and over the life course

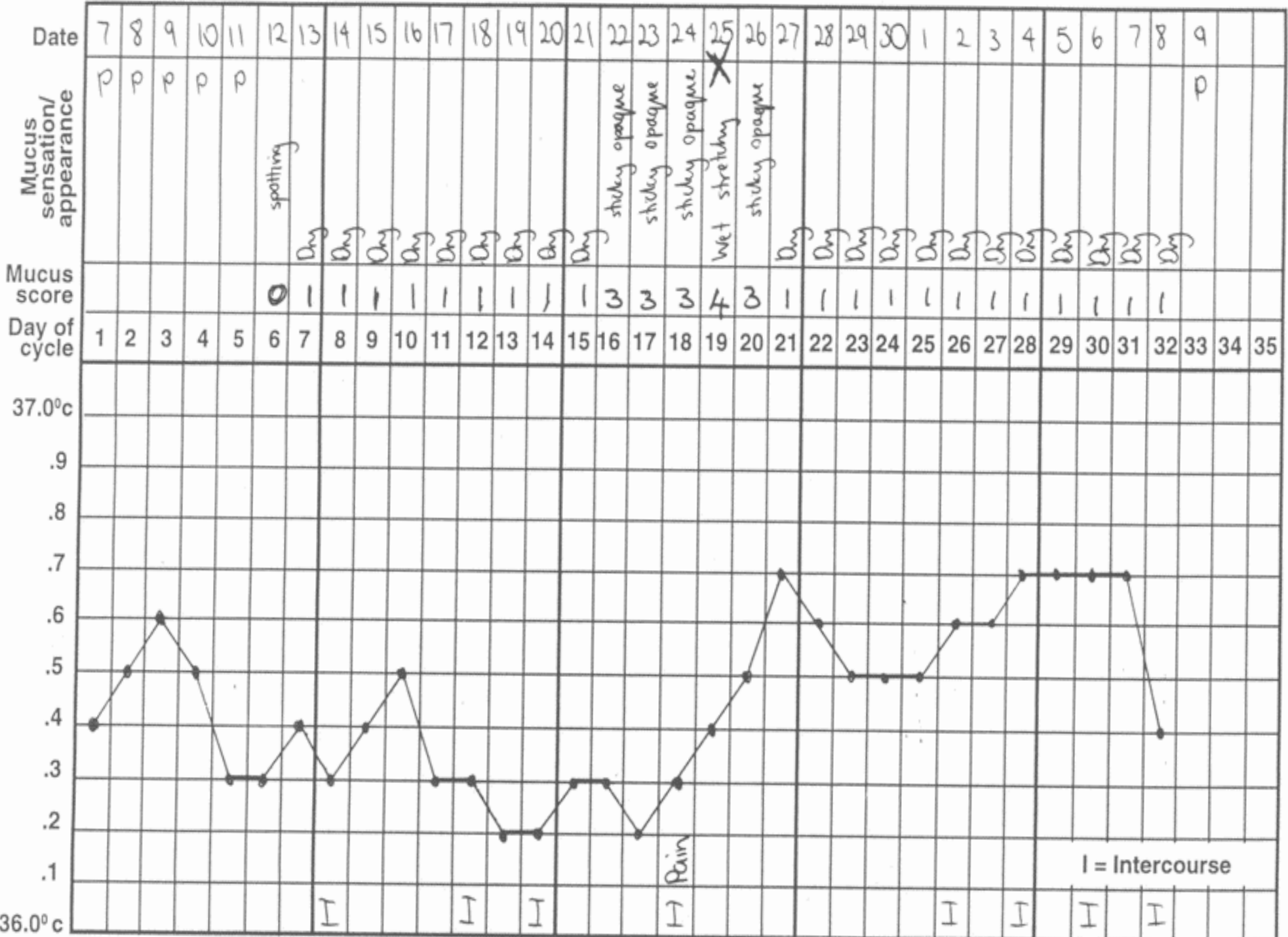
# *Age pattern of fecundability & sterility*

• difficult to estimate the **(unobserved)**

**age pattern of fecundability and sterility**

- model waiting time to conception
- model probability of sterility
- how to model female & male age effects?
- **how to model effects of coital pattern relative to ovulation?**
- unobserved heterogeneity

Month November



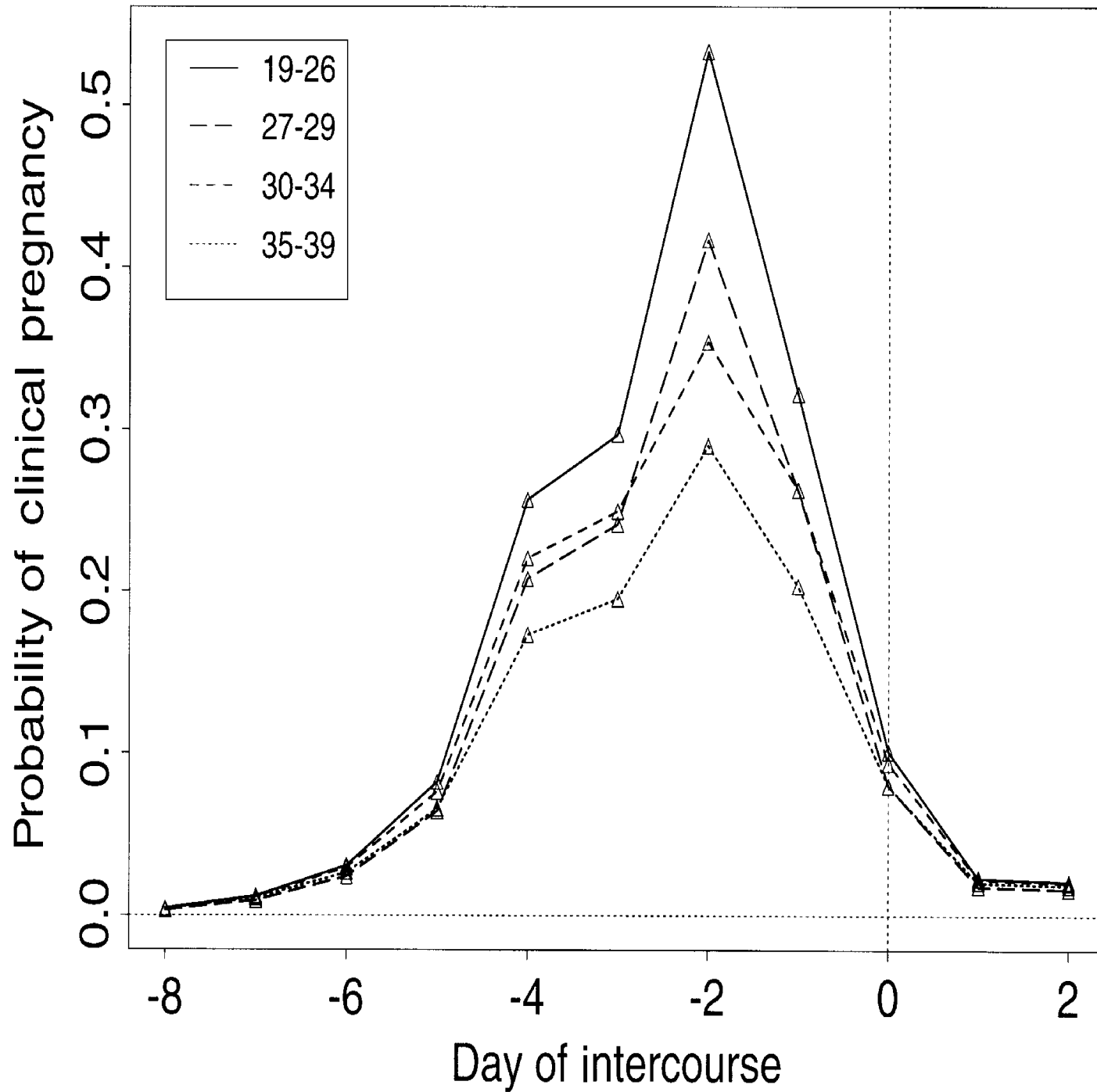
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## ***Dunson, Colombo & Baird (2002)***

- Menstrual Cycle Fecundability Study (MCFS) data
- Dunson D, Colombo B & Baird D (2002) Changes with age in the level and duration of fertility in the menstrual cycle. Human Reproduction 17, 1399-1403
- **all pregnancies studied**
- "to evaluate the effects of male and female age on natural fertility by carefully controlling for variation in sexual behaviour"?

## ***Dunson, Colombo & Baird (2002)***

- **"women's fertility begins to decline in the late 20s with substantial decreases by the late 30s"**
- "Fertility for men is less affected by age, but shows significant decline by the late 30s."
- estimated daily probabilities of conception relative to ovulation for women aged 19-26, 27-29, 30-34 and 35-39



# ***Menstrual Cycle Fecundability Study***

- **multinational longitudinal study of users of natural family planning**
- women had no sign of infertility at entry
- women aged 18-40
- **cervical mucus quality used to identify day of ovulation (day 0)**
- **presence of intercourse collected for each day**
- 7,017 cycles from 881 couples & 575 pregnancies

# ***Our study with MCFS data***

- **first clinical pregnancies to women aged 20-36**
- husband/partner is aged less than 40
- **342 nulliparous couples with 1,595 menstrual cycles**
- only include cycles with at least one intercourse in the 12-day interval (-8, 3) [no pregnancies when intercourse only outside of interval (-8, 3)]
- **210 with first pregnancy (uncensored data)**
- **132 did not conceive (censored data & possibly sterile)**

# *Mixture model for two populations*

## sterile and nonsterile populations

$$Y = \begin{cases} 1 & \text{if eventually having the event (fecund)} \\ 0 & \text{if zero risk (sterile), i.e., long-term survivor} \end{cases}$$

## $Y$ is partially observable

$$Y = \begin{cases} \text{known} & \text{for uncensored observation} \\ \text{missing} & \text{for right-censored observation} \end{cases}$$

## logistic model for distribution of $Y$

$$\text{logit}(\text{pr}(Y = 1)) = F' \beta$$

## ***Mixture model for two populations . . .***

- **'sterility/conditional fecundability' mixture model**
- **discrete-time survival model for cycle-specific probability of first conception for those fecund**
- **time starts at entry into MCFS study**
- **logistic regression model for primary sterility**

# *Mixture model for two populations ...*

- see for further details

McDonald JW & Rosina A (2001) Mixture modelling of recurrent event times with long-term survivors: Analysis of Hutterite birth intervals. *Statistical Methods & Applications* 15, 257-272

- **Bayesian estimation** with non-informative or 'mildly' informative priors with posterior distribution summarized by mean or median and/or 2.5% & 97.5% percentiles for 95% credible interval

# ***Logistic-normal-geometric model***

- **geometric distribution when discrete hazard**

$P(T = t \mid T \geq t)$  **is constant over time**

- **unobserved heterogeneity in risk is modelled by a mixed-geometric model for waiting times**

$$\text{logit}(\text{hazard} \mid \text{fecund}) = X'\beta + Z\sigma$$

$$Z \sim N(0, 1)$$

- $Z$  unobserved covariate value
- $\sigma$  standard deviation parameter
- $Z\sigma$  random effect

# ***Our model specification***

- **female age effects: restricted cubic spline** with knots at age 24, 28 & 32
- **male age effects:** dummy variable < 35 and 35+
- **center effects:**
  - Verona (reference category)
  - Milano
  - Lugano
  - Paris
  - Düsseldorf
  - London
  - Brussels

# ***Our model specification***

- **windows - day 0 is ovulation**
  - A (-2, -1, 0), B (-4, -3, 1), C (-8, -7, -6, -5, 2, 3)
- **coital pattern and frequency categorized**
  - 2+ acts of intercourse in A (reference category)
  - one act of intercourse in A
    - A no, B yes, C yes
    - A no, B yes, C no
    - A no, B no, C yes

# ***No. of couples, cycles & pregnancies***

**Number of Couples, Menstrual Cycles and Pregnancies After Applying Successive Selection Criteria. The Last Row Is the Analytic Sample.**

	Number of couples	Number of cycles	Number of pregnancies
total in Menstrual Cycle Fecundability Study	881	7,017	575
only European centers	782	6,724	487
& women's first entry in the study	782	5,641	413
& women aged 20-36 years old*	739	5,188	397
& partner aged less than 40**	718	5,021	389
& <b>nulliparous women</b>	<b>420</b>	<b>2,860</b>	<b>241</b>
& cycles with peak mucous day identified	411	2,725	222
& at least five cycles after stopping contraceptive pill	387	2,641	210
& <b>cycles at risk of conception***</b>	<b>342</b>	<b>1,595</b>	<b>210</b>

Notes: \* woman's age at first entry and first observed cycle

\*\* partner age at woman's first entry and first observed cycle

\*\*\* **only cycles with at least one intercourse in the 12-day interval (-8, 3)**

# ***Prob. of conception by age of woman***

## **Probability of Conception by Age of Woman**

Age of woman	Number of women*	Number of cycles**	Number of pregnancies	Probability of conception
< 24	30	106	12	0.113
24 – 27	155	568	91	0.160
28 – 31	154	771	89	0.115
32+	35	150	18	0.120

Notes: \* at least one cycle in the age group

\*\*at least one cycle in the age group

# *Coital patterns by age*

## **Percentage Distribution of Coital Patterns by Age of Woman\***

Coital pattern	All ages	< 24	24 – 27	28 – 31	32+
A no, B no, C yes	37.6	48.0	44.5	33.7	23.3
A no, B yes, C no	3.7	4.7	1.9	4.5	5.3
A no, B yes, C yes	11.0	12.3	9.9	12.2	8.7
Only 1 act in A	30.5	20.8	25.0	33.6	42.0
2 or 3 acts in A	17.2	14.2	18.7	16.0	20.7

Notes: \* age at the beginning of the menstrual cycle

Windows relative to day 0 (mucus reference day)

A : (-2, -1, 0)

B : (-4, -3, 1)

C : (-8, -7, -6, -5, 2, 3)

# ***Logistic model for primary sterility***

- **only covariate was age of woman**
- mean of posterior distribution was .728
- median of posterior distribution was .685
- 95% credible interval was [-.077, 1.775]
- **linear effect in the expected positive direction, but not significant**

## ***Logistic model for primary sterility ...***

- probabilities of being fecund can be estimated for individual women who did not conceive**
- posterior probability that a woman with vector of covariates  $x$  comes from population  $Y = 1$  (fecund), given that no conception has occurred by time  $t$ , is

$$\mathbf{P}(Y = 1 | x, T > t) = \frac{\mathbf{P}(Y = 1 | x) S(t | Y = 1, x)}{\mathbf{P}(Y = 0 | x) + \mathbf{P}(Y = 1 | x) S(t | Y = 1, x)}$$

## ***Logistic model for primary sterility ...***

- posterior medians were 1 for all non-conceiving women, **except for 3 women in their 20s with long periods of exposure**
- for these 3 women, posterior medians were 0
  - posterior mean .842 (26 cycles observed)
  - posterior mean .778 (20 cycles observed)
  - **posterior mean .004 (20 cycles observed)**
- **last: aged 22 with young partner, 4 cycles with intercourse pattern A no, B yes, C yes, 9 with only 1 act in A & 7 cycles with 2+ acts in A**

# Waiting time to conception models

	cubic spline model*			linear model		
	mean	2.5%	97.5%	mean	2.5%	97.5%
constant	0.411	-0.857	1.642	0.194	-0.528	0.922
Age of woman						
age	-0.139	-0.330	0.042	<b>-0.103</b>	<b>-0.176</b>	<b>-0.028</b>
knot at age 24	0.001	-0.004	0.005			
knot at age 28	-0.000	-0.018	0.017			
knot at age 32	-0.008	-0.049	0.030			
Age of man						
< 35						
35+	-0.674	-1.536	0.150	-0.664	-1.474	0.129

# Waiting time to conception models ...

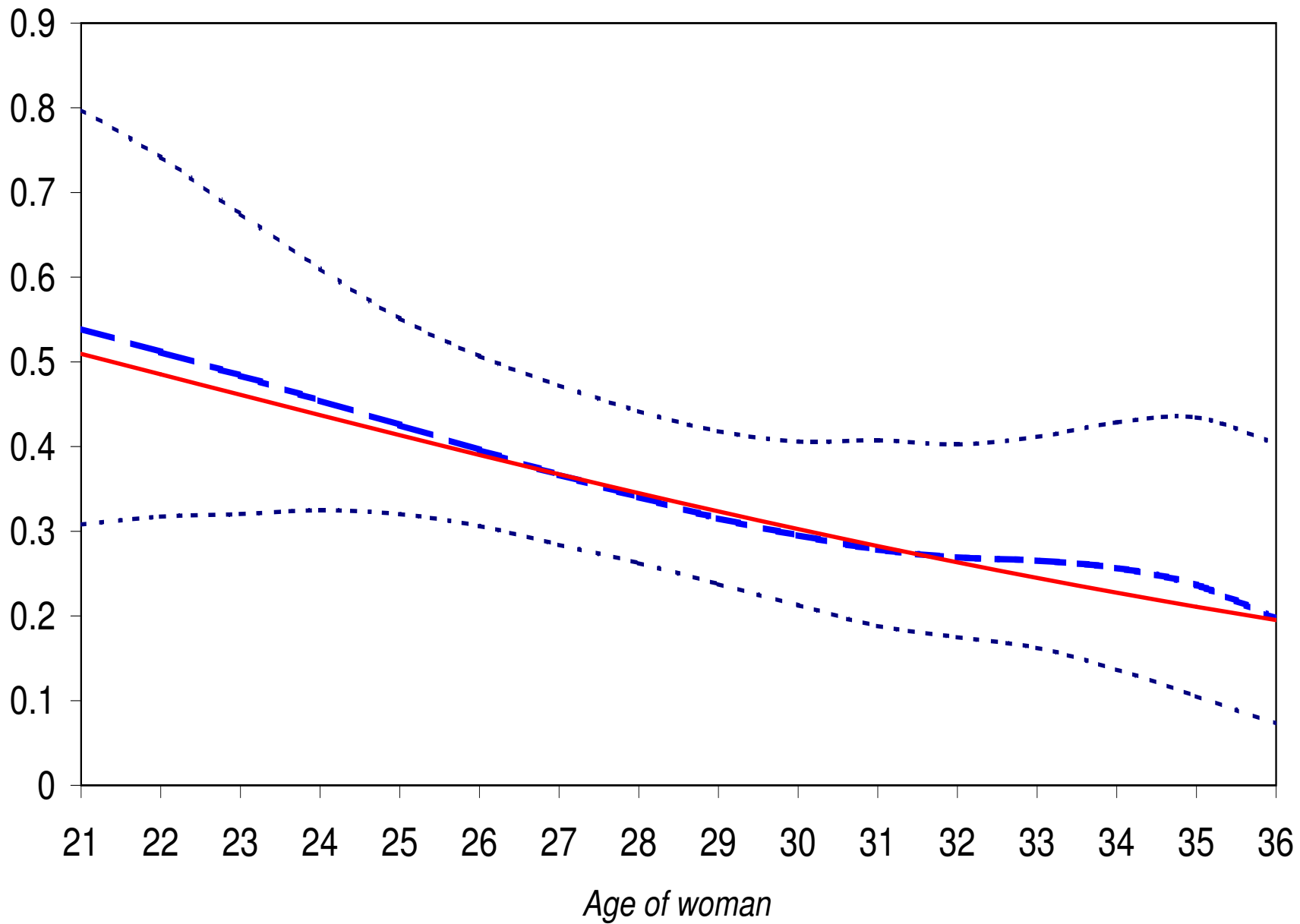
Study center	cubic spline model*			linear model		
	mean	2.5%	97.5%	mean	2.5%	97.5%
Verona						
Milano	-0.287	-0.679	0.105	-0.276	-0.702	0.144
<b>Lugano</b>	<b>2.198</b>	<b>0.663</b>	<b>3.861</b>	<b>2.145</b>	<b>0.643</b>	<b>3.747</b>
Paris	-0.251	-1.251	0.704	-0.230	-1.221	0.708
Düsseldorf	0.663	-0.207	1.499	0.693	-0.179	1.527
London	0.695	-0.391	1.757	0.652	-0.447	1.717
Brussels	0.088	-1.315	1.427	0.146	-1.216	1.443

**NB Lugano mostly enrolled couples planning a pregnancy**

(8 couples and 7 pregnancies among nulliparous women)

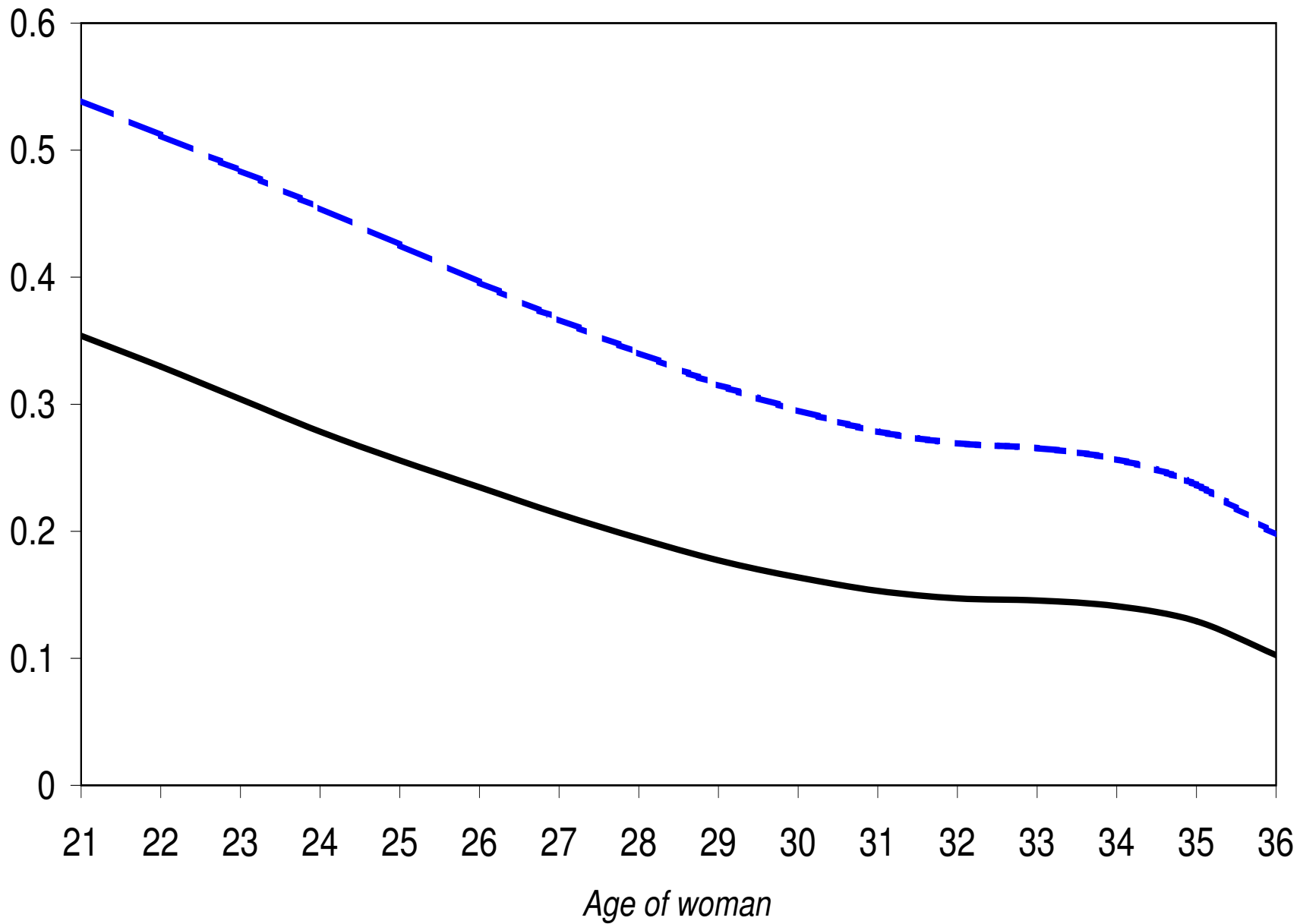
# Waiting time to conception models ...

	cubic spline model*			linear model		
	mean	2.5%	97.5%	mean	2.5%	97.5%
Pattern of intercourse						
A no B no C yes	-3.945	-4.852	-3.127	-3.925	-4.853	-3.098
A no B yes C no	-0.938	-1.845	-0.130	-0.936	-1.825	-0.137
A no B yes C yes	-0.797	-1.348	-0.267	-0.790	-1.342	-0.261
Only 1 act in A	-0.593	-0.996	-0.206	-0.586	-0.990	-0.194
2 or 3 acts in A						
Random effect						
$\sigma$	0.631	0.104	1.052	0.621	0.119	1.012



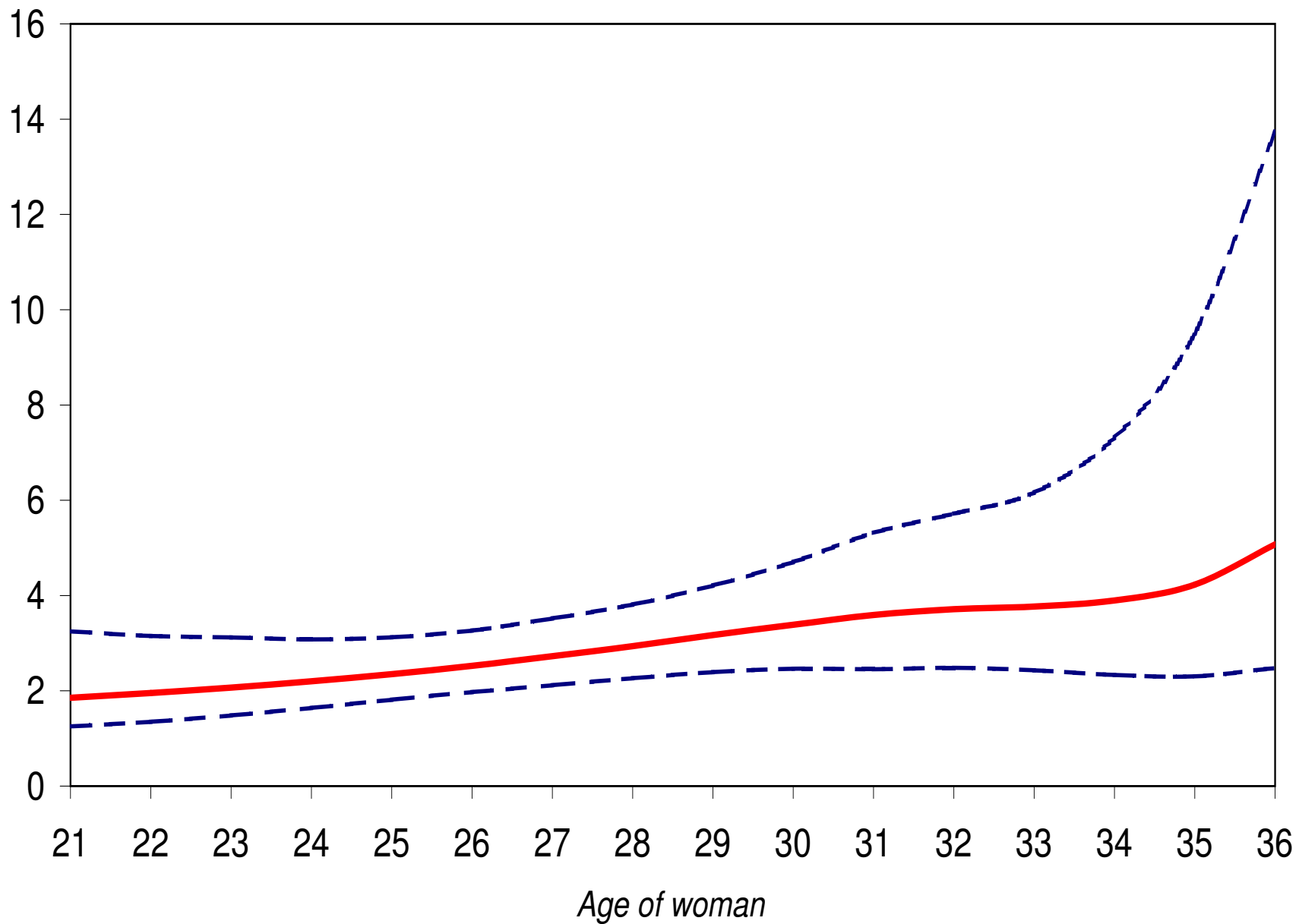
Median hazard for the cubic spline (dashed line) & linear models (solid line) with 95% credible interval for the cubic spline model

2+ acts in A (-2, -1, 0), Verona, young partner



Median hazard - **dashed line**: 2+ Acts window A (-2, -1, 0)

solid line: no in A, but yes in B (-4, -3, 1) & C (-8, -7, -6, -5, 2, 3)



**solid line:** estimated mean waiting time to first conception in menstrual cycles with 95% credible interval

**2+ acts in A (-2, -1, 0), Verona, young partner**

# Results

- present results from the cubic spline model as it is more robust to model misspecification of age effects
- Figure 1 - **decline in the median hazard for the reference group is almost linear with age**
- median hazard at age 21 is 0.54 and at 35 is 0.24
- from 28 to 33, median hazard ↓ from 0.34 to 0.27
- size of the decline depends on our choice of reference group, namely those with 2+ acts of intercourse in window A (-2, -1, 0)

## *Results ...*

- Figure 3 - **increase in estimated mean waiting time is almost linear** with age of woman until age 34 when there is an upturn
- estimate at age 21 is 1.85 cycles and at age 34 is 3.90 cycles
- from 28 to 33, estimated mean waiting time for our reference group  $\uparrow$  from 2.94 to 3.77 cycles
- **very modest increase of little practical importance**

## *Results ...*

- our random effects model should capture time-constant unobserved heterogeneity at the couple level, whether behavioral or environmental, so that our conclusions are expected to be more robust than those based on an event history model that did not include a random effect
- **substantial unobserved heterogeneity that is not accounted for by age of woman, coital pattern or the other covariates included in the model**

## ***Results ...***

- **we found the result of a decline in fecundability from the early 20s surprising** as we expected an increase in fecundability to the middle 20s and then a decline
- evidence that a woman's fecundability declines before the age of 30 is not new in demography, see Larsen and Vaupel (1993)

Larsen U & Vaupel JW (1993) Hutterite fecundability by age and parity: Strategies for frailty modeling of event histories. *Demography* 30, 81-102

# *How late can you wait?*

- can you wait until your 30s? Yes, providing you are not sterile
- can you wait until your 40s? Linear extrapolation
  - ⇒ median hazard at age 41 of .1 for 2+ acts in A
    - conditional on not being sterile
    - but large uncertainty on estimate

# ***Sterility***

- little information on age pattern of sterility
- limited followup on too few couples
- only 6.3% followed for 12+ cycles

## ***Limited information on couples***

- no intentions for each cycle, i.e. trying to achieve or avoid conception
- no covariate information, except
  - when married
  - number of previous pregnancies
  - previous use of pill

# ***Sample selection & selection effects?***

- time origin for the waiting time to conception is entry into study
- some couples intending to enroll in the study might have become pregnant before entry and therefore, ineligible for our study of first pregnancies
- categorised time from marriage to entry into study:  
1) same month as marriage, 2) 1-11 months after marriage, 3) 12+ months after marriage and 4) NA
- this variable was not significantly related to the waiting time to conception