Omega-3-T1D Mendelian Randomization

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2023-04-03

This R Markdown details a Mendelian randomization(MR) analysis for a study that aims to investigate the causal association between omega-3 fatty acids and type 1 diabetes (T1D) using a two-sample MR approach. MR utilizes genetic variants as instrumental variables to estimate causal effects between an exposure and an outcome. The hypothesis being tested in this study is that omega-3 fatty acids may have a protective effect against T1D risk.

The data used in this analysis includes publicly available GWAS summary data from the OpenGWAS repository. The TwoSampleMR package, which provides functions for performing two-sample Mendelian randomization analyses, is used.

INSTALL PACKAGES

```
# Install TwoSampleMR package

install.packages("plyr", repos = "http://cran.us.r-project.org")
```

```
##
## The downloaded binary packages are in
##  /var/folders/2y/z3g4d8r132j6m0_l9skqmw6c0000gp/T//RtmprfdCpX/downloaded_packages
```

```
remotes::install_github("MRCIEU/TwoSampleMR")
```

```
## Skipping install of 'TwoSampleMR' from a github remote, the SHA1 (b93ca5d9) has not changed since las
##   Use 'force = TRUE' to force installation
```

```
library(TwoSampleMR)
```

```
## TwoSampleMR version 0.5.6
## [>] New: Option to use non-European LD reference panels for clumping etc
## [>] Some studies temporarily quarantined to verify effect allele
## [>] See news(package='TwoSampleMR') and https://gwas.mrcieu.ac.uk for further details
```

EXTRACTING EXPOSURE INSTRUMENTS

The 'extract_instruments' function searches for GWAS-significant snps from the supplied dataset at a given p-value threshold and applies linkage disequilibrium (LD) based clumping to select only the independent SNPs that show significant associations with the exposure.

```
exposure_om <- extract_instruments("met-d-Omega_3")
```

```
## API: public: http://gwas-api.mrcieu.ac.uk/
```

```
exposure_om
```

```
##    samplesize.exposure chr.exposure pval.exposure pos.exposure beta.exposure
## 1                   NA            1   4.79999e-09      2330190     0.0229488
## 2                   NA            1   3.59998e-66     62931632     0.0713574
## 3                   NA            1   1.29987e-14    109818306     0.0382887
## 4                   NA            2   8.40040e-88     27730940    -0.0820592
## 5                   NA            2   2.00000e-08    136820960    -0.0251255
## 6                   NA            2   3.89996e-08     20363666    -0.0208868
## 7                   NA            2   2.19999e-08    241214158     0.0221268
## 8                   NA            2   5.60015e-15     21203877    -0.0361462
## 9                   NA            2   3.20000e-08    234679384     0.0349727
## 10                  NA            4   1.20005e-21     69491284     0.0463493
## 11                  NA            5   2.39999e-09    131677047     0.0240622
## 12                  NA            5   1.90020e-13    156397673     0.0288844
## 13                  NA            6   1.20005e-15     31311912    -0.0461429
## 14                  NA            6   2.80027e-17    161010118    -0.0629576
## 15                  NA            6   1.79999e-09     32379383    -0.0392017
## 16                  NA            6   1.39991e-15    160922870    -0.1159450
## 17                  NA            7   1.20005e-45     73042085    -0.0721329
## 18                  NA            7   9.20005e-10     44785800    -0.0349475
## 19                  NA            7   1.00000e-11     25990597    -0.0288196
## 20                  NA            8   3.50026e-98    126506694    -0.0873719
## 21                  NA            8   3.19963e-16      9183358     0.0566995
## 22                  NA            8   1.79999e-10     19844415    -0.0396447
## 23                  NA            9   5.19996e-09    107665978    -0.0373414
## 24                  NA           10   4.60045e-12     96728169     0.0341853
## 25                  NA           10   5.49997e-10     65191645     0.0233527
## 26                  NA           10   8.50002e-10      5247302     0.0350603
## 27                  NA           11   1.10002e-34     75450576    -0.0669996
## 28                  NA           11   1.10002e-22     61823630    -0.0506080
## 29                  NA           11   1.99986e-14     61248776    -0.0353357
## 30                  NA           11   4.20001e-08    116916060     0.1071340
## 31                  NA           11   9.39940e-14     61453822    -0.1541380
## 32                  NA           11  1.00000e-200     61588305    -0.3370940
## 33                  NA           11   8.90020e-87    116648917    -0.1166370
## 34                  NA           11   3.40017e-12     61701898    -0.1029590
## 35                  NA           12   1.20000e-10    121423376    -0.0253039
## 36                  NA           15  3.89942e-161     58678720    -0.1143830
## 37                  NA           15   2.29985e-21     44027885     0.1179870
## 38                  NA           15   4.39997e-10     58569330     0.0356728
## 39                  NA           15   9.09913e-80     58725839     0.0840069
## 40                  NA           16   2.99999e-08     15501099     0.0251849
## 41                  NA           16   5.60015e-75     15127534    -0.0810999
## 42                  NA           17   3.90032e-14     44186063    -0.0355285
## 43                  NA           18   5.19996e-24     47158234     0.0528854
## 44                  NA           18   7.19946e-22     47109955     0.1617490
## 45                  NA           19   3.50026e-11     11347657    -0.0726631
## 46                  NA           19   1.10002e-27     19458388    -0.2095710
```

```
## 47                  NA           19  1.39959e-113     19379549    -0.1716660
## 48                  NA           19   9.09913e-30     45430280     0.0476852
## 49                  NA           19   8.60003e-11     45448036     0.0270834
## 50                  NA           19   3.59998e-09     45424514     0.0284296
## 51                  NA           20   5.10000e-10     39167592    -0.0257607
## 52                  NA           21   2.19999e-10     40555561    -0.0370966
##    se.exposure   id.exposure         SNP effect_allele.exposure
## 1   0.00407772 met-d-Omega_3   rs6693447                      G
## 2   0.00425038 met-d-Omega_3   rs1167998                      A
## 3   0.00488385 met-d-Omega_3    rs629301                      T
## 4   0.00415340 met-d-Omega_3   rs1260326                      C
## 5   0.00448600 met-d-Omega_3  rs11681659                      T
## 6   0.00408348 met-d-Omega_3  rs35135293                      T
## 7   0.00408591 met-d-Omega_3  rs13424225                      T
## 8   0.00486548 met-d-Omega_3  rs10184054                      G
## 9   0.00647476 met-d-Omega_3  rs11563251                      T
## 10  0.00491057 met-d-Omega_3   rs4860987                      T
## 11  0.00406580 met-d-Omega_3  rs11242109                      T
## 12  0.00421159 met-d-Omega_3   rs6882345                      A
## 13  0.00550837 met-d-Omega_3   rs2394976                      T
## 14  0.00753435 met-d-Omega_3  rs10455872                      G
## 15  0.00603734 met-d-Omega_3   rs3129962                      A
## 16  0.01507310 met-d-Omega_3 rs117733303                      G
## 17  0.00506371 met-d-Omega_3  rs62466318                      T
## 18  0.00621600 met-d-Omega_3  rs73109460                      A
## 19  0.00446039 met-d-Omega_3   rs4000713                      A
## 20  0.00422001 met-d-Omega_3 rs112875651                      A
## 21  0.00707191 met-d-Omega_3   rs9987289                      G
## 22  0.00628878 met-d-Omega_3   rs7819706                      G
## 23  0.00619432 met-d-Omega_3   rs1800978                      G
## 24  0.00508075 met-d-Omega_3  rs55891451                      C
## 25  0.00406452 met-d-Omega_3   rs7924036                      T
## 26  0.00563873 met-d-Omega_3   rs6601924                      C
## 27  0.00554146 met-d-Omega_3    rs673335                      C
## 28  0.00524839 met-d-Omega_3  rs12226389                      C
## 29  0.00456603 met-d-Omega_3   rs3018731                      G
## 30  0.02049000 met-d-Omega_3 rs144018203                      C
## 31  0.02040730 met-d-Omega_3 rs143355652                      T
## 32  0.00424185 met-d-Omega_3    rs174564                      G
## 33  0.00596503 met-d-Omega_3    rs964184                      C
## 34  0.01482120 met-d-Omega_3  rs11230829                      G
## 35  0.00419603 met-d-Omega_3   rs7970695                      A
## 36  0.00428189 met-d-Omega_3    rs261290                      C
## 37  0.01280750 met-d-Omega_3 rs139974673                      C
## 38  0.00602277 met-d-Omega_3  rs34663616                      A
## 39  0.00448287 met-d-Omega_3    rs633695                      G
## 40  0.00469670 met-d-Omega_3   rs1672811                      C
## 41  0.00446068 met-d-Omega_3  rs72789541                      A
## 42  0.00487720 met-d-Omega_3  rs16940904                      T
## 43  0.00527814 met-d-Omega_3   rs9304381                      T
## 44  0.01775740 met-d-Omega_3  rs77960347                      G
## 45  0.01103540 met-d-Omega_3    rs737338                      T
## 46  0.01957770 met-d-Omega_3 rs182611493                      G
## 47  0.00775231 met-d-Omega_3  rs58542926                      T
```

```
## 48  0.00437178 met-d-Omega_3      rs5112                    G
## 49  0.00410188 met-d-Omega_3   rs1132899                    C
## 50  0.00536368 met-d-Omega_3    rs157592                    C
## 51  0.00437946 met-d-Omega_3   rs6129624                    A
## 52  0.00584700 met-d-Omega_3 rs117143374                    C
##    other_allele.exposure eaf.exposure                              exposure
## 1                      T     0.461686 Omega-3 fatty acids || id:met-d-Omega_3
## 2                      C     0.644674 Omega-3 fatty acids || id:met-d-Omega_3
## 3                      G     0.778033 Omega-3 fatty acids || id:met-d-Omega_3
## 4                      T     0.604010 Omega-3 fatty acids || id:met-d-Omega_3
## 5                      C     0.716465 Omega-3 fatty acids || id:met-d-Omega_3
## 6                      C     0.516750 Omega-3 fatty acids || id:met-d-Omega_3
## 7                      G     0.449809 Omega-3 fatty acids || id:met-d-Omega_3
## 8                      C     0.224107 Omega-3 fatty acids || id:met-d-Omega_3
## 9                      C     0.110601 Omega-3 fatty acids || id:met-d-Omega_3
## 10                     A     0.258609 Omega-3 fatty acids || id:met-d-Omega_3
## 11                     G     0.479016 Omega-3 fatty acids || id:met-d-Omega_3
## 12                     G     0.632863 Omega-3 fatty acids || id:met-d-Omega_3
## 13                     G     0.161648 Omega-3 fatty acids || id:met-d-Omega_3
## 14                     A     0.078988 Omega-3 fatty acids || id:met-d-Omega_3
## 15                     G     0.129765 Omega-3 fatty acids || id:met-d-Omega_3
## 16                     A     0.018513 Omega-3 fatty acids || id:met-d-Omega_3
## 17                     C     0.204178 Omega-3 fatty acids || id:met-d-Omega_3
## 18                     G     0.123622 Omega-3 fatty acids || id:met-d-Omega_3
## 19                     G     0.295408 Omega-3 fatty acids || id:met-d-Omega_3
## 20                     G     0.392346 Omega-3 fatty acids || id:met-d-Omega_3
## 21                     A     0.909151 Omega-3 fatty acids || id:met-d-Omega_3
## 22                     A     0.118291 Omega-3 fatty acids || id:met-d-Omega_3
## 23                     C     0.123991 Omega-3 fatty acids || id:met-d-Omega_3
## 24                     A     0.201728 Omega-3 fatty acids || id:met-d-Omega_3
## 25                     G     0.504205 Omega-3 fatty acids || id:met-d-Omega_3
## 26                     T     0.845765 Omega-3 fatty acids || id:met-d-Omega_3
## 27                     T     0.159762 Omega-3 fatty acids || id:met-d-Omega_3
## 28                     T     0.185820 Omega-3 fatty acids || id:met-d-Omega_3
## 29                     A     0.717549 Omega-3 fatty acids || id:met-d-Omega_3
## 30                     G     0.010653 Omega-3 fatty acids || id:met-d-Omega_3
## 31                     C     0.010467 Omega-3 fatty acids || id:met-d-Omega_3
## 32                     A     0.347013 Omega-3 fatty acids || id:met-d-Omega_3
## 33                     G     0.867229 Omega-3 fatty acids || id:met-d-Omega_3
## 34                     A     0.027786 Omega-3 fatty acids || id:met-d-Omega_3
## 35                     G     0.620549 Omega-3 fatty acids || id:met-d-Omega_3
## 36                     T     0.654653 Omega-3 fatty acids || id:met-d-Omega_3
## 37                     T     0.025918 Omega-3 fatty acids || id:met-d-Omega_3
## 38                     C     0.137654 Omega-3 fatty acids || id:met-d-Omega_3
## 39                     A     0.292348 Omega-3 fatty acids || id:met-d-Omega_3
## 40                     T     0.748488 Omega-3 fatty acids || id:met-d-Omega_3
## 41                     T     0.295970 Omega-3 fatty acids || id:met-d-Omega_3
## 42                     C     0.226571 Omega-3 fatty acids || id:met-d-Omega_3
## 43                     C     0.818434 Omega-3 fatty acids || id:met-d-Omega_3
## 44                     A     0.013239 Omega-3 fatty acids || id:met-d-Omega_3
## 45                     C     0.035186 Omega-3 fatty acids || id:met-d-Omega_3
## 46                     A     0.012519 Omega-3 fatty acids || id:met-d-Omega_3
## 47                     C     0.074383 Omega-3 fatty acids || id:met-d-Omega_3
## 48                     C     0.533736 Omega-3 fatty acids || id:met-d-Omega_3
```

```
## 49                    T     0.509603 Omega-3 fatty acids || id:met-d-Omega_3
## 50                    A     0.185267 Omega-3 fatty acids || id:met-d-Omega_3
## 51                    G     0.335237 Omega-3 fatty acids || id:met-d-Omega_3
## 52                    T     0.142254 Omega-3 fatty acids || id:met-d-Omega_3
##    mr_keep.exposure pval_origin.exposure data_source.exposure
## 1              TRUE             reported                 igd
## 2              TRUE             reported                 igd
## 3              TRUE             reported                 igd
## 4              TRUE             reported                 igd
## 5              TRUE             reported                 igd
## 6              TRUE             reported                 igd
## 7              TRUE             reported                 igd
## 8              TRUE             reported                 igd
## 9              TRUE             reported                 igd
## 10             TRUE             reported                 igd
## 11             TRUE             reported                 igd
## 12             TRUE             reported                 igd
## 13             TRUE             reported                 igd
## 14             TRUE             reported                 igd
## 15             TRUE             reported                 igd
## 16             TRUE             reported                 igd
## 17             TRUE             reported                 igd
## 18             TRUE             reported                 igd
## 19             TRUE             reported                 igd
## 20             TRUE             reported                 igd
## 21             TRUE             reported                 igd
## 22             TRUE             reported                 igd
## 23             TRUE             reported                 igd
## 24             TRUE             reported                 igd
## 25             TRUE             reported                 igd
## 26             TRUE             reported                 igd
## 27             TRUE             reported                 igd
## 28             TRUE             reported                 igd
## 29             TRUE             reported                 igd
## 30             TRUE             reported                 igd
## 31             TRUE             reported                 igd
## 32             TRUE             reported                 igd
## 33             TRUE             reported                 igd
## 34             TRUE             reported                 igd
## 35             TRUE             reported                 igd
## 36             TRUE             reported                 igd
## 37             TRUE             reported                 igd
## 38             TRUE             reported                 igd
## 39             TRUE             reported                 igd
## 40             TRUE             reported                 igd
## 41             TRUE             reported                 igd
## 42             TRUE             reported                 igd
## 43             TRUE             reported                 igd
## 44             TRUE             reported                 igd
## 45             TRUE             reported                 igd
## 46             TRUE             reported                 igd
## 47             TRUE             reported                 igd
## 48             TRUE             reported                 igd
## 49             TRUE             reported                 igd
```

```
## 50             TRUE             reported                  igd
## 51             TRUE             reported                  igd
## 52             TRUE             reported                  igd
```

EXTRACTING SNP EFFECTS FROM OUTCOME GWAS

The 'extract_outcome_data' function queries the outcome dataset against the exposure data to extract snp effects from the outcome GWAS.

```
outcome_om <- extract_outcome_data(snps = exposure_om$SNP, outcomes = "ebi-a-GCST010681")
```

```
## Extracting data for 52 SNP(s) from 1 GWAS(s)

## Finding proxies for 5 SNPs in outcome ebi-a-GCST010681

## Extracting data for 5 SNP(s) from 1 GWAS(s)
```

```
outcome_om
```

```
##            SNP chr       pos beta.outcome se.outcome samplesize.outcome
## 1   rs34663616  15  58569330       0.0193     0.0353               24840
## 2    rs6129624  20  39167592       0.0295     0.0250               24840
## 3    rs2394976   6  31311912       0.5843     0.0330               24840
## 4    rs6882345   5 156397673      -0.0004     0.0242               24840
## 5    rs4860987   4  69491284      -0.0085     0.0328               24840
## 6    rs4000713   7  25990597      -0.0200     0.0263               24840
## 7  rs144018203  11 116916060       0.0105     0.1258               24840
## 8  rs182611493  19  19458388       0.0457     0.1158               24840
## 9    rs1800978   9 107665978       0.0889     0.0348               24840
## 10   rs6601924  10   5247302      -0.0029     0.0324               24840
## 11   rs1167998   1  62931632       0.0359     0.0246               24840
## 12   rs1260326   2  27730940       0.0331     0.0239               24840
## 13  rs35135293   2  20363666      -0.0254     0.0236               24840
## 14  rs11563251   2 234679384      -0.0048     0.0381               24840
## 15   rs3129962   6  32379383      -0.3573     0.0367               24840
## 16   rs3129962   6  32379383       0.7618     0.0353               24840
## 17  rs10455872   6 161010118      -0.0114     0.0440               24840
## 18 rs139974673  15  44027885      -0.0223     0.0742               24840
## 19    rs737338  19  11347657      -0.0097     0.0620               24840
## 20  rs72789541  16  15127534       0.0089     0.0263               24840
## 21  rs10184054   2  21203877      -0.0042     0.0280               24840
## 22   rs9304381  18  47158234      -0.0359     0.0306               24840
## 23  rs13424225   2 241214158      -0.0224     0.0244               24840
## 24  rs62466318   7  73042085      -0.0244     0.0302               24840
## 25   rs9987289   8   9183358       0.0321     0.0412               24840
## 26    rs964184  11 116648917       0.0272     0.0342               24840
## 27    rs261290  15  58678720       0.0146     0.0248               24840
## 28 rs117733303   6 160922870      -0.0544     0.0870               24840
## 29 rs143355652  11  61453822       0.1419     0.1073               24840
## 30  rs12226389  11  61823630      -0.0231     0.0308               24840
## 31      rs5112  19  45430280      -0.0174     0.0291               24840
```

```
## 32    rs633695  15  58725839      -0.0205     0.0272              24840
## 33  rs77960347  18  47109955       0.0274     0.1030              24840
## 34   rs1132899  19  45448036      -0.0664     0.0254              24840
## 35 rs117143374  21  40555561      -0.0416     0.0346              24840
## 36   rs3018731  11  61248776      -0.0338     0.0281              24840
## 37    rs174564  11  61588305      -0.0487     0.0248              24840
## 38   rs6693447   1   2330190       0.0495     0.0255              24840
## 39  rs11242109   5 131677047       0.0137     0.0235              24840
## 40 rs112875651   8 126506694       0.0385     0.0255              24840
## 41  rs58542926  19  19379549      -0.0157     0.0436              24840
## 42  rs16940904  17  44186063      -0.0952     0.0281              24840
## 43    rs629301   1 109818306       0.0582     0.0284              24840
## 44   rs7819706   8  19844415       0.0159     0.0354              24840
## 45    rs673335  11  75450576       0.0229     0.0316              24840
## 46   rs7924036  10  65191645       0.0052     0.0234              24840
## 47   rs1672811  16  15501099      -0.0214     0.0271              24840
## 48   rs7970695  12 121423376      -0.0010     0.0240              24840
## 49  rs73109460   7  44792326       0.0351     0.0373              24840
## 50  rs55891451  10  96731788      -0.0525     0.0296              24840
##    pval.outcome eaf.outcome effect_allele.outcome other_allele.outcome
## 1   5.84300e-01      0.1452                     A                    C
## 2   2.38000e-01      0.3375                     A                    G
## 3   2.89868e-70      0.1720                     T                    G
## 4   9.87800e-01      0.6326                     A                    G
## 5   7.94500e-01      0.2575                     T                    A
## 6   4.48200e-01      0.2921                     A                    G
## 7   9.33200e-01      0.0115                     C                    G
## 8   6.93201e-01      0.0146                     G                    A
## 9   1.05801e-02      0.1270                     G                    C
## 10  9.28600e-01      0.8470                     C                    T
## 11  1.44800e-01      0.6504                     A                    C
## 12  1.66300e-01      0.5993                     C                    T
## 13  2.82000e-01      0.5163                     T                    C
## 14  8.98900e-01      0.1179                     T                    C
## 15  1.85183e-22      0.2079                     C                    G
## 16 3.65595e-103      0.1358                     A                    G
## 17  7.95000e-01      0.0878                     G                    A
## 18  7.64100e-01      0.0267                     C                    T
## 19  8.75200e-01      0.0418                     T                    C
## 20  7.35401e-01      0.2922                     A                    T
## 21  8.80900e-01      0.2247                     G                    C
## 22  2.42000e-01      0.8251                     T                    C
## 23  3.59100e-01      0.4475                     T                    G
## 24  4.19200e-01      0.2029                     T                    C
## 25  4.37100e-01      0.9100                     G                    A
## 26  4.26500e-01      0.8628                     C                    G
## 27  5.55300e-01      0.6507                     C                    T
## 28  5.31300e-01      0.0197                     G                    A
## 29  1.86000e-01      0.0127                     T                    C
## 30  4.53600e-01      0.1875                     C                    T
## 31  5.50201e-01      0.5420                     G                    C
## 32  4.51000e-01      0.2900                     G                    A
## 33  7.90300e-01      0.0154                     G                    A
## 34  9.01094e-03      0.5099                     C                    T
```

```
## 35  2.29600e-01      0.1409                    C                   T
## 36  2.28800e-01      0.6983                    G                   A
## 37  4.92901e-02      0.3445                    G                   A
## 38  5.18704e-02      0.4572                    G                   T
## 39  5.60101e-01      0.4788                    T                   G
## 40  1.30700e-01      0.4062                    A                   G
## 41  7.18399e-01      0.0829                    T                   C
## 42  6.88098e-04      0.2355                    T                   C
## 43  4.01301e-02      0.7769                    T                   G
## 44  6.53800e-01      0.1218                    G                   A
## 45  4.68600e-01      0.1592                    C                   T
## 46  8.23000e-01      0.5034                    T                   G
## 47  4.30700e-01      0.7498                    C                   T
## 48  9.67700e-01      0.6208                    A                   G
## 49  3.46600e-01      0.1249                    A                   G
## 50  7.61798e-02      0.2043                    C                   A
##                                      outcome       id.outcome originalname.outcome
## 1  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 2  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 3  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 4  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 5  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 6  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 7  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 8  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 9  Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 10 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 11 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 12 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 13 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 14 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 15 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 16 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 17 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 18 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 19 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 20 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 21 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 22 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 23 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 24 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 25 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 26 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 27 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 28 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 29 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 30 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 31 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 32 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 33 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 34 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 35 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 36 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 37 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
```

```
## 38 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 39 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 40 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 41 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 42 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 43 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 44 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 45 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 46 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 47 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 48 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 49 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
## 50 Type 1 diabetes || id:ebi-a-GCST010681 ebi-a-GCST010681      Type 1 diabetes
##         outcome.deprecated mr_keep.outcome data_source.outcome proxy.outcome
## 1  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 2  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 3  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 4  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 5  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 6  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 7  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 8  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 9  Type 1 diabetes ||  ||             TRUE                 igd            NA
## 10 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 11 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 12 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 13 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 14 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 15 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 16 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 17 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 18 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 19 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 20 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 21 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 22 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 23 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 24 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 25 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 26 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 27 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 28 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 29 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 30 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 31 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 32 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 33 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 34 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 35 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 36 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 37 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 38 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 39 Type 1 diabetes ||  ||             TRUE                 igd            NA
## 40 Type 1 diabetes ||  ||             TRUE                 igd            NA
```

```
## 41 Type 1 diabetes ||  ||            TRUE                igd            NA
## 42 Type 1 diabetes ||  ||            TRUE                igd            NA
## 43 Type 1 diabetes ||  ||            TRUE                igd            NA
## 44 Type 1 diabetes ||  ||            TRUE                igd            NA
## 45 Type 1 diabetes ||  ||            TRUE                igd            NA
## 46 Type 1 diabetes ||  ||            TRUE                igd            NA
## 47 Type 1 diabetes ||  ||            TRUE                igd            NA
## 48 Type 1 diabetes ||  ||            TRUE                igd            NA
## 49 Type 1 diabetes ||  ||            TRUE                igd          TRUE
## 50 Type 1 diabetes ||  ||            TRUE                igd          TRUE
##    target_snp.outcome proxy_snp.outcome target_a1.outcome target_a2.outcome
## 1                <NA>              <NA>              <NA>              <NA>
## 2                <NA>              <NA>              <NA>              <NA>
## 3                <NA>              <NA>              <NA>              <NA>
## 4                <NA>              <NA>              <NA>              <NA>
## 5                <NA>              <NA>              <NA>              <NA>
## 6                <NA>              <NA>              <NA>              <NA>
## 7                <NA>              <NA>              <NA>              <NA>
## 8                <NA>              <NA>              <NA>              <NA>
## 9                <NA>              <NA>              <NA>              <NA>
## 10               <NA>              <NA>              <NA>              <NA>
## 11               <NA>              <NA>              <NA>              <NA>
## 12               <NA>              <NA>              <NA>              <NA>
## 13               <NA>              <NA>              <NA>              <NA>
## 14               <NA>              <NA>              <NA>              <NA>
## 15               <NA>              <NA>              <NA>              <NA>
## 16               <NA>              <NA>              <NA>              <NA>
## 17               <NA>              <NA>              <NA>              <NA>
## 18               <NA>              <NA>              <NA>              <NA>
## 19               <NA>              <NA>              <NA>              <NA>
## 20               <NA>              <NA>              <NA>              <NA>
## 21               <NA>              <NA>              <NA>              <NA>
## 22               <NA>              <NA>              <NA>              <NA>
## 23               <NA>              <NA>              <NA>              <NA>
## 24               <NA>              <NA>              <NA>              <NA>
## 25               <NA>              <NA>              <NA>              <NA>
## 26               <NA>              <NA>              <NA>              <NA>
## 27               <NA>              <NA>              <NA>              <NA>
## 28               <NA>              <NA>              <NA>              <NA>
## 29               <NA>              <NA>              <NA>              <NA>
## 30               <NA>              <NA>              <NA>              <NA>
## 31               <NA>              <NA>              <NA>              <NA>
## 32               <NA>              <NA>              <NA>              <NA>
## 33               <NA>              <NA>              <NA>              <NA>
## 34               <NA>              <NA>              <NA>              <NA>
## 35               <NA>              <NA>              <NA>              <NA>
## 36               <NA>              <NA>              <NA>              <NA>
## 37               <NA>              <NA>              <NA>              <NA>
## 38               <NA>              <NA>              <NA>              <NA>
## 39               <NA>              <NA>              <NA>              <NA>
## 40               <NA>              <NA>              <NA>              <NA>
## 41               <NA>              <NA>              <NA>              <NA>
## 42               <NA>              <NA>              <NA>              <NA>
## 43               <NA>              <NA>              <NA>              <NA>
```

```
## 44              <NA>              <NA>              <NA>              <NA>
## 45              <NA>              <NA>              <NA>              <NA>
## 46              <NA>              <NA>              <NA>              <NA>
## 47              <NA>              <NA>              <NA>              <NA>
## 48              <NA>              <NA>              <NA>              <NA>
## 49       rs73109460        rs56230523                 A                 G
## 50       rs55891451         rs9332172                 C                 A
##    proxy_a1.outcome proxy_a2.outcome
## 1              <NA>             <NA>
## 2              <NA>             <NA>
## 3              <NA>             <NA>
## 4              <NA>             <NA>
## 5              <NA>             <NA>
## 6              <NA>             <NA>
## 7              <NA>             <NA>
## 8              <NA>             <NA>
## 9              <NA>             <NA>
## 10             <NA>             <NA>
## 11             <NA>             <NA>
## 12             <NA>             <NA>
## 13             <NA>             <NA>
## 14             <NA>             <NA>
## 15             <NA>             <NA>
## 16             <NA>             <NA>
## 17             <NA>             <NA>
## 18             <NA>             <NA>
## 19             <NA>             <NA>
## 20             <NA>             <NA>
## 21             <NA>             <NA>
## 22             <NA>             <NA>
## 23             <NA>             <NA>
## 24             <NA>             <NA>
## 25             <NA>             <NA>
## 26             <NA>             <NA>
## 27             <NA>             <NA>
## 28             <NA>             <NA>
## 29             <NA>             <NA>
## 30             <NA>             <NA>
## 31             <NA>             <NA>
## 32             <NA>             <NA>
## 33             <NA>             <NA>
## 34             <NA>             <NA>
## 35             <NA>             <NA>
## 36             <NA>             <NA>
## 37             <NA>             <NA>
## 38             <NA>             <NA>
## 39             <NA>             <NA>
## 40             <NA>             <NA>
## 41             <NA>             <NA>
## 42             <NA>             <NA>
## 43             <NA>             <NA>
## 44             <NA>             <NA>
## 45             <NA>             <NA>
## 46             <NA>             <NA>
```

```
## 47             <NA>             <NA>
## 48             <NA>             <NA>
## 49                T                G
## 50                G                A
```

HARMONIZING EXPOSURE AND OUTCOME INSTRUMENTS

At this stage, the outcome and exposure snps are matched so that they are relative to the same allele. 'action=3' corrects strands for non-palindromic SNPs, and drops all palindromic SNPs from the analysis.

```
dat_om <- harmonise_data(exposure_om, outcome_om, action = 3)
```

```
## Harmonising Omega-3 fatty acids || id:met-d-Omega_3 (met-d-Omega_3) and Type 1 diabetes || id:ebi-a-(
```

```
## Removing the following SNPs for being palindromic:
## rs10184054, rs144018203, rs1800978, rs4860987, rs5112, rs72789541, rs964184
```

```
## Removing the following SNPs for incompatible alleles:
## rs3129962
```

```
dat_om
```

```
##            SNP effect_allele.exposure other_allele.exposure
## 1   rs10184054                      G                     C
## 2   rs10455872                      G                     A
## 3   rs11242109                      T                     G
## 4  rs112875651                      A                     G
## 5    rs1132899                      C                     T
## 6   rs11563251                      T                     C
## 7    rs1167998                      A                     C
## 8  rs117143374                      C                     T
## 9  rs117733303                      G                     A
## 10  rs12226389                      C                     T
## 11   rs1260326                      C                     T
## 12  rs13424225                      T                     G
## 13 rs139974673                      C                     T
## 14 rs143355652                      T                     C
## 15 rs144018203                      C                     G
## 16   rs1672811                      C                     T
## 17  rs16940904                      T                     C
## 18    rs174564                      G                     A
## 19   rs1800978                      G                     C
## 20 rs182611493                      G                     A
## 21   rs2394976                      T                     G
## 22    rs261290                      C                     T
## 23   rs3018731                      G                     A
## 24   rs3129962                      A                     G
## 25   rs3129962                      A                     G
## 26  rs34663616                      A                     C
## 27  rs35135293                      T                     C
## 28   rs4000713                      A                     G
```

```
## 29   rs4860987                    T                   A
## 30      rs5112                    G                   C
## 31  rs55891451                    C                   A
## 32  rs58542926                    T                   C
## 33   rs6129624                    A                   G
## 34  rs62466318                    T                   C
## 35    rs629301                    T                   G
## 36    rs633695                    G                   A
## 37   rs6601924                    C                   T
## 38   rs6693447                    G                   T
## 39    rs673335                    C                   T
## 40   rs6882345                    A                   G
## 41  rs72789541                    A                   T
## 42  rs73109460                    A                   G
## 43    rs737338                    T                   C
## 44  rs77960347                    G                   A
## 45   rs7819706                    G                   A
## 46   rs7924036                    T                   G
## 47   rs7970695                    A                   G
## 48   rs9304381                    T                   C
## 49    rs964184                    C                   G
## 50   rs9987289                    G                   A
##    effect_allele.outcome other_allele.outcome beta.exposure beta.outcome
## 1                      G                    C    -0.0361462      -0.0042
## 2                      G                    A    -0.0629576      -0.0114
## 3                      T                    G     0.0240622       0.0137
## 4                      A                    G    -0.0873719       0.0385
## 5                      C                    T     0.0270834      -0.0664
## 6                      T                    C     0.0349727      -0.0048
## 7                      A                    C     0.0713574       0.0359
## 8                      C                    T    -0.0370966      -0.0416
## 9                      G                    A    -0.1159450      -0.0544
## 10                     C                    T    -0.0506080      -0.0231
## 11                     C                    T    -0.0820592       0.0331
## 12                     T                    G     0.0221268      -0.0224
## 13                     C                    T     0.1179870      -0.0223
## 14                     T                    C    -0.1541380       0.1419
## 15                     C                    G     0.1071340       0.0105
## 16                     C                    T     0.0251849      -0.0214
## 17                     T                    C    -0.0355285      -0.0952
## 18                     G                    A    -0.3370940      -0.0487
## 19                     G                    C    -0.0373414       0.0889
## 20                     G                    A    -0.2095710       0.0457
## 21                     T                    G    -0.0461429       0.5843
## 22                     C                    T    -0.1143830       0.0146
## 23                     G                    A    -0.0353357      -0.0338
## 24                     G                    C    -0.0392017      -0.3573
## 25                     A                    G    -0.0392017       0.7618
## 26                     A                    C     0.0356728       0.0193
## 27                     T                    C    -0.0208868      -0.0254
## 28                     A                    G    -0.0288196      -0.0200
## 29                     T                    A     0.0463493      -0.0085
## 30                     G                    C     0.0476852      -0.0174
## 31                     C                    A     0.0341853      -0.0525
```

```
## 32                    T                    C    -0.1716660      -0.0157
## 33                    A                    G    -0.0257607       0.0295
## 34                    T                    C    -0.0721329      -0.0244
## 35                    T                    G     0.0382887       0.0582
## 36                    G                    A     0.0840069      -0.0205
## 37                    C                    T     0.0350603      -0.0029
## 38                    G                    T     0.0229488       0.0495
## 39                    C                    T    -0.0669996       0.0229
## 40                    A                    G     0.0288844      -0.0004
## 41                    A                    T    -0.0810999       0.0089
## 42                    A                    G    -0.0349475       0.0351
## 43                    T                    C    -0.0726631      -0.0097
## 44                    G                    A     0.1617490       0.0274
## 45                    G                    A    -0.0396447       0.0159
## 46                    T                    G     0.0233527       0.0052
## 47                    A                    G    -0.0253039      -0.0010
## 48                    T                    C     0.0528854      -0.0359
## 49                    C                    G    -0.1166370       0.0272
## 50                    G                    A     0.0566995       0.0321
##    eaf.exposure eaf.outcome remove palindromic ambiguous       id.outcome chr
## 1      0.224107      0.2247  FALSE        TRUE     FALSE ebi-a-GCST010681   2
## 2      0.078988      0.0878  FALSE       FALSE     FALSE ebi-a-GCST010681   6
## 3      0.479016      0.4788  FALSE       FALSE     FALSE ebi-a-GCST010681   5
## 4      0.392346      0.4062  FALSE       FALSE     FALSE ebi-a-GCST010681   8
## 5      0.509603      0.5099  FALSE       FALSE     FALSE ebi-a-GCST010681  19
## 6      0.110601      0.1179  FALSE       FALSE     FALSE ebi-a-GCST010681   2
## 7      0.644674      0.6504  FALSE       FALSE     FALSE ebi-a-GCST010681   1
## 8      0.142254      0.1409  FALSE       FALSE     FALSE ebi-a-GCST010681  21
## 9      0.018513      0.0197  FALSE       FALSE     FALSE ebi-a-GCST010681   6
## 10     0.185820      0.1875  FALSE       FALSE     FALSE ebi-a-GCST010681  11
## 11     0.604010      0.5993  FALSE       FALSE     FALSE ebi-a-GCST010681   2
## 12     0.449809      0.4475  FALSE       FALSE     FALSE ebi-a-GCST010681   2
## 13     0.025918      0.0267  FALSE       FALSE     FALSE ebi-a-GCST010681  15
## 14     0.010467      0.0127  FALSE       FALSE     FALSE ebi-a-GCST010681  11
## 15     0.010653      0.0115  FALSE        TRUE     FALSE ebi-a-GCST010681  11
## 16     0.748488      0.7498  FALSE       FALSE     FALSE ebi-a-GCST010681  16
## 17     0.226571      0.2355  FALSE       FALSE     FALSE ebi-a-GCST010681  17
## 18     0.347013      0.3445  FALSE       FALSE     FALSE ebi-a-GCST010681  11
## 19     0.123991      0.1270  FALSE        TRUE     FALSE ebi-a-GCST010681   9
## 20     0.012519      0.0146  FALSE       FALSE     FALSE ebi-a-GCST010681  19
## 21     0.161648      0.1720  FALSE       FALSE     FALSE ebi-a-GCST010681   6
## 22     0.654653      0.6507  FALSE       FALSE     FALSE ebi-a-GCST010681  15
## 23     0.717549      0.6983  FALSE       FALSE     FALSE ebi-a-GCST010681  11
## 24     0.129765      0.2079   TRUE       FALSE     FALSE ebi-a-GCST010681   6
## 25     0.129765      0.1358  FALSE       FALSE     FALSE ebi-a-GCST010681   6
## 26     0.137654      0.1452  FALSE       FALSE     FALSE ebi-a-GCST010681  15
## 27     0.516750      0.5163  FALSE       FALSE     FALSE ebi-a-GCST010681   2
## 28     0.295408      0.2921  FALSE       FALSE     FALSE ebi-a-GCST010681   7
## 29     0.258609      0.2575  FALSE        TRUE     FALSE ebi-a-GCST010681   4
## 30     0.533736      0.5420  FALSE        TRUE      TRUE ebi-a-GCST010681  19
## 31     0.201728      0.2043  FALSE       FALSE     FALSE ebi-a-GCST010681  10
## 32     0.074383      0.0829  FALSE       FALSE     FALSE ebi-a-GCST010681  19
## 33     0.335237      0.3375  FALSE       FALSE     FALSE ebi-a-GCST010681  20
## 34     0.204178      0.2029  FALSE       FALSE     FALSE ebi-a-GCST010681   7
```

```
## 35     0.778033      0.7769  FALSE       FALSE     FALSE ebi-a-GCST010681   1
## 36     0.292348      0.2900  FALSE       FALSE     FALSE ebi-a-GCST010681  15
## 37     0.845765      0.8470  FALSE       FALSE     FALSE ebi-a-GCST010681  10
## 38     0.461686      0.4572  FALSE       FALSE     FALSE ebi-a-GCST010681   1
## 39     0.159762      0.1592  FALSE       FALSE     FALSE ebi-a-GCST010681  11
## 40     0.632863      0.6326  FALSE       FALSE     FALSE ebi-a-GCST010681   5
## 41     0.295970      0.2922  FALSE        TRUE     FALSE ebi-a-GCST010681  16
## 42     0.123622      0.1249  FALSE       FALSE     FALSE ebi-a-GCST010681   7
## 43     0.035186      0.0418  FALSE       FALSE     FALSE ebi-a-GCST010681  19
## 44     0.013239      0.0154  FALSE       FALSE     FALSE ebi-a-GCST010681  18
## 45     0.118291      0.1218  FALSE       FALSE     FALSE ebi-a-GCST010681   8
## 46     0.504205      0.5034  FALSE       FALSE     FALSE ebi-a-GCST010681  10
## 47     0.620549      0.6208  FALSE       FALSE     FALSE ebi-a-GCST010681  12
## 48     0.818434      0.8251  FALSE       FALSE     FALSE ebi-a-GCST010681  18
## 49     0.867229      0.8628  FALSE        TRUE     FALSE ebi-a-GCST010681  11
## 50     0.909151      0.9100  FALSE       FALSE     FALSE ebi-a-GCST010681   8
##          pos se.outcome samplesize.outcome pval.outcome
## 1   21203877     0.0280              24840  8.80900e-01
## 2  161010118     0.0440              24840  7.95000e-01
## 3  131677047     0.0235              24840  5.60101e-01
## 4  126506694     0.0255              24840  1.30700e-01
## 5   45448036     0.0254              24840  9.01094e-03
## 6  234679384     0.0381              24840  8.98900e-01
## 7   62931632     0.0246              24840  1.44800e-01
## 8   40555561     0.0346              24840  2.29600e-01
## 9  160922870     0.0870              24840  5.31300e-01
## 10  61823630     0.0308              24840  4.53600e-01
## 11  27730940     0.0239              24840  1.66300e-01
## 12 241214158     0.0244              24840  3.59100e-01
## 13  44027885     0.0742              24840  7.64100e-01
## 14  61453822     0.1073              24840  1.86000e-01
## 15 116916060     0.1258              24840  9.33200e-01
## 16  15501099     0.0271              24840  4.30700e-01
## 17  44186063     0.0281              24840  6.88098e-04
## 18  61588305     0.0248              24840  4.92901e-02
## 19 107665978     0.0348              24840  1.05801e-02
## 20  19458388     0.1158              24840  6.93201e-01
## 21  31311912     0.0330              24840  2.89868e-70
## 22  58678720     0.0248              24840  5.55300e-01
## 23  61248776     0.0281              24840  2.28800e-01
## 24  32379383     0.0367              24840  1.85183e-22
## 25  32379383     0.0353              24840 3.65595e-103
## 26  58569330     0.0353              24840  5.84300e-01
## 27  20363666     0.0236              24840  2.82000e-01
## 28  25990597     0.0263              24840  4.48200e-01
## 29  69491284     0.0328              24840  7.94500e-01
## 30  45430280     0.0291              24840  5.50201e-01
## 31  96731788     0.0296              24840  7.61798e-02
## 32  19379549     0.0436              24840  7.18399e-01
## 33  39167592     0.0250              24840  2.38000e-01
## 34  73042085     0.0302              24840  4.19200e-01
## 35 109818306     0.0284              24840  4.01301e-02
## 36  58725839     0.0272              24840  4.51000e-01
## 37   5247302     0.0324              24840  9.28600e-01
```

```
## 38   2330190     0.0255              24840  5.18704e-02
## 39  75450576     0.0316              24840  4.68600e-01
## 40 156397673     0.0242              24840  9.87800e-01
## 41  15127534     0.0263              24840  7.35401e-01
## 42  44792326     0.0373              24840  3.46600e-01
## 43  11347657     0.0620              24840  8.75200e-01
## 44  47109955     0.1030              24840  7.90300e-01
## 45  19844415     0.0354              24840  6.53800e-01
## 46  65191645     0.0234              24840  8.23000e-01
## 47 121423376     0.0240              24840  9.67700e-01
## 48  47158234     0.0306              24840  2.42000e-01
## 49 116648917     0.0342              24840  4.26500e-01
## 50   9183358     0.0412              24840  4.37100e-01
##                                    outcome originalname.outcome
## 1  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 2  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 3  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 4  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 5  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 6  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 7  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 8  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 9  Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 10 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 11 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 12 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 13 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 14 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 15 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 16 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 17 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 18 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 19 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 20 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 21 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 22 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 23 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 24 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 25 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 26 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 27 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 28 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 29 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 30 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 31 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 32 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 33 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 34 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 35 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 36 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 37 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 38 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 39 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 40 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
```

```
## 41 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 42 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 43 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 44 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 45 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 46 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 47 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 48 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 49 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
## 50 Type 1 diabetes || id:ebi-a-GCST010681      Type 1 diabetes
##         outcome.deprecated mr_keep.outcome data_source.outcome proxy.outcome
## 1  Type 1 diabetes ||  ||             TRUE                igd            NA
## 2  Type 1 diabetes ||  ||             TRUE                igd            NA
## 3  Type 1 diabetes ||  ||             TRUE                igd            NA
## 4  Type 1 diabetes ||  ||             TRUE                igd            NA
## 5  Type 1 diabetes ||  ||             TRUE                igd            NA
## 6  Type 1 diabetes ||  ||             TRUE                igd            NA
## 7  Type 1 diabetes ||  ||             TRUE                igd            NA
## 8  Type 1 diabetes ||  ||             TRUE                igd            NA
## 9  Type 1 diabetes ||  ||             TRUE                igd            NA
## 10 Type 1 diabetes ||  ||             TRUE                igd            NA
## 11 Type 1 diabetes ||  ||             TRUE                igd            NA
## 12 Type 1 diabetes ||  ||             TRUE                igd            NA
## 13 Type 1 diabetes ||  ||             TRUE                igd            NA
## 14 Type 1 diabetes ||  ||             TRUE                igd            NA
## 15 Type 1 diabetes ||  ||             TRUE                igd            NA
## 16 Type 1 diabetes ||  ||             TRUE                igd            NA
## 17 Type 1 diabetes ||  ||             TRUE                igd            NA
## 18 Type 1 diabetes ||  ||             TRUE                igd            NA
## 19 Type 1 diabetes ||  ||             TRUE                igd            NA
## 20 Type 1 diabetes ||  ||             TRUE                igd            NA
## 21 Type 1 diabetes ||  ||             TRUE                igd            NA
## 22 Type 1 diabetes ||  ||             TRUE                igd            NA
## 23 Type 1 diabetes ||  ||             TRUE                igd            NA
## 24 Type 1 diabetes ||  ||             TRUE                igd            NA
## 25 Type 1 diabetes ||  ||             TRUE                igd            NA
## 26 Type 1 diabetes ||  ||             TRUE                igd            NA
## 27 Type 1 diabetes ||  ||             TRUE                igd            NA
## 28 Type 1 diabetes ||  ||             TRUE                igd            NA
## 29 Type 1 diabetes ||  ||             TRUE                igd            NA
## 30 Type 1 diabetes ||  ||             TRUE                igd            NA
## 31 Type 1 diabetes ||  ||             TRUE                igd          TRUE
## 32 Type 1 diabetes ||  ||             TRUE                igd            NA
## 33 Type 1 diabetes ||  ||             TRUE                igd            NA
## 34 Type 1 diabetes ||  ||             TRUE                igd            NA
## 35 Type 1 diabetes ||  ||             TRUE                igd            NA
## 36 Type 1 diabetes ||  ||             TRUE                igd            NA
## 37 Type 1 diabetes ||  ||             TRUE                igd            NA
## 38 Type 1 diabetes ||  ||             TRUE                igd            NA
## 39 Type 1 diabetes ||  ||             TRUE                igd            NA
## 40 Type 1 diabetes ||  ||             TRUE                igd            NA
## 41 Type 1 diabetes ||  ||             TRUE                igd            NA
## 42 Type 1 diabetes ||  ||             TRUE                igd          TRUE
## 43 Type 1 diabetes ||  ||             TRUE                igd            NA
```

```
## 44 Type 1 diabetes ||  ||            TRUE                igd            NA
## 45 Type 1 diabetes ||  ||            TRUE                igd            NA
## 46 Type 1 diabetes ||  ||            TRUE                igd            NA
## 47 Type 1 diabetes ||  ||            TRUE                igd            NA
## 48 Type 1 diabetes ||  ||            TRUE                igd            NA
## 49 Type 1 diabetes ||  ||            TRUE                igd            NA
## 50 Type 1 diabetes ||  ||            TRUE                igd            NA
##    target_snp.outcome proxy_snp.outcome target_a1.outcome target_a2.outcome
## 1                <NA>              <NA>              <NA>              <NA>
## 2                <NA>              <NA>              <NA>              <NA>
## 3                <NA>              <NA>              <NA>              <NA>
## 4                <NA>              <NA>              <NA>              <NA>
## 5                <NA>              <NA>              <NA>              <NA>
## 6                <NA>              <NA>              <NA>              <NA>
## 7                <NA>              <NA>              <NA>              <NA>
## 8                <NA>              <NA>              <NA>              <NA>
## 9                <NA>              <NA>              <NA>              <NA>
## 10               <NA>              <NA>              <NA>              <NA>
## 11               <NA>              <NA>              <NA>              <NA>
## 12               <NA>              <NA>              <NA>              <NA>
## 13               <NA>              <NA>              <NA>              <NA>
## 14               <NA>              <NA>              <NA>              <NA>
## 15               <NA>              <NA>              <NA>              <NA>
## 16               <NA>              <NA>              <NA>              <NA>
## 17               <NA>              <NA>              <NA>              <NA>
## 18               <NA>              <NA>              <NA>              <NA>
## 19               <NA>              <NA>              <NA>              <NA>
## 20               <NA>              <NA>              <NA>              <NA>
## 21               <NA>              <NA>              <NA>              <NA>
## 22               <NA>              <NA>              <NA>              <NA>
## 23               <NA>              <NA>              <NA>              <NA>
## 24               <NA>              <NA>              <NA>              <NA>
## 25               <NA>              <NA>              <NA>              <NA>
## 26               <NA>              <NA>              <NA>              <NA>
## 27               <NA>              <NA>              <NA>              <NA>
## 28               <NA>              <NA>              <NA>              <NA>
## 29               <NA>              <NA>              <NA>              <NA>
## 30               <NA>              <NA>              <NA>              <NA>
## 31        rs55891451         rs9332172                 C                 A
## 32               <NA>              <NA>              <NA>              <NA>
## 33               <NA>              <NA>              <NA>              <NA>
## 34               <NA>              <NA>              <NA>              <NA>
## 35               <NA>              <NA>              <NA>              <NA>
## 36               <NA>              <NA>              <NA>              <NA>
## 37               <NA>              <NA>              <NA>              <NA>
## 38               <NA>              <NA>              <NA>              <NA>
## 39               <NA>              <NA>              <NA>              <NA>
## 40               <NA>              <NA>              <NA>              <NA>
## 41               <NA>              <NA>              <NA>              <NA>
## 42        rs73109460        rs56230523                 A                 G
## 43               <NA>              <NA>              <NA>              <NA>
## 44               <NA>              <NA>              <NA>              <NA>
## 45               <NA>              <NA>              <NA>              <NA>
## 46               <NA>              <NA>              <NA>              <NA>
```

```
## 47              <NA>             <NA>             <NA>             <NA>
## 48              <NA>             <NA>             <NA>             <NA>
## 49              <NA>             <NA>             <NA>             <NA>
## 50              <NA>             <NA>             <NA>             <NA>
##    proxy_a1.outcome proxy_a2.outcome samplesize.exposure chr.exposure
## 1              <NA>             <NA>                  NA            2
## 2              <NA>             <NA>                  NA            6
## 3              <NA>             <NA>                  NA            5
## 4              <NA>             <NA>                  NA            8
## 5              <NA>             <NA>                  NA           19
## 6              <NA>             <NA>                  NA            2
## 7              <NA>             <NA>                  NA            1
## 8              <NA>             <NA>                  NA           21
## 9              <NA>             <NA>                  NA            6
## 10             <NA>             <NA>                  NA           11
## 11             <NA>             <NA>                  NA            2
## 12             <NA>             <NA>                  NA            2
## 13             <NA>             <NA>                  NA           15
## 14             <NA>             <NA>                  NA           11
## 15             <NA>             <NA>                  NA           11
## 16             <NA>             <NA>                  NA           16
## 17             <NA>             <NA>                  NA           17
## 18             <NA>             <NA>                  NA           11
## 19             <NA>             <NA>                  NA            9
## 20             <NA>             <NA>                  NA           19
## 21             <NA>             <NA>                  NA            6
## 22             <NA>             <NA>                  NA           15
## 23             <NA>             <NA>                  NA           11
## 24             <NA>             <NA>                  NA            6
## 25             <NA>             <NA>                  NA            6
## 26             <NA>             <NA>                  NA           15
## 27             <NA>             <NA>                  NA            2
## 28             <NA>             <NA>                  NA            7
## 29             <NA>             <NA>                  NA            4
## 30             <NA>             <NA>                  NA           19
## 31                G                A                  NA           10
## 32             <NA>             <NA>                  NA           19
## 33             <NA>             <NA>                  NA           20
## 34             <NA>             <NA>                  NA            7
## 35             <NA>             <NA>                  NA            1
## 36             <NA>             <NA>                  NA           15
## 37             <NA>             <NA>                  NA           10
## 38             <NA>             <NA>                  NA            1
## 39             <NA>             <NA>                  NA           11
## 40             <NA>             <NA>                  NA            5
## 41             <NA>             <NA>                  NA           16
## 42                T                G                  NA            7
## 43             <NA>             <NA>                  NA           19
## 44             <NA>             <NA>                  NA           18
## 45             <NA>             <NA>                  NA            8
## 46             <NA>             <NA>                  NA           10
## 47             <NA>             <NA>                  NA           12
## 48             <NA>             <NA>                  NA           18
## 49             <NA>             <NA>                  NA           11
```

```
## 50             <NA>             <NA>                   NA            8
##    pval.exposure pos.exposure se.exposure   id.exposure
## 1    5.60015e-15     21203877  0.00486548 met-d-Omega_3
## 2    2.80027e-17    161010118  0.00753435 met-d-Omega_3
## 3    2.39999e-09    131677047  0.00406580 met-d-Omega_3
## 4    3.50026e-98    126506694  0.00422001 met-d-Omega_3
## 5    8.60003e-11     45448036  0.00410188 met-d-Omega_3
## 6    3.20000e-08    234679384  0.00647476 met-d-Omega_3
## 7    3.59998e-66     62931632  0.00425038 met-d-Omega_3
## 8    2.19999e-10     40555561  0.00584700 met-d-Omega_3
## 9    1.39991e-15    160922870  0.01507310 met-d-Omega_3
## 10   1.10002e-22     61823630  0.00524839 met-d-Omega_3
## 11   8.40040e-88     27730940  0.00415340 met-d-Omega_3
## 12   2.19999e-08    241214158  0.00408591 met-d-Omega_3
## 13   2.29985e-21     44027885  0.01280750 met-d-Omega_3
## 14   9.39940e-14     61453822  0.02040730 met-d-Omega_3
## 15   4.20001e-08    116916060  0.02049000 met-d-Omega_3
## 16   2.99999e-08     15501099  0.00469670 met-d-Omega_3
## 17   3.90032e-14     44186063  0.00487720 met-d-Omega_3
## 18  1.00000e-200     61588305  0.00424185 met-d-Omega_3
## 19   5.19996e-09    107665978  0.00619432 met-d-Omega_3
## 20   1.10002e-27     19458388  0.01957770 met-d-Omega_3
## 21   1.20005e-15     31311912  0.00550837 met-d-Omega_3
## 22  3.89942e-161     58678720  0.00428189 met-d-Omega_3
## 23   1.99986e-14     61248776  0.00456603 met-d-Omega_3
## 24   1.79999e-09     32379383  0.00603734 met-d-Omega_3
## 25   1.79999e-09     32379383  0.00603734 met-d-Omega_3
## 26   4.39997e-10     58569330  0.00602277 met-d-Omega_3
## 27   3.89996e-08     20363666  0.00408348 met-d-Omega_3
## 28   1.00000e-11     25990597  0.00446039 met-d-Omega_3
## 29   1.20005e-21     69491284  0.00491057 met-d-Omega_3
## 30   9.09913e-30     45430280  0.00437178 met-d-Omega_3
## 31   4.60045e-12     96728169  0.00508075 met-d-Omega_3
## 32  1.39959e-113     19379549  0.00775231 met-d-Omega_3
## 33   5.10000e-10     39167592  0.00437946 met-d-Omega_3
## 34   1.20005e-45     73042085  0.00506371 met-d-Omega_3
## 35   1.29987e-14    109818306  0.00488385 met-d-Omega_3
## 36   9.09913e-80     58725839  0.00448287 met-d-Omega_3
## 37   8.50002e-10      5247302  0.00563873 met-d-Omega_3
## 38   4.79999e-09      2330190  0.00407772 met-d-Omega_3
## 39   1.10002e-34     75450576  0.00554146 met-d-Omega_3
## 40   1.90020e-13    156397673  0.00421159 met-d-Omega_3
## 41   5.60015e-75     15127534  0.00446068 met-d-Omega_3
## 42   9.20005e-10     44785800  0.00621600 met-d-Omega_3
## 43   3.50026e-11     11347657  0.01103540 met-d-Omega_3
## 44   7.19946e-22     47109955  0.01775740 met-d-Omega_3
## 45   1.79999e-10     19844415  0.00628878 met-d-Omega_3
## 46   5.49997e-10     65191645  0.00406452 met-d-Omega_3
## 47   1.20000e-10    121423376  0.00419603 met-d-Omega_3
## 48   5.19996e-24     47158234  0.00527814 met-d-Omega_3
## 49   8.90020e-87    116648917  0.00596503 met-d-Omega_3
## 50   3.19963e-16      9183358  0.00707191 met-d-Omega_3
##                                    exposure mr_keep.exposure
## 1  Omega-3 fatty acids || id:met-d-Omega_3             TRUE
```

```
## 2  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 3  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 4  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 5  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 6  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 7  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 8  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 9  Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 10 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 11 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 12 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 13 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 14 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 15 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 16 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 17 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 18 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 19 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 20 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 21 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 22 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 23 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 24 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 25 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 26 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 27 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 28 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 29 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 30 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 31 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 32 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 33 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 34 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 35 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 36 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 37 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 38 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 39 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 40 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 41 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 42 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 43 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 44 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 45 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 46 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 47 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 48 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 49 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
## 50 Omega-3 fatty acids || id:met-d-Omega_3            TRUE
##    pval_origin.exposure data_source.exposure action mr_keep
## 1              reported                 igd      3   FALSE
## 2              reported                 igd      3    TRUE
## 3              reported                 igd      3    TRUE
## 4              reported                 igd      3    TRUE
```

```
## 5              reported                 igd      3    TRUE
## 6              reported                 igd      3    TRUE
## 7              reported                 igd      3    TRUE
## 8              reported                 igd      3    TRUE
## 9              reported                 igd      3    TRUE
## 10             reported                 igd      3    TRUE
## 11             reported                 igd      3    TRUE
## 12             reported                 igd      3    TRUE
## 13             reported                 igd      3    TRUE
## 14             reported                 igd      3    TRUE
## 15             reported                 igd      3   FALSE
## 16             reported                 igd      3    TRUE
## 17             reported                 igd      3    TRUE
## 18             reported                 igd      3    TRUE
## 19             reported                 igd      3   FALSE
## 20             reported                 igd      3    TRUE
## 21             reported                 igd      3    TRUE
## 22             reported                 igd      3    TRUE
## 23             reported                 igd      3    TRUE
## 24             reported                 igd      3   FALSE
## 25             reported                 igd      3    TRUE
## 26             reported                 igd      3    TRUE
## 27             reported                 igd      3    TRUE
## 28             reported                 igd      3    TRUE
## 29             reported                 igd      3   FALSE
## 30             reported                 igd      3   FALSE
## 31             reported                 igd      3    TRUE
## 32             reported                 igd      3    TRUE
## 33             reported                 igd      3    TRUE
## 34             reported                 igd      3    TRUE
## 35             reported                 igd      3    TRUE
## 36             reported                 igd      3    TRUE
## 37             reported                 igd      3    TRUE
## 38             reported                 igd      3    TRUE
## 39             reported                 igd      3    TRUE
## 40             reported                 igd      3    TRUE
## 41             reported                 igd      3   FALSE
## 42             reported                 igd      3    TRUE
## 43             reported                 igd      3    TRUE
## 44             reported                 igd      3    TRUE
## 45             reported                 igd      3    TRUE
## 46             reported                 igd      3    TRUE
## 47             reported                 igd      3    TRUE
## 48             reported                 igd      3    TRUE
## 49             reported                 igd      3   FALSE
## 50             reported                 igd      3    TRUE
```

DETERMINING VARIANCE EXPLAINED BY INSTRUMENTAL VARIABLES

The F-statistic is calculated to determine if the instrumental variables explain a substantial proportion of the variance in the exposure and that the MR study has enough power to detect a causal effect of the exposure on the outcome.

```r
# Extract effect allele and minor allele frequencies
dat_om$EAF2 <- (1 - dat_om$eaf.exposure)
dat_om$MAF <- pmin(dat_om$eaf.exposure, dat_om$EAF2)

# Function to determine the proportion of variance explained
PVEfx <- function(BETA, MAF, SE, N) {
    pve <- (2 * (BETA^2) * MAF * (1 - MAF))/((2 * (BETA^2) * MAF * (1 - MAF)) + ((SE^2) *
        2 * N * MAF * (1 - MAF)))
    return(pve)
}

# Apply function to exposure effects
dat_om$PVE <- mapply(PVEfx, dat_om$beta.exposure, dat_om$MAF, dat_om$se.exposure,
    N = 114999)

# Calculate per-SNP F statistic
dat_om$FSTAT <- ((114999 - 1 - 1)/1) * (dat_om$PVE/(1 - dat_om$PVE))

# Calculate total instrument F statistic Total PVE
PVEtot_om <- sum(dat_om$PVE)
print(paste0("The proportion of variance expalained by the instrumental variables is ",
    PVEtot_om))
```

```
## [1] "The proportion of variance expalained by the instrumental variables is 0.102277621102368"
```

```r
# F-statistic
FSTATtot_om <- ((114999 - 50 - 1)/50) * (PVEtot_om/(1 - PVEtot_om))
print(paste0("The F-statistic is ", FSTATtot_om))
```

```
## [1] "The F-statistic is 261.92079571218"
```

PRIMARY MR ANALYSIS

This includes single SNP analysis using the inverse variance weighted method followed by an all SNPs analysis using the same method and then analysis using each of three other methods including the MR-Egger, Weighted median and Weighted mode. The 'generate_odds_ratios' function computes odds ratios and their corresponding confidence intervals for effects measured by each of the MR analysis methods.

```r
# Single snp analysis using IVW method
MR_ss_om <- mr_singlesnp(dat_om, parameters = default_parameters(), single_method = "mr_wald_ratio",
    all_method = "mr_ivw")

# MR analysis with all 4 methods
mr_res_om <- mr(dat_om, method_list = c("mr_ivw", "mr_egger_regression", "mr_weighted_median",
    "mr_weighted_mode"))
```

```
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
```

```r
# Generate odds ratios and confidence intervals
mr_res_om_ORs <- generate_odds_ratios(mr_res_om)
mr_res_om_ORs
```

```
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   42
## 2 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger   42
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   42
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   42
##             b         se       pval       lo_ci     up_ci        or  or_lci95
## 1 -0.08165236 0.25068226 0.74463580 -0.57298960 0.4096849 0.9215923 0.5638373
## 2  0.18433818 0.34223511 0.59312716 -0.48644264 0.8551190 1.2024224 0.6148096
## 3  0.14080825 0.07039665 0.04547732  0.00283083 0.2787857 1.1512039 1.0028348
## 4  0.11469216 0.06669397 0.09303268 -0.01602802 0.2454123 1.1215281 0.9840997
##   or_uci95
## 1 1.506343
## 2 2.351654
## 3 1.321524
## 4 1.278148
```

SENSITIVITY ANALYSES

In order to assess the validity of the causal inference made from the instrumental variable analyses above and to provide a more robust and reliable estimation of the causal effect between omega 3 and T1D, several other sensitivity analyses are performed. Pleiotropy and heterogeneity tests for the main analysis and for each of the other analyses are also done as detailed below.

Pleiotropy and heterogeneity test for main analysis

The 'mr_pleiotropy_test' method performs MR-Egger and returns intercept values while 'mr_heterogeneity' calculates Cochran's Q statistic and its corresponding p-value as measures of heterogeneity.

```
# pleiotropy
ple_om <- mr_pleiotropy_test(dat_om)
ple_om
```

```
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.03273187 0.02878808 0.2623063
```

```
# heterogeneity
het_om <- mr_heterogeneity(dat_om)
het_om
```

```
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 807.2030
```

```
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 833.2909
##   Q_df        Q_pval
## 1   40 1.468886e-143
## 2   41 2.669900e-148
```

MR and sensitivity analysis excluding proxy snps

To check whether the observed causal effect is due to the proxy SNPs, we extract these from our harmonized data and repeat the MR analysis, and heterogeneity tests using the remaining SNPS.

```
# Extract outcome snps excluding proxies
outcome_om_rmprx <- extract_outcome_data(snps = exposure_om$SNP, outcomes = "ebi-a-GCST010681",
    proxies = FALSE)
```

```
## Extracting data for 52 SNP(s) from 1 GWAS(s)
```

```
# Harmonize snp data for IVs excluding proxies
dat_om_rmprx <- harmonise_data(exposure_om, outcome_om_rmprx, action = 3)
```

```
## Harmonising Omega-3 fatty acids || id:met-d-Omega_3 (met-d-Omega_3) and Type 1 diabetes || id:ebi-a-
```

```
## Removing the following SNPs for being palindromic:
## rs10184054, rs144018203, rs1800978, rs4860987, rs5112, rs72789541, rs964184
```

```
## Removing the following SNPs for incompatible alleles:
## rs3129962
```

```
# MR analysis without proxy snps
mr_res_om_rmprx <- mr(dat_om_rmprx, method_list = c("mr_ivw", "mr_egger_regression",
    "mr_weighted_median", "mr_weighted_mode"))
```

```
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
```

```
# Generate ORs and CIs
mr_res_om_rmprx_ORs <- generate_odds_ratios(mr_res_om_rmprx)

# pleiotropy test excluding proxy snps
ple_om_rmprx <- mr_pleiotropy_test(dat_om_rmprx)

# heterogeneity test excluding proxy snps
het_om_rmprx <- mr_heterogeneity(dat_om_rmprx)
```

Phenoscanner search for potentially pleiotropic snp-trait associations

The PhenoScanner package is installed, loaded and then used to query the database to identify the SNPS among the instrumental variables that have associations with potentially confounding traits.

```r
# Install PhenoScanner package
install.packages("remotes", repos = "https://cran.r-project.org")
```

```
##
## The downloaded binary packages are in
##  /var/folders/2y/z3g4d8r132j6m0_l9skqmw6c0000gp/T//RtmprfdCpX/downloaded_packages
```

```r
remotes::install_github("phenoscanner/phenoscanner")
```

```
## Skipping install of 'phenoscanner' from a github remote, the SHA1 (06dadfc0) has not changed since la
##   Use 'force = TRUE' to force installation
```

```r
library(phenoscanner)

# Run phenoscanner analysis
Pheno <- phenoscanner(snpquery = dat_om$SNP, pvalue = 5e-08)
```

```
## PhenoScanner V2
## Cardiovascular Epidemiology Unit
## University of Cambridge
## Email: phenoscanner@gmail.com
##
## Information: Each user can query a maximum of 10,000 SNPs (in batches of 100), 1,000 genes (in batch
## Terms of use: Please refer to the terms of use when using PhenoScanner V2 (www.phenoscanner.medschl.
##
## [1] "1 -- chunk of 10 SNPs queried"
## [1] "2 -- chunk of 10 SNPs queried"
## [1] "3 -- chunk of 10 SNPs queried"
## [1] "4 -- chunk of 10 SNPs queried"
## [1] "5 -- chunk of 10 SNPs queried"
```

```r
# Extract results from PhenoScanner search
Pheno_res <- Pheno$results

# Extract SNP-trait associations in data frame
Pheno_res2 <- data.frame(Pheno_res$snp, Pheno_res$trait)
```

SNP-trait associations are grouped into trait categories and categories likely to confound the omega3-T1D association are selected for further analysis.

Extract harmonized data excluding lipid, blood, inflammation, body composition and T2D SNPs

In this is step, harmonized data is extracted excluding snps from individual trait categories, that can potentially affect the Omega-3-T1D relationship, obtained through PhenoScanner.

```r
# harmonized data excluding lipid-associated snps
dat_om_lipid <- dat_om[!((dat_om$SNP) %in% c("rs10184054", "rs10455872", "rs10184054",
    "rs10455872", "rs112875651", "rs1132899", "rs11563251", "rs1167998", "rs117733303",
    "rs1260326", "rs1800978", "rs261290", "rs5112", "rs58542926", "rs6129624", "rs62466318",
```

```
    "rs629301", "rs633695", "rs6601924", "rs7819706", "rs7970695", "rs9304381", "rs964184",
    "rs9987289", "rs9987289")), ]

# harmonized data excluding blood-associated snps
dat_om_blood <- dat_om[!((dat_om$SNP) %in% c("rs10184054", "rs11242109", "rs112875651",
    "rs1167998", "rs117143374", "rs1260326", "rs139974673", "rs16940904", "rs174564",
    "rs2394976", "rs5112", "rs58542926", "rs62466318", "rs673335", "rs6882345", "rs7819706",
    "rs7924036", "rs964184", "rs9987289", "rs7970695")), ]

# harmonized data excluding inflammation-associated snps
dat_om_inflam <- dat_om[!((dat_om$SNP) %in% c("rs11242109", "rs1260326", "rs174564",
    "rs2394976", "rs7970695", "rs9987289")), ]

# harmonized data excluding T2D-associated snps
dat_om_T2D <- dat_om[!((dat_om$SNP) %in% c("rs1260326", "rs58542926")), ]

# harmonized data excluding body composition-associated snps
dat_om_bodycomp <- dat_om[!((dat_om$SNP) %in% c("rs11242109", "rs112875651", "rs1260326",
    "rs139974673", "rs16940904", "rs2394976", "rs58542926", "rs62466318", "rs6601924",
    "rs72789541", "rs7924036")), ]
```

MR and sensitivity analyses excluding lipid, blood, inflammation, body composition and T2D SNPs

MR and sensitivity analyses with harmonized data from the previous step are conducted. Odds ratios and CIs for these analyses are also generated.

```
# Create list for PhenoScanner categories
dat_om_phenoexcl <- list(dat_om_blood, dat_om_bodycomp, dat_om_inflam, dat_om_lipid,
    dat_om_T2D)

# Initialize an empty list to store the results
phenoexcl_res_list <- list()

# Loop over each dataset and run the mr() function
for (i in seq_along(dat_om_phenoexcl)) {
    phenoexcl_res_list[[i]] <- mr(dat = dat_om_phenoexcl[[i]], method_list = c("mr_ivw",
        "mr_egger_regression", "mr_weighted_median", "mr_weighted_mode"))
}
```

```
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
```

```
## GENERATE ODDS RATIOS AND CIS initialize an empty list to store the results
OR_list <- list()

# loop over each dataset from mr analysis to generate odds ratios
for (i in seq_along(phenoexcl_res_list)) {
```

```
    OR_list[[i]] <- generate_odds_ratios(phenoexcl_res_list[[i]])
}

OR_list
```

```
## [[1]]
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                  exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   25
## 2 Omega-3 fatty acids || id:met-d-Omega_3                  MR Egger   25
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   25
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   25
##             b        se      pval      lo_ci     up_ci        or  or_lci95
## 1 -0.46875373 0.5512296 0.3951147 -1.5491637 0.6116562 0.6257817 0.2124256
## 2 -0.04618121 1.0040474 0.9637112 -2.0141141 1.9217517 0.9548689 0.1334386
## 3 -0.13025803 0.1874123 0.4870336 -0.4975861 0.2370701 0.8778689 0.6079965
## 4 -0.13188007 0.1799773 0.4708018 -0.4846355 0.2208754 0.8764461 0.6159217
##   or_uci95
## 1 1.843482
## 2 6.832917
## 3 1.267530
## 4 1.247168
##
## [[2]]
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                  exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   32
## 2 Omega-3 fatty acids || id:met-d-Omega_3                  MR Egger   32
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   32
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   32
##              b         se       pval        lo_ci     up_ci       or  or_lci95
## 1 0.001496313 0.24590988 0.99514506 -0.480487054 0.4834797 1.001497 0.6184821
## 2 0.201690757 0.32279460 0.53680845 -0.430986659 0.8343682 1.223470 0.6498676
## 3 0.142810382 0.07369083 0.05262726 -0.001623637 0.2872444 1.153511 0.9983777
## 4 0.124717622 0.07119464 0.08969988 -0.014823881 0.2642591 1.132829 0.9852855
##   or_uci95
## 1 1.621708
## 2 2.303358
## 3 1.332750
## 4 1.302466
##
## [[3]]
##     id.exposure       id.outcome                                outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
```

```
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   36
## 2 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger   36
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   36
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   36
##             b        se      pval      lo_ci     up_ci        or  or_lci95
## 1 -0.20932215 0.3471904 0.5465732 -0.8898154 0.4711711 0.8111339 0.4107316
## 2  0.01289283 0.6392338 0.9840263 -1.2400055 1.2657911 1.0129763 0.2893826
## 3 -0.11076144 0.1394309 0.4269730 -0.3840460 0.1625232 0.8951523 0.6811001
## 4 -0.11201105 0.1307466 0.3974367 -0.3682744 0.1442523 0.8940344 0.6919273
##   or_uci95
## 1 1.601869
## 2 3.545897
## 3 1.176476
## 4 1.155175
##
## [[4]]
##     id.exposure       id.outcome                                  outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   24
## 2 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger   24
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   24
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   24
##             b         se       pval        lo_ci     up_ci        or  or_lci95
## 1 -0.07804552 0.39821084 0.84461764 -0.858538771 0.7024477 0.9249223 0.4237809
## 2  0.18557706 0.48761179 0.70716225 -0.770142051 1.1412962 1.2039130 0.4629473
## 3  0.14420677 0.06918161 0.03711772  0.008610818 0.2798027 1.1551229 1.0086480
## 4  0.11916298 0.07155623 0.10941646 -0.021087242 0.2594132 1.1265535 0.9791335
##   or_uci95
## 1 2.018688
## 2 3.130824
## 3 1.322869
## 4 1.296169
##
## [[5]]
##     id.exposure       id.outcome                                  outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 3 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 4 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method nsnp
## 1 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted   40
## 2 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger   40
## 3 Omega-3 fatty acids || id:met-d-Omega_3           Weighted median   40
## 4 Omega-3 fatty acids || id:met-d-Omega_3             Weighted mode   40
##             b         se       pval        lo_ci     up_ci       or  or_lci95
## 1 -0.07790752 0.26834009 0.77156282 -0.603854096 0.4480391 0.925050 0.5467005
## 2  0.18251902 0.35961602 0.61471019 -0.522328377 0.8873664 1.200237 0.5931379
```

```
## 3  0.14241511 0.07011030 0.04222449  0.004998924 0.2798313 1.153055 1.0050114
## 4  0.12269680 0.06823691 0.07990553 -0.011047547 0.2564411 1.130542 0.9890133
##   or_uci95
## 1 1.565240
## 2 2.428725
## 3 1.322907
## 4 1.292323
```

Further sensitivity analyses are performed using snps associated with blood and inflammation categories combined and independently to test for their contribution to the observed causal effects in the previous step.

```
# MR analysis using blood/inflammation snps
bld_snps <- dat_om[((dat_om$SNP) %in% c("rs10184054", "rs11242109", "rs112875651",
    "rs1167998", "rs117143374", "rs1260326", "rs139974673", "rs16940904", "rs174564",
    "rs2394976", "rs5112", "rs58542926", "rs62466318", "rs673335", "rs6882345", "rs7819706",
    "rs7924036", "rs964184", "rs9987289", "rs7970695")), ]

# MR analysis using only blood snps
bld_snps_mr <- mr(dat = bld_snps, method_list = c("mr_ivw", "mr_egger_regression",
    "mr_weighted_median", "mr_weighted_mode"))
```

```
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
```

```
# Extracting harmonized data for only inflammation snps
infl_snps <- dat_om[((dat_om$SNP) %in% c("rs11242109", "rs1260326", "rs174564", "rs2394976",
    "rs7970695", "rs9987289")), ]

# MR analysis using only inflammation snps
infl_snps_mr <- mr(dat = infl_snps, method_list = c("mr_ivw", "mr_egger_regression",
    "mr_weighted_median", "mr_weighted_mode"))
```

```
## Analysing 'met-d-Omega_3' on 'ebi-a-GCST010681'
```

Pleiotropy and heterogeneity tests excluding lipid, blood, inflammation, body composition and T2D SNPs

This step performs the pleiotropy and heterogeneity analyses with the five snp-trait categories excluded.

```
# #initialize an empty vector to store the results
ple_pheno <- c()
het_pheno <- c()

for (i in seq_along(dat_om_phenoexcl)) {
    ple_pheno[[i]] <- mr_pleiotropy_test(dat_om_phenoexcl[[i]])
    het_pheno[[i]] <- mr_heterogeneity(dat_om_phenoexcl[[i]])

    print(ple_pheno[[i]])
    print(het_pheno[[i]])
}
```

```
##     id.exposure       id.outcome                                  outcome
```

```
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.02624965 0.05176955 0.6169482
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 476.3978
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 481.7230
##   Q_df       Q_pval
## 1   23 2.840364e-86
## 2   24 1.031988e-86
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.02762246 0.02880011 0.3451702
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 489.9725
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 504.9965
##   Q_df       Q_pval
## 1   30 1.370381e-84
## 2   31 4.730203e-87
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.01514672 0.03639914 0.6799311
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 507.3401
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 509.9239
##   Q_df       Q_pval
## 1   34 1.019453e-85
## 2   35 1.187261e-85
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.04304142 0.04571712 0.3566866
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 779.5653
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 810.9736
##   Q_df        Q_pval
## 1   22 1.200245e-150
## 2   23 1.655415e-156
##    id.exposure       id.outcome                                 outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                 exposure egger_intercept         se      pval
```

```
## 1 Omega-3 fatty acids || id:met-d-Omega_3     -0.03221034 0.02969471 0.2848814
##     id.exposure       id.outcome                                  outcome
## 1 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
## 2 met-d-Omega_3 ebi-a-GCST010681 Type 1 diabetes || id:ebi-a-GCST010681
##                                  exposure                    method        Q
## 1 Omega-3 fatty acids || id:met-d-Omega_3                 MR Egger 806.6262
## 2 Omega-3 fatty acids || id:met-d-Omega_3 Inverse variance weighted 831.6021
##   Q_df        Q_pval
## 1   38 9.085395e-145
## 2   39 2.793430e-149
```

Run Mendelian Randomization- Pleiotropy RESidual Sum and Outlier(MR-PRESSO) test

The 'run_mr_presso' method uses the MR-PRESSO wrapper within the TwoSampleMR package to detect and correct for outliers and pleiotropic effects in MR analyses. 'NbDistribution = 1000' specifies the number of Monte Carlo simulations performed by MR-PRESSO to estimate the empirical distribution of the test statistic under the null hypothesis. The analysis is performed under a Significance value threshold of 0.05 below which implies statistical significance.

```
presso <- run_mr_presso(dat_om, NbDistribution = 1000, SignifThreshold = 0.05)
```

```
## Omega-3 fatty acids || id:met-d-Omega_3 - Type 1 diabetes || id:ebi-a-GCST010681
```

```
presso
```

```
## [[1]]
## [[1]]$`Main MR results`
##        Exposure       MR Analysis Causal Estimate         Sd     T-stat
## 1 beta.exposure               Raw     -0.08165236 0.25068226 -0.3257205
## 2 beta.exposure Outlier-corrected     -0.06468136 0.09022143 -0.7169179
##     P-value
## 1 0.7462924
## 2 0.4779262
##
## [[1]]$`MR-PRESSO results`
## [[1]]$`MR-PRESSO results`$`Global Test`
## [[1]]$`MR-PRESSO results`$`Global Test`$RSSobs
## [1] 883.4384
##
## [[1]]$`MR-PRESSO results`$`Global Test`$Pvalue
## [1] "<0.001"
##
##
## [[1]]$`MR-PRESSO results`$`Outlier Test`
##          RSSobs Pvalue
## 2  2.770897e-04      1
## 3  2.469826e-04      1
## 4  1.059328e-03      1
## 5  4.149295e-03  0.336
## 6  3.800454e-06      1
## 7  1.835356e-03      1
```

```
## 8  2.005984e-03      1
## 9  4.124190e-03      1
## 10 7.541343e-04      1
## 11 7.506686e-04      1
## 12 4.262487e-04      1
## 13 1.629679e-04      1
## 14 1.693763e-02      1
## 16 3.761810e-04      1
## 17 9.719651e-03 <0.042
## 18 3.160818e-02 <0.042
## 20 8.340836e-04      1
## 21 3.411298e-01 <0.042
## 22 3.170492e-05      1
## 23 1.359064e-03      1
## 25 5.798866e-01 <0.042
## 26 4.965379e-04      1
## 27 7.382775e-04      1
## 28 5.033961e-04      1
## 31 2.491462e-03      1
## 32 9.742547e-04      1
## 33 7.555251e-04      1
## 34 9.507179e-04      1
## 35 3.803555e-03      1
## 36 1.975479e-04      1
## 37 1.397190e-09      1
## 38 2.652538e-03      1
## 39 3.124057e-04      1
## 40 3.869657e-06      1
## 42 1.045502e-03      1
## 43 2.464834e-04      1
## 44 1.674381e-03      1
## 45 1.616004e-04      1
## 46 5.081916e-05      1
## 47 9.466071e-06      1
## 48 1.016091e-03      1
## 50 1.365007e-03      1
##
## [[1]]$`MR-PRESSO results`$`Distortion Test`
## [[1]]$`MR-PRESSO results`$`Distortion Test`$`Outliers Indices`
## [1] 15 16 18 21
##
## [[1]]$`MR-PRESSO results`$`Distortion Test`$`Distortion Coefficient`
## beta.exposure
##     -26.23785
##
## [[1]]$`MR-PRESSO results`$`Distortion Test`$Pvalue
## [1] 0.509
##
##
##
##
## attr(,"id.exposure")
## [1] "met-d-Omega_3"
## attr(,"id.outcome")
```

```
## [1] "ebi-a-GCST010681"
## attr(,"exposure")
## [1] "Omega-3 fatty acids || id:met-d-Omega_3"
## attr(,"outcome")
## [1] "Type 1 diabetes || id:ebi-a-GCST010681"
```

CREATE VISUALIZATIONS FOR MR ANALYSES

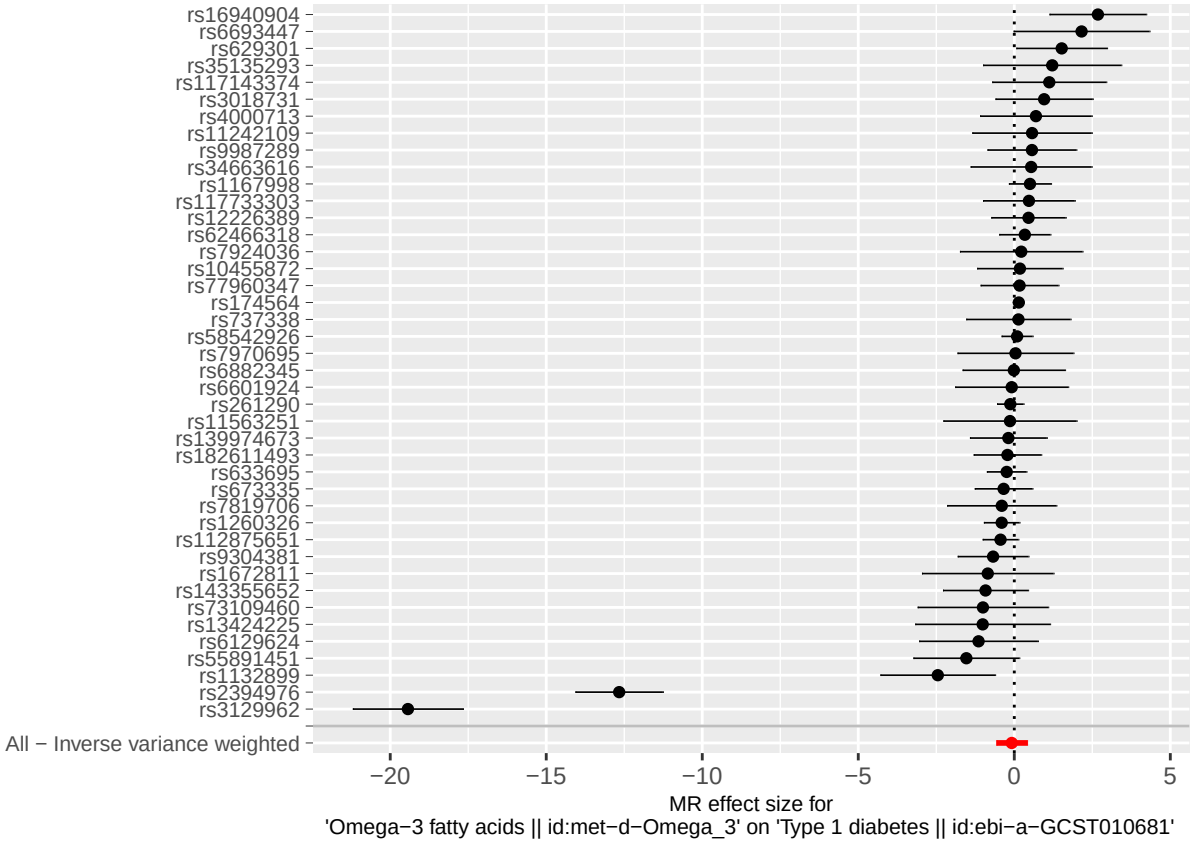
Generate forest plot for main MR single snp analysis

```
p1_om <- mr_forest_plot(MR_ss_om, exponentiate = FALSE)
p1_om
```

```
## $`met-d-Omega_3.ebi-a-GCST010681`
```

```
## Warning: Removed 1 rows containing missing values (`geom_errorbarh()`).
```

```
## Warning: Removed 1 rows containing missing values (`geom_point()`).
```




```
##
## attr(,"split_type")
## [1] "data.frame"
```

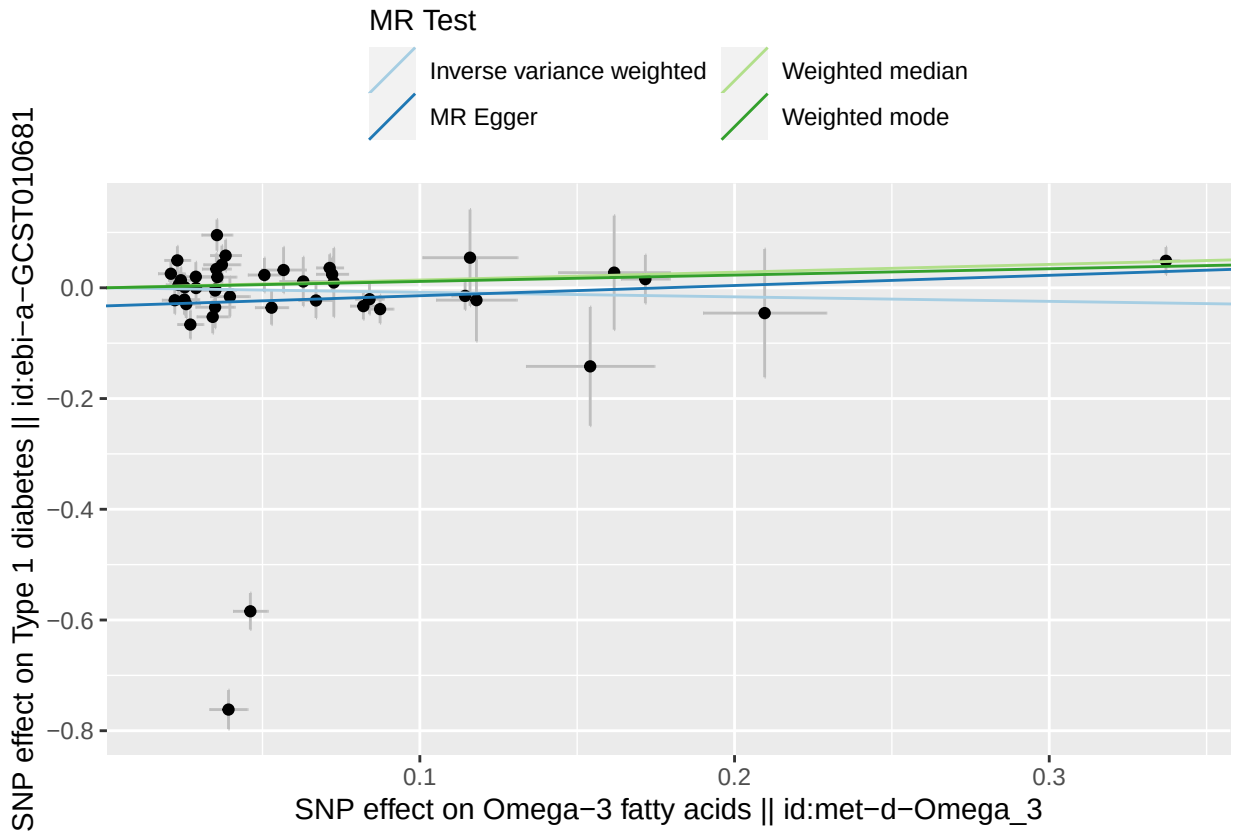
```
## attr(,"split_labels")
##     id.exposure       id.outcome
## 1 met-d-Omega_3 ebi-a-GCST010681
```

Generate scatterplot

Create scatter plot with lines showing the causal estimate for different MR tests. The arguments used by the 'mr_scatter_plot' function are the results from the MR analysis and harmonized data used for that analysis.

```
p2_om <- mr_scatter_plot(mr_res_om, dat_om)
p2_om
```

```
## $`met-d-Omega_3.ebi-a-GCST010681`
```




```
##
## attr(,"split_type")
## [1] "data.frame"
## attr(,"split_labels")
##     id.exposure       id.outcome
## 1 met-d-Omega_3 ebi-a-GCST010681
```

Generate forest plots for main MR and all sensitivity analyses

```
install.packages("forestplot", repos ="https://cran.r-project.org")
```

```
##
## The downloaded binary packages are in
##  /var/folders/2y/z3g4d8r132j6m0_l9skqmw6c0000gp/T//RtmprfdCpX/downloaded_packages
```

```
library(forestplot)
```

```
## Loading required package: grid
```

```
## Loading required package: checkmate
```

```
## Loading required package: abind
```

```
# Create vector for y-axis label names
tabs <- c("MR Analyses", "Main Analysis", "AXP", "AXB","AXBC","AXI","AXL", "AXT2D")

# Odds ratios for each MR method
IVW_ORs <-c(NA,0.92,0.92,0.63,1.00,0.81,0.92,0.92)
MR_Egger_ORs <-c(NA,1.20,1.20,0.95,1.22,1.01,1.20,1.20)
Weighted_median_ORs<-c(NA,1.15,1.15,0.88,1.15,0.90,1.16,1.15)
Weighted_mode_ORs<-c(NA,1.12,1.12,0.88,1.13,0.89,1.13,1.13)

#Lower confidence intervals for each MR method
IVW_LCI<- c(NA,0.56,0.56,0.21,0.62,0.41,0.42,0.55)
MR_Egger_LCI<- c(NA,0.61,0.60,0.13,0.65,0.29,0.46,0.59)
Weighted_median_LCI<- c(NA,1.00,1.00,0.62,1.00,0.68,1.00,1.00)
Weighted_mode_LCI <- c(NA,0.98,0.98,0.62,0.98,0.68,0.98,0.98)

#Upper confidence intervals for each method
IVW_UCI <- c(NA,1.51,1.54,1.84,1.62,1.60,2.02,1.57)
MR_Egger_UCI<- c(NA,2.35,2.38,6.83,2.30,3.55,3.13,2.43)
Weighted_median_UCI<- c(NA,1.32,1.32,1.24,1.32,1.18,1.33,1.33)
Weighted_mode_UCI<- c(NA,1.28,1.28,1.23,1.31,1.18,1.30,1.30)

# Generate forest plot
forestplot(tabs,
           txt_gp=fpTxtGp(ticks = gpar(cex=.8),
                          xlab = gpar(cex=.8),
                          label = gpar(cex=.8)),
           legend=c("IVW","MR-Egger","Weighted median", "Weighted mode"),
           fn.ci_norm=c(fpDrawNormalCI,fpDrawDiamondCI,fpDrawCircleCI,fpDrawPointCI),
           is.summary= c(TRUE,rep(FALSE,7)),
           mean= cbind(IVW_ORs,MR_Egger_ORs,Weighted_median_ORs,Weighted_mode_ORs),
           lower= cbind(IVW_LCI,MR_Egger_LCI,Weighted_median_LCI,Weighted_mode_LCI),
           upper= cbind(IVW_UCI,MR_Egger_UCI,Weighted_median_UCI,Weighted_mode_UCI),
           clip= c(0,7.0),
           lty.ci= c(1,1,1,1),
           lwd.ci= 1,
```

```
        col = fpColors(box=c("blue","darkred","lightgreen","purple")),
        vertices= TRUE,
        xlab= "Odds Ratios for T1D per 1 SD change in omega-3 levels",
        new_page= TRUE,
        boxsize=.1,
        #grid= TRUE
        grid=structure(c(0,1,2,3,4,5,6,7), gp=gpar(lty=2,lwd=1)))
```