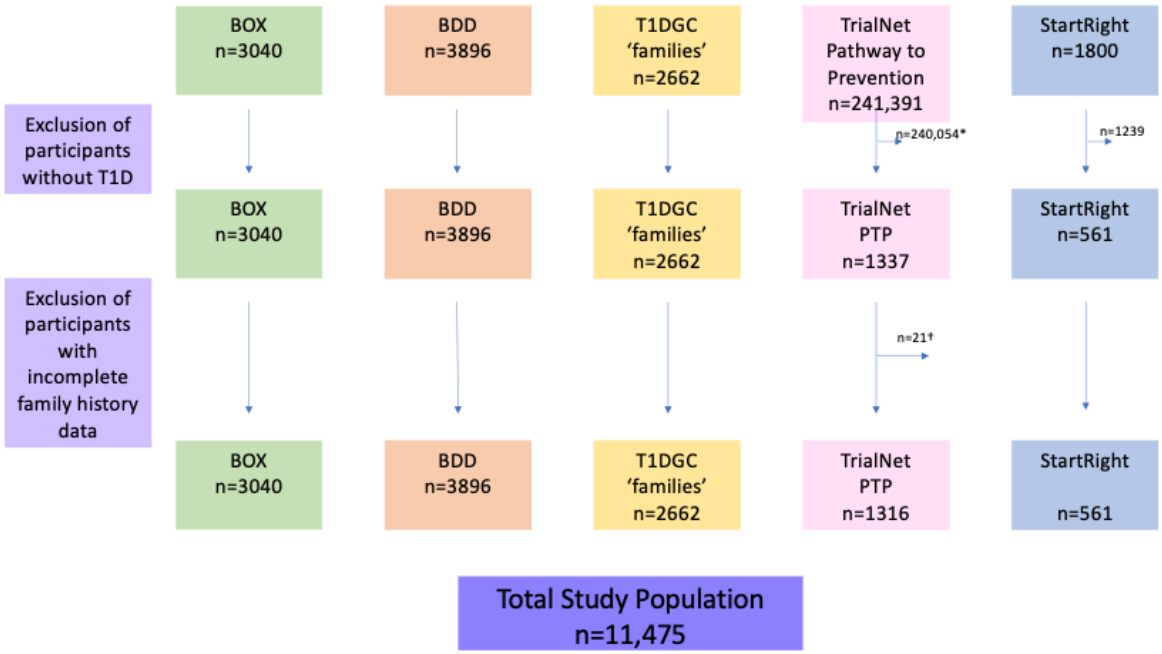
Supplementary Table 1: Summary of the studies from which participants were included

Study	Number of participants meeting eligibility criteria for inclusion in this study	Age at diagnosis of type 1 diabetes	Recruitment Area	Recruitment period	Type 1 diabetes at enrolment?
BOX[19, 20]	3,040	<21 years Median 10 years (IQR 6, 13 years)	Oxfordshire Health Authority Region, UK	Since 1985	Yes (newly diagnosed). Diagnosis of type 1 diabetes based on WHO criteria and clinical requirement for insulin treatment.
BDD[21]	3,896	<18 years Median 10 years (IQR 6, 14 years)	Sweden (nationwide)	Since 2005	Yes (newly diagnosed) since 2005. Since 2011 estimated to have captured over 95% of new diagnoses of type 1 diabetes under age 18. To establish diabetes classification, the study included analyses of HLA-DQ genotypes, autoantibodies and levels of c-peptide at first recruitment.
TrialNet PTP[23, 47]	1,316	0-55 years Median 12 years (IQR 8, 16 years)	International, multi-centre Participating countries include the United States of America, Canada, United Kingdom, Germany, Italy, Sweden, Finland, Australia and New Zealand	Since 2000	No. Recruitment of first-degree relatives of individuals with type 1 diabetes found to be positive for at least one type 1 diabetes associated autoantibody. Progression to type 1 diabetes (on the basis of the results of oral glucose tolerance test (OGTT), HbA1c level and antibody testing results) was recorded.
T1DGC 'Families Dataset' [22].	2,662	0-32 years Median 7 years (IQR 4, 12 years)	International, multi centre. Data collected across 4 regional networks: Asia-Pacific (participating countries	2004-2009	Yes. Recruitment of predominantly affected sibling pairs and a smaller group of parent-child trios to generate a "families

			Australia, India, Malaysia, New Zealand, Philippines, Singapore, Thailand) Europe (Austria, Belgium, Cameroon, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Israel, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Russia, Slovenia, Spain, Sweden, Switzerland, Turkey) North America (57 data collection sites in the United States of America) United Kingdom Network (48 data collection sites in the United Kingdom)		dataset" within the T1DGC.
StartRight[26, 32].	561	17-88 years Median 35 years (IQR 27, 49 years)	55 UK sites	2015-2020	Recruited participants with newly diagnosed diabetes (<12 months' duration). Type of diabetes recorded and validated using autoantibody testing and clinical information.

Supplementary figure 1: Flow chart illustrating contribution of each individual study



Flow chart showing the number of individuals from each study who were eligible for inclusion in this study, with reasons for exclusions shown.
* In the TrialNet Pathway to Prevention (PTP) Study, as of 31st August 2023, 241,391 participants were screened and had provided at least one blood sample for antibody testing. Of these individuals, 1337 developed clinical type 1 diabetes during follow up (as confirmed by the combined results of oral glucose tolerance test (OGTT), HbA1c and antibody testing.
†In 21 individuals in TrialNet PTP, due to an administrative issue, it was unclear whether a parent with type 1 diabetes was a mother or father, and thus these individuals were excluded from the study.

Supplementary table 2: Comparison of results obtained utilising different definitions of parental type 1 diabetes in StartRight.

	Parent with diabetes treated with insulin only	**Parent with diabetes diagnosed ≤25 and treated with insulin only**	**Parent with diabetes diagnosed ≤30 and treated with insulin only**	**Parent with diabetes diagnosed ≤35 and treated with insulin only**	**Parent with diabetes diagnosed ≤40 and treated with insulin only**	**Parent with diabetes diagnosed ≤45 and treated with insulin only**	**Parent with diabetes diagnosed ≤50 and treated with insulin only**
% with affected mother	25 (4·5%)	7 (1·2%)	8 (1·4%)	11 (2·0%)	13 (2·3%)	16 (2·9%)	18 (3·2%)
% with affected father	44 (7·8%)	13 (2·3%)	17 (3·0%)	19 (3·4%)	27 (4·8%)	31 (5·5%)	34 (6·1%)
Odds ratio	0.55 (0.33,0.91) p=0.02	0.53 (0.21, 1.35) p=0.18	0.46 (0.20, 1.08) p=0.08	0.57 (0.27, 1.21) p=0.14	0.47 (0.24, 0.92) p=0.03	0.50 (0.27, 0.93) p=0.03	0.51 (0.29, 0.92) p=0.03

Parental diabetes was recorded in StartRight. However, the type of diabetes was not routinely recorded. We used data regarding parental diabetes treatment and age at diagnosis as surrogate markers of diabetes type. This table illustrates the number and proportion (%) of individuals with affected fathers and mothers (from total number of participants of 561) depending on the definition of parental diabetes employed. The odds ratios shown represent the odds of an individual in the study having an affected mother compared with father. As the results obtained were consistent regardless of the definition used, the least restrictive definition of parental diabetes (parent with diabetes treated with insulin only) was employed.

Supplementary Text 1: *SNP Genotyping and GRS computation in Trialnet*

Participants were genotyped on an Illumina Infinium T1DExomeChip SNP array. TrialNet participants genotyping data was imputed using the TOPMed reference panel [25]. We included 30 SNPs which were directly genotyped. We imputed 32 non-HLA SNPs with a median R^2 of 0.997 (min = 0.858 and max = 0.999) using the TOPMed Imputation Server with the multi-ethnic TOPMed reference panel which includes 97,256 reference samples and > 308 million genetic variants [48, 49]. We also imputed 5 SNPs in the HLA region (rs72848653 (R^2 = 0.999), rs9266268 (R^2 = 0.999), rs16899379 (R^2 = 0.998), rs2524277 (R^2 = 0.995), and rs9268500 (R^2 = 0.925)) using the Michigan Imputation Server with the high-resolution HLA reference panel spanning five global populations (n = 21,546) based on whole-genome sequencing data [50]. Updated code which provides a complete algorithm for generating the T1D T1D-GRS2 (now described as T1D-GRS2x) is freely available online (https://github.com/sethsh7/prsedm).

Supplementary table 3: Comparison of the proportion of individuals in each study with an affected mother versus father

Study	Individuals with affected mothers				Individuals with affected fathers				Individuals with both parents affected				Individuals with no affected parents			
	Age at onset (median (IQR) in years)	Females	Males	Total	Age at onset (median (IQR) in years)	Females	Males	Total	Age at onset (median (IQR) in years)	Females	Males	Total	Age at onset (median (IQR) in years	Females	Males	Total
BOX (n=3,040)	10.6 (5.7, 13.8)	36 (1.2%)	42 (1.4%)	78 (2.6%)	9.2 (4.8, 12.9)	54 (1.8%)	91(3.0%)	145 (4.8%)	11.8 (7.5, 12.7)	3 (0.1%)	4 (0.1%)	7 (0.2%)	10.3 (6.3, 13.2)	1,293 (42.5%)	1,517 (49.9%)	2,810 (92.4%)
BDD (n=3,896)	10.3 (5.8, 14.0)	42 (1.1%)	64 (1.6%)	106 (2.7%)	10.2 (6.1, 13.4)	95 (2.4%)	111 (2.8%)	206 (5.3%)	8.4 (1.7, 12.7)	4 (0.1%)	3 (0.1%)	7 (0.2%)	10.4 (6.4, 13.7)	1,604 (41.2%)	1,973 (50.6%)	3,577 (91.8%)
TrialNet (n=1,316) 1 missing sex	8.0 (11.0, 15.0)	68 (5.2%)	80 (6.1%)	148 (11.2%)	12.0 (9.0, 16.0)	89 (6.8%)	127 (9.7%)	216 (16.4%)	9.0 (8.0, 10.0)	3 (0.2%)	8 (0.6%)	11 (0.8%)	12.0 (9.0, 17.0)	446 (33.9%)	494 (37.5%)	940 (71.5%)
T1DGC (n=2,662)	6.0 (2.8, 10.3)	26 (1.0%)	25 (0.9%)	51 (1.9%)	6.0 (3.0, 9.0)	56 (2.1%)	55 (2.1%)	111 (4.2%)	4.0 (1.0, -)	1 0.04%)	2 (0.1%)	3 (0.1%)	7.0 (4.0, 12.0)	1,236 (46.4%)	1,261 (47.3%)	2,497 (93.8%)
StartRight (n=561)	36.0 (28.0, 47.0)	13 (2.3%)	10 (1.8%)	23 (4.1%)	39.5 (27.5, 47.5)	21 (3.7%)	21 (3.7%)	42 (7.5%)	39.5 (38.0, --)	1 (0.2%)	1 (0.2%)	2 (0.4%	35.0 (26.0, 50.0)	240 (42.8%)	254 (45.3%	494 (88.1%)

Supplementary table 4: More detailed breakdown of proportion of individuals with affected first degree relatives across the studies

Study	Number with mother as only affected first-degree relative	Number with father as only affected first-degree relative	Number with sibling or siblings but no parent affected	Number with mother and at least one other first-degree relative affected	Number with father and at least one other first-degree relative affected	No affected first-degree relatives
BOX (n=3,040)	73 (2.4%)	125 (4.1%)	142 (4.7%)	12 (0.4%)	20 (0.7%)	2,668 (87.8%)
TrialNet (n=1,316)	117 (8.9%)	150 (11.4%)	768 (58.4%)	42 (3.2%)	66 (5.0%)	173 (13.1%)
T1DGC (n=2,662)	1 (0.04%)	2 (0.1%)	2,436 (91.5%)	53 (2.0%)	110 (4.1%)	60 (2.3%)
StartRight (n=561)	21 (3.7%)	36 (6.4%)	46 (8.2%)	4 (0.7%)	6 (1.1%)	448 (79.9%)

*BDD did not include sibling data to facilitate inclusion of BDD in this table.

Supplementary table 5: Comparison of the results generated when using different ages to divide the study into those diagnosed with type 1 diabetes at a younger versus older age.

	Individual with age at diagnosis ≤ chosen cut off			**Individuals with age at diagnosis > chosen cut off**		
Cut off	**Number of individuals with affected mothers**	**Number of individuals with affected fathers**	**Odds ratio (odds of having an affected fathers/odds of having an affected mother**	**Number of individuals with affected mothers**	**Number of individuals with affected fathers**	**Odds ratio (odds of having an affected fathers/odds of having an affected mother**
13 years	295	515	0.54 (0.43, 0,68) p<0.001	139	227	0.59 (0.47, 0.73) p<0.001
14 years	311	536	0.55 (0.44, 0.68) p<0.001	112	181	0.60 (0.47, 0.77) p<0.001
15 years	336	591	0.54 (0.45, 0.65) p<0.001	98	151	0.63 (0.48, 0.82) p=0.001
16 years	356	621	0.54 (0.45, 0.65) p<0.001	78	121	0.62 (0.46, 0.84) p=0.002
17 years	459	644	0.64 (0.45, 0.90) p-0.01	66	98	0.65 (0.47, 0.91) p=0.01
18 years	381	659	0.55 (0.47, 0.64) p<0.001	53	83	0.61 (0.43, 0.88) p=0.01
19 years	386	673	0.55 (0.48, 0.63) p<0.001	48	69	0.67 (0.45, 0.98) p=0.04

In our main results we compared the number and proportion of individuals with type 1 diabetes who had affected mothers and fathers after subdividing the study based on age of participant (offspring) at diagnosis (≤18 years vs >18 years). We chose to divide the study on the basis of the age of 18 as it is widely accepted that this represents the age at which individuals are considered to have transitioned from childhood to adulthood. However, to demonstrate that the precise cut off chosen did not significantly impact the results, we report in this supplementary table, the results obtained using different age cut offs between ages 13-19 years. We consistently found that individuals in both subgroups were significantly more likely to have an affected father than mother regardless of the age cut off chosen.

Supplementary table 6: Sex distribution of participants

	Participants with T1D		
	Male	**Female**	**Ratio of males to females**
BOX (n=3,040)	1,654	1,386	1.2
<15 years	1,417	1,232	1.2
≥15 years	237	153	1.5
Missing	0	1	
BDD (n=3,896)	2,151	1.745	1.2
<15 years	1,741	1,475	1.2
≥15 years	377	229	1.6
Missing	33	41	
TrialNet PTP (n=1,316)	709	606	1.2
<15 years	480	411	1.2
≥15 years	229	195	1.2
Missing	0	0	
T1DGC (n=2,662)	1,343	1,319	1.02
<15 years	1,124	1,145	0.98
≥15 years	213	169	1.3
Missing	6	5	
StartRight (n=561)	286	275	1.04
<15 years	0	0	n/a
≥15 years	286	275	1.04
Missing	0	0	
Overall (n=11,475)	6,143	5,331	1.15
<15 years	4,762	4,263	1.12
≥15 years	1,342	1,021	1.31
Missing	39	47	

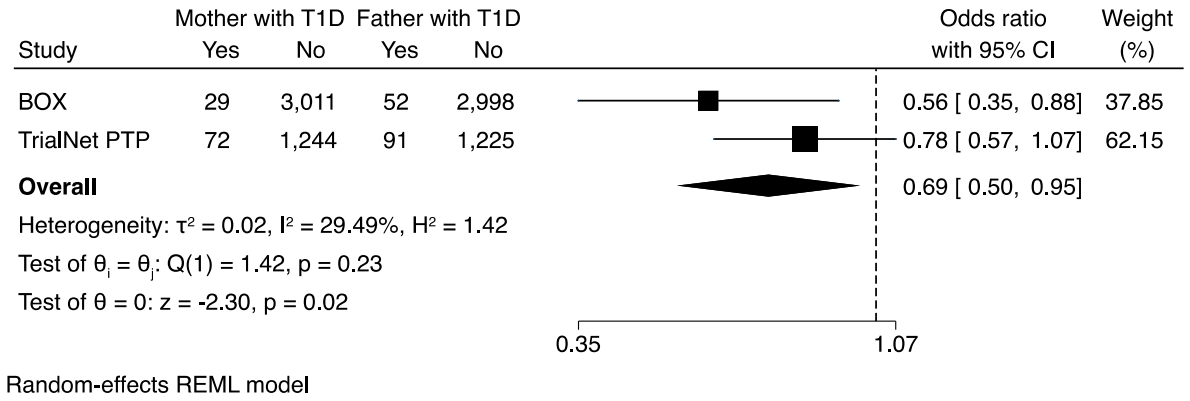
Sex distribution of participants shown as number of males and females as well as the ratio of males to females by study, and overall. In addition, the number of males and females and the ratio of males to females by age of participant at diagnosis (<15 years versus ≥15 years) is shown.

Abbreviations: T1D: Type 1 diabetes

Missing data regarding age at onset is shown in the table.

Missing data regarding participant sex: TrialNet PTP n=1.

Supplementary figure 2: Sensitivity Analysis – Meta-analysis of odds of having a mother with type 1 diabetes compared with the odds of having a father with type 1 diabetes amongst individuals with type 1 diabetes restricted to those with parents diagnosed prior to age 15 years.



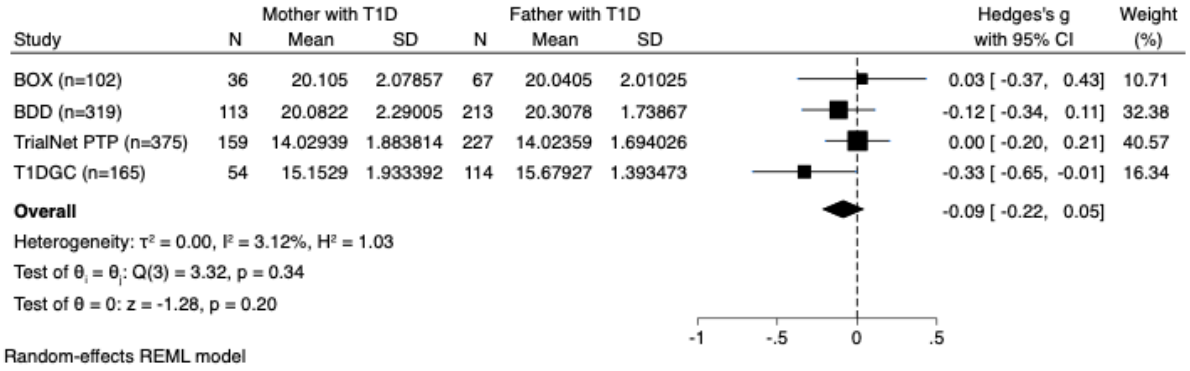
Unadjusted odds ratios shown for the odds of individuals with type 1 diabetes having an affected mother vs father when analysis confined to parents diagnosed before age 15 years. The odds ratios for each individual study are shown, as well as the overall odds ratio as derived from a random effects meta-analysis. This data was only available from BOX and TrialNet PTP. p<0·001. *Abbreviations: T1D: Type 1 Diabetes*

Supplementary table 7: Descriptive data regarding the number of children born to men and women with type 1 diabetes in BOX

	Fathers with T1D n=152	Mothers with T1D n=85
Parental age at diagnosis (years) Median (IQR) Missing	21 (11, 29) 1	23 (12, 33) 3
Number of children (total number, mean (standard deviation))	363 (2.4 (1.24))	204 (2.4 (1.05))
Number of affected children (total number, mean (standard deviation))	176 (1.2 (0.45))	92 (1.1 (0.28))

Number of children born to men and women with type 1 diabetes overall, and by type 1 diabetes status. The mean number of children born to men and women with type 1 diabetes was similar.

Supplementary Figure 3: Comparison of Type 1 Diabetes-GRS (T1D-GRS2) between participants with mothers and fathers with type 1 diabetes after excluding StartRight



Hedges's g standardised mean difference in type 1 diabetes genetic risk score (T1D-GRS2) for those with an affected father compared with those with an affected mother. The results are shown for the individual studies, alongside an overall estimate of effect as derived from random effects meta-analysis. Missing data regarding T1D-GRS2 amongst individuals with parents with type 1 diabetes: BOX n=134, BDD missing n=0, TrialNet PTP n=0, T1DGC n=0). Complete case analysis was performed. p=0·20.