Family matters: a genealogical inquiry into the familial component of longevity

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CHAPTER 8

SUPPLEMENTARY MATERIAL

CHAPTER 4 - CHAPTER 5 - CHAPTER 6

Chapter 4

Supplementary Table 1: Survival analysis for IPs by top 5% siblings and top 5% parents

		UPDB			LINKS	
	N (mean)	HR (95% CI)	P-value	N (mean)	HR (95% CI)	P-value
Top 5% parents (F1)						
0 (ref)	8149 (0.79)			8975 (0.88)		
1	1961 (0.19)	0.83 (0.79-0.88)	8.19*10-11	1097 (0.11)	0.79 (0.74-0.84)	2.07*10-12
2	136 (0.02)	0.70 (0.57-0.86)	5.97*10-4	42 (0.01)	0.83 (0.60-1.16)	2.75*10-1
Top 5% sibs (F2)						
0 (ref)	8169 (0.79)			9331 (0.92)		
1	1667 (0.17)	0.82 (0.74-0.91)	1.48*10-4	712 (0.07)	0.79 (0.67-0.93)	4.74*10-3
2+	410 (0.04)	0.75 (0.63-0.89)	9.30*10-4	71 (0.01)	0.65 (0.42-1.02)	6.12*10-2
LDS (F2)						
0 - non-religious(ref)	2753 (0.27)					
1 – baptized	512 (0.05)	0.69 (0.62-0.77)	4.47*10-12	NA	NA	NA
2 - baptized + endowment	6736 (0.66)	0.82 (0.78-0.86)	4.60*10-15	NA	NA	NA
3 - missing	245 (0.02)	0.87 (0.78-1.00)	5.78*10-2	NA	NA	NA
Sibship size (F2)	10246 (6.28)	1.01 (1.00-1.02)	1.04*10-1	10114 (6.34)	1.00 (0.99-1.01)	4.35*10-1
Birth cohort, years (F2)	10246 (1868)	0.99 (>0.99<1.00)	1.28*10-10	10114 (1835)	0.99 (>0.99<1.00)	<1.00*10-15
Sex (F2)						
Man (ref)	5053 (0.49)			4776 (0.48)		
Women	5193 (0.51)	0.69 (0.65-0.74)	<1.00*10-15	5338 (0.52)	1.01 (0.97-1.06)	4.35*10-1
SES – OCC_1950 (F2)						
0 - High (ref)	315 (0.03)			67 (0.01)		
1	1482 (0.14)	1.12 (0.98-1.28)	1.11*10-1	645 (0.06)	0.89 (0.69-1.15)	3.64*10-1
2	400 (0.04)	1.14 (0.97-1.33)	1.20*10-1	536 (0.05)	0.98 (0.76-1.27)	8.66*10-1
3	352 (0.03)	1.22 (1.03-1.44)	1.81*10-2	62 (0.01)	0.77 (0.54-1.10)	1.51*10-1
4	187 (0.02)	1.10 (0.91-1.34)	3.17*10-1	71 (0.01)	0.95 (0.67-1.34)	7.67*10-1
5	891 (0.09)	1.23 (1.07-1.42)	3.59*10-3	733 (0.07)	0.80 (0.62-1.03)	8. 59*10-2
6	668 (0.07)	1.29 (1.12-1.49)	5.11*10-4	311 (0.03)	0.86 (0.66-1.13)	2.81*10-1
7	522 (0.05)	1.25 (1.07-1.45)	4.92*10-3	759 (0.08)	0.82 (0.63-1.06)	2.31*10-1
8	168 (0.02)	1.22 (0.99-1.50)	5.94*10-2	574 (0.06)	0.85 (0.66-1.10)	2.11*10-1
9 – Low	562 (0.05)	1.39 (1.19-1.61)	2.11*10-5	3656 (0.36)	0.83 (0.65-1.07)	1.47*10-1
999 - missing	4699 (0.46)	1.59 (1.40-1.81)	1.74*10-12	2700 (0.26)	0.92 (0.72-1.18)	4.93*10-1

Table corresponds to the CH curves in the top and bottom right panel of supplementary Figure 2. Means represent a mean for a ontinuous variable and a proportion for a categorical variable. Additional covariates are: age mom at birth, birth order, birth intervals (in years), twin birth. When the p-value was lower than 1.00e-15 we indicated the P-value as <1.00e-15. LDS: the church of Jesus Christ of latter-day saints (Mormon church), SES: socio-economic status, OCC: occupational coding scheme of 1950. P-values are estimated with cox regression.

Supplementary Table 2: Frailty survival analysis for Children of IPs by top 5% IP's and aunt and uncles of children

		UPDB			LINKS	
	N (mean)	**HR (95% CI)**	**P-value**	**N (mean)**	**HR (95% CI)**	**P-value**
Top 5% IP (F2)						
0 non LL (ref.)	54607 (0.90)			58196 (0.93)		
1 LL	6191 (0.10)	0.83 (0.80-0.86)	<1.00*10-15	4278 (0.07)	0.83 (0.79-0.88)	5.66*10-13
Top 5% aunts and uncles (F2)						
0 (ref.)	48154 (0.79)			57508 (0.92)		
1	10166 (0.17)	0.95 (0.92-0.98)	3.79*10-4	4465 (0.07)	0.93 (0.89-0.97)	2.40*10-3
2+	2478 (0.04)	0.91 (0.86-0.96)	1.60*10-3	501 (0.01)	0.78 (0.68-0.90)	4.94*10-4
Sibshipsize (F3)	60798 (8.89)	1.02 (1.01-1.02)	<1.00*10-15	62474 (8.52)	1.00 (0.99-1.00)	5.92*10-1
Birth year (F3)	60798 (1892)	0.99 (>0.99<1.00)	<1.00*10-15	62474 (1867)	0.99 (>0.99<1.00)	6.52*10-12
Sex (F3)						
Man (ref.)	31258 (0.51)			32136 (0.52)		
Women	29540 (0.49)	0.62 (0.60-0.63)	<1.00*10-15	30338 (0.48)	0.64 (0.63-0.66)	<1.00*10-15
Famid intercept (variance)	60798 (1.00)	0.34 (0.11)		62474 (1.00)	0.34 (0.11)	
BIC	60798 (1.00)	-23798.10		62474 (1.00)	-21555.34	

Additional covariates are: birth order, birth intervals (years), age mom at birth. Religion, Socio-economic status, twin birth have been stratified. When the p-value was lower than 1.00e-15 we indicated the P-value as <1.00e-15. BIC: Bayesian Information Criterion, Famid: family identifier. P-values are estimated with cox regression.

Supplementary Table 3: Survival analysis for IP's by top 5% siblings for IPs without top 5% parents

		UPDB non-longevous parents	
	N (mean)	**HR (CI)**	**P-value**
Top 5% sibs of RP			
0 (ref.)	6665 (0.82)		
1	1219 (0.15)	0.79 (0.70-0.90)	<0.0001
2+	165 (0.02)	0.77 (0.62-0.95)	0.0168
		LINKS non-longevous parents	
	N (mean)	**HR (CI)**	**P-value**
Top 5% sibs of RP			
0 (ref.)	8354 (0.93)		
1	567 (0.06)	0.76 (0.63-0.92)	0.0045
2+	54 (0.01)	0.61 (0.37-0.99)	0.0500

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 4:
frailty survival analysis for Children of IP's by top 5% aunt and uncles of children without top 5% parents

		UPDB non-longevous RP + non longevous spouse	
	N (mean)	**HR (CI)**	**P-value**
Top 5% aunts and uncles			
0 (ref.)	39338 (80)		
1	7934 (16)	0.93 (0.90-0.96)	<0.0001
2+	1816 (4)	0.91 (0.85-0.97)	0.0047
		LINKS non-longevous RP + non longevous spouse	
	N (mean)	**HR (CI)**	**P-value**
Top 5% aunts and uncles			
0 (ref.)	50165 (92)		
1	3737 (7)	0.93 (0.88-0.98)	0.0037
2+	345 (1)	0.73 (0.62-0.86)	<0.0001

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 5: Survival analysis for IP's by top 5% fathers and mothers

			UPDB			LINKS	
		N (mean)	**HR (95% CI)**	**P-value**	**N (mean)**	**HR (95% CI)**	**P-value**
F1-F2 (IP)	Top 5% parents						
	0 Both parents NL	7798 (0.79)			8927 (0.88)		
	1 Pa LL / Ma NL	1037 (0.10)	0.83 (0.77-0.89)	<0.0001	495 (0.5)	0.789(0.77-0.86)	<0.0001
	2 Ma LL / Pa NL	876 (0.9)	0.83 (0.78-0.89)	<0.0001	601 (0.6)	0.77 (0.70-0.84)	<0.0001
	3 Both parents LL	136 (0.2)	0.69 (0.58-0.82)	<0.0001	42 (0.1)	0.86 (0.63-1.16)	0.3368
F2-F3 (full)	Top 5% parents						
	0 Both parents NL	47960 (0.80)			53422 (0.86)		
	1 Pa LL / Ma NL	6176 (0.10)	0.86 (0.83-0.89)	<0.0001	4668 (0.07)	0.85 (0.81-0.89)	<0.0001
	2 Ma LL / Pa NL	5352 (0.09)	0.83 (0.79-0.86)	<0.0001	3783 (0.06)	0.82 (0.78-0.86)	<0.0001
	3 Both parents LL	754 (0.01)	0.68 (0.61-0.76)	<0.0001	438 (0.01)	0.63 (0.54-0.73)	<0.0001

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. PA=father, MA=mother, NL=non-longevous, LL=longevous, NL=non-longevous, longevous was defined as belonging to the top 10% of a persons' birth cohort. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 6 - construction of final statistical models UPDB - 10 percent

	Model 1		Model 2		Model 3		Model 4	
	N (mean)	HR (95% CI)	N (mean)	HR (95% CI)	N (mean)	HR (95% CI)	N (mean	HR (95% CI)
Top 10% parents (F1)								
0 (ref)	6640 (0.65)				7861 (0.78)		6640 (0.65)	
1	3167 (0.31)	0.89 (0.84-0.93)			2096 (0.20)	0.90 (0.86-0.95)	3167 (0.31)	0.88 (0.83-0.92)
2	439 (0.4)	0.74 (0.66-0.83)			184 (0.2)	0.76 (0.67-0.85)	439 (0.4)	0.73 (0.65-0.83)
Top 10% sibs (F2)								
0 (ref)			6720 (0.66)		8644 (0.85)		6720 (0.66)	
1			2495 (0.24)	0.82 (0.75-0.89)	1256 (0.13)	0.83 (0.76-0.90)	2495 (0.24)	0.82 (0.76-0.90)
2+			1031 (0.10)	0.74 (0.66-0.82)	214 (0.2)	0.76 (0.68-0.84)	1031 (0.10)	0.74 (0.66-0.82)
LDS (F2)								
0 - non-religious(ref)							2753 (0.27)	
1 – baptized							512 (0.05)	NA
2 - baptized + endowment							6736 (0.66)	NA
3 - missing							245 (0.02)	NA
Sibship size (F2)							10246 (6.28)	1.01 (1.00-1.02)
Birth cohort, years (F2)							10246 (1868)	0.99 (>0.99<1.00)
Sex (F2)								
Man (ref)							5053 (0.49)	
Women							5193 (0.51)	0.71 (0.67-0.76)
SES – OCC_1950 (F2)								
0 - High (ref)							315 (0.03)	
1							1482 (0.14)	1.16 (1.01-1.34)
2							400 (0.04)	1.19 (1.00-1.40)
3							352 (0.03)	1.24 (1.05-1.48)
4							187 (0.02)	1.14 (0.93-1.40)
5							891 (0.09)	1.31 (1.13-1.52)
6							668 (0.07)	1.34 (1.15-1.56)
7							522 (0.05)	1.27 (1.08-1.50)
8							168 (0.02)	1.21 (0.97-1.50)
9 - Low							562 (0.05)	1.48 (1.26-1.73)
999 - missing							4699 (0.46)	1.61 (1.40-1.84)

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: age mom at birth, birth order, birth intervals (in years), and twin birth. LDS: the church of Jesus Christ of latter-day saints (Mormon church), SES: socio-economic status, OCC: occupational coding scheme of 1950. P-values are estimated with cox regression.

Supplementary Table 7 - construction of final statistical models LINKS - 10 percent

	Model 1		Model 2		Model 3		Model 4	
	N (mean)	HR (95% CI)	N (mean)	HR (95% CI)	N (mean)	HR (95% CI)	N (mean	HR (95% CI)
Top 10% parents (F1)								
0 (ref)	7861 (0.78)				7861 (0.78)		7861 (0.78)	
1	2096 (0.20)	0.81 (0.77-0.86)			2096 (0.20)	0.82 (0.78-0.86)	2096 (0.20)	0.82 (0.78-0.86)
2	184 (0.2)	0.68 (0.58-0.81)			184 (0.2)	0.69 (0.58-0.82)	184 (0.2)	0.69 (0.58-0.82)
Top 10% sibs (F2)								
0 (ref)			8644 (0.85)		8644 (0.85)		8644 (0.85)	
1			1256 (0.13)	0.82 (0.72-0.92)	1256 (0.13)	0.83 (0.73-0.94)	1256 (0.13)	0.82 (0.73-0.93)
2+			214 (0.2)	0.72 (0.56-0.92)	214 (0.2)	0.76 (0.59-0.97)	214 (0.2)	0.75 (0.58-0.96)
LDS (F2)								
0 - non-religious(ref)								
1 – baptized							NA	NA
2 - baptized + endowment							NA	NA
3 - missing							NA	NA
Sibship size (F2)							10114 (6.34)	1.01 (1.00-1.02)
Birth cohort, years (F2)							10114 (1835)	0.99 (>0.99<1.00)
Sex (F2)								
Man (ref)							4776 (0.48)	
Women							5338 (0.52)	1.01 (0.96-1.06)
SES – OCC_1950 (F2)								
0 - High (ref)							67 (0.01)	
1							645 (0.06)	0.88 (0.68-1.14)
2							536 (0.05)	0.97 (0.75-1.27)
3							62 (0.01)	0.76 (0.53-1.10)
4							71 (0.01)	0.99 (0.70-1.40)
5							733 (0.07)	0.80 (0.62-1.04)
6							311 (0.03)	0.86 (0.65-1.13)
7							759 (0.08)	0.84 (0.65-1.10)
8							574 (0.06)	0.85 (0.65-1.11)
9 - Low							3656 (0.36)	0.83 (0.65-1.07)
999 - missing							2700 (0.26)	0.93 (0.72-1.20)

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: age mom at birth, birth order, birth intervals (in years), twin birth. LDS: the church of Jesus Christ of latter-day saints (Mormon church), SES: socio-economic status, OCC: occupational coding scheme of 1950. P-values are estimated with cox regression.

Supplementary Table 8: Survival analysis for IP's by top 10% siblings among IPs without top 10% parents

		UPDB non-longevous parents	
	N (mean)	**HR (CI)**	**P-value**
Top 10% sibs of RP			
0 (ref.)	4639 (0.70)		
1	1473 (0.22)	0.85 (0.79-0.91)	<0.0001
2+	528 (0.8)	0.78 (0.67-0.90)	<0.0001
		LINKS non-longevous parents	
	N (mean)	**HR (CI)**	**P-value**
Top 10% sibs of RP			
0 (ref.)	6867 (0.87)		
1	886 (0.11)	0.78 (0.72-0.85)	<0.0001
2+	108 (0.2)	0.72 (0.53-0.99)	0.0429

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 9: Survival analysis for IP's by top 10% fathers and mothers

			UPDB			LINKS	
		N (mean)	**HR (95% CI)**	**P-value**	**N (mean)**	**HR (95% CI)**	**P-value**
F1-F2 (IP)	Top 10% parents						
	0 Both parents NL	6334 (0.64)			7817 (0.77)		
	1 Pa LL / Ma NL	1653 (0.17)	0.88 (0.84-0.93)	<0.0001	1124 (0.11)	0.83 (0.78-0.89)	<0.0001
	2 Ma LL / Pa NL	1421 (0.15)	0.84 (0.79-0.89)	<0.0001	940 (0.09)	0.80 (0.75-0.86)	<0.0001
	3 Both parents LL	439 (0.4)	0.73 (0.66-0.80)	<0.0001	184 (0.03)	0.72 (0.62-0.83)	<0.0001
F2-F3 (full)	Top 10% parents						
	0 Both parents NL	38423 (0.64)			45644 (0.73)		
	1 Pa LL / Ma NL	10522 (0.17)	0.89 (0.86-0.92)	<0.0001	8643 (0.14)	0.86 (0.83-0.89)	<0.0001
	2 Ma LL / Pa NL	8969 (0.15)	0.86 (0.83-0.89)	<0.0001	6360 (0.10)	0.82 (0.79-0.86)	<0.0001
	3 Both parents LL	2328 (0.4)	0.72 (0.68-0.76)	<0.0001	1664 (0.03)	0.73 (0.67-0.79)	<0.0001

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. PA=father, MA=mother, NL=non-longevous, LL=longevous, NL=non-longevous, longevous was defined as belonging to the top 10% of a persons' birth cohort. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 10: Sex specific survival analysis for IP's by top 10% parents

		UPDB			LINKS		
		N (mean)	HR (95% CI)	P-value	N (mean)	HR (95% CI)	P-value
F1-F2 (IP)	Top 10% parents (F1)						
	0	6640 (0.65)			7861 (0.78)		
	1	3167 (0.31)	0.85 (0.75-0.96)	0.0067	2096 (0.20)	0.83 (0.78-0.91)	<0.0001
	2	439 (0.4)	0.68 (0.59-0.80)	<0.0001	184 (0.2)	0.61 (0.48-0.76)	<0.0001
	Sex						
	Man (ref)	5053 (0.49)			4776 (0.48)		
	Women	5193 (0.51)	0.73 (0.68-0.78)	<0.0001	5338 (0.52)	1.02 (0.97-1.08)	0.3600
	Sex* Top 10% parents (F1)						
	0 Top 10 parents | women (ref)	6640 (0.65)			7861 (0.78)		
	1 Top 10 parents | women	3167 (0.31)	0.92 (0.78-1.10)	0.3440	2096 (0.20)	0.96 (0.86-1.10)	0.4041
	2 Top 10 parents | women	439 (0.4)	1.10 (0.89-1.35)	0.4010	184 (0.2)	1.36 (0.97-1.91)	0.0748
F2-F3 (Child of IP - one LL parent)	Top 10% parents (F1)						
	0	48619 (0.80)			53378 (0.85)		
	1	12179 (0.20)	0.83 (0.77-0.89)	<0.0001	9096 (0.15)	0.86 (0.78-0.94)	<0.0017
	Sex						
	Man (ref)	31258 (0.51)			32136 (0.52)		
	Women	29540 (0.49)	0.56 (0.55-0.58)	<0.0001	30338 (0.48)	0.64 (0.63-0.66)	<0.0001
	Sex* Top 10% parents (F1)						
	0 Top 10 parents | women (ref)	48619 (0.80)			53378 (0.85)		
	1 Top 10 parents | women	12179 (0.20)	1.03 (0.98-1.08)	0.2390	9096 (0.15)	1.00 (0.94-1.05)	0.1863
F2-F3 (Child of IP - two LL parents)	Top 10% parents (F1)						
	0	58672 (0.96)			60962 (0.97)		
	2	2126 (0.04)	0.68 (0.57-0.80)	<0.0001	1512 (0.03)	0.78 (0.63-0.96)	0.0138
	Sex						
	Man (ref)	31258 (0.51)			32136 (0.52)		
	Women	29540 (0.49)	0.56 (0.55-0.58)	<0.0001	30338 (0.48)	0.64 (0.63-0.66)	<0.0001
	Sex* Top 10% parents (F1)						
	0 Top 10 parents | women (ref)	58672 (0.96)			60962 (0.97)		
	2 Top 10 parents | women	2126 (0.04)	1.09 (0.99-1.21)	0.0812	1512 (0.03)	1.00 (0.87-1.13)	0.1947

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. PA=father, MA=mother, NL=non-longevous, LL=longevous, NL=non-longevous, longevous was defined as belonging to the top 10% of a persons' birth cohort. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 11:

Frailty survival analysis for Children of IP's By top 10% aunt and uncles of children without top 10% parents

		UPDB non-longevous RP + non-longevous spouse	
	N (mean)	**HR (CI)**	**P-value**
Top 10% aunts and uncles			
0 (ref.)	26475 (0.67)		
1	9374 (0.24)	0.96 (0.93-0.99)	0.0170
2+	3516 (0.8)	0.90 (0.86-0.95)	<0.0001
		LINKS **non-longevous RP + non-longevous spouse**	
	N (mean)	**HR (CI)**	**P-value**
Top 10% aunts and uncles			
0 (ref.)	40031 (0.86)		
1	5651 (0.12)	0.95 (0.91-0.99)	0.0134
2+	890 (0.2)	0.81 (0.73-0.90)	<0.0001

Means represent a mean for a continuous variable and a proportion for a categorical variable. Additional covariates are: religion, sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, and twin birth. Here P-values were rounded to 4 digits. P-values are estimated with cox regression.

Supplementary Table 12: Selection criteria for the random sampling of F2 IPs

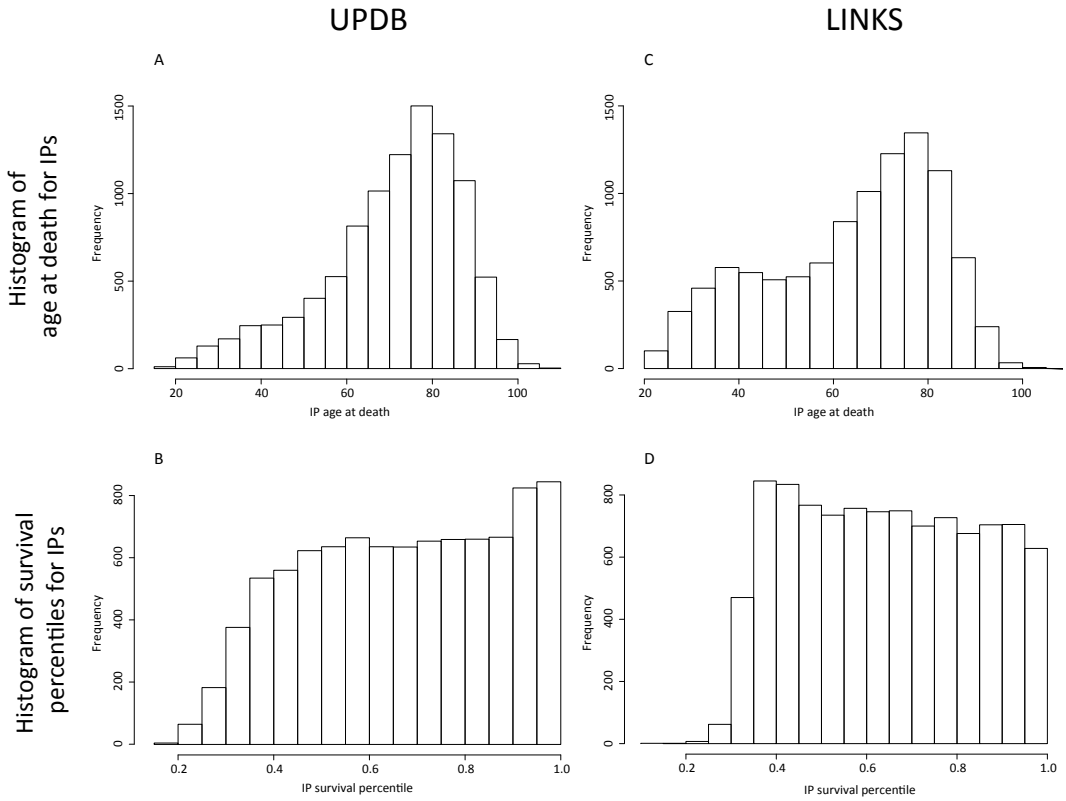
Selection	**Motivation**
At least 1 identifiable child	**Part of the study focused on children, hence children needed to be available for the index persons**
At least 1 identifiable sibling	To ensure that the influence of siblings could be analyzed we excluded families with only a single child. In addition this was a method to make sure that dummy families were excluded
A spouse should be identified	Part of the study focused on spouses who married to longevous index persons. For this, and because index persons needed to have a child, a spouse was required to be available
A known sex	To be able to distinguish between males and females, the sex of at least the index persons needed to be available
Availability of a birth date	To be able to study the survival of the complete group of index persons with the best possible data, a date of birth and a date of death needed to be available. In addition, in the LINKS data selecting on an available birth and death date was a quality check that made sure that index person was indeed part of the identified family.
Availability of a death	
In the UPDB: should be identified on a genealogy record	All genealogy records are verified. Hence, this was a double check to make sure that the index person was indeed part of the identified family.

UPDB: Utah Population Database, LINKS: LINKing System for historical family reconstruction.

Supplementary Table 13: Demographic spread for included UPDB persons

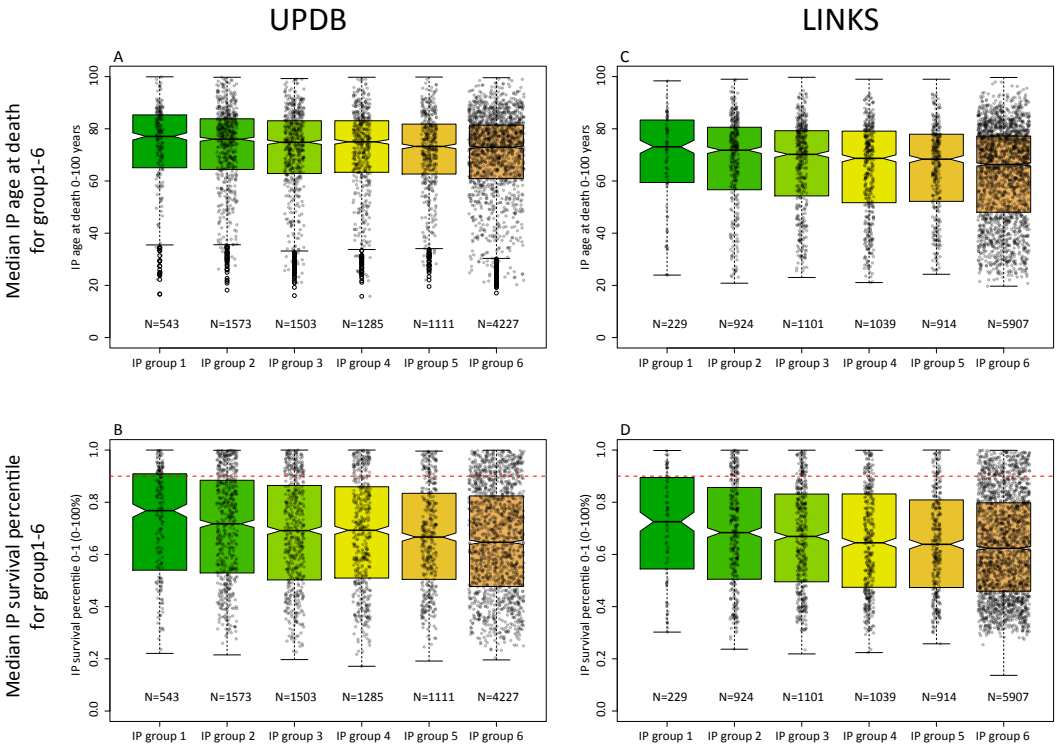
Role	**Fathers**	**Mothers**	**IPs**	**Siblings**	**Spouses**	**Children**
Lived in Utah (%)	7600 (80)	8478 (87)	9901 (97)	32026 (70)	9998 (97)	49839 (92)
Not lived in Utah (%)	1884 (20)	1229 (13)	345 (3)	13674 (30)	356 (3)	4236 (8)
Birth continent	**America**	**Europe**	**Asia**	**Africa**	**Australia**	**Other**
Lived in Utah	85141 (91)	11490 (73)	35 (65)	4 (100)	195 (73)	171 (34)
Not lived in Utah	8310 (9)	4363 (27)	19 (45)	0 (0)	73 (27)	329 (66)

Numbers are based on uncensored individuals. Numbers are based on the UPDB only.



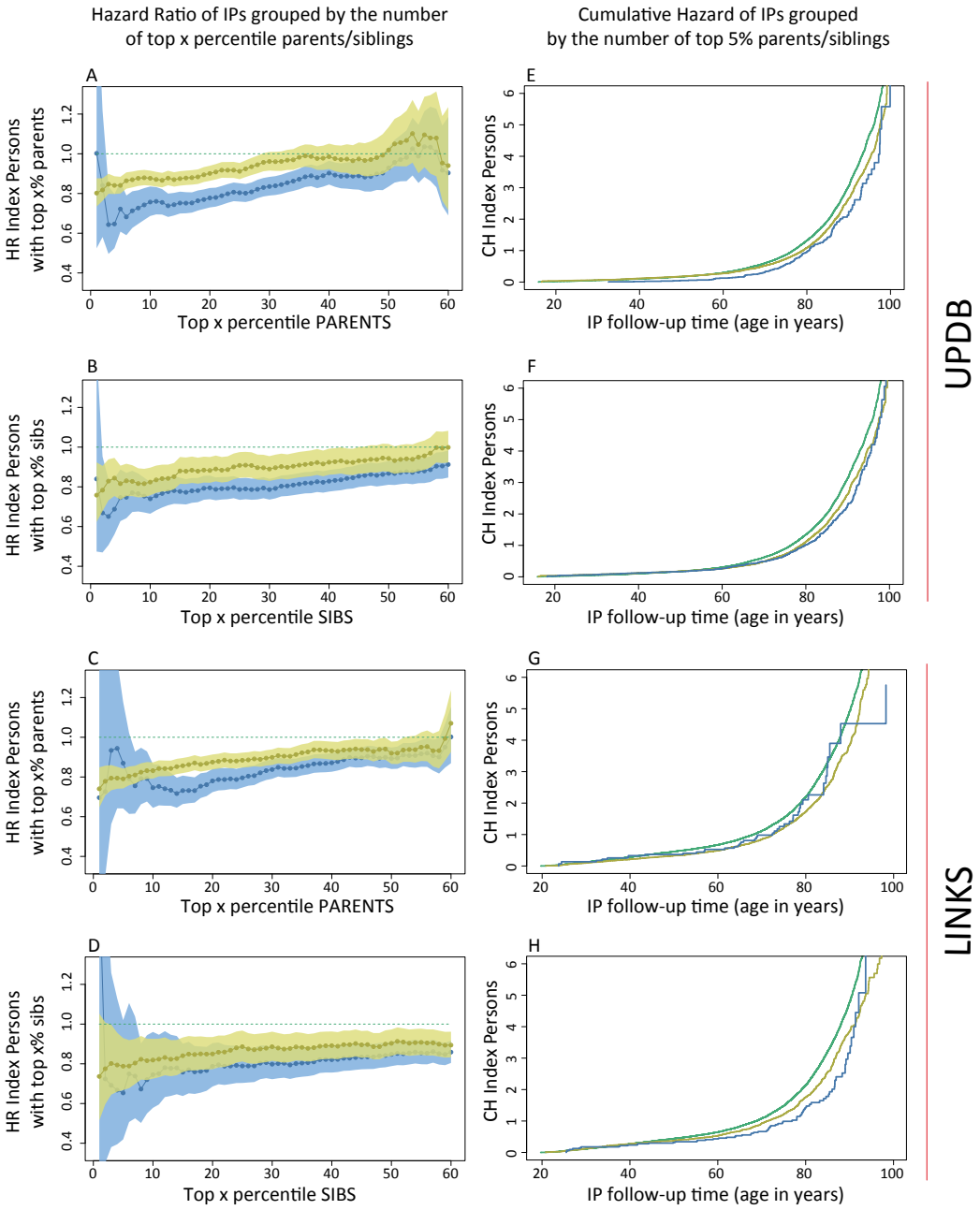
Supplementary Figure 1: Histogram of IP age at death and IP survival percentiles

Panel A and C depict a histogram for the IPs ages at death with the UPDB and LINKS data respectively. Panel B and D depict a histogram for the IPs survival percentiles with the UPDB and LINKS data respectively. IP=Index Person.



Supplementary Figure 2: Median age at death and survival percentile for IPs grouped by their parental and sibling survival in mutual exclusive groups

This figure relates to main Figure 3 and shows the median + quantiles and variation for IPs' age at death on the top row (panel A and C). The bottom row (panel B and D) shows the median + quantiles and variation for IPs' survival percentiles. Nodes are based on 1/6th of the total sample size for illustrative purposes. The red lines on the bottom row represent the cut-off for the top 10 percent surviving IPs for the different groups. Similar to the decrease in HR for the different groups illustrated in main Figure 2 and the increase in age at death or survival percentile for the different groups illustrated in this figure, there is an increase in top 10% surviving IPs. For the UPDB data 17% of the total number of IPs in group 6 belongs to the top 10% survivors, this is 19% for group 5, 23% for group 4, 26% for group 3, 29% for group 2, and 37% for group 1. For the LINKS data the numbers, in similar order, are 13%, 14%, 16%, 18%, 23% and 32%.

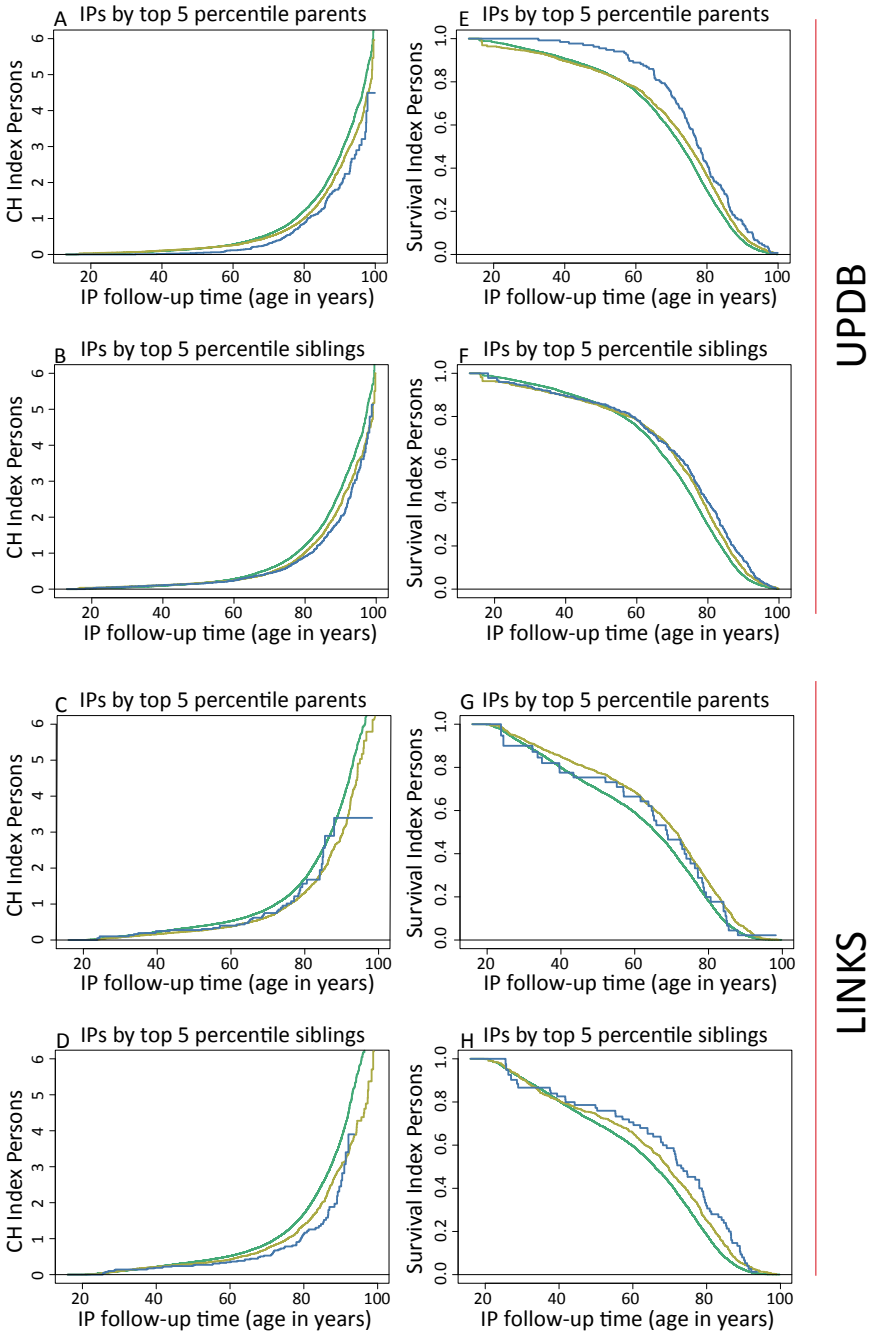


Supplementary Figure 3:

Survival of IPs with parents and siblings belonging to the 1st until 60th percentile survivors of their birth cohort

This figure depicts the Hazard Ratio (HR) for IPs (left column, panel A-D) with 1 and 2 parents or 1 and 2+ siblings belonging to the top x percentile (x = 1,2,3, ..., 60) of survivors of their birth cohort. The percentile groups (x-axis) are mutually inclusive, meaning that a first-degree family member who belonged to the top 1% also belonged to the top 5% etc. The figure also depicts the Cumulative Hazard (CH) for index persons (IPs, right column,

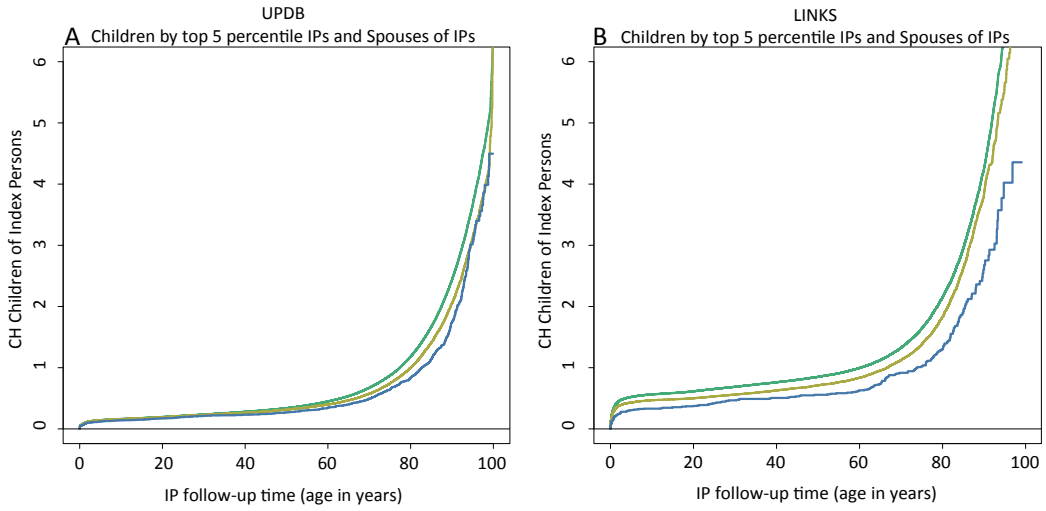
panel E-H) with 1 and 2 parents or 1 and 2+ siblings who belong to the top 5%. Green (dotted) lines present the reference group of 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ top x percentile siblings. Left column: x-axes represent the top x birth cohort based survival percentile, the y-axes represent the hazard ratio (HR) of dying for IPs having 1 and 2 or 2+ top x percentile parents or siblings compared to having 0 top x percentile parents or siblings. Right column: x-axes represent IP years of survival, y-axes represent the IPs' cumulative hazard of dying while having 1 and 2 or 2+ top 5th percentile parents or siblings compared to having 0 top 5th percentile parents or siblings. All estimates are adjusted for religion (UPDB only), sibship size, birth cohort, sex, socio-economic status, mother's age at birth, birth order, birth intervals, twin birth, and number of top 5% parents or number of top 5% siblings for the sibling and parent analyses respectively. Error bars represent confidence intervals.



Supplementary Figure 4:

Kaplan-Meier and Nelson-Aalen plots for IPs by the longevity of their parents and siblings at the top 5%

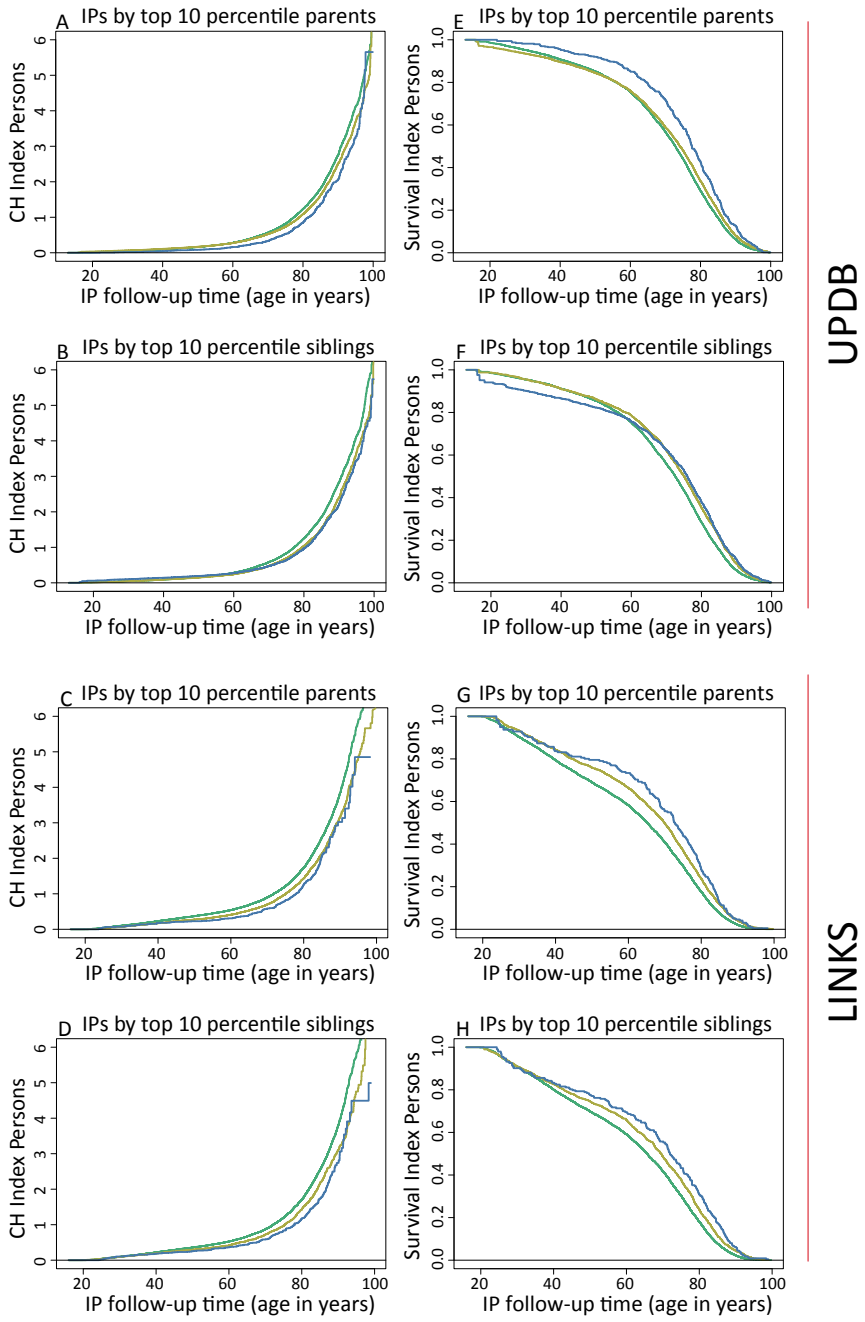
Green lines present 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ longevous parents or siblings. CH=Cumulative Hazard, IP=Index Person. Left column depicts the Kaplan-Meier curves, right column depicts the Nelson-Aalen curves. Panel A, B, E, and F represent UPDB IPs, panel C, D, G, and H represent LINKS IPs. CH=Cumulative Hazard, IP=Index Person.



Supplementary Figure 5:

Nelson-Aalen plots for children of IPs by the longevity of their parents (IPs and spouses of IPs) at the top 5%

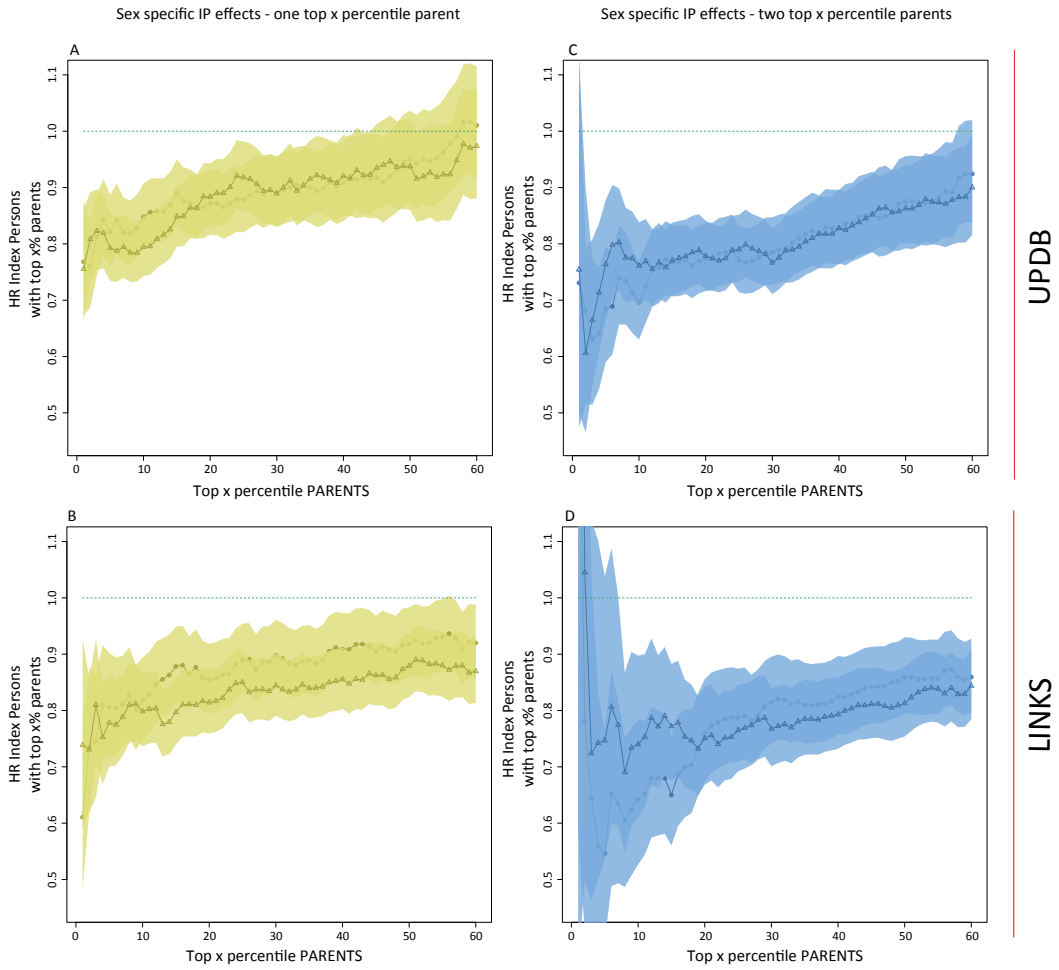
Green lines present 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ longevous parents or siblings. Panel A represents UPDB children of IPs and panel B represents LINKS children of IPs. CH=Cumulative Hazard, IP=Index Person.



Supplementary Figure 6:

Kaplan Meier and Nelson-Aalen plots for IPs by the longevity of their parents and siblings at the top 10%

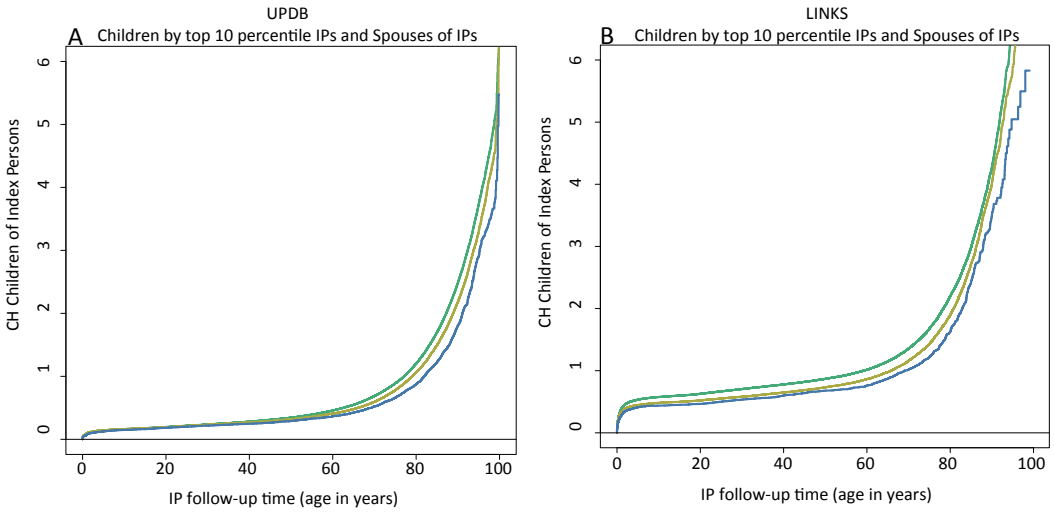
Green lines present 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ longevous parents or siblings. CH=Cumulative Hazard, IP=Index Person. Left column depicts the Kaplan-Meier curves, right column depicts the Nelson-Aalen curves. Panel A, B, E, and F represent UPDB IPs, panel C, D, G, and H represent LINKS IPs. CH=Cumulative Hazard, IP=Index Person.



Supplementary Figure 7:

Sex specific survival of IPs with parents belonging to the 1st until 60th percentile survivors of their birth cohort

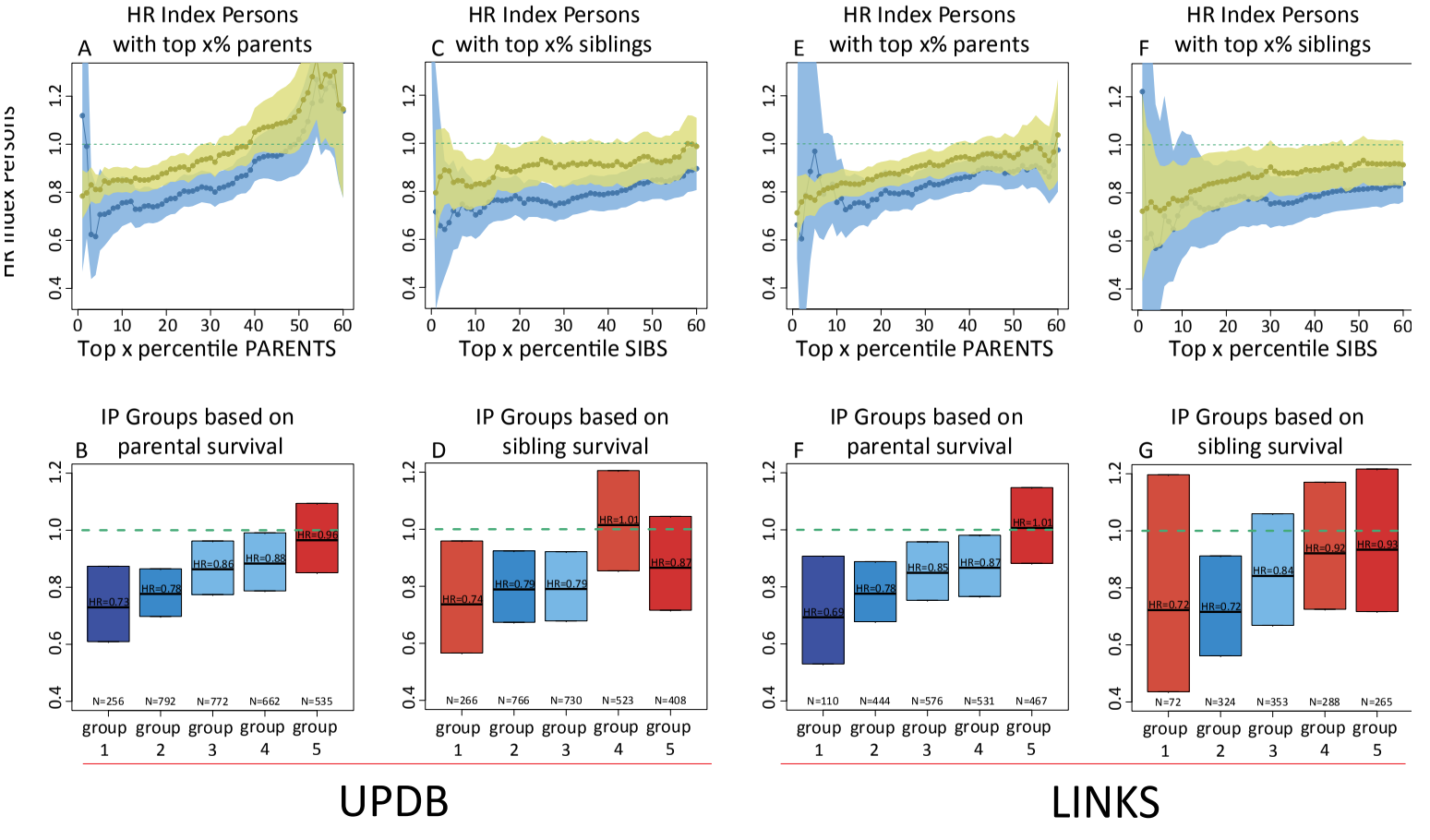
Green lines present 0 top x percentile parents, yellow lines represent 1 top x percentile parents, blue lines represent 2 or 2+ longevous parents. Round nodes=males, triangle nodes=females. Top row (panel A and C) represent UPDB IPs, bottom row (panel B and D) represents LINKS IPs. HR=Hazard Ratio, IP=Index Person. Error bars represent confidence intervals.



Supplementary Figure 8:

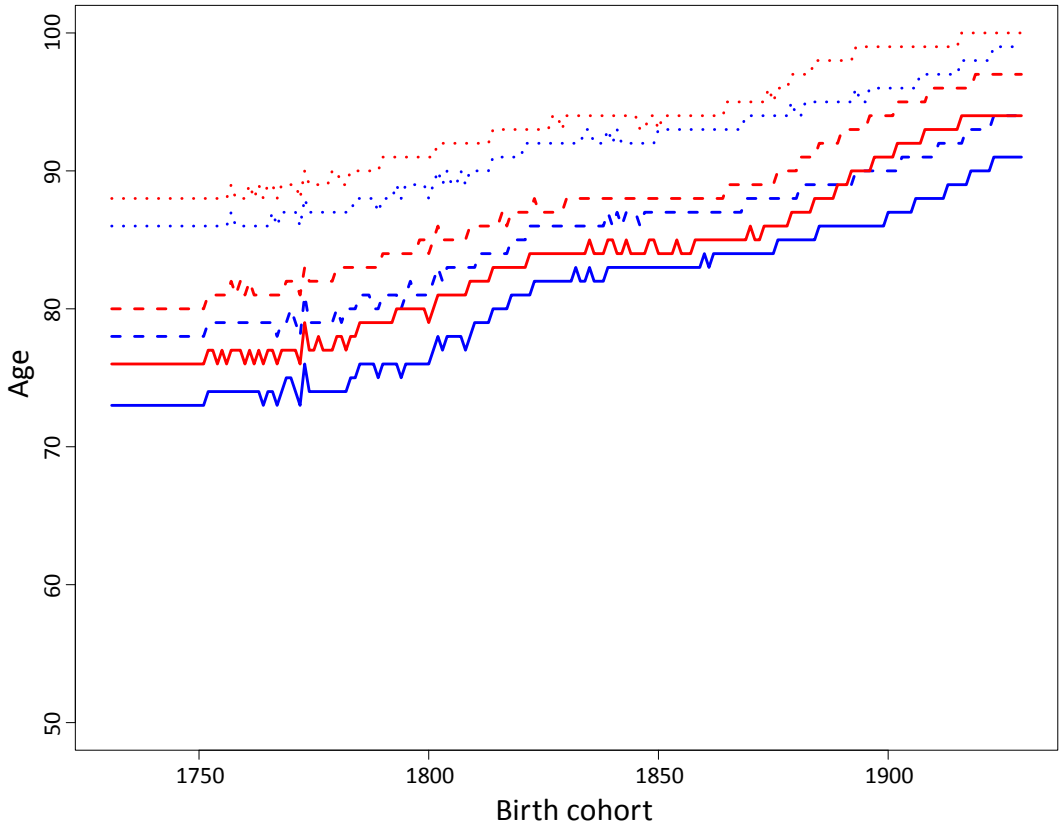
Nelson-Aalen plots for children of IPs by the longevity of their parents (IPs and spouses of IPs) at the top 10%

Green lines present 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ longevous parents or siblings. Panel A represents UPDB children of IPs and panel B represents LINKS children of IPs. CH=Cumulative Hazard, IP=Index Person.



Supplementary Figure 9: Results represented by main Figure 2 and 3 with the IP numbers split in half

Figure illustrates results similar to main Figure 2 and 3 with the number of IPs cut in half. Top row: green lines present 0 top x percentile parents or siblings, yellow lines represent 1 top x percentile parents or siblings, blue lines represent 2 or 2+ longevous parents or siblings. Bottom row: green lines represent the reference category, which is group 6. Top column (Panel A, C, D, and E) represents Figure 2, bottom column (Panel B, D, F, and G) represents Figure 3. HR=Hazard Ratio, IP=Index Person. Error bars represent confidence intervals.



Supplementary Figure 10: UPDB and LINKS birth cohorts mapping of age by top 1, 5, and 10th percentile

This figure represents the the percentile-age pairings from the Swedish lifetables used to calculate survival percentiles in both the UPDB and LINKS datasets. Line colors: Blue: men, Red: women. Line patterns: Dotted lines represent the top 1% survivors of the specific birth cohorts. Broken lines represent the top 5% survivors of the specific birth cohorts. Unbroken lines represent the top 10% survivors of the specific birth cohorts.

Chapter 5

Table A1: Lifetable conditioning by group

Group	Conditioning (age)	Reason
Parents (F0)	**First death in the group, 28 years**	**Parents are indirectly selected to have reached an age to be able to have at least 2 offspring that could be enrolled as participants**
Participants (F1)	Age at inclusion, differs per individual	Participants are directly selected to be alive until the age of inclusion
Siblings (F1)	No conditioning was applied	Siblings are not directly or indirectly selected
Spouses (F1)	First death in the group, 28 years	Spouses are indirectly selected to be old enough to marry

Table A2: Exact SMR values, CIs and N connected to Figure 3

Age	Parents	N parents	Siblings	N siblings	Spouses	N spouses
1			**0.69 (0.65-0.73)**	**2269**		
2			0.66 (0.64-0.7)	2075		
3			0.67 (0.64-0.7)	2058		
4			0.67 (0.64-0.7)	2044		
5			0.67 (0.64-0.7)	2037		
6			0.67 (0.64-0.7)	2035		
7			0.67 (0.64-0.7)	2028		
8			0.67 (0.64-0.7)	2028		
9			0.67 (0.64-0.7)	2025		
10			0.67 (0.64-0.7)	2022		
11			0.67 (0.64-0.7)	2021		
12			0.67 (0.64-0.7)	2016		
13			0.67 (0.64-0.7)	2016		
14			0.67 (0.64-0.7)	2014		
15			0.67 (0.64-0.7)	2012		
16			0.67 (0.64-0.7)	2010		
17			0.67 (0.64-0.7)	2009		
18			0.67 (0.64-0.7)	2004		
19			0.67 (0.64-0.7)	2000		
20			0.67 (0.64-0.7)	1998		
21			0.67 (0.64-0.7)	1992		
22			0.67 (0.64-0.7)	1987		
23			0.67 (0.64-0.7)	1984		
24			0.67 (0.64-0.7)	1981		

Age	Parents	N parents	Siblings	N siblings	Spouses	N spouses
25			0.67 (0.64-0.7)	1977		
26			0.67 (0.64-0.7)	1972		
27			0.66 (0.63-0.69)	1965		
28	0.68 (0.64-0.72)	820	0.66 (0.63-0.69)	1960	1.02 (0-1.08)	690
29	0.68 (0.64-0.72)	819	0.66 (0.63-0.69)	1956	1.02 (0-1.09)	685
30	0.68 (0.65-0.72)	819	0.66 (0.63-0.69)	1953	1.02 (0.95-1.09)	685
31	0.69 (0.65-0.73)	819	0.66 (0.63-0.69)	1950	1.02 (0.95-1.09)	685
32	0.69 (0.65-0.73)	819	0.66 (0.63-0.69)	1947	1.02 (0.95-1.09)	683
33	0.69 (0.65-0.73)	818	0.66 (0.63-0.69)	1945	1.03 (0.96-1.1)	681
34	0.69 (0.65-0.73)	817	0.66 (0.63-0.69)	1941	1.03 (0.96-1.1)	681
35	0.69 (0.65-0.73)	815	0.66 (0.63-0.69)	1937	1.03 (0.97-1.1)	679
36	0.69 (0.65-0.73)	813	0.66 (0.63-0.69)	1933	1.03 (0.97-1.1)	676
37	0.69 (0.66-0.74)	811	0.66 (0.63-0.69)	1930	1.03 (0.97-1.1)	675
38	0.69 (0.66-0.74)	809	0.66 (0.63-0.69)	1927	1.03 (0.97-1.1)	675
39	0.7 (0.66-0.74)	808	0.66 (0.63-0.69)	1923	1.03 (0.97-1.1)	674
40	0.7 (0.66-0.74)	807	0.66 (0.63-0.69)	1919	1.03 (0.98-1.11)	673
41	0.7 (0.66-0.74)	804	0.66 (0.63-0.69)	1915	1.04 (0.98-1.11)	670
42	0.7 (0.66-0.74)	800	0.66 (0.63-0.69)	1909	1.04 (0.98-1.11)	669
43	0.7 (0.66-0.74)	798	0.66 (0.63-0.69)	1906	1.04 (0.98-1.11)	667
44	0.7 (0.66-0.74)	792	0.66 (0.63-0.69)	1901	1.04 (0.98-1.11)	666
45	0.69 (0.66-0.74)	788	0.66 (0.63-0.69)	1898	1.04 (0.98-1.11)	663
46	0.69 (0.66-0.74)	783	0.66 (0.63-0.69)	1891	1.04 (0.98-1.11)	660
47	0.69 (0.66-0.74)	780	0.66 (0.63-0.69)	1885	1.04 (0.98-1.11)	660
48	0.69 (0.66-0.74)	778	0.66 (0.63-0.69)	1884	1.04 (0.98-1.11)	659
49	0.69 (0.66-0.74)	774	0.66 (0.63-0.69)	1880	1.04 (0.98-1.11)	655
50	0.69 (0.66-0.74)	769	0.66 (0.63-0.69)	1873	1.05 (0.99-1.12)	651
51	0.69 (0.65-0.74)	763	0.66 (0.63-0.69)	1866	1.04 (0.99-1.12)	648
52	0.69 (0.65-0.74)	760	0.66 (0.63-0.69)	1860	1.04 (0.98-1.12)	642
53	0.69 (0.65-0.74)	755	0.66 (0.63-0.69)	1856	1.05 (0.98-1.12)	640
54	0.69 (0.66-0.74)	752	0.66 (0.63-0.69)	1848	1.04 (0.98-1.12)	633
55	0.7 (0.66-0.74)	748	0.66 (0.63-0.69)	1843	1.05 (0.98-1.12)	627
56	0.7 (0.66-0.74)	743	0.66 (0.63-0.69)	1835	1.05 (0.98-1.12)	623
57	0.7 (0.66-0.74)	739	0.66 (0.63-0.69)	1828	1.05 (0.98-1.12)	619
58	0.7 (0.66-0.74)	734	0.66 (0.63-0.69)	1820	1.05 (0.99-1.13)	614
59	0.7 (0.66-0.75)	728	0.66 (0.63-0.69)	1809	1.06 (0.99-1.13)	609
60	0.7 (0.66-0.75)	722	0.67 (0.64-0.7)	1804	1.06 (1-1.14)	593
61	0.7 (0.66-0.75)	713	0.66 (0.63-0.7)	1786	1.07 (1-1.14)	584

Age	Parents	N parents	Siblings	N siblings	Spouses	N spouses
62	0.7 (0.66-0.75)	706	0.67 (0.64-0.7)	1776	1.06 (0.99-1.14)	571
63	0.7 (0.66-0.75)	695	0.67 (0.64-0.7)	1762	1.06 (0.99-1.14)	563
64	0.7 (0.66-0.74)	683	0.67 (0.64-0.7)	1744	1.06 (0.99-1.13)	551
65	0.7 (0.66-0.74)	672	0.67 (0.64-0.7)	1722	1.06 (0.99-1.14)	542
66	0.69 (0.65-0.74)	654	0.67 (0.63-0.7)	1699	1.06 (0.99-1.15)	530
67	0.69 (0.65-0.74)	642	0.67 (0.63-0.7)	1674	1.07 (1-1.16)	512
68	0.69 (0.65-0.74)	628	0.67 (0.64-0.71)	1654	1.08 (1.01-1.16)	494
69	0.68 (0.65-0.73)	608	0.67 (0.64-0.7)	1624	1.08 (1-1.16)	483
70	0.69 (0.65-0.74)	597	0.67 (0.64-0.71)	1601	1.07 (1-1.16)	462
71	0.69 (0.64-0.74)	581	0.67 (0.64-0.71)	1571	1.09 (1.02-1.17)	440
72	0.68 (0.64-0.73)	562	0.68 (0.64-0.71)	1544	1.08 (1.01-1.17)	425
73	0.68 (0.64-0.74)	547	0.68 (0.64-0.71)	1506	1.08 (1-1.16)	405
74	0.68 (0.64-0.73)	526	0.68 (0.65-0.72)	1471	1.09 (1.01-1.17)	390
75	0.69 (0.65-0.74)	512	0.68 (0.65-0.72)	1425	1.09 (1.02-1.18)	372
76	0.68 (0.64-0.73)	486	0.69 (0.65-0.72)	1382	1.12 (1.03-1.21)	356
77	0.69 (0.64-0.74)	469	0.69 (0.65-0.73)	1330	1.13 (1.05-1.24)	331
78	0.7 (0.65-0.76)	452	0.69 (0.65-0.73)	1273	1.17 (1.07-1.27)	300
79	0.7 (0.65-0.76)	428	0.7 (0.66-0.74)	1214	1.17 (1.08-1.29)	279
80	0.7 (0.65-0.76)	404	0.7 (0.66-0.74)	1147	1.17 (1.07-1.29)	249
81	0.71 (0.66-0.78)	383	0.7 (0.67-0.74)	1076	1.2 (1.1-1.34)	223
82	0.73 (0.67-0.79)	363	0.71 (0.67-0.76)	1001	1.2 (1.09-1.34)	192
83	0.72 (0.67-0.79)	330	0.73 (0.69-0.78)	940	1.22 (1.1-1.38)	169
84	0.73 (0.67-0.8)	301	0.73 (0.68-0.77)	837	1.22 (1.09-1.37)	135
85	0.75 (0.68-0.83)	279	0.72 (0.68-0.77)	740	1.27 (1.13-1.45)	112
86	0.75 (0.68-0.83)	249	0.74 (0.69-0.8)	667	1.21 (1.07-1.39)	87
87	0.78 (0.71-0.88)	228	0.78 (0.71-0.84)	589	1.26 (1.12-1.47)	69
88	0.8 (0.72-0.9)	202	0.8 (0.73-0.86)	508	1.24 (1.07-1.44)	49
89	0.77 (0.69-0.88)	165	0.78 (0.71-0.86)	409	1.31 (1.12-1.57)	32
90	0.73 (0.63-0.83)	129	0.83 (0.75-0.92)	350	1.32 (1.09-1.6)	22
91	0.74 (0.63-0.85)	108	0.86 (0.78-0.96)	292	1.25 (0.99-1.55)	10
92	0.75 (0.64-0.87)	90	0.8 (0.71-0.9)	221	1.3 (0.97-1.73)	5
93	0.74 (0.61-0.87)	71	0.82 (0.71-0.94)	175	1.23 (0.78-1.86)	NA
94	0.73 (0.59-0.88)	55	0.75 (0.64-0.88)	125	1.23 (0.63-2.05)	NA
95	0.82 (0.66-1.03)	48	0.78 (0.65-0.93)	93		NA
96	0.94 (0.72-1.21)	40	0.75 (0.6-0.91)	65		NA
97	0.83 (0.54-1.14)	25	0.72 (0.5-0.97)	44		NA
98	0.8 (0.4-1.22)	17	0.82 (0.52-1.19)	34		NA
99	0.44 (0-1.04)	10	0.42 (0.03-0.8)	18		NA

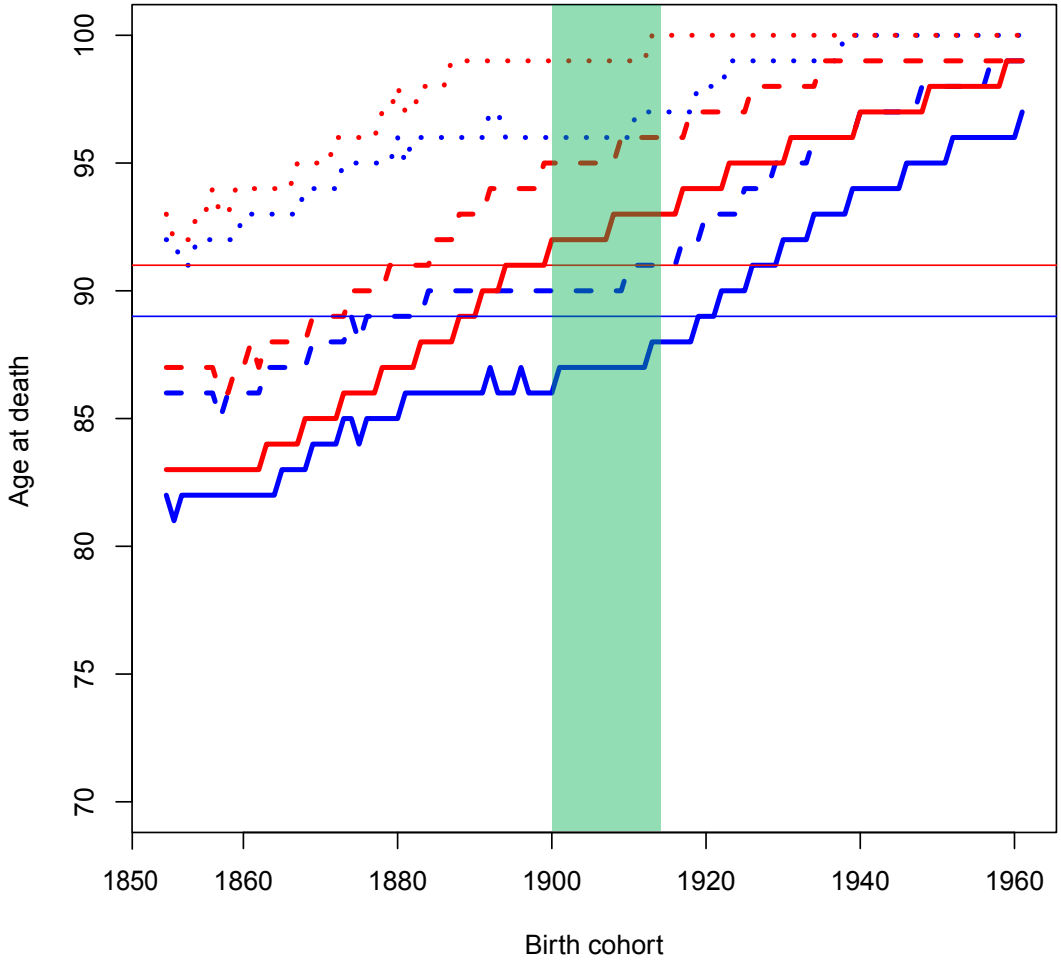


Figure A1: LLS birth cohorts top 10, 5, 1 percentile by participants

The horizontal lines represent the minimal inclusion criteria for the LLS participants (men >=89 and women >=91). The green rectangle represents the birth cohorts for the LLS participants (1900 - 1916). Line colors: Blue: men, Red: women. Line patterns: Dotted lines represent the top 1% survivors of the specific birth cohorts, broken lines represent the top 5% survivors of the specific birth cohorts, unbroken lines represent the top 10% survivors of the specific birth cohorts.

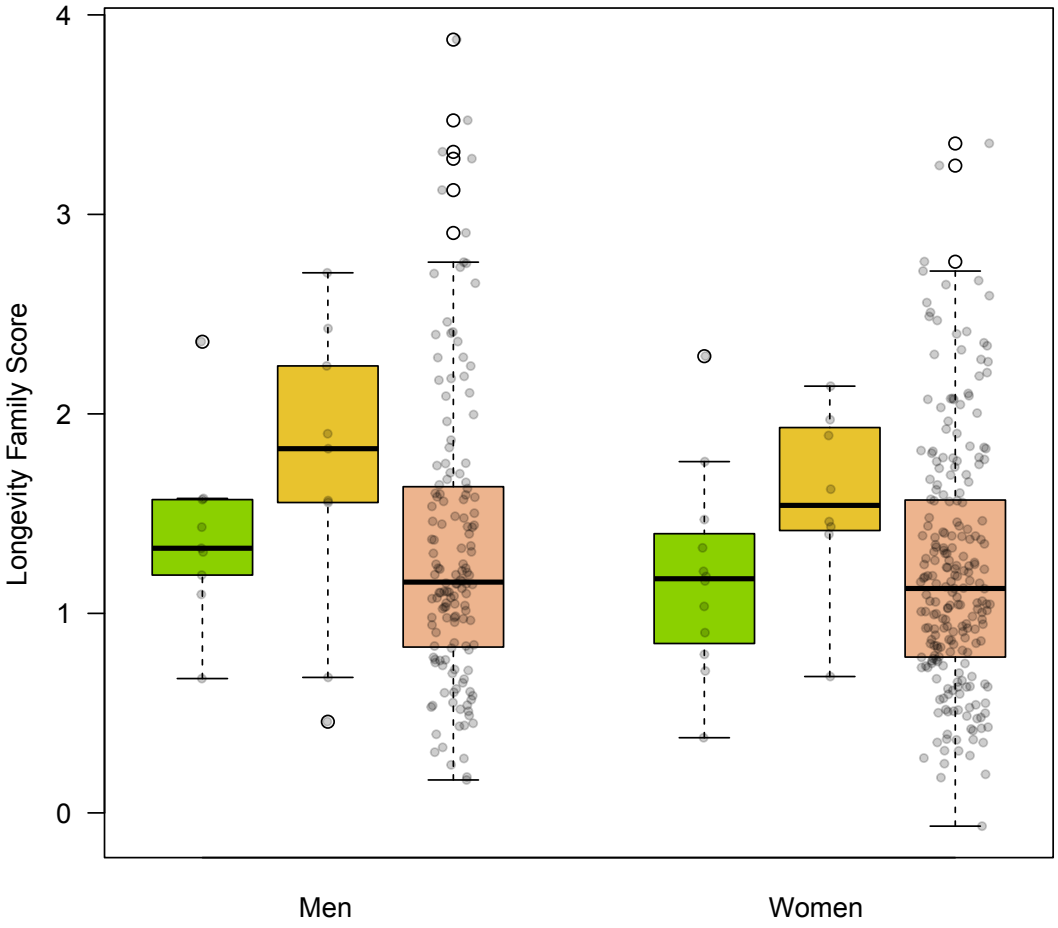


Figure A2: Median sex specific Longevity family score per sibship with one or none long-lived parent

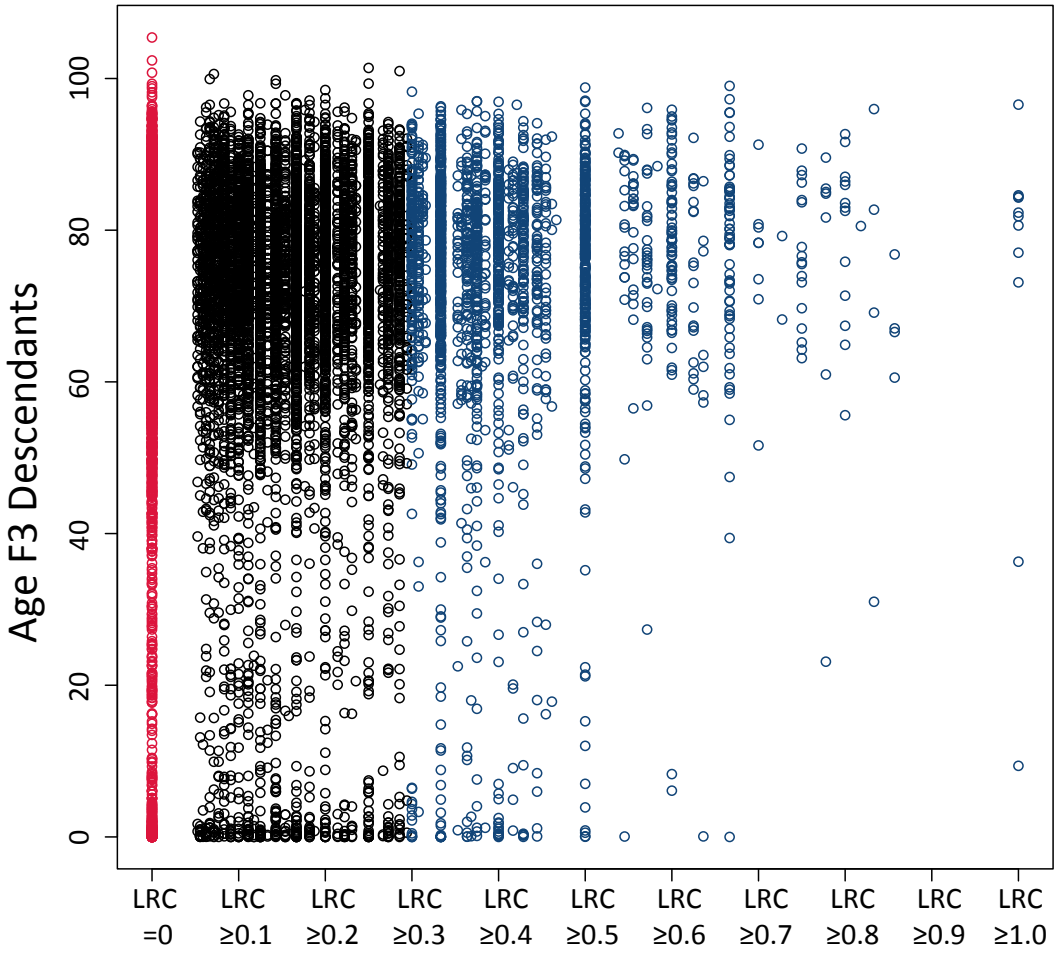
Each gray dot represents a complete sibship. Green boxplot represents the group of sibships with long-lived father and a non-long-lived mother (N=21). Orange boxplot represents the group of sibships with a long-lived mother and a non-long-lived father (N=17). Light brown boxplot represents the group of sibships with both parents not long-lived (N=371).

Chapter 6

Supplementary Table 1: Increase in excess survival with an increase in parental survival percentile

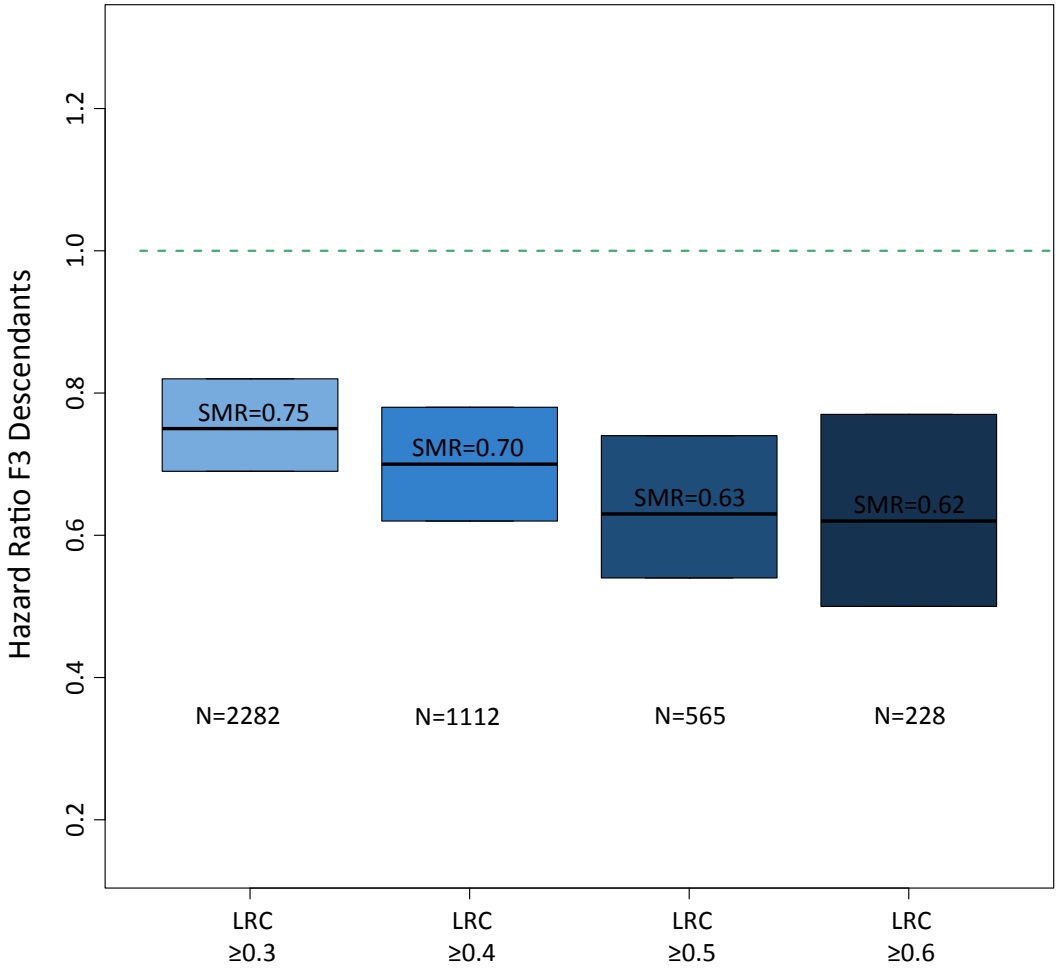
Percentile threshold	SMR (CI)	Number (N)
F2 children (original design - case)		
No parental selection	0.87 (0.84-0.89)	4416
≥85% surviving parent	0.85 (0.83-0.88)	3770
≥90% surviving parent	0.85 (0.82-0.88)	2565
≥95% surviving parent	0.86 (0.81-0.9)	1336
≥99% surviving parent	0.80 (0.7-0.9)	239
≥99.5% surviving parent	0.77 (0.65-0.9)	130
F3 children (original design - case)		
No parental selection	0.86 (0.84-0.89)	9010
≥50% surviving parent	0.84 (0.82-0.87)	7476
≥60% surviving parent	0.83 (0.81-0.86)	6357
≥70% surviving parent	0.81 (0.78-0.84)	5144
≥80% surviving parent	0.77 (0.74-0.81)	3434
≥85% surviving parent	0.76 (0.72-0.8)	2639
≥90% surviving parent	0.71 (0.67-0.76)	1813
≥95% surviving parent	0.69 (0.63-0.76)	798
≥99% surviving parent	0.65 (0.49-0.85)	78
F3 children (original design - control)		
No selection	0.96 (0.93-1)	4353
≥50% surviving parent	0.95 (0.91-0.99)	3425
≥60% surviving parent	0.92 (0.87-0.96)	2828
≥70% surviving parent	0.89 (0.84-0.93)	2168
≥80% surviving parent	0.85 (0.79-0.91)	1479
≥85% surviving parent	0.84 (0.78-0.91)	1107
≥90% surviving parent	0.84 (0.76-0.92)	772
≥95% surviving parent	0.77 (0.67-0.89)	317
≥99% surviving parent	0.94 (0.62-1.38)	41

Surviving parent refers to the proband IP for the F2 children. It refers to having at least 1 parent belonging to the specified survival percentile threshold for the F3 children. Estimates are only based on the proband line and not on the spousal line.



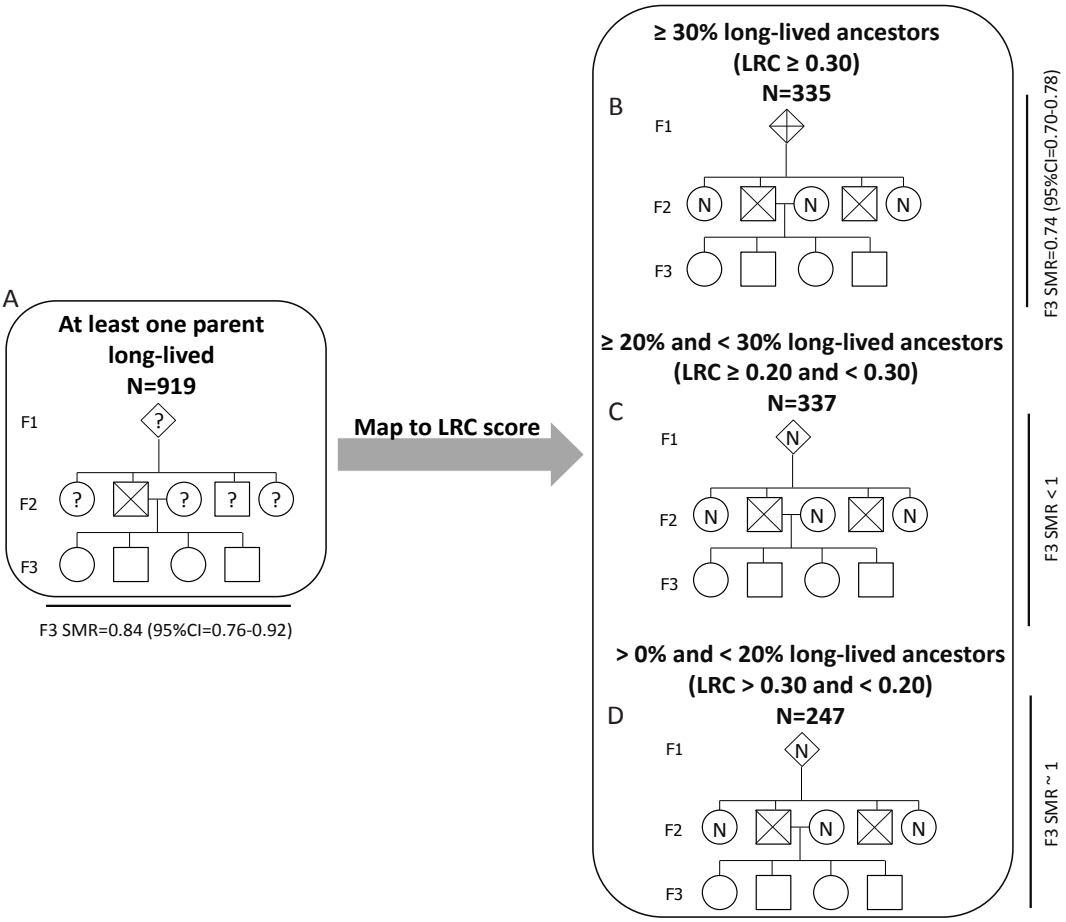
Supplementary Figure 1: Family cases and controls distributed by their reached age

The x-axis represents the Longevity Relatives Count (LRC) scores of the F3 descendants. The y-axis represents the attained age of the F3 descendants. The attained age can either be an age at death or an age at last observation. Around 50% of the F3 descendants is still alive (Table 1). The red color shows the family controls (those without any long-lived ancestors) and the blue color shows the family cases (those with an LRC ≥0.30).



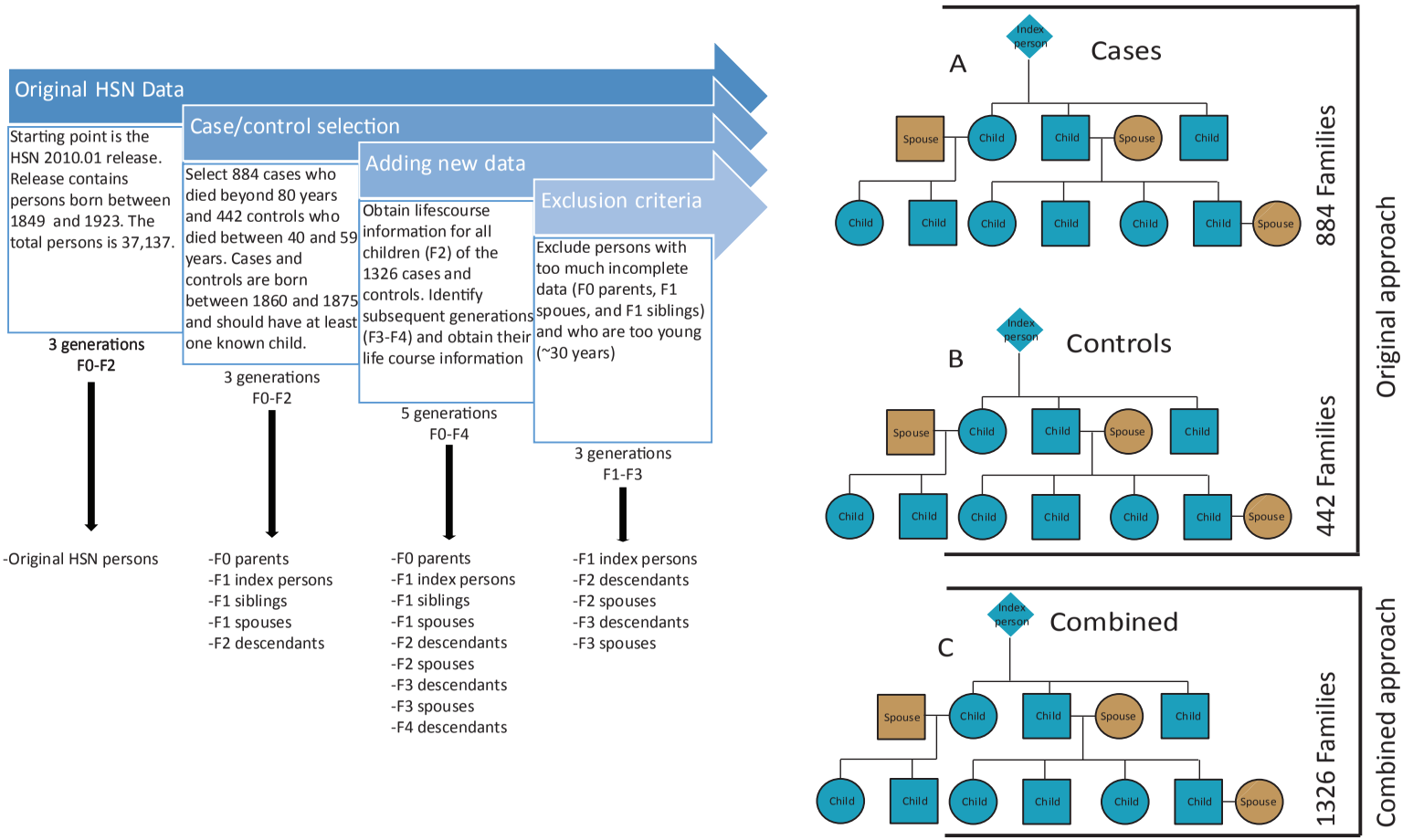
Supplementary Figure 2: SMR of F3 descendants with an increasing proportion of long-lived ancestors

The x-axis represents the Longevity Relatives Count (LRC) score for the F3 descendants. The y-axis shows the Hazard Ratios (HRs) for the F3 descendants. The stronger the effect (lower HR) the darker the blue color.



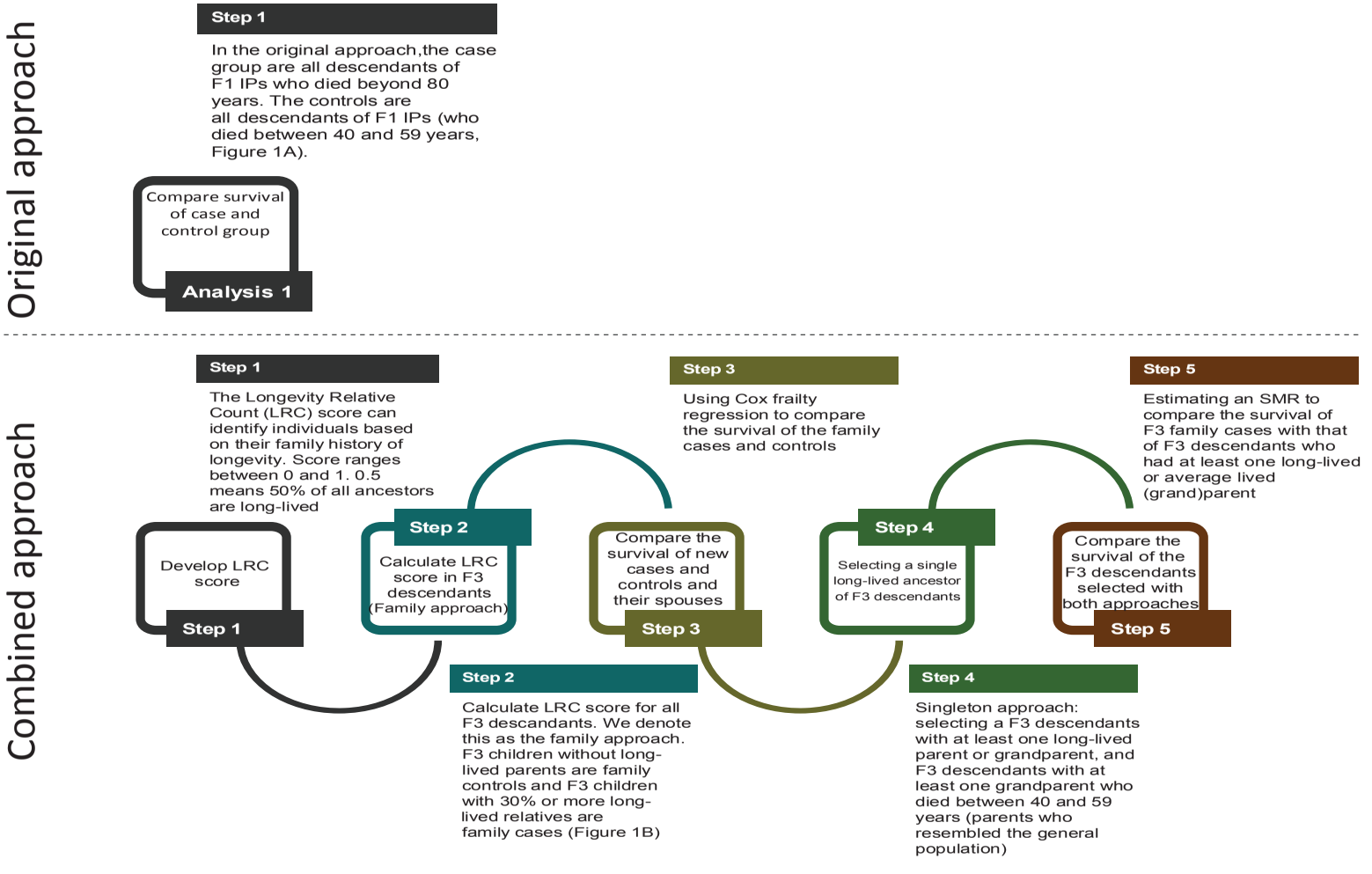
Supplementary Figure 3: Selection of F3 descendants based on the LRC and on at least one long-lived parent

The ? sign shows that the survival of that specific ancestor was unknown. The N sign shows that the ancestor was nog long-lived (top 10% survivor). The X sign shows that the ancestor was long-lived. Panel A shows the F3 descendants with at least one long-lived parent. As illustrated, at least one means that we actively selected F3 descendants with one long-lived parent. That means that the other ancestors could also be long-lived but we did not take that information into account. This resembles the selection procedure of genetic longevity studies which focus on singletons. Panel B shows the ancestors with 30% long-lived ancestors or more and the corresponding standardized mortality ratio (SMR) observed for that group of F3 descendants. Panel C shows the F3 descendants who had between 20% and 30% long-lived ancestors and the corresponding SMR observed for that group. Panel D shows the F3 descendants with more than 0 and less than 20% long-lived ancestors and the corresponding SMR to that group.



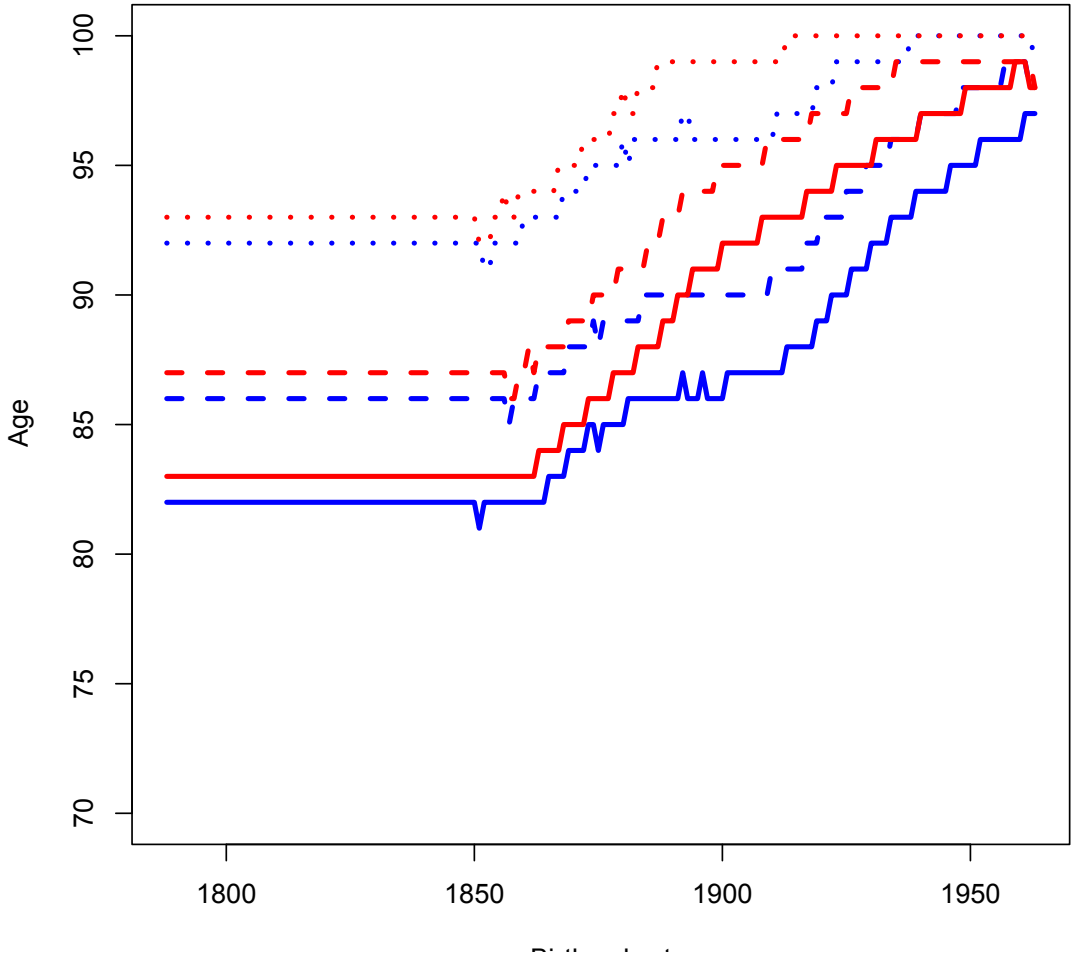
Supplementary Figure 4: Data cleaning procedure into the original and combined approach

Figure provides an overview of the specific sample selection for this study. It starts with the original Historical Sample of the Netherlands data and works towards the specific study persons for this study and finally to the two different approaches used in this study.



Supplementary Figure 5: Subsequent analyses steps in the original and combined approach

This figure shows the different steps used for the analyses in the original and the combined approach



Supplementary Figure 6: HSN birth cohorts mapping of age by top 1, 5, and 10th percentile

This figure represents the percentile-age pairings from the Dutch lifetables used to calculate survival percentiles in HSN case/control datasets. Line colors: Blue: men, Red: women. Line patterns: Dotted lines represent the top 1% survivors of the specific birth cohorts. Broken lines represent the top 5% survivors of the specific birth cohorts. Unbroken lines represent the top 10% survivors of the specific birth cohorts.