

Supplementary Online Content

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eFigure. Schematics of Exclusions in the Enrollment of Swedish Born Adoptees

eTable 1. International Classification of Diseases and Related Health Problems (ICD) Codes Used for Studied Comorbidities

eTable 2. Comorbidities in Biological and Adoptive Parents With and Without Heart Failure

eTable 3. Odds Ratio of Heart Failure (HF) in Adoptees, Stratified by Number of Affected Biological Parents (Cohort Study). Individuals With Cardiomyopathies Included

eTable 4. Hazard Ratio of Heart Failure in Adoptees, Stratified by Affected Parent

eTable 5. Heritability of Heart Failure Based on Estimated Population Prevalence and Tetrachoric Correlation in the Case-Control Study. Individuals With Cardiomyopathies Included

eTable 6. Heritability of Heart Failure Based on Estimated Population Prevalence and Tetrachoric Correlation in the Case-Control study. Individuals With Cardiomyopathy Excluded

eTable 7. Odds Ratio of Heart Failure in Adoptees, Stratified by Affected Parent (Cohort Study). Only Adoptees With Both Biological and Both Adoptive Parents Identified Included

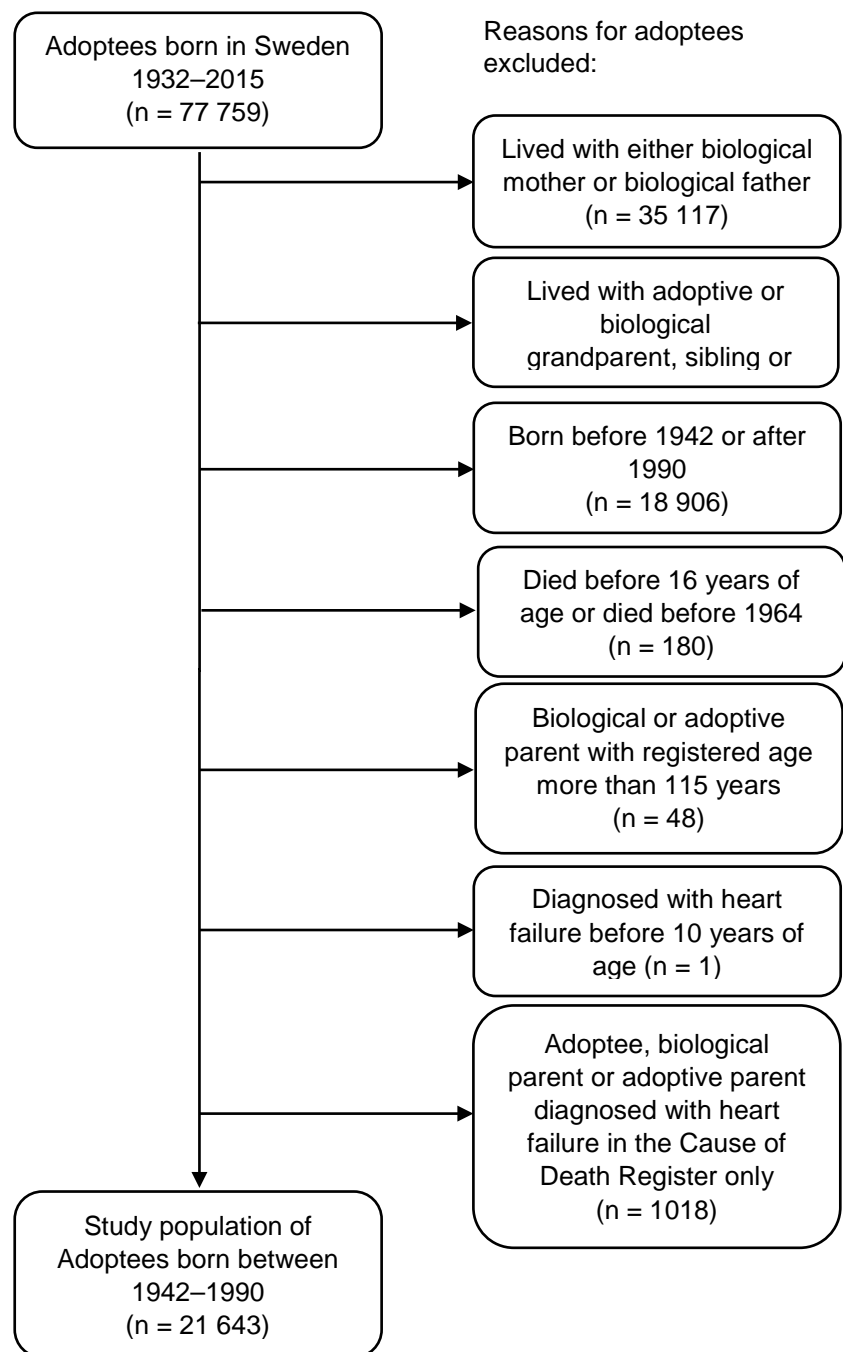
eTable 8. Odds Ratio of Heart Failure (HF) in Adoptees, Stratified by Affected Parent (Case-Control Study). Only Adoptees With Both Biological and Both Adoptive Parents Identified included

eTable 9. Odds Ratio of Heart Failure (HF) in Adoptees, Stratified by Affected Biological Parents, in Relation to Coronary Heart Disease (CHD) (Cohort Design). Individuals With Cardiomyopathies Included

eTable 10. Odds Ratio of Heart Failure (HF) in Adoptees, Stratified by Affected Biological Parents and by Sex (Cohort Study). Individuals with cardiomyopathies included

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Schematics of Exclusions in the Enrollment of Swedish-Born Adoptees



eTable 1. International Classification of Diseases and Related Health Problems (ICD) Codes Used for Studied Comorbidities

Diagnosis	ICD 10	ICD 9	ICD 8	ICD 7
Coronary heart disease	I20-I25	410-414	410-414	420
Hypertension	I10-I15	401-405	400-404	440-447
Valvular heart disease	I05-I09, I33-I39	391, 394-398, 421, 424	391, 393, 394-398, 421, 424	401.10, 401.11, 410-414, 421, 430
Diabetes mellitus	E10-E14	250	250	260
Chronic obstructive pulmonary disease	J40-J47	490-496	490-493	241, 502, 527.10, 527.11

eTable 2. Comorbidities in Biological and Adoptive Parents With and Without Heart Failure

	No heart failure	Heart failure	P-value^a
Biological parents	(n = 39 629)	(n = 3 657)	
Coronary heart disease (CHD) ^b	7 310 (18.45)	2 305 (63.03)	<0.0001
Hypertension ^b	10 824 (27.31)	1 929 (52.75)	<0.0001
Valvular heart disease ^b	1 120 (2.83)	645 (17.64)	<0.0001
Diabetes mellitus ^b	5 318 (13.42)	1 302 (35.60)	<0.0001
Chronic obstructive pulmonary disease ^b	5 614 (14.17)	1 281 (35.03)	<0.0001
Cardiomyopathy ^b	216 (0.55)	310 (8.48)	<0.0001
Adoptive parents	(n = 31 044)	(n = 3 972)	
Coronary heart disease ^b	7 090 (22.84)	2 477 (62.36)	<0.0001
Hypertension ^b	9 458 (30.47)	1 984 (49.95)	<0.0001
Valvular heart disease ^b	1 228 (3.96)	829 (20.87)	<0.0001
Diabetes mellitus ^b	4 076 (13.13)	1 041 (26.21)	<0.0001
Chronic obstructive pulmonary disease ^b	3 013 (9.71)	867 (21.83)	<0.0001
Cardiomyopathy ^b	167 (0.54)	219 (5.51)	<0.0001

^a Chi-square test. ^b number of observations (%).

eTable 3. Odds Ratio^a of Heart Failure (HF) in Adoptees, Stratified by Number of Affected Biological Parents (Cohort Study). Individuals With Cardiomyopathies Included

	No biological parental HF	One biological parent with HF only	Both biological parents affected with HF
Person-years at risk	844 228	156 859	10 151
Cases/persons at risk	135/18192	53/3245	6/206
Incidence rate per 1000 person years	0.16 (0.13-0.19)	0.34 (0.26-0.44)	0.59 (0.27-1.32)
Incidence ratio	1 [Reference]	2.11 (1.53-2.89)	3.70 (1.48-7.86)
<i>Odds ratio (95% CI)</i>			
Model 1	1 [Reference]	2.22 (1.61-3.06)	4.01 (1.75-9.20)
Model 2	1 [Reference]	1.47 (1.06-2.03)	2.12 (0.91-4.91)
Model 3	1 [Reference]	1.40 (0.99-1.98)	1.97 (0.80-4.87)

Abbreviations: CI, confidence interval. Model 1=univariate model; Model 2=adjusted for adoptee birth year, sex, county, and education; Model 3=adjusted for adoptee birth year, sex, county, education, coronary heart disease, hypertension, valvular heart disease, diabetes mellitus, and chronic obstructive pulmonary disease. ^a Risks are presented as odds ratios (95 % confidence interval) derived from unconditional logistic regression. ^b Reference group.

eTable 4. Hazard Ratio^a of Heart Failure in Adoptees, Stratified by Affected Parent

	No biological parental heart failure	Biological parental heart failure	No adoptive parental heart failure	Adoptive parental heart failure
Cardiomyopathies included				
Person-years at risk	844 228	167 010	828 375	182 863
Cases/persons at risk	135/18192	59/3451	155/17887	39/3756
Incidence rate per 1000 person years	0.16 (0.13-0.19)	0.35 (0.27-0.46)	0.19 (0.16-0.22)	0.21 (0.15-0.29)
Incidence ratio	1 [Reference]	2.21 (1.62-2.99)	1 [Reference]	1.14 (0.79-1.61)
	<i>Odds ratio (95% CI)</i>		<i>Odds ratio (95% CI)</i>	
Model 1	1 [Reference]	1.78 (1.31 – 2.41)	1 [Reference]	0.88 (0.62 – 1.25)
Model 2	1 [Reference]	1.49 (1.01 – 2.03)	1 [Reference]	0.81 (0.57 – 1.15)
Model 3	1 [Reference]	1.40 (1.01 – 1.94)	1 [Reference]	0.83 (0.58 – 1.18)
Cardiomyopathies excluded^b				
Person-years at risk	825 608	150 032	807 625	168 015
Cases/persons at risk	79/17796	37/3092	93/17444	23/3444
Incidence rate per 1000 person years	0.10 (0.076-0.12)	0.25 (0.17-0.34)	0.12 (0.093-0.14)	0.14 (0.087-0.21)
Incidence ratio	1 [Reference]	2.58 (1.73-3.79)	1 [Reference]	1.19 (0.74-1.85)
	<i>Odds ratio (95% CI)</i>		<i>Odds ratio (95% CI)</i>	
Model 1	1 [Reference]	2.04 (1.38 – 3.03)	1 [Reference]	0.91 (0.58 – 1.43)
Model 2	1 [Reference]	1.59 (1.07 – 2.36)	1 [Reference]	0.80 (0.51 – 1.26)
Model 3	1 [Reference]	1.50 (0.98 – 2.28)	1 [Reference]	0.77 (0.48 – 1.24)

Abbreviations: CI, confidence interval. Model 1=univariate model; Model 2=adjusted for adoptee birth year, sex, county, and education; Model 3=adjusted for adoptee birth year, sex, county, education, coronary heart disease, hypertension, valvular heart disease, diabetes mellitus, and chronic obstructive pulmonary disease. ^a Risks are presented as hazard ratios (95 % confidence interval) derived from Cox regression models with time ranging from 1964 or date of birth to date of emigration, death, diagnosis of HF or end of follow-up December 31 2015). ^b All adoptees diagnosed with cardiomyopathy, or that had a biological or adoptive parent diagnosed with cardiomyopathy, were excluded.

eTable 5. Heritability of Heart Failure Based on Estimated Population Prevalence and Tetrachoric Correlation in the Case-Control Study. Individuals With Cardiomyopathies Included

Exposed cases	Unexposed cases	OR	Prevalence %	Tetrachoric correlation (SE)	$h^2 \pm SE \%$
58	133	1.49	0.1	0.07 (0.03)	14 ± 6
58	133	1.49	0.6	0.08 (0.03)	16 ± 6
58	133	1.49	1.0	0.09 (0.04)	18 ± 8
58	133	1.49	5.0	0.11 (0.05)	22 ± 10
58	133	1.49	8.0	0.12 (0.05)	24 ± 10
58	133	1.49	10.0	0.12 (0.05)	25 ± 10
58	133	1.49	12.0	0.13 (0.05)	25 ± 10

Abbreviations: SE, Standard error; OR, Odds ratio.

eTable 6. Heritability of Heart Failure Based on Estimated Population Prevalence and Tetrachoric Correlation in the Case-Control study. Individuals With Cardiomyopathy Excluded

Exposed cases	Unexposed cases	OR	Prevalence %	Tetrachoric correlation (SE)	$h^2 \pm SE \%$
37	77	1.64	0.1	0.09 (0.04)	18±8
37	77	1.64	0.5	0.10 (0.04)	20±8
37	77	1.64	1.0	0.11 (0.05)	22±10
37	77	1.64	5.0	0.14 (0.06)	28±12
37	77	1.64	8.0	0.15 (0.06)	30±12
37	77	1.64	10.0	0.15 (0.07)	31±14
37	77	1.64	12.0	0.16 (0.07)	32±14

Abbreviations: SE, Standard error; OR, Odds ratio.

eTable 7. Odds Ratio^a of Heart Failure in Adoptees, Stratified by Affected Parent (Cohort Study). Only Adoptees With Both Biological and Both Adoptive Parents Identified Included

	No biological parental heart failure	Biological parental heart failure	No adoptive parental heart failure	Adoptive parental heart failure
Cardiomyopathies included				
Person-years at risk	513 358	122 205	481 733	153 830
Cases/persons at risk	107/10 862	49/2511	122/10 222	34/3151
Incidence rate per 1000 person years	0.21 (0.17-0.25)	0.40 (0.30-0.53)	0.25 (0.21-0.31)	0.22 (0.15-0.31)
Incidence ratio	1 [Reference]	1.92 (1.36-2.69)	1 [Reference]	0.87 (0.59-1.27))
	<i>Odds ratio (95% CI)</i>		<i>Odds ratio (95% CI)</i>	
Model 1	1 [Reference]	2.00 (1.42–2.81)	1 [Reference]	0.90 (0.62-1.32)
Model 2	1 [Reference]	1.48 (1.04–2.09)	1 [Reference]	0.75 (0.51 – 1.10)
Model 3	1 [Reference]	1.46 (1.01–2.11)	1 [Reference]	0.77 (0.51 – 1.15)
Cardiomyopathies excluded^b				
Person-years at risk	494 703	109 464	462 495	141 672
Cases/persons at risk	67/10 468	31/2245	78/9815	20/2898
Incidence rate per 1000 person years	0.14 (0.11-0.17)	2.09 (1.35-3.18)	0.17 (0.13-0.21)	0.14 (0.86-0.22)
Incidence ratio	1 [Reference]	2.58 (1.73-3.79)	1 [Reference]	0.84 (0.50-1.35))
	<i>Odds ratio (95% CI)</i>		<i>Odds ratio (95% CI)</i>	
Model 1	1 [Reference]	2.17 (1.42–3.34)	1 [Reference]	0.87 (0.53–1.42)
Model 2	1 [Reference]	1.52 (0.98–2.35)	1 [Reference]	0.69 (0.42 – 1.14)
Model 3	1 [Reference]	1.54 (0.97–2.44)	1 [Reference]	0.70 (0.42–1.16)

Abbreviations: CI, confidence interval. Model 1=univariate model; Model 2=adjusted for adoptee birth year, sex, county, and education; Model 3=adjusted for adoptee birth year, sex, county, education, coronary heart disease, hypertension, valvular heart disease, diabetes mellitus, and chronic obstructive pulmonary disease. ^a Risks are presented as odds ratios (95 % confidence interval) derived from unconditional logistic regression. ^b All adoptees diagnosed with cardiomyopathy, or that had a biological or adoptive parent diagnosed with cardiomyopathy, were excluded.

eTable 8. Odds Ratio^a of Heart Failure (HF) in Adoptees, Stratified by Affected Parent (Case-Control Study)^b. Only Adoptees With Both Biological and Both Adoptive Parents Identified included

	No. of cases	No. of controls	All ages ^c	Age ≤ 45 yr. ^d	Age 46-59 yr. ^e	Age ≥60 yr. ^f
Cardiomyopathies included			<i>Odds ratio (95% Confidence Interval)</i>			
Biological parental HF	46	172	1.51 (1.02 – 2.25)	1.17 (0.39– 3.50)	1.85 (1.09– 3.12)	1.16 (0.55– 2.43)
No biological parental HF	105	583	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Adoptive parental HF			<i>Odds ratio (95% Confidence Interval)</i>			
Adoptive parental HF	31	206	0.68 (0.45 – 1.05)	0.46 (0.11– 1.85)	0.52 (0.28– 0.95)	1.16 (0.58– 2.29)
No adoptive parental HF	120	549	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Cardiomyopathies excluded^g			<i>Odds ratio (95% Confidence Interval)</i>			
Biological parental HF	30	104	1.69 (1.03 – 2.78)	1.00 (0.19– 5.28)	2.23 (1.14– 4.35)	1.26 (0.53– 2.98)
No biological parental HF	65	371	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Adoptive parental HF			<i>Odds ratio (95% Confidence Interval)</i>			
Adoptive parental HF	18	119	0.70 (0.40 – 1.22)	0.46 (0.05– 4.70)	0.59 (0.26– 1.32)	0.89 (0.39– 2.03)
No adoptive parental HF	77	356	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Abbreviations: HF, heart failure. ^a Odds ratios derived from unconditional logistic regression. ^b Cases and controls matched by sex, birth year (± 5 years), county of birth and level of education, and stratified by adoptee age at diagnosis. ^c Numbers of adoptee cases and controls per category of affected parents as specified in left columns. ^d Total number of 37 cases and 185 controls; 17 cases and 102 controls with cardiomyopathies excluded. ^e 99 cases and 495 controls; 58 cases and 348 controls with cardiomyopathies excluded. ^f 55 cases and 275 controls; 39 cases and 234 controls with cardiomyopathies excluded. ^g All adoptees diagnosed with cardiomyopathy, or that had a biological or adoptive parent diagnosed with cardiomyopathy, were excluded.						

eTable 9. Odds Ratio^a of Heart Failure (HF) in Adoptees, Stratified by Affected Biological Parents, in Relation to Coronary Heart Disease (CHD) (Cohort Design). Individuals With Cardiomyopathies Included

	No Biological Parental HF	Biological parental HF without CHD	Biological parental HF and CHD ^b
Adoptee HF without CHD	<i>Odds ratio (95% CI)</i>		
Model 1	1 [Reference]	2.67 (1.58-4.49)	1.95 (1.21-3.14)
Model 2	1 [Reference]	1.88 (1.11-3.20)	1.38 (0.85-2.24)
Model 3	1 [Reference]	1.93 (1.12-3.34)	1.13 (0.68-1.88)
Adoptee HF and CHD^b	<i>Odds ratio (95% CI)</i>		
Model 1	1 [Reference]	2.13 (0.96-4.72)	2.70 (1.50-4.84)
Model 2	1 [Reference]	1.22 (0.54-2.73)	1.49 (0.83-2.71)
Model 3	1 [Reference]	1.46 (0.63-3.36)	1.25 (0.67-2.35)

Abbreviations: CHD, coronary heart disease; HF, heart failure; CI, confidence interval. Model 1=univariate model; Model 2=adjusted for adoptee birth year, sex, county, and education; Model 3=adjusted for adoptee birth year, sex, county, education, coronary heart disease, hypertension, valvular heart disease, diabetes mellitus, and chronic obstructive pulmonary disease.^a Risks are presented as odds ratios (95 % confidence interval) derived from unconditional logistic regression.^b Patients registered with both CHD and HF regardless of order of events.

eTable 10. Odds Ratio^a of Heart Failure (HF) in Adoptees^b, Stratified by Affected Biological Parents and by Sex (Cohort Study). Individuals with cardiomyopathies included

	No Biological Parental HF	Biological paternal HF	Biological maternal HF
All adoptees	<i>Odds ratio (95% CI)</i>		
Model 1	1 [Reference]	1.65 (1.07–2.55)	3.11 (2.07–4.67)
Model 2	1 [Reference]	1.20 (0.77–1.87)	1.81 (1.19 – 2.74)
Model 3	1 [Reference]	1.14 (0.71–1.81)	1.77 (1.14 – 2.77)
Male adoptees	<i>Odds ratio (95% CI)</i>		
Model 1	1 [Reference]	1.67 (1.04-2.67)	2.15 (1.30-3.55)
Model 2	1 [Reference]	1.25 (0.78-2.01)	1.29 (0.77-2.15)
Model 3	1 [Reference]	1.03 (0.62-1.71)	1.11 (0.63-1.95)
Female adoptees	<i>Odds ratio (95% CI)</i>		
Model 1	1 [Reference]	1.56 (0.77-3.18)	5.31 (3.02-9.32)
Model 2	1 [Reference]	1.10 (0.54-2.25)	3.08 (1.72-5.51)
Model 3	1 [Reference]	1.45 (0.68-3.06)	3.65 (1.97-6.77)

Abbreviations: HF, heart failure; CI, confidence interval. Model 1=univariate model; Model 2=adjusted for adoptee birth year, sex, county, and education; Model 3=adjusted for adoptee birth year, sex, county, education, coronary heart disease, hypertension, valvular heart disease, diabetes mellitus, and chronic obstructive pulmonary disease. ^a Risks are presented as odds ratios (95 % confidence interval) derived from unconditional logistic regression. ^b Adoptees with both biological parents affected with HF were excluded.