Supplementary file 4

MR Results of sleeplessness/insomnia, anxiety/panic attacks and depression on the risk of localized pain with scatter plots

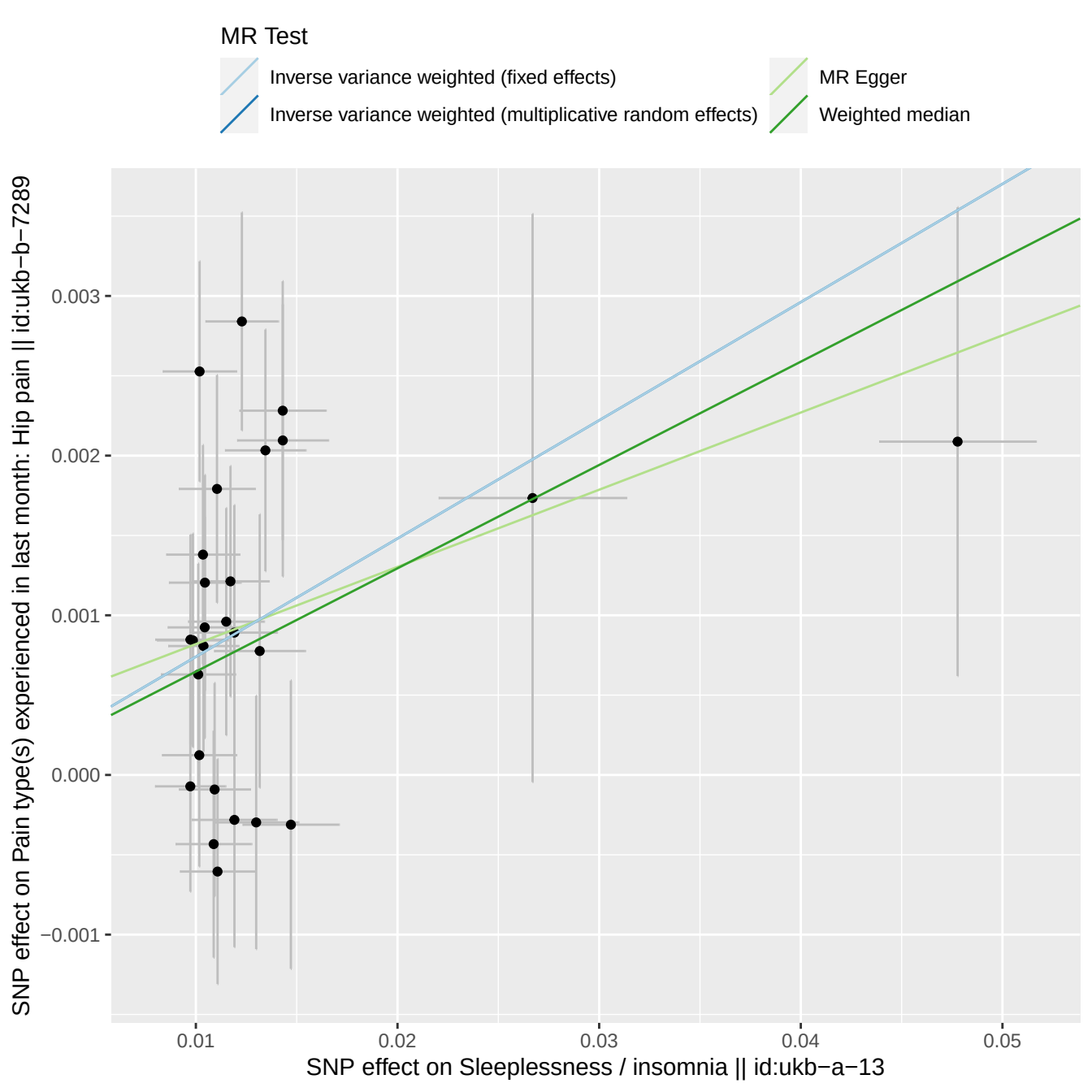
Single-Variable MR Results of sleeplessness/insomnia, anxiety/panic attacks and depression on the risk of localized pain

		Sleeplessness / insomnia			Anxiety/panic attacks*			Depression*		
Outcome	**Method**	**N SNV**	**OR (95%CI)**	***P* value**	**N SNV**	**OR (95%CI)**	***P* value**	**N SNV**	**OR (95%CI)**	***P* value**
Headache	IVW (FEM)	27	1.09 (1.06-1.12)	<0.001	12	1.98 (1.41-2.78)	<0.001	32	1.28 (1.13-1.45)	<0.001
	IVW (REM)	27	1.09 (1.03-1.15)	0.002	12	1.98 (1.40-2.81)	<0.001	32	1.28 (1.08-1.52)	0.004
	Weighted median	27	1.07 (1.02-1.13)	0.005	12	2.31 (1.44-3.69)	<0.001	32	1.21 (1.00-1.46)	0.05
	MR Egger	27	1.00 (0.84-1.19)	0.99	12	0.65 (0.28-1.55)	0.36	32	1.58 (0.95-2.65)	0.09
Facial pain	IVW (FEM)	26	1.01 (1.00-1.02)	0.02	8	1.12 (0.97-1.28)	0.12	25	1.07 (1.02-1.12)	0.006
	IVW (REM)	26	1.01 (1.00-1.02)	0.03	8	1.12 (0.98-1.27)	0.09	25	1.07 (1.03-1.11)	<0.001
	Weighted median	26	1.01 (1.00-1.03)	0.09	8	1.11 (0.92-1.33)	0.29	25	1.05 (0.99-1.12)	0.12
	MR Egger	26	1.03 (0.99-1.07)	0.13	8	0.89 (0.49-1.60)	0.70	25	1.28 (1.00-1.65)	0.07
Neck or shoulder pain	IVW (FEM)	27	1.12 (1.08-1.15)	<0.001	12	1.83 (1.28-2.62)	<0.001	32	1.32 (1.16-1.50)	<0.001
	IVW (REM)	27	1.12 (1.07-1.16)	<0.001	12	1.83 (1.28-2.62)	<0.001	32	1.32 (1.14-1.51)	<0.001
	Weighted median	27	1.07 (1.02-1.12)	0.005	12	1.78 (1.08-2.93)	0.25	32	1.25 (1.04-1.50)	0.02
	MR Egger	27	1.05 (0.93-1.18)	0.42	12	1.34 (0.53-3.42)	0.55	32	1.52 (0.99-2.31)	0.06
Back pain	IVW (FEM)	27	1.12 (1.09-1.16)	<0.001	12	1.54 (1.20-1.97)	0.02	32	1.35 (1.18-1.55)	<0.001
	IVW (REM)	27	1.12 (1.07-1.18)	<0.001	12	1.54 (1.06-2.23)	<0.001	32	1.35 (1.10-1.66)	0.004
	Weighted median	27	1.11 (1.05-1.17)	<0.001	12	1.64 (1.01-2.68)	0.05	32	1.30 (1.04-1.62)	0.02
	MR Egger	27	1.14 (0.97-1.33)	0.13	12	1.23 (0.48-3.16)	0.68	32	1.75 (0.94-3.32)	0.09
Stomach and abdominal pain	IVW (FEM)	27	1.06 (1.04-1.08)	<0.001	12	0.97 (0.76-1.23)	0.80	32	1.14 (1.05-1.25)	0.002
	IVW (REM)	27	1.06 (1.03-1.08)	<0.001	12	0.97 (0.78-1.20)	0.78	32	1.14 (1.04-1.25)	0.004
	Weighted median	27	1.04 (1.01-1.07)	0.006	12	1.05 (0.76-1.45)	0.77	32	1.16 (1.03-1.32)	0.02
	MR Egger	27	1.01 (0.97-1.07)	0.76	12	1.27 (0.69-2.32)	0.46	32	0.95 (0.73-1.25)	0.74
Hip pain	IVW (FEM)	27	1.08 (1.05-1.10)	<0.001	12	1.20 (0.91-1.57)	0.19	32	1.17 (1.06-1.29)	0.002
	IVW (REM)	27	1.08 (1.05-1.11)	<0.001	12	1.20 (0.80-1.80)	0.39	32	1.17 (1.04-1.31)	0.01
	Weighted median	27	1.07 (1.03-1.10)	<0.001	12	1.26 (0.83-1.92)	0.27	32	1.14 (0.98-1.31)	0.08
	MR Egger	27	1.05 (0.96-1.15)	0.31	12	0.67 (0.24-1.85)	0.46	32	0.98 (0.68-1.40)	0.90
Knee pain	IVW (FEM)	27	1.09 (1.06-1.12)	<0.001	12	1.14 (0.80-1.62)	0.46	32	1.16 (1.02-1.32)	0.02
	IVW (REM)	27	1.09 (1.04-1.13)	<0.001	12	1.14 (0.78-1.66)	0.49	32	1.16 (0.99-1.36)	0.06
	Weighted median	27	1.05 (1.00-1.10)	0.06	12	1.23 (0.76-1.98)	0.40	32	1.20 (0.99-1.46)	0.06
	MR Egger	27	0.98 (0.87-1.11)	0.78	12	0.65 (0.26-1.66)	0.39	32	1.00 (0.62-1.60)	1.00
None of above	IVW (FEM)	27	0.86 (0.83-0.89)	<0.001	12	0.55 (0.37-0.84)	0.005	32	0.71 (0.61-0.83)	<0.001
	IVW (REM)	27	0.86 (0.81-0.92)	<0.001	12	0.55 (0.36-0.86)	0.008	32	0.71 (0.58-0.87)	<0.001
	Weighted median	27	0.92 (0.86-0.97)	0.004	12	0.44 (0.25-0.77)	0.004	32	0.68 (0.54-0.85)	<0.001
	MR Egger	27	0.93 (0.77-1.13)	0.49	12	1.83 (0.64-5.28)	0.29	32	0.64 (0.35-1.18)	0.16

Abbreviations: N SNV, number of single-nucleotide variants; IVW, inverse-variance weighted; FEM, fixed effects models; REM, random effects models; OR, odds ratio; GWAS, genome-wide association studies.

Genetic instruments selected from sleeplessness/insomnia, anxiety/panic attacks and depression GWASs, selection threshold *P* less than 5×10^{-8}, pruned at linkage disequilibrium R^2 less than 0.001 (10 000 kilobase pair window).

* If the number of SNPs available for analysis is less than 3, the selection threshold *P* will be adjusted to 5×10^{-6}.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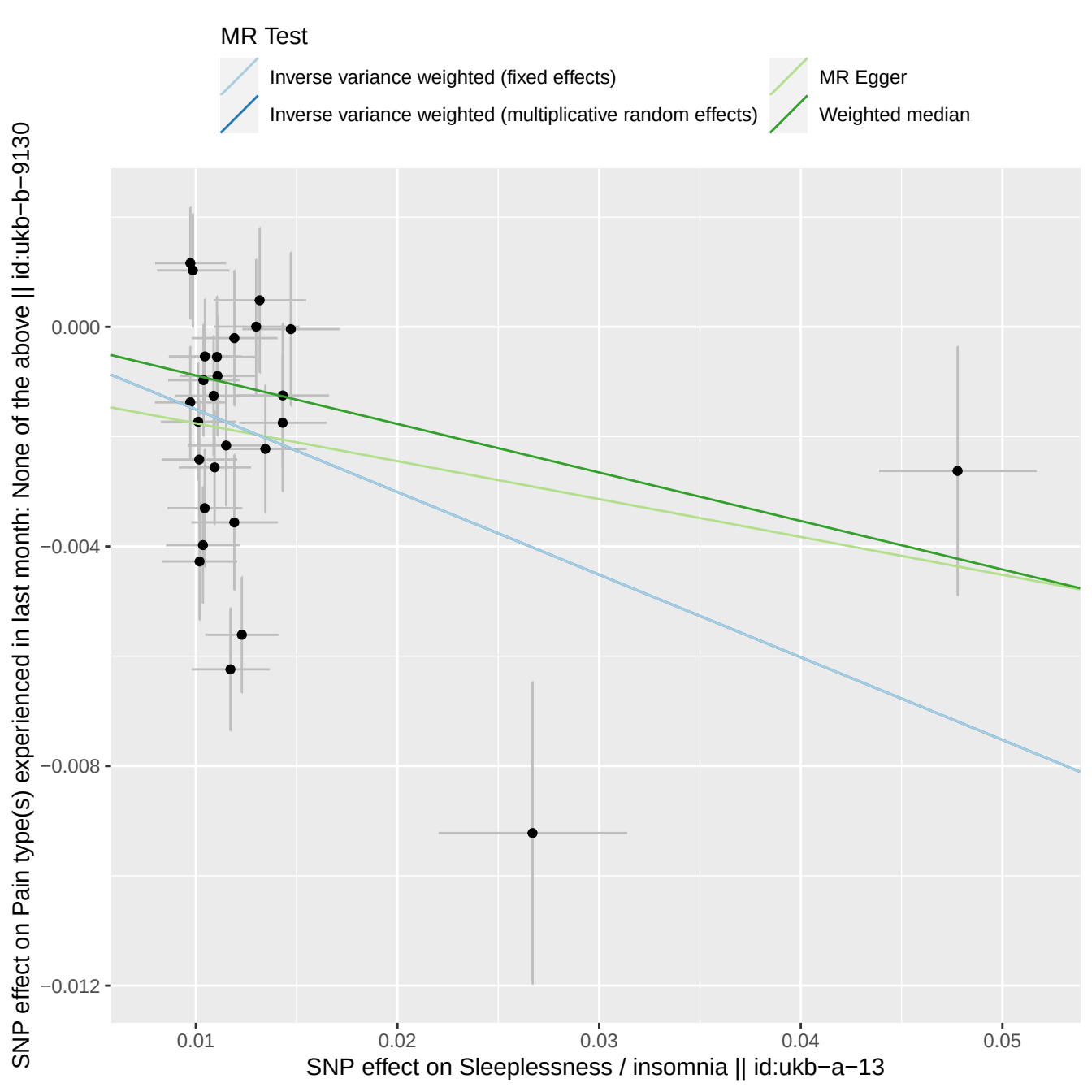
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Hip pain || id:ukb−b−7289
0.003
0.002
0.001
0.000
−0.001
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13


MR Test
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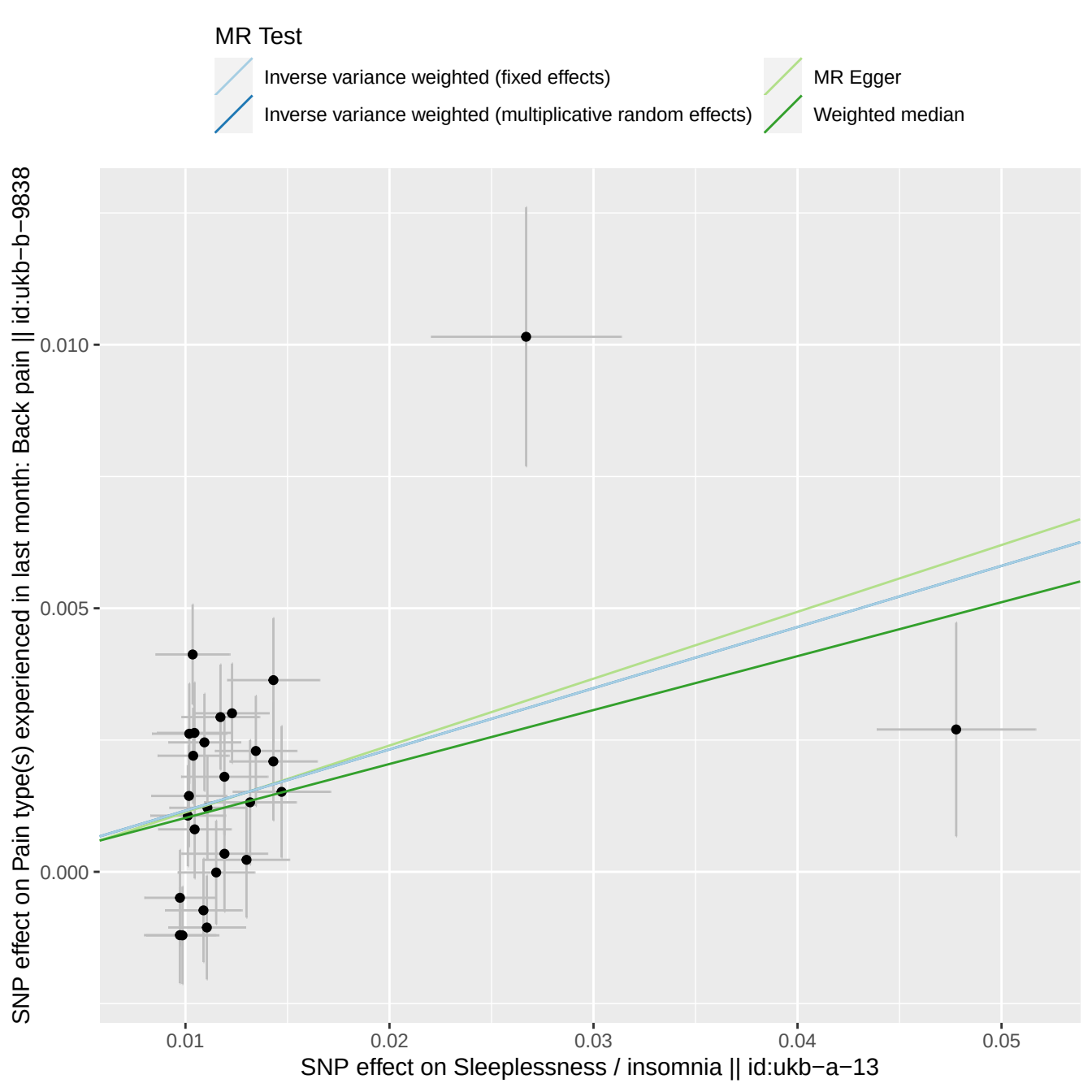
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: None of the above || id:ukb−b−9130
0.000
−0.004
−0.008
−0.012
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13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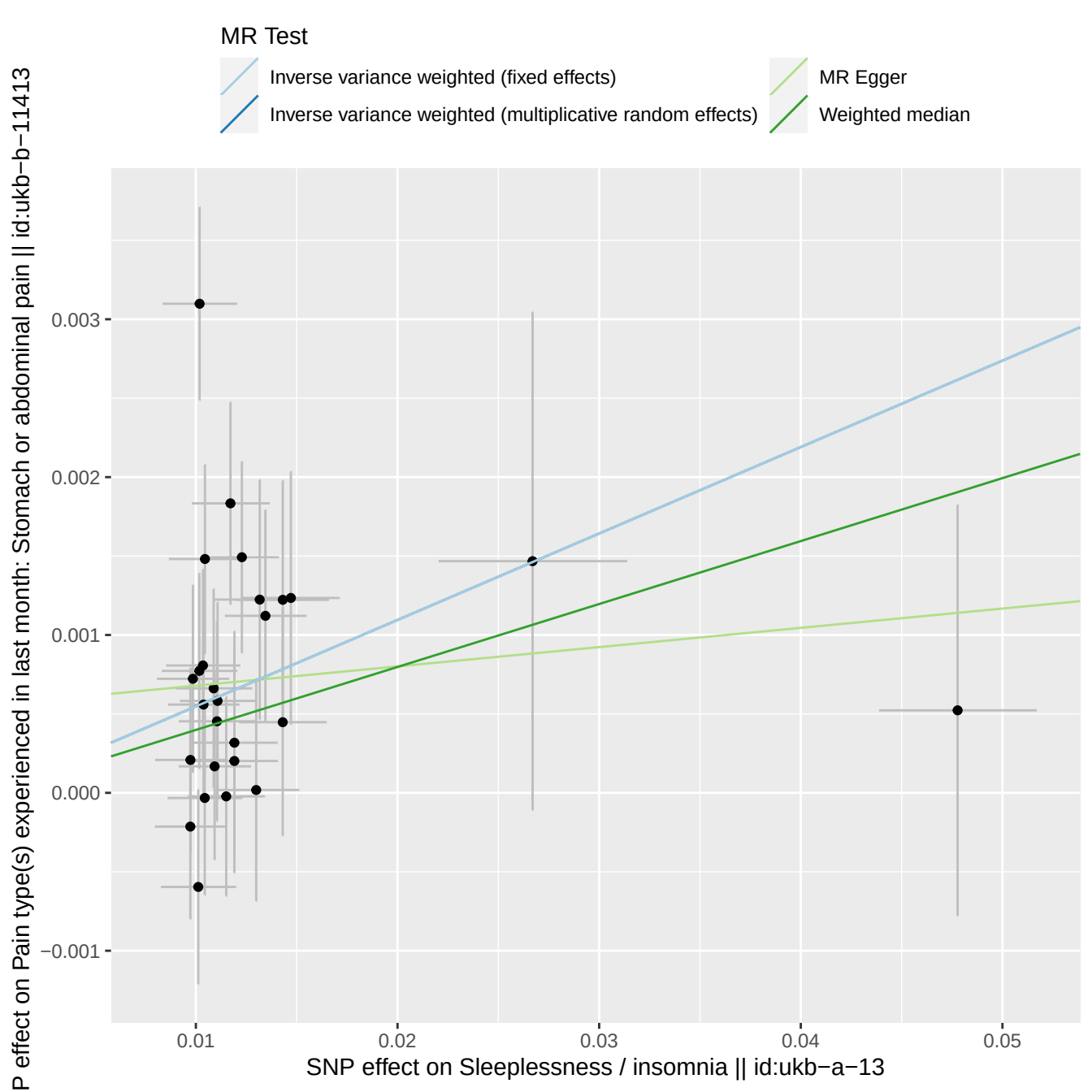
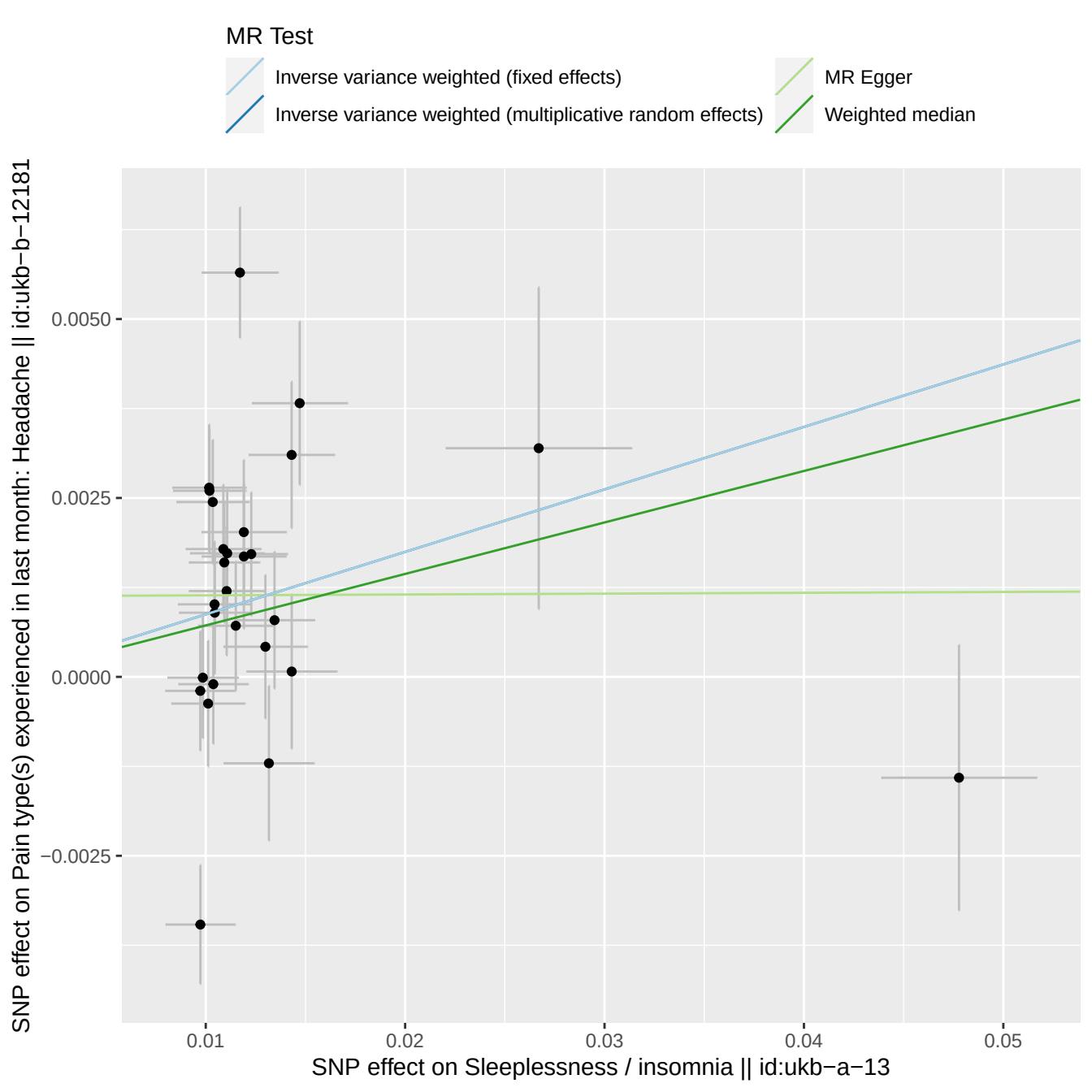
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Back pain || id:ukb−b−9838
0.010
0.005
0.000
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
0.003
0.002
0.001
0.000
−0.001
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13
P effect on Pain type(s) experienced in last month: Stomach or abdominal pain || id:ukb−b−11413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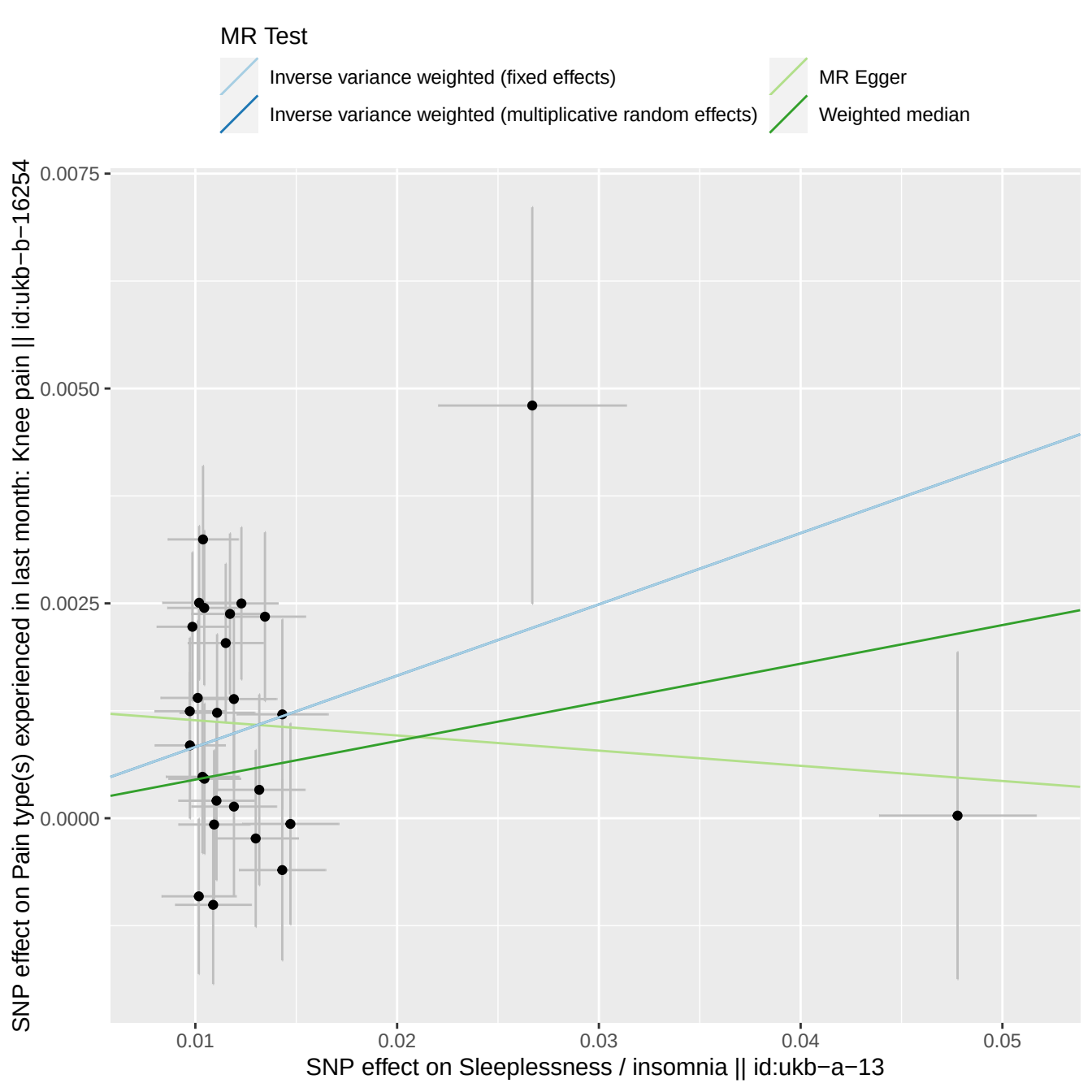
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Headache || id:ukb−b−12181
0.0050
0.0025
0.0000
−0.0025
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13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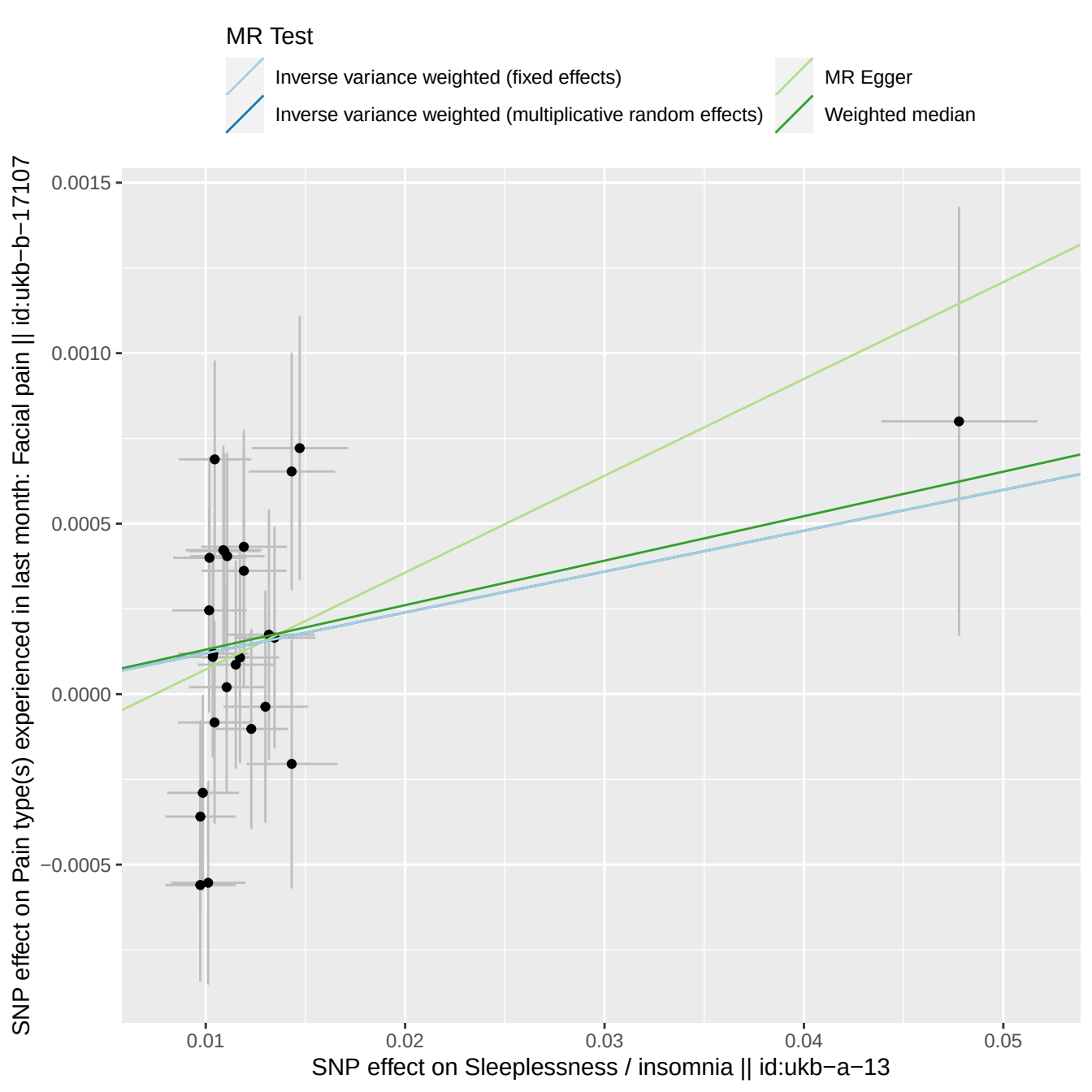
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Knee pain || id:ukb−b−16254
0.0075
0.0050
0.0025
0.0000
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13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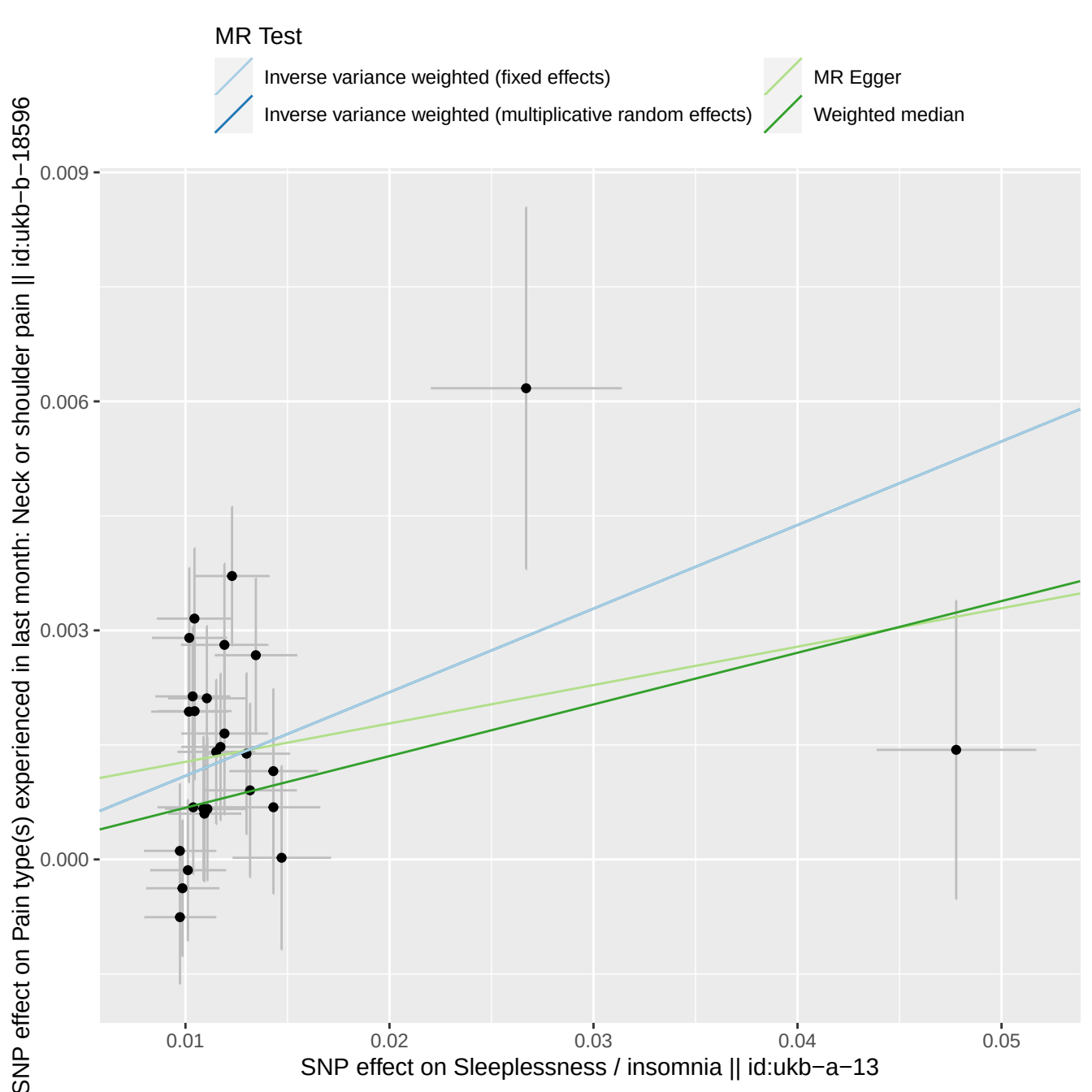
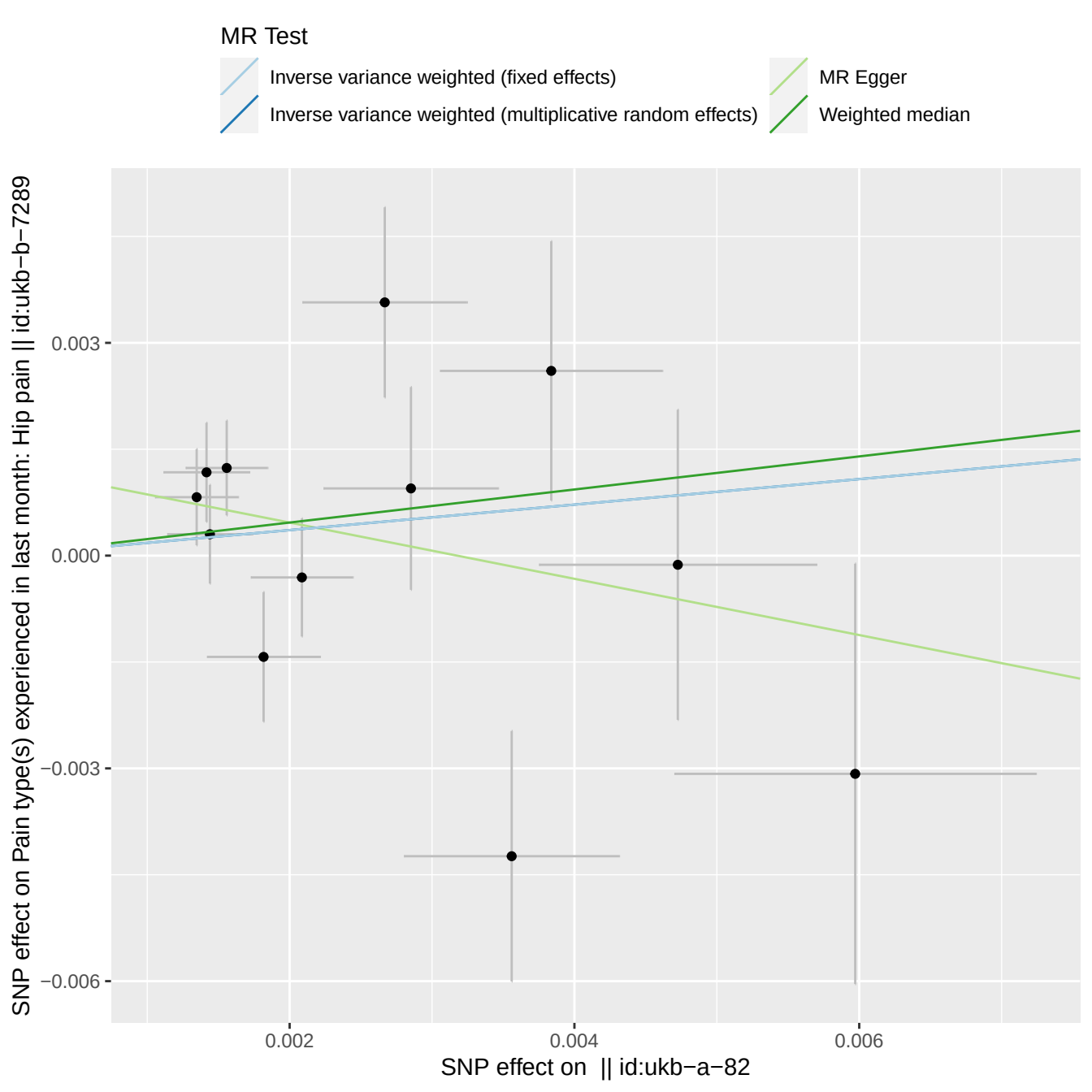
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Facial pain || id:ukb−b−17107
0.0015
0.0010
0.0005
0.0000
−0.0005
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
0.009
0.006
0.003
0.000
0.01
0.02
0.03
0.04
0.05
SNP effect on Sleeplessness / insomnia || id:ukb−a−13
SNP effect on Pain type(s) experienced in last month: Neck or shoulder pain || id:ukb−b−18596


MR Test
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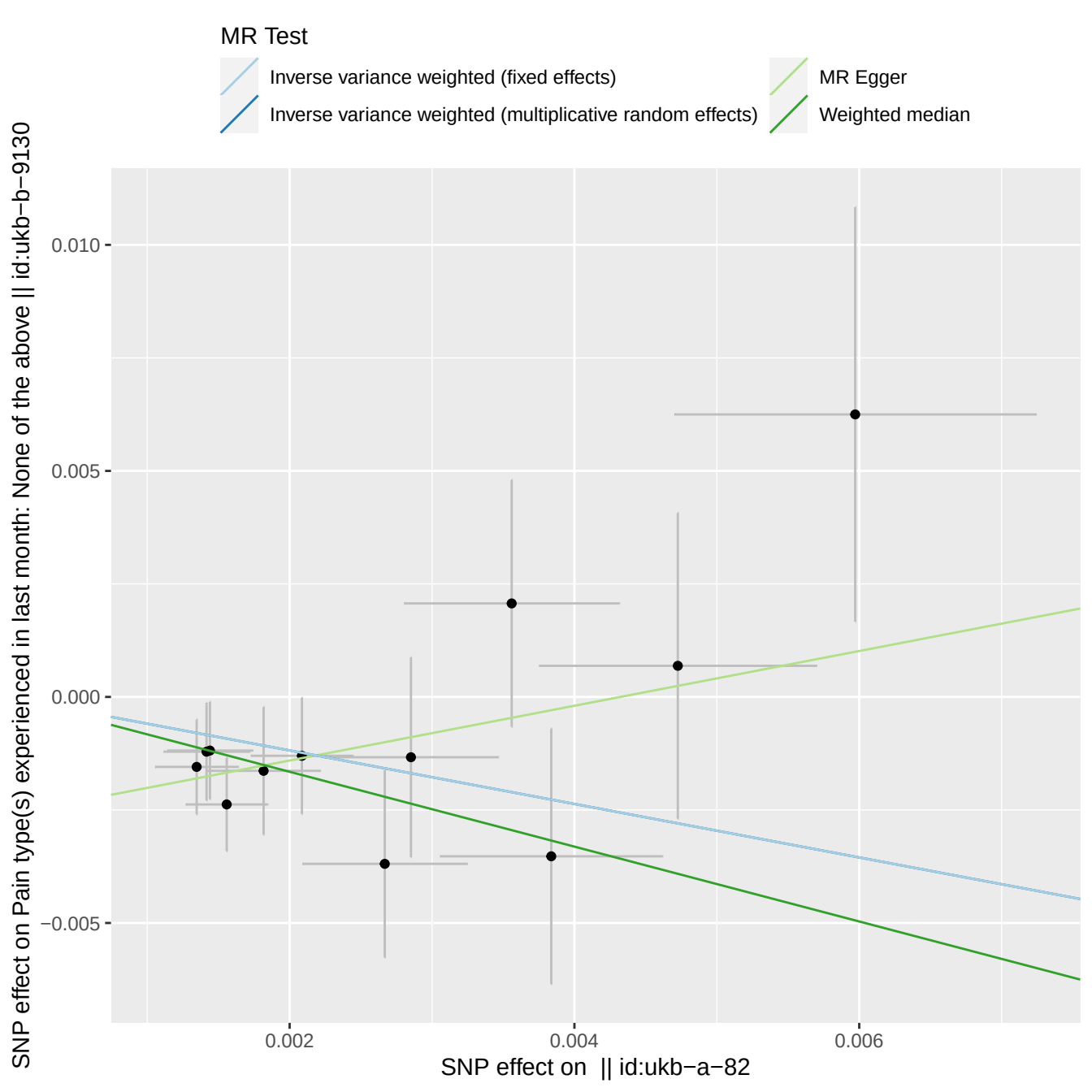
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Hip pain || id:ukb−b−7289
0.003
0.000
−0.003
−0.006
0.002
0.004
0.006
SNP effect on || id:ukb−a−82


MR Test
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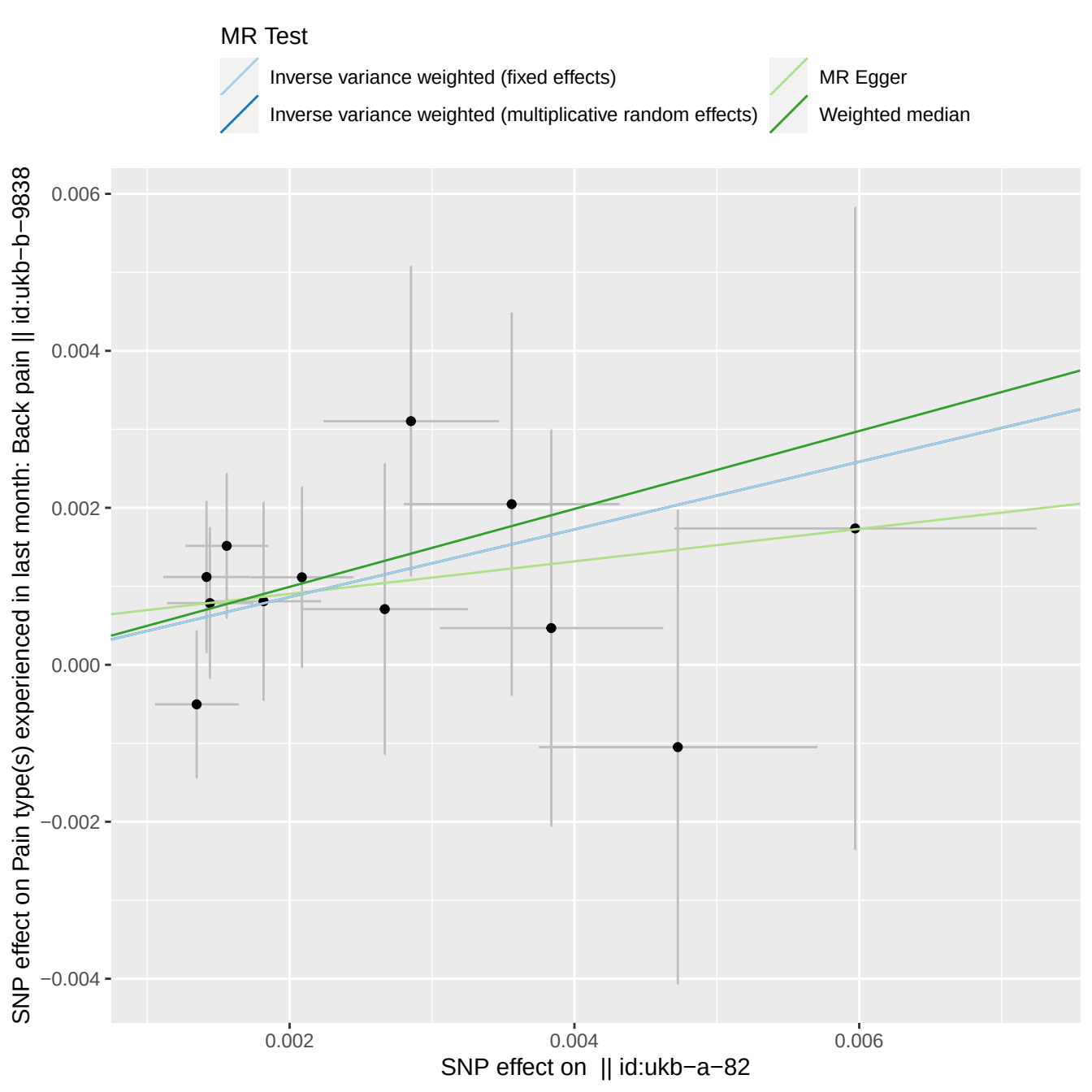
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: None of the above || id:ukb−b−9130
0.010
0.005
0.000
−0.005
0.002
0.004
0.006
SNP effect on || id:ukb−a−82


MR Test
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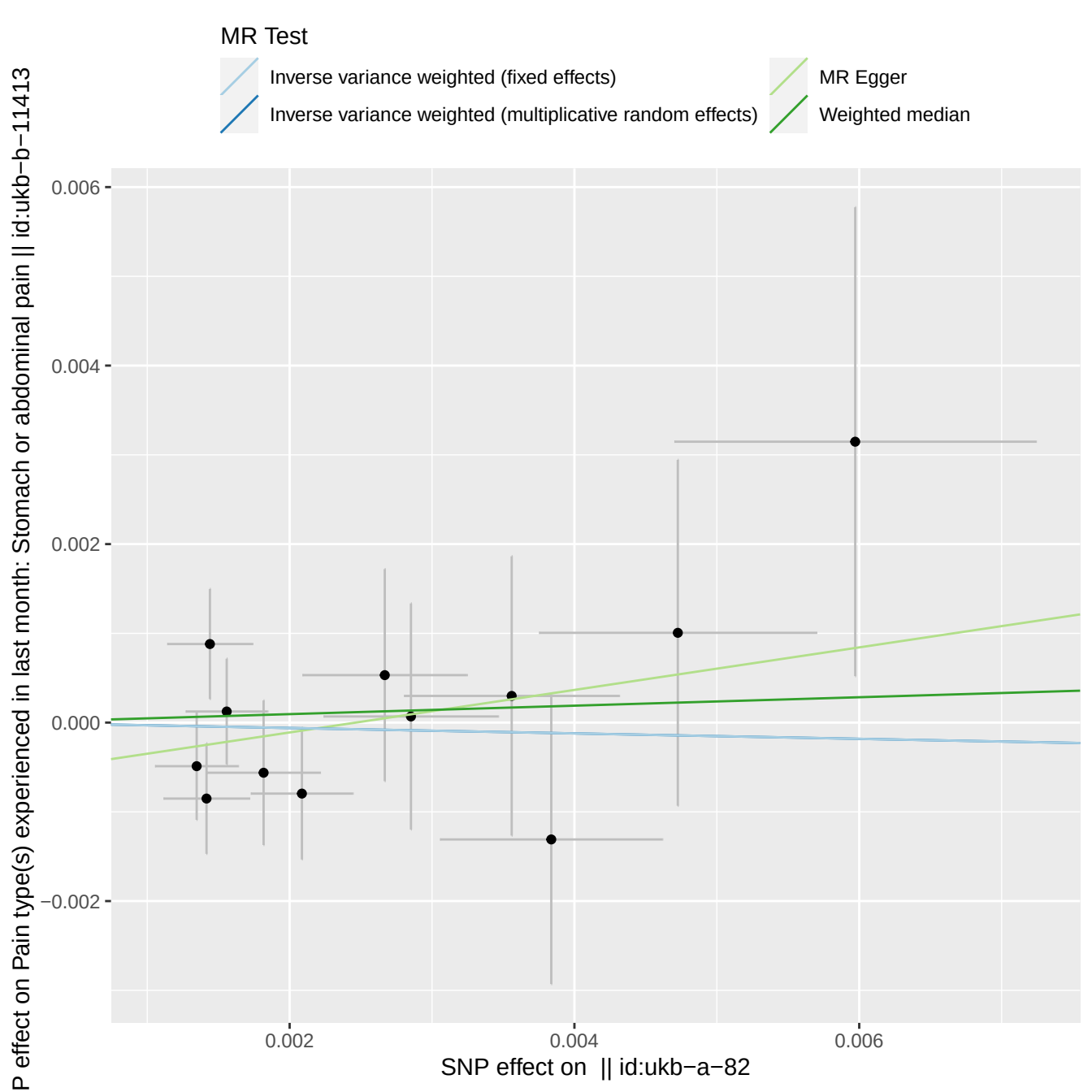
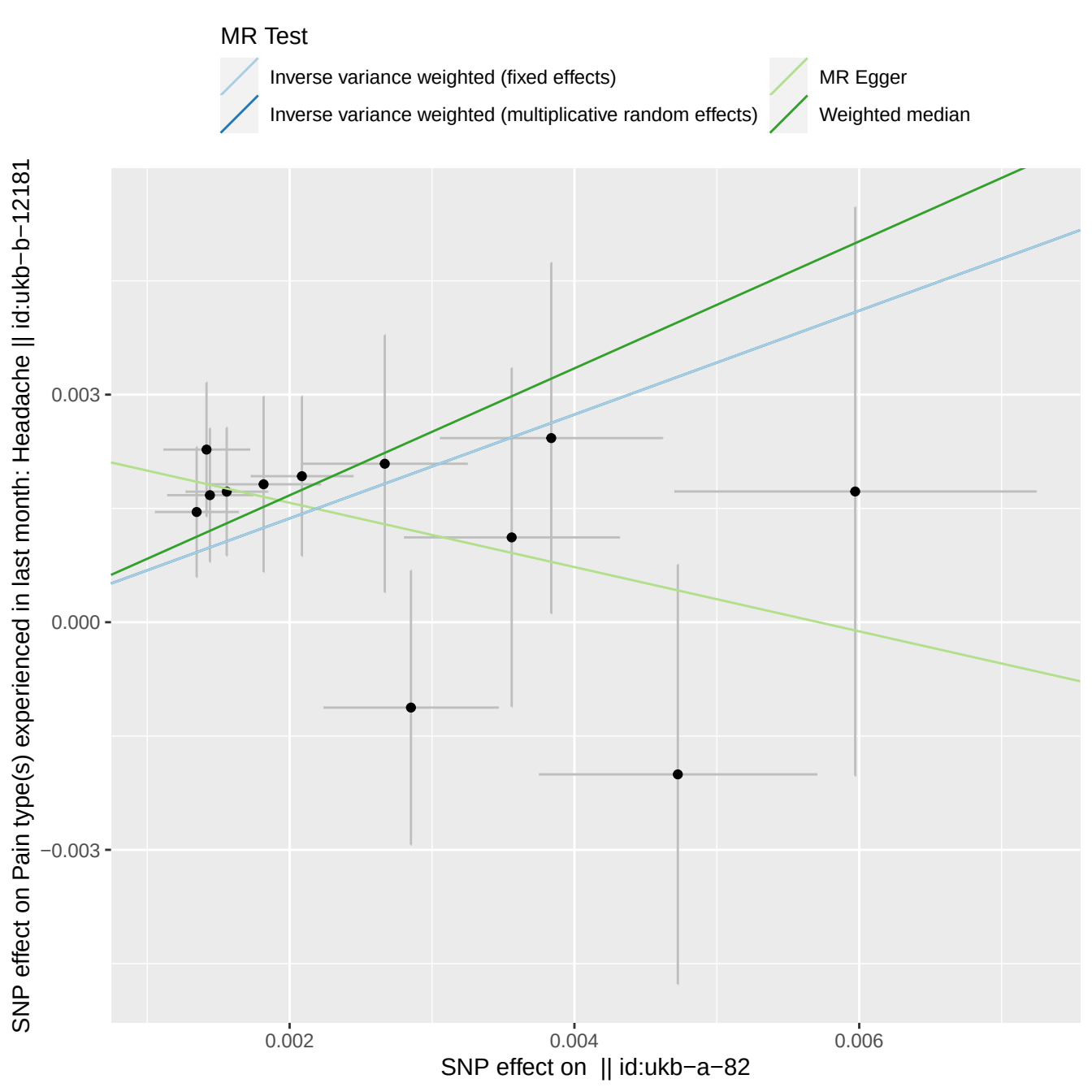
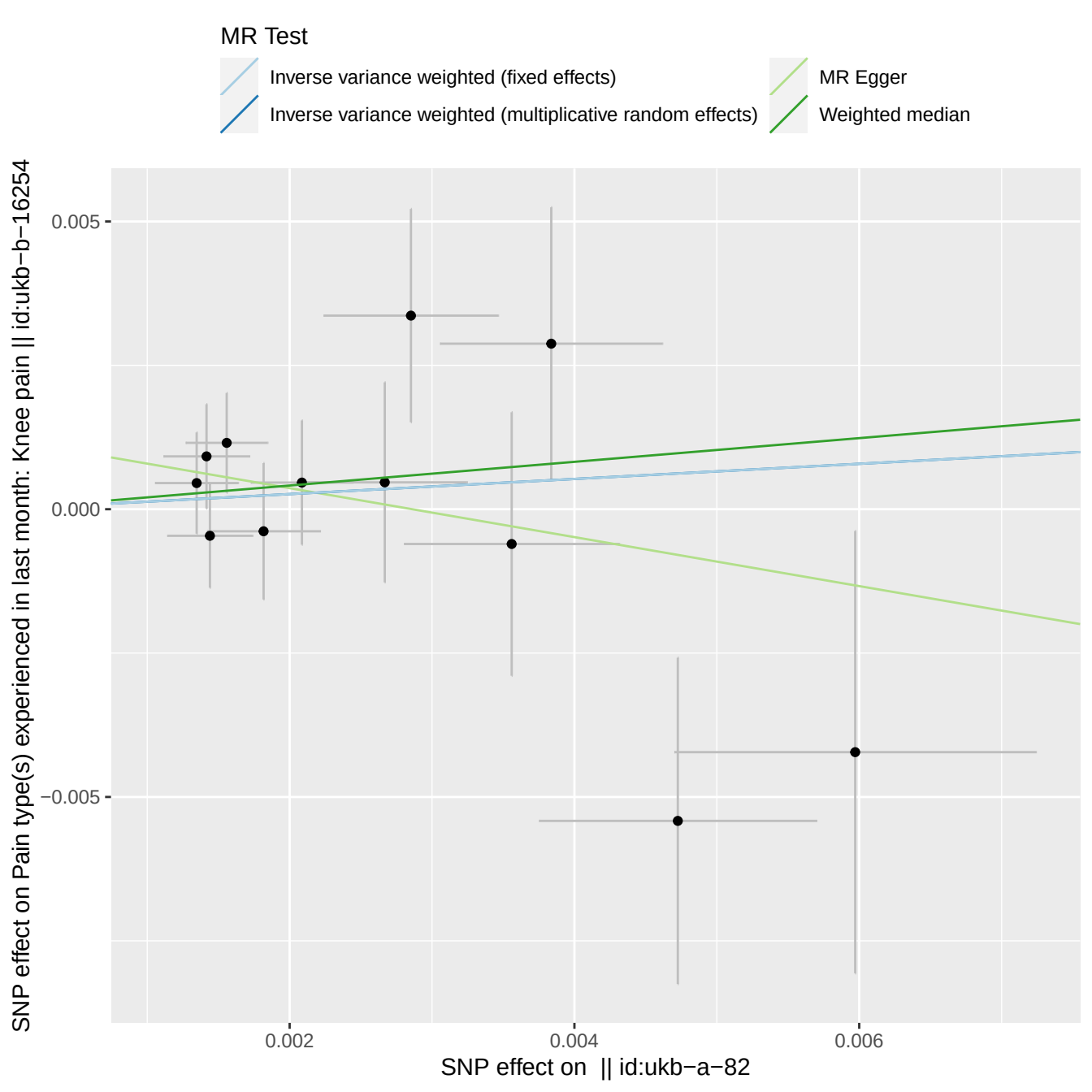
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Back pain || id:ukb−b−9838
0.006
0.004
0.002
0.000
−0.002
−0.004
0.002
0.004
0.006
SNP effect on || id:ukb−a−82


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
0.006
0.004
0.002
0.000
−0.002
0.002
0.004
0.006
SNP effect on || id:ukb−a−82
P effect on Pain type(s) experienced in last month: Stomach or abdominal pain || id:ukb−b−11413


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Headache || id:ukb−b−12181
0.003
0.000
−0.003
0.002
0.004
0.006
SNP effect on || id:ukb−a−82


MR Test
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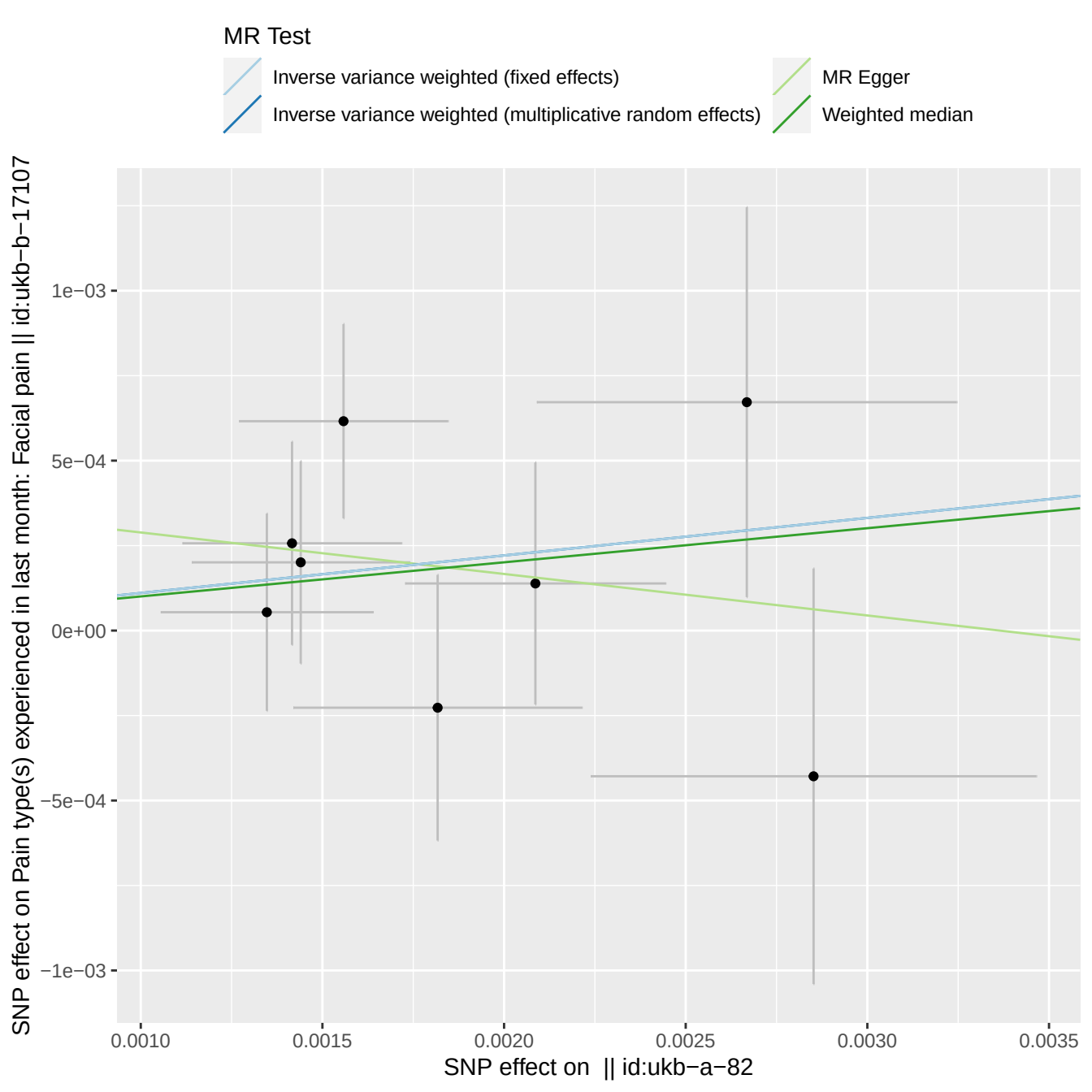
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Knee pain || id:ukb−b−16254
0.005
0.000
−0.005
0.002
0.004
0.006
SNP effect on || id:ukb−a−82


MR Test
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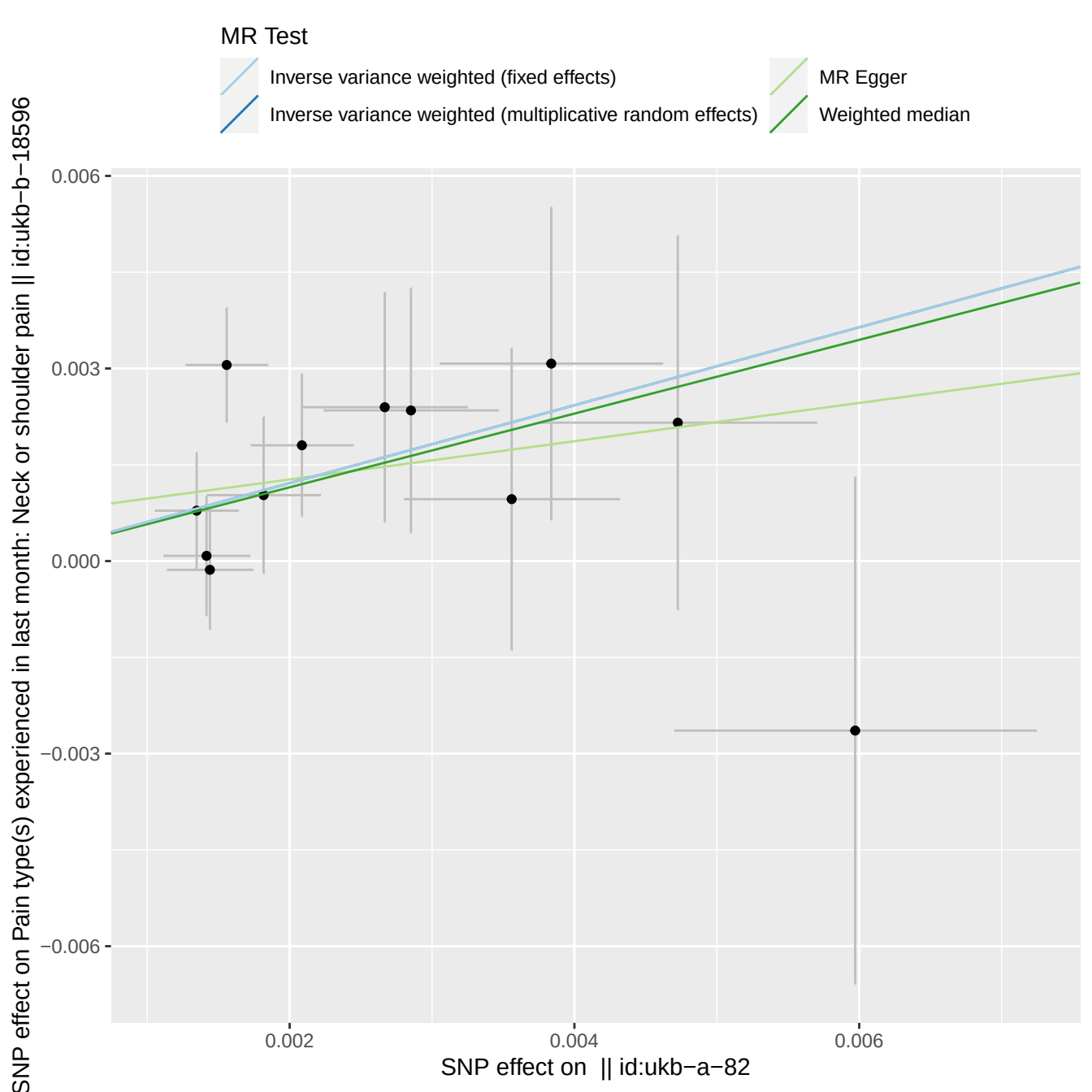
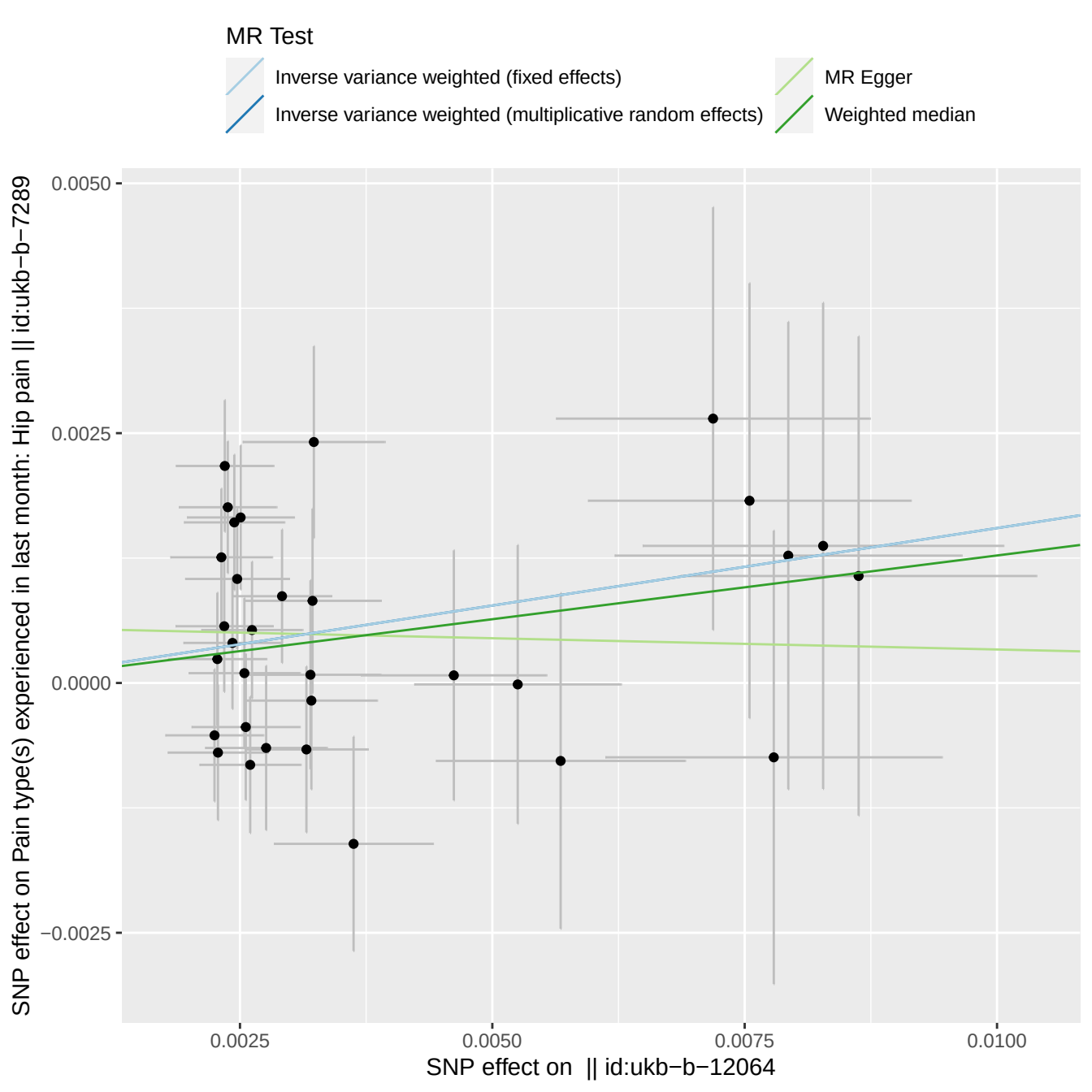
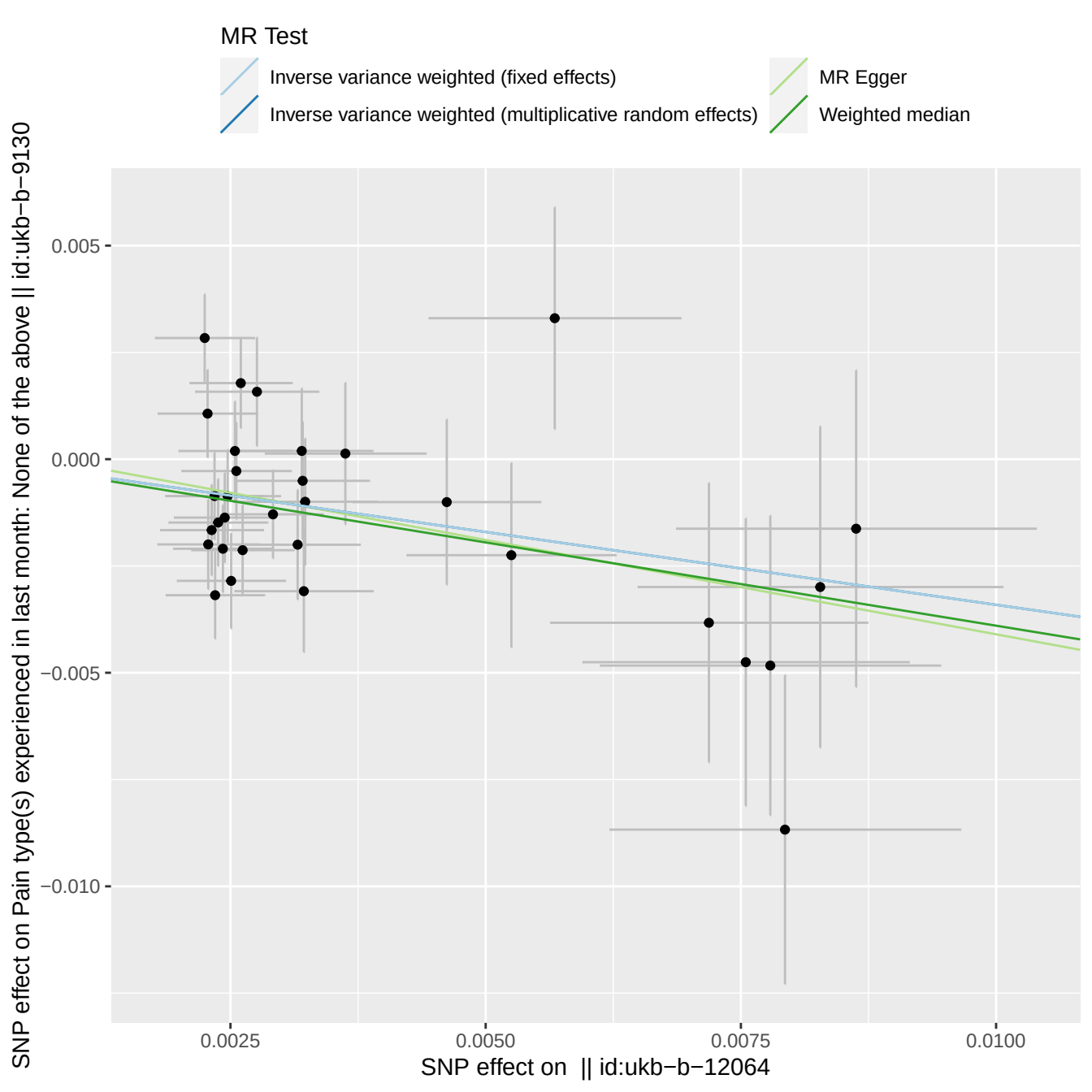
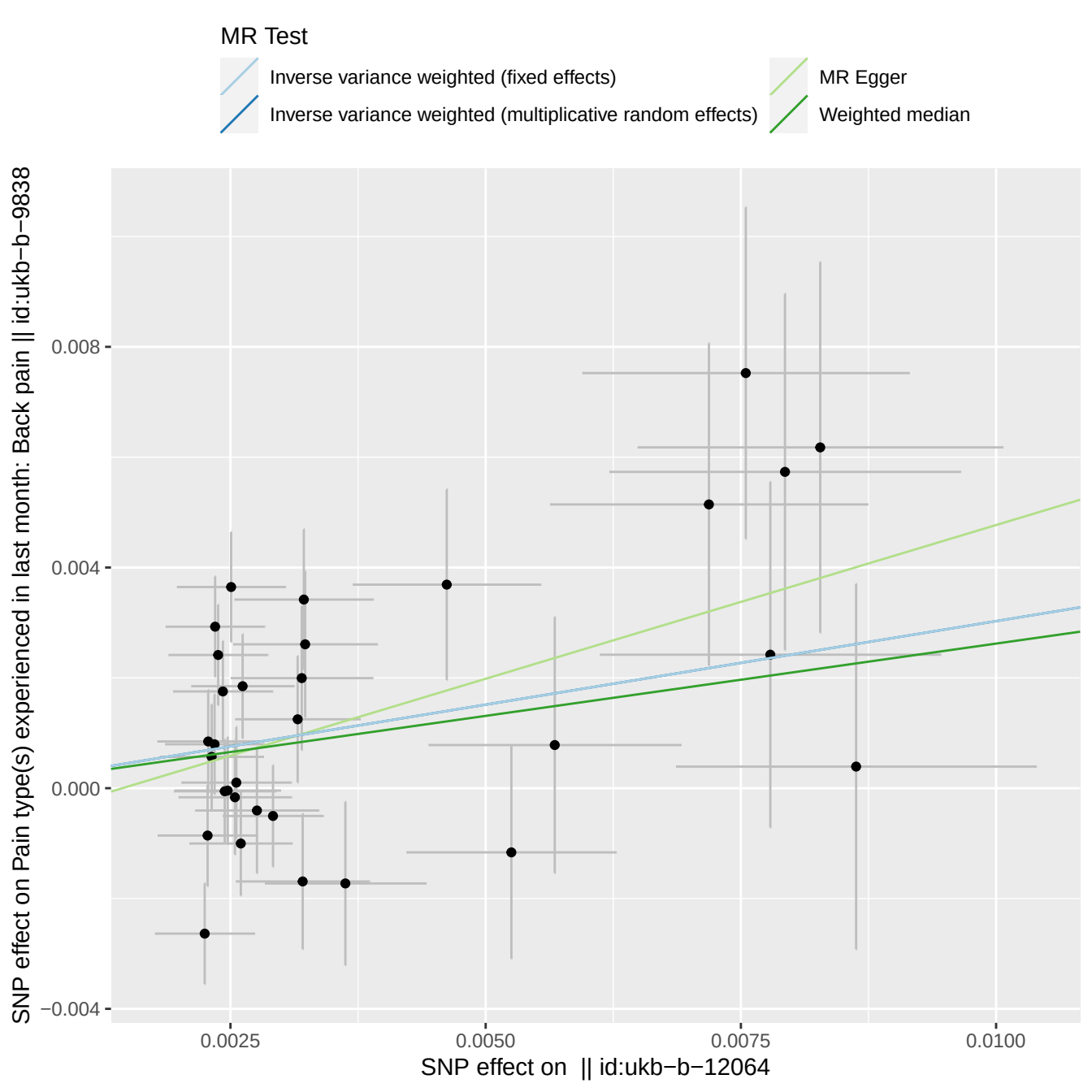
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Facial pain || id:ukb−b−17107
1e−03
5e−04
0e+00
−5e−04
−1e−03
0.0010
0.0015
0.0020
0.0025
0.0030
0.0035
SNP effect on || id:ukb−a−82


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
0.006
0.003
0.000
−0.003
−0.006
0.002
0.004
0.006
SNP effect on Pain type(s) experienced in last month: Neck or shoulder pain || id:ukb−b−18596
SNP effect on || id:ukb−a−82


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Hip pain || id:ukb−b−7289
0.0050
0.0025
0.0000
−0.0025
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: None of the above || id:ukb−b−9130
0.005
0.000
−0.005
−0.010
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064


MR Test
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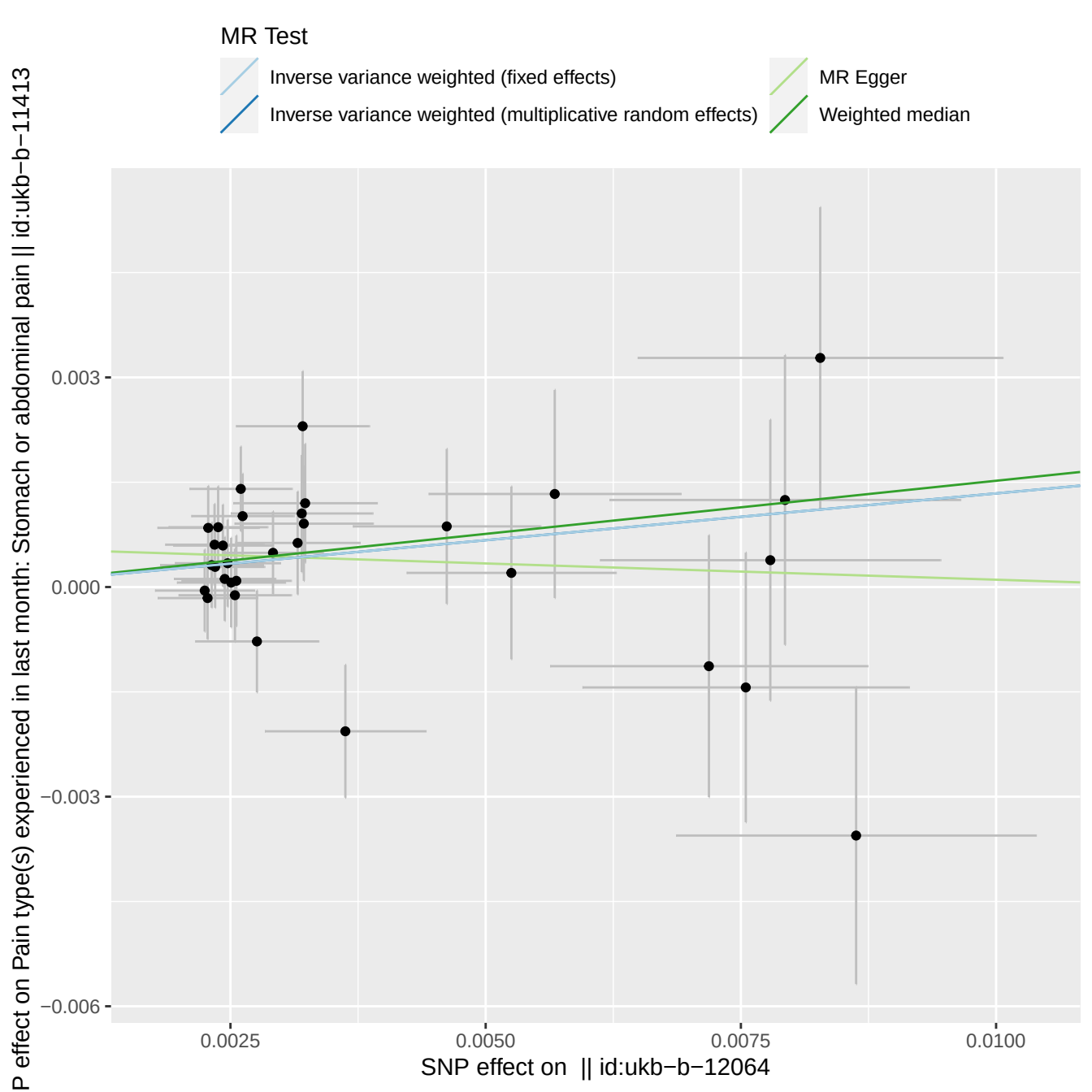
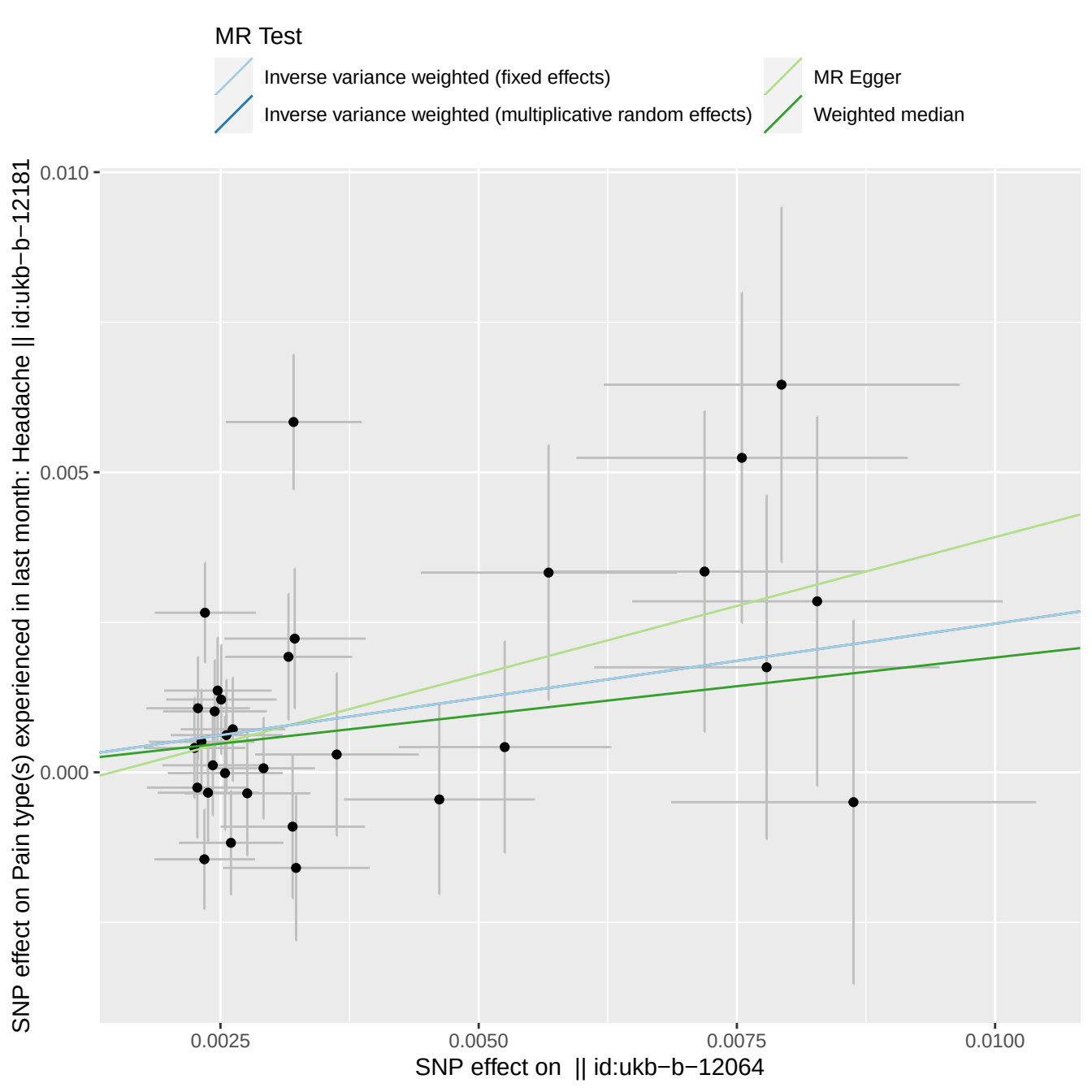
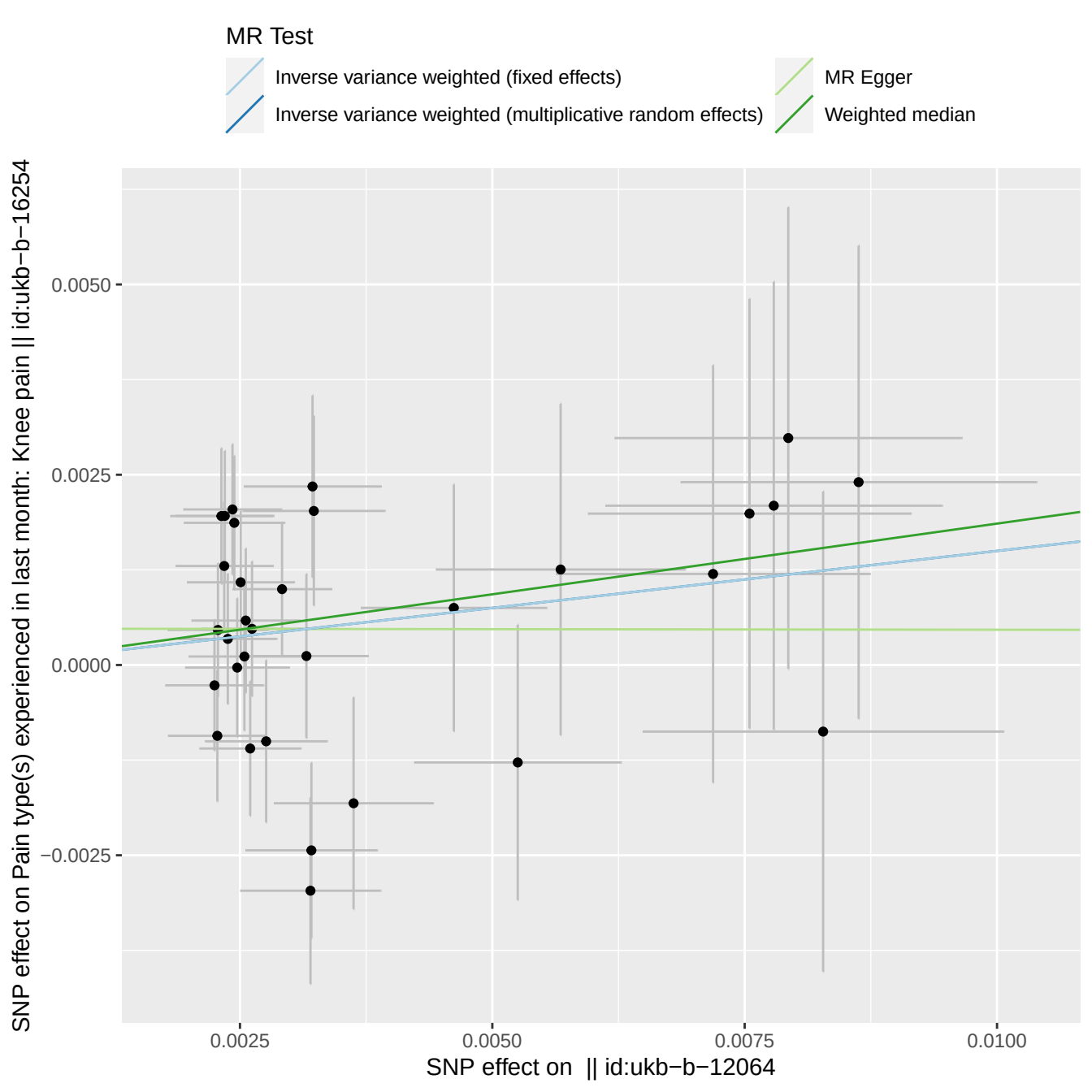
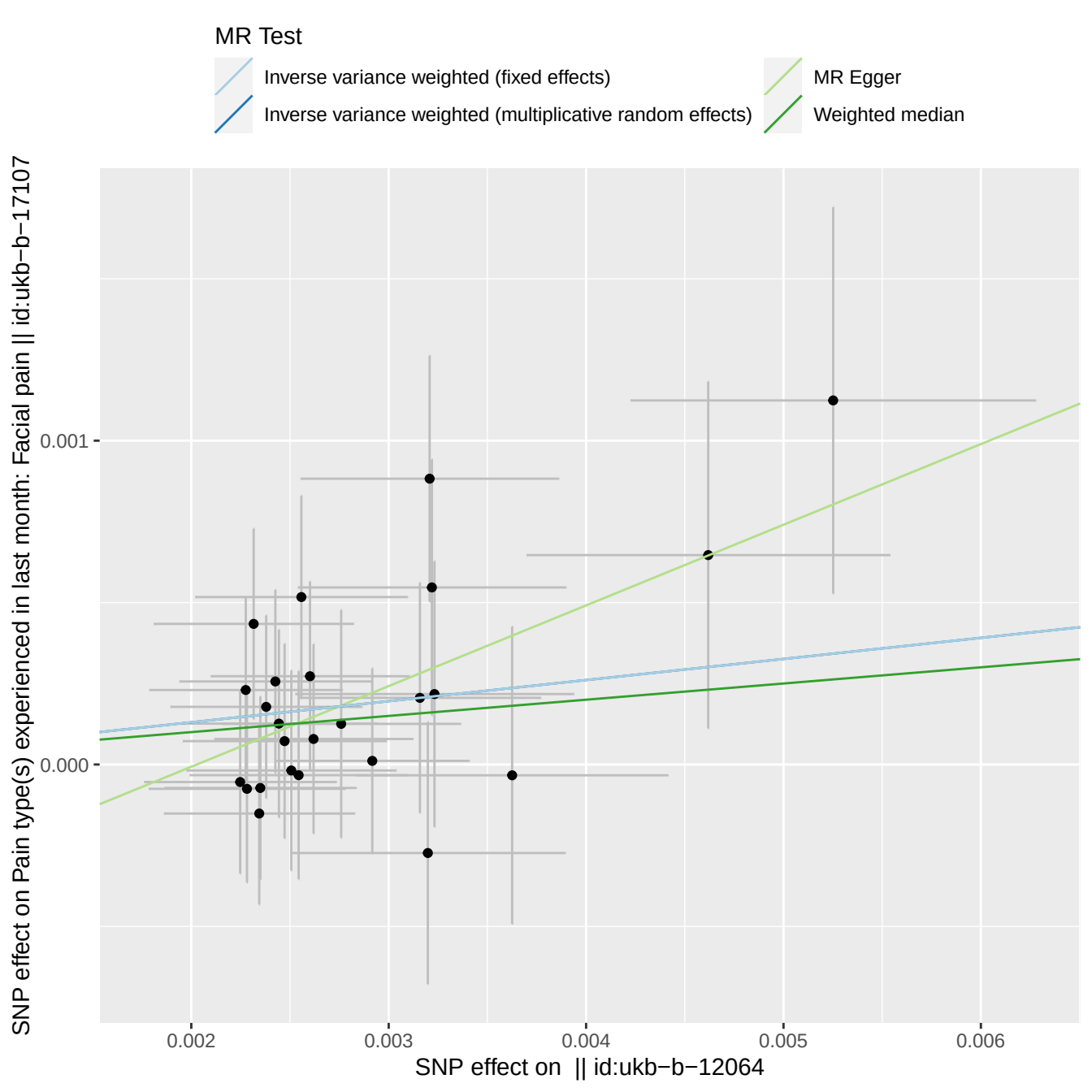
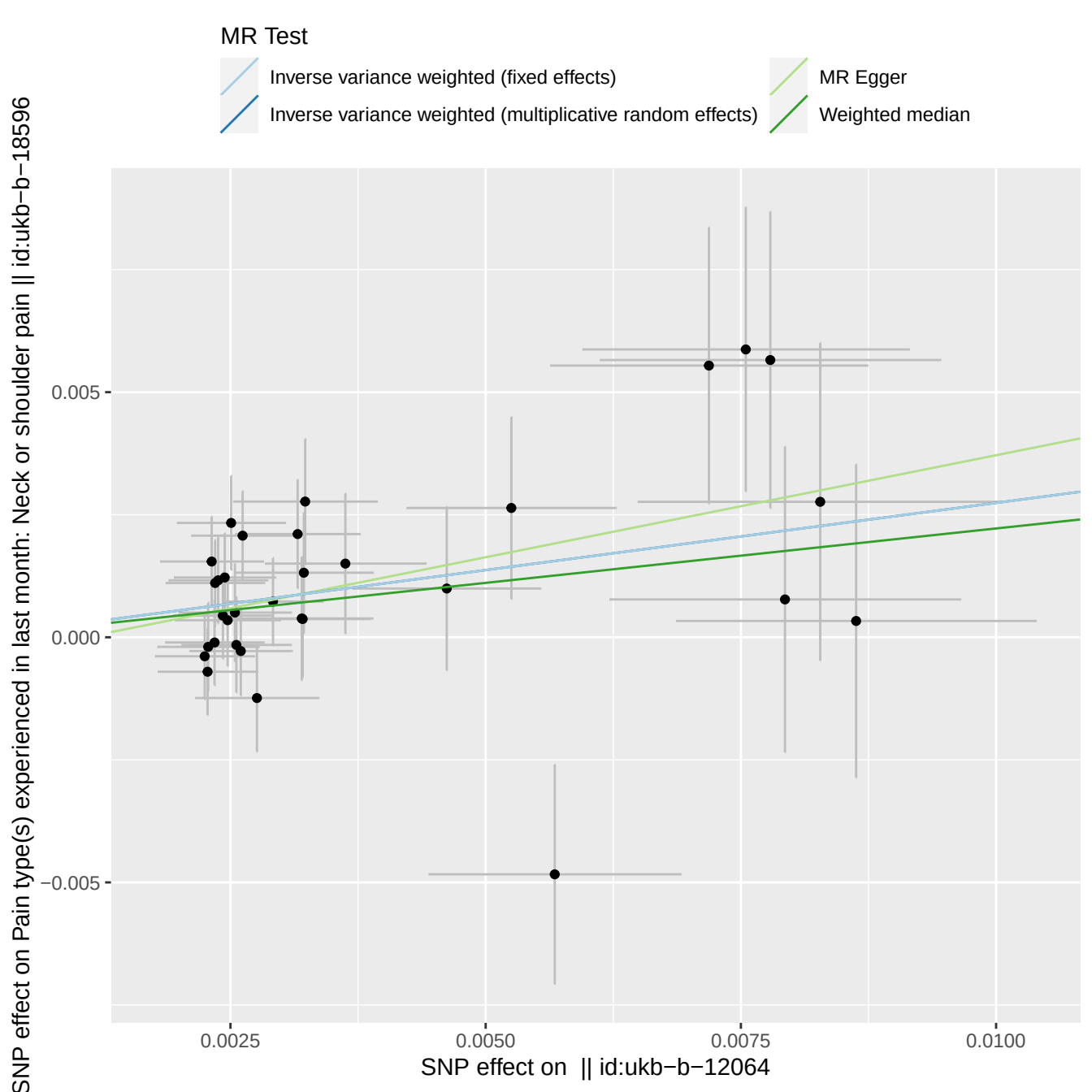
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Back pain || id:ukb−b−9838
0.008
0.004
0.000
−0.004
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
0.003
0.000
−0.003
−0.006
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064
P effect on Pain type(s) experienced in last month: Stomach or abdominal pain || id:ukb−b−11413


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Headache || id:ukb−b−12181
0.010
0.005
0.000
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Knee pain || id:ukb−b−16254
0.0050
0.0025
0.0000
−0.0025
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Facial pain || id:ukb−b−17107
0.001
0.000
0.002
0.003
0.004
0.005
0.006
SNP effect on || id:ukb−b−12064


MR Test
Inverse variance weighted (fixed effects)
Inverse variance weighted (multiplicative random effects)
MR Egger
Weighted median
SNP effect on Pain type(s) experienced in last month: Neck or shoulder pain || id:ukb−b−18596
0.005
0.000
−0.005
0.0025
0.0050
0.0075
0.0100
SNP effect on || id:ukb−b−12064