

Supplementary Files

S1: Completeness of variables (for the purpose of linkage and analysis) on the HFEA register

Variable	Useable* entry	Entry 'Null'	No entry	Other**	% useable out of total no. of entries
DOB	110,204	374	0	18	99.6%
Sex of Child	110,484	112	0	0	99.9%
Male	56,265				
Female	54,219				
BW	109,157	534	0	905 records with BW <600g ***	98.7%
Child's Surname	12,332	97,671	0	593	11.2%
Child's Forename	11,402	97,670	0	1524	10.3%
Child's Town of Birth	70,738	39,689	61	108	64.0%
Child's District of Birth	18,833	91,452	298	13	17.0%
Child's Town <i>or</i> District of Birth	71,650	38,787	51	108	64.8%
Country of Birth	67554	38,861	0	4181 cases born outside of Great Britain	61.1%
Mother's Surname	110,596	0	0	0	100%
Mother's Forename	110,588	0	8	0	100.0%
Mother's Surname at Birth	51,237	58,714	209	436	46.3%
Mother's Forename at Birth	3,323	106,895	377	1	3.0%
Mother's DOB	110,569	1	0	26	100.0%
Father's Surname	110,450	138	8	0	99.9%
Father's Forename	110,384	202	8	2	99.8%
Father's DOB	110,282	257	0	57	99.7%
Mother's Town or District of Birth	62,505	47,045	0	1046	56.5%
Mother's Country of Birth	64,396	46,190	0	10	58.2%
Father's Town or District of Birth	61,143	48,354	0	1099	55.3%
Father's Country of Birth	63,100	47,485	0	11	57.1%
Treatment Cycle Start Date	110,596	0	0	0	100%
Treatment Centre No/ Name	110,594	0	0	2	100.0%

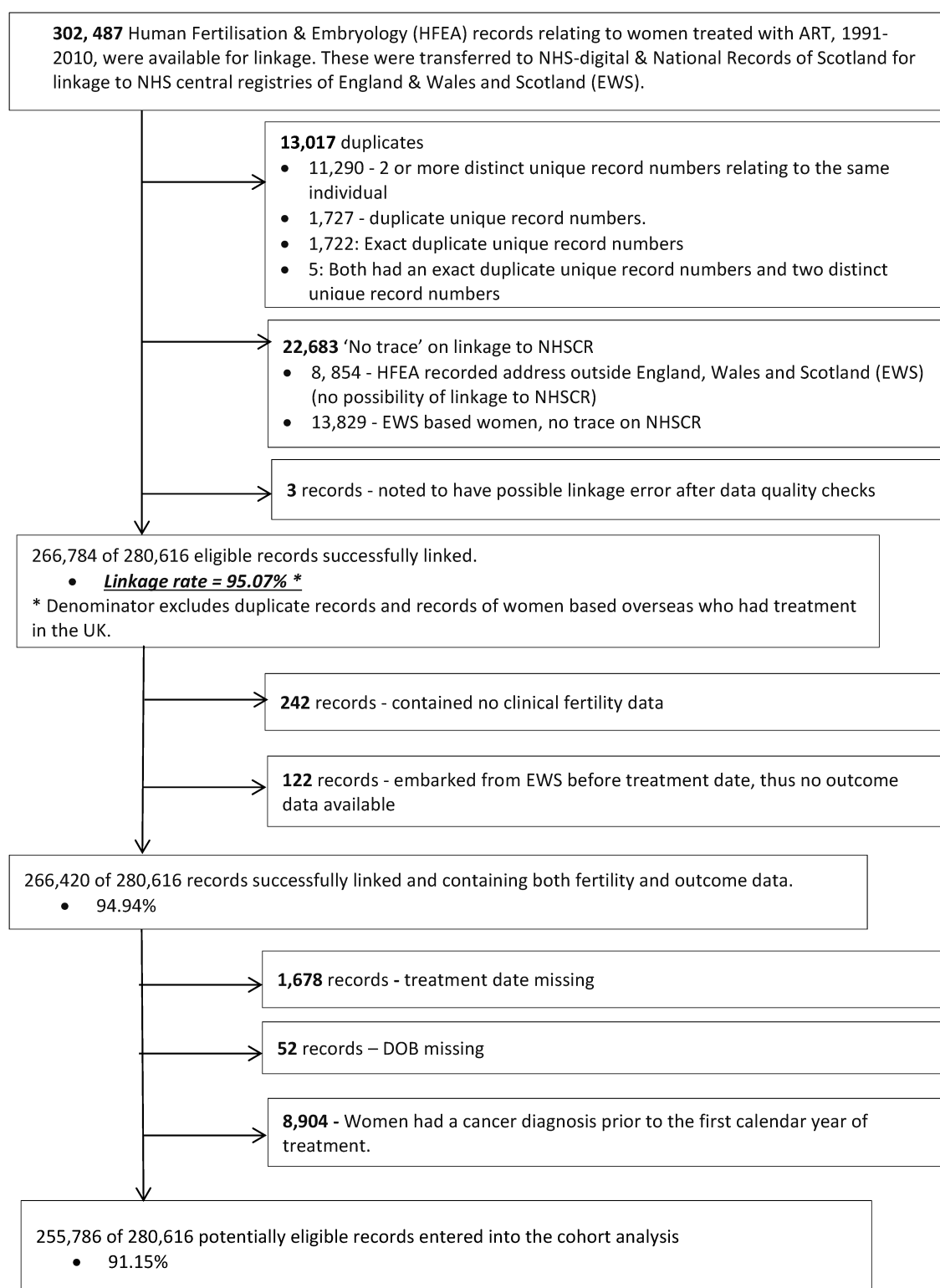
HFEA: Human Fertilization and Embryology Authority; DOB: date of birth; BW: birth weight

* 'Useable' data refers to records which contain data that appears useable in some analyses, including initial quality control analyses.

** 'Other' refers to unusable information for the variable in question, most commonly variations of 'Not known', 'Unknown' etc.

***905 records with documented BWs less than 600g were considered as invalid information for the purpose of deterministic linkage. Whilst a small number of these BWs (<600g) are likely to be correct, many more are likely to be data errors within the HFEA register. All actual recorded BWs were used when manually viewing potential matches.

This table was shared with us by HFEA at the start of the study.

S2- Flow diagram showing derivation of File 2 in Figure 1.

HFEA: Human Fertilization and Embryology Authority; DOB: date of birth; EWS: England, Wales & Scotland; NHSCR: National Health Service Central Register

S3: Order of pregnancy (HFEA-ONS cohort)

No. of pregnancies	Order of pregnancy	ART		Spontaneously conceived siblings	
		Singleton pregnancy	Twin Pregnancy	Singleton pregnancy	Twin Pregnancy
2 (n=8441)	1	5135	1182	2095	29
	2	1596	528	6161	156
3 (n=1336)	1	918	107	304	7
	2	453	96	777	10
	3	126	26	1155	29
4 (n=125)	1	83	9	33	0
	2	42	5	77	1
	3	19	6	99	1
	4	7	4	113	1
5 (n=12)	1	8	1	2	1
	2	5	1	6	0
	3	2	0	10	0
	4	0	0	12	0
	5	0	0	12	0
6 (n=1)	1	1	0	0	0
	2	0	0	1	0
	3	0	0	1	0
	4	0	0	1	0
	5	0	0	1	0
	6	0	0	1	0
7 (n=1)	1	0	1	0	0
	2	0	0	1	0
	3	0	0	1	1
	4	0	0	0	0
	5	0	0	1	0
	6	0	0	1	0
	7	0	0	1	0

HFEA: Human Fertilization and Embryology Authority; ONS: Office for National Statistics.

S4: Multiple regression coefficients for adjusted mean BW- ART vs NCP (HFEA-ONS)

Variables	BW Coefficient	95% Confidence interval
<u>Embryo transfer status</u>		
Fresh	-131.4	(-139.5 - -123.4)
Frozen	35.24	(18.97 - 51.52)
<u>Sex</u>		
Male	119.1	(112.7 - 125.5)
<u>Maternal age group</u>		
25-29	66.68	(55.89 - 77.48)
30-34	111.9	(102.2 - 121.6)
35-39	129.2	(118.7 - 139.7)
40-44	132.3	(118.0 - 146.5)
>=45	72.66	(-13.46 - 158.8)
Constant	3,215	(3,207 - 3,223)
Observations	129,304	
R-squared	0.021	

BW: birth weight; NCP: naturally conceived population controls; HFEA: Human Fertilization and Embryology Authority; ONS: Office for National Statistics.

S5: Multiple regression coefficients for adjusted mean BW- sART vs NCS (HFEA-ONS)

VARIABLES	BW coefficient	95% Confidence interval
<u>Embryo transfer status</u>		
Fresh	-54.69	(-72.64 - -36.73)
Frozen	138.6	(101.3 - 175.9)
<u>Sex</u>		
Male	115.6	(97.78 - 133.4)
<u>Maternal age group</u>		
25-29	-43.23	(-114.2 - 27.74)
30-34	-98.50	(-176.5 - -20.46)
35-39	-117.1	(-206.8 - -27.41)
40-44	-161.8	(-266.1 - -57.52)
>=45	-198.7	(-409.2 - 11.79)
<u>Order of pregnancy</u>		
2	165.6	(142.2 - 188.9)
>=3	237.0	(194.4 - 279.6)
Constant	3,337	(3,263 - 3,411)
Observations	22,086	
R-squared	0.081	

BW: birth weight; sART: ART with siblings; NCS- naturally conceived siblings; HFEA: Human Fertilization and Embryology

Authority; ONS: Office for National Statistics.

S6: Multiple regression coefficients for adjusted mean BW- ART vs NCP (HFEA-ONS-HES cohort)

Variables	BW coefficient	95% confidence interval
<u>Embryo transfer status</u>		
Fresh	-152.2	(-162.2 - -142.3)
Frozen	2.855	(-16.61 - 22.32)
<u>Sex</u>		
Male	120.6	(112.7 - 128.6)
<u>Maternal age group</u>		
25-29	57.25	(43.52 - 70.99)
30-34	86.40	(73.80 - 99.00)
35-39	91.20	(77.62 - 104.8)
40-44	98.57	(80.37 - 116.8)
45-49	4.103	(-63.56 - 71.77)
Missing	94.69	(60.19 - 129.2)
<u>IMD at earliest appointment</u>		
2	25.95	(8.336 - 43.57)
3	56.66	(38.69 - 74.64)
4	58.78	(40.66 - 76.91)
5	75.13	(56.93 - 93.34)
6	93.33	(75.06 - 111.6)
7	93.21	(75.17 - 111.2)
8	111.8	(93.76 - 129.8)
9	117.3	(99.48 - 135.1)
10	134.7	(116.5 - 152.8)
<u>Derived ethnicity</u>		
Asian/Asian British	-247.8	(-264.2 - -231.4)
Black/African/Caribbean/Black British	-138.2	(-161.2 - -115.2)
Chinese	-120.1	(-195.7 - -44.43)
Mixed/multiple ethnic groups	-66.13	(-94.92 - -37.33)
Not stated/Not known	5.034	(-5.060 - 15.13)
Other ethnic group	-49.19	(-82.25 - -16.13)
Constant	3,177	(3,162 - 3,192)
Observations	85,366	
R-squared	0.040	

BW: birth weight; NCP- naturally conceived population controls; HFEA: Human Fertilization and Embryology Authority; ONS: Office for National Statistics; HES: Hospital Episode Statistics; IMD: Index of Multiple Deprivation

S7: Multiple regression coefficients for adjusted mean BW- sART vs NCS (HFEA-ONS-HES cohort)

Variables	BW coefficient	95% Confidence interval
<u>Embryo transfer status</u>		
Fresh	-57.01	(-75.79 - -38.23)
Frozen	152.1	(113.5 - 190.7)
<u>Sex</u>		
Male	115.6	(96.95 – 134.2)
<u>Maternal age group</u>		
25-29	-28.73	(-104.3 - -46.84)
30-34	-81.27	(-164.9 – 2.335)
35-39	-96.01	(-192.0 - -0.010)
40-44	-135.4	(-246.9 - -23.89)
>=45	-141.6	(-308.8 - -25.69)
<u>Order of pregnancy</u>		
2	152.2	(127.8 – 176.6)
>=3	229.6	(184.3 – 274.8)
Constant	3,332	(3,252 - 3,412)
Observations	19180	
R-squared	0.09	

BW: birth weight; sART: ART with siblings; NCS- naturally conceived siblings; HFEA: Human Fertilization and Embryology Authority; ONS: Office for National Statistics.

S8: Distribution of maternal age in records born before 1997 and not linked to HES

	ART	CONTROL	SIBLING
<u>Maternal age group</u>			
<=25	91 (0.79%)	5804 (15.57%)	84 (2.45%)
25-29	1360 (11.84%)	5496 (14.74%)	179 (5.22%)
30-34	4781 (41.62%)	7592 (20.37%)	636 (18.55%)
35-39	4318 (37.59%)	4738 (12.71%)	873 (25.46%)
40-44	921 (8.02%)	1160 (3.11%)	357 (10.41%)
>=45	11 (0.10%)	132 (0.35%)	27 (0.79%)
Missing	5 (0.04%)	12357 (33.15%)	1273 (37.12%)

HES: Hospital Episode Statistics

