

## Supplementary Online Content

Maguire A, Tseliou F, O'Reilly D. Consanguineous marriage and the psychopathology of progeny: a population-wide data linkage study. *JAMA Psychiatry*. Published online April 4, 2018. doi:10.1001/jamapsychiatry.2018.0133

**eFigure.** Flowchart Illustrating the Generation of the Study Data Set

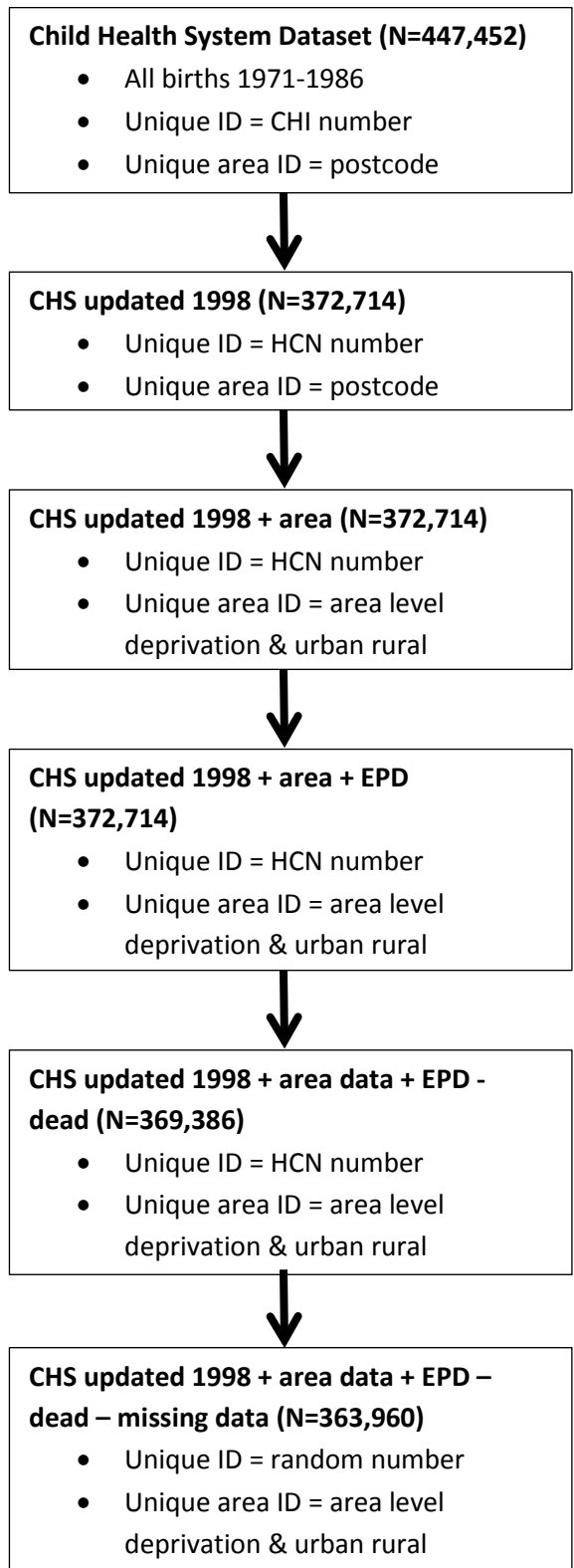
**eTable 1.** Multilevel Regression Models to Investigate the Likelihood of  $\geq 3$  Months' Antidepressant and/or Anxiolytic or  $\geq 3$  Months' Antipsychotic Medication Prescriptions Given Parental Consanguinity, Adjusting for the Clustering of Individuals Within GP Practices

**eTable 2.** Regression Analysis to Investigate the Likelihood of Missing HCN Given Neonatal Factors and Consanguinity of Parents

**eTable 3.** Multilevel Regression Models to Investigate the Likelihood of Antidepressant and/or Anxiolytic Medication Given Parental Consanguinity for Singleton Births Only, Adjusting for the Clustering of Individuals Within GP Practices

**eTable 4.** Multilevel Regression Models to Investigate the Likelihood of Antipsychotic Medication Given Parental Consanguinity for Singleton Births Only, Adjusting for the Clustering of Individuals Within GP Practices

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



minus 74,738 unable to be assigned new Health and Care Number (HCN)

Link area level deprivation data from the NIMDM via postcode

remove postcode

Link area level settlement band to identify urban/rural areas via postcode

Link EPD data on all psychotropic medications 2010-2014 via HCN number

Link deaths from General Register Office via HCN number

minus 3,328 dead

minus 5,426 missing data  
remove HCN

**eFigure.** Flowchart Illustrating the Generation of the Study Data Set

**eTable 1.** Multilevel Regression Models to Investigate the Likelihood of  $\geq 3$  Months' Antidepressant and/or Anxiolytic or  $\geq 3$  Months' Antipsychotic Medication Prescriptions Given Parental Consanguinity, Adjusting for the Clustering of Individuals Within GP Practices. Figures represent Odds Ratios (95% Confidence Intervals)

		CMD $\geq 3$		AP $\geq 3$	
		Model 1	Model 2	Model 1	Model 2
<b>Parents Related</b>	<b>Not related</b>	1.00	1.00	1.00	1.00
	<b>First cousins</b>	1.99 (1.27,3.12)	2.01 (1.28,3.15)	1.98 (1.04,3.77)	2.03 (1.07,3.85)
	<b>Second cousins</b>	1.06 (0.73,1.54)	1.06 (0.73,1.54)	1.83 (0.94,3.55)	1.82 (0.94,3.52)
	<b>Not known</b>	0.98 (0.92,1.03)	0.98 (0.92,1.03)	0.95 (0.84,1.07)	0.95 (0.84,1.08)
<b>Gender</b>	<b>Male</b>	1.00	1.00	1.00	1.00
	<b>Female</b>	1.47 (1.43,1.50)	1.46 (1.42,1.50)	0.49 (0.46,0.52)	0.49 (0.46,0.52)
<b>Age (years)</b>	<b>26-29</b>	1.00	1.00	1.00	1.00
	<b>30-33</b>	1.16 (1.12,1.21)	1.16 (1.12,1.21)	1.12 (1.03,1.22)	1.12 (1.03,1.22)
	<b>34-37</b>	1.34 (1.29,1.39)	1.34 (1.29,1.39)	1.22 (1.12,1.33)	1.22 (1.12,1.33)
	<b>38-41</b>	1.44 (1.39,1.50)	1.44 (1.39,1.49)	1.45 (1.33,1.58)	1.45 (1.33,1.57)
<b>SGA</b>	<b>No</b>	1.00	1.00	1.00	1.00
	<b>Yes</b>	1.11 (1.06,1.16)	1.12 (1.06,1.17)	1.25 (1.13,1.39)	1.27 (1.15,1.41)
<b>Delivery Method</b>	<b>Natural</b>	1.00	1.00	1.00	1.00
	<b>Assisted</b>	1.02 (0.98,1.06)	1.02 (0.97,1.06)	1.03 (0.94,1.13)	1.02 (0.93,1.11)
<b>Parity</b>	<b>First Born</b>	1.00	1.00	1.00	1.00
	<b>1</b>	0.97 (0.94,1.01)	0.97 (0.94,1.01)	1.06 (0.97,1.14)	1.06 (0.98,1.15)
	<b>2</b>	0.97 (0.93,1.01)	0.97 (0.94,1.01)	1.08 (0.99,1.18)	1.09 (1.00,1.19)
	<b>&gt;3</b>	1.02 (0.97,1.06)	1.03 (0.99,1.07)	1.18 (1.08,1.29)	1.22 (1.11,1.33)
	<b>Unknown</b>	0.92 (0.87,0.98)	0.92 (0.87,0.98)	1.04 (0.90,1.19)	1.04 (0.91,1.19)
<b>Mother's Age</b>	<b>&lt;18</b>	1.09 (0.97,1.22)	1.10 (0.98,1.24)	1.26 (1.00,1.60)	1.30 (1.02,1.64)
	<b>18-35</b>	1.00	1.00	1.00	1.00
	<b>&gt;35</b>	0.99 (0.94,1.04)	0.98 (0.93,1.04)	1.02 (0.91,1.13)	1.01 (0.90,1.13)
	<b>Not known</b>	0.88 (0.69,1.13)	0.88 (0.69,1.13)	1.03 (0.62,1.70)	1.01 (0.61,1.67)
<b>Father's Age</b>	<b>&lt;18</b>	1.22 (0.85,1.77)	1.24 (0.86,1.79)	1.19 (0.57,2.46)	1.21 (0.58,2.51)
	<b>18-35</b>	1.00	1.00	1.00	1.00
	<b>&gt;35</b>	0.97 (0.93,1.01)	0.97 (0.93,1.01)	1.08 (0.99,1.19)	1.07 (0.97,1.17)
	<b>Not known</b>	1.10 (1.05,1.15)	1.12 (1.07,1.17)	1.28 (1.17,1.40)	1.31 (1.19,1.44)
<b>Deprivation at Birth</b>	<b>Not Deprived</b>	1.00	-	1.00	-
	<b>Deprived</b>	1.14 (1.11,1.18)	-	1.35 (1.27,1.44)	-
<b>Urbanicity at Birth</b>	<b>Urban</b>	-	1.00	-	1.00
	<b>Rural</b>	-	0.91 (0.87,0.95)	-	0.93 (0.85,1.01)
<b>Variance</b>		0.159565	0.1584288	0.2210672	0.2385557
<b>p</b>		<0.001	<0.001	<0.001	<0.001
<b>VPC*</b>		0.046	0.046	0.063	0.068

\*VPC = Variance Partition Co-efficient

**eTable 2.** Regression Analysis to Investigate the Likelihood of Missing HCN Given Neonatal Factors and Consanguinity of Parents

		<b>Model 1</b>
<b>Consanguineous Parents</b>	<b>No</b>	1.00
	<b>First Cousins</b>	1.74 (1.35,2.25)
	<b>Second Cousins</b>	1.18 (0.92,1.52)
	<b>Not Known</b>	1.72 (1.67,1.77)
<b>Gender</b>	<b>Male</b>	1.00
	<b>Female</b>	1.35 (1.33,1.37)
<b>Age (years)</b>	<b>26-29</b>	1.00
	<b>30-33</b>	1.27 (1.23,1.31)
	<b>34-37</b>	1.53 (1.50,1.58)
	<b>38-41</b>	3.09 (3.02,3.17)
<b>SGA</b>	<b>No</b>	1.00
	<b>Yes</b>	1.89 (1.83,1.93)
<b>Delivery Method</b>	<b>Natural</b>	1.00
	<b>Other</b>	1.06 (1.04,1.08)
<b>Parity</b>	<b>First Born</b>	1.00
	<b>1</b>	0.85 (0.83,0.87)
	<b>2</b>	0.78 (0.76,0.80)
	<b>&gt;3</b>	0.75 (0.73,0.76)
	<b>Unknown</b>	1.26 (1.22,1.31)

**eTable 3.** Multilevel Regression Models to Investigate the Likelihood of Antidepressant and/or Anxiolytic Medication Given Parental Consanguinity for Singleton Births Only, Adjusting for the Clustering of Individuals Within GP Practices. Figures represent Odds Ratios (95% Confidence Intervals)

		<b>Unadjusted</b>	<b>Model 1</b>	<b>Model 2</b>
<b>Consanguineous Parents</b>	<b>No</b>	1.00	1.00	1.00
	<b>First Cousins</b>	3.00 (1.22,7.36)	3.00 (1.22,7.38)	3.01 (1.23,7.41)
	<b>Second Cousins</b>	1.32 (0.64,2.72)	1.30 (0.63,2.70)	1.31 (0.63,2.71)
	<b>Not Known</b>	1.02 (0.92,1.13)	0.98 (0.89,1.09)	0.98 (0.89,1.09)
<b>Gender</b>	<b>Male</b>		1.00	1.00
	<b>Female</b>		1.79 (1.71,1.87)	1.78 (1.70,1.86)
<b>Age (years)</b>	<b>26-29</b>		1.00	1.00
	<b>30-33</b>		1.06 (0.99,1.13)	1.06 (0.99,1.13)
	<b>34-37</b>		1.10 (1.03,1.18)	1.10 (1.03,1.17)
	<b>38-41</b>		1.12 (1.05,1.19)	1.11 (1.04,1.19)
<b>SGA</b>	<b>No</b>		1.00	1.00
	<b>Yes</b>		1.07 (0.98,1.18)	1.08 (0.98,1.19)
<b>Delivery Method</b>	<b>Natural</b>		1.00	1.00
	<b>Natural Assisted</b>		1.04 (0.97,1.12)	1.04 (0.96,1.12)
	<b>C-section</b>		0.98 (0.90,1.07)	0.98 (0.90,1.07)
<b>Parity</b>	<b>First Born</b>		1.00	1.00
	<b>1</b>		0.98 (0.92,1.05)	0.98 (0.92,1.05)
	<b>2</b>		0.94 (0.88,1.01)	0.95 (0.88,1.02)
	<b>&gt;3</b>		1.00 (0.93,1.08)	1.02 (0.94,1.10)
	<b>Unknown</b>		0.94 (0.84,1.04)	0.94 (0.85,1.04)
<b>Mother's Age</b>	<b>&lt;18</b>		1.06 (0.85,1.33)	1.07 (0.86,1.34)
	<b>18-35</b>		1.00	1.00
	<b>&gt;35</b>		0.99 (0.91,1.09)	0.99 (0.90,1.09)
	<b>Not known</b>		1.05 (0.67,1.65)	1.04 (0.67,1.64)
<b>Father's Age</b>	<b>&lt;18</b>		1.90 (0.86,4.21)	1.92 (0.87,4.24)
	<b>18-35</b>		1.00	1.00
	<b>&gt;35</b>		0.93 (0.87,1.01)	0.93 (0.86,1.01)
	<b>Not known</b>		1.11 (1.02,1.20)	1.12 (1.03,1.22)
<b>Deprivation at Birth</b>	<b>Not Deprived</b>		1.00	-
	<b>Deprived</b>		1.10 (1.04,1.15)	-
	<b>Not known</b>		0.87 (0.73,1.05)	-
<b>Urbanicity at Birth</b>	<b>Urban</b>		-	1.00
	<b>Rural</b>		-	0.91 (0.86,0.97)
	<b>Not known</b>		-	0.79 (0.65,0.94)
<b>Variance</b>		0.3550799	0.3542844	0.3554447
<b>p</b>		<0.001	<0.001	<0.001
<b>VPC*</b>		0.100	0.097	0.098

\*VPC = Variance Partition Co-efficient

**eTable 4.** Multilevel Regression Models to Investigate the Likelihood of Antipsychotic Medication Given Parental Consanguinity for Singleton Births Only, Adjusting for the Clustering of Individuals Within GP Practices. Figures represent Odds Ratios (95% Confidence Intervals)

		<b>Unadjusted</b>	<b>Model 1</b>	<b>Model 2</b>
<b>Consanguineous Parents</b>	<b>No</b>	1.00	1.00	1.00
	<b>First Cousins</b>	2.37 (1.44,3.89)	2.13 (1.29,3.53)	2.19 (1.32,3.61)
	<b>Second Cousins</b>	1.39 (0.80,2.41)	1.38 (0.79,2.42)	1.37 (0.78,2.40)
	<b>Not Known</b>	0.97 (0.89,1.07)	0.92 (0.84,1.01)	0.92 (0.84,1.01)
<b>Gender</b>	<b>Male</b>		1.00	1.00
	<b>Female</b>		0.57 (0.55,0.60)	0.57 (0.55,0.60)
<b>Age (years)</b>	<b>26-29</b>		1.00	1.00
	<b>30-33</b>		1.04 (0.98,1.11)	1.04 (0.98,1.11)
	<b>34-37</b>		1.10 (1.03,1.17)	1.10 (1.03,1.17)
	<b>38-41</b>		1.15 (1.08,1.22)	1.14 (1.07,1.22)
<b>SGA</b>	<b>No</b>		1.00	1.00
	<b>Yes</b>		1.18 (1.09,1.28)	1.20 (1.11,1.30)
<b>Delivery Method</b>	<b>Natural</b>		1.00	1.00
	<b>Natural Assisted</b>		1.04 (0.97,1.12)	1.03 (0.96,1.11)
	<b>C-section</b>		1.09 (1.00,1.18)	1.08 (1.00,1.17)
<b>Parity</b>	<b>First Born</b>		1.00	1.00
	<b>1</b>		1.05 (0.99,1.12)	1.05 (0.99,1.12)
	<b>2</b>		1.08 (1.01,1.16)	1.09 (1.02,1.17)
	<b>&gt;3</b>		1.16 (1.08,1.24)	1.18 (1.10,1.27)
	<b>Unknown</b>		1.03 (0.93,1.14)	1.03 (0.94,1.14)
<b>Mother's Age</b>	<b>&lt;18</b>		1.12 (0.93,1.35)	1.14 (0.95,1.38)
	<b>18-35</b>		1.00	1.00
	<b>&gt;35</b>		0.97 (0.89,1.06)	0.97 (0.89,1.05)
	<b>Not known</b>		0.90 (0.60,1.36)	0.89 (0.59,1.34)
<b>Father's Age</b>	<b>&lt;18</b>		1.44 (0.85,2.45)	1.47 (0.86,2.50)
	<b>18-35</b>		1.00	1.00
	<b>&gt;35</b>		1.02 (0.94,1.09)	1.01 (0.93,1.08)
	<b>Not known</b>		1.32 (1.23,1.42)	1.35 (1.25,1.44)
<b>Deprivation at Birth</b>	<b>Not Deprived</b>		1.00	-
	<b>Deprived</b>		1.34 (1.28,1.41)	-
	<b>Not known</b>		1.10 (0.92,1.33)	-
<b>Urbanicity at Birth</b>	<b>Urban</b>		-	1.00
	<b>Rural</b>		-	0.92 (0.86,0.99)
	<b>Not known</b>		-	0.88 (0.72,1.06)
<b>Variance</b>		0.3562542	0.3519837	0.350317
<b>p</b>		<0.001	<0.001	<0.001
<b>VPC*</b>		0.098	0.097	0.096

\*VPC = Variance Partition Co-efficient