

Assisted reproduction and fertility: The case of Denmark

Tomáš Sobotka

W. Lutz (VID)

T. K. Jensen, R. Jacobsen, A. T. Pedersen, M. Hansen, and N. E. Skakkebak
(Department of Growth and Reproduction, Rigshospitalet, Copenhagen)



OAW
Austrian Academy
of Sciences

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INTRODUCTION

Rising importance of assisted reproduction for fertility in developed countries:

- Increasing number of births after an ART (1-3 % in most Western & Northern European countries in 2003; ESHRE 2007)
- Huge increase in the number of multiple births in the 1990s
- Contributes to a rise of fertility rates at ages 40+
- Helps realising fertility desires among infertile couples
- Helps offsetting part of the effect of increasing infertility due to fertility postponement (Leridon 2004)

INTRODUCTION

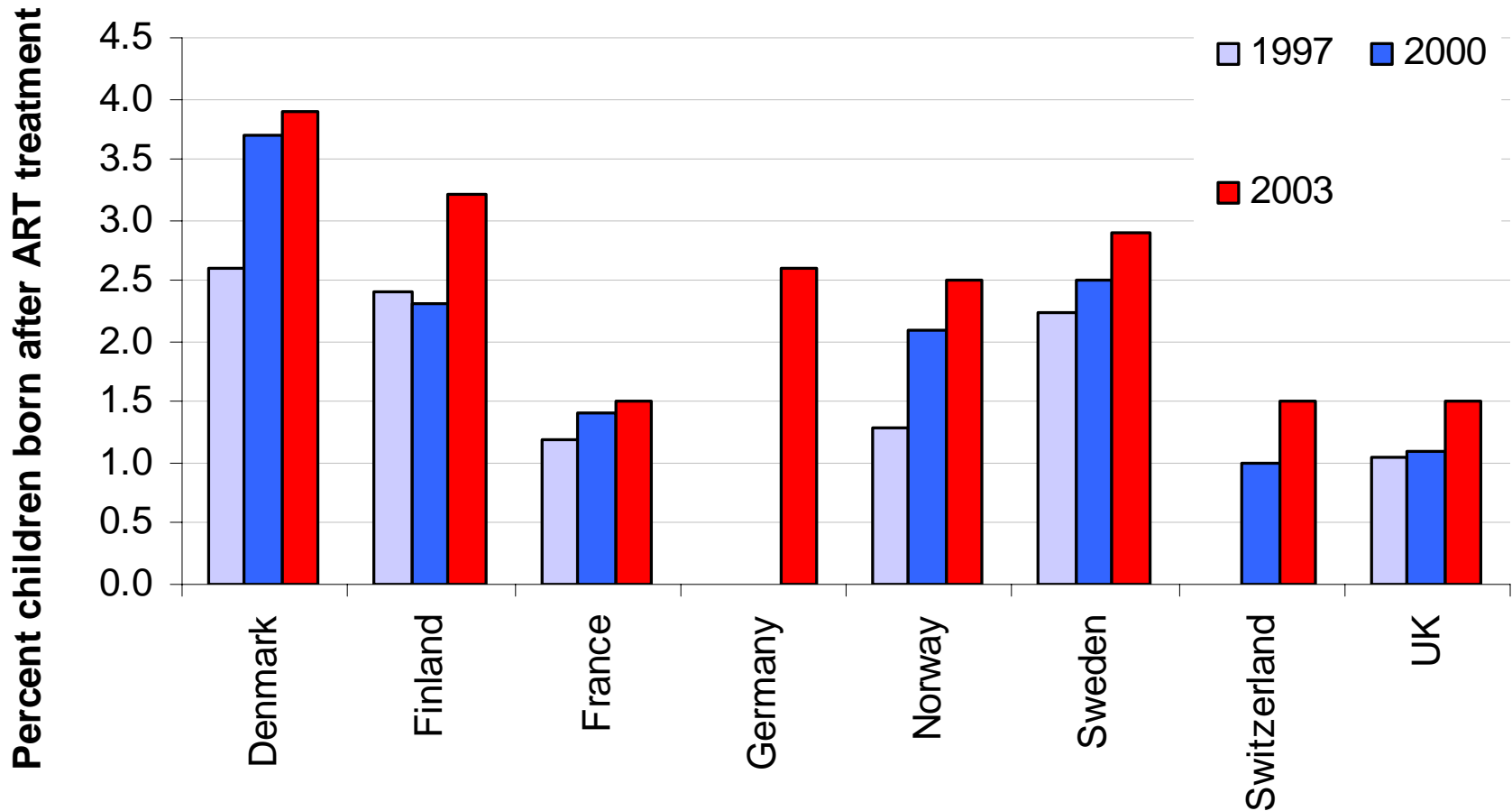
➤ Pushing the age limits of childbearing



- **January 2007:** a single woman from Spain named Carmela Bousada gave birth to healthy twins one week before her 67th birthday (and 18 years after reaching menopause)

- **March 2007:** Austrian woman gave birth to her third child in March 2007 after undergoing an ART treatment outside the country. This followed a birth of her second child at age 61 and a first child at age 31.

Denmark: highest percentage of ART-children in Europe



Austria: ca. 1% of ART births in 2003

The unique position of Denmark

- Highest ART use in Europe (6% children born after infertility treatment when Intrauterine Inseminations included)
- Late childbearing, mean age of first-time mothers 29 years
- Delayed childbearing not linked to fertility decline: stable or increasing cohort fertility (1.94 in cohort 1968)
- Possible role of rising male infertility: declining sperm count and quality among younger men (Jørgensen et al. 2002)
- Availability of register-based data on births, incl. ART database

Our project: analysis and projection of fertility rates and ART / IVF use in Denmark

Collaboration of VID and Department of Growth and Reproduction, Rigshospitalet, Copenhagen

Main objectives of research conducted in 2006-2008:

- o Analysis & projection of fertility and IVF fertility by cohort, age and birth order
- o Analysis of the importance of assisted reproduction for cohort fertility trends
- o Analysis of educational differences in IVF fertility
- o Discussion on the possible role of rising male factor infertility on ART use and fertility rates
 - **FOCUS: Native Danish women only**

THIS TALK

...focuses on:

- The rising contribution of ART to completed fertility
 - Sobotka, T. et al. 2008. “The contribution of assisted reproduction to completed fertility: An analysis of Danish data” Forthcoming in *Population and Development Review*
 - Emerging debate on the (potential) contribution of ART to fertility (e.g., Hoorens et al. 2007, Beets et al. 2008)
 - Difficulties to estimate the ‘net’ impact of ART, all analyses employ many assumptions

Methodology: IVF vs. ART

RESEARCH QUESTIONS

- What are cohort trends in IVF fertility by age?
- Can relatively high cohort fertility rate be further sustained for women born after 1970?
- If so, what would be the role of assisted reproduction?
 - Estimating the ,net impact‘ of ART on fertility

DATA

DATA: register-based data provided by Statistics Denmark & Danish National Board of Health

➤ linked records on total population (1-1-2004), births in 1973-2003 and ART treatments in 1995-2003

➤ Only the date of first treatment leading to pregnancy available!

ART data: only IVF & ICSI (intracytoplasmic sperm injections) included

POPULATION: focus on native Danish women born in 1960-78

ART in Denmark in 2003

Treatment	Cycles	Deliveries	Del. per cycle (%)	Total births	Births per delivery	% ART cycles	% ART births	Share of total births (%)
IVF + ICSI	9,292	1,854	20.0	2,291	1.24	85.3	92.3	3.53
FER	1,519	145	9.5	172	1.19	13.9	6.9	0.27
ED	82	20	24.4	(20) ^{b)}	n.a.	0.8	0.8	0.03
ART total	10,893	2,019	18.5	2,483	1.23	100.0	100.0	3.83
IUI	9,805	1,369	12.9	1,546	1.13			2.38
ART+IUI	20,698	3,388	16.6	4,029	1.19			6.21
Total births		63,433		64,838	1.02			100.0

ART = assisted reproduction

IVF = vitro fertilisation

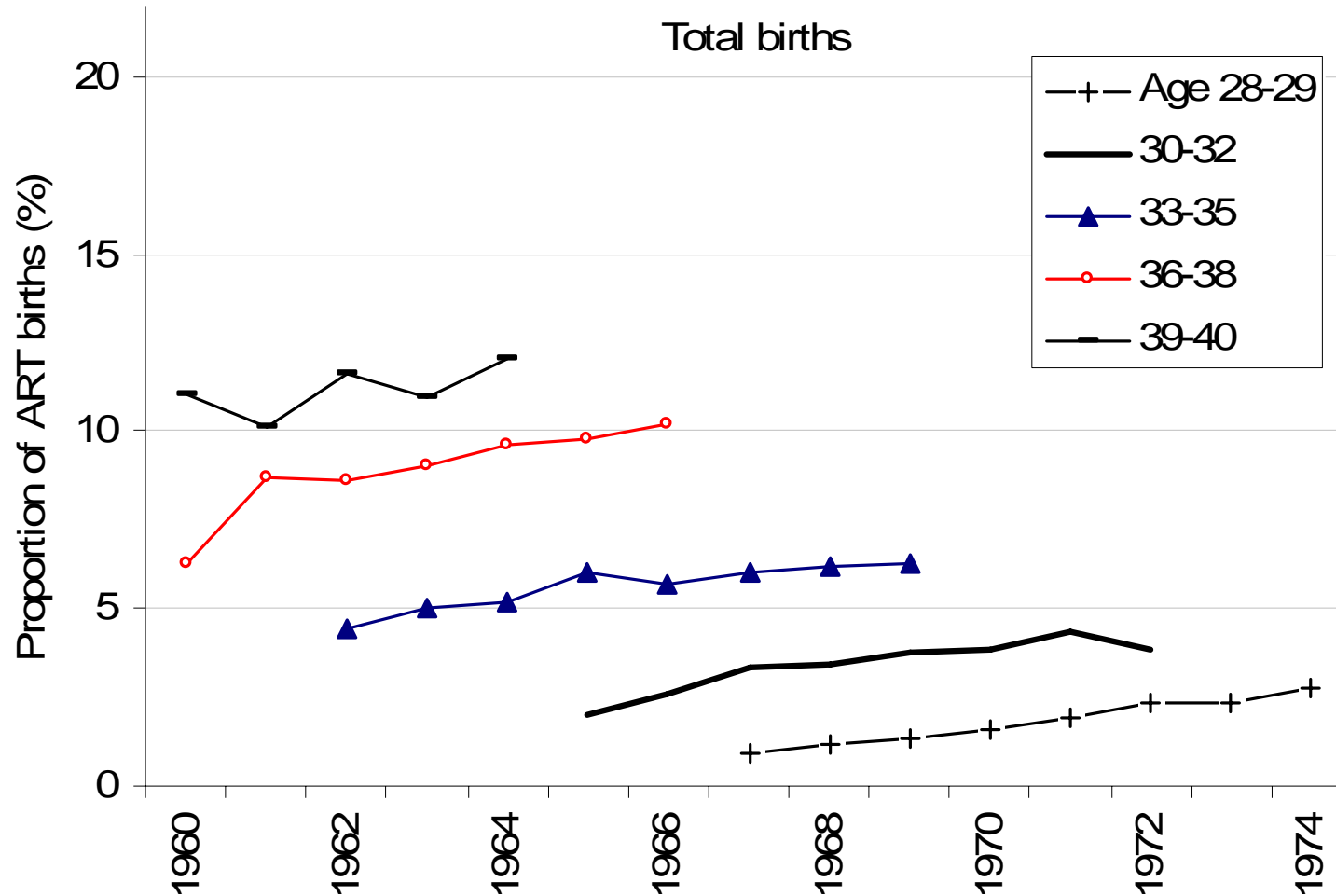
ED = egg donation

FER = frozen embryo replacement

ICSI = intracytoplasmic sperm injection

IUI = intrauterine insemination

Proportion of IVF births by mother's age and birth cohort



Note: Not adjusted for 'spontaneous conceptions'

PROJECTION SCENARIOS: IVF fertility

PROJECTION: Age-parity specific fertility rates, completed fertility and age-specific ART use since 2004

- Focus: Cohorts 1960-78

PROJECTION SCENARIOS:

- **3 scenarios of fertility (S1-S3; modelling by age & parity)**
- **2 scenarios of IVF fertility by age**

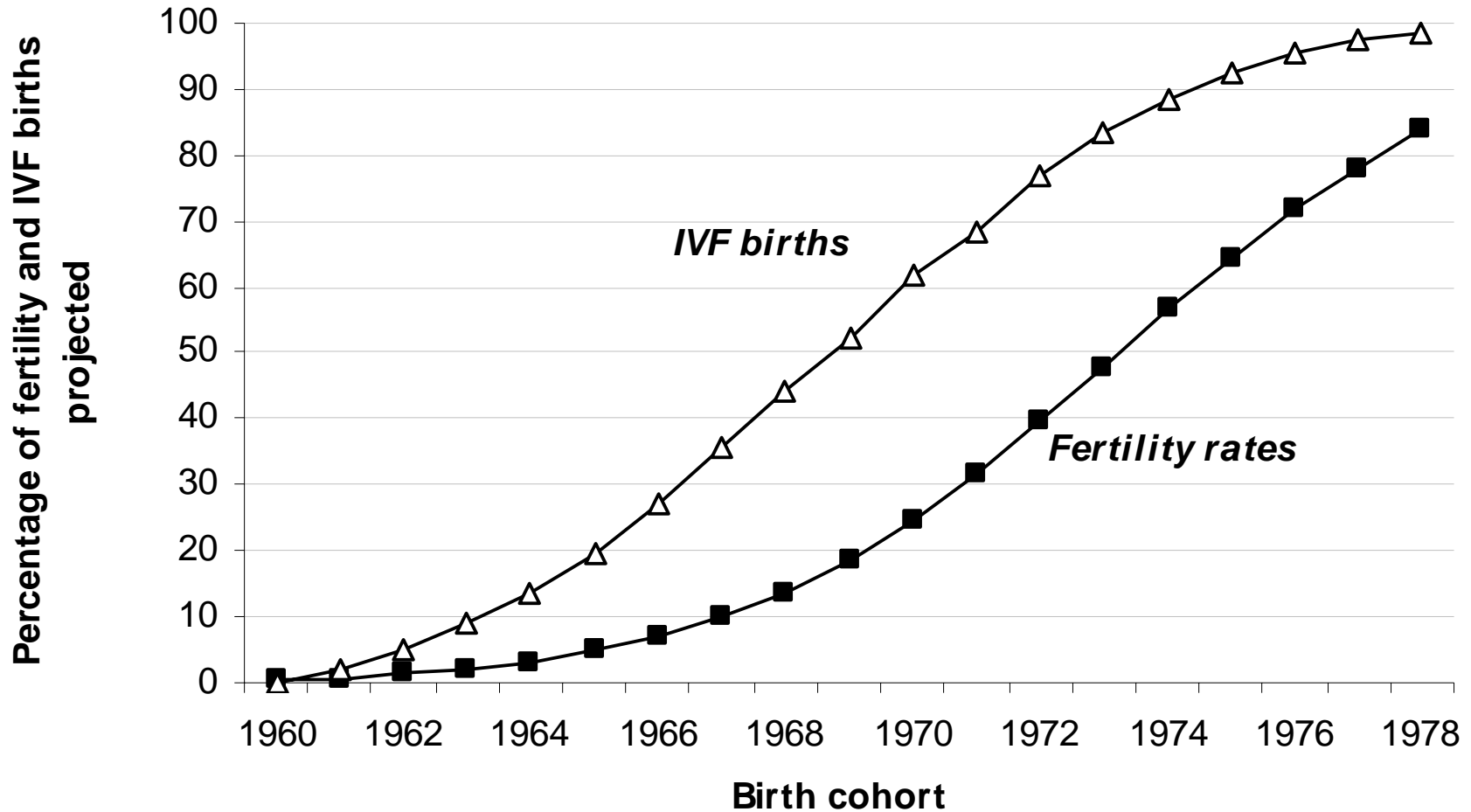
Main Assumptions rather conservative:

- first birth postponement as a driving force of trends in period & cohort fertility trends
- IVF use projection by age conditional on fertility scenarios

Results adjusted for spontaneous conceptions after ART (5% first births and 25% of second and later births)

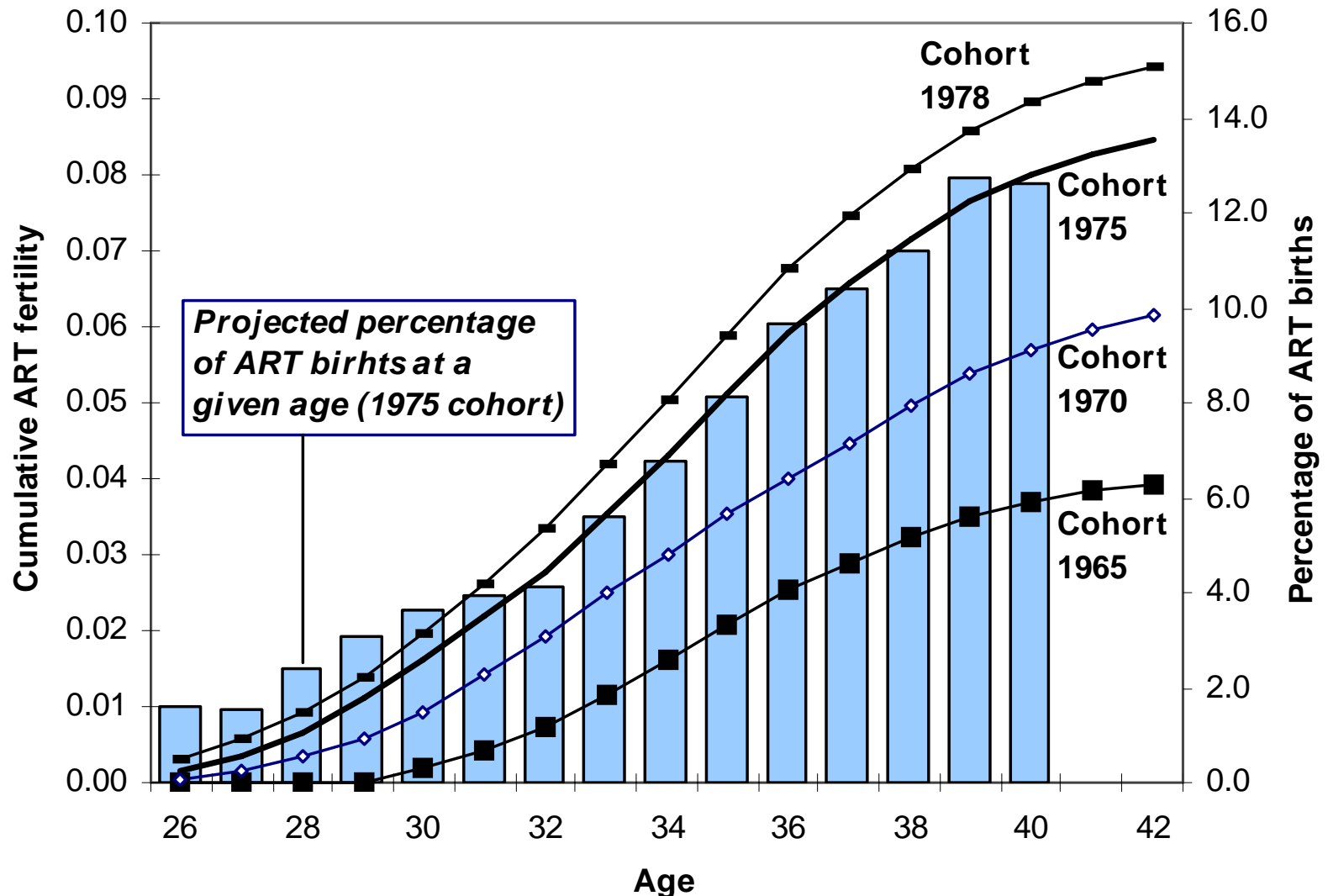
Focus: Trend projections of fertility and IVF (S3 and IVF-2)

Estimated fraction of projected fertility rates and IVF births

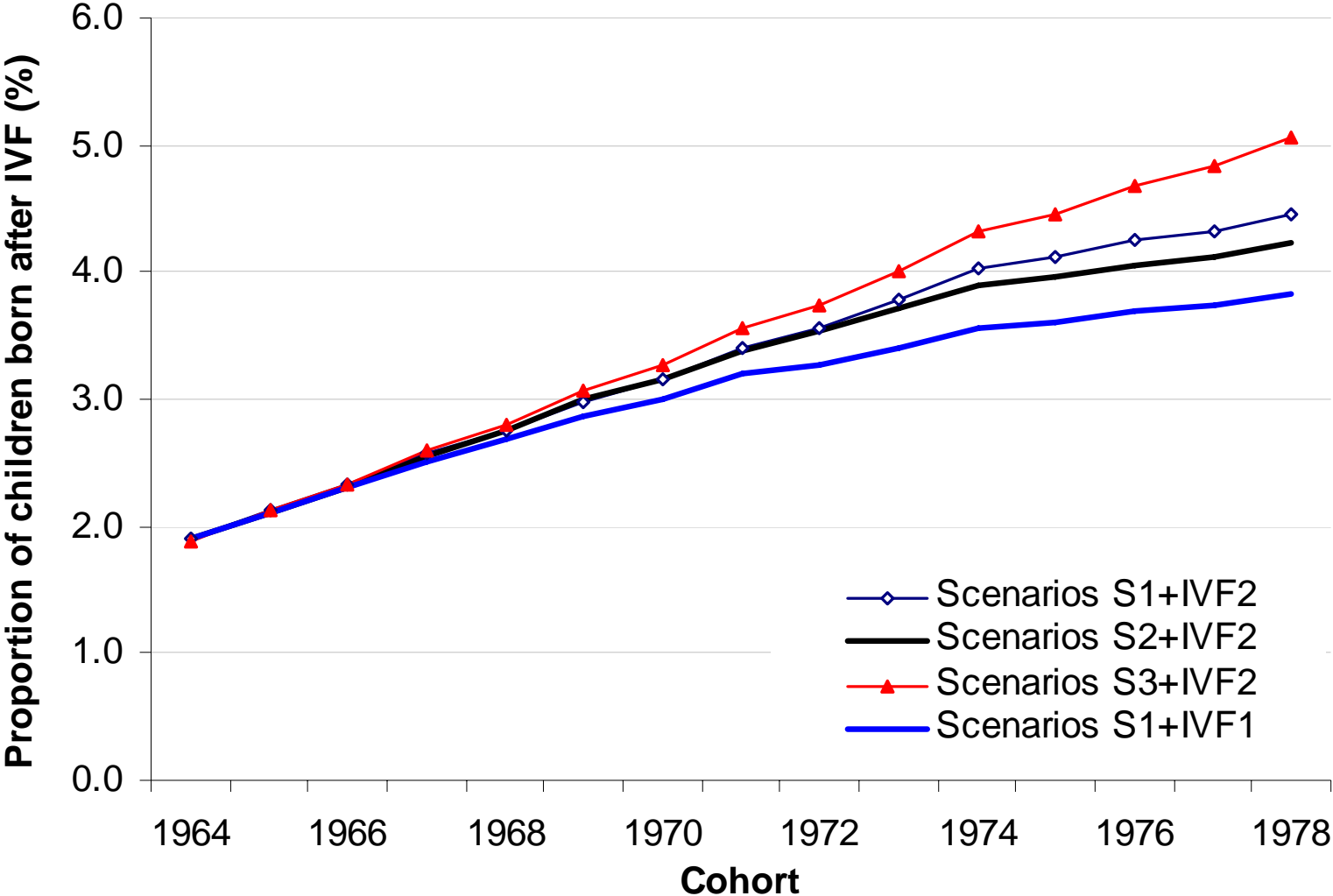


PROJECTIONS: MAIN RESULTS

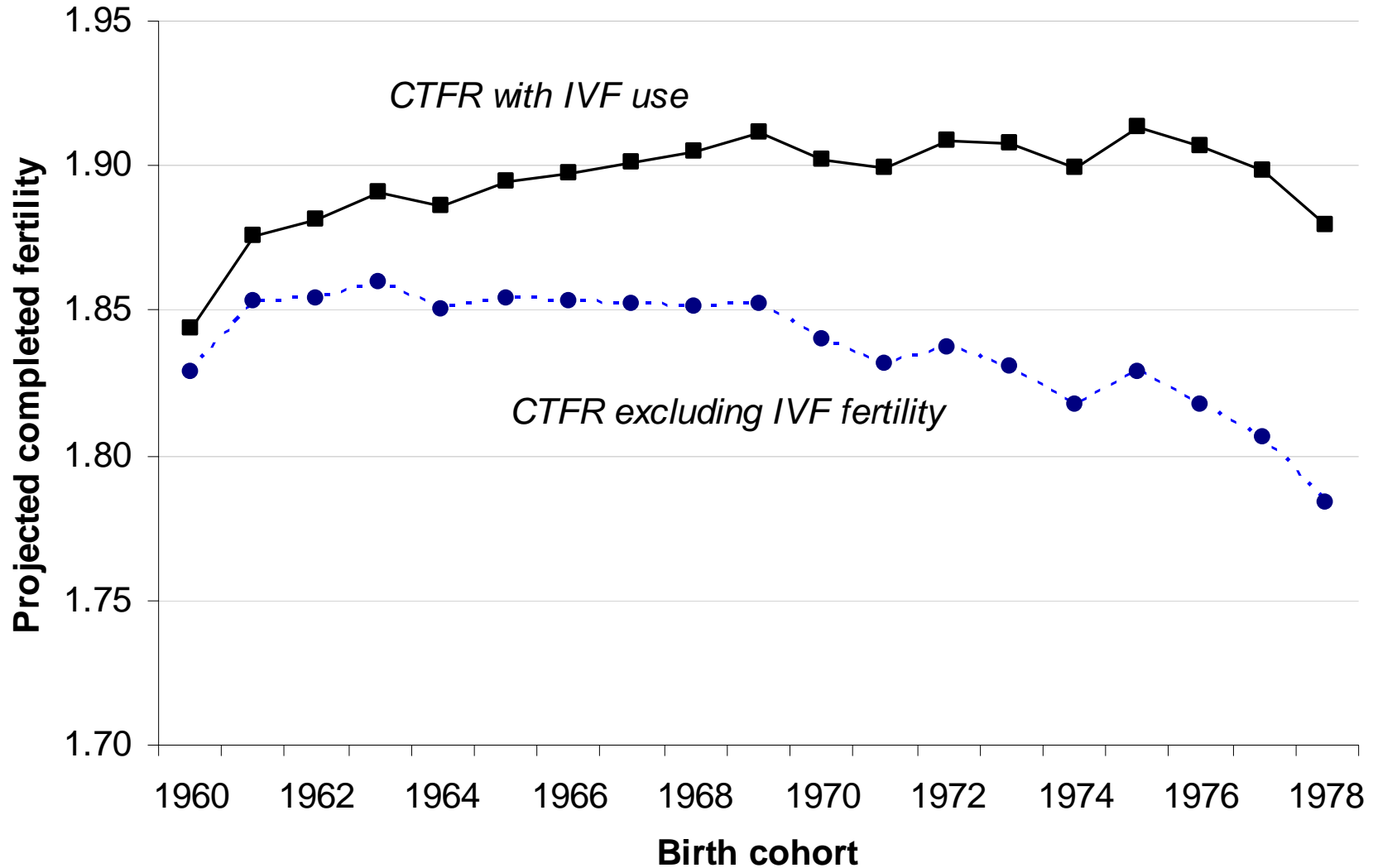
Cumulative IVF fertility by cohort and age (trend scenarios)



Projected proportion of children born after IVF treatment, different scenarios



Completed cohort TFR with and without ART (trend scenario)



Estimating the ‘net impact’ of ART

- **‘Crude impact’:** How many births can be attributed to ART / IVF
- **‘Net impact:’** Excluding ART births that would eventually take place without ART use:

“How would fertility rates differ if assisted reproduction were not available?”

Difficulties in assessing the net impact of ART

How to assess multiple births after ART use?

- Giving an important boost to ART fertility
- Medical experts often see them as undesirable (Land & Evers 2003)
- However, for many infertile couples twin births after ART wished and desired (van Wely et al. 2006)

How many sub-fertile couples using ART would eventually get pregnant without ART?

- Different estimates depending on study design, response rate, data collection method, length of observation, type of treatment, infertility diagnosis
 - Schmidt 2006: Annual rates of spontaneous conc.: 1.4-4.9%
 - Evers et al. 1998: Annual rates: 2.4-6.6%
 - Osmanagaoglu et al. (2002): 36-month cum. rate: 9.6-27.6%

Estimating the net impact of ART in Denmark

SCENARIO 1 (upper bound, stronger impact of ART):

- ART twinning rate kept at present levels (ca 24%)
- Spontaneous conceptions would replace 15% of ART births

SCENARIO 2 (lower bound)

- ART twinning rate reduced to the ‘natural’ twinning rate (1%)
- Spontaneous conceptions would replace 35% of ART births

Computing the net impact of ART in Denmark

Example of SCENARIO 2, 1965 cohort

1) Estimating the 'crude' effect of ART	
TFR	1.894
TFR following IVF use	0.040
adjustment for other ART methods	0.003
Total ART-related TFR (crude effect)	0.043
Hypothetical TFR without ART (crude)	1.851
Relative ART effect (crude, in %)	2.3
<i>Percentage TFR projected</i>	<i>4.8</i>
<i>Percentage IVF births projected</i>	<i>19.6</i>

2) Estimating the 'net' effect of ART	
Total TFR following ART (crude effect)	0.043
-reduction due to decline in twinning rate (24 to 1%)	-0.008
Crude ART effect with normal twinning rate	0.035
-reduction due to spontaneous conceptions (35%)	-0.012
Net effect ART	0.023
TFR without ART (net)	1.871
Net effect of ART (%)	1.2

Estimating the net impact of ART on cohort fertility in Denmark: Summary of results

	Birth cohort		
	1965	1970	1975
Crude effect (summary)			
TFR	1.894	1.902	1.914
Total ART-related TFR (crude effect)	0.043	0.068	0.093
Hypothetical TFR without ART (crude)	1.851	1.834	1.821
Relative ART effect (crude, in %)	2.3	3.7	5.1
Net effect, scenario 1			
Net effect ART	0.037	0.057	0.079
Relative net ART effect (in %)	2.0	3.1	4.3
Net effect, scenario 2			
Net effect ART	0.023	0.036	0.049
Relative net ART effect (in %)	1.2	1.9	2.6

Will our projections hold?

Assumptions & factors that might affect projection accuracy:

- Overall stability in fertility trends
- No dramatic improvement in ART success rates
- No dramatic increase in male-factor infertility
- No larger changes in the public funding of ART
- Possible decline in multiple embryo transfers & multiple pregnancies
 - Since January 2007, Danish Board of Health banned transfer of multiple embryos to women aged <37
 - Likely to result in a significant decline in (crude) ART fertility; maximum effect ~ 20 %. Real effect much lower.

SUMMARY

- ✓ The net impact of assisted reproduction on fertility remains relatively small, even in Denmark
- ✓ However, this effect not negligible
 - *ART likely to become an important factor contributing to the stability in cohort fertility rates*
- ✓ Growth in ART fuelled by fertility postponement, ART availability, technological advances in ART methods, and possibly also by rising (male) infertility
- ✓ The widespread use of ART also signals ‘unmet demand’ for children among women who postponed childbearing for too long

Discussion: Policy (ir)relevance of ART

RAND report (Grant 2006): Policies supporting ART use may have a positive affect on fertility rates

- ART as a part of population policy mix?

Thaele and Uszkoreit (2007): “...*fertility treatment is more than a medical need: fertility treatment plays a major role in battling negative population growth*”

However: ART potential to increase fertility and slow-down population ageing limited at best

- ‘Net effect’ of ART rather small & less important than some other factors
- Hoorens et al. (2007): TFR in the UK may increase by 0.04 (2 %) to 1.68 if UK women had the same ART use as women in Denmark (many assumptions involved)

More troubles with ART

- Many couples referred to ART too soon (Beets et al. 2008)
- Very low success rates at ages 40+

ART is ill-suited as a means of helping women who postponed motherhood to (very) late reproductive ages

- Nature, 4 November 2004: “*Age is no barrier*“
- New Scientist April 2007: „*Reproductive revolution*“

But: ART particularly ineffective for a rapidly rising number of women who postponed childbearing past age 40

- Leridon 2004: ART makes up for one half of births lost by postponing childbearing from age 30 to 35, but is as ineffective as spontaneous conceptions for women aged 42
- Live birth rate after non-donor ART in the US in 2003: 15.6 % at age 40, 12.6 % at age 41, 8.9 % at age 42 (CDC 2005)

Technology advances fuel a false perception of reproductive control

Reproductive biology still imposes strict limits on most prospective mothers and their partners

Further plans for our research

Database management:

- Updating database of men's and women's reproductive history
- Getting complete records on all ART cycles, 1994(95)-2006

Substantive issues (long-term plans):

- Life table analysis of ART cycles, pregnancies, and deliveries by age, education, birth order, and partner's characteristics
- Long-term success of ART and spontaneous conceptions after ART
- Sex ratios of ART children
- Multipartner fertility among Danish men and women
- Updating analysis and projections of fertility and ART use