Congenital heart disease and fertility

Do the patients have an increased risk of impaired fertility?

Disclosure:
Since submission of abstract, part of the study was accepted in JAHA (2023)

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Department of Public Health, Epidemiology, Aarhus University

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Fertility clinics will receive more couples affected by congenital heart disease

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Fertility clinics will receive more couples affected by congenital heart disease

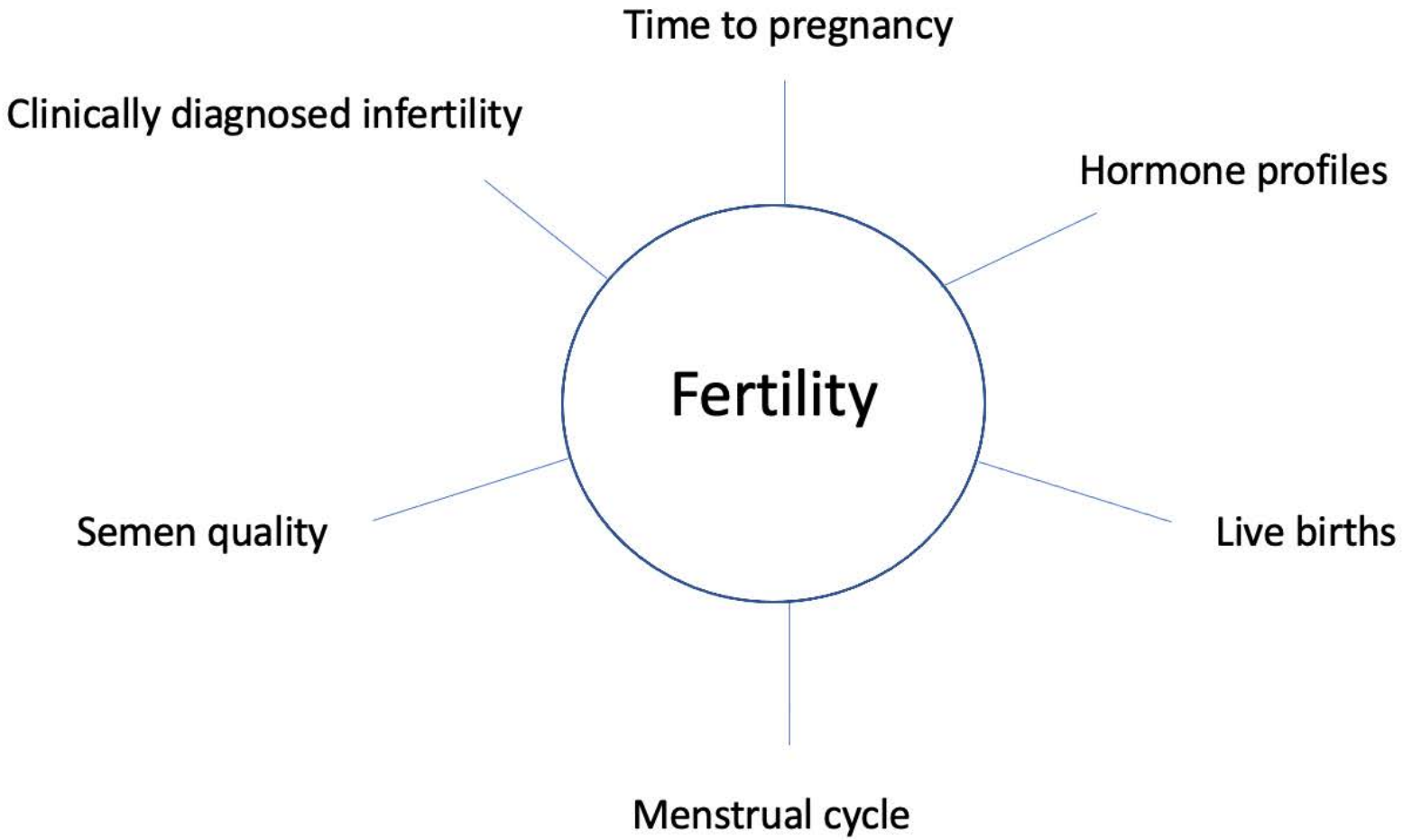
Do CHD patients have an increased risk of impaired fertility?

”The fertility in women with more simple defects is probably the same as the background population”

Aim

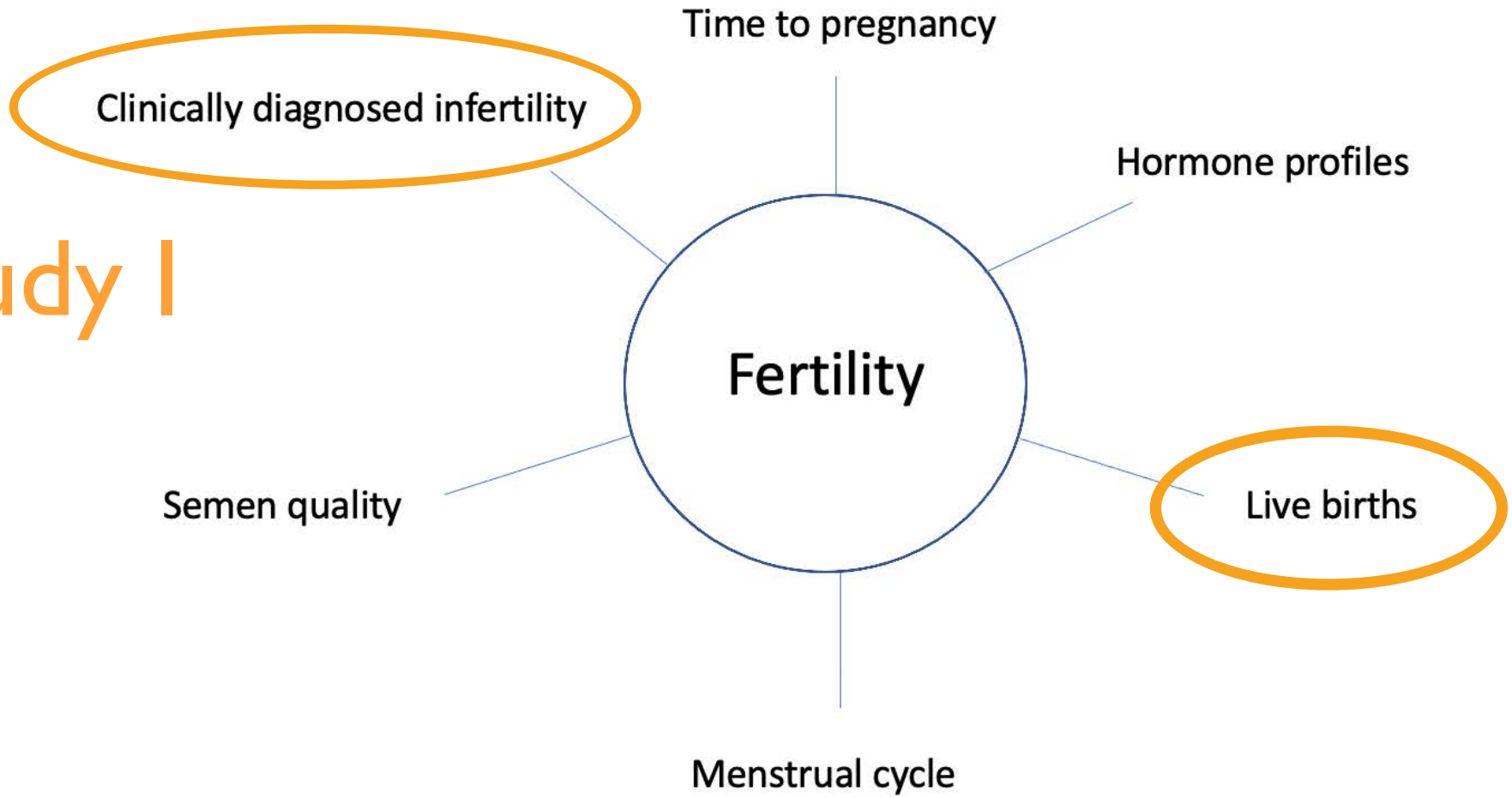
To evaluate the fertility in men and women with congenital heart disease compared with background populations

Proxy measures of fertility



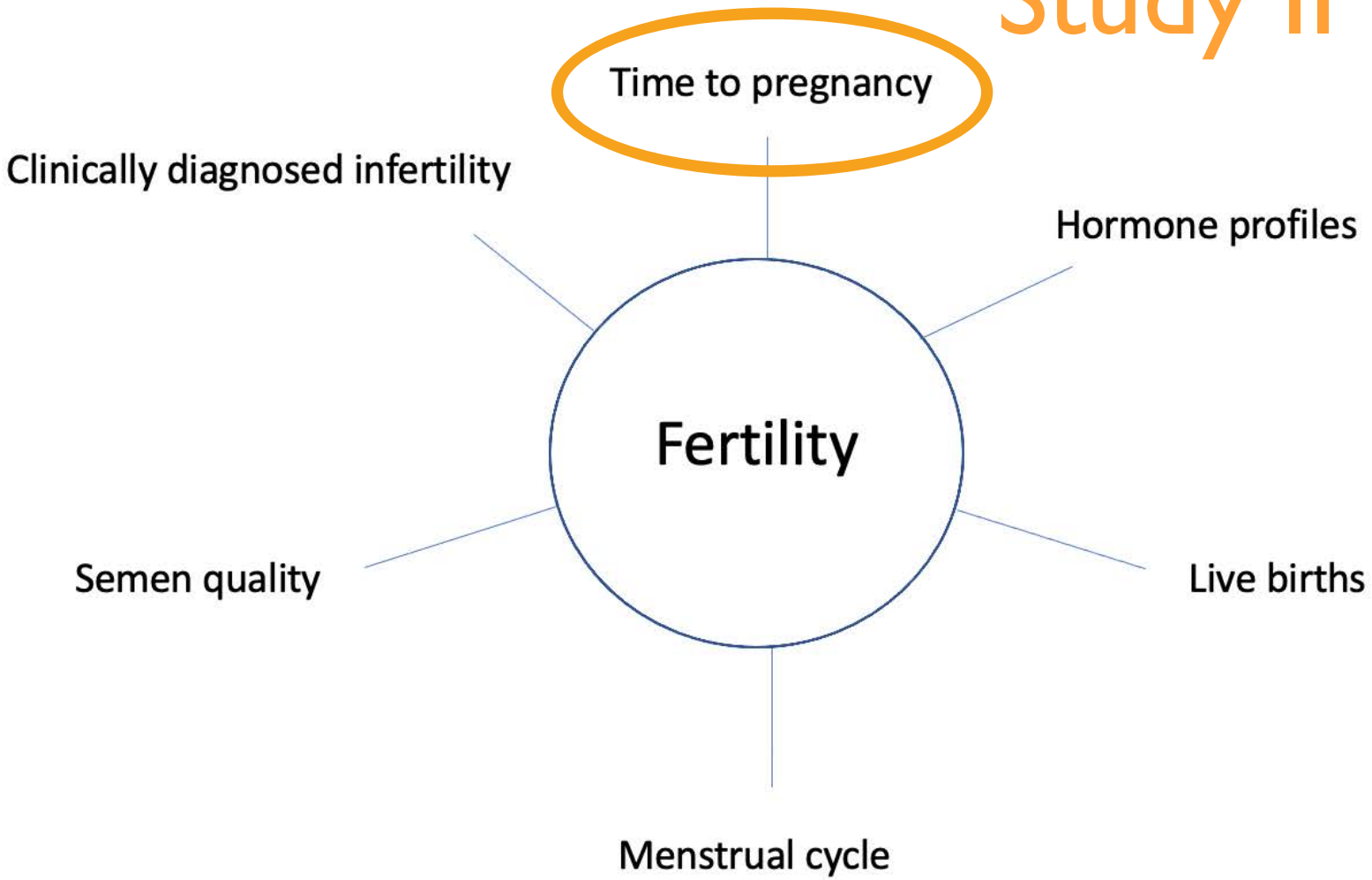
Proxy measures of fertility

Study I



Proxy measures of fertility

Study II



Study I

Born between 1977 and 2000

N = 1,472,258

Study I

The Danish national registries

The Danish Civil Registry

The In Vitro Fertilization registry

The National Patient Registry

The Death Registry

The Education Registry

The Danish Birth Registry

The Income Registry

The Danish national registries

Study I

The In Vitro Fertilization registry

The National Patient Registry

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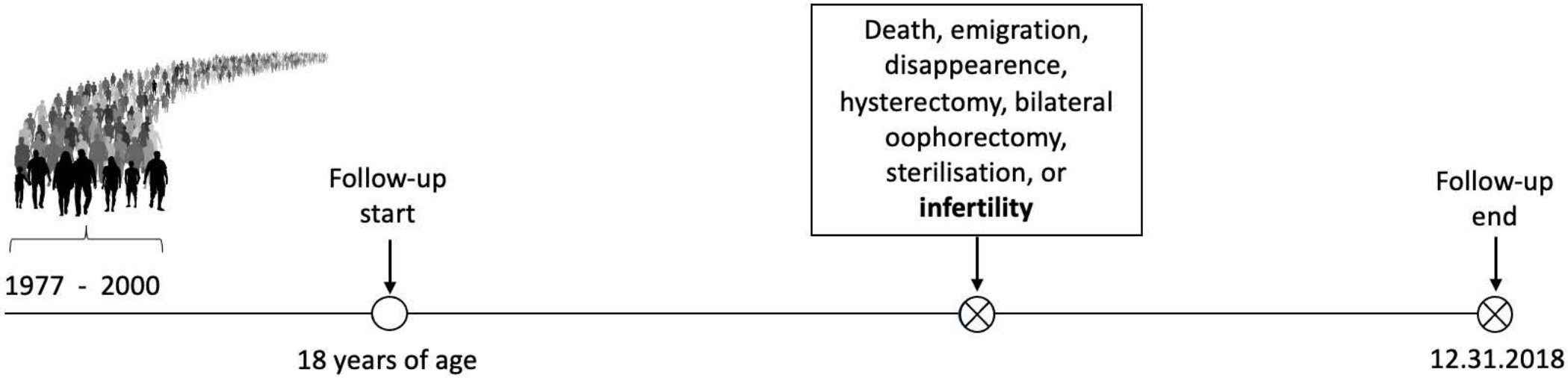
Study I

Statistical analyses

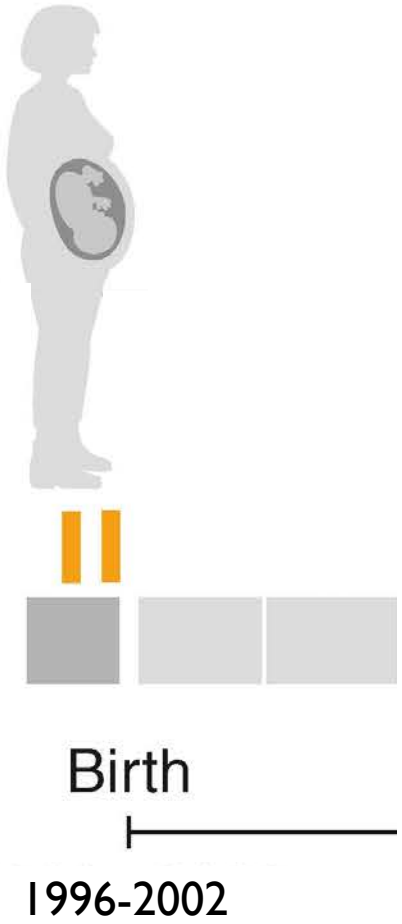


Statistics: Cox regression model performed separately for each sex

Adjustments for birth period, maternal age, and maternal socioeconomic status

Study II

Study II



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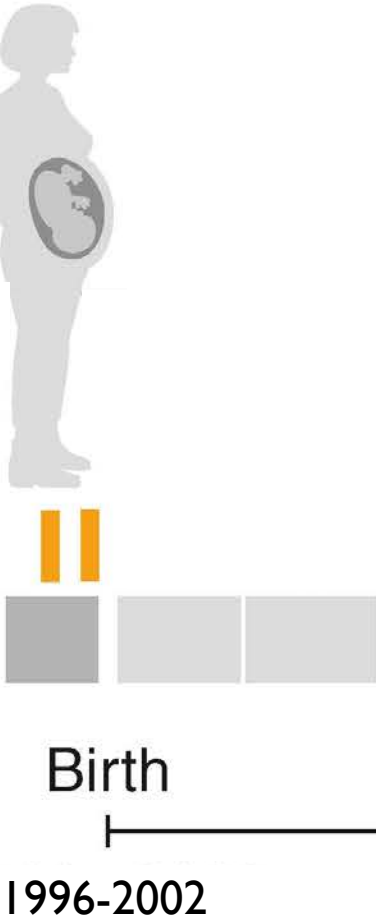

84,000 pregnant women with > **100,000** pregnancies

Interview in first trimester (including questions on time to pregnancy)

The National Patient Register

Questions on waiting time to pregnancy (TTP)

Study II

A018	Is this pregnancy planned, partly planned or not planned at all?

1. planned →A019
2. partly planned →A019
3. not planned → A020
4. do not know
5. do not want to answer
9. Undefined
10. Irrelevant

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A019 For how long did you try to get pregnant before you succeeded?
Dependent on: A018

1. did not try to get pregnant → A020
2. got pregnant immediately→A029
3. 1-2 months → A029
4. 3-5 months →A029
5. 6-12 months → A024
6. For more than 12 months → A024
7. Do not know → A024
8. Do not want to answer → A024
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Study II

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A024 Did you get any infertility treatment prior to this pregnancy?
Dependent on: A019 A020 A021 A022 A023

1. yes
2. no →A029
3. do not know →A029
4. do not want to answer →A029
9. Undefined
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Questions on waiting time to pregnancy (TTP)

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Two outcome variables:

Subfertile TTP > 6 months or infertility treatment received

Infertile TTP > 12 months or infertility treatment received

Statistical analyses

Study II

Pregnancies in women with CHD were compared with pregnancies in women without CHD

Binomial logistic regression model

Risk ratio of being subfertile *(*TTP > 6 mo/MAR vs. TTP < 6 mo)

Risk ratio of being infertile *(*TTP > 12 mo/MAR vs. TTP < 12 mo)

Crude and adjusted analyse (women's age)

Study I

- Clinically diagnosed infertility
- Live births

Study I

CHD prevalence of 0.6%

Females with no CHD (n = 669,711)	
Females with CHD (n = 4,337)	
	Simple (n = 2,461)
	Moderat (n = 1,291)
	Complex (n = 258)
	Unspecific (n = 327)
Males with no CHD (n = 707,505)	
Males with CHD (n = 4,342)	
	Simple (n = 1,958)
	Moderat (n = 1,668)
	Complex (n = 351)
	Unspecific (n = 365)

Study I

No association observed...

	Men		Women	
	CHD n = 4,342	No CHD n = 707,505	CHD n = 4,337	No CHD n = 669,711
Model 1*				
Number of infertile individuals (n = 81,344)	194	36,696	236	44,218
Crude HR (95% CI)	1.04 (0.90-1.20)	1.00 (reference)	0.99 (0.87-1.13)	1.00 (reference)
Adjusted HR (95% CI)†	1.04 (0.90-1.19)	1.00 (reference)	1.00 (0.88-1.14)	1.00 (reference)
Model 2‡				
Number of infertile individuals (n = 63,061)	141	25,381	206	37,333
Crude HR (95% CI)	1.09 (0.92-1.28)	1.00 (reference)	1.02 (0.89-1.18)	1.00 (reference)
Adjusted HR (95% CI)†	1.09 (0.92-1.29)	1.00 (reference)	1.03 (0.90-1.19)	1.00 (reference)

Study I

No association observed...

	Men		Women	
	CHD n = 4,342	No CHD n = 707,505	CHD n = 4,337	No CHD n = 669,711
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Study I

No association observed...

Model 1*	Infertile, n =	Crude HR (95% CI)	Adjusted HR (95% CI)†
Women			
No CHD (n = 669,711)	44,218	1.00 (reference)	1.00 (reference)
Simple CHD (n = 2,461)	119	0.97 (0.81-1.16)	0.97 (0.81-1.17)
Moderate CHD (n = 1,291)	91	0.99 (0.81-1.22)	1.00 (0.82-1.23)
Complex CHD (n = 258)	15	1.40 (0.82-2.25)	1.36 (0.81-2.30)
Unspecific CHD (n = 327)	11	0.88 (0.49-1.60)	0.88 (0.49-1.60)
Men			
No CHD (n = 707,505)	36,696	1.00 (reference)	1.00 (reference)
Simple CHD (n = 1,958)	80	1.07 (0.86-1.33)	1.06 (0.85-1.32)
Moderate CHD (n = 1,668)	84	0.93 (0.75-1.15)	0.93 (0.75-1.16)
Complex CHD (n = 351)	13	1.25 (0.73-2.15)	1.24 (0.72-2.13)
Unspecific CHD (n = 365)	17	1.49 (0.93-2.40)	1.50 (0.92-2.46)

Study I

Parenthood

Individuals born 1977-1984 (N = 425,445)	Childless, *n* (%)	Parent, *n* (%)	Mean number of children per parent (sd)	Median age at first child (IQI)
Women with no CHD (n = 205,326)	40,210 (19.6)	165,116 (80.4)	2.1 (0.8)	28.0 (25.0-30.0)
Women with CHD (n = 1,097)	290 (26.4)	807 (73.6)	2.1 (0.8)	27.4 (25.0-30.0)
Simple (n = 542)	141 (26.0)	401 (74.0)	2.1 (0.8)	27.0 (25.0-30.0)
Moderat (n = 452)	122 (27.0)	330 (73.0)	2.0 (0.8)	28.0 (25.0-30.0)
Complex (n = 45)	15 (33.3)	30 (66.7)	2.2 (0.8)	26.2 (23.1-28.9)
Unspecific (n = 58)	12 (20.7)	46 (79.3)	2.1 (0.8)	27.8 (24.8-30.6)
Men with no CHD (n = 216,987)	69,702 (32.1)	147,285 (67.9)	2.0 (0.8)	29.0 (26.0-32.0)
Men with CHD (n = 1,035)	382 (36.9)	653 (63.1)	2.0 (0.8)	29.0 (26.0-32.0)
Simple (n = 412)	141 (34.2)	271 (65.8)	1.9 (0.8)	29.0 (26.0-32.0)
Moderat (n = 499)	185 (37.1)	314 (62.9)	1.9 (0.8)	29.0 (26.0-32.0)
Complex (n = 51)	24 (47.1)	27 (52.9)	2.0 (0.8)	28.4 (24.7-30.9)
Unspecific (n = 73)	32 (43.8)	41 (56.2)	2.0 (0.8)	27.8 (25.5-31.4)

Study I

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Study I

Parenthood

34-41 years of age

Individuals born 1977-1984 (N = 425,445)	Childless, *n* (%)	Parent, *n* (%)	Mean number of children per parent (sd)	Median age at first child (IQI)
Women with no CHD (n = 205,326)	40,210 (19.6)	165,116 (80.4)	2.1 (0.8)	28.0 (25.0-30.0)
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More were found childless...

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Study I

Same number of children...

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Study I

Women with complex CHD were youngest...

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Study II

- Time to pregnancy (TTP)

Study II

Results

Study population for TTP analyses:

Women with CHD = 333 (0.4%), including 360 pregnancies

Women without CHD = 84,589 (99.6%), including 93,472 pregnancies

Study II

Results

Study population for TTP analyses:

Women with CHD = 333 (0.4%), including 360 pregnancies → 87% diagnosed with a simple heart defect

Women without CHD = 84,589 (99.6%), including 93,472 pregnancies

Study II

No increased risk of neither subfertility nor infertility...

	Subfertility (TTP > 6 months/MAR)			Infertility (TTP > 12 months/MAR)		
	Cases n =	Crude RR	Adjusted RR (95% CI)*	Cases n =	Crude RR	Adjusted RR (95% CI)*
Pregnancies in women without CHD	24,544	1.00 (ref)	1.00 (ref.)	12,806	1.00 (ref.)	1.00 (ref.)
Pregnancies in women with CHD	87	0.92	0.96 (0.80-1.15)	40	0.81	0.87 (0.66-1.17)

*adjustment for age at pregnancy

Conclusion

- **No evidence of impaired fertility** in patients with CHD when compared with the background population

- The available data did **not allow for firm conclusions on patients with more complex CHD**

- CHD patients were **more often childless**, but…

- **Parents** with CHD had the **same number of children per individual** as the background population

Still, we cannot exclude a higher risk among CHD patients not embarking on pregnancy and among patients with complex or less frequent lesions