**Supplementary files**

**Association between** **hemostatic profile and migraine: a Mendelian randomization analysis**

**Short title for the running head:** Hemostatic profile and migraine: an MR study

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# **Supplementary Table 1** **Detailed information for the genome-wide association study summary statistics used in the current study.**

|  |  |  |  |
| --- | --- | --- | --- |
| Trait | PMID | Title | N |
| Migraine, MA, MO | 27322543 | Meta-analysis of 375,000 individuals identifies 38 susceptibility loci for migraine. | 59,674 cases and 316,078 controls |
| aPTT | 22703881 | Genetic Associations for Activated Partial Thromboplastin Time and Prothrombin Time, their Gene Expression Profiles, and Risk of Coronary Artery Disease | 11,851 |
| D-dimer | 21502573 | Genetic predictors of fibrin D-dimer levels in healthy adults | 21,052 |
| Fibrinogen | 26561523 | A meta-analysis of 120 246 individuals identifies 18 new loci for fibrinogen concentration | 120,246 |
| FVII | 30642921 | A genome-wide association study identifies new loci for factor VII and implicates factor VII in ischemic stroke etiology | 20,014 |
| FVIII | 30586737 | Genome-Wide Association Transethnic Meta-Analyses Identifies Novel Associations Regulating Coagulation Factor VIII and von Willebrand Factor Plasma Levels | 25,897 |
| FXI | 28053049 | Genome-wide association study with additional genetic and post-transcriptional analyses reveals novel regulators of plasma factor XI levels | 16,169 |
| VWF | 30586737 | Genome-Wide Association Transethnic Meta-Analyses Identifies Novel Associations Regulating Coagulation Factor VIII and von Willebrand Factor Plasma Levels | 42,379 |
| PT/INR | 22703881 | Genetic Associations for Activated Partial Thromboplastin Time and Prothrombin Time, their Gene Expression Profiles, and Risk of Coronary Artery Disease | 3,569 |
| PAI-1 | 22990020 | Genome-wide association study for circulating levels of PAI-1 provides novel insights into its regulation | 19,599 |
| tPA | 24578379 | Genome-Wide Association Study for Circulating Tissue Plasminogen Activator (tPA) Levels and Functional Follow-up Implicates Endothelial *STXBP5* and *STX2* | 26,929 |
| ADSGEGDFXAEGGGVR\* and ADpSGEGDFXAEGGGVR\* | 24816252 | An atlas of genetic influences on human blood metabolites | 7,824 |

Abbreviations: MA: migraine with aura; MO: migraine without aura; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A.

# **Supplementary Table 2** **Distribution of the instruments for all the hemostatic profiles used in the current study.**

| SNP | CHR | BP | A1 | A2 | freq | aPTT | D-dimer | fibrinogen | FVII | FVIII | FXI | PT/INR | PAI-1 | tPA | ADSGEGDFXAEGGGVR\* | ADpSGEGDFXAEGGGVR\* | VWF |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| rs1892534 | 1 | 66105944 | T | C | 0.39 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2794475 | 1 | 95025193 | T | G | 0.17 | - | Yes | - | - | - | - | - | - | - | - | - | - |
| rs12029080 | 1 | 95053353 | T | G | 0.70 | - | Yes | - | - | - | - | - | - | - | - | - | - |
| rs12083537 | 1 | 154381103 | A | G | 0.81 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2228145 | 1 | 154426970 | A | C | 0.65 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs9426829 | 1 | 154592201 | T | C | 0.53 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6687813 | 1 | 169477574 | A | C | 0.07 | - | Yes | - | - | - | - | - | - | - | - | - | - |
| rs1557570 | 1 | 169507844 | T | G | 0.32 | - | Yes | - | - | - | - | - | - | - | - | - | - |
| rs6028 | 1 | 169551682 | T | C | 0.70 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs12239046 | 1 | 247601595 | T | C | 0.36 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs4925671 | 1 | 247622874 | T | C | 0.28 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6542680 | 2 | 3640142 | T | C | 0.78 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs1260326 | 2 | 27730940 | T | C | 0.41 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs780094 | 2 | 27741237 | T | C | 0.42 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs1558643 | 2 | 102731691 | T | C | 0.43 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs11897907 | 2 | 113727061 | T | C | 0.50 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs4145013 | 2 | 113830688 | A | G | 0.69 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6734238 | 2 | 113841030 | A | G | 0.59 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs766271 | 2 | 135667131 | T | C | 0.55 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs715 | 2 | 211543055 | T | C | 0.71 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs59104589 | 2 | 242237902 | T | C | 0.34 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs62246343 | 3 | 9543642 | T | C | 0.13 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs11128603 | 3 | 12385828 | A | G | 0.88 | - | - | - | - | - | - | - | Yes | - | - | - | - |
| rs6775517 | 3 | 58358967 | T | G | 0.38 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs2717219 | 3 | 122868438 | A | G | 0.65 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs66505225 | 3 | 129241528 | T | C | 0.11 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs7628146 | 3 | 135998453 | T | G | 0.24 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs1868146 | 3 | 186221871 | A | G | 0.11 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs1071592 | 3 | 186338425 | A | C | 0.24 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs35799453 | 3 | 186338540 | T | C | 0.98 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs78954048 | 3 | 186383709 | A | G | 0.97 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs9898 | 3 | 186390627 | T | C | 0.33 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs2378117 | 3 | 186422256 | A | G | 0.88 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs55746367 | 3 | 186429140 | A | G | 0.18 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs5030103 | 3 | 186448928 | T | C | 0.98 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs35477316 | 3 | 186451584 | T | C | 0.05 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs5030094 | 3 | 186461158 | T | C | 0.99 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs266767 | 3 | 186464731 | T | G | 0.85 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs111444674 | 3 | 186476193 | A | G | 0.11 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs266714 | 3 | 186498925 | T | C | 0.21 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs266771 | 3 | 186545338 | A | G | 0.62 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs822387 | 3 | 186556037 | T | C | 0.92 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs75050741 | 3 | 186589499 | T | C | 0.85 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs59950280 | 4 | 3452345 | A | G | 0.31 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6532796 | 4 | 100042242 | A | G | 0.30 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs6855246 | 4 | 103112470 | A | G | 0.91 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs4696532 | 4 | 155072373 | T | C | 0.22 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs78997818 | 4 | 155215322 | A | C | 0.97 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs1352713 | 4 | 155243811 | T | G | 0.02 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6811038 | 4 | 155299346 | T | C | 0.69 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs13133450 | 4 | 155369941 | A | G | 0.04 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs73856419 | 4 | 155432364 | T | C | 0.19 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs80325712 | 4 | 155445115 | T | G | 0.14 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs72681206 | 4 | 155478278 | A | G | 0.78 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2227432 | 4 | 155485742 | T | C | 0.99 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs13109457 | 4 | 155514879 | A | G | 0.24 | - | Yes | - | - | - | - | - | - | - | - | - | - |
| rs35147053 | 4 | 155517842 | A | G | 0.76 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs13137121 | 4 | 155548453 | A | G | 0.58 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs4696598 | 4 | 155553408 | T | C | 0.47 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs75357674 | 4 | 186990842 | T | G | 0.95 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs10866290 | 4 | 187114479 | T | C | 0.67 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs34852777 | 4 | 187139062 | T | C | 0.86 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs4253236 | 4 | 187148071 | T | C | 0.34 | - | - | - | - | - | - | - | - | - | Yes | - | - |
| rs4253325 | 4 | 187178473 | A | G | 0.12 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs4253408 | 4 | 187193858 | A | G | 0.08 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs4253414 | 4 | 187196853 | T | C | 0.97 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs7687352 | 4 | 187239747 | A | G | 0.51 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs7688348 | 4 | 187247239 | A | G | 0.97 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs78134251 | 4 | 187263919 | T | G | 0.03 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs75440104 | 4 | 187267791 | T | C | 0.93 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs4456995 | 4 | 187270966 | T | G | 0.84 | - | - | - | - | - | Yes | - | - | - | - | - | - |
| rs12517661 | 5 | 71745716 | T | C | 0.87 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs548630 | 5 | 72406659 | A | C | 0.45 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs114283007 | 5 | 131777682 | A | G | 0.04 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2057655 | 5 | 131807624 | A | G | 0.21 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2070729 | 5 | 131819921 | A | C | 0.47 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs1295683 | 5 | 131998876 | A | G | 0.12 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs11954311 | 5 | 176554850 | A | G | 0.02 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs13159114 | 5 | 176661808 | T | C | 0.10 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs8119 | 5 | 176758786 | T | C | 0.03 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs11749830 | 5 | 176766547 | A | G | 0.34 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs2545801 | 5 | 176841339 | T | C | 0.23 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs2731672 | 5 | 176842474 | T | C | 0.23 | - | - | - | - | - | - | - | - | - | Yes | - | - |
| rs2731664 | 5 | 176859848 | A | C | 0.50 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs1165165 | 6 | 25862466 | T | C | 0.23 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs78593564 | 6 | 31906828 | A | G | 0.02 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs3798228 | 6 | 116321156 | T | C | 0.59 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs9390460 | 6 | 147694334 | T | C | 0.48 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs9390462 | 6 | 147701221 | A | G | 0.44 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs7765526 | 6 | 147713764 | A | G | 0.48 | - | - | - | - | - | - | - | - | Yes | - | - | - |
| rs2177652 | 7 | 17894933 | A | G | 0.45 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs71520386 | 7 | 22853521 | T | C | 0.18 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs498475 | 7 | 28256240 | A | G | 0.64 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs2700938 | 7 | 36085142 | T | C | 0.62 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs35866503 | 7 | 73005776 | T | C | 0.19 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs6976053 | 7 | 100512119 | T | C | 0.46 | - | - | - | - | - | - | - | Yes | - | - | - | - |
| rs2227631 | 7 | 100769538 | A | G | 0.60 | - | - | - | - | - | - | - | Yes | - | - | - | - |
| rs35512856 | 7 | 150294291 | T | C | 0.78 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs35464700 | 7 | 150308090 | A | G | 0.78 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs7012814 | 8 | 9173358 | A | G | 0.47 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs10104221 | 8 | 27791780 | T | G | 0.60 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs4276643 | 8 | 27803599 | T | C | 0.68 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs62496810 | 8 | 27815481 | T | C | 0.04 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs11780263 | 8 | 27823832 | A | G | 0.19 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs3136739 | 8 | 42205080 | A | G | 0.96 | - | - | - | - | - | - | - | - | Yes | - | - | - |
| rs7010330 | 8 | 145036615 | T | C | 0.59 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs13291088 | 9 | 13929919 | T | G | 0.14 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs3138493 | 9 | 92219260 | T | C | 0.47 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs10985344 | 9 | 124416940 | A | G | 0.22 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs10901192 | 9 | 135480259 | T | C | 0.18 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs191197998 | 9 | 135711405 | A | G | 0.01 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs615667 | 9 | 135863485 | A | G | 0.62 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs77643237 | 9 | 135889210 | A | G | 0.06 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs117405640 | 9 | 135891267 | A | G | 0.97 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs4962090 | 9 | 135903038 | A | G | 0.51 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs3761824 | 9 | 135985796 | T | C | 0.27 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs671050 | 9 | 136001966 | T | C | 0.29 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs2073927 | 9 | 136031346 | A | G | 0.49 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs4962095 | 9 | 136031751 | T | G | 0.51 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs117804300 | 9 | 136034364 | A | G | 0.03 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs7034230 | 9 | 136043357 | T | C | 0.67 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs7033553 | 9 | 136043471 | A | G | 0.67 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs4962110 | 9 | 136105687 | A | G | 0.08 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs35664240 | 9 | 136117495 | T | C | 0.11 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs8176744 | 9 | 136131350 | T | G | 0.04 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs687621 | 9 | 136137065 | A | G | 0.63 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs687289 | 9 | 136137106 | A | G | 0.37 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs66697526 | 9 | 136144593 | T | G | 0.03 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs491626 | 9 | 136144873 | T | C | 0.37 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs651007 | 9 | 136153875 | T | C | 0.22 | - | - | - | - | - | - | - | - | - | - | Yes | - |
| rs55988407 | 9 | 136156064 | A | G | 0.04 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs558240 | 9 | 136157133 | A | G | 0.39 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs7859913 | 9 | 136171550 | A | C | 0.91 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs4962127 | 9 | 136178277 | A | G | 0.04 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs590488 | 9 | 136178951 | T | C | 0.47 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs551924 | 9 | 136181539 | A | G | 0.28 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs554710 | 9 | 136181848 | T | C | 0.70 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs150148506 | 9 | 136209558 | A | G | 0.01 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs117509822 | 9 | 136240909 | A | G | 0.95 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs3124747 | 9 | 136268084 | A | G | 0.31 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs36220944 | 9 | 136303993 | T | C | 0.97 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs117164445 | 9 | 136317767 | T | C | 0.02 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs3124758 | 9 | 136344853 | A | G | 0.16 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs79135817 | 9 | 136349643 | T | C | 0.13 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs4962156 | 9 | 136350478 | A | C | 0.87 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs112151537 | 9 | 136455785 | T | C | 0.02 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs75505227 | 9 | 136466678 | T | G | 0.95 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs3025336 | 9 | 136469322 | T | G | 0.95 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs10822168 | 10 | 65165184 | A | G | 0.49 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs10761778 | 10 | 65273782 | A | G | 0.51 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs73362918 | 10 | 122853958 | T | G | 0.92 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6486122 | 11 | 13361524 | T | C | 0.70 | - | - | - | - | - | - | - | Yes | - | - | - | - |
| rs7934094 | 11 | 43505707 | T | G | 0.81 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs7946992 | 11 | 59944810 | T | C | 0.60 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs72920867 | 11 | 60005424 | T | C | 0.60 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs1149616 | 11 | 76498369 | T | C | 0.15 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs35458154 | 11 | 126296825 | A | G | 0.02 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs12423482 | 12 | 6070845 | A | G | 0.95 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs34230288 | 12 | 6103094 | A | C | 0.02 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs2854871 | 12 | 6133079 | T | C | 0.90 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs80336293 | 12 | 6142205 | T | C | 0.04 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs216324 | 12 | 6145225 | A | G | 0.09 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs216335 | 12 | 6148005 | T | C | 0.09 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs2283335 | 12 | 6157394 | T | C | 0.63 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs112814955 | 12 | 6225931 | A | G | 0.07 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs4762707 | 12 | 21715049 | A | G | 0.75 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2684898 | 12 | 51046825 | T | C | 0.37 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs10467022 | 12 | 103813706 | T | C | 0.87 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs11111614 | 12 | 103892504 | T | C | 0.91 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs2723889 | 12 | 104000470 | T | C | 0.32 | - | - | - | - | Yes | - | - | - | - | - | - | Yes |
| rs1032450 | 12 | 104046601 | A | G | 0.84 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs703632 | 12 | 104051407 | A | G | 0.60 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs73192004 | 12 | 104127353 | A | G | 0.05 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs35102665 | 12 | 104136289 | A | G | 0.02 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs3751198 | 12 | 104147207 | A | G | 0.37 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs7296626 | 12 | 104149251 | T | C | 0.94 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs4981022 | 12 | 104149874 | A | G | 0.69 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs10774625 | 12 | 111910219 | A | G | 0.48 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs6486599 | 12 | 131287011 | T | C | 0.34 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs7301826 | 12 | 131291101 | T | C | 0.56 | - | - | - | - | - | - | - | - | Yes | - | - | - |
| rs35786512 | 13 | 113669874 | A | G | 0.30 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs117989138 | 13 | 113697671 | A | G | 0.01 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs116980211 | 13 | 113717241 | A | G | 0.03 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs9549655 | 13 | 113725367 | A | G | 0.15 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs912196 | 13 | 113733335 | T | C | 0.35 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs72663544 | 13 | 113739126 | A | G | 0.08 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs553702 | 13 | 113744669 | A | G | 0.11 | - | - | - | - | - | - | Yes | - | - | - | - | - |
| rs3093230 | 13 | 113757968 | A | G | 0.22 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs561241 | 13 | 113760034 | T | C | 0.88 | - | - | - | - | - | - | Yes | - | - | - | - | - |
| rs1475931 | 13 | 113763926 | T | G | 0.22 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs569557 | 13 | 113769917 | A | G | 0.12 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs3211719 | 13 | 113777509 | A | G | 0.77 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs3213001 | 13 | 113784540 | A | C | 0.92 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs3211756 | 13 | 113789282 | T | C | 0.04 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs3213004 | 13 | 113796138 | A | G | 0.05 | - | - | - | - | - | - | Yes | - | - | - | - | - |
| rs34201467 | 13 | 113830329 | T | C | 0.81 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs9549731 | 13 | 113944627 | T | C | 0.16 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs34264706 | 13 | 113992885 | A | G | 0.10 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs59416814 | 13 | 114006151 | A | G | 0.95 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs1274953 | 14 | 69297212 | A | G | 0.74 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs61988257 | 14 | 92217670 | A | G | 0.32 | - | - | - | - | Yes | - | - | - | - | - | - | - |
| rs2402074 | 14 | 92293518 | A | G | 0.45 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs28364388 | 15 | 42676437 | A | G | 0.13 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs10467994 | 15 | 51008687 | T | C | 0.67 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs141272690 | 15 | 51188758 | T | C | 0.95 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs11637089 | 15 | 62458184 | T | C | 0.40 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs2469184 | 15 | 87191977 | A | G | 0.46 | Yes | - | - | - | - | - | - | - | - | - | - | - |
| rs8062405 | 16 | 28837906 | A | G | 0.67 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs62047987 | 16 | 53163796 | T | C | 0.73 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2278027 | 16 | 72051369 | A | G | 0.59 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs9903204 | 17 | 40288062 | A | G | 0.24 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2277998 | 19 | 7831628 | A | G | 0.30 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs601338 | 19 | 49206674 | A | G | 0.44 | - | - | - | - | - | - | - | - | - | - | Yes | - |
| rs73058052 | 19 | 50099422 | T | C | 0.17 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs2295888 | 20 | 33722863 | A | G | 0.91 | - | - | - | - | - | - | Yes | - | - | - | - | - |
| rs112928119 | 20 | 33726451 | T | C | 0.23 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs11907011 | 20 | 33767770 | T | C | 0.09 | - | - | - | Yes | - | - | - | - | - | - | - | - |
| rs1800961 | 20 | 43042364 | T | C | 0.04 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs9808651 | 21 | 40466468 | A | G | 0.26 | - | - | Yes | - | - | - | - | - | - | - | - | - |
| rs5757680 | 22 | 39844793 | T | C | 0.28 | - | - | - | - | - | - | - | - | - | - | - | Yes |
| rs68174505 | 22 | 51108072 | A | G | 0.22 | - | - | Yes | - | - | - | - | - | - | - | - | - |

Abbreviations: CHR: chromosome; BP: position based on build37; A1:allele 1; A2: Allele 2; freq: allele 1 frequency; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A. SNPS highlighted with yellow: instruments within ABO gene; . SNPS highlighted with yellow and green: instruments within 200kb of ABO gene.

# **Supplementary Table 3** **Instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO).**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Instrumental estimate** | **se** | **OR** | **95%CI** | ***P*** | **nsnp** | **global\_heidi\_outlier** |
| **aPTT** | | | | | | | |
| Anymigraine | -0.02 | 0.01 | 0.98 | 0.96, 1.00 | 0.01 | 18 | 0.18 |
| MA | -0.07 | 0.03 | 0.93 | 0.87, 1.00 | 0.02 | 19 | 0.14 |
| MO | 0.00 | 0.02 | 1.00 | 0.96, 1.05 | 0.96 | 17 | 0.65 |
| **D-dimer** † | | | | | | | |
| Anymigraine | 0.06 | 0.04 | 1.06 | 0.99, 1.14 | 0.11 | 5 |  |
| MA | 0.09 | 0.13 | 1.10 | 0.85, 1.41 | 0.48 | 5 |  |
| MO | -0.04 | 0.10 | 0.96 | 0.79, 1.18 | 0.74 | 5 |  |
| **Fibrinogen** | | | | | | | |
| Anymigraine | -0.08 | 0.03 | 0.93 | 0.87, 0.98 | 9.68E-03 | 58 | 0.09 |
| MA | -0.27 | 0.09 | 0.76 | 0.64, 0.91 | 2.32E-03 | 63 | 0.52 |
| MO | 0.01 | 0.08 | 1.01 | 0.86, 1.18 | 0.91 | 63 | 0.19 |
| **FVII** | | | | | | | |
| Anymigraine | 0.02 | 0.01 | 1.02 | 1.00, 1.04 | 0.11 | 23 | 0.06 |
| MA | 0.05 | 0.04 | 1.05 | 0.98, 1.13 | 0.20 | 25 | 0.12 |
| MO | 0.00 | 0.03 | 1.00 | 0.94, 1.07 | 0.91 | 25 | 0.81 |
| **FVIII** | | | | | | | |
| Anymigraine | 0.05 | 0.01 | 1.05 | 1.03, 1.08 | 6.08E-05 | 31 | 0.32 |
| MA | 0.12 | 0.04 | 1.13 | 1.05, 1.22 | 1.74E-03 | 31 | 0.98 |
| MO | 0.04 | 0.03 | 1.04 | 0.97, 1.11 | 0.27 | 31 | 0.96 |
| **FXI** | | | | | | | |
| Anymigraine | 0.03 | 0.02 | 1.03 | 0.99, 1.07 | 0.18 | 20 | 0.47 |
| MA | -0.05 | 0.07 | 0.95 | 0.83, 1.09 | 0.50 | 20 | 0.61 |
| MO | -0.06 | 0.06 | 0.94 | 0.84, 1.06 | 0.33 | 20 | 0.19 |
| **vWF** | | | | | | | |
| Anymigraine | 0.05 | 0.01 | 1.05 | 1.03, 1.08 | 2.25E-06 | 55 | 0.18 |
| MA | 0.11 | 0.03 | 1.12 | 1.05, 1.20 | 7.98E-04 | 55 | 0.50 |
| MO | 0.00 | 0.03 | 1.00 | 0.95, 1.06 | 0.93 | 55 | 0.89 |
| **PT/INR** | | | | | | | |
| Anymigraine | -0.01 | 0.02 | 0.99 | 0.96, 1.03 | 0.76 | 5 |  |
| MA | -0.01 | 0.06 | 0.99 | 0.87, 1.11 | 0.82 | 5 |  |
| MO | 0.03 | 0.04 | 1.03 | 0.95, 1.12 | 0.44 | 5 |  |
| **PAI-1** † | | | | | | | |
| Anymigraine | -0.07 | 0.05 | 0.93 | 0.84, 1.03 | 0.17 | 4 |  |
| MA | -0.08 | 0.15 | 0.93 | 0.68, 1.25 | 0.62 | 4 |  |
| MO | 0.01 | 0.15 | 1.01 | 0.76, 1.34 | 0.93 | 4 |  |
| **tPA** † | | | | | | | |
| Anymigraine | 0.14 | 0.15 | 1.15 | 0.86, 1.55 | 0.34 | 3 |  |
| MA | 0.48 | 0.44 | 1.61 | 0.67, 3.84 | 0.29 | 3 |  |
| MO | 0.09 | 0.18 | 1.10 | 0.77, 1.57 | 0.61 | 3 |  |
| **ADSGEGDFXAEGGGVR\* (fibrinogen A-alpha)** † | | | | | | | |
| Anymigraine | 0.03 | 0.04 | 1.03 | 0.98, 1.08 | 0.26 | 2 |  |
| MA | -0.01 | 0.03 | 0.99 | 0.88, 1.11 | 0.87 | 2 |  |
| MO | 0.03 | 0.06 | 1.03 | 0.93, 1.14 | 0.59 | 2 |  |
| **ADpSGEGDFXAEGGGVR\* (fibrinogen peptide A phosphorylated)** † | | | | | | | |
| Anymigraine | 0.12 | 0.03 | 1.13 | 1.07, 1.19 | 5.44E-06 | 2 |  |
| MA | 0.20 | 0.03 | 1.22 | 1.01, 1.48 | 0.04 | 2 |  |
| MO | -0.02 | 0.10 | 0.98 | 0.84, 1.14 | 0.77 | 2 |  |

Abbreviations: MA: migraine with aura; MO: migraine without aura; OR: odds ratio; CI: confidence interval; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A.

All the analyses were conducted using Generalized Summary-data-based Mendelian Randomization (GSMR) except for D-dimer, PT/INR, PAI-1, tPA, fibrinopeptide A, and phosphorylated fibrinopeptide A, which were estimated using inverse-variance weighted (IVW) MR implemented in the R package TwoSampleMR due to limited number of instruments (less than 10).

All the instrumental estimates were interpreted as the odds ratio of per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided.

# **Supplementary Table 4** **Instrumental estimates of migraine and migraine without aura (MO) with hemostatic profiles.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure** | **Outcome** | **Causal Estimate** | **se** | ***P*** |
| **Anymigraine** | **aPTT** | -0.04 | 0.08 | 0.43 |
| **d-dimer** | 0.01 | 0.01 | 0.45 |
| **Fibrinogen** | 0.00 | 0.00 | 0.64 |
| **FVII** | 0.00 | 0.00 | 0.82 |
| **FVIII** | -0.01 | 0.00 | 0.21 |
| **FXI** | 0.01 | 0.00 | 0.41 |
| **PT/INR** | 0.00 | 0.00 | 0.38 |
| **VWF** | -0.01 | 0.00 | 0.15 |
| **PAI-1** | 0.00 | 0.03 | 0.95 |
| **tPA** | 0.00 | 0.01 | 0.80 |
| **ADSGEGDFXAEGGGVR\* (fibrinogen A-alpha)** | 0.00 | 0.00 | 0.85 |
| **ADpSGEGDFXAEGGGVR\* (fibrinogen peptide A phosphorylated)** | 0.02 | 0.00 | 0.30 |
| **MO** † | **aPTT** | -0.02 | 0.08 | 0.74 |
| **d-dimer** | 0.00 | 0.01 | 0.69 |
| **Fibrinogen** | 0.00 | 0.00 | 0.53 |
| **FVII** | -0.01 | 0.00 | 0.27 |
| **FVIII** | -0.02 | 0.00 | 0.04 |
| **FXI** | 0.00 | 0.00 | 0.83 |
| **PT/INR** | 0.00 | 0.00 | 0.70 |
| **VWF** | -0.01 | 0.00 | 0.18 |
| **PAI-1** | 0.01 | 0.03 | 0.71 |
| **tPA** | 0.00 | 0.01 | 0.68 |
| **ADSGEGDFXAEGGGVR\* (fibrinogen A-alpha)** | -0.01 | 0.00 | 0.48 |
| **ADpSGEGDFXAEGGGVR\* (fibrinogen peptide A phosphorylated)** | -0.02 | 0.00 | 0.41 |

Abbreviations: MO: migraine without aura; OR: odds ratio; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A.

†All the analyses for migraine without aura were conducted using inverse-variance weighted (IVW) MR implemented in the R package TwoSampleMR due to limited number of instruments (less than 10).

As migraine is a binary variable, we interpreted the reverse causal estimates as the average change in hemostatic factors per doubling (2-fold increase) in the odds of migraine, which could be obtained by multiplying the reverse causal estimate by 0.693 (loge2). *P* values are two-sided.

# **Supplementary Table 5** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) using MR-PRESSO.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **MR\_PRESSO** | | | | | | |
| **aPTT** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| **Anymigraine** | **-0.03** | **0.01** | **0.98** | **0.96, 0.99** | **-2.48** | **0.02** |
| MA | -0.06 | 0.03 | 0.94 | 0.88, 1.00 | -1.90 | 0.07 |
| MO | 0.01 | 0.02 | 1.00 | 0.96, 1.05 | 0.17 | 0.87 |
| **D-dimer** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | 0.06 | 0.04 | 1.06 | 0.99, 1.14 | 1.61 | 0.18 |
| MA | 0.09 | 0.13 | 1.09 | 0.85, 1.41 | 0.70 | 0.52 |
| MO | -0.04 | 0.10 | 0.97 | 0.79, 1.18 | -0.34 | 0.75 |
| **fibrinogen** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | -0.06 | 0.03 | 0.94 | 0.88, 1.01 | -1.78 | 0.08 |
| **MA** | **-0.25** | **0.08** | **0.78** | **0.66, 0.92** | **-2.90** | **0.01** |
| MO | 0.01 | 0.08 | 1.01 | 0.86, 1.18 | 0.09 | 0.93 |
| **FVII** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | 0.01 | 0.01 | 1.01 | 0.98, 1.03 | 0.51 | 0.61 |
| MA | 0.03 | 0.04 | 1.03 | 0.95, 1.11 | 0.74 | 0.47 |
| MO | 0.00 | 0.03 | 1.00 | 0.95, 1.05 | -0.03 | 0.98 |
| **FVIII** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| **Anymigraine** | **0.05** | **0.01** | **1.05** | **1.04, 1.08** | **4.27** | **1.81E-04** |
| **MA** | **0.12** | **0.03** | **1.13** | **1.10, 1.19** | **4.76** | **4.52E-05** |
| MO | 0.04 | 0.02 | 1.04 | 1.01, 1.09 | 1.44 | 0.16 |
| **FXI** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | 0.03 | 0.02 | 1.03 | 0.99, 1.08 | 1.46 | 0.16 |
| MA | -0.06 | 0.06 | 0.95 | 0.83, 1.07 | -0.86 | 0.40 |
| MO | -0.06 | 0.07 | 0.94 | 0.82, 1.07 | -0.95 | 0.36 |
| **VWF** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| **Anymigraine** | **0.05** | **0.01** | **1.05** | **1.03, 1.07** | **4.75** | **1.51E-05** |
| **MA** | **0.11** | **0.03** | **1.12** | **1.06, 1.19** | **3.85** | **3.11E-04** |
| MO | -0.00 | 0.02 | 1.00 | 0.96, 1.04 | -0.06 | 0.95 |
| **PT/INR** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | -0.01 | 0.02 | 0.99 | 0.95, 1.04 | -0.28 | 0.80 |
| MA | -0.03 | 0.07 | 0.97 | 0.85, 1.11 | -0.45 | 0.68 |
| MO | 0.06 | 0.01 | 1.06 | 1.03, 1.08 | 4.44 | 0.02 |
| **PAI-1** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | -0.07 | 0.04 | 0.93 | 0.87, 1.00 | -1.91 | 0.15 |
| MA | -0.08 | 0.11 | 0.93 | 0.75, 1.14 | -0.71 | 0.53 |
| MO | 0.01 | 0.14 | 1.01 | 0.76, 1.34 | 0.08 | 0.94 |
| **tPA** | | | | | | |
| Outcome | Causal Estimate | Sd | OR | 95%CI | T-stat | P-value |
| Anymigraine | 0.14 | 0.15 | 1.15 | 0.86, 1.55 |  | 0.33 |
| MA | 0.47 | 0.44 | 1.61 | 0.67, 3.84 |  | 0.29 |
| MO | 0.09 | 0.19 | 1.10 | 0.76, 1.58 |  | 0.61 |

Abbreviations: MR-PRESSO: Mendelian Randomization pleiotropy residual sum and outlier test; OR: odds ratio; MA: migraine with aura; MO: migraine without aura; CI: confidence interval; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A.

All the instrumental estimates were interpreted as the odds ratio of per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided.

# **Supplementary Table 6** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) using IVW, simple median, weighted median, and MR-Egger.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | IVW | | |  | Simple Median | | |  | Weighted Median | | |  | MR-Egger | | |
| **aPTT** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| **Anymigraine** | 0.97 | 0.95, 0.99 | 0.01 |  | 0.99 | 0.95, 1.03 | 0.56 |  | 0.97 | 0.95, 1.00 | 0.07 |  | 0.97 | 0.92, 1.01 | 0.15 |
| MA | 0.94 | 0.88, 1.00 | 0.06 |  | 0.91 | 0.82, 1.01 | 0.07 |  | 0.90 | 0.83, 0.98 | 0.01 |  | 0.95 | 0.84, 1.08 | 0.43 |
| MO | 0.98 | 0.91, 1.05 | 0.48 |  | 0.95 | 0.87, 1.03 | 0.20 |  | 0.99 | 0.93, 1.06 | 0.81 |  | 1.00 | 0.87, 1.14 | 0.98 |
| **D-dimer** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 1.06 | 0.99, 1.14 | 0.11 |  | 1.12 | 1.01, 1.23 | 0.03 |  | 1.05 | 0.97, 1.13 | 0.22 |  | 0.91 | 0.76, 1.09 | 0.39 |
| MA | 1.09 | 0.85, 1.41 | 0.48 |  | 1.43 | 0.99, 2.08 | 0.06 |  | 1.08 | 0.83, 1.41 | 0.56 |  | 0.63 | 0.36, 1.10 | 0.20 |
| MO | 0.97 | 0.79, 1.18 | 0.74 |  | 0.95 | 0.72, 1.25 | 0.71 |  | 1.01 | 0.80, 1.26 | 0.95 |  | 0.97 | 0.50, 1.90 | 0.93 |
| **fibrinogen** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 0.93 | 0.86, 1.00 | 0.04 |  | 0.95 | 0.87, 1.04 | 0.25 |  | 0.89 | 0.81, 0.98 | 0.01 |  | 0.88 | 0.75, 1.02 | 0.09 |
| **MA** | 0.78 | 0.66, 0.92 | 3.83E-03 |  | 0.77 | 0.59, 1.01 | 0.06 |  | 0.81 | 0.61, 1.08 | 0.14 |  | 0.73 | 0.51, 1.03 | 0.08 |
| MO | 1.01 | 0.86, 1.18 | 0.93 |  | 1.03 | 0.82, 1.30 | 0.78 |  | 1.05 | 0.80, 1.38 | 0.70 |  | 1.04 | 0.74, 1.45 | 0.82 |
| **FVII** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 1.01 | 0.98, 1.04 | 0.51 |  | 1.02 | 0.97, 1.06 | 0.44 |  | 1.01 | 0.99, 1.04 | 0.29 |  | 1.00 | 0.96, 1.04 | 0.90 |
| MA | 1.03 | 0.95, 1.11 | 0.46 |  | 1.05 | 0.92, 1.19 | 0.49 |  | 1.04 | 0.95, 1.14 | 0.40 |  | 1.00 | 0.89, 1.12 | 0.98 |
| MO | 1.00 | 0.94, 1.06 | 0.98 |  | 1.03 | 0.92, 1.15 | 0.63 |  | 0.97 | 0.89, 1.05 | 0.44 |  | 0.98 | 0.90, 1.07 | 0.65 |
| **FVIII** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| **Anymigraine** | 1.05 | 1.03, 1.08 | 1.96E-05 |  | 1.04 | 0.99, 1.08 | 0.11 |  | 1.05 | 1.02, 1.09 | 9.08e-04 |  | 1.06 | 1.02, 1.10 | 4.29E-3 |
| **MA** | 1.13 | 1.05, 1.21 | 5.92E-04 |  | 1.14 | 1.01, 1.29 | 0.04 |  | 1.11 | 1.02, 1.22 | 0.02 |  | 1.11 | 0.99, 1.24 | 0.07 |
| MO | 1.04 | 0.97, 1.10 | 0.27 |  | 1.04 | 0.93, 1.17 | 0.51 |  | 1.04 | 0.93, 1.17 | 0.51 |  | 1.06 | 0.96, 1.17 | 0.24 |
| **FXI** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 1.03 | 0.99, 1.08 | 0.15 |  | 1.03 | 0.97, 1.09 | 0.35 |  | 1.02 | 0.96, 1.08 | 0.56 |  | 1.02 | 0.90, 1.16 | 0.74 |
| MA | 0.95 | 0.83, 1.08 | 0.42 |  | 0.92 | 0.76, 1.11 | 0.36 |  | 0.92 | 0.76, 1.11 | 0.36 |  | 1.07 | 0.72, 1.59 | 0.75 |
| MO | 0.94 | 0.82, 1.07 | 0.34 |  | 0.98 | 0.82, 1.16 | 0.79 |  | 0.99 | 0.83, 1.17 | 0.89 |  | 0.92 | 0.62, 1.38 | 0.69 |
| **VWF** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| **Anymigraine** | 1.05 | 1.03, 1.07 | 1.97E-06 |  | 1.05 | 1.01, 1.09 | 0.02 |  | 1.04 | 1.02, 1.07 | 1.00E-03 |  | 1.04 | 1.01, 1.07 | 0.01 |
| **MA** | 1.12 | 1.06, 1.19 | 1.25E-04 |  | 1.14 | 1.02, 1.27 | 0.02 |  | 1.10 | 1.02, 1.19 | 0.02 |  | 1.11 | 1.02, 1.21 | 0.01 |
| MO | 1.00 | 0.95, 1.05 | 0.96 |  | 1.00 | 0.90, 1.11 | 0.99 |  | 1.04 | 0.97, 1.12 | 0.29 |  | 1.02 | 0.94, 1.10 | 0.62 |
| **PT/INR** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 0.99 | 0.95, 1.04 | 0.78 |  | 0.99 | 0.95, 1.02 | 0.47 |  | 0.98 | 0.95, 1.02 | 0.39 |  | 0.87 | 0.77, 0.97 | 0.13 |
| MA | 0.97 | 0.85, 1.11 | 0.65 |  | 0.97 | 0.86, 1.09 | 0.59 |  | 0.97 | 0.86, 1.08 | 0.53 |  | 0.70 | 0.48, 1.02 | 0.20 |
| MO | 1.06 | 0.97, 1.16 | 0.21 |  | 1.05 | 0.95, 1.16 | 0.35 |  | 1.05 | 0.95, 1.17 | 0.34 |  | 1.09 | 0.78, 1.52 | 0.65 |
| **PAI-1** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 0.93 | 0.85, 1.03 | 0.17 |  | 0.89 | 0.79, 1.00 | 0.06 |  | 0.90 | 0.79, 1.01 | 0.07 |  | 1.06 | 0.67, 1.69 | 0.82 |
| MA | 0.93 | 0.68, 1.25 | 0.62 |  | 0.92 | 0.65, 1.30 | 0.63 |  | 0.93 | 0.64, 1.34 | 0.68 |  | 0.55 | 0.13, 2.30 | 0.50 |
| MO | 1.01 | 0.76, 1.34 | 0.93 |  | 1.08 | 0.78, 1.49 | 0.63 |  | 1.07 | 0.78, 1.47 | 0.68 |  | 1.50 | 0.32, 7.07 | 0.65 |
| **tPA** | | | | | | | | | | | | | | | |
| Outcome | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  | OR | 95%CI | P-value |  |
| Anymigraine | 1.15 | 0.86, 1.55 | 0.34 |  | 1.03 | 0.85, 1.25 | 0.75 |  | 1.03 | 0.86, 1.24 | 0.73 |  | 0.62 | 0.23, 1.67 | 0.51 |
| MA | 1.61 | 0.67, 3.84 | 0.29 |  | 1.09 | 0.56, 2.13 | 0.81 |  | 1.08 | 0.63, 1.86 | 0.78 |  | 0.32 | 0.01, 15.29 | 0.66 |
| MO | 1.10 | 0.76, 1.58 | 0.61 |  | 1.00 | 0.62, 1.61 | 0.99 |  | 1.02 | 0.68, 1.52 | 0.93 |  | 0.70 | 0.18, 2.79 | 0.70 |

Abbreviations: OR: odds ratio; CI: confidence interval; MA: migraine with aura; MO: migraine without aura; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A.

All the analyses were conducted using inverse-variance weighted (IVW), simple median, weighted median, and MR-Egger implemented in the R package TwoSampleMR.

As migraine is a binary variable, we interpreted the reverse causal estimates as the average change in hemostatic factors per doubling (2-fold increase) in the odds of migraine, which could be obtained by multiplying the reverse causal estimate by 0.693 (loge2). *P* values are two-sided.

# **Supplementary Table 7** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) after removing instruments on ABO gene.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **trait1** | **trait2** | **CausalEstimate** | **se** | **OR** | **95%CI** | **P-value** |
| D-dimer | Anymigraine | 0.06 | 0.04 | 1.06 | 0.99, 1.14 | 0.18 |
| D-dimer | MA | 0.09 | 0.13 | 1.09 | 0.85, 1.41 | 0.52 |
| D-dimer | MO | -0.04 | 0.10 | 0.97 | 0.79, 1.18 | 0.75 |
| fibrinogen | Anymigraine | -0.06 | 0.03 | 0.94 | 0.88, 1.01 | 0.08 |
| fibrinogen | MA | -0.25 | 0.08 | 0.78 | 0.66, 0.92 | 0.00 |
| fibrinogen | MO | 0.01 | 0.08 | 1.01 | 0.86, 1.18 | 0.93 |
| FVII | Anymigraine | 0.01 | 0.01 | 1.01 | 0.98, 1.03 | 0.61 |
| FVII | MA | 0.03 | 0.04 | 1.03 | 0.95, 1.11 | 0.47 |
| FVII | MO | 0.00 | 0.03 | 1.00 | 0.95, 1.05 | 0.98 |
| FVIII | Anymigraine | 0.05 | 0.02 | 1.05 | 1.02, 1.09 | 0.01 |
| FVIII | MA | 0.14 | 0.04 | 1.14 | 1.06, 1.23 | 1.43E-03 |
| FVIII | MO | 0.02 | 0.04 | 1.02 | 0.95, 1.09 | 0.62 |
| FXI | Anymigraine | 0.03 | 0.02 | 1.03 | 0.99, 1.08 | 0.16 |
| FXI | MA | -0.06 | 0.06 | 0.95 | 0.83, 1.07 | 0.40 |
| FXI | MO | -0.06 | 0.07 | 0.94 | 0.82, 1.07 | 0.36 |
| VWF | Anymigraine | 0.05 | 0.01 | 1.05 | 1.02, 1.08 | 8.10E-04 |
| VWF | MA | 0.13 | 0.04 | 1.14 | 1.05, 1.24 | 3.82E-03 |
| VWF | MO | -0.05 | 0.03 | 0.95 | 0.90, 1.01 | 0.14 |
| PAI-1 | Anymigraine | -0.07 | 0.04 | 0.93 | 0.87, 1.00 | 0.15 |
| PAI-1 | MA | -0.08 | 0.11 | 0.93 | 0.75, 1.14 | 0.53 |
| PAI-1 | MO | 0.01 | 0.14 | 1.01 | 0.76, 1.34 | 0.94 |
| tPA | Anymigraine | 0.14 | 0.15 | 1.15 | 0.86, 1.55 | 0.34 |
| tPA | MA | 0.47 | 0.44 | 1.61 | 0.67, 3.84 | 0.29 |
| tPA | MO | 0.09 | 0.19 | 1.10 | 0.76, 1.58 | 0.61 |
| aPTT | Anymigraine | -0.02 | 0.01 | 0.98 | 0.97, 1.01 | 0.17 |
| aPTT | MA | -0.04 | 0.04 | 0.96 | 0.89, 1.03 | 0.26 |
| aPTT | MO | 0.02 | 0.03 | 1.02 | 0.97, 1.07 | 0.43 |
| PT/INR | Anymigraine | -0.01 | 0.02 | 0.99 | 0.95, 1.04 | 0.80 |
| PT/INR | MA | -0.03 | 0.07 | 0.97 | 0.85, 1.11 | 0.68 |
| PT/INR | MO | 0.06 | 0.01 | 1.06 | 1.03, 1.08 | 0.02 |
| Fibrinopeptide A | Anymigraine | 0.03 | 0.04 | 1.03 | 0.98, 1.08 | 0.26 |
| Fibrinopeptide A | MA | -0.01 | 0.03 | 0.99 | 0.88, 1.11 | 0.87 |
| Fibrinopeptide A | MO | 0.03 | 0.06 | 1.03 | 0.93, 1.14 | 0.59 |
| Phosphorylated fibrinopeptide A | Anymigraine | 0.12 | 0.03 | 1.13 | 1.07, 1.19 | 5.44E-06 |
| Phosphorylated fibrinopeptide A | MA | 0.20 | 0.03 | 1.22 | 1.01, 1.48 | 0.04 |
| Phosphorylated fibrinopeptide A | MO | -0.02 | 0.10 | 0.98 | 0.84, 1.14 | 0.77 |

Abbreviations: OR: odds ratio; CI: confidence interval; MA: migraine with aura; MO: migraine without aura; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A. *P* values are two-sided.

# **Supplementary Table 8** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) after removing instruments within 200kb of ABO gene.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **trait1** | **trait2** | **CausalEstimate** | **se** | **OR** | **95%CI** | **P-value** |
| D-dimer | Anymigraine | 0.06 | 0.04 | 1.06 | 0.99, 1.14 | 0.18 |
| D-dimer | MA | 0.09 | 0.13 | 1.09 | 0.85, 1.41 | 0.52 |
| D-dimer | MO | -0.04 | 0.10 | 0.97 | 0.79, 1.18 | 0.75 |
| fibrinogen | Anymigraine | -0.06 | 0.03 | 0.94 | 0.88, 1.01 | 0.08 |
| fibrinogen | MA | -0.25 | 0.08 | 0.78 | 0.66, 0.92 | 4.84E-03 |
| fibrinogen | MO | 0.01 | 0.08 | 1.01 | 0.86, 1.18 | 0.93 |
| FVII | Anymigraine | 0.01 | 0.01 | 1.01 | 0.98, 1.03 | 0.61 |
| FVII | MA | 0.03 | 0.04 | 1.03 | 0.95, 1.11 | 0.47 |
| FVII | MO | 0.00 | 0.03 | 1.00 | 0.95, 1.05 | 0.98 |
| FVIII | Anymigraine | 0.02 | 0.02 | 1.02 | 0.97, 1.07 | 0.45 |
| FVIII | MA | 0.10 | 0.05 | 1.11 | 1.00, 1.23 | 0.06 |
| FVIII | MO | -0.02 | 0.06 | 0.98 | 0.88, 1.10 | 0.77 |
| FXI | Anymigraine | 0.03 | 0.02 | 1.03 | 0.99, 1.08 | 0.16 |
| FXI | MA | -0.06 | 0.06 | 0.95 | 0.83, 1.07 | 0.40 |
| FXI | MO | -0.06 | 0.07 | 0.94 | 0.82, 1.07 | 0.36 |
| VWF | Anymigraine | 0.05 | 0.02 | 1.05 | 1.01, 1.08 | 0.01 |
| VWF | MA | 0.10 | 0.06 | 1.11 | 0.99, 1.24 | 0.07 |
| VWF | MO | -0.07 | 0.04 | 0.93 | 0.86, 1.01 | 0.09 |
| PAI-1 | Anymigraine | -0.07 | 0.04 | 0.93 | 0.87, 1.00 | 0.15 |
| PAI-1 | MA | -0.08 | 0.11 | 0.93 | 0.75, 1.14 | 0.53 |
| PAI-1 | MO | 0.01 | 0.14 | 1.01 | 0.76, 1.34 | 0.94 |
| tPA | Anymigraine | 0.14 | 0.15 | 1.15 | 0.86, 1.55 | 0.34 |
| tPA | MA | 0.47 | 0.44 | 1.61 | 0.67, 3.84 | 0.29 |
| tPA | MO | 0.09 | 0.19 | 1.10 | 0.76, 1.58 | 0.61 |
| aPTT | Anymigraine | -0.02 | 0.01 | 0.98 | 0.96, 1.01 | 0.16 |
| aPTT | MA | -0.04 | 0.04 | 0.96 | 0.89, 1.04 | 0.31 |
| aPTT | MO | 0.02 | 0.03 | 1.02 | 0.96, 1.07 | 0.54 |
| PT/INR | Anymigraine | -0.01 | 0.02 | 0.99 | 0.95, 1.04 | 0.80 |
| PT/INR | MA | -0.03 | 0.07 | 0.97 | 0.85, 1.11 | 0.68 |
| PT/INR | MO | 0.06 | 0.01 | 1.06 | 1.03, 1.08 | 0.02 |
| Fibrinopeptide A | Anymigraine | 0.03 | 0.03 | 1.03 | 0.98, 1.08 | 0.26 |
| Fibrinopeptide A | MA | -0.01 | 0.06 | 0.99 | 0.88, 1.11 | 0.87 |
| Fibrinopeptide A | MO | 0.03 | 0.05 | 1.03 | 0.93, 1.14 | 0.59 |
| Phosphorylated fibrinopeptide A | Anymigraine | 0.09 | 0.05 | 1.10 | 1.00, 1.20 | 0.04 |
| Phosphorylated fibrinopeptide A | MA | 0.07 | 0.14 | 1.07 | 0.82, 1.41 | 0.60 |
| Phosphorylated fibrinopeptide A | MO | -0.06 | 0.12 | 0.94 | 0.74, 1.20 | 0.63 |

Abbreviations: OR: odds ratio; CI: confidence interval; MA: migraine with aura; MO: migraine without aura; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A. *P* values are two-sided.

# **Supplementary Table 9** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) after removing instruments on chromosome 9.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| trait1 | trait2 | CausalEstimate | Sd | OR | 95%CI | P-value |
| D-dimer | Anymigraine | 0.06 | 0.04 | 1.06 | 0.99, 1.14 | 0.18 |
| D-dimer | MA | 0.09 | 0.13 | 1.09 | 0.85, 1.41 | 0.52 |
| D-dimer | MO | -0.04 | 0.10 | 0.97 | 0.79, 1.18 | 0.75 |
| fibrinogen | Anymigraine | -0.06 | 0.03 | 0.94 | 0.88, 1.00 | 0.07 |
| fibrinogen | MA | -0.24 | 0.09 | 0.78 | 0.66, 0.93 | 0.01 |
| fibrinogen | MO | 0.01 | 0.08 | 1.01 | 0.86, 1.18 | 0.95 |
| FVII | Anymigraine | 0.01 | 0.01 | 1.01 | 0.98, 1.03 | 0.61 |
| FVII | MA | 0.03 | 0.04 | 1.03 | 0.95, 1.11 | 0.47 |
| FVII | MO | 0.00 | 0.03 | 1.00 | 0.95, 1.05 | 0.98 |
| FVIII | Anymigraine | 0.03 | 0.03 | 1.03 | 0.97, 1.09 | 0.41 |
| FVIII | MA | 0.09 | 0.08 | 1.10 | 0.93, 1.29 | 0.29 |
| FVIII | MO | -0.06 | 0.08 | 0.94 | 0.81, 1.10 | 0.45 |
| FXI | Anymigraine | 0.03 | 0.02 | 1.03 | 0.99, 1.08 | 0.16 |
| FXI | MA | -0.06 | 0.06 | 0.95 | 0.83, 1.07 | 0.40 |
| FXI | MO | -0.06 | 0.07 | 0.94 | 0.82, 1.07 | 0.36 |
| VWF | Anymigraine | 0.06 | 0.02 | 1.06 | 1.01, 1.11 | 0.02 |
| VWF | MA | 0.12 | 0.08 | 1.12 | 0.96, 1.31 | 0.15 |
| VWF | MO | -0.04 | 0.05 | 0.96 | 0.88, 1.05 | 0.43 |
| PAI-1 | Anymigraine | -0.07 | 0.04 | 0.93 | 0.87, 1.00 | 0.15 |
| PAI-1 | MA | -0.08 | 0.11 | 0.93 | 0.75, 1.14 | 0.53 |
| PAI-1 | MO | 0.01 | 0.14 | 1.01 | 0.76, 1.34 | 0.94 |
| tPA | Anymigraine | 0.14 | 0.15 | 1.15 | 0.86, 1.55 | 0.34 |
| tPA | MA | 0.47 | 0.44 | 1.61 | 0.67, 3.84 | 0.29 |
| tPA | MO | 0.09 | 0.19 | 1.10 | 0.76, 1.58 | 0.61 |
| aPTT | Anymigraine | -0.02 | 0.01 | 0.98 | 0.96, 1.01 | 0.16 |
| aPTT | MA | -0.04 | 0.04 | 0.96 | 0.89, 1.04 | 0.31 |
| aPTT | MO | 0.02 | 0.03 | 1.02 | 0.96, 1.07 | 0.54 |
| PT/INR | Anymigraine | -0.01 | 0.02 | 0.99 | 0.95, 1.04 | 0.80 |
| PT/INR | MA | -0.03 | 0.07 | 0.97 | 0.85, 1.11 | 0.68 |
| PT/INR | MO | 0.06 | 0.01 | 1.06 | 1.03, 1.08 | 0.02 |
| Fibrinopeptide A | Anymigraine | 0.03 | 0.03 | 1.03 | 0.98, 1.08 | 0.26 |
| Fibrinopeptide A | MA | -0.01 | 0.06 | 0.99 | 0.88, 1.11 | 0.87 |
| Fibrinopeptide A | MO | 0.03 | 0.05 | 1.03 | 0.93, 1.14 | 0.59 |
| Phosphorylated fibrinopeptide A | Anymigraine | 0.09 | 0.05 | 1.10 | 1.00, 1.20 | 0.04 |
| Phosphorylated fibrinopeptide A | MA | 0.07 | 0.14 | 1.07 | 0.82, 1.41 | 0.60 |
| Phosphorylated fibrinopeptide A | MO | -0.06 | 0.12 | 0.94 | 0.74, 1.20 | 0.63 |

Abbreviations: OR: odds ratio; CI: confidence interval; MA: migraine with aura; MO: migraine without aura; aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time; ADSGEGDFXAEGGGVR\*: fibrinopeptide A; ADpSGEGDFXAEGGGVR\*: phosphorylated fibrinopeptide A. *P* values are two-sided.

# **Supplementary Table 10** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine, migraine with aura (MA), and migraine without aura (MO) with cis-only variants.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| exposure | outcome | Number of instruments | OR | 95%CI | P value |
| fibrinogen | Anymigraine | 12 | 0.91 | 0.83, 1.00 | 0.06 |
| MA | 12 | 0.75 | 0.56, 1.01 | 0.06 |
| MO | 12 | 1.02 | 0.79, 1.31 | 0.89 |
| FVII | Anymigraine | 16 | 1.01 | 0.98, 1.03 | 0.55 |
| MA | 16 | 1.04 | 0.96, 1.13 | 0.36 |
| MO | 16 | 1.01 | 0.95, 1.08 | 0.80 |
| FXI | Anymigraine | 10 | 1.05 | 0.99, 1.11 | 0.14 |
| MA | 10 | 0.87 | 0.71, 1.06 | 0.16 |
| MO | 10 | 0.94 | 0.76, 1.15 | 0.55 |
| PAI-1 | Anymigraine | 2 | 0.96 | 0.85, 1.09 | 0.56 |
| MA | 2 | 1.05 | 0.71, 1.57 | 0.80 |
| MO | 2 | 1.07 | 0.76, 1.52 | 0.69 |
| VWF | Anymigraine | 6 | 1.07 | 1.00, 1.14 | 0.06 |
| MA | 6 | 1.21 | 0.99, 1.49 | 0.06 |
| MO | 6 | 0.84 | 0.70, 1.01 | 0.06 |

Abbreviations: OR: odds ratio; CI: confidence interval; MA: migraine with aura; MO: migraine without aura; OR: odds ratio; FVII: coagulation factors VII; FXI: coagulation factors XI; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1. *P* values are two-sided.

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# **Supplementary Figure 1** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine after removing instruments on ABO gene (A), within 200kb of ABO gene (B), and on chromosome 9 (C).** Abbreviations: aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time.The x-axis in on log scale.All the instrumental estimates were interpreted as the odds ratio of per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided.

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# **Supplementary Figure 2** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine with aura (MA) after removing instruments on ABO gene (A), within 200kb of ABO gene (B), and on chromosome 9 (C).** Abbreviations: aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time. The x-axis in on log scale.All the instrumental estimates were interpreted as the odds ratio of per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 3** **Sensitivity analysis of instrumental estimates of hemostatic profiles with migraine without aura (MO) after removing instruments on ABO gene (A), within 200kb of ABO gene (B), and on chromosome 9 (C).** Abbreviations: aPTT: activated partial thromboplastin time; FVII: coagulation factors VII; FVIII: coagulation factors VIII; VWF: von Willebrand factor; PAI-1: plasminogen activator inhibitor-1; tPA: tissue plasminogen activator; PT/INR: prothrombin time.The x-axis in on log scale.All the instrumental estimates were interpreted as the odds ratio of per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 4** **Leave-one-out sensitivity analysis of instrumental estimates of D-dimer with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 5** **Leave-one-out sensitivity analysis of instrumental estimates of fibrinogen with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR.All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 6** **Leave-one-out sensitivity analysis of instrumental estimates of coagulation factor VII (FVII) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 7** **Leave-one-out sensitivity analysis of instrumental estimates of coagulation factor VIII (FVIII) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 8** **Leave-one-out sensitivity analysis of instrumental estimates of coagulation factor XI (FXI) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 9** **Leave-one-out sensitivity analysis of instrumental estimates of von Willebrand factor (VWF) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 10** **Leave-one-out sensitivity analysis of instrumental estimates of plasminogen activator inhibitor-1 (PAI-1)** **with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 11** **Leave-one-out sensitivity analysis of instrumental estimates of tissue plasminogen activator (tPA) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 12** **Leave-one-out sensitivity analysis of instrumental estimates of activated partial thromboplastin time (aPTT) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 13** **Leave-one-out sensitivity analysis of instrumental estimates of** **prothrombin time ( PT/INR) with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using leave-one-out method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 14** **Single SNP sensitivity analysis of instrumental estimates of** **fibrinopeptide A with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using single SNP method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**

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# **Supplementary Figure 15** **Single SNP sensitivity analysis of instrumental estimates of** **Phosphorylated fibrinopeptide A with migraine, migraine with aura (MA), and migraine without aura (MO).** All the analyses were conducted using single SNP method implemented in the R package TwoSampleMR. All the instrumental estimates were corresponding to per standard deviation (SD) change of the hemostatic profiles being tested. *P* values are two-sided**.**