The biological obstacles to late childbearing and the limits of ART

Henri Leridon

Ined-Inserm, Paris

# What are the risks of wanting a child late in reproductive life?

1. For the newborn
2. For the mother (pregnancy and delivery)
3. Of miscarriage
4. Of a long delay before conceiving
5. Of not getting pregnant

Risks 1and 2 will not be considered here

What do we know about the effect of age on these risks?

- **Miscarriage**: many data available, showing a *substantial increase beyond 30-35 years* (woman's age)

- **Fecundability**: less clear trends, at least before 40 years (*but the decline in fecundability may be related to the age at sterility onset*)

- **Sterility**: somewhat overestimated in the past, because estimates included the effect of miscarriages. *But to be considered!*

Figure 2. Mean proportion of pregnancies ending in a miscarriage (per 1000 pregnancies), by age of woman at conception
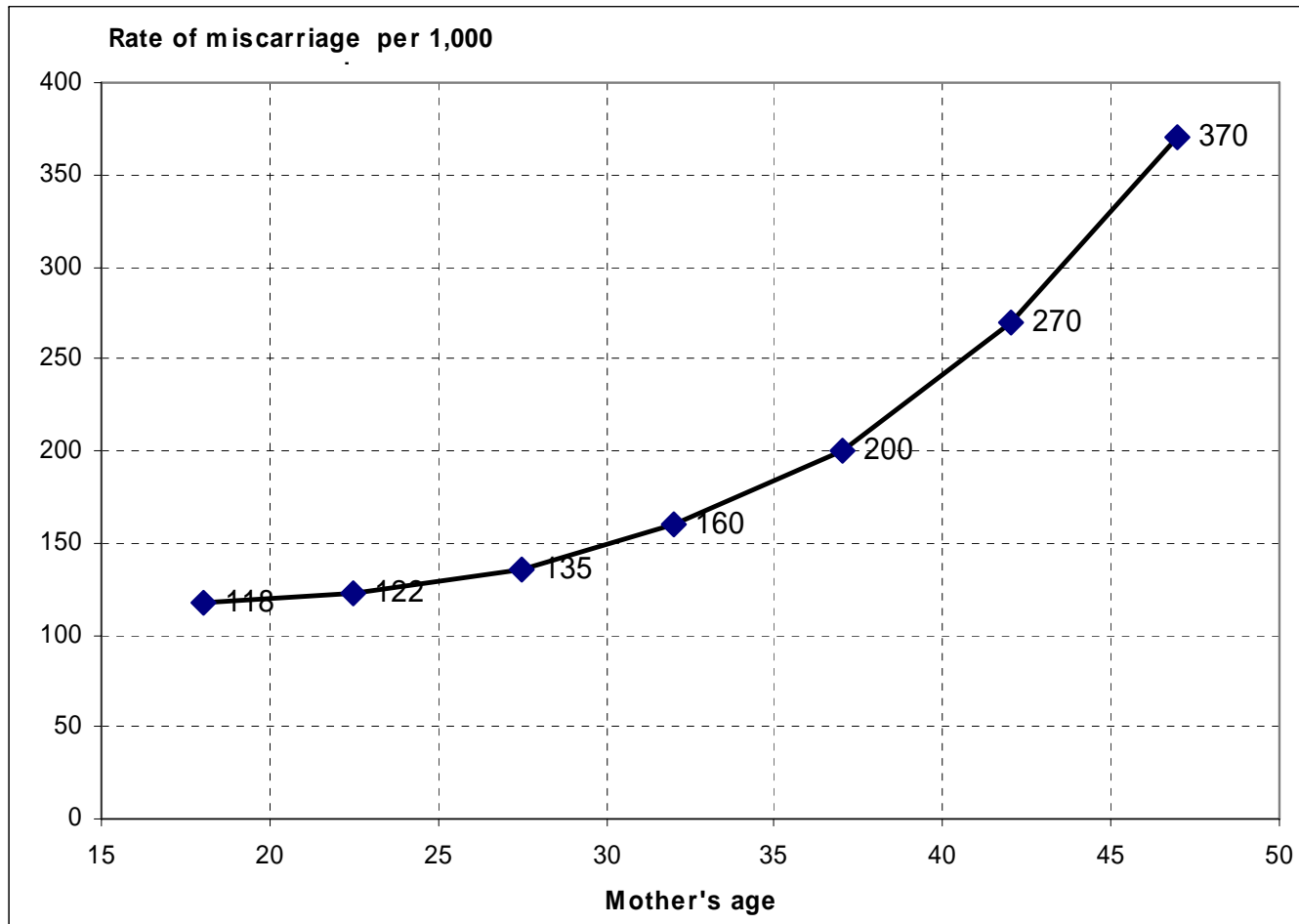
Sterility and age
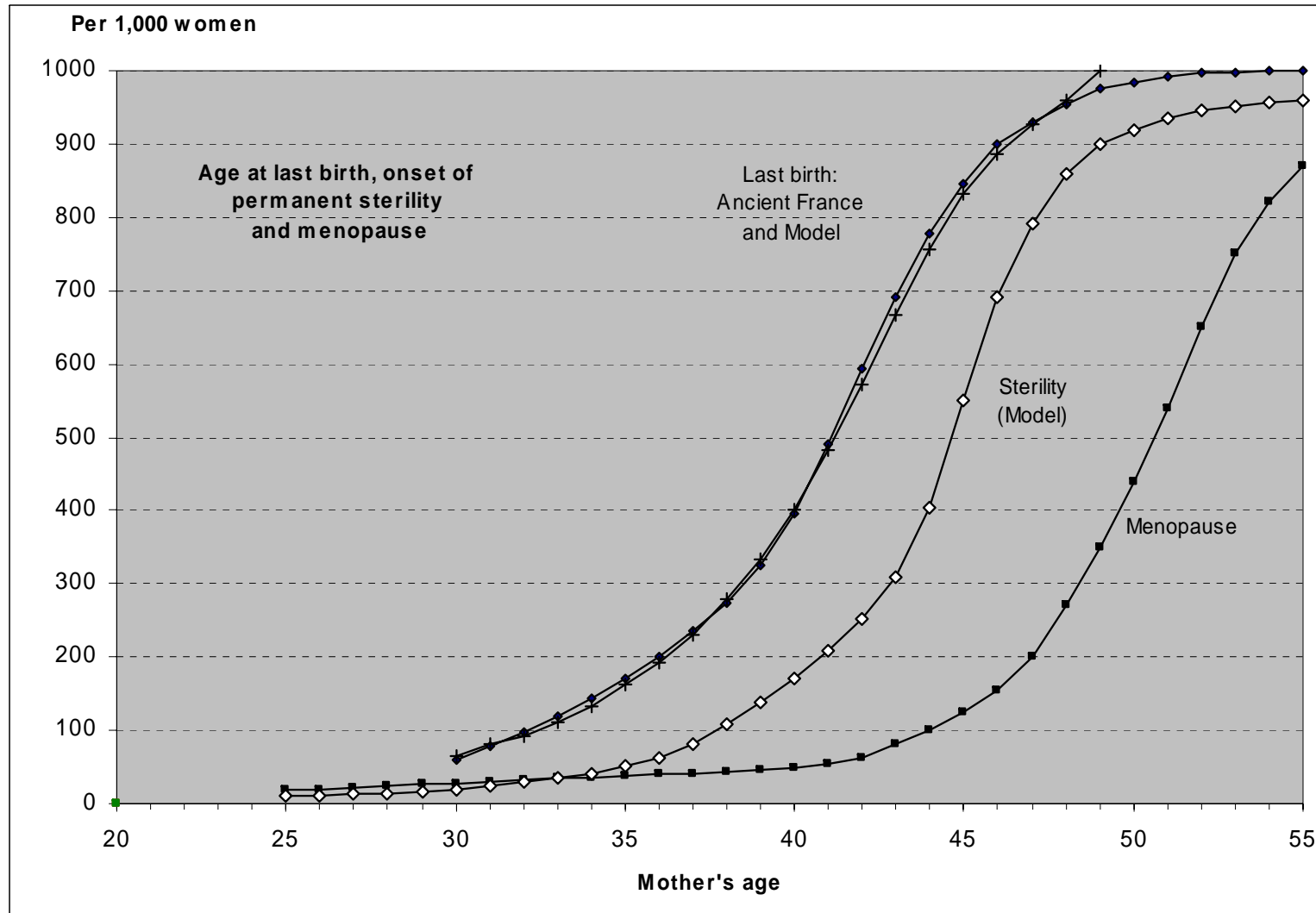
Proportion (%) of couples definitively sterile by woman's age:

previous and new estimates

Age	No more live birth							No more conception
	Vincent (1950)	Henry (1953) Angleterre	Henry (1953) Norvège	Pittenger (1973)	Leridon (1977)	Trussell-Wilson (1985)	Menken-Larsen (1986)	**Leridon (Sim56)**
20	4	3.5	3.5	2.2	3		4	
25	6	6	5	3.3	6	6	7	**1**
30	10	11	8	6.5	10	11	12	**2**
35	17	19	13	16	17	16	22	**5**
40	37	33	24	40	29	24	46	**17**
45	75	58	50	79	50	58		**55**
Median	42.0	43.3	45.0	41.5	45.0	44.0	40.8	**44.7**

- **To understand how these factors interplay, we need aggregated models.**

>>>> SIMULA (a Montecarlo simulation)

H. Leridon:

Can assisted reproductive technology compensate for the natural decline in fertility with age? *Human reproduction 2004, 19(7):1548-53*

How effective is assisted reproduction technology? A model assessment. *Rev. Epidemiol Sante Publique 2005, 53: 2S119-127*

A new estimate of permanent sterility by age *(submitted)*

Interplay between biological variables and demographic fertility/fecundity. *(Copenhagen Workshop on Environment, Reproductive Health and Fertility, Jan 15-18, 2005)*

Success rates without ART, by age of woman (p = 0.23)
(Pregnancies ending in live births)

	Woman's age when starting to try to get pregnant		
	30 yrs	**35 yrs**	**40 yrs**
Per 100 women of each age:			
Results without ART			
Success: conception (LB) within 12 mo	**75,4**	**66,0**	**44,3**
Delay: conception (LB) in 12-23 mo	10,9	12,3	12,7
conception (LB) in 24-35 mo	3,0	3,9	4,7
conception (LB) in 36-47 mo	1,4	1,7	2,0
Total Conceptions (LB) within 4 years	*90,7*	*83,9*	*63,7*
Total conceptions (LB) ever	*93,9*	*85,9*	*65,1*
At least 1 miscarriage before LB	*14,4*	*15,7*	*16,3*
Age Y when starting ART (in case of failure)	***34 yrs***	***38 yrs***	***42 yrs***
No conception at age Y	9,3	17,8	43,0

Success rates without ART, by age of woman (p = 0.40)

	Woman's age when starting to try to get pregnant		
	30 yrs	**35 yrs**	**40 yrs**
Per 100 women of each age:			
Results without ART			
Success: conception (LB) within 12 mo	**83,7**	**76,3**	**53,8**
Delay: conception (LB) in 12-23 mo	6,3	8,3	10,9
conception (LB) in 24-35 mo	2,0	2,1	3,2
conception (LB) in 36-47 mo	1,0	0,8	1,3
Total Conceptions (LB) within 4 years	*93,0*	*87,5*	*69,2*
Total conceptions (LB) ever	*95,6*	*88,9*	*70,1*
At least 1 miscarriage before LB	*14,4*	*16,0*	*17,2*
Age Y when starting ART (in case of failure)	*34 yrs*	*38 yrs*	*42 yrs*
No conception at age Y	7,0	13,3	35,3

Success rates with ART, by age of woman (p=0.23)

		Woman's age when starting to try to get pregnant		
		30 yrs	**35 yrs**	**40 yrs**
	Per 100 women of each age:			
	Age Y when starting ART (in case of failure)	*34 yrs*	*38 yrs*	*42 yrs*
a	No conception at age Y (failure)	9,3	17,8	43,0
	Total conceptions (LB) with ART			
	Success : conception (LB) within 12 mo	2,0	3,0	5,1
	Delay : conception (LB) in 12-23 mo	0,8	1,2	2,0
b	*Total conceptions (LB) within 2 years*	*2,8*	*4,2*	*7,1*
c	*Apparent rate of success for ART (%) = 100*b/a*	*30,1*	*23,6*	*16,5*
	No conception at age Y + 2	*6,5*	*13,6*	*35,9*
	Spontaneous conceptions (no treatment)			
d	Within 2 years	1,4	2,5	6,7
e	*Net rate of success for ART (%) = 100*(b-d)/a*	*15,1*	*9,6*	*0,9*
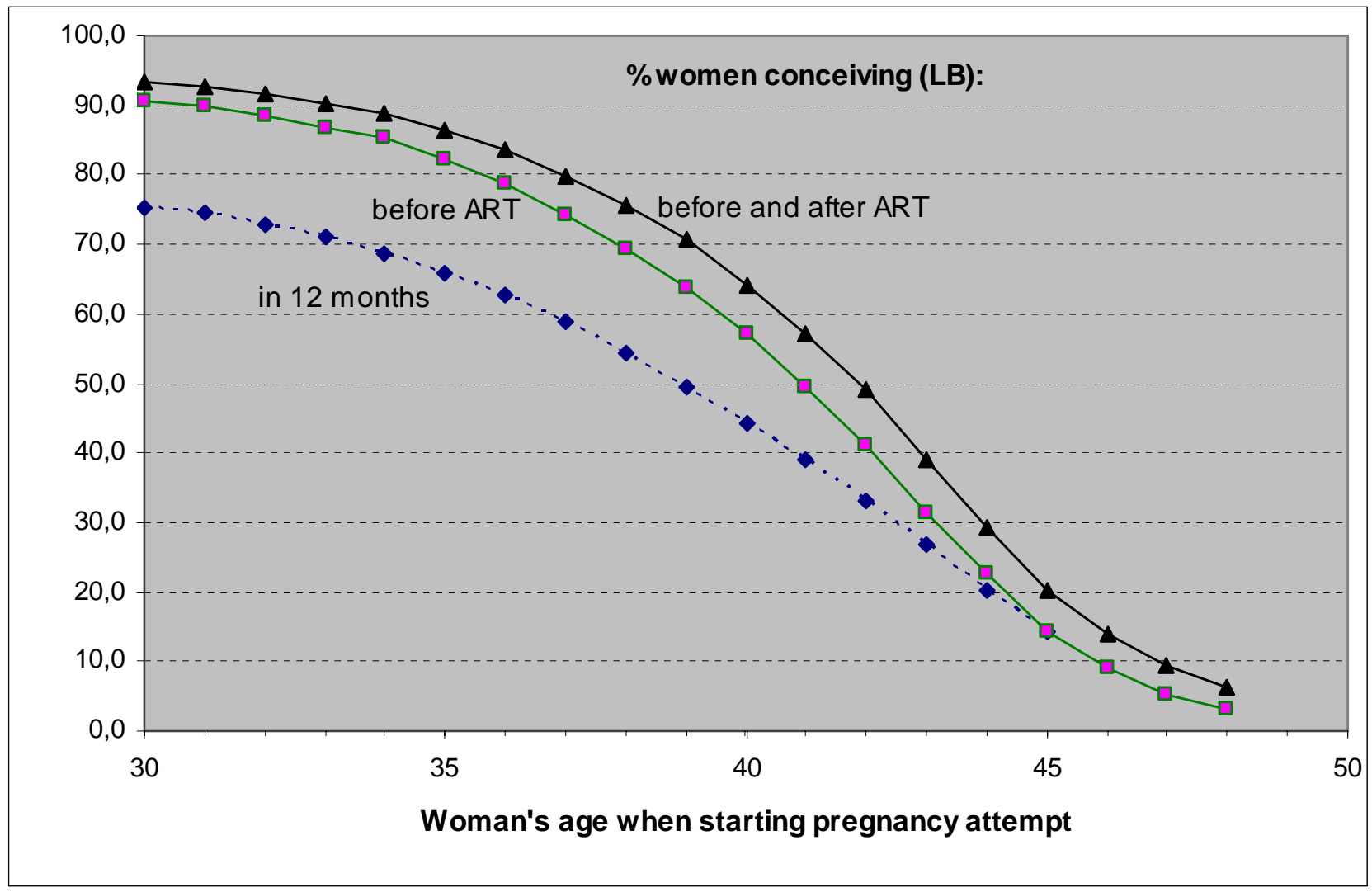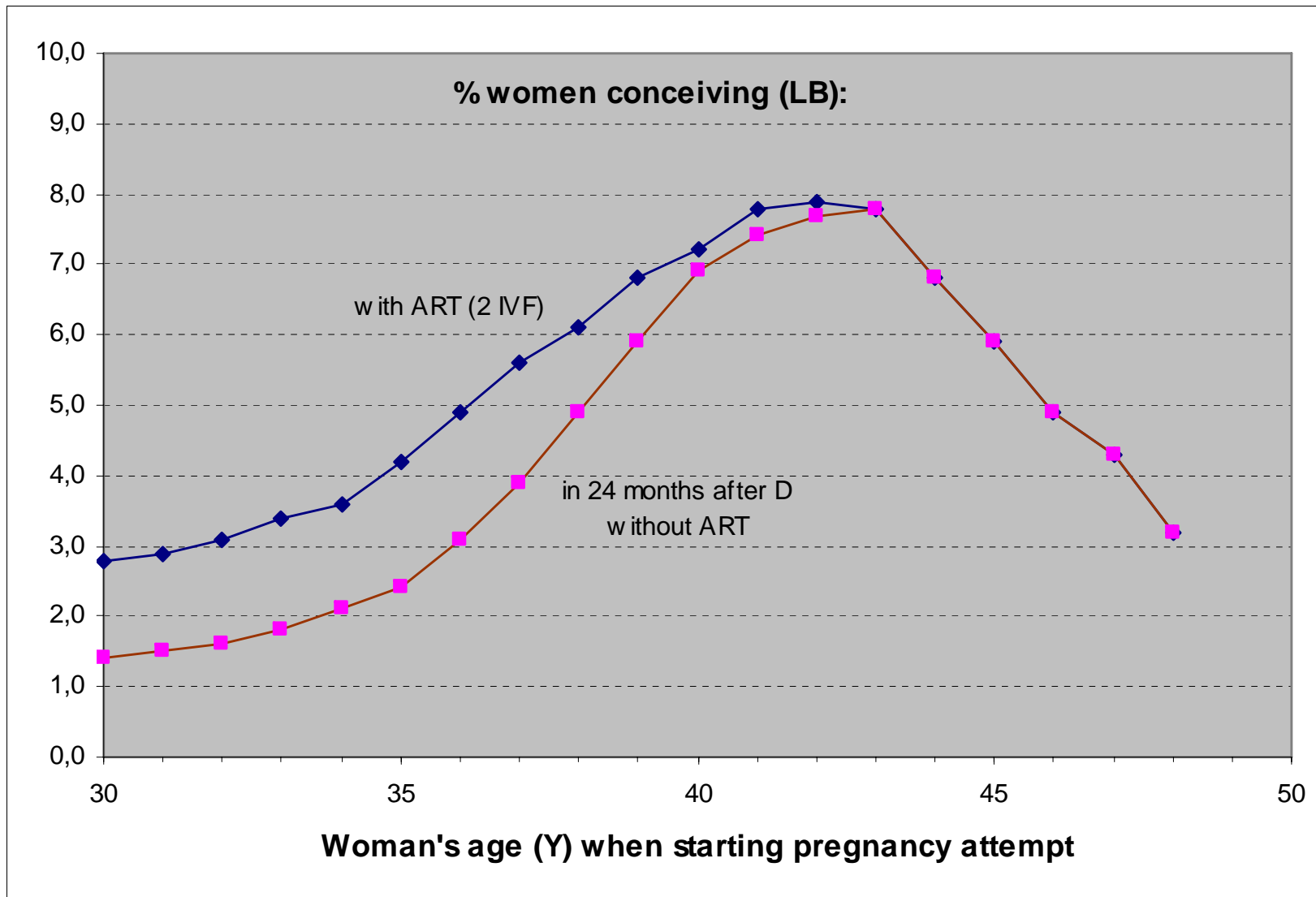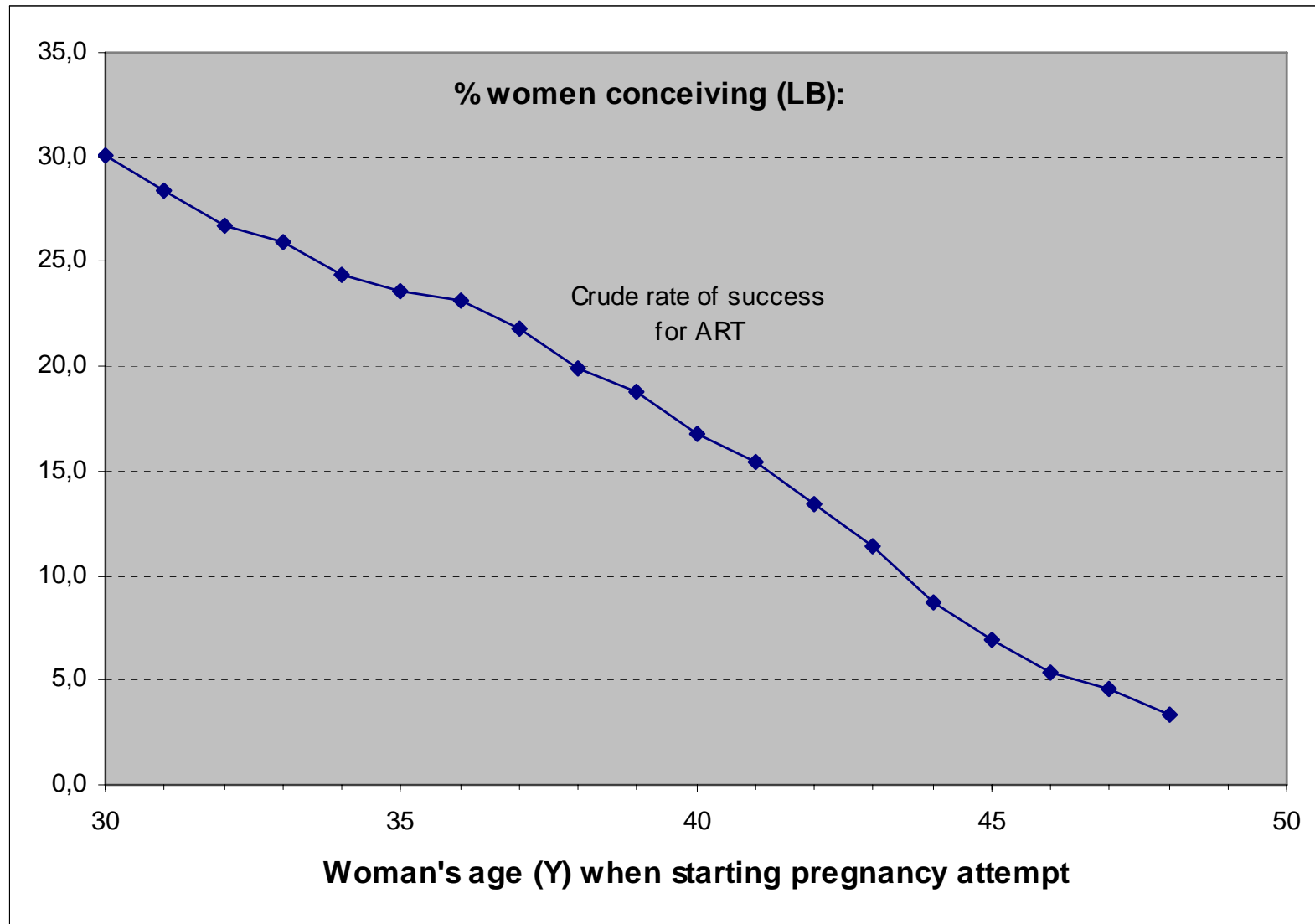
Table III - Fertility characteristics of couples turning to ART (model's value)

	30	35	40	45
Woman's age (Y) when starting pregnancy attempt (years)	**30**	**35**	**40**	**45**
Woman's age at the end delay D (years)	34	38	42	46
Among those having not conceived at age Y+D:				
% sterile at age Y+D	30.2	40.4	47.2	63.9
Mean fecundability at age Y+D	0.016	0.025	0.039	0.035

Assessing the effects of a decline in fecundability

	France (circa 2000)	**Model standard run**
Mean desired family size	2.21**	2.20(a)
Mean final number of births	2.00*	1.95
Mean age at 1st birth	27.9	27.9
Mean age at childbearing	29.4	30.1
% Childless women	10*	5
% Women with 1 child	19*	15
% women with 2 children	42*	45
% women with 3 children	22*	31
% women with 4 children +	7*	4
% unwanted births	7 % ***	8%

* Estimation for generation 1965
** Women 25-34 years (1998 Ined Survey)
*** Cocon survey (Inserm-Ined, 2000)
(a) 13% want 1child, 54 % want 2, and 33% want 3.

Leridon -LateChild - Vienna-2005

Assessing the effects of a decline in fecundability: results (1)

	Mean natural fecundability (at age 25)	Mean number of children (achieved)	Fertility reduction	Proportion childless (p. 100)
Standard run	0.230	1.950	-	4.7
Fecundability: - 7%	0.214	1.913	- 1.9 %	5.9
Fecundability: - 15%	0.195	1.905	- 2.3 %	5.8
Fecundability: - 50%	0.115	1.807	- 7.3 %	6.5
Marriage delayed by 2 yrs	0.230	1.858	- 4.7 %	6.8

Assessing the effects of a decline in fecundability: results (2)

	Mean fecundability (at age 25)	Proportion with more births than wanted (p.100 women)	Proportion of births unplanned (p.100 births)	Mean time to conception (1st birth) (months)	TTC > 1 year (1st birth) (%)
Standard run	0.230	13.9	42.2	8.9	18.3
Fecundability: - 7%	0.214	12.8	40.8	9.5	19.7
Fecundability: - 15%	0.195	11.7	39.0	10.1	21.8
Fecundability: - 50%	0.115	6.7	28.4	14.2	35.4
Marriage delayed by 2 yrs	0.230	11.0	40.9	8.7	18.9

CONCLUSION

- *Postponing births beyond age 30-35 is a problem, mainly at the individual level but also for its demographic consequences*

- *Assisted reproduction techniques will not solve 100% of the problem*