

**Appendix 1.** Details of the studies included in the Mendelian randomization analyses.

| Phynotype                                  | GWAS data source                | Sample size                      | Year | Number of SNP |
|--|---------------------------------|----------------------------------|------|---------------|
| Helicobacter pylori infection <sup>a</sup> | EBI                             | 1,058 cases and 3,625 controls   | 2021 | 7,247,045     |
| IDA <sup>b</sup>                           | UK Biobank                      | 2,941 cases and 481,657 controls | 2021 | 9,886,868     |
| HBG <sup>c</sup>                           | A genome-wide meta-analysis     | 408,112 participants             | 2020 | 41,261,840    |
| Iron serum <sup>d</sup>                    | Iceland, FinnGen and UK Biobank | 163,511 participants             | 2021 | 19,689,928    |
| Total iron binding capacity <sup>d</sup>   | Iceland, FinnGen and UK Biobank | 135,430 participants             | 2021 | 19,293,087    |
| Ferritin <sup>d</sup>                      | Iceland, FinnGen and UK Biobank | 246,139 participants             | 2021 | 21,642,116    |
| Transferrin saturation <sup>d</sup>        | Iceland, FinnGen and UK Biobank | 131,471 participants             | 2021 | 19,330,058    |

1: All datasets are of European ethnicity

2: EBI: European Bioinformatic institute; IDA: Iron Deficiency Anemia; HBG: Hemoglobin

3: Web source:

a:<https://gwas.mrcieu.ac.uk/datasets/ieu-b-4905/>

b:<https://www.ebi.ac.uk/gwas/studies/GCST90038659>

c:<https://www.ebi.ac.uk/gwas/studies/GCST90002384>

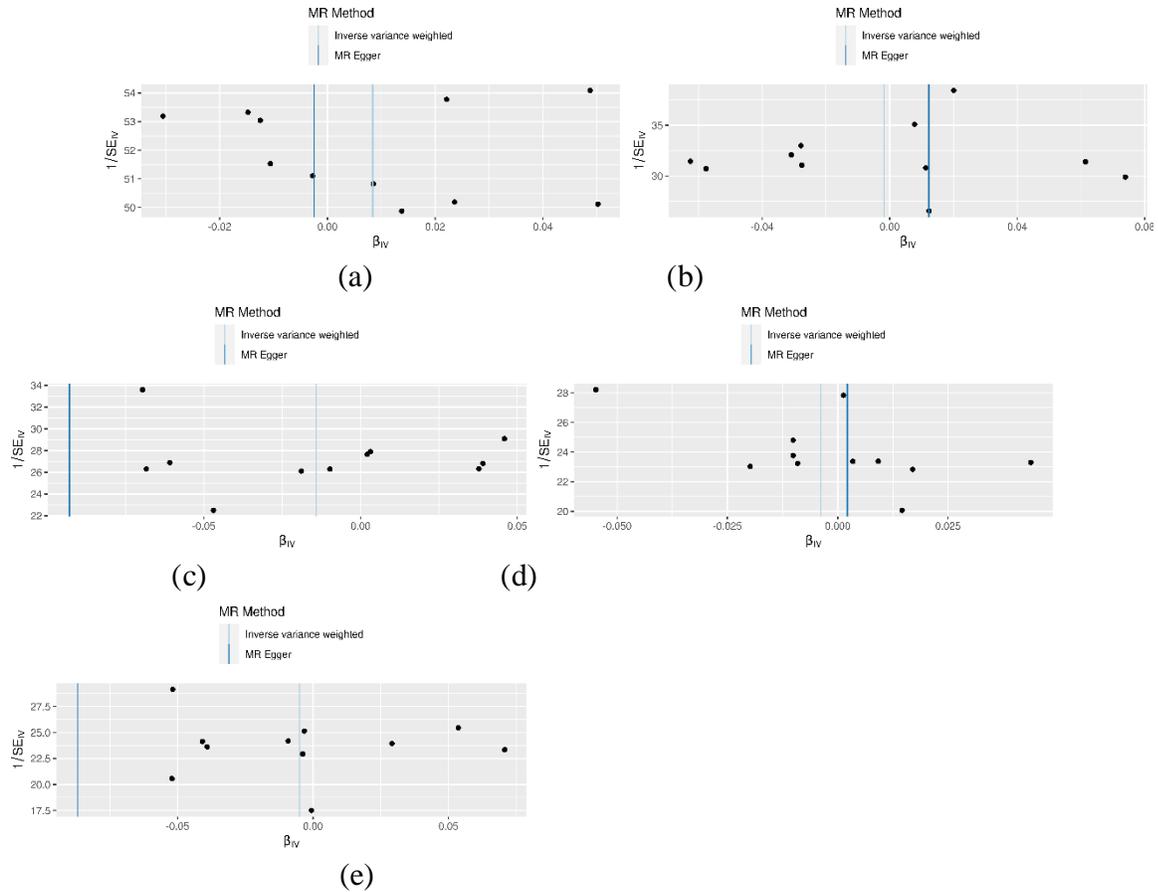
d:<https://www.decode.com/summarydata/>

4.The study includ: Airwave Health Monitoring Study, BioMe™ BioBank Program, Caerphilly Prospective Study, Cardiovascular Health Study, Estonia SNP Chip, Estonia Whole Genome Sequencing, Framingham Heart Study, The Finnish Cardiovascular Study, Genetic Epidemiology Research on Adult Health and Aging , Health2006, Health2008, Health2010, INTERVAL Study, The Multi-Ethnic Study of Atherosclerosis, Montreal Heart Institute Biobank phase1, Montreal Heart Institute Biobank phase2, Million Veteran Program , Rotterdam Study I, Rotterdam Study II, Rotterdam Study III, Study of Helath in Pomerania, Study of Health in Pomerania Trend, UK Biobank European-ancestry, Womens' Health Initiative , The Cardiovascular Risk in Young Finns Study.

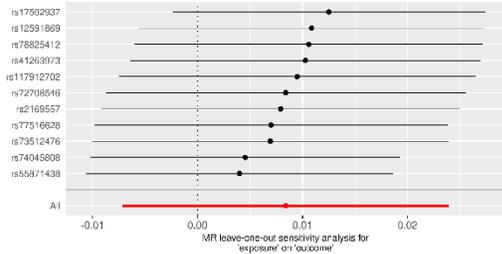
**Appendix 2.** Instrumental SNPs of *H. pylori* infection from EBI and F statistics

| <b>SNP</b>              | <b>effect_al<br/>lele</b> | <b>other_al<br/>lele</b> | <b>C<br/>hr</b> | <b>Pos</b>    | <b>EAF</b>   | <b>BETA</b>  | <b>SE</b>     | <b>P</b>     | <b>F</b>        |
|-------------------------|---------------------------|--------------------------|-----------------|---------------|--------------|--------------|---------------|--------------|-----------------|
| <b>rs412639<br/>73</b>  | A                         | G                        | 1               | 321628<br>10  | 0.033<br>534 | 0.315<br>775 | 0.0672<br>338 | 2.74<br>E-06 | 22.05871<br>308 |
| <b>rs216955<br/>7</b>   | T                         | C                        | 2               | 202449<br>54  | 0.488<br>46  | -<br>0.105   | 0.0230<br>674 | 4.55<br>E-06 | 21.08069<br>108 |
| <b>rs775166<br/>28</b>  | T                         | A                        | 4               | 621256<br>18  | 0.088<br>953 | 0.187<br>87  | 0.0401<br>253 | 2.94<br>E-06 | 21.92190<br>472 |
| <b>rs727085<br/>46</b>  | A                         | G                        | 4               | 170153<br>219 | 0.059<br>115 | -<br>0.229   | 0.0481<br>386 | 1.90<br>E-06 | 22.76694<br>861 |
| <b>rs350305<br/>89*</b> | A                         | G                        | 6               | 326729<br>03  | 0.132<br>05  | -<br>0.175   | 0.0342<br>852 | 3.40<br>E-07 | 26.10185<br>513 |
| <b>rs117912<br/>702</b> | A                         | G                        | 6               | 166062<br>930 | 0.019<br>949 | 0.405<br>025 | 0.0865<br>994 | 3.02<br>E-06 | 21.87428<br>646 |
| <b>rs735124<br/>76</b>  | T                         | G                        | 11              | 865859<br>00  | 0.076<br>735 | 0.212<br>576 | 0.0440<br>791 | 1.47<br>E-06 | 23.25749<br>972 |
| <b>rs175029<br/>37</b>  | T                         | G                        | 13              | 304407<br>40  | 0.020<br>036 | -<br>0.396   | 0.0846<br>646 | 2.89<br>E-06 | 21.95557<br>239 |
| <b>rs740458<br/>08</b>  | T                         | C                        | 14              | 344573<br>96  | 0.107<br>56  | -<br>0.174   | 0.0380<br>12  | 4.49<br>E-06 | 21.10794<br>745 |
| <b>rs558714<br/>38</b>  | C                         | T                        | 15              | 754111<br>20  | 0.039<br>419 | 0.299<br>19  | 0.0647<br>964 | 4.02<br>E-06 | 21.32025<br>487 |
| <b>rs788254<br/>12</b>  | A                         | C                        | 15              | 835126<br>21  | 0.032<br>426 | 0.317<br>81  | 0.0685<br>235 | 3.64<br>E-06 | 21.51077<br>421 |
| <b>rs125918<br/>69</b>  | A                         | C                        | 15              | 966742<br>67  | 0.269<br>81  | -<br>0.128   | 0.0265<br>143 | 1.29<br>E-06 | 23.52273<br>597 |

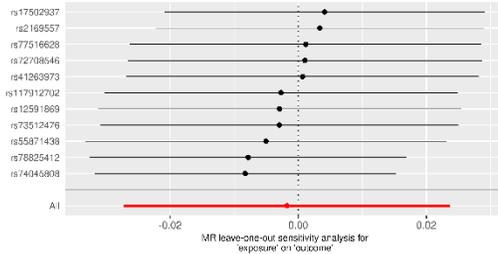
\*Deleted in relation to confounding factors



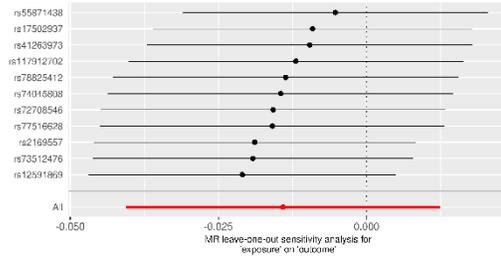
**Appendix 3.** Funnel plots of significant estimates from genetically predicted *Helicobacter pylori* infection on (a) HGB; (b) Ferritin; (c) Iron; (d) TIBC; and (e) TSAT.



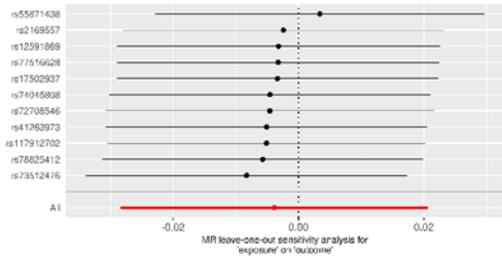
(a)



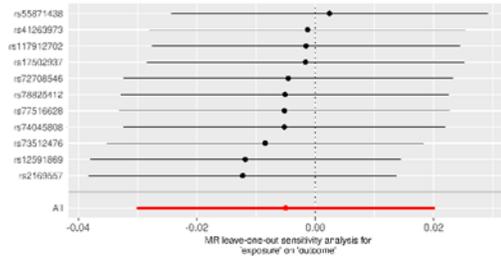
(b)



(c)

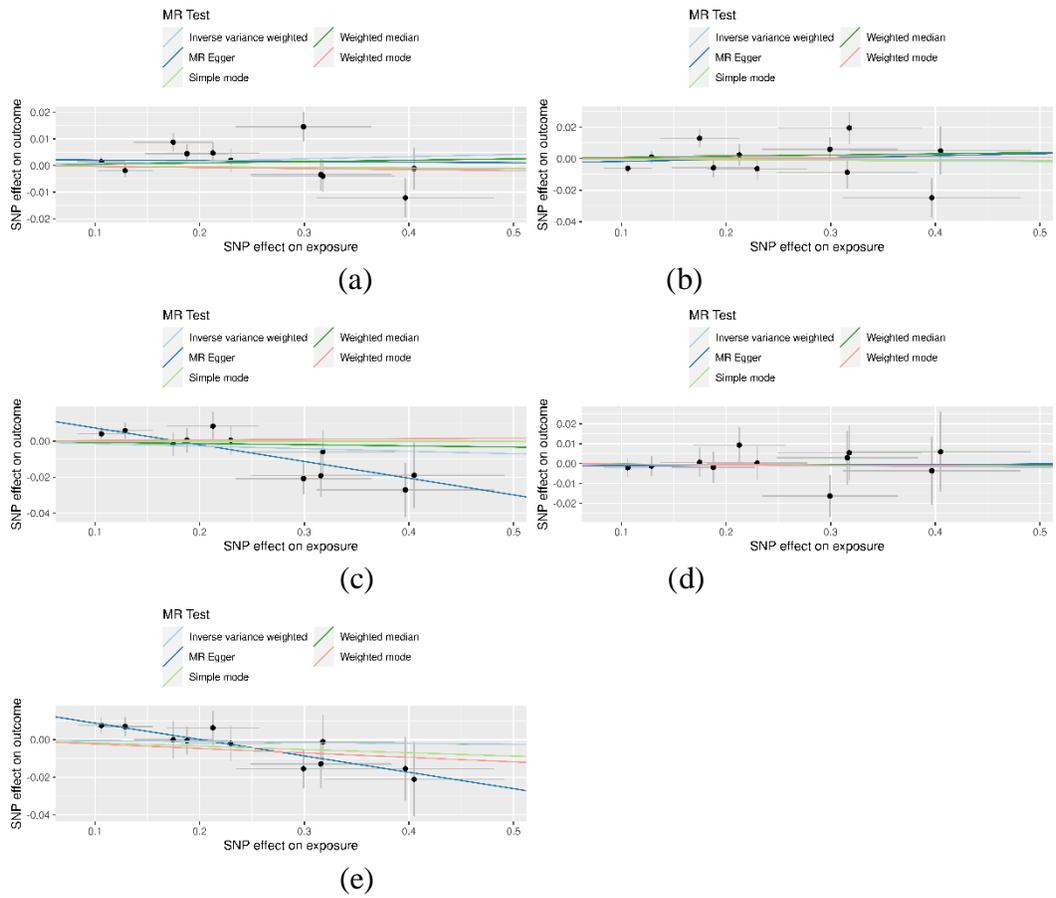


(d)



(e)

**Appendix 4.** Leave-one-out plots of significant estimates from genetically predicted *Helicobacter pylori* infection on (a) HGB; (b) Ferritin; (c) Iron; (d) TIBC; and (e) TSAT.



**Appendix 5.** Scatter plots of significant estimates from genetically predicted *Helicobacter pylori* infection on (a) HGB; (b) Ferritin; (c) Iron; (d) TIBC; and (e) TSAT.