Non-linear MR: evaluating Vitamin D and CRP

Overview

- Re-investigation of the non-linear association between Vitamin D and CRP described by Zhou et al using the residual nlmr method.
- Univariable MR analyses on UKB by Townsend Deprivation Index Quartile (TDI-Q) and by season.

Method details

Instrumental variables

Vitamin D Zhou/GWAS score As described by Zhou et al, the vitamin D instrument was based on a GWAS of Vitamin D in UKB. Effects taken from an earlier independent study (SUNLIGHT consortium). 143 SNPs were identified for Vitamin in UKB. After QC 122 were remaining. 3 of these were not present in the SUNLIGHT consortium and of the remaining SNPs only 35 replicated in the SUNLIGHT consortium GWAS. Therefore, the main score was constructed with the 35 SNPs which replicated between studies.

Vitamin D focused score Used instruments as derived and described in this Burgess et al study (UKB + other studies). In this analysis, a focused score based on 21 variants mapping to 4 genetic loci relevant to VitD metabolism was considered; but only 18 were available in UKB, the missing 3 were rare variants (MAF<0.005).

CRP score Taken from Zhou et al: This score was constructed using 46 SNPs associated with CRP/weights from a 'non-UKB meta-analysis'. They also log-transformed the CRP measurements in UKB.

Covariates Covariates based on the Zhou study: sex + age.at.assessment + assessmenth.centre + month.of.assessment + fasting.time + PC1 + (. . .) PC10

Sample Individuals of white British ancestry in the UKB (to match the Zhou study)

Outcomes/Phenotypes All UKB - Used log(CRP), to match the Zhou study - Measured Vitamin D (nmol/L)

Mean phenotypic values in TFI-Quartile groups by season, where Winter = (October->March) and Summer = (April->September).

Summer

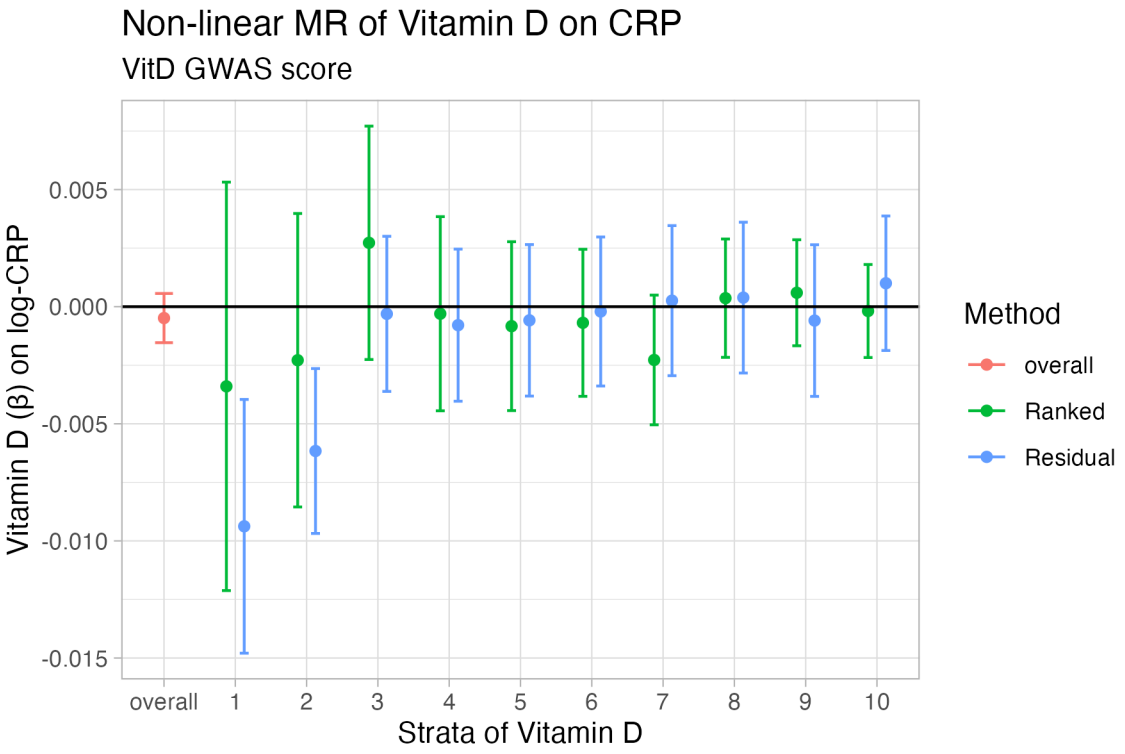
Townsend Deprivation Index	N	mean Vitamin D nmol/L	mean CRP mg/L
Q1	43639	56.23449406	2.2730053
Q2	44645	55.62643913	2.378077166
Q3	44818	53.92306312	2.480660404
Q4	43201	50.18716136	2.965550361

Winter

Townsend Deprivation Index	N	mean Vitamin D nmol/L	mean CRP mg/L
Q1	40837	47.24170804	2.405773514
Q2	39435	46.65011687	2.49998469
Q3	38757	45.30158562	2.625797655
Q4	40901	41.51274673	3.031211241

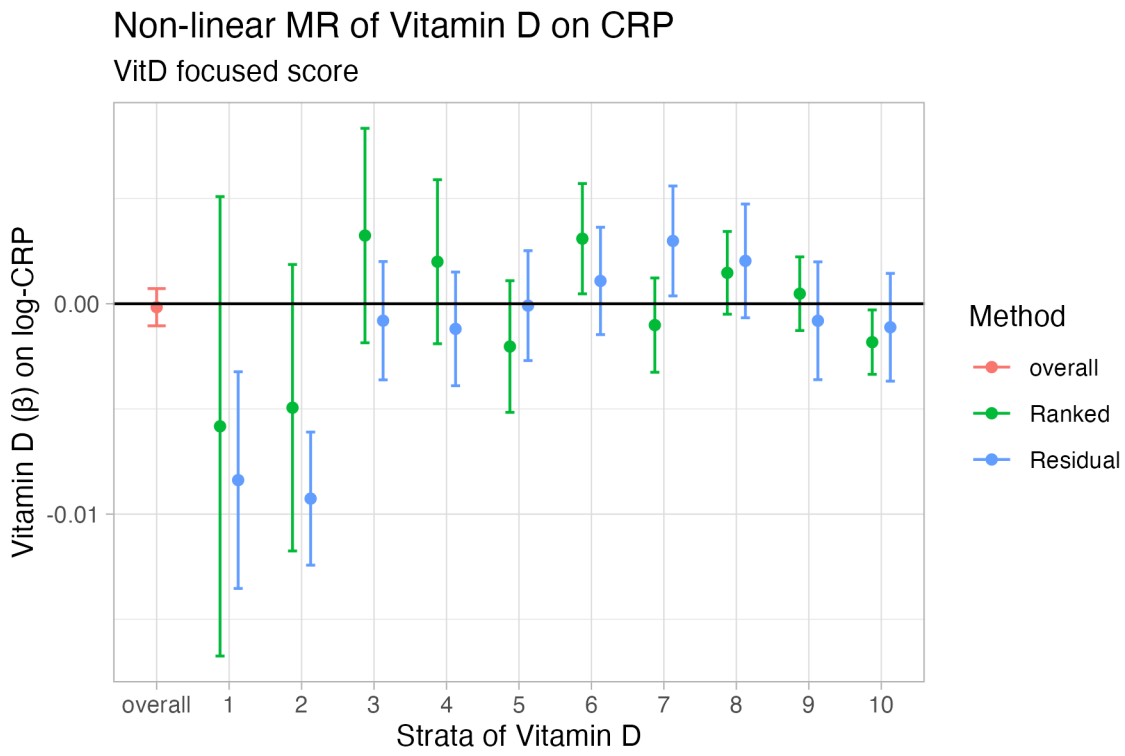
Results

Non-linear MR results



Evidence of a significant effects:

- Evidence of a non-linear effect of Vitamin D on CRP using the residual method.
- No evidence using the doubly-ranked method.



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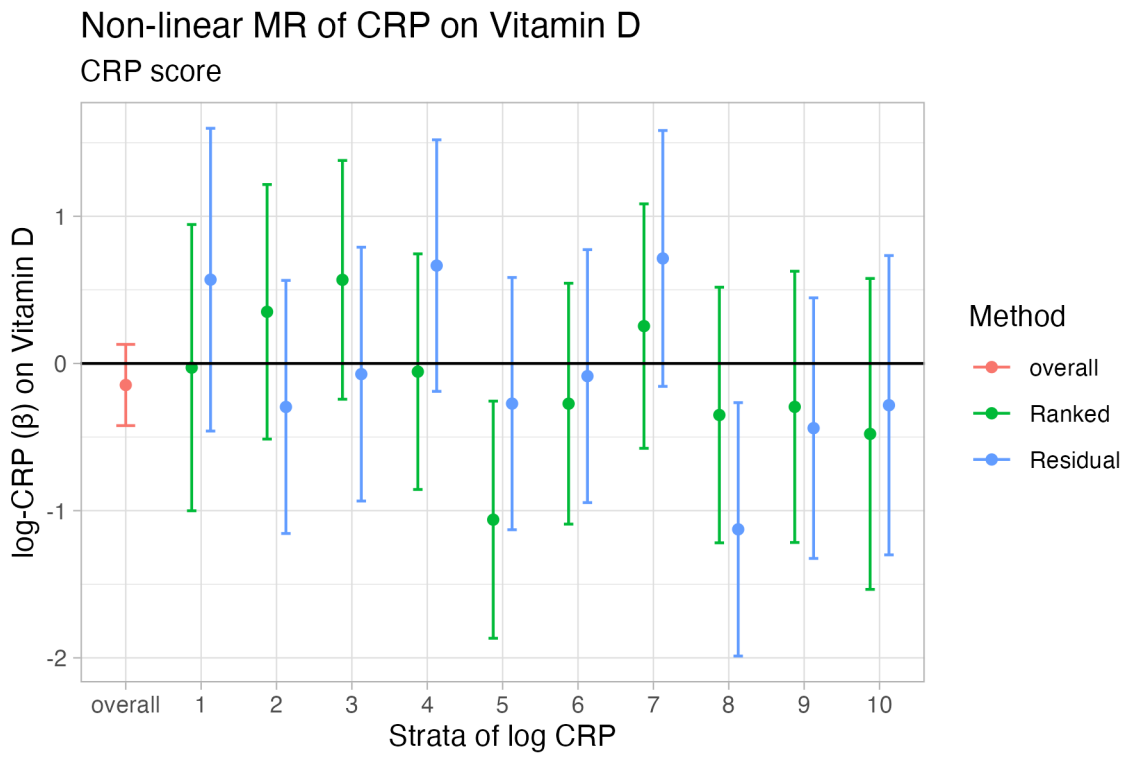
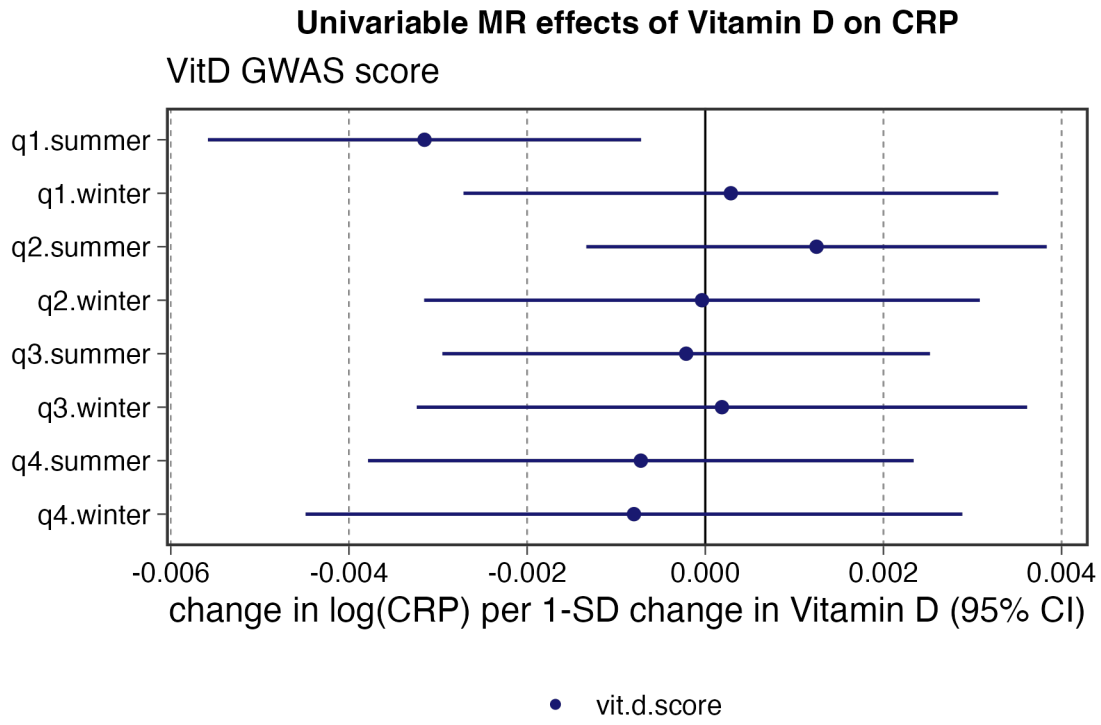


Evidence of a significant effects:

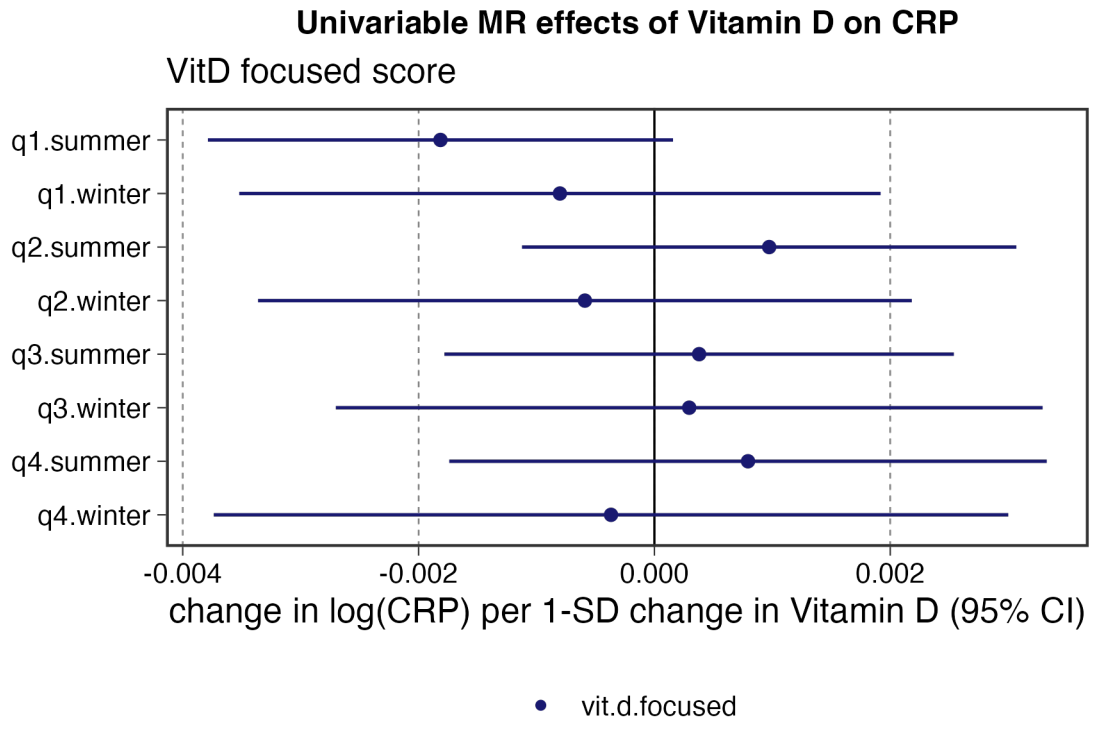
- Putative evidence for a non-linear effect of CRP on Vitamin D using the residual method in Quartile 8 of CRP only.
- Putative evidence for a non-linear effect of CRP on Vitamin D using the doubly-ranked method in Quartile 5 of CRP only.

Univaraible MR by TDI Quartile and by Season



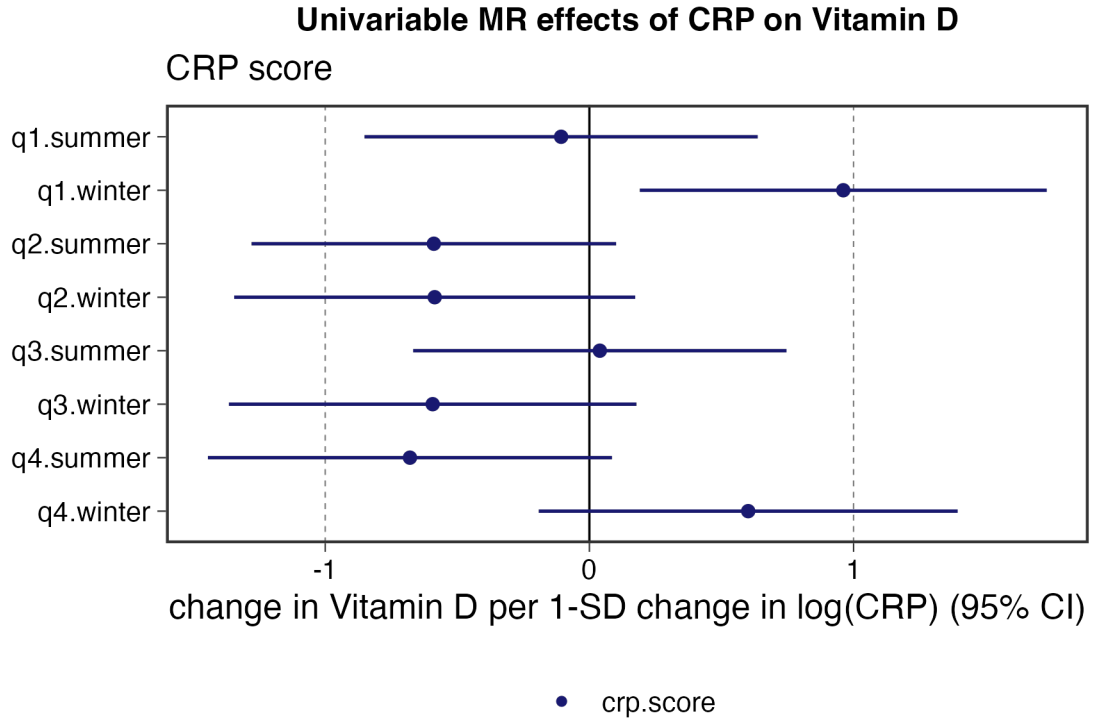
Evidence of a significant effects:

- Vitamin D on CRP in Q1 (least deprived) during Summer.



Evidence of a significant effects:

- No evidence of a significant effect of VIT D on CRP using the focused score.



Evidence of a significant effects:

- CRP on Vitamin D in Q1 (least deprived) during Winter

N (Sample) with Vitamin D deficiency (Vitamin D <25nmol/L)

Townsend Deprivation Quartile	Summer (N)	Winter (N)
Q1	2106	5033
Q2	2235	5021
Q3	2778	5788
Q4	4374	8682