

### **Supplemental Data**

Supplemental Figure 1: Meta-analyses results of A) PRS<sub>BD</sub> in replication cohorts and B) PRS<sub>BD</sub> in discovery and replication cohorts, C) PRS<sub>SCZ</sub> in replication cohorts, D) PRS<sub>SCZ</sub> in discovery and replication cohorts. Where: Effect, odds ratio; 95%CI, 95% confidence interval; weight, relative weight in the analyses, based on sample size;  $I^2$ , measure of heterogeneity; p, p-value for heterogeneity measure.

Supplemental Figure 2: Meta-analyses results of A) PRS<sub>MDD</sub> and DVT, B) PRS<sub>MDD</sub> and PE, C) PRS<sub>BD</sub> and DVT, D) PRS<sub>BD</sub> and PE, E) PRS<sub>SCZ</sub> and DVT and F) PRS<sub>SCZ</sub> and PE in discovery and replication cohorts. Where: Effect, odds ratio; 95%CI, 95% confidence interval; weight, relative weight in the analyses, based on sample size;  $I^2$ , measure of heterogeneity; p, p-value for heterogeneity measure.

Supplementary Table 1: Characteristics of the UK Biobank study without mental illness

	Men		Women		Combined	
	cases	controls	cases	controls	cases	controls
N (% male)	3866 (100)	124458 (100)	5130 (0)	131701 (0)	8996 (43.0)	256159 (48.6)
Age (years)	59.6 (7.4)	57.0 (8.1)	59.3 (7.3)	56.6 (8.0)	59.4 (7.3)	56.8 (8.10)
BMI (Kg/m <sup>2</sup> )	29.4 (5.0)	27.8 (4.1)	28.8 (5.8)	26.7 (4.9)	29.1 (5.5)	27.2 (4.6)
Ever Smoker	2243 (58.3)	63134 (50.9)	2171 (42.5)	51576 (39.3)	4414 (49.3)	114710 (45.0)
Oral contraceptives			48 (0.01)	3233 (2.5)		
HRT			301 (5.9)	8476 (6.5)		
PE	1339 (34.6)		1495 (29.1)		2834	
Age at PE diagnosis	48.6 (12.3)		43.6 (13.2)		45.9 (13.0)	
DVT	3040 (78.6)		4065 (79.2)		7105	
Age at DVT diagnosis	48.5 (11.9)		39.4 (13.7)		43.3 (13.7)	
DVT and PE	513 (13.3)		430 (8.4)		943	

Where: HRT, hormone replacement therapy; PE, pulmonary embolism; DVT, deep vein thrombosis

Supplementary Table 2: Associations between PRS and risk of VTE in individuals without mental illness

PRS	Model	men					women					sex-combined				
		R2*	OR	CI	P	N	R2*	OR	CI	P	N	R2*	OR	CI	P	N
SCZ	1	0.011	0.96	0.92-0.99	<b>0.015</b>	105471	0.013	1.01	0.97-1.04	0.701	110563	0.01	0.98	0.96-1.01	0.183	216034
	2	0.018	0.96	0.92-1.00	0.260	105467	0.160	1.01	0.98-1.04	0.659	110556	0.02	0.99	0.96-1.01	0.251	216023
	3	0.033	0.97	0.93-1.00	0.075	104747	0.030	1.02	0.99-1.05	0.286	109899	0.03	1.00	0.97-1.02	0.712	214646
	4						0.031	1.02	0.98-1.05	0.298	109517					
BD	1	0.110	1.04	1.00-1.07	0.550	105471	0.013	1.04	1.00-1.07	0.031	110563	0.01	1.04	1.01-1.06	<b>0.004</b>	216034
	2	0.018	1.04	1.00-1.08	0.046	105467	0.160	1.04	1.00-1.07	0.030	110556	0.02	1.04	1.01-1.06	<b>0.003</b>	216023
	3	0.034	1.04	1.00-1.08	0.030	104747	0.030	1.04	1.00-1.07	0.240	109899	0.03	1.04	1.01-1.06	<b>0.002</b>	214646
	4						0.031	1.04	1.00-1.07	0.270	109517					
MDD	1	0.122	1.05	1.01-1.09	<b>0.016</b>	124206	0.150	1.07	1.04-1.11	<b>&lt;0.001</b>	131157	0.01	1.06	1.04-1.09	<b>&lt;0.001</b>	255363
	2	0.018	1.05	1.01-1.09	<b>0.018</b>	124177	0.018	1.07	1.04-1.01	<b>&lt;0.001</b>	131112	0.02	1.06	1.03-1.09	<b>&lt;0.001</b>	255289
	3	0.034	1.04	1.00-1.08	0.051	123138	0.032	1.06	1.03-1.10	<b>&lt;0.001</b>	150213	0.03	1.05	1.03-1.08	<b>&lt;0.001</b>	253351
	4						0.032	1.06	1.03-1.10	<b>&lt;0.001</b>	129626					
VTE	1	0.040	1.63	1.57-1.70	<b>&lt;0.001</b>	103603	0.027	1.38	1.34-1.42	<b>&lt;0.001</b>	108458	0.03	1.48	1.45-1.52	<b>&lt;0.001</b>	212061
	2	0.042	1.76	1.69-1.83	<b>&lt;0.001</b>	103600	0.027	1.46	1.40-1.51	<b>&lt;0.001</b>	108454	0.03	1.58	1.54-1.63	<b>&lt;0.001</b>	212054
	3	0.058	1.76	1.69-1.84	<b>&lt;0.001</b>	102904	0.041	1.46	1.40-1.51	<b>&lt;0.001</b>	107818	0.05	1.58	1.54-1.63	<b>&lt;0.001</b>	204619
	4						0.04	1.46	1.41-1.52	<b>&lt;0.001</b>	107456					

Where: R2\*, Pseudo R2; Model 1: age, principle genetic components 1-8 (PGC1-8) and genotyping chip; Model 2: Model 1 plus blood group; Model 3: model 2 plus BMI, ever smoking and any anti-psychotic medication; Model 4 (women only), model 3 plus exogenous hormones (hormone replacement therapy and oral contraceptives)

Supplementary Table 3: Effect of family history of MDD on VTE risk.

Model	men (N=120724)				women				sex-combined (N= 257487)			
	R2*	OR	CI	P	R2*	OR	CI	P	R2*	OR	CI	P
1	0.012	1.19	1.08-1.32	<b>&lt;0.0001</b>	0.015	1.29	1.20-1.39	<b>&lt;0.0001</b>	0.015	1.26	1.19-1.33	<b>&lt;0.0001</b>
2	0.019	1.20	1.09-1.33	<b>&lt;0.0001</b>	0.018	1.29	1.20-1.39	<b>&lt;0.0001</b>	0.020	1.26	1.19-1.33	<b>&lt;0.0001</b>
3	0.036	1.20	1.09-1.33	<b>&lt;0.0001</b>	0.034	1.27	1.18-1.37	<b>&lt;0.0001</b>	0.036	1.24	1.17-1.32	<b>&lt;0.0001</b>
4					0.035	1.27	1.17-1.36	<b>&lt;0.0001</b>				

Where: R2\*, Pseudo R2; Model 1: age, principle genetic components 1-8 (PGC1-8) and genotyping chip; Model 2: Model 1 plus blood group; Model 3: model 2 plus BMI, ever smoking and any anti-psychotic medication; Model 4 (women only), model 3 plus exogenous hormones (hormone replacement therapy and oral contraceptives)

STable 4: Descriptive statistics of the replication cohorts

	RETROVE		HVH1		HVH3		EOVT		FARIVE		MARTHA	
	cases	controls	cases	controls	cases	controls	cases	contr ols	cases	controls	cases	controls
	196	194	716	877	976	757		370				522
Sex (%), male	(49.0)	(48.50)	(4.61)	(30.9)	(54.61)	(40.16)	229 (56)	(30)	241 (40)	259 (43)	522 (34)	(34)
	61.73	47.09	66.24	66.88	61.01	63.55	35.19		53.16	51.46	40.94	68.07
Age (SD)	(18.56)	(18.18)	(12.12)	(9.33)	(15.24)	(13.09)	(11.25)		(19.65)	(18.56)	(15.70)	(2.24)
BMI (SD), kg/m2	28.08	25.36	31.68	29.43	31.51	30.12			26.35	25.87	26.02	
	(5.22)	(4.08)	(8.17)	(6.31)	(7.53)	(6.49)			(5.85)	(6.04)	(4.81)	
Ever Smoker (yes)	55	75	299	440	499	395			294	336	157	
	(13.75)	(18.75)	(41.76)	(50.17)	(51.13)	(52.18)			(48.43)	(55.44)	(10.18)	
Exogenous hormones	73	125	25	2	72	19						
	(35.78)	(60.68)	(3.49)	(0.23)	(7.38)	(2.51)						
HRT	9 (4.43)	23 (11.17)	198 (27.65)	184 (20.98)	21 (2.15)	64 (8.45)			47 (12.84)	50 (14.37)		
	181		234		294							
PE	(45.25)	0 (0)	(32.7)		(30.1)		143 (42)		245(40)		44 (7.7)	
Age at PE diagnosis			67.02		62.38							
			(11.56)		(16.03)							
DVT	280		365		476							
	(70.00)	0 (0)	(51.0)		(48.8)		196 (58)		173(29)		444 (78)	
Age at DVT diagnosis			65.89		59.59							
			(12.49)		(14.89)							
DVT and PE	70		117		206							
	(17.50)	0 (0)	(16.3)		(21.1)				188 (31)		81 (14)	
Blood group (type O)	93	153	234	374	301	342						
	(23.48)	(38.54)	(32.68)	(42.65)	(30.84)	(45.18)			157 (30)	239 (45)		
anti-psychotics	16	7	23	3	19	2						
	(4.00)	(1.75)	(3.21)	(0.34)	(1.95)	(0.26)						

STable 5: Individual replication cohort results for VTE

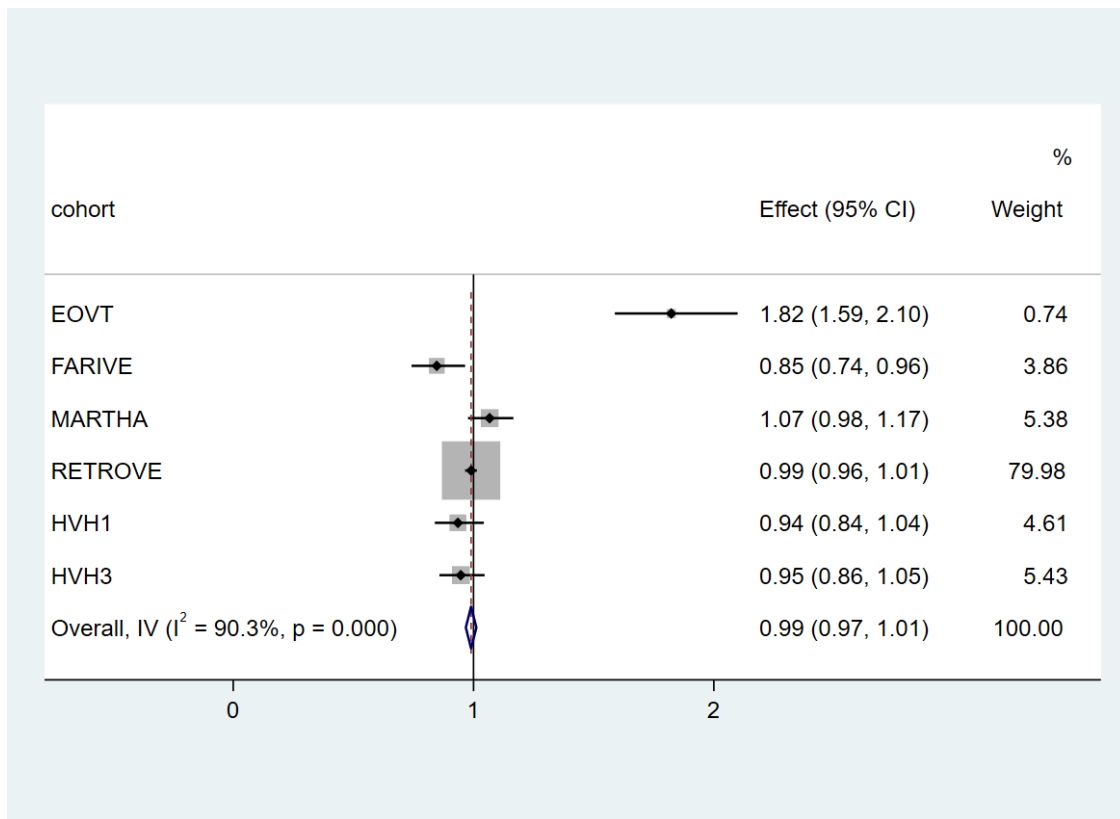
PR S	RETROVE				HVH1				HVH3				P thres hold	EO VT	FARIVE				MARTH A							
	O	L9	U9	P	OR	L95	U95	P	OR	L95	U95	P			OR	L95	U95	P	O	L9	U9	P	O	L9	U9	P
	R	5	5																R	5	5		R	5	5	
BD													5e.05	1.1	1.	1.	<b>0.032</b>	0.	0.	1.	0.77	1.	0.	1.	0.33	
														5	01	30	<b>0</b>	98	86	12	41	04	96	13	61	
													0.05	1.6	1.	1.	<b>1.30E</b>	0.	0.	0.	<b>0.01</b>	1.	0.	1.	0.52	
													8	47	93	<b>-13</b>	84	74	96	<b>09</b>	03	94	12	98		
	0.	0.	1.	0.40	0.9	0.8	1.0	0.22	0.9	0.8	1.0	0.2	1	1.8	1.	2.	<b>2.97E</b>	0.	0.	0.	<b>0.01</b>	1.	0.	1.	0.14	
	99	97	01	78	35	39	43	80	47	58	46	83		2	59	10	<b>-17</b>	85	74	97	<b>30</b>	07	98	17	84	
SC Z													5e.05	1.0	0.	1.	0.852	1.	0.	1.	0.99	1.	0.	1.	0.11	
														2	87	19	9	00	88	14	23	08	98	19	26	
													0.05	1.0	0.	1.	0.362	1.	0.	1.	0.49	1.	1.	1.	0.06	
														6	93	22	2	05	92	19	82	09	00	19	64	
	1.	0.	1.	0.33	0.8	0.8	0.9	0.03	0.9	0.8	1.0	0.6	1	1.1	0.	1.	0.175	1.	0.	1.	0.95	1.	0.	1.	0.22	
	00	98	01	11	93	03	93	75	79	87	8	66		0	96	25	0	00	88	15	24	06	97	16	52	
M DD													5e.05	0.9	0.	1.	0.771	0.	0.	1.	0.31	1.	0.	1.	0.80	
														8	86	12	7	94	82	06	05	01	93	10	85	
													0.05	1.1	1.	1.	<b>0.032</b>	0.	0.	1.	0.28	1.	1.	1.	<b>0.01</b>	
														5	01	30	<b>7</b>	93	82	06	92	12	03	21	<b>07</b>	
	1.	0.	1.	0.50	1.1	1.0	1.2	0.02	1.0	0.9	1.1	0.6	1	1.1	1.	1.	<b>0.015</b>	0.	0.	1.	0.37	1.	1.	1.	<b>0.01</b>	
	12	79	44	59	31	17	59	37	22	27	28	57		7	03	33	<b>3</b>	94	83	08	62	11	02	20	<b>97</b>	

Where: RETROVE, HVH1 and HVH3 PRS were calculated using LDpred (includes all SNPs). RETROVE adjusted for age, sex, principle components 1-20. HVH1 and HVH3 adjusting for age, sex and PCs 1-2.

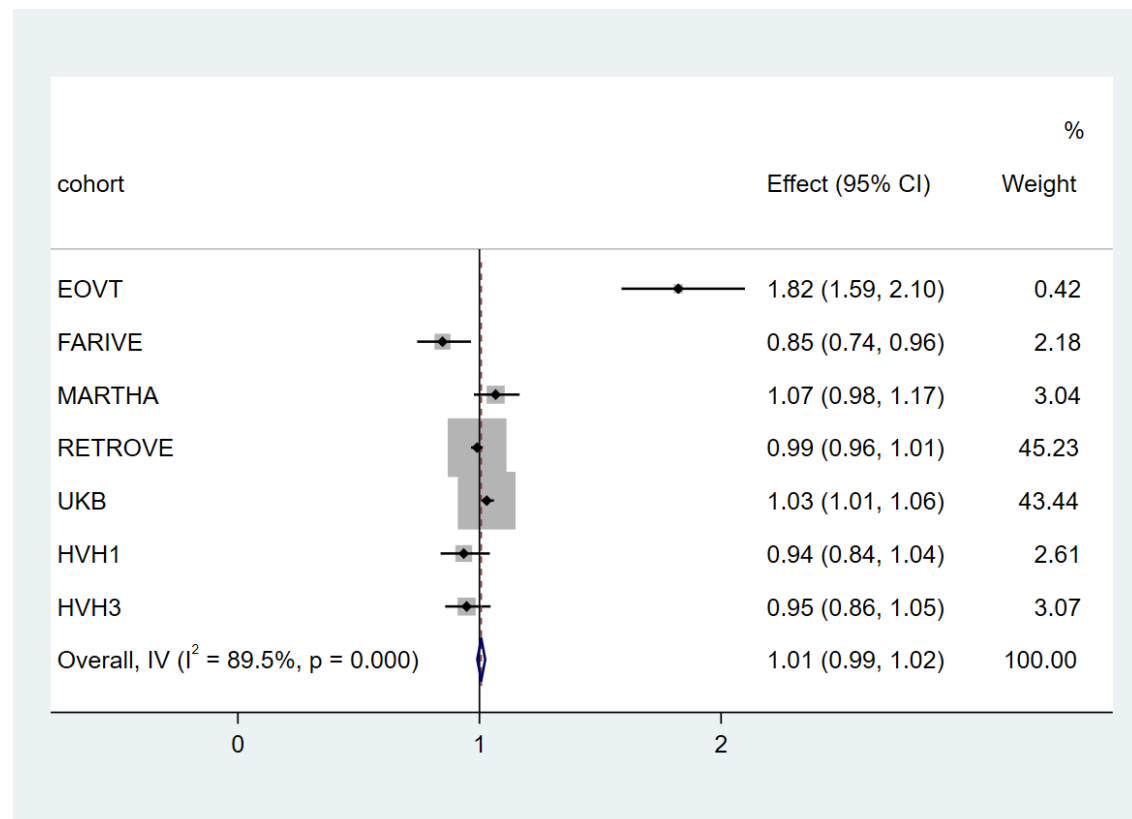


SFigure 1

A)

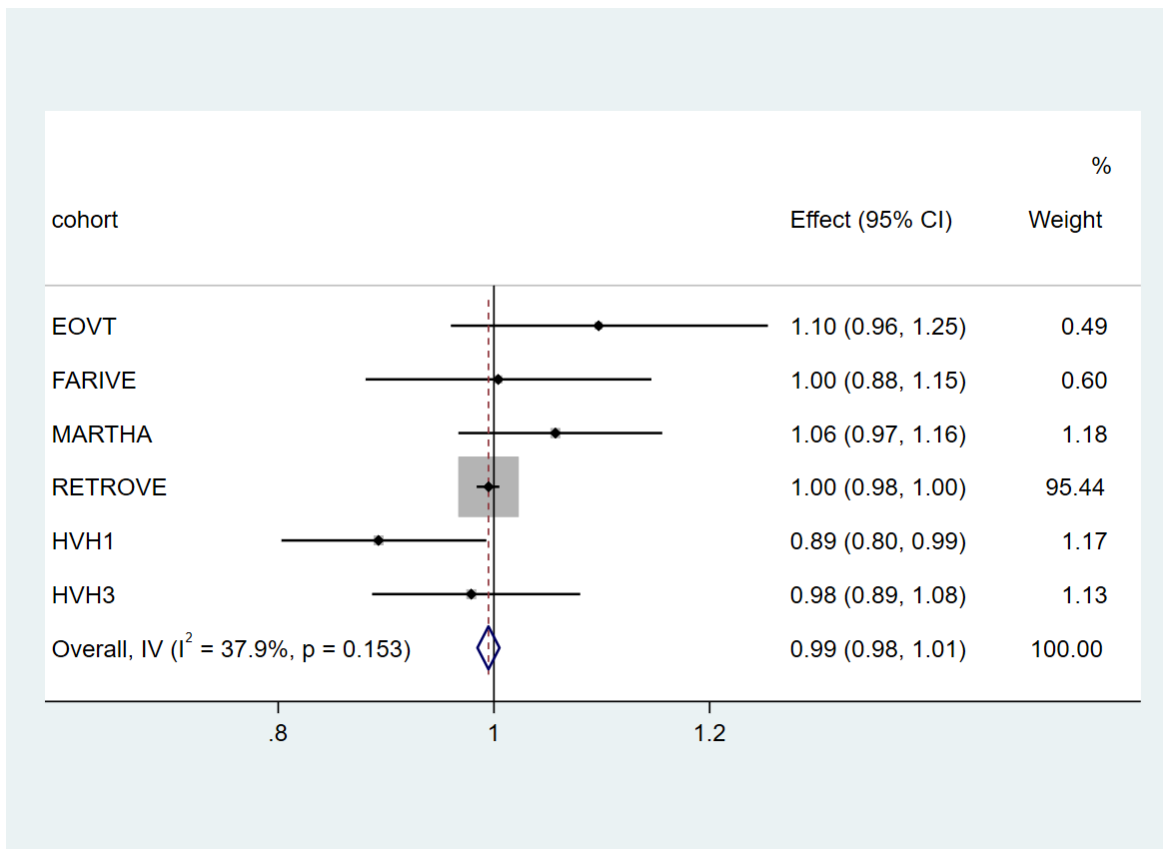


B)





C)



D)

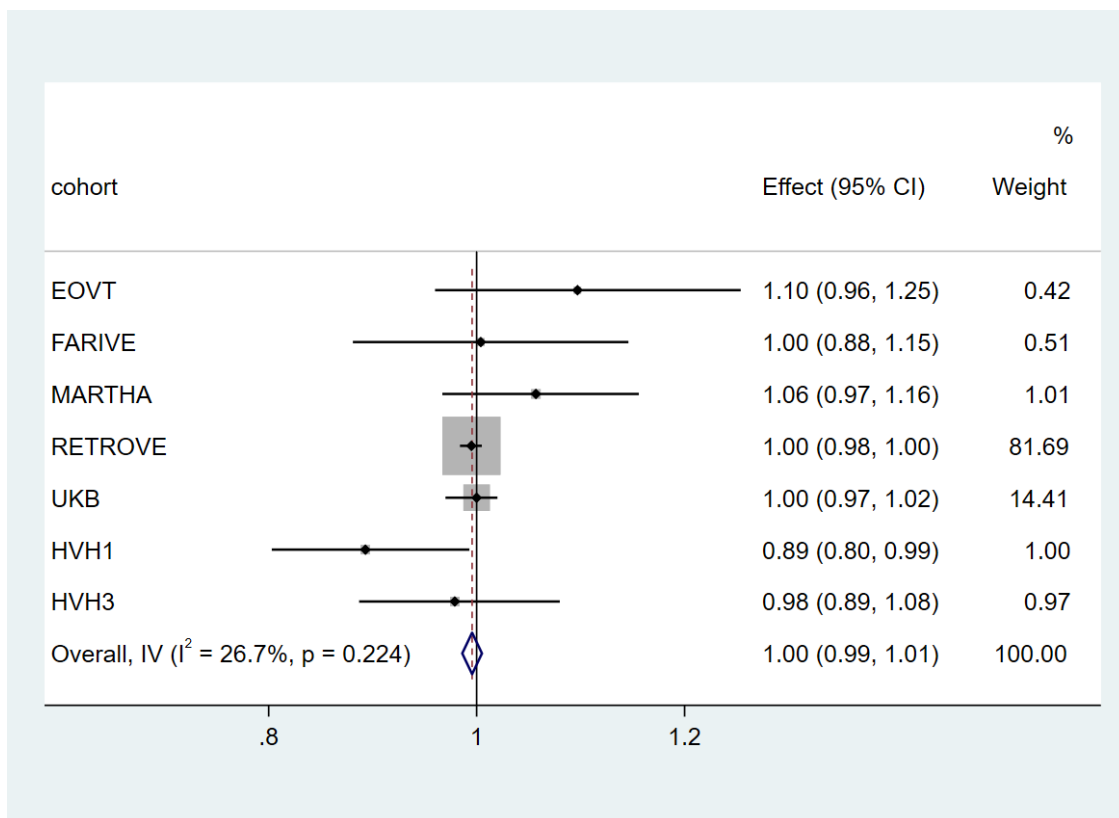
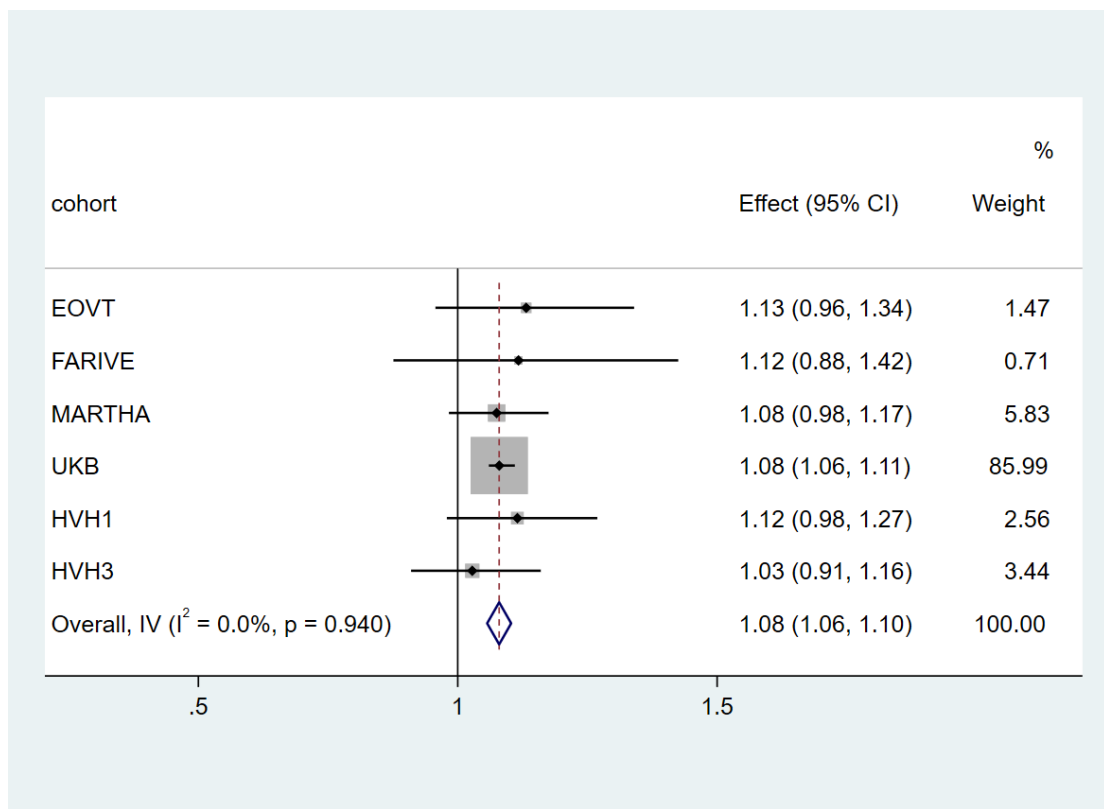
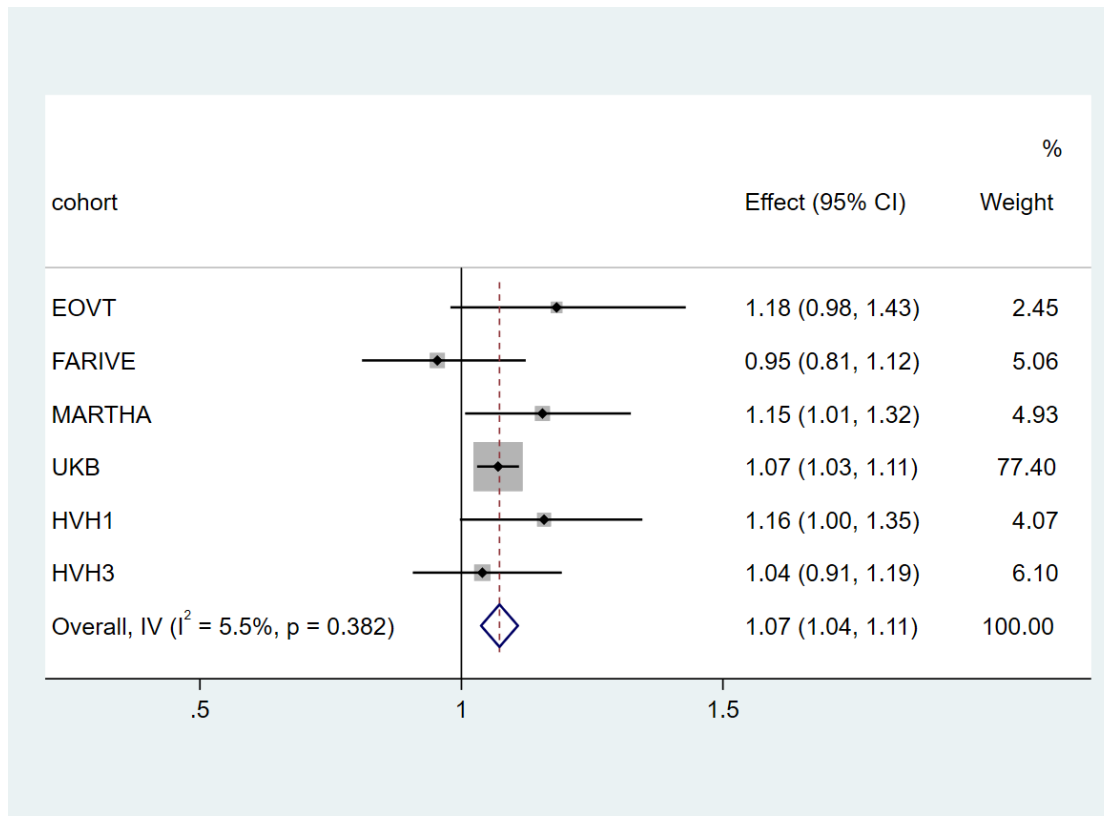


Figure 2

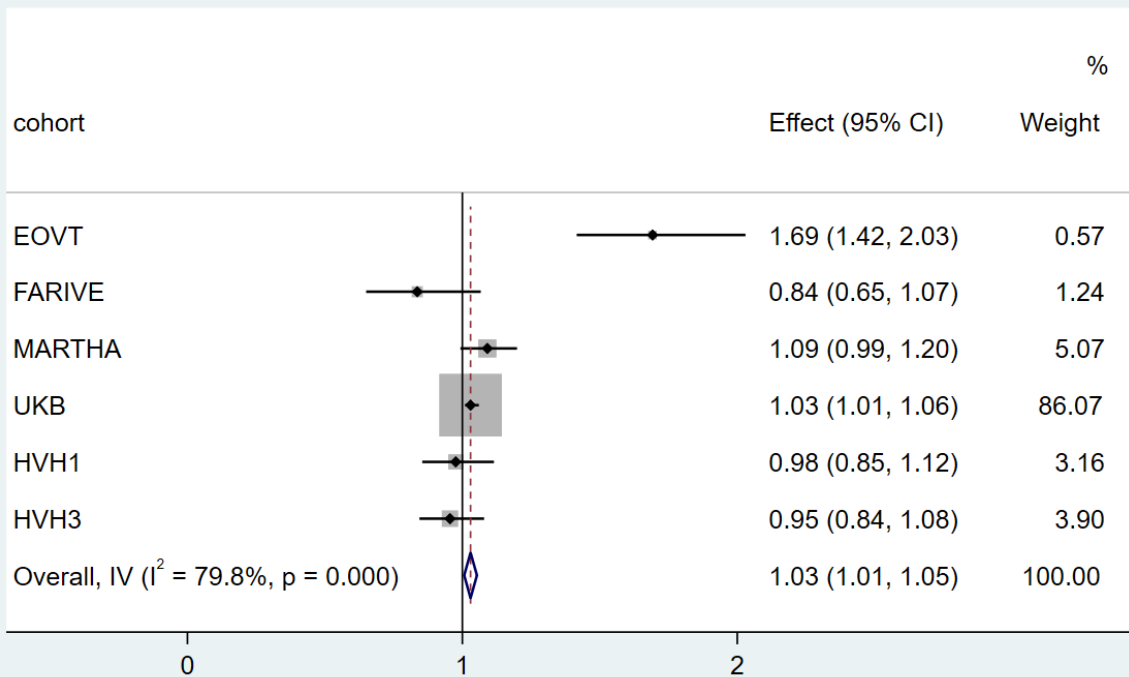
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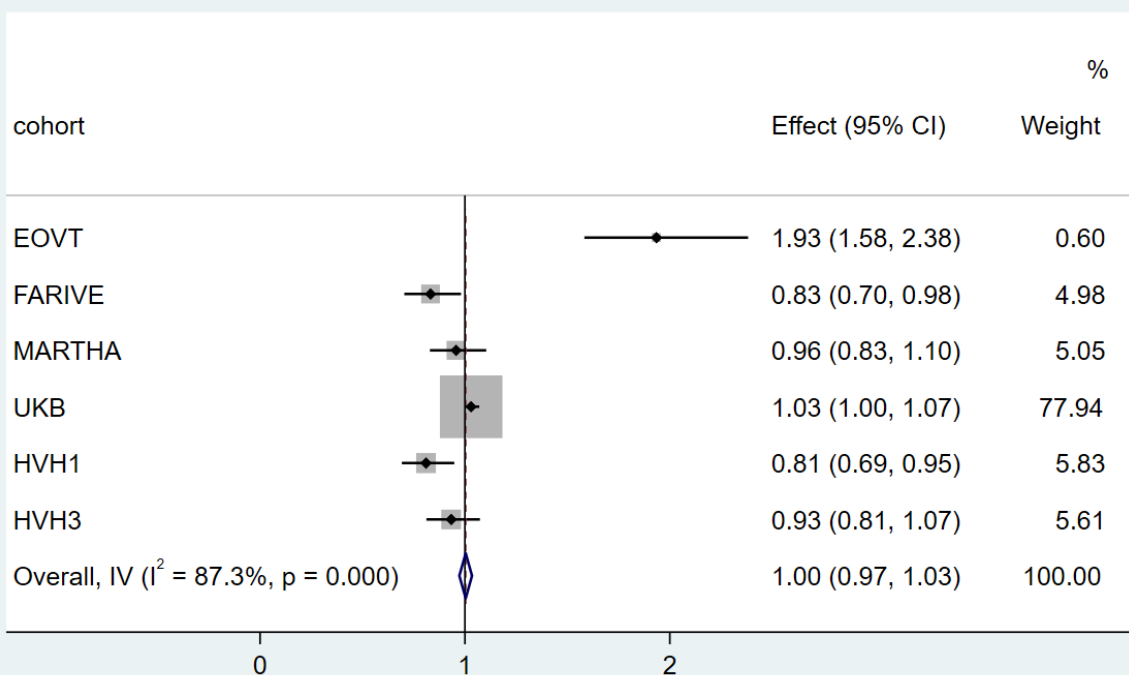
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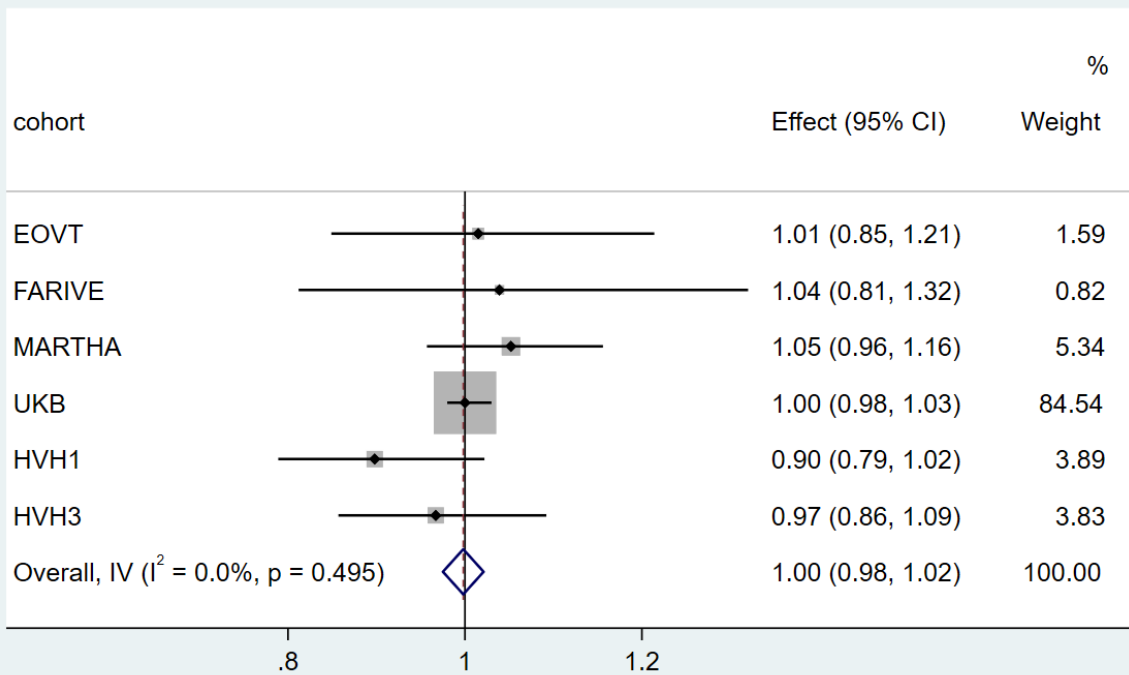
C)



D)



E)



F)

