Supplementary figures

Genetic architecture of lumbar spinal stenosis

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References

Supplementary Note. FinnGen R12 Ethics statement

Study subjects in FinnGen provided informed consent for biobank research, based on the Finnish Biobank Act. Alternatively, separate research cohorts, collected prior the Finnish Biobank Act came into effect (in September 2013) and start of FinnGen (August 2017), were collected based on study-specific consents and later transferred to the Finnish biobanks after approval by Fimea (Finnish Medicines Agency), the National Supervisory Authority for Welfare and Health. Recruitment protocols followed the biobank protocols approved by Fimea. The Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa (HUS) statement number for the FinnGen study is Nr HUS/990/2017.

The FinnGen study is approved by Finnish Institute for Health and Welfare (permit numbers: THL/2031/6.02.00/2017, THL/1101/5.05.00/2017, THL/341/6.02.00/2018, THL/2222/6.02.00/2018, THL/283/6.02.00/2019, THL/1721/5.05.00/2019 and THL/1524/5.05.00/2020), Digital and population data service agency (permit numbers: VRK43431/2017-3, VRK/6909/2018-3, VRK/4415/2019-3), the Social Insurance Institution (permit numbers: KELA 58/522/2017, KELA 131/522/2018, KELA 70/522/2019, KELA 98/522/2019, KELA 134/522/2019, KELA 138/522/2019, KELA 2/522/2020, KELA 16/522/2020), Findata permit numbers THL/2364/14.02/2020, THL/4055/14.06.00/2020, THL/3433/14.06.00/2020, THL/4432/14.06/2020, THL/5189/14.06/2020, THL/5894/14.06.00/2020, THL/6619/14.06.00/2020, THL/209/14.06.00/2021, THL/688/14.06.00/2021, THL/1284/14.06.00/2021, THL/1965/14.06.00/2021, THL/5546/14.02.00/2020, THL/2658/14.06.00/2021, THL/4235/14.06.00/2021, Statistics Finland (permit numbers: TK-53-1041-17 and TK/143/07.03.00/2020 (earlier TK-53-90-20) TK/1735/07.03.00/2021, TK/3112/07.03.00/2021) and Finnish Registry for Kidney Diseases permission/extract from the meeting minutes on 4th July 2019.

The Biobank Access Decisions for FinnGen samples and data utilized in FinnGen Data Freeze 12 include: THL Biobank BB2017_55, BB2017_111, BB2018_19, BB_2018_34, BB_2018_67, BB2018_71, BB2019_7, BB2019_8, BB2019_26, BB2020_1, BB2021_65, Finnish Red Cross Blood Service Biobank 7.12.2017, Helsinki Biobank HUS/359/2017, HUS/248/2020, HUS/430/2021 §28, §29, HUS/150/2022 §12, §13, §14, §15, §16, §17, §18, §23, §58, §59, HUS/128/2023 §18, Auria Biobank AB17-5154 and amendment #1 (August 17 2020) and amendments BB_2021-0140, BB_2021-0156 (August 26 2021, Feb 2 2022), BB_2021-0169, BB_2021-0179, BB_2021-0161, AB20-5926 and amendment #1 (April 23 2020) and it´s modifications (Sep 22 2021), BB_2022-0262, BB_2022-0256, Biobank Borealis of Northern Finland_2017_1013, 2021_5010, 2021_5010 Amendment, 2021_5018, 2021_5018 Amendment, 2021_5015, 2021_5015 Amendment, 2021_5015 Amendment_2, 2021_5023, 2021_5023 Amendment, 2021_5023 Amendment_2, 2021_5017, 2021_5017 Amendment, 2022_6001, 2022_6001 Amendment, 2022_6006 Amendment, 2022_6006 Amendment, 2022_6006 Amendment_2, BB22-0067, 2022_0262, 2022_0262 Amendment, Biobank of Eastern Finland 1186/2018 and amendment 22§/2020, 53§/2021, 13§/2022, 14§/2022, 15§/2022, 27§/2022, 28§/2022, 29§/2022, 33§/2022, 35§/2022, 36§/2022, 37§/2022, 39§/2022, 7§/2023, 32§/2023, 33§/2023, 34§/2023, 35§/2023, 36§/2023, 37§/2023, 38§/2023, 39§/2023, 40§/2023, 41§/2023, Finnish Clinical Biobank Tampere MH0004 and amendments (21.02.2020 & 06.10.2020), BB2021-0140 8§/2021, 9§/2021, §9/2022, §10/2022, §12/2022, 13§/2022, §20/2022, §21/2022, §22/2022, §23/2022, 28§/2022, 29§/2022, 30§/2022, 31§/2022, 32§/2022, 38§/2022, 40§/2022, 42§/2022, 1§/2023, Central Finland Biobank 1-2017, BB_2021-0161, BB_2021-0169, BB_2021-0179, BB_2021-0170, BB_2022-0256, BB_2022-0262, BB22-0067, Decision allowing to continue data processing until 31st Aug 2024 for projects: BB_2021-0179, BB22-0067,BB_2022-0262, BB_2021-0170, BB_2021-0164, BB_2021-0161, and BB_2021-0169, and Terveystalo Biobank STB 2018001 and amendment 25th Aug 2020, Finnish Hematological Registry and Clinical Biobank decision 18th June 2021, Arctic biobank P0844: ARC_2021_1001.

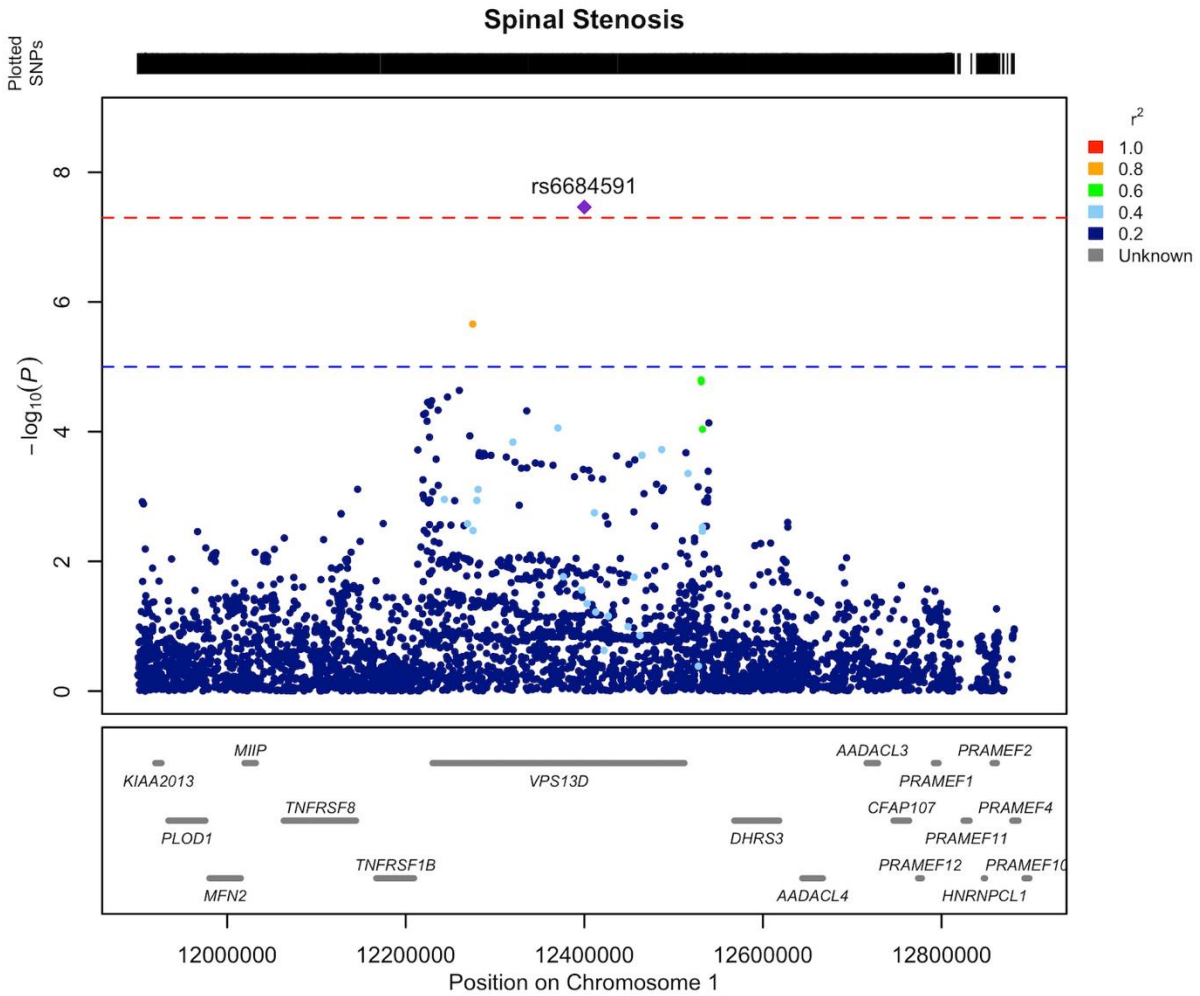

Fig S1. Regional association plot of previously unreported LSS association on chromosome 1 area of 11.9-12.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TNFRSF1B (TNF receptor superfamily member 1B).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

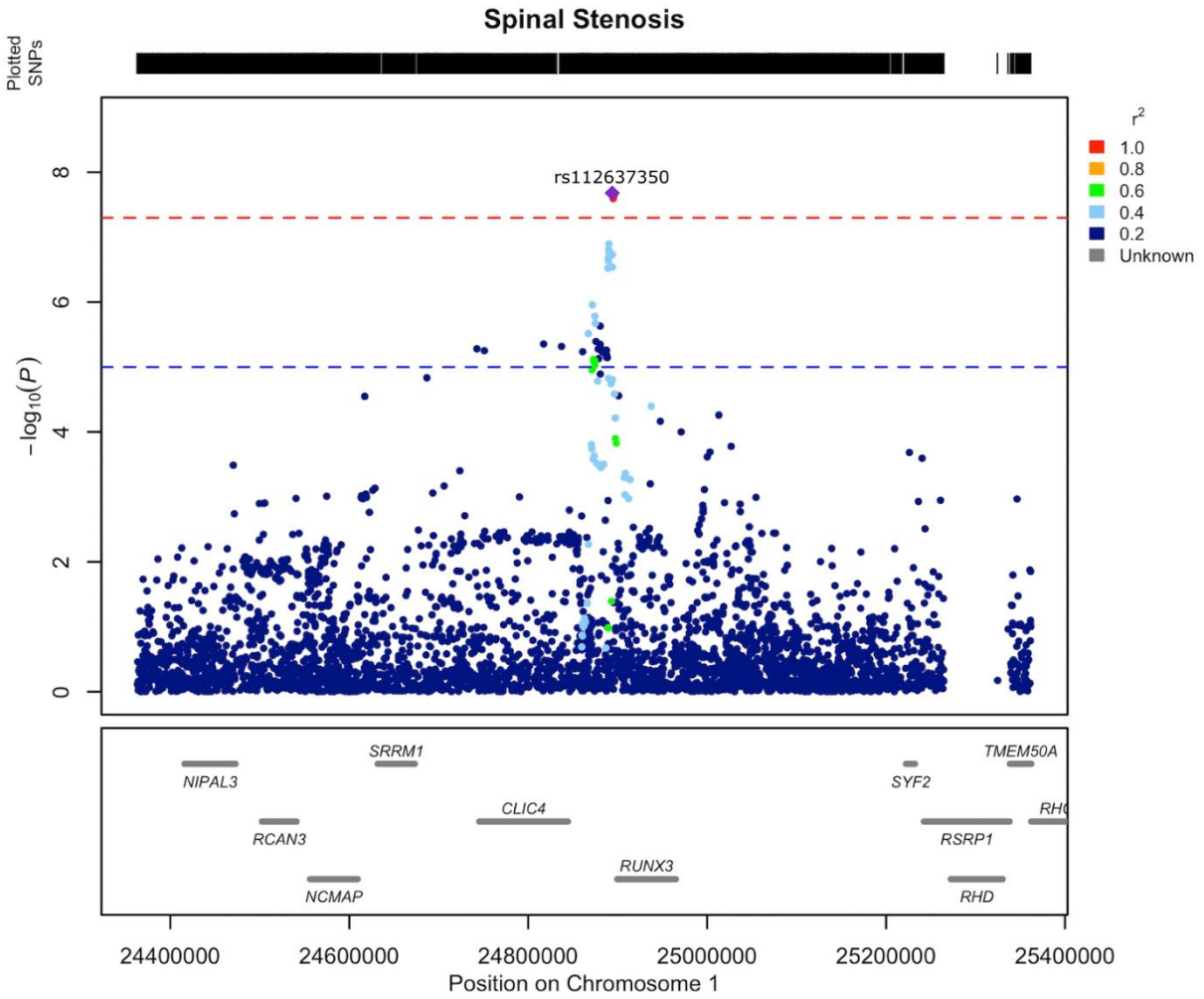

Fig S2. Regional association plot of previously unreported LSS association on chromosome 1 area of 24.4-25.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *RUNX3 (RUNX family transcription factor 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

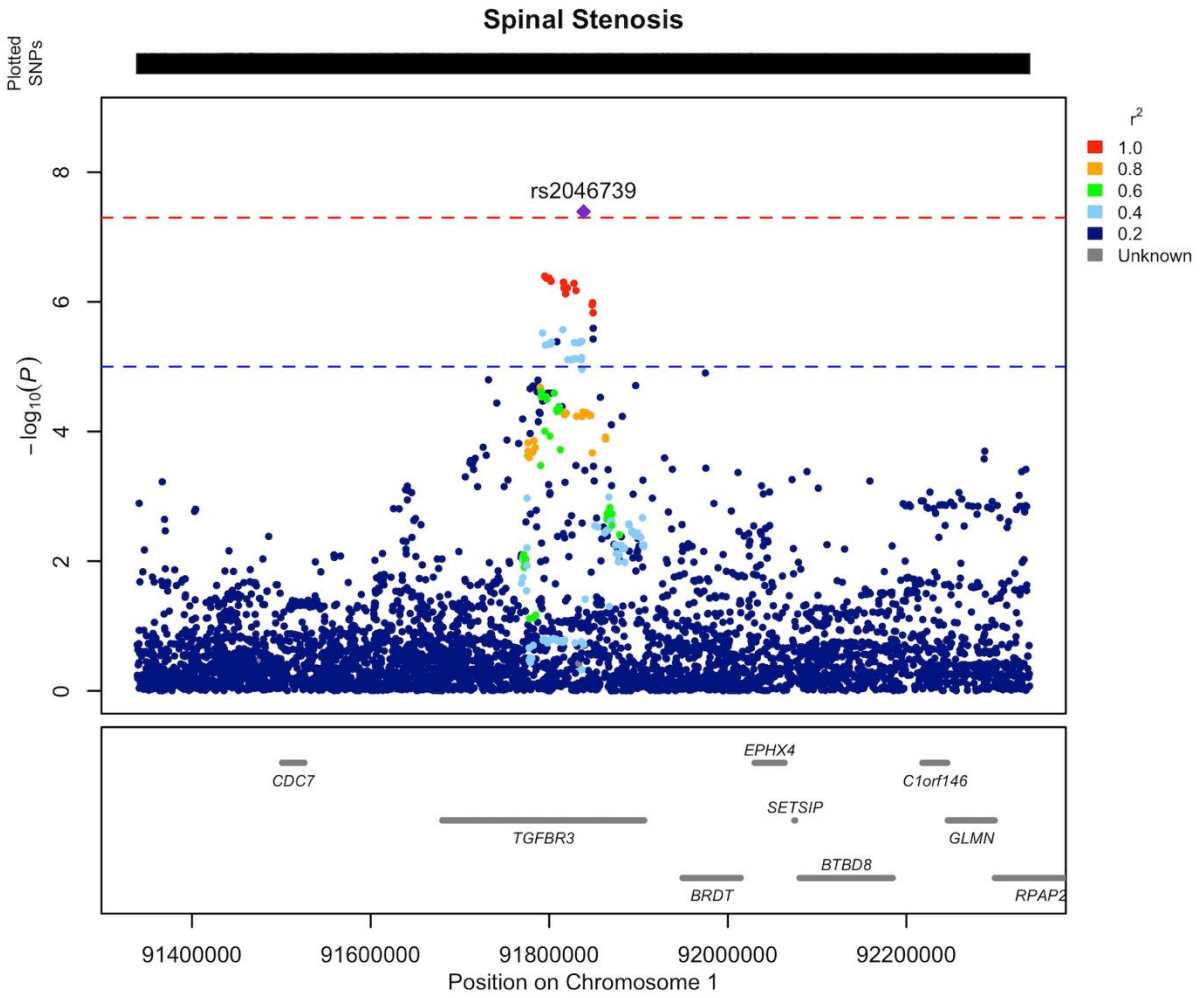

Fig S3. Regional association plot of previously unreported LSS association on chromosome 1 area of 91.3-92.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TGFBR3 (transforming growth factor beta receptor 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

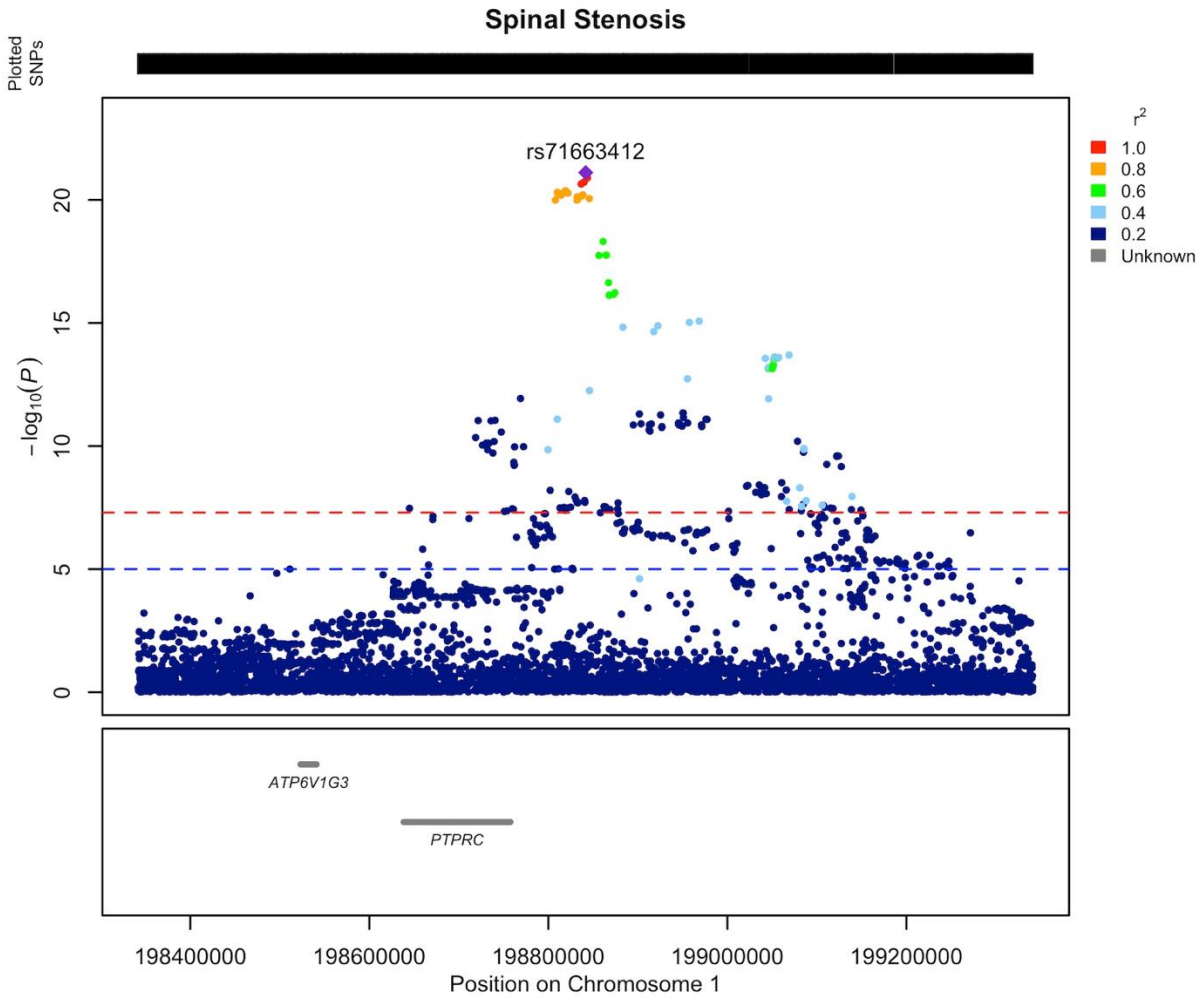

Fig S4. Regional association plot of previously unreported LSS association on chromosome 1 area of 198.3-199.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *PTPRC (protein tyrosine phosphatase receptor type C).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

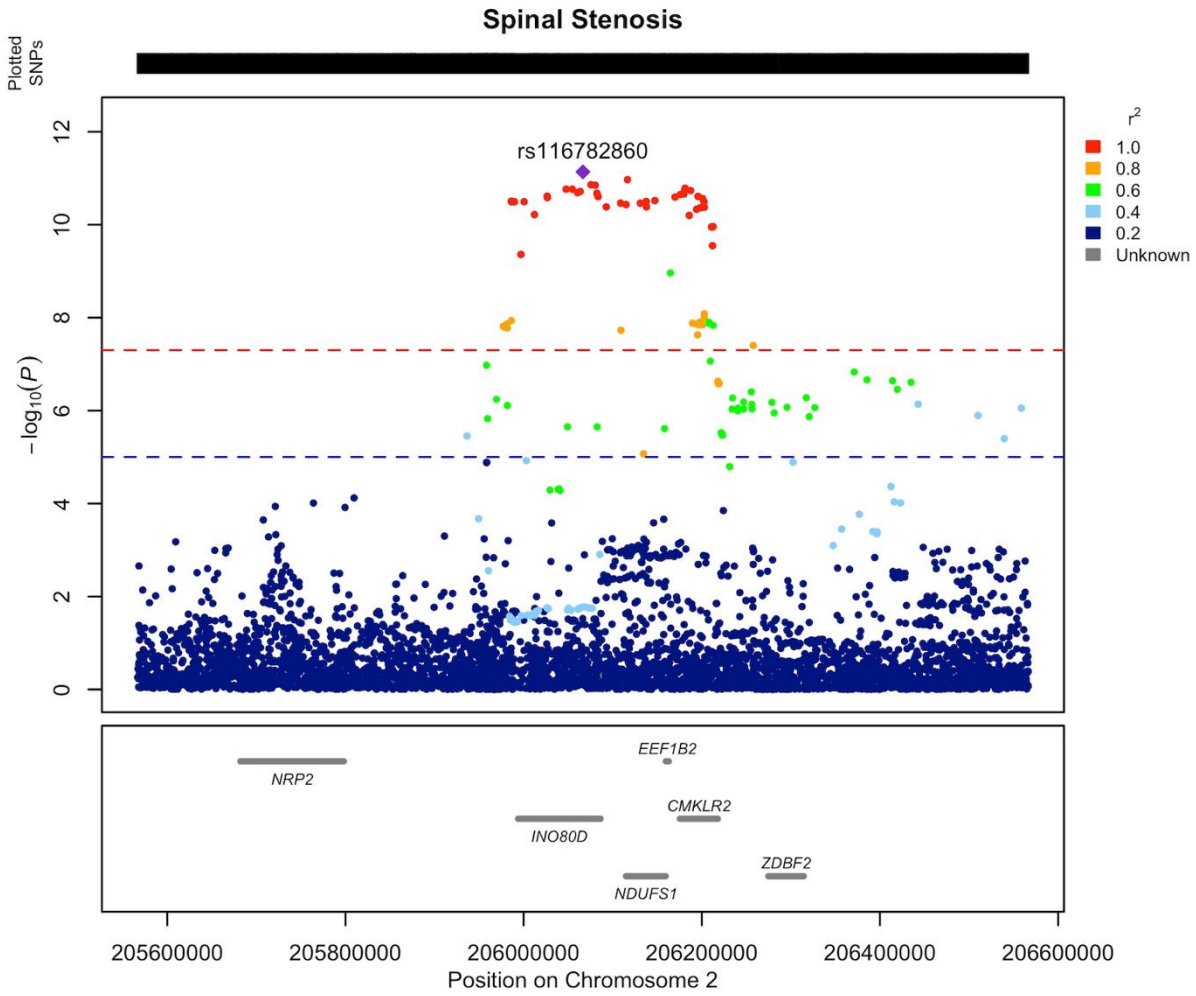

Fig S5. Regional association plot of previously unreported LSS association on chromosome 2 area of 205.6-206.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *GPR1 (chemerin-like receptor 2, also known as CMKLR2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

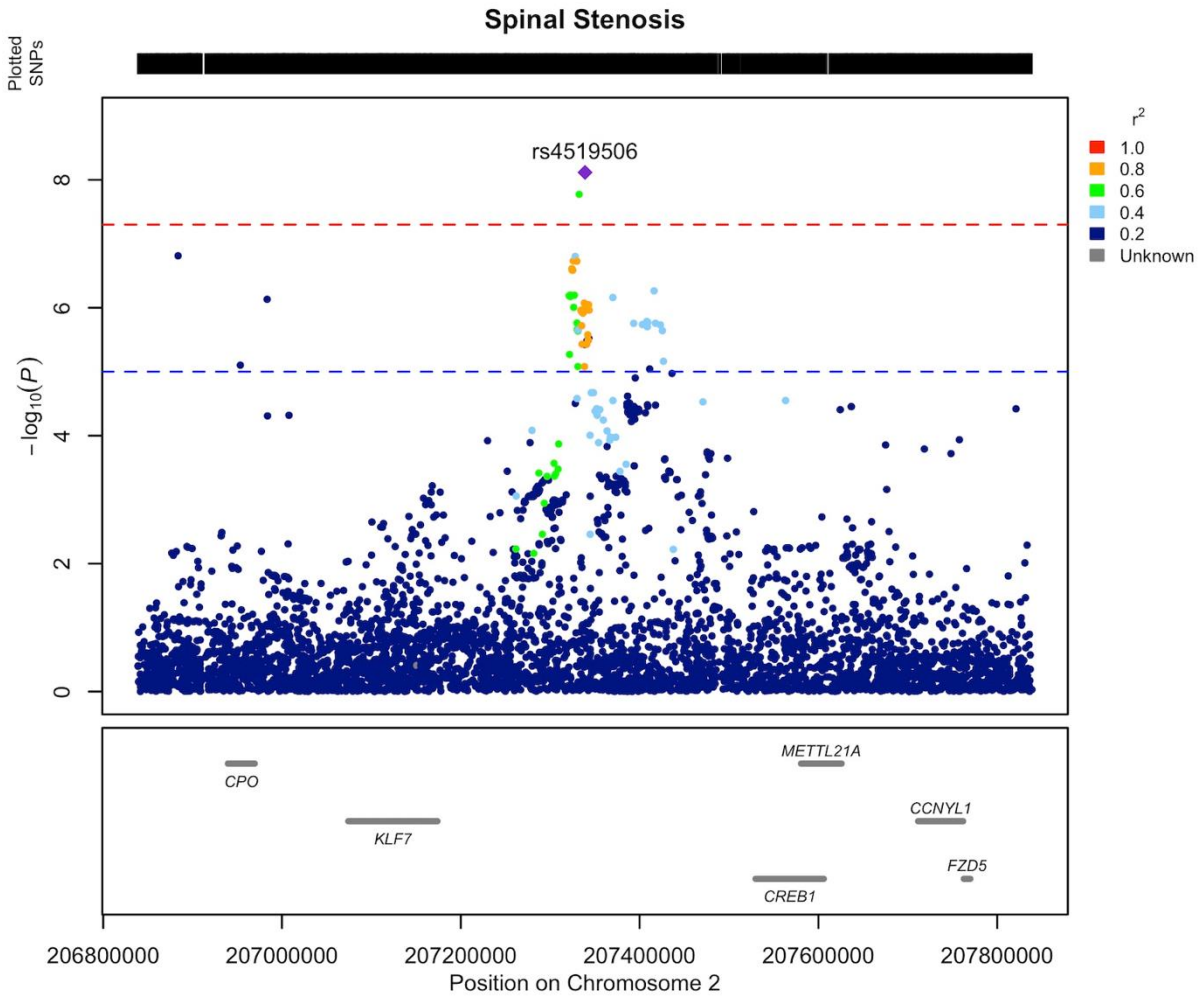

Fig S6. Regional association plot of previously unreported LSS association on chromosome 2 area of 206.8-207.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *KLF7 (KLF transcription factor 7).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

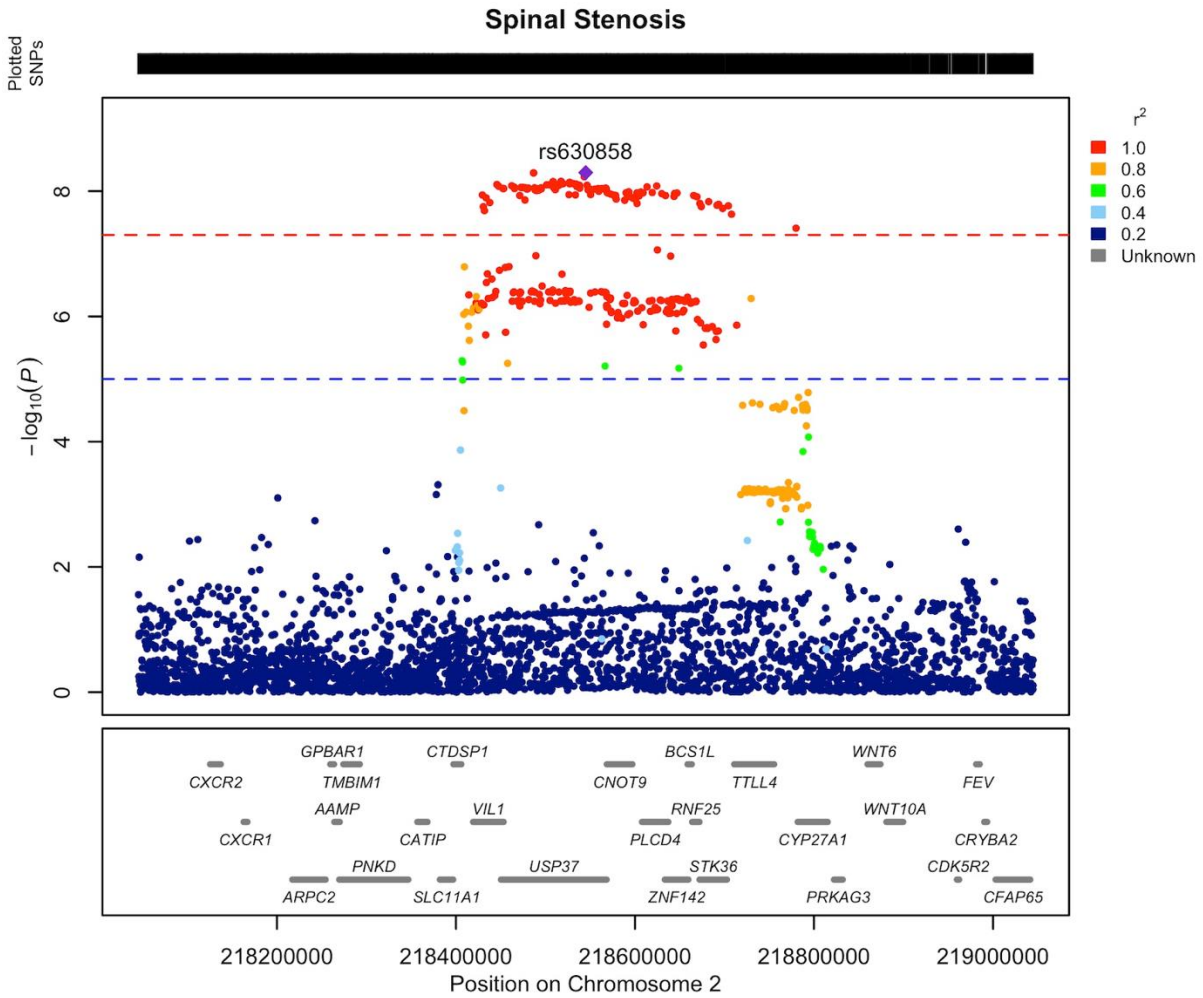

Fig S7. Regional association plot of previously unreported LSS association on chromosome 2 area of 218.1-219.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *USP37 (ubiquitin specific peptidase 37).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

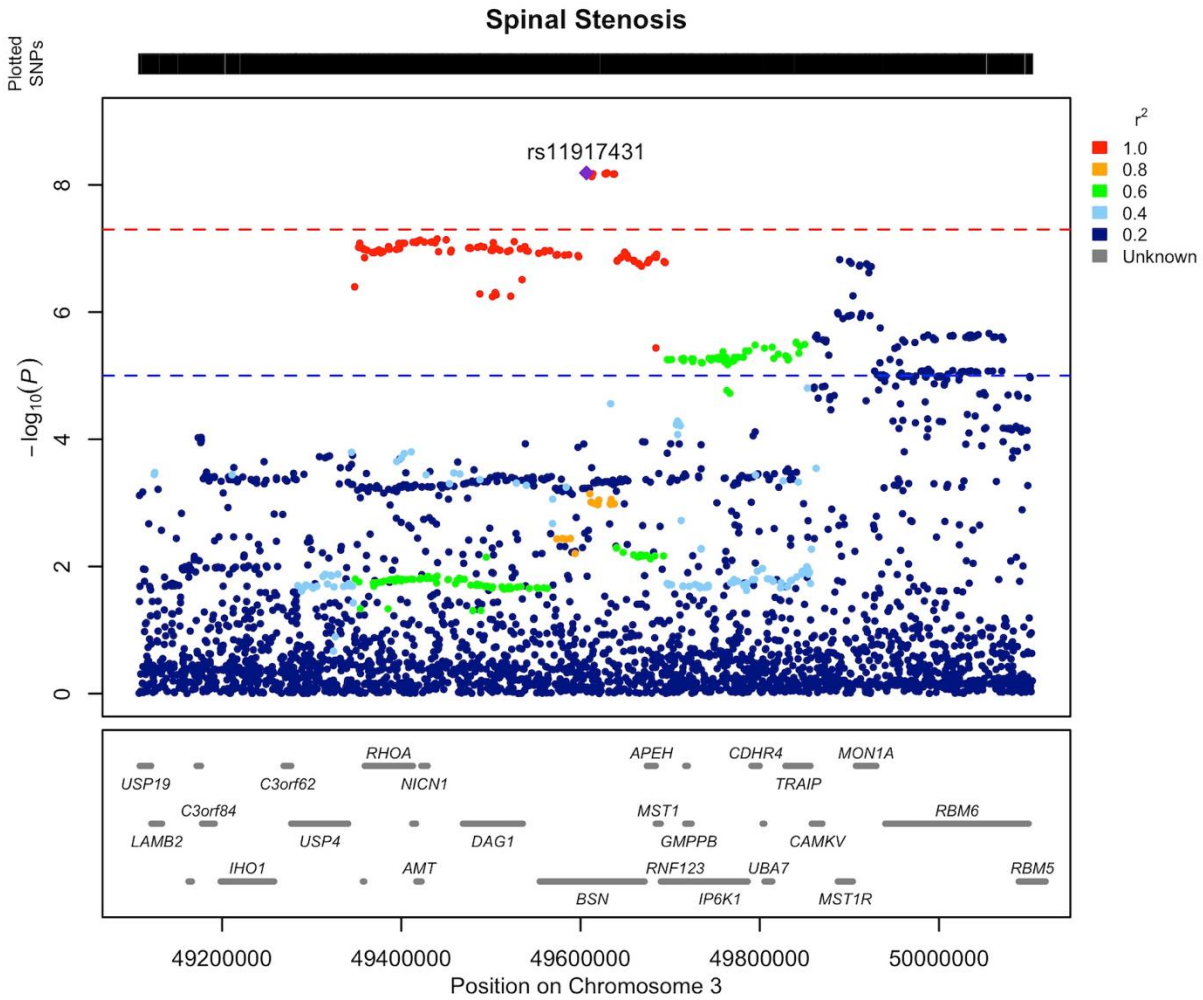

Fig S8. Regional association plot of previously unreported LSS association on chromosome 3 area of 49.1-50.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *DAG1 (dystroglycan 1)*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

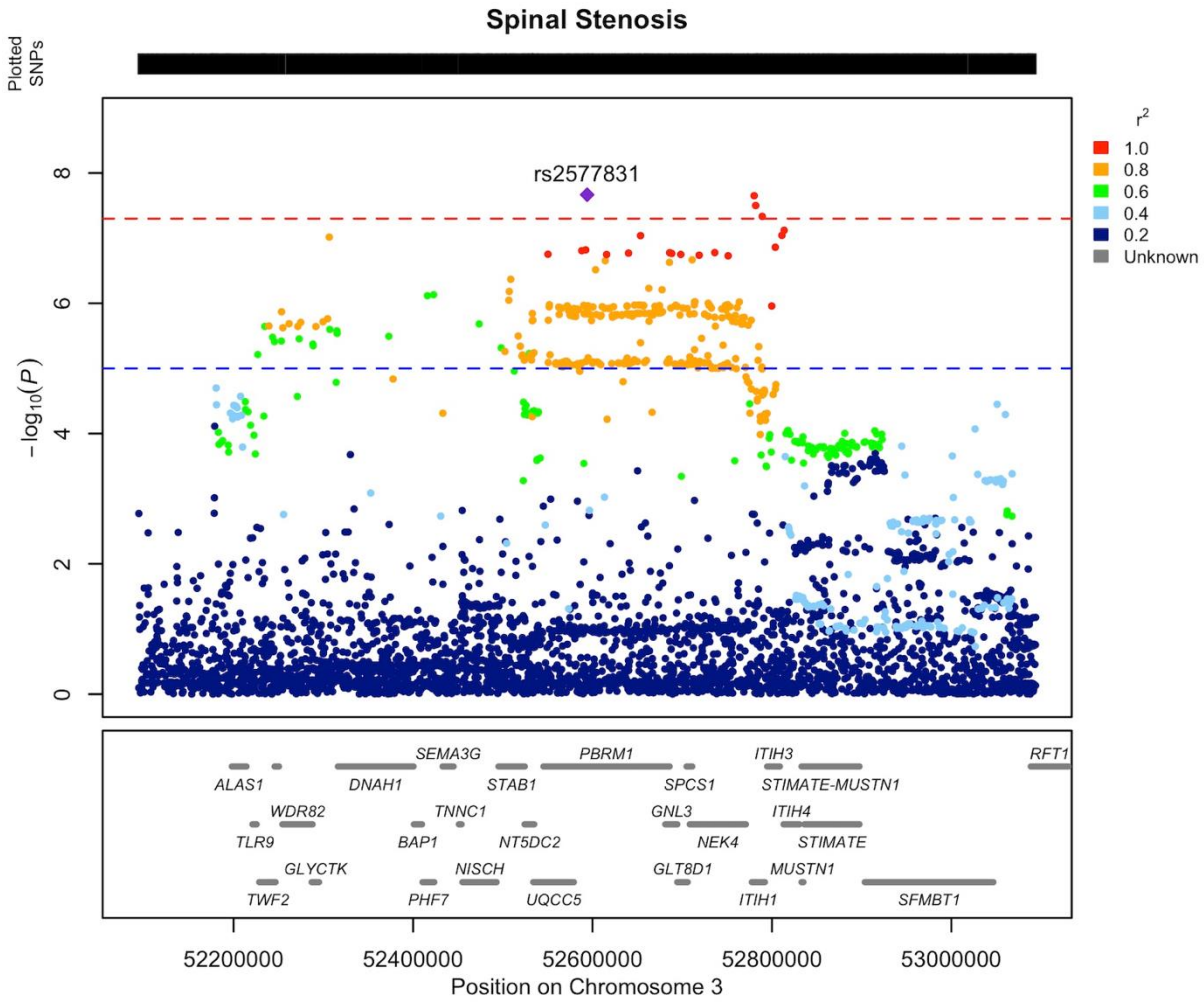

Fig S9. Regional association plot of previously unreported LSS association on chromosome 3 area of 52.1-53.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *GNL3 (G protein nucleolar 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

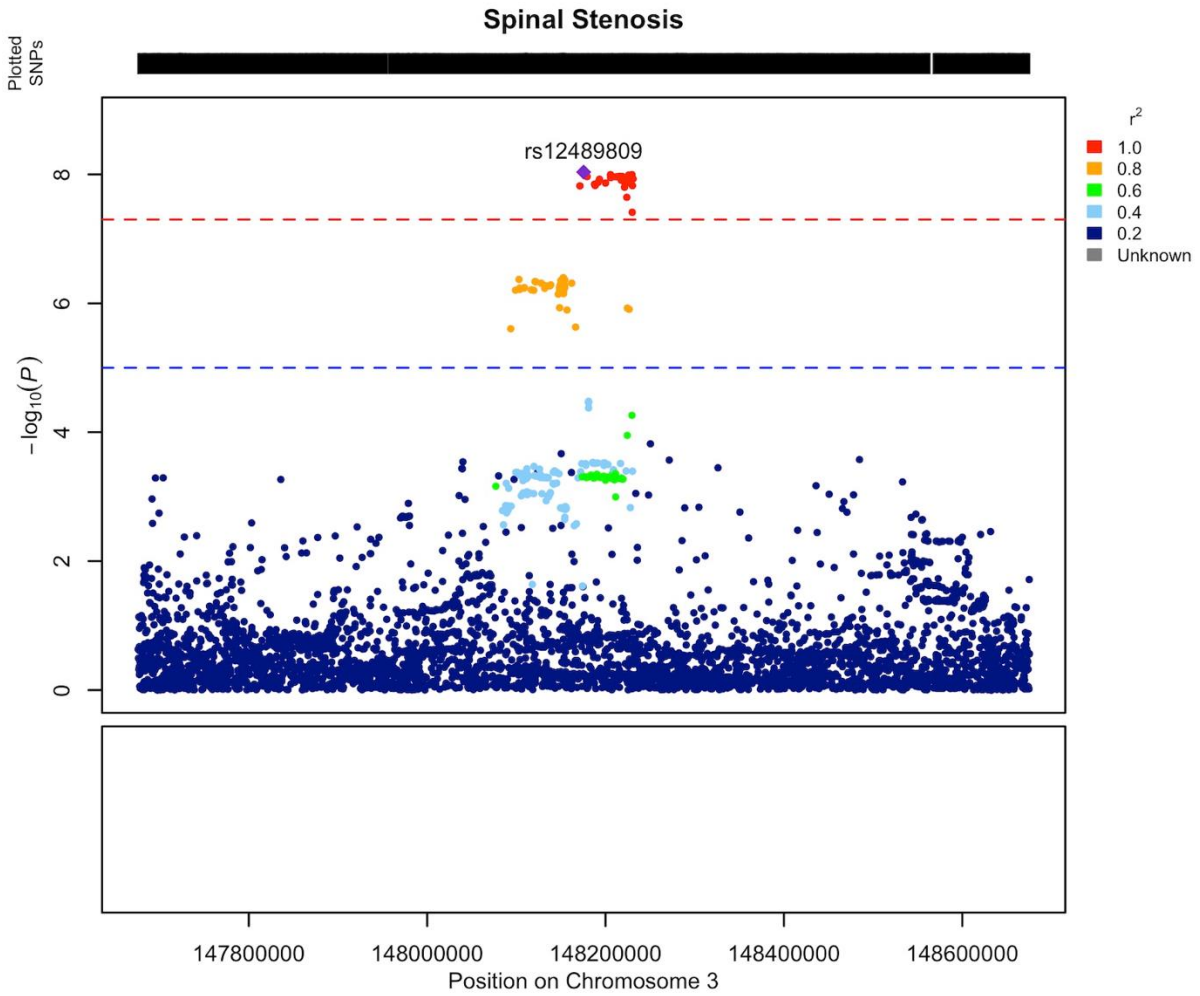

Fig S10. Regional association plot of previously unreported LSS association on chromosome 3 area of 147.7-148.7 MB. There was not any protein coding gene in this locus, so it was classified as *LINC02045 (long intergenic non-protein coding RNA 2045).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

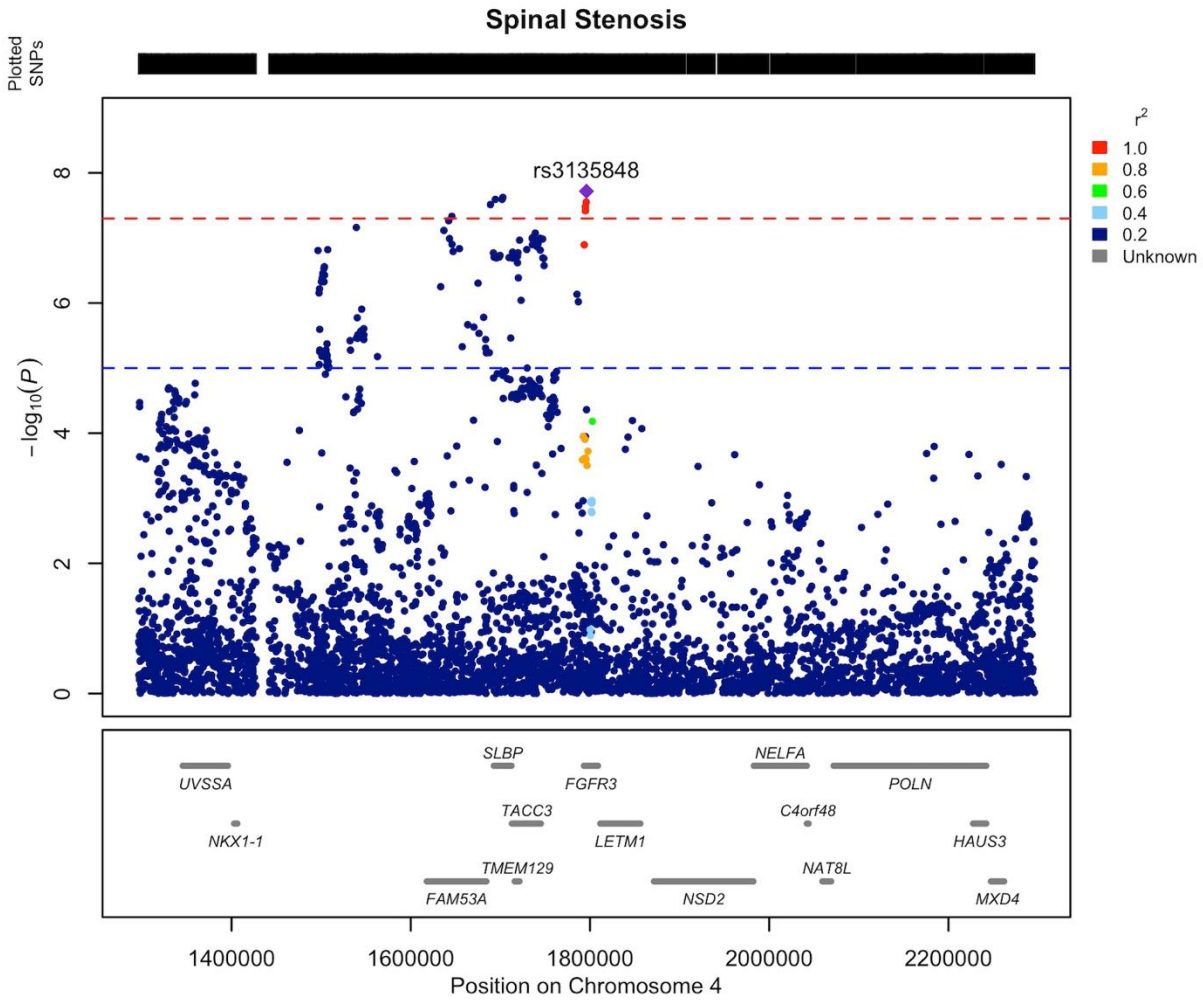

Fig S11. Regional association plot of previously unreported LSS association on chromosome 4 area of 1.4-2.2 MB. Our findings indicate that the gene responsible for the locus's association is most likely *FGFR3 (fibroblast growth factor receptor 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

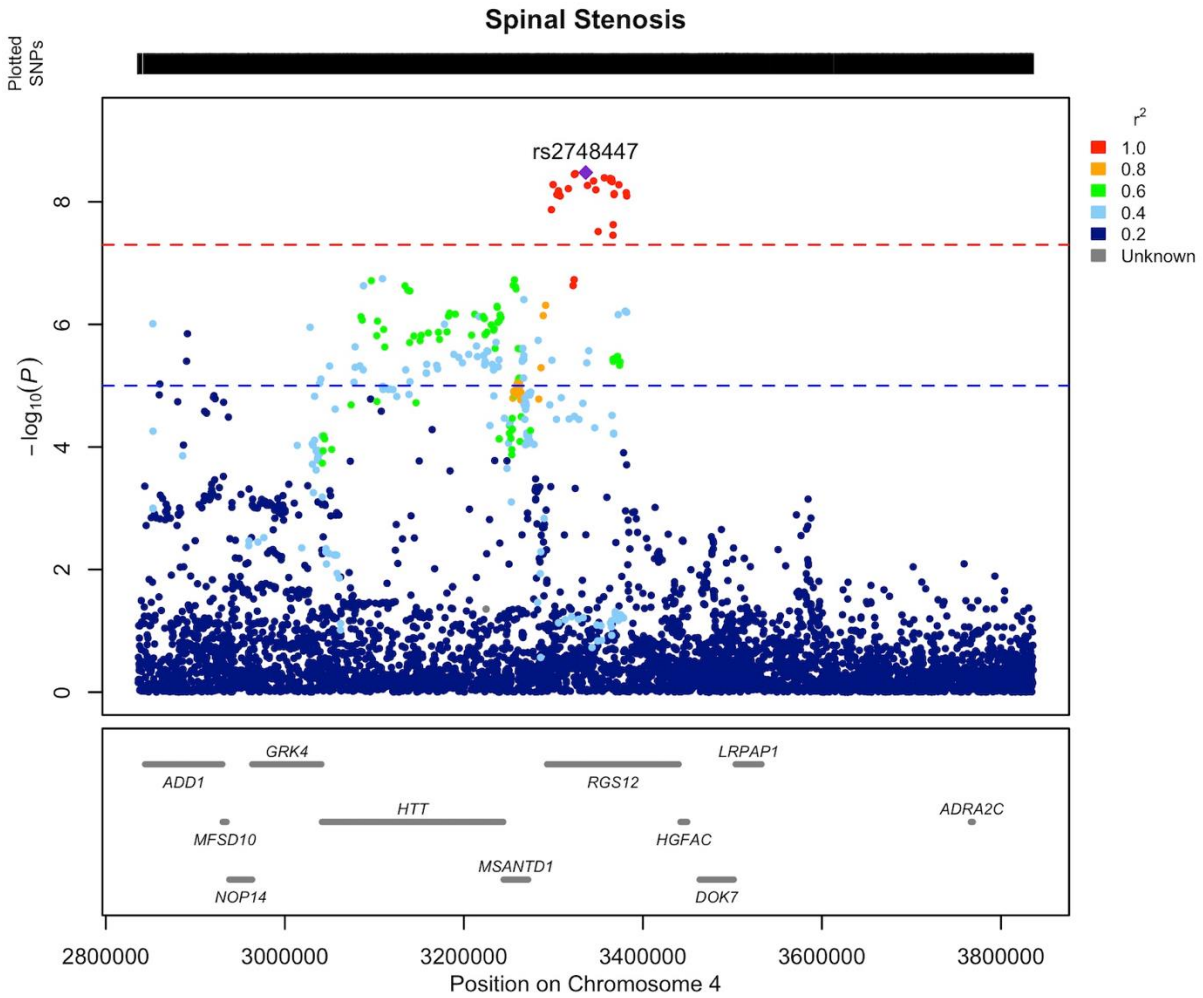

Fig S12. Regional association plot of previously unreported LSS association on chromosome 4 area of 2.8-3.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *RGS12 (regulator of G protein signaling 12).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

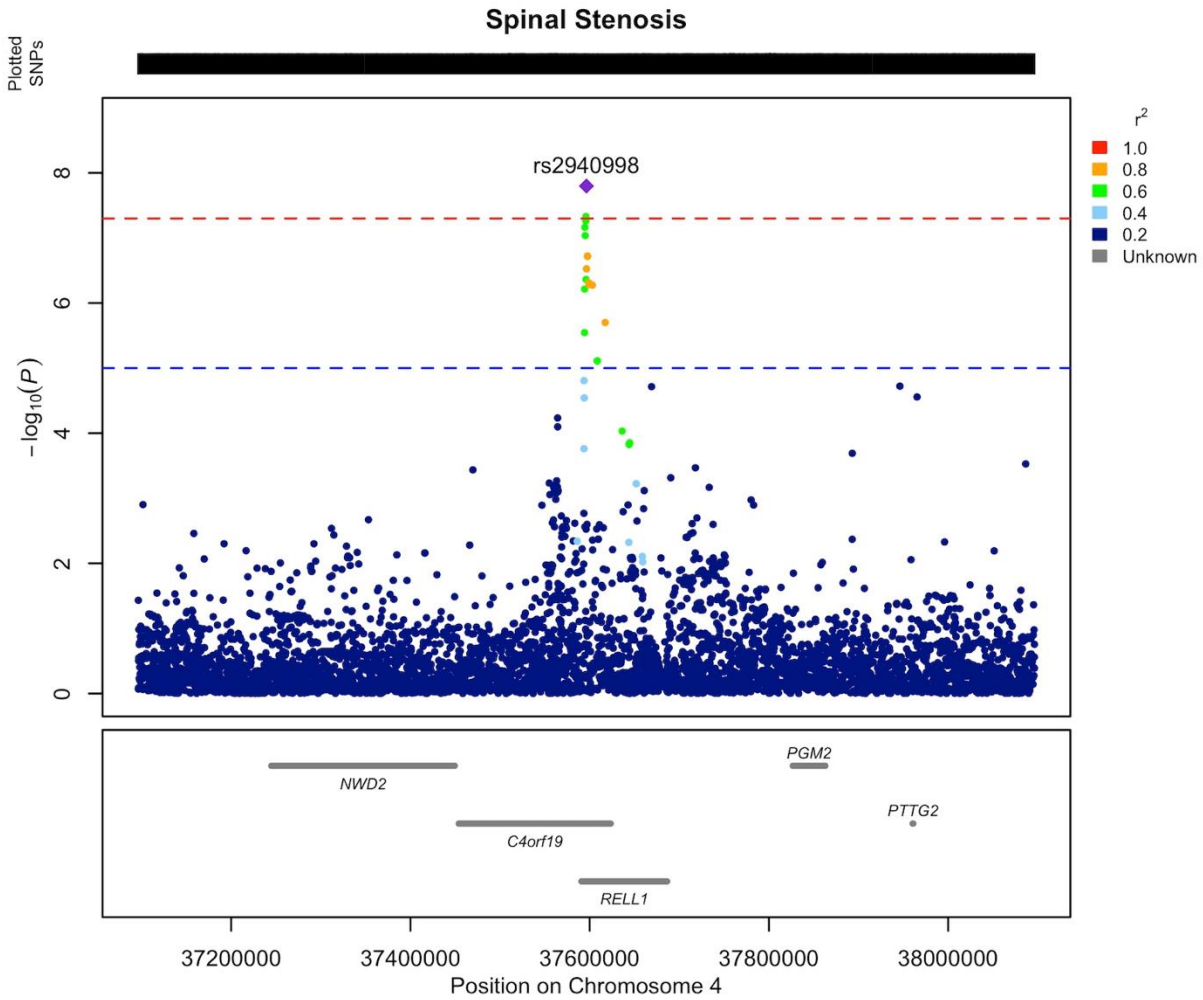

Fig S13. Regional association plot of previously unreported LSS association on chromosome 4 area of 37.1-38.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *RELL1 (RELT like 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

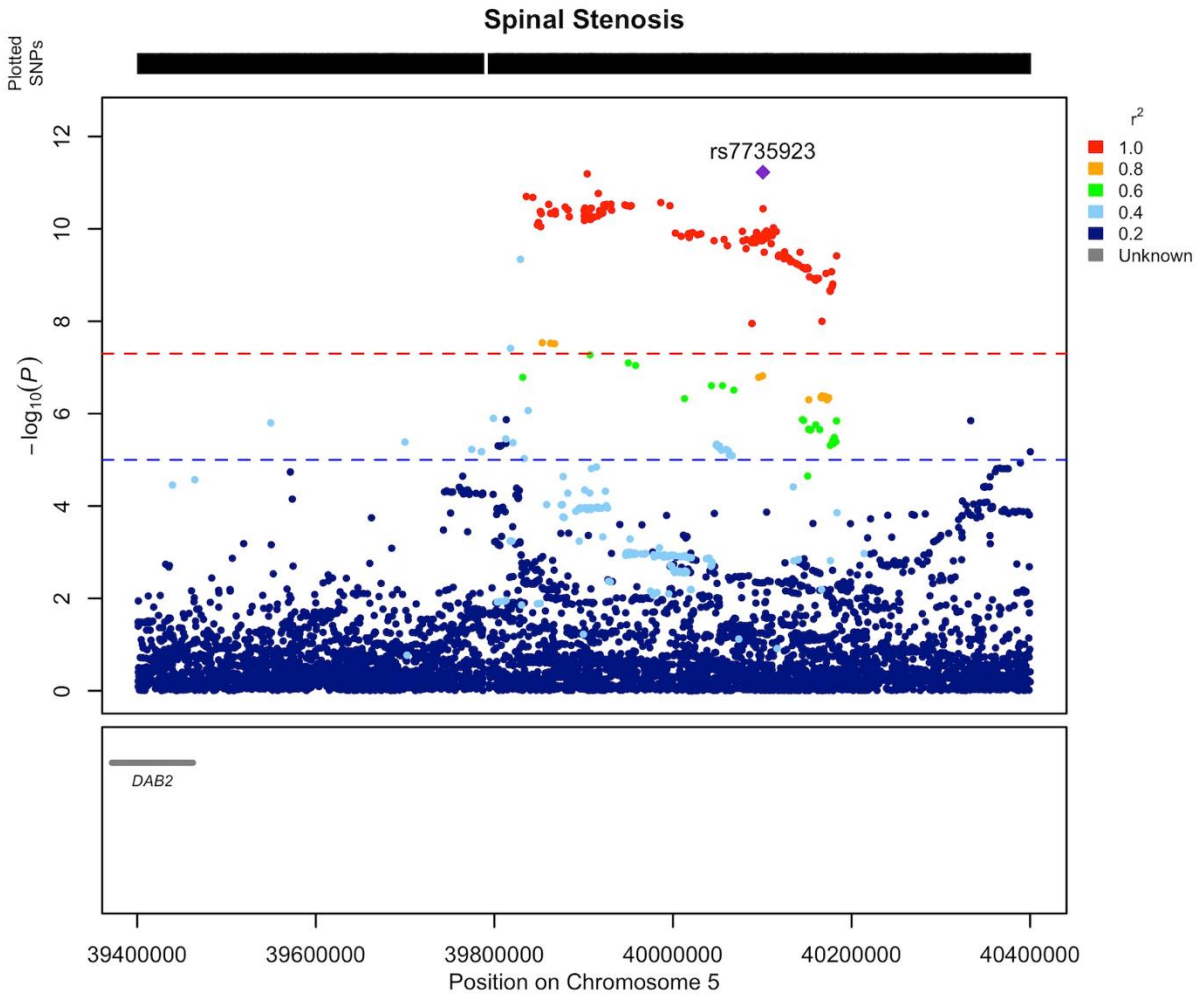

Fig S14. Regional association plot of previously unreported LSS association on chromosome 5 area of 39.4-40.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *DAB2 (DAB adaptor protein 2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

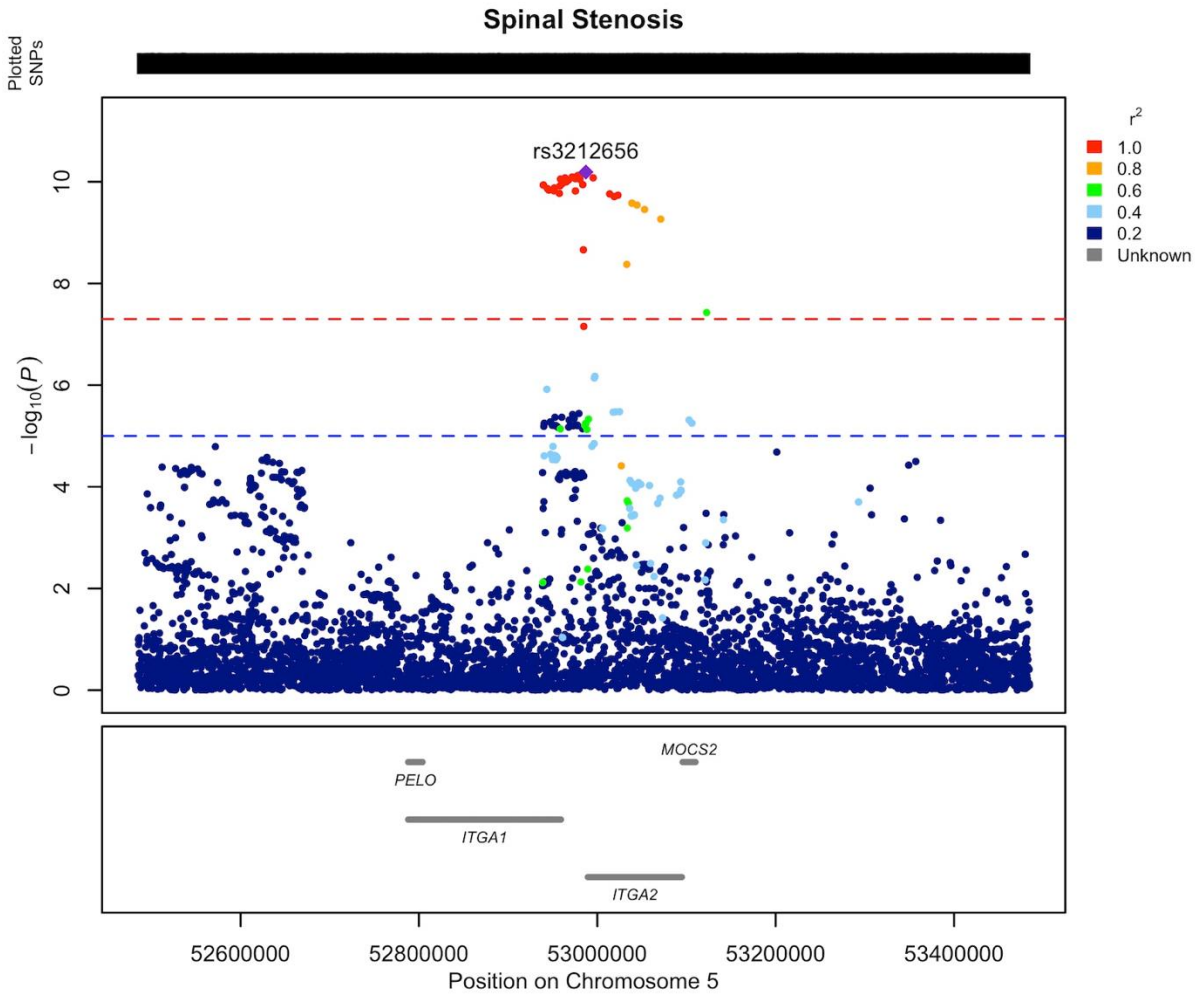

Fig S15. Regional association plot of previously unreported LSS association on chromosome 5 area of 52.5-53.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ITGA2 (integrin subunit alpha 2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

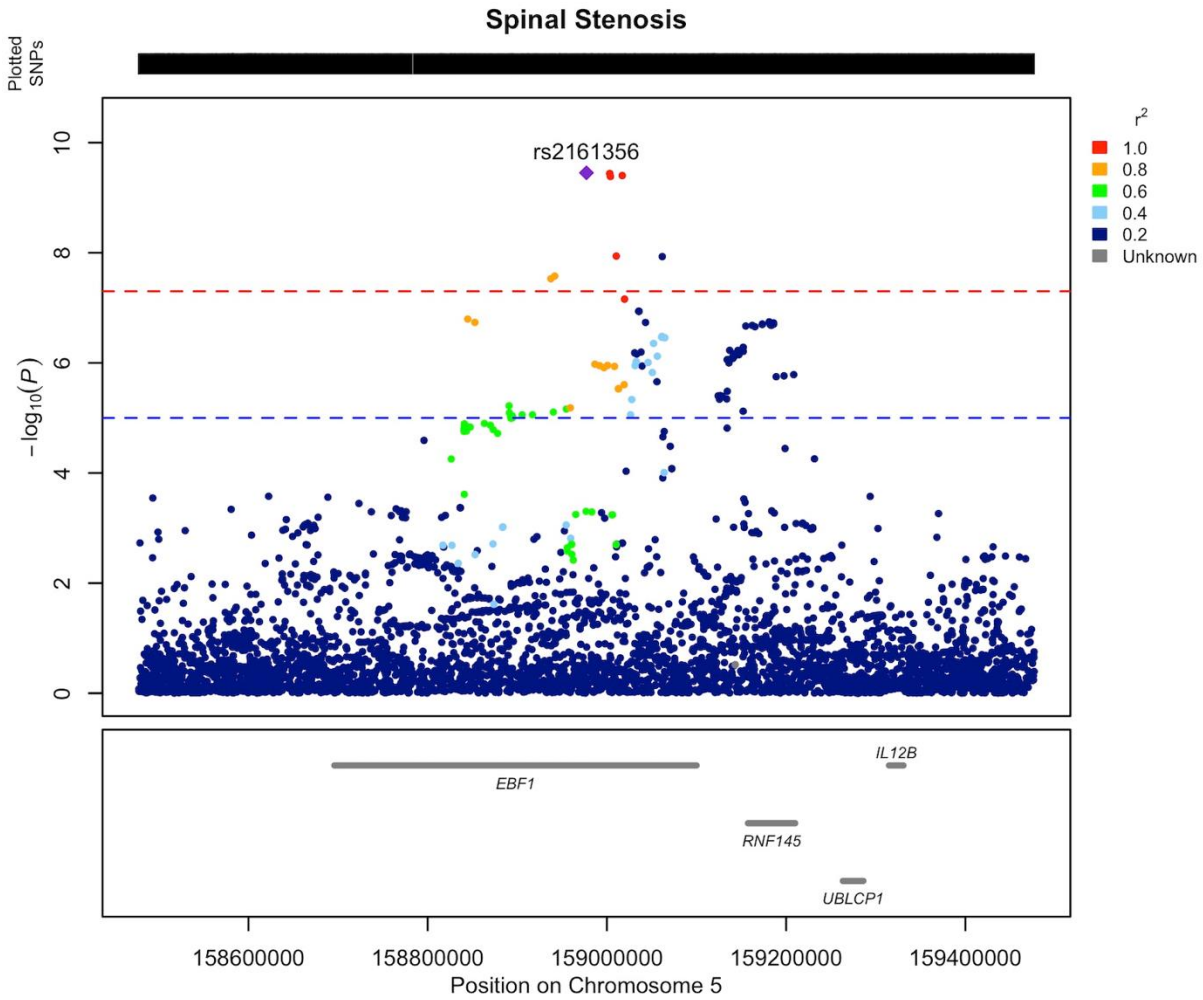

Fig S16. Regional association plot of previously unreported LSS association on chromosome 5 area of 158.5-159.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *EBF1 (EBF transcription factor 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

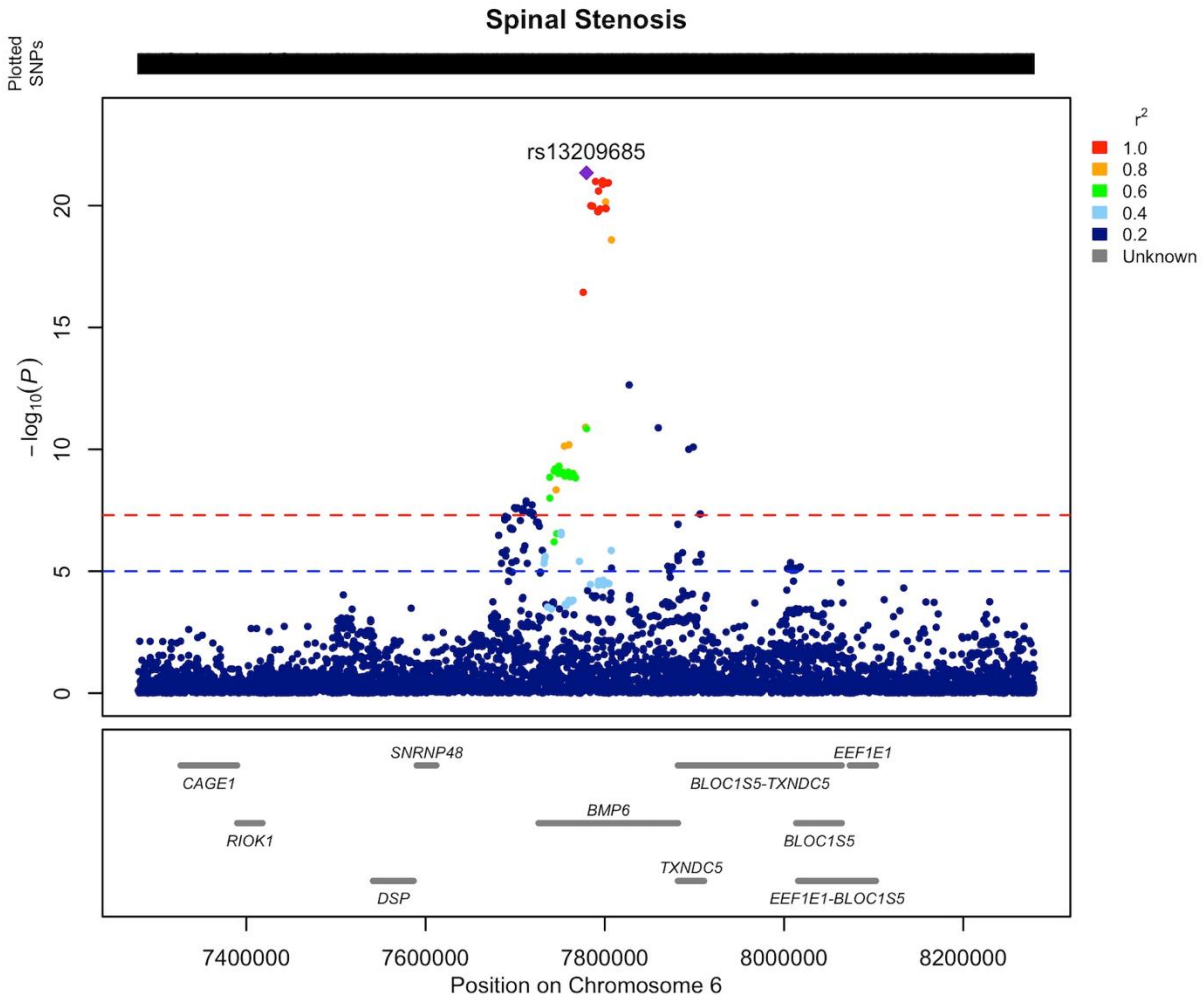

Fig S17. Regional association plot of previously unreported LSS association on chromosome 6 area of 7.3-8.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *BMP6 (bone morphogenetic protein 6)*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

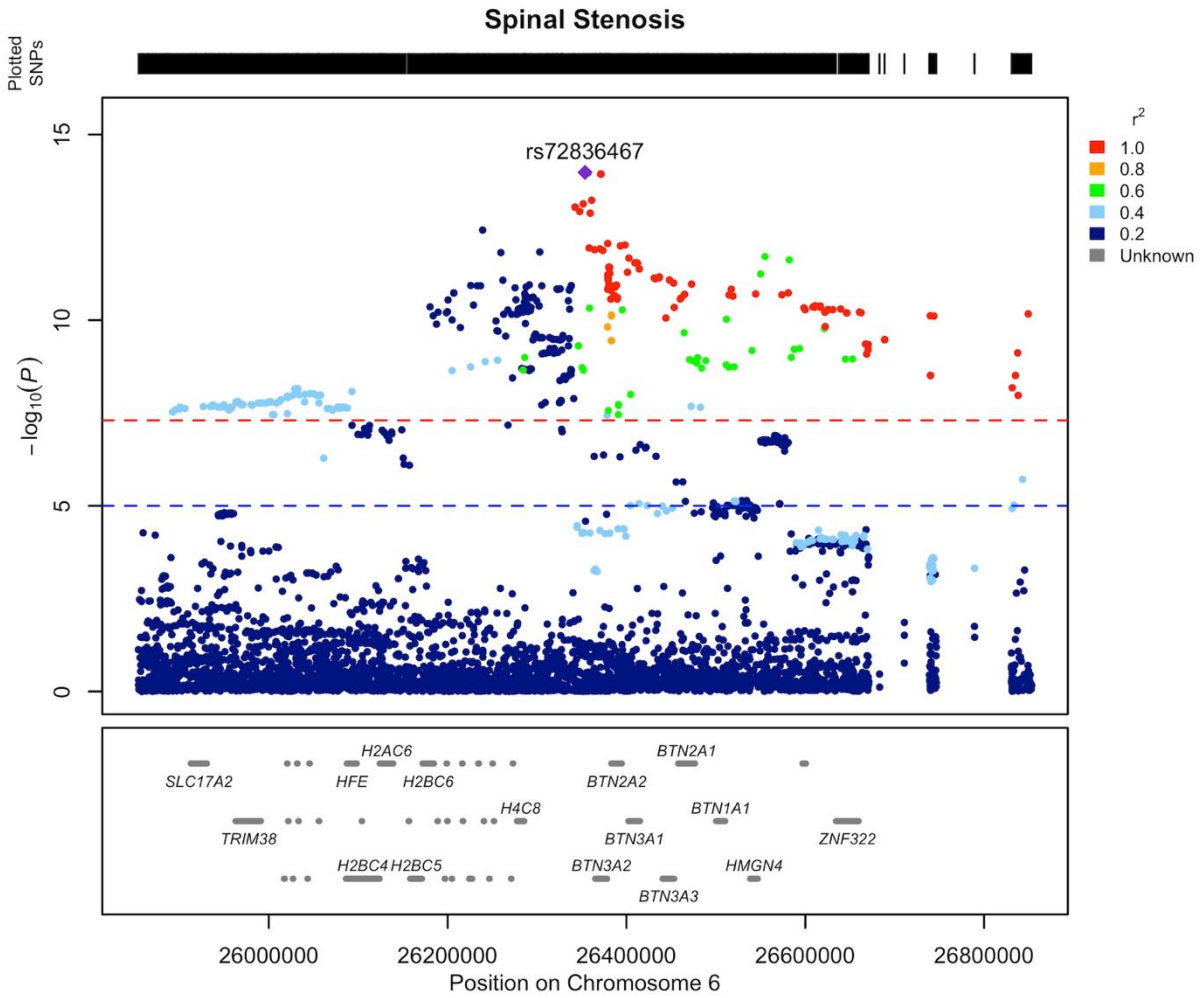

Fig S18. Regional association plot of previously unreported LSS association on chromosome 6 area of 25.8-26.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *HLA*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list. 30 genes omitted from the plot.

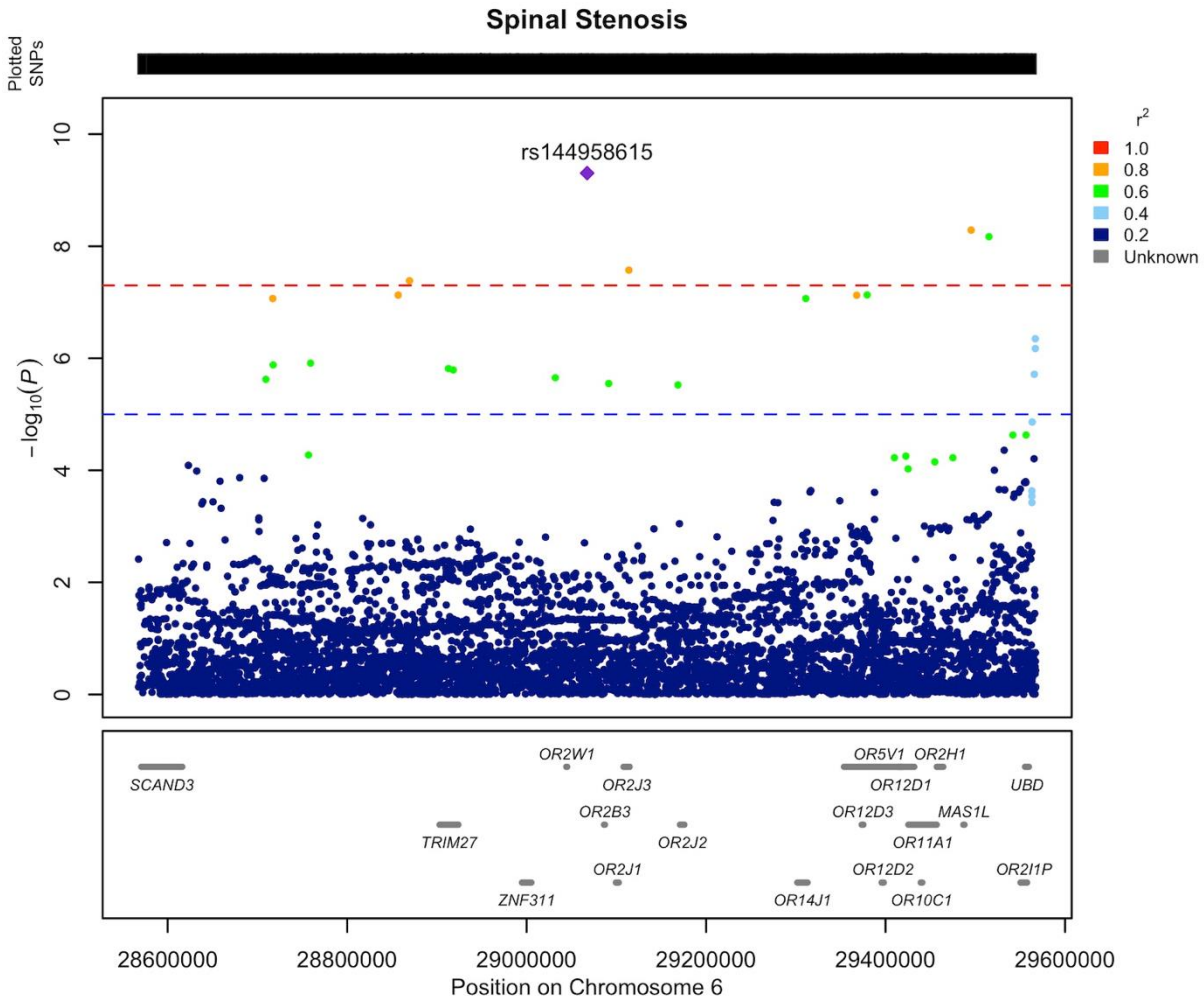

Fig S19. Regional association plot of previously unreported LSS association on chromosome 6 area of 28.6-29.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *HLA*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

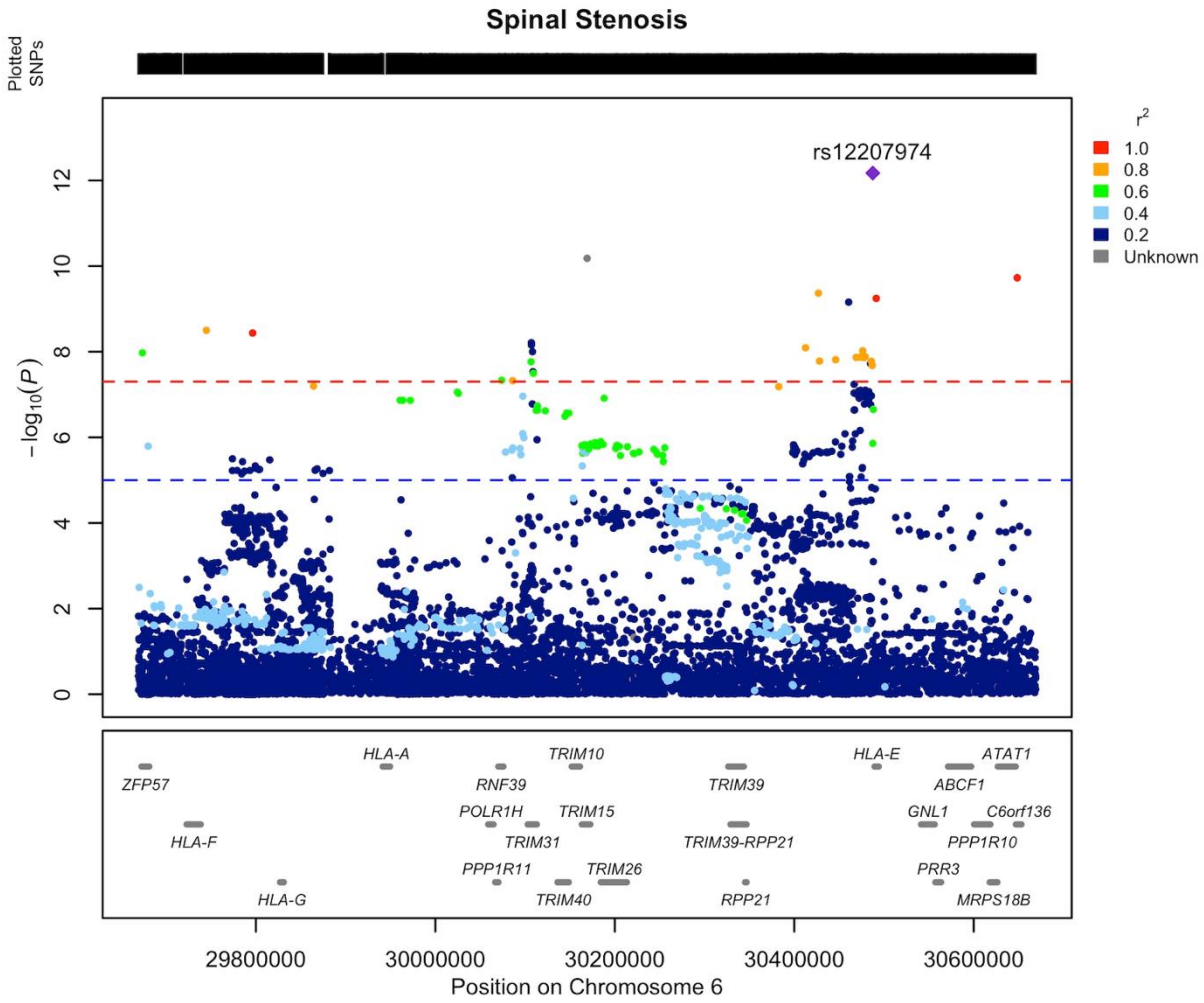

Fig S20. Regional association plot of previously unreported LSS association on chromosome 6 area of 29.7-30.7 MB. Our findings indicate that the gene responsible for the locus's association is most likely *HLA*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

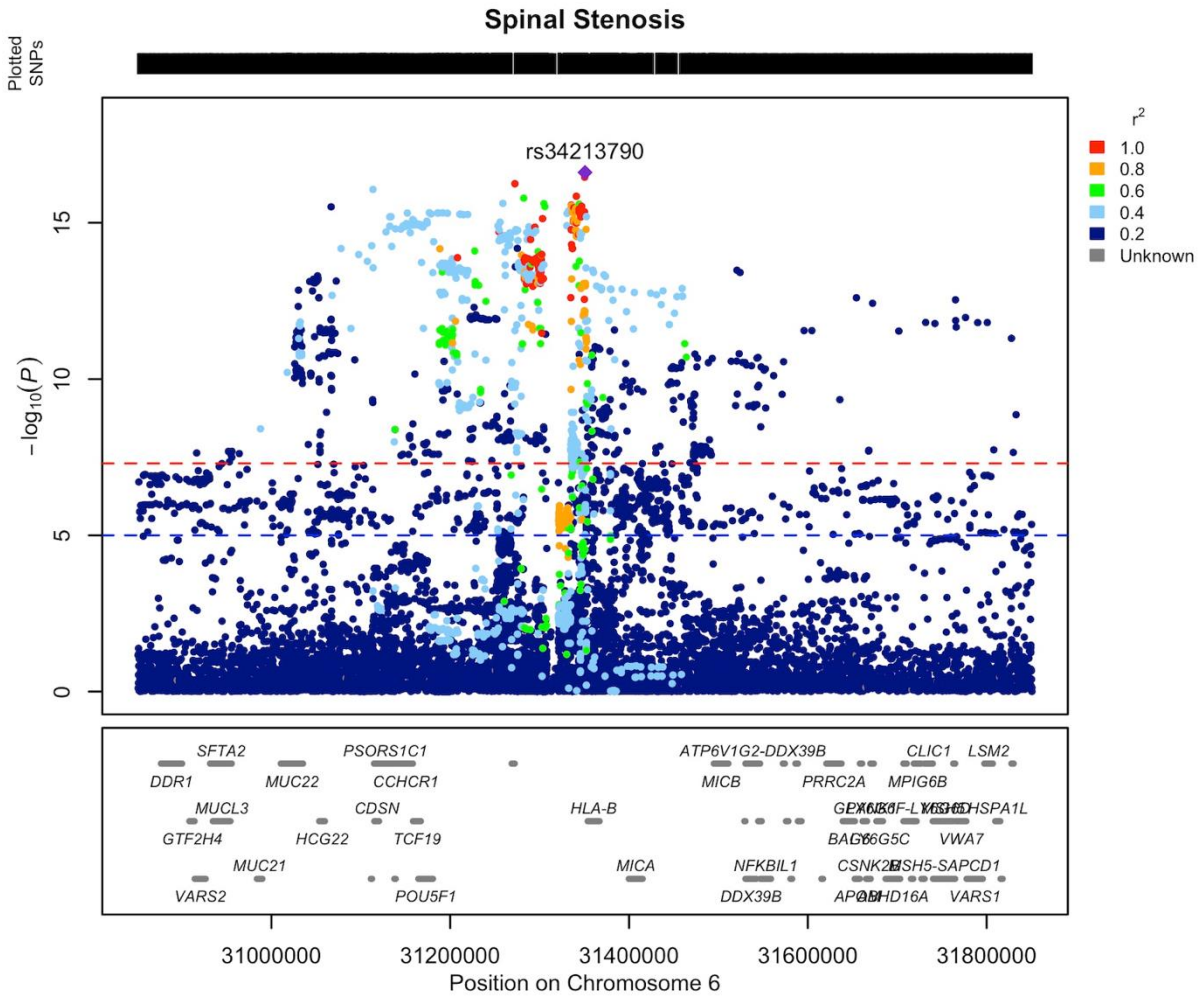

Fig S21. Regional association plot of previously unreported LSS association on chromosome 6 area of 30.9-31.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *HLA*. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

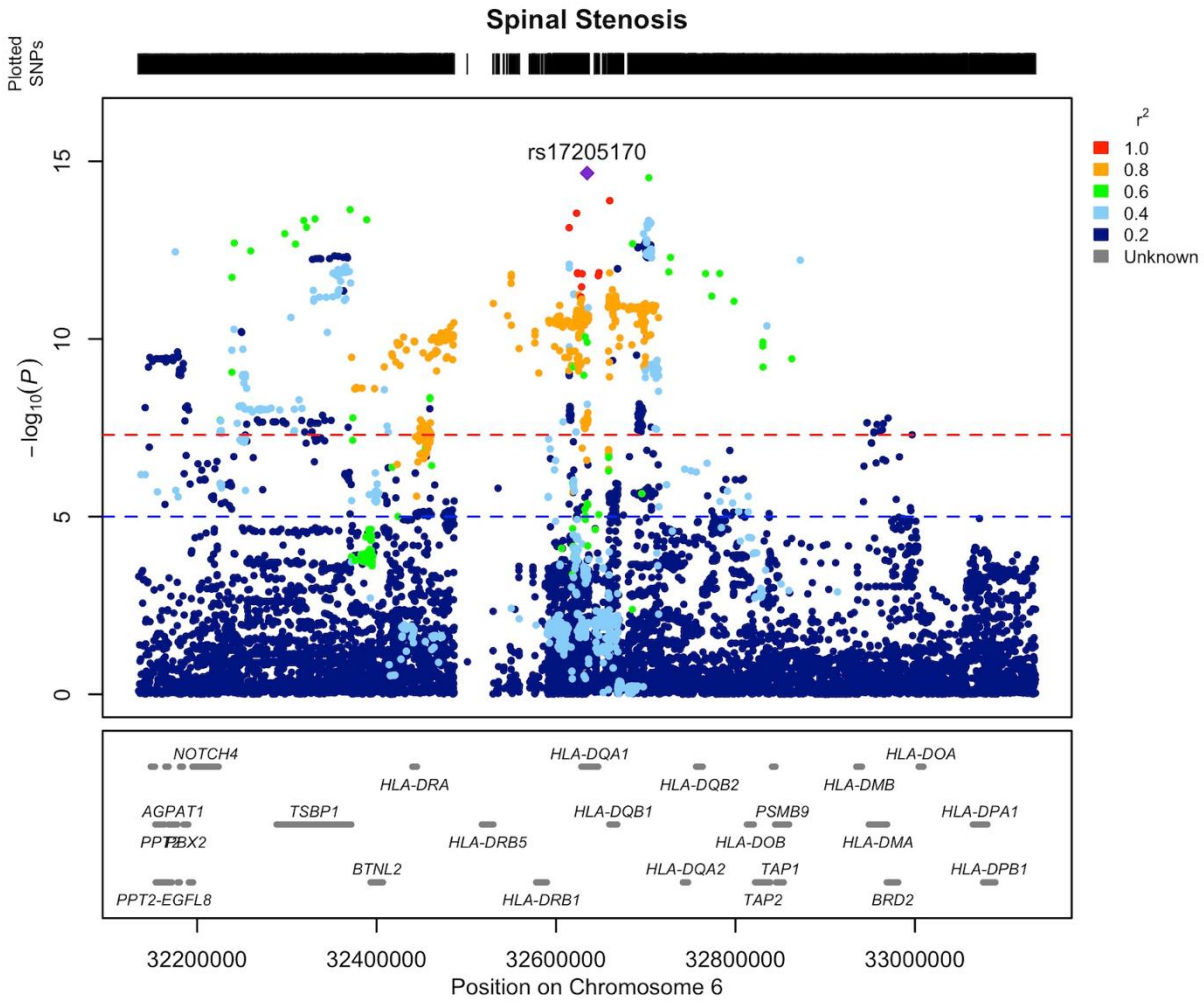

Fig S22. Regional association plot of previously unreported LSS association on chromosome 6 area of 32.2-33.2 MB. Our findings indicate that the gene responsible for the locus's association is most likely *HLA.* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

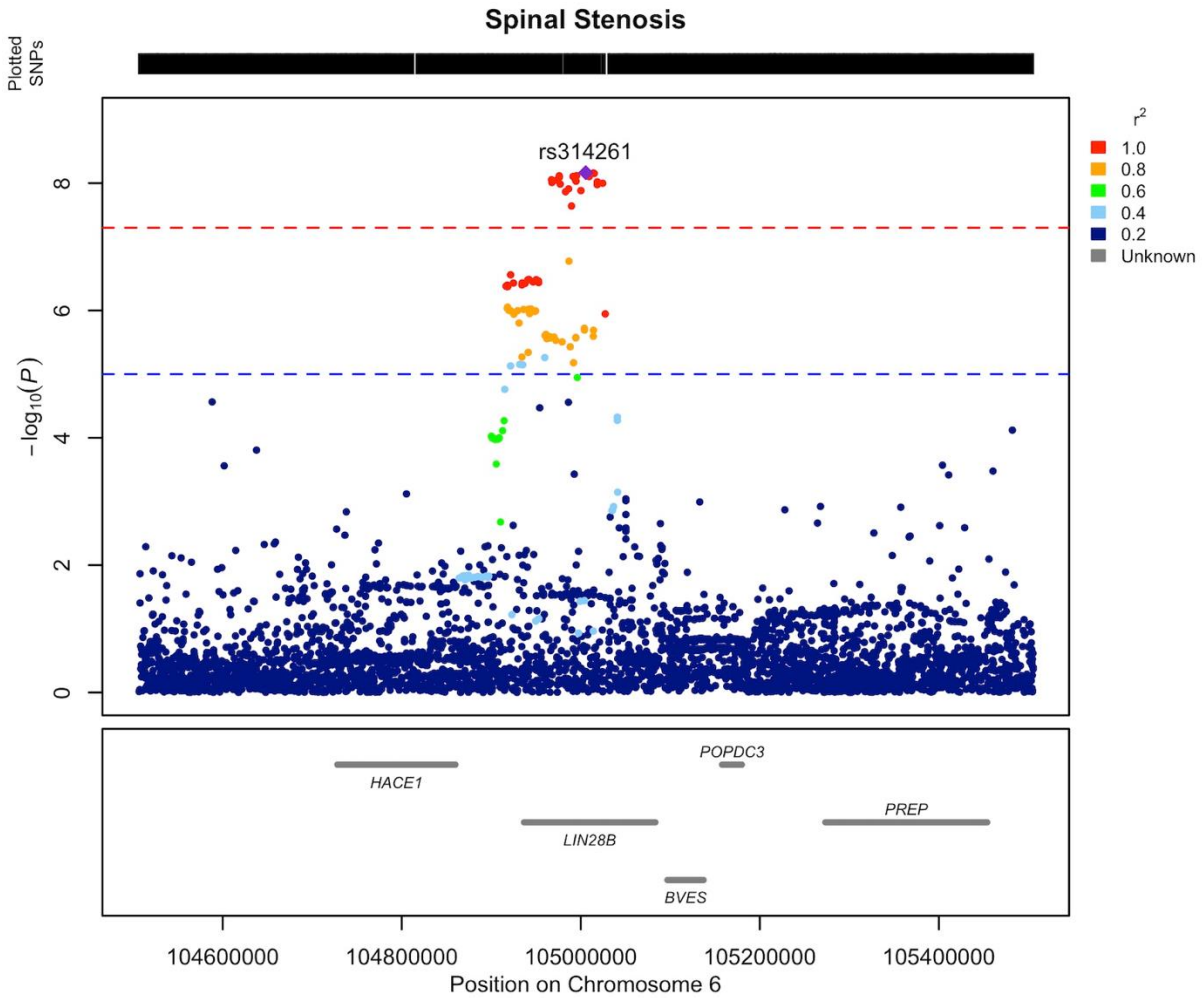

Fig S23. Regional association plot of previously unreported LSS association on chromosome 6 area of 104.5-105.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *LIN28B (lin-28 homolog B).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

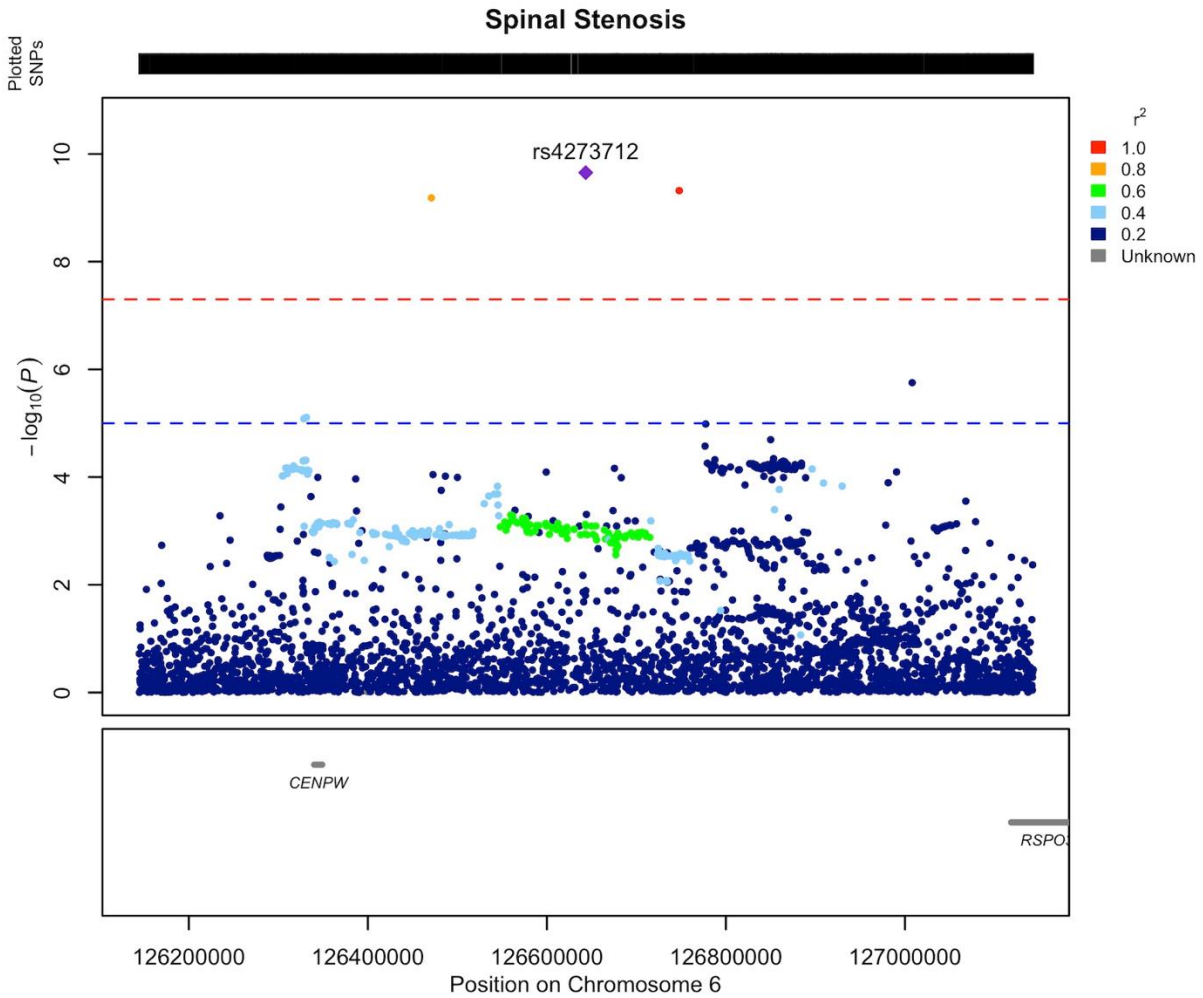

Fig S24. Regional association plot of previously unreported LSS association on chromosome 6 area of 126.1-127.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *RSPO3 (R-spondin 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

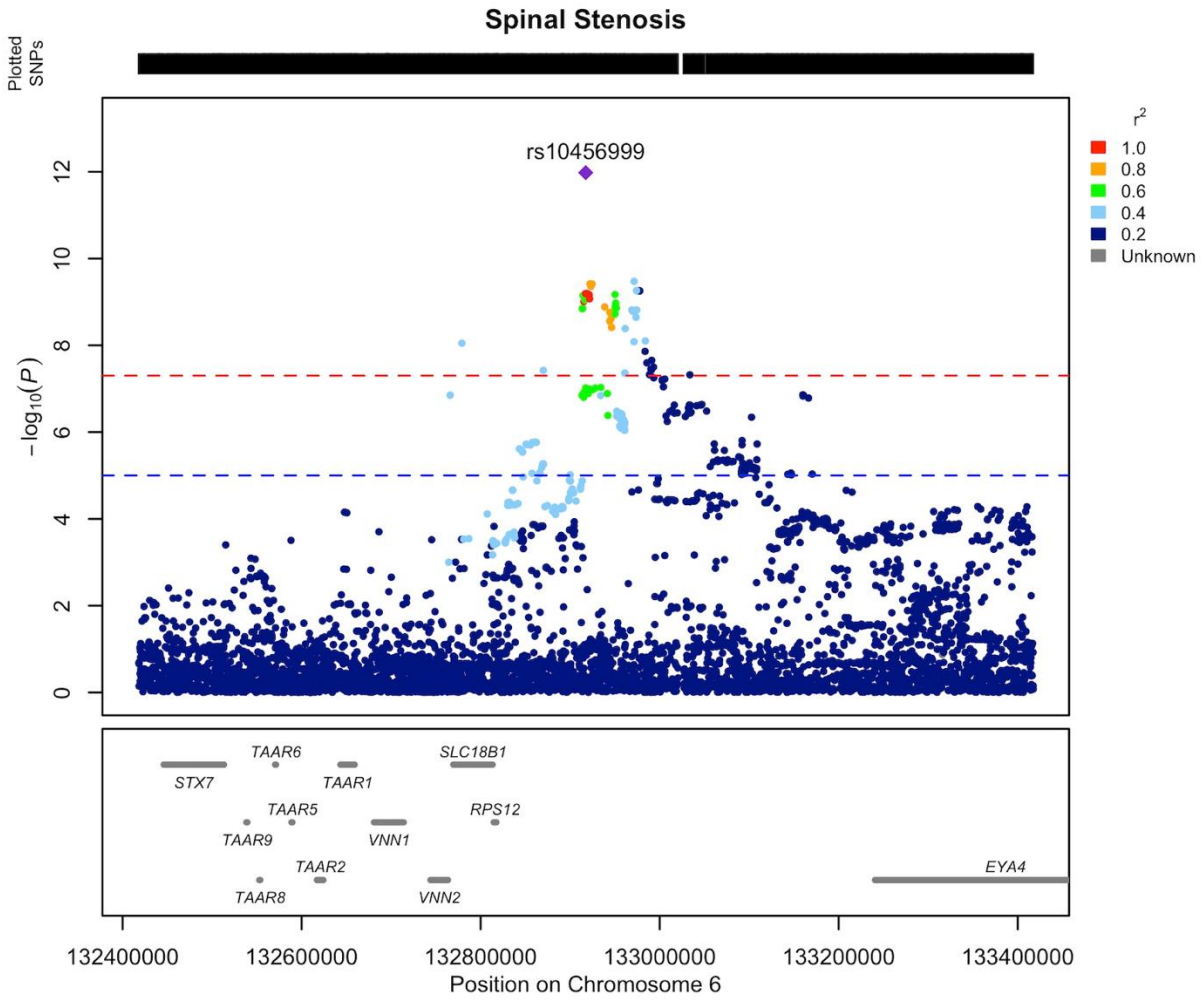

Fig S25. Regional association plot of previously unreported LSS association on chromosome 6 area of 132.4-133.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *EYA4 (EYA transcriptional coactivator and phosphatase 4).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

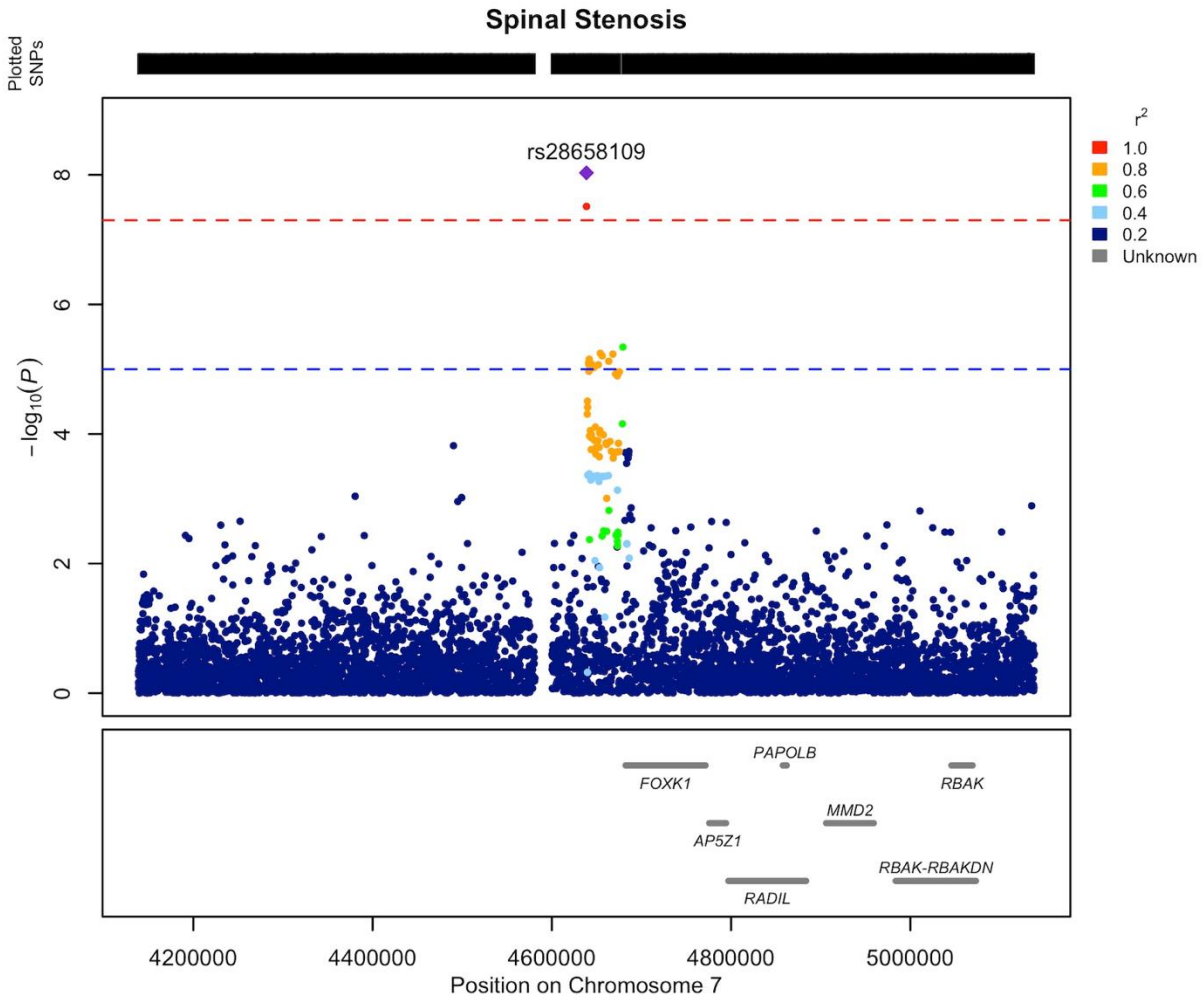

Fig S26. Regional association plot of previously unreported LSS association on chromosome 7 area of 4.1-5.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *FOXK1 (forkhead box K1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

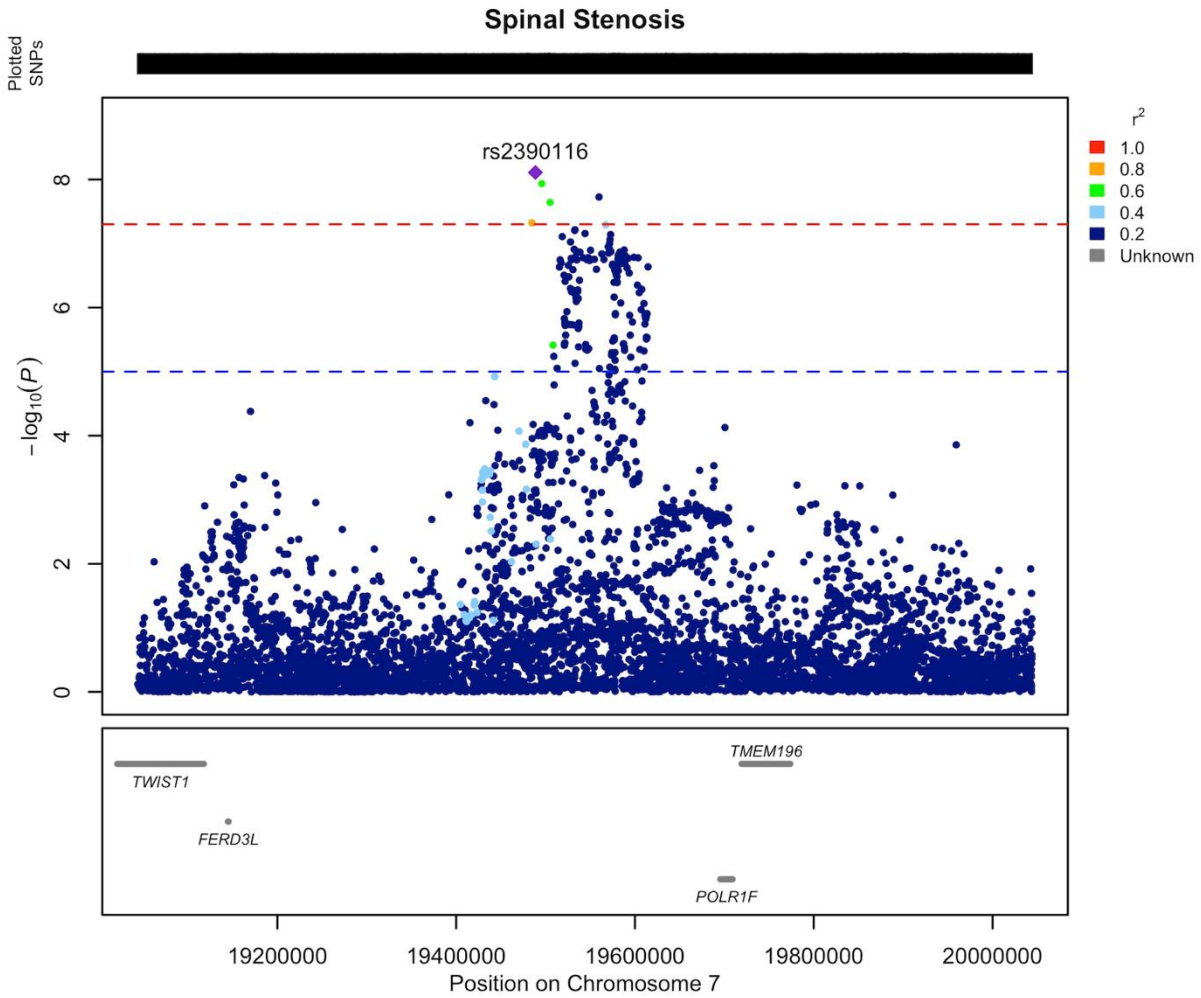

Fig S27. Regional association plot of previously unreported LSS association on chromosome 7 area of 19.1-20.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TWIST1 (twist family bHLH transcription factor 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

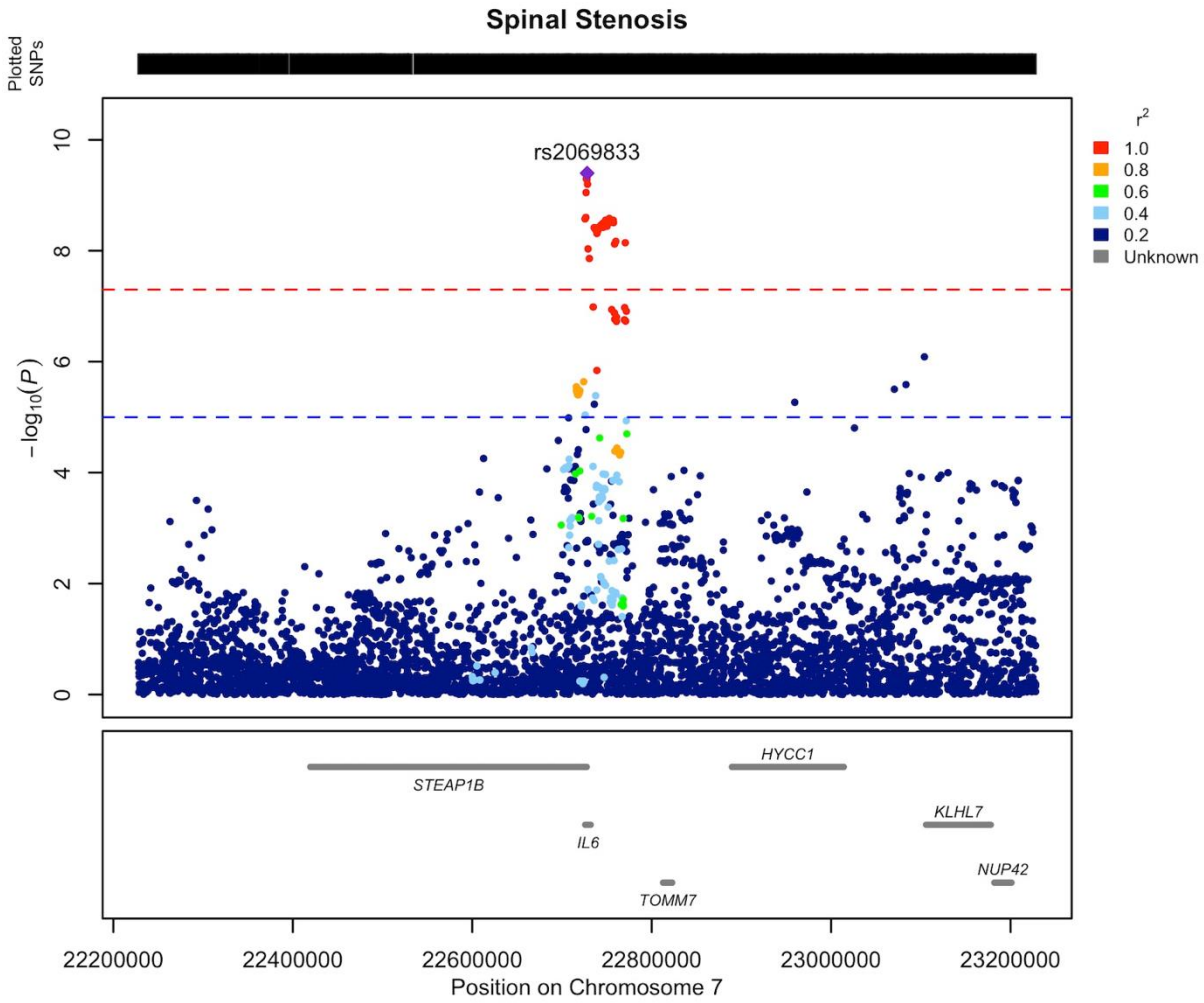

Fig S28. Regional association plot of previously unreported LSS association on chromosome 7 area of 22.2-23.2 MB. Our findings indicate that the gene responsible for the locus's association is most likely *IL6 (interleukin 6).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

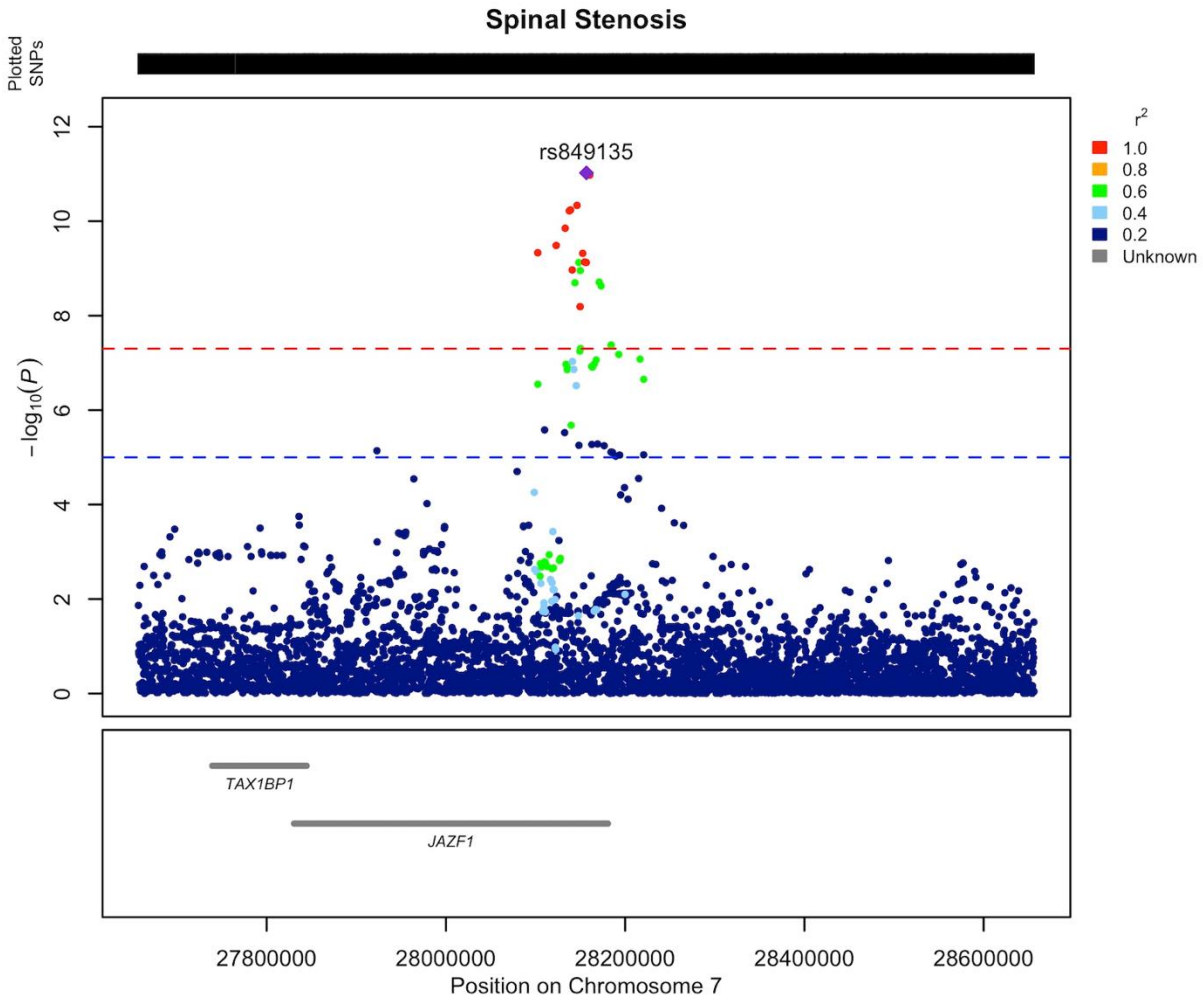

Fig S29. Regional association plot of previously unreported LSS association on chromosome 7 area of 27.7-28.7 MB. Our findings indicate that the gene responsible for the locus's association is most likely *JAZF1 (JAZF1 zinc finger 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

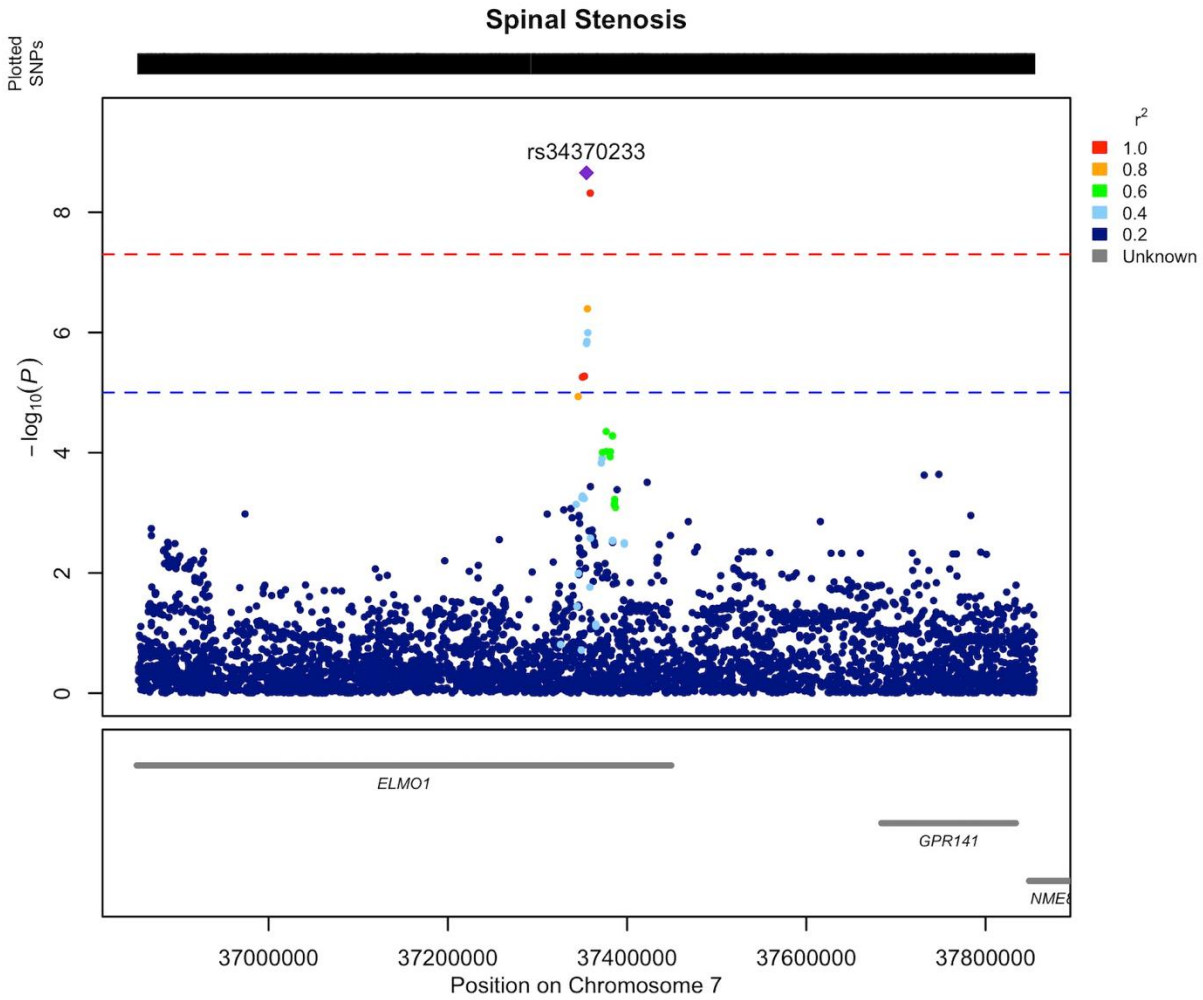

Fig S30. Regional association plot of previously unreported LSS association on chromosome 7 area of 367.8-37.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ELMO1 (engulfment and cell motility 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

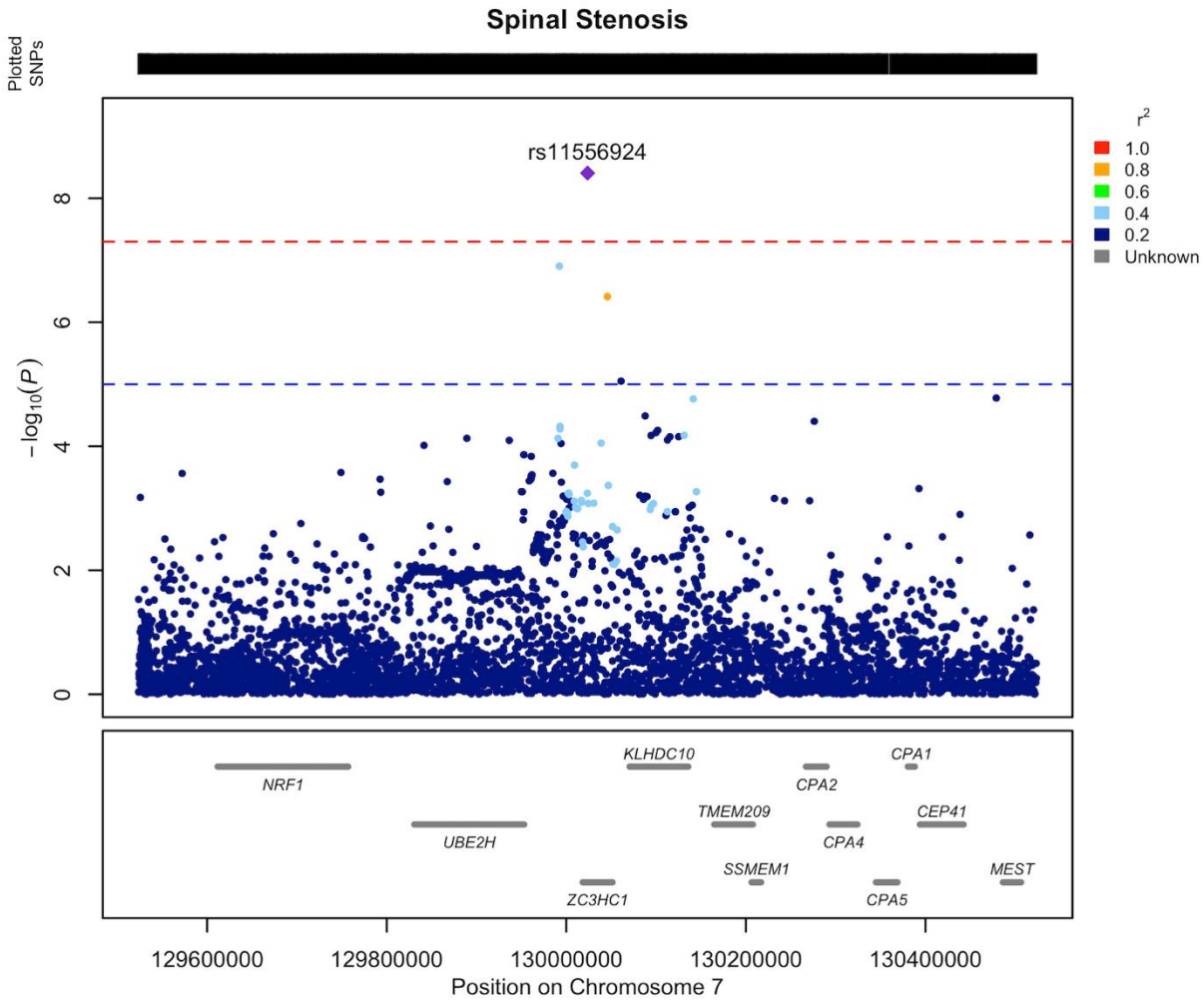

Fig S31. Regional association plot of previously unreported LSS association on chromosome 7 area of 129.5-130.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ZC3HC1 (zinc finger C3HC-type containing 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

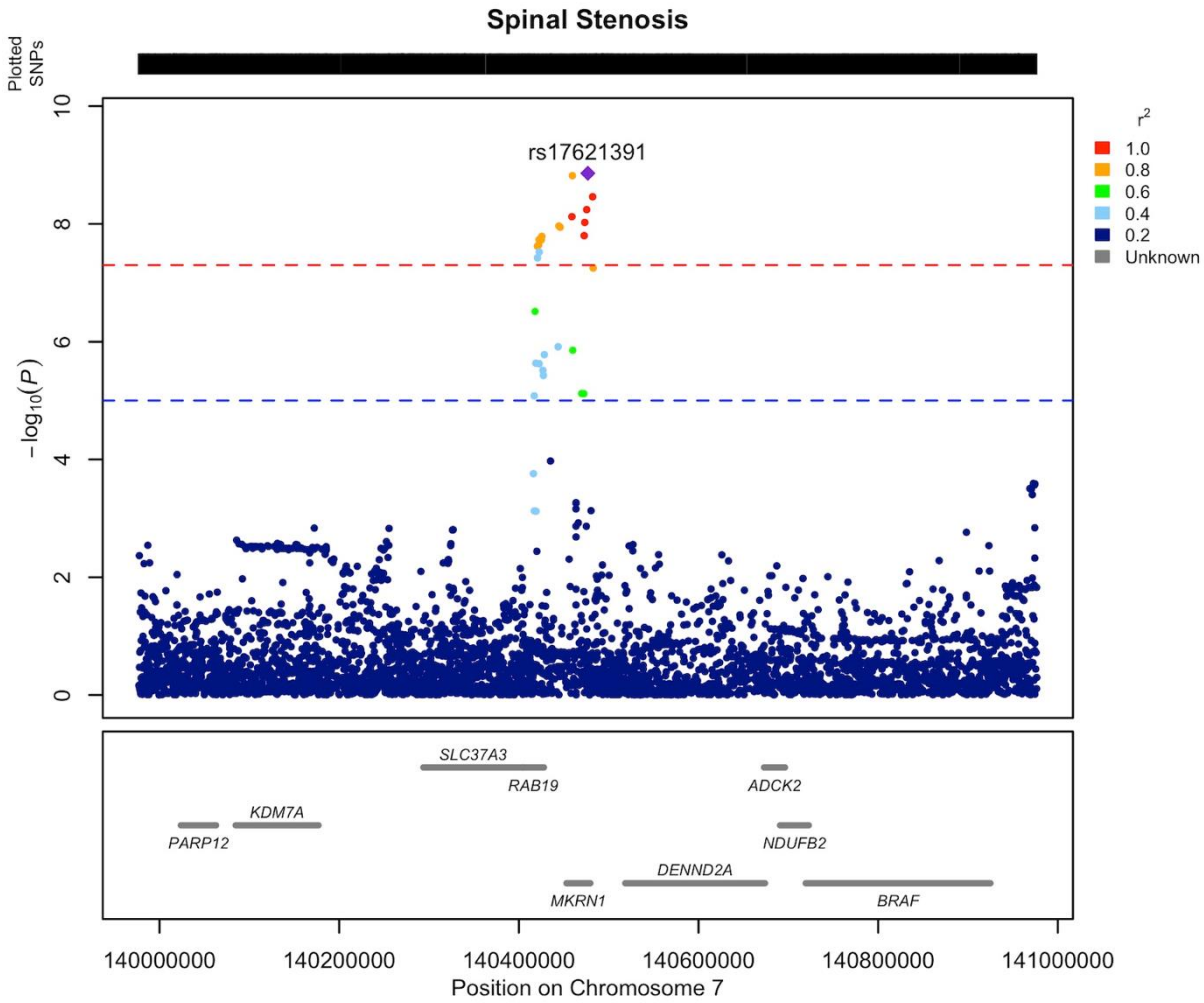

Fig S32. Regional association plot of previously unreported LSS association on chromosome 7 area of 140.0-141.0 MB. Our findings indicate that the gene responsible for the locus's association is most likely *MKRN1 (makorin ring finger protein 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

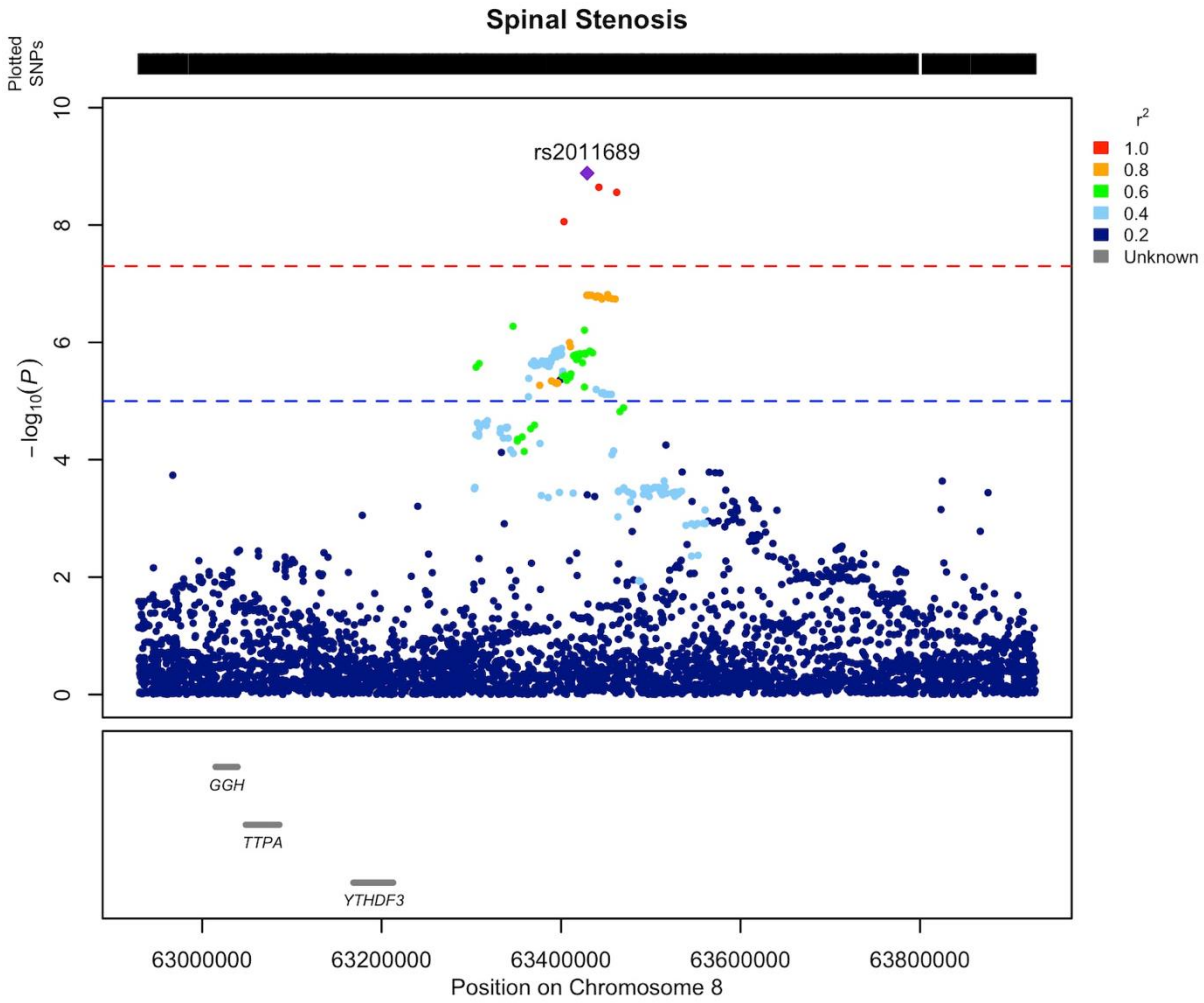

Fig S33. Regional association plot of previously unreported LSS association on chromosome 8 area of 62.9-63.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *YTHDF3 (YTH N6-methyladenosine RNA binding protein F3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

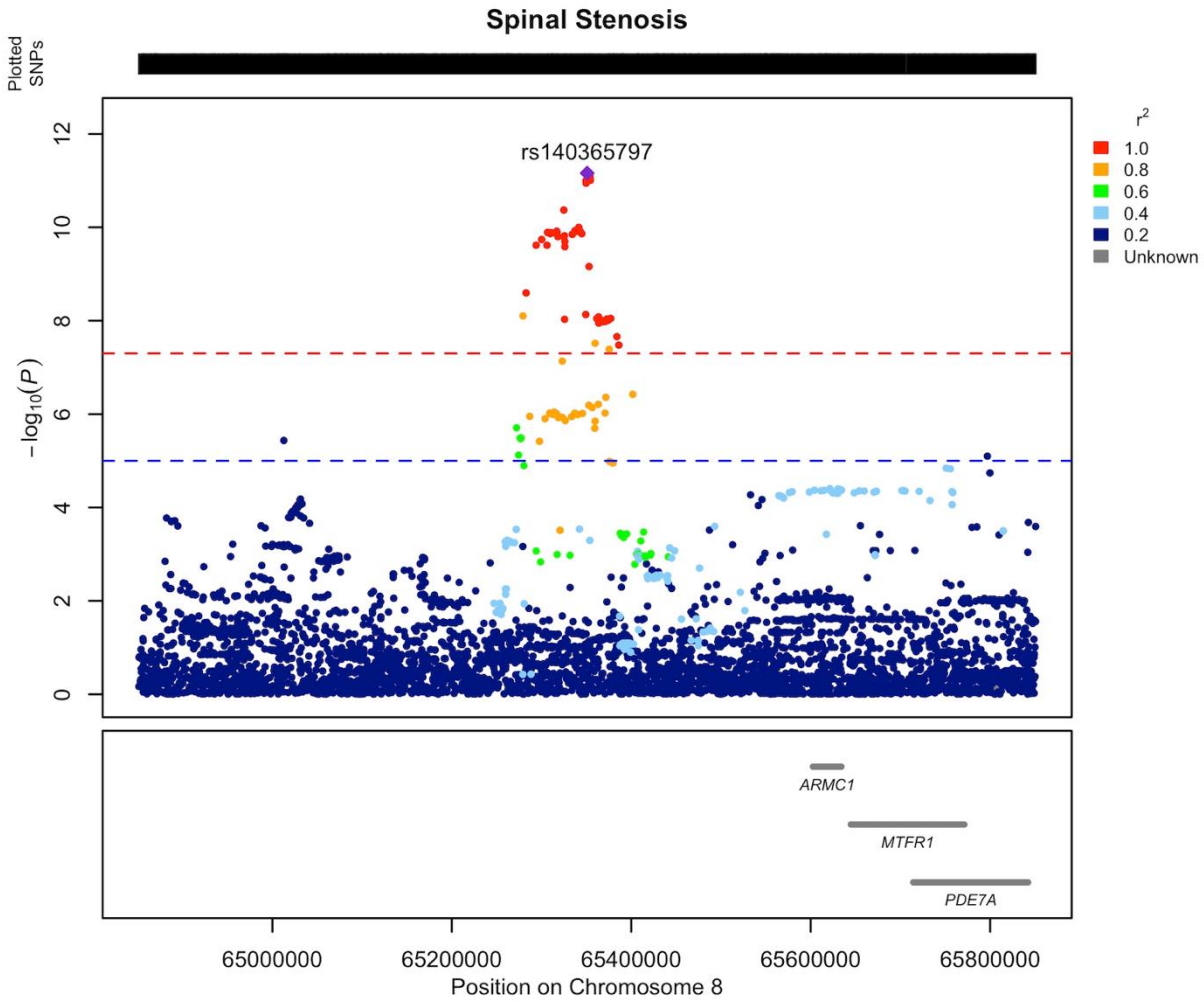

Fig S34. Regional association plot of previously unreported LSS association on chromosome 8 area of 64.8-65.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *PDE7A (phosphodiesterase 7A).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

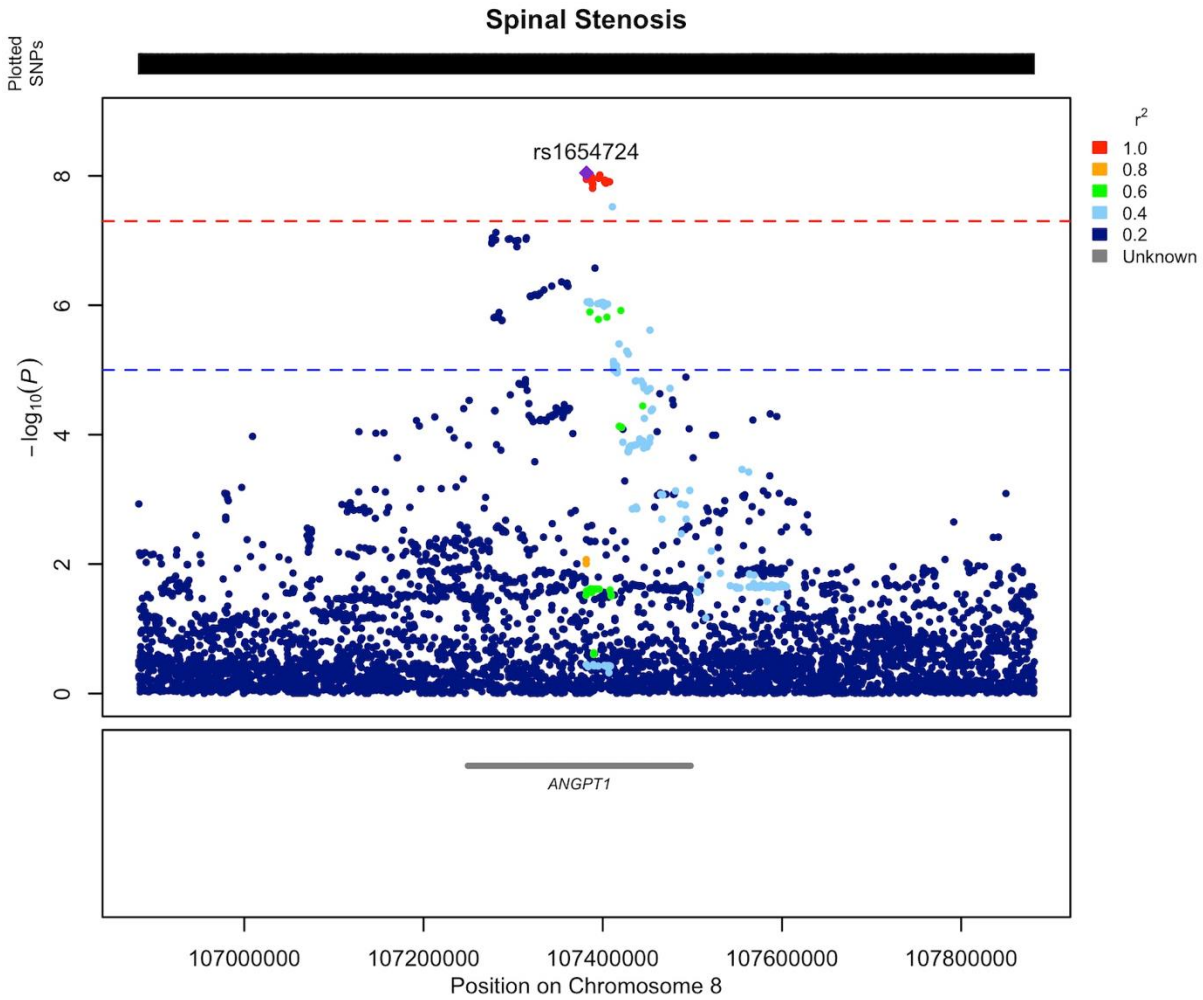

Fig S35. Regional association plot of previously unreported LSS association on chromosome 8 area of 106.9-107.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ANGPT1 (angiopoietin 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

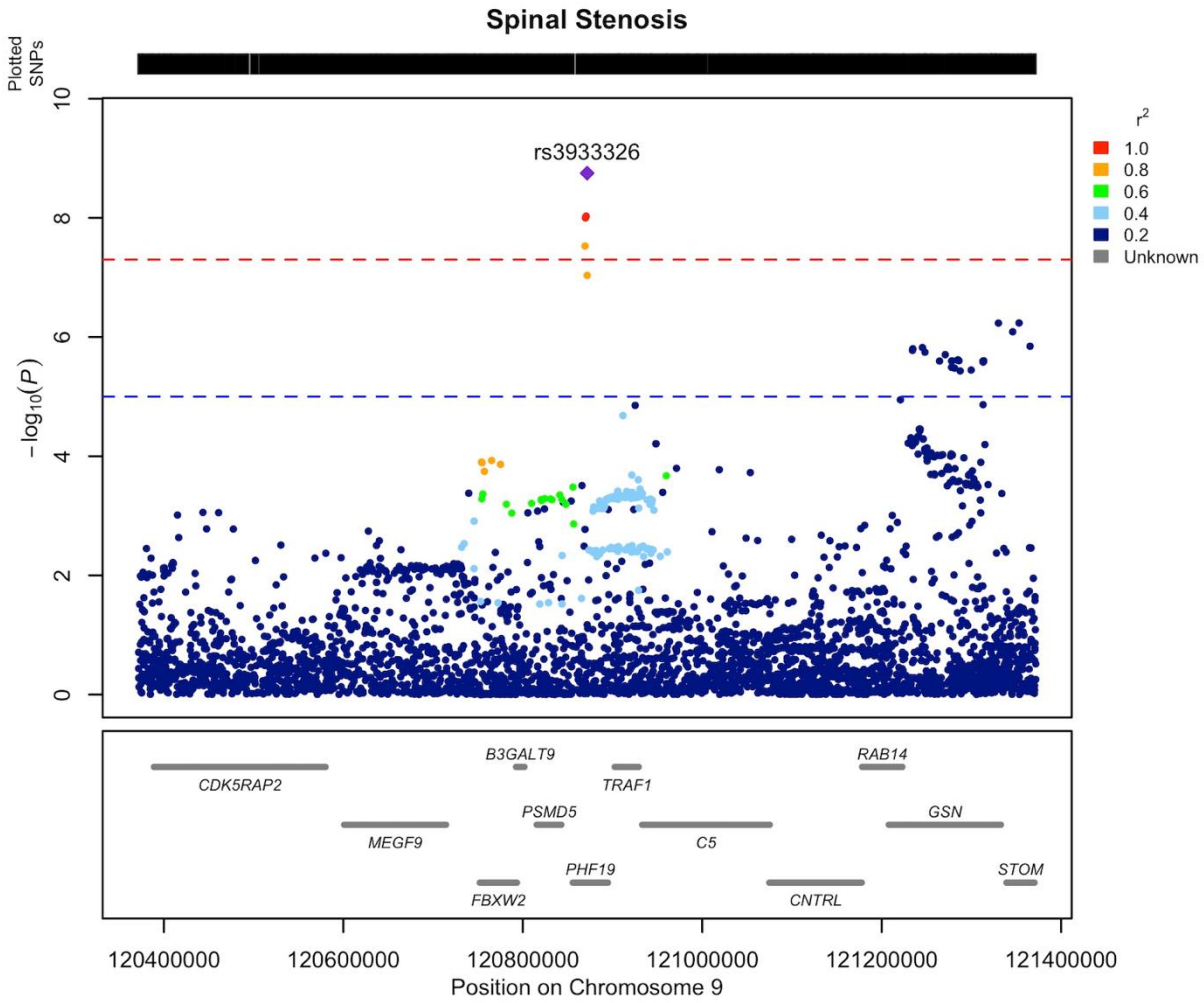

Fig S36. Regional association plot of previously unreported LSS association on chromosome 9 area of 120.4-121.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TRAF1 (TNF receptor associated factor 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

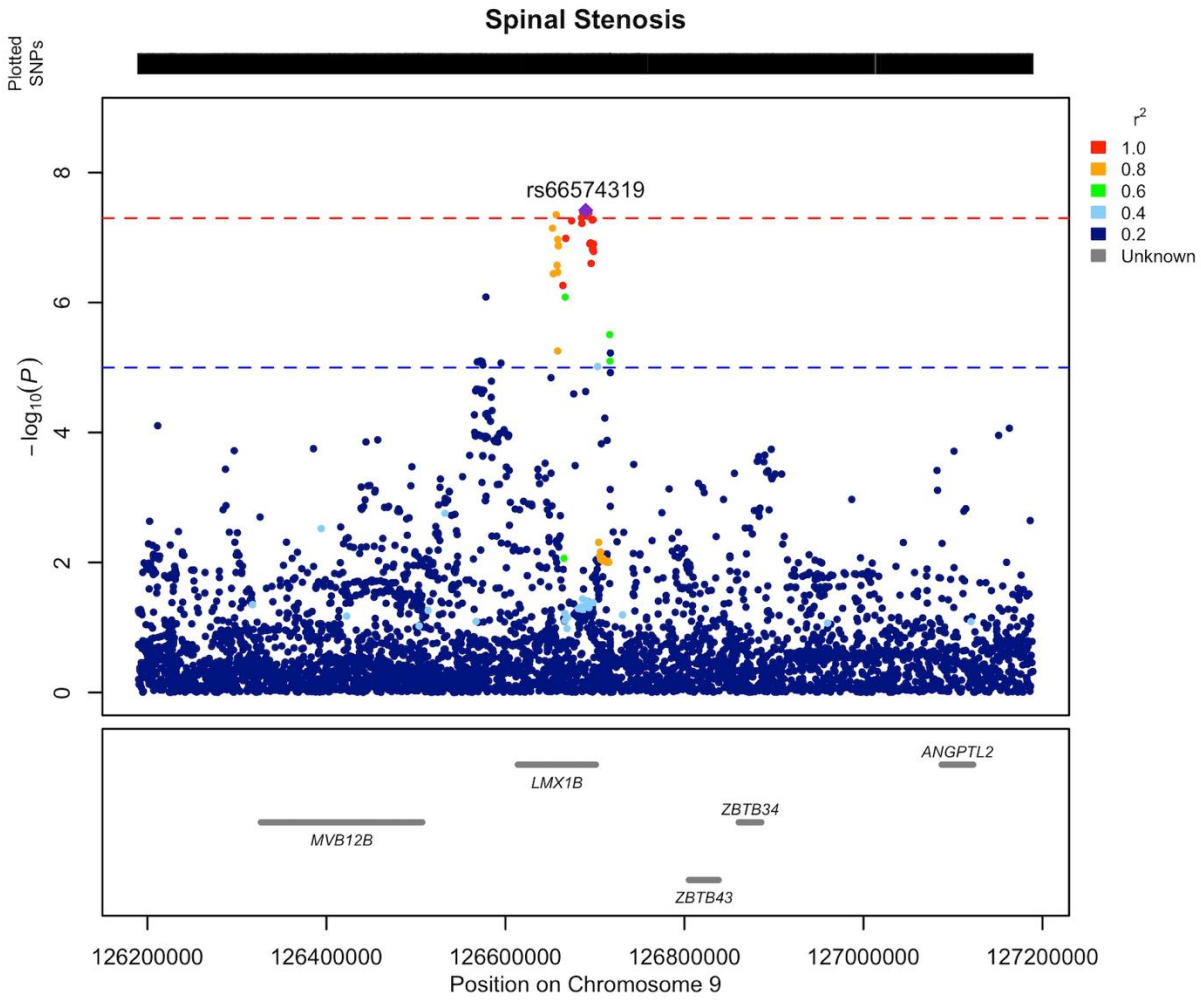

Fig S37. Regional association plot of previously unreported LSS association on chromosome 9 area of 126.2-127.2 MB. Our findings indicate that the gene responsible for the locus's association is most likely *LMX1B (LIM homeobox transcription factor 1 beta).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

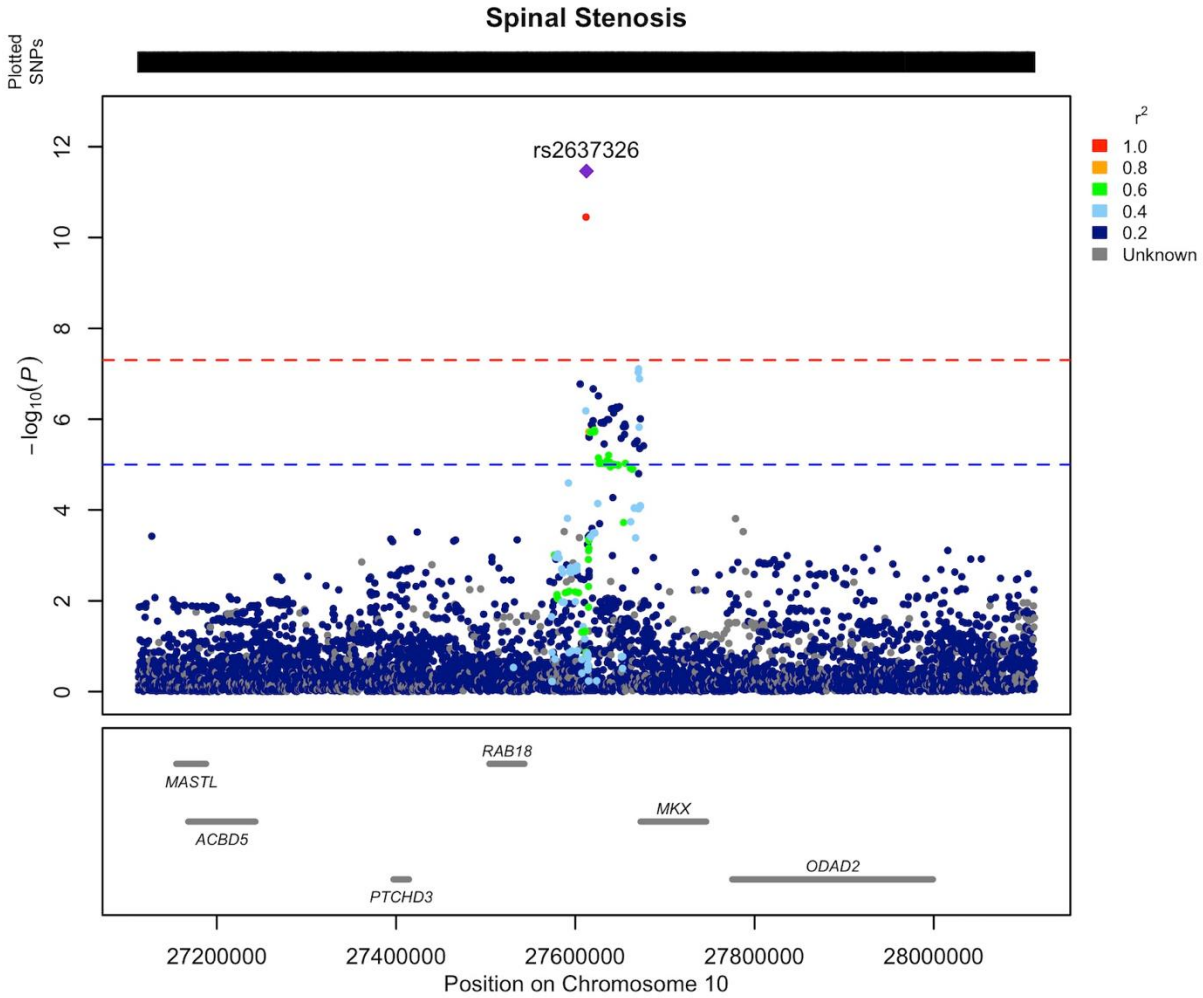

Fig S38. Regional association plot of previously unreported LSS association on chromosome 10 area of 27.1-28.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *MKX (mohawk homeobox).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

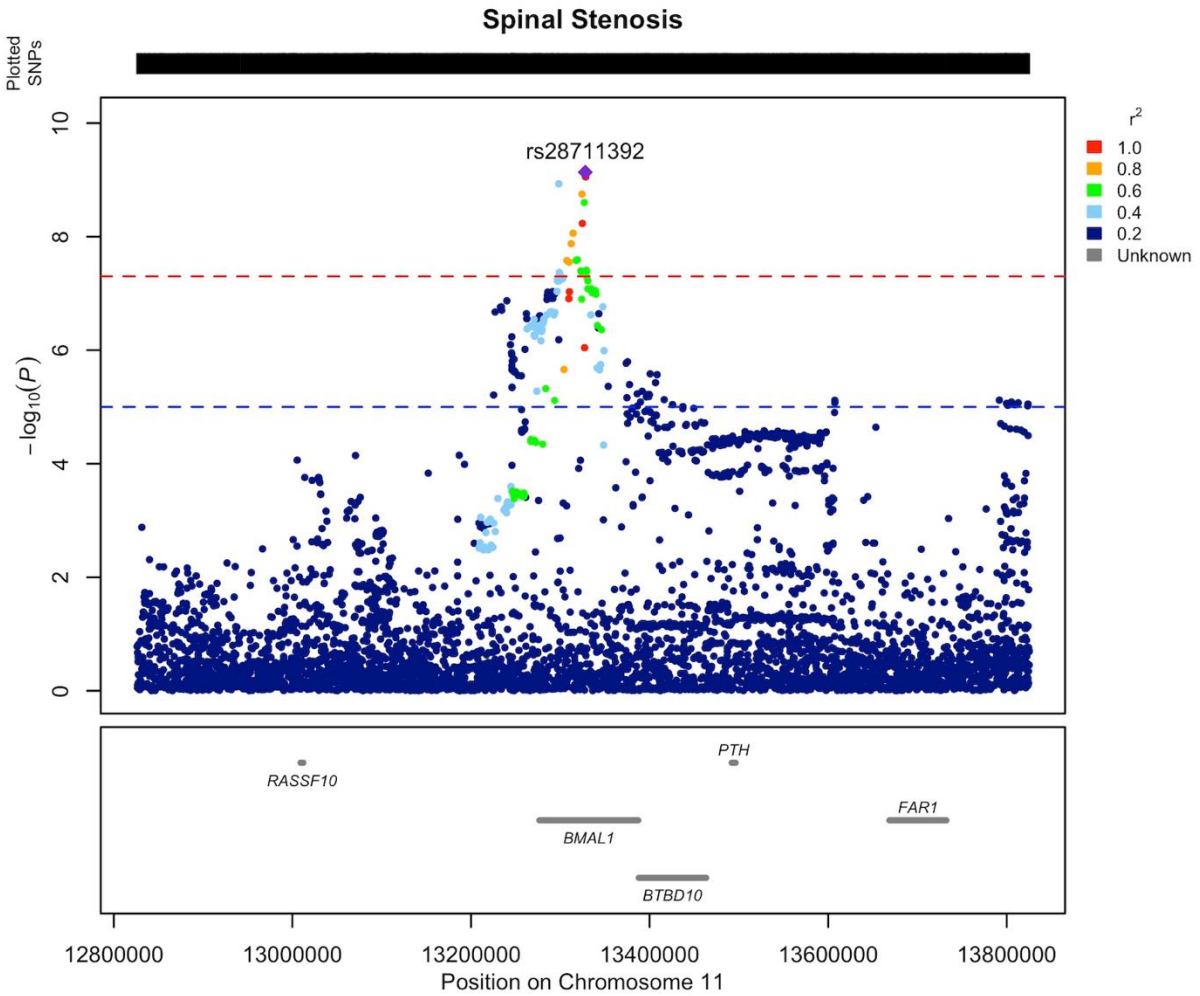

Fig S39. Regional association plot of previously unreported LSS association on chromosome 11 area of 128.0-129.0 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ARNTL (basic helix-loop-helix ARNT like 1, also known as BMAL1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

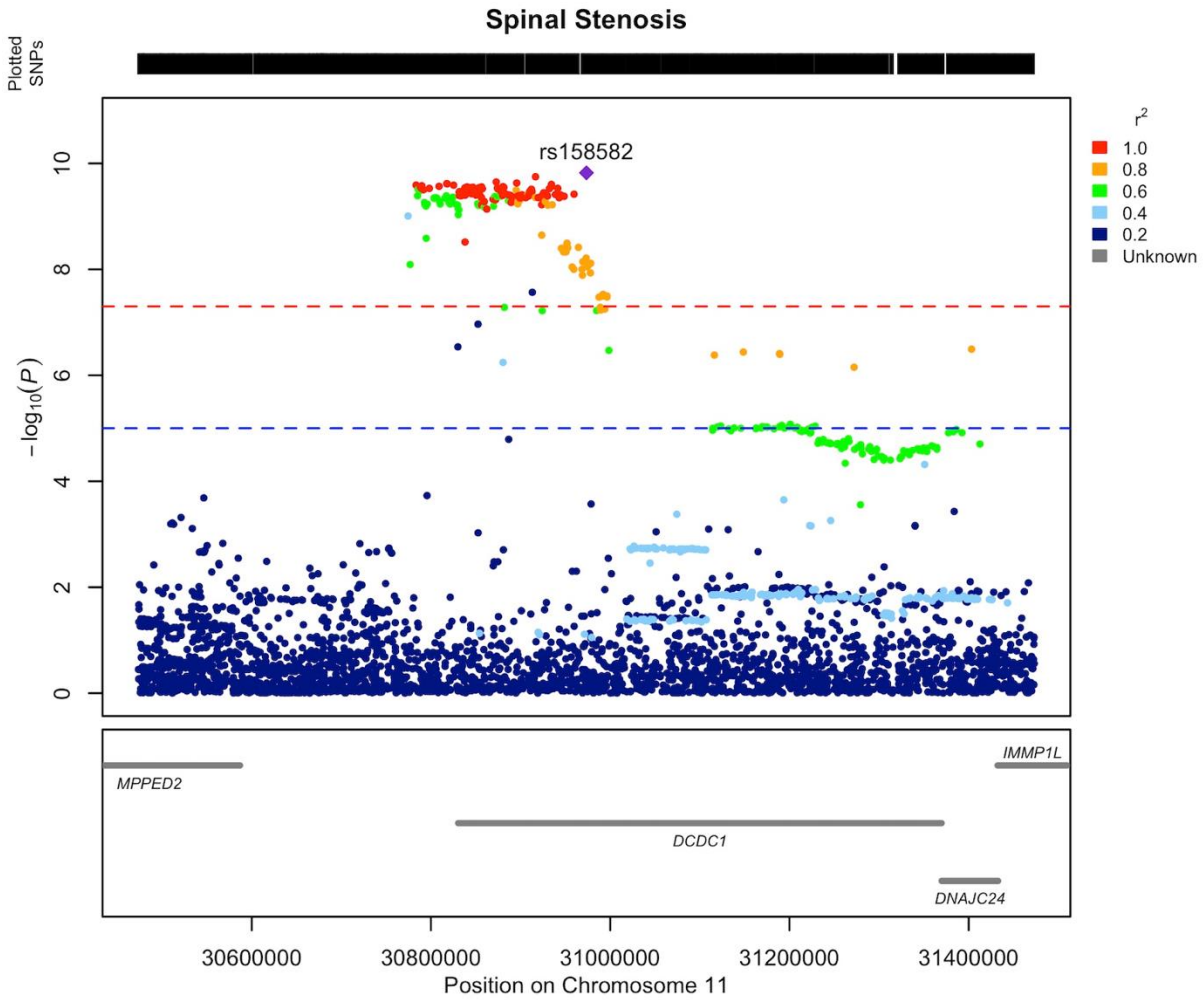

Fig S40. Regional association plot of previously unreported LSS association on chromosome 11 area of 30.5-31.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *MPPED2 (metallophosphosterase domain containing 2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

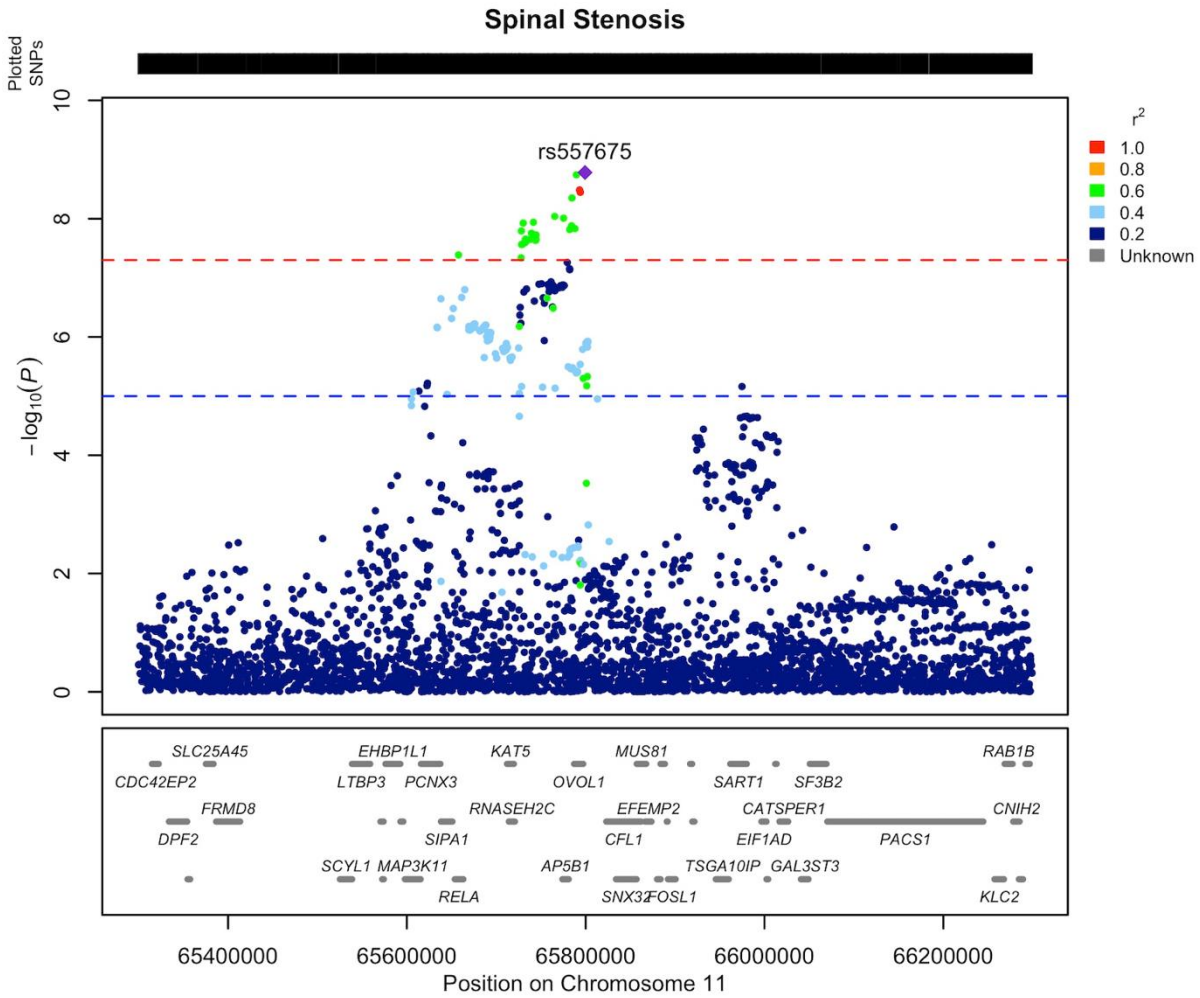

Fig S41. Regional association plot of previously unreported LSS association on chromosome 11 area of 65.3-66.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *OVOL1 (ovo like transcriptional repressor 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

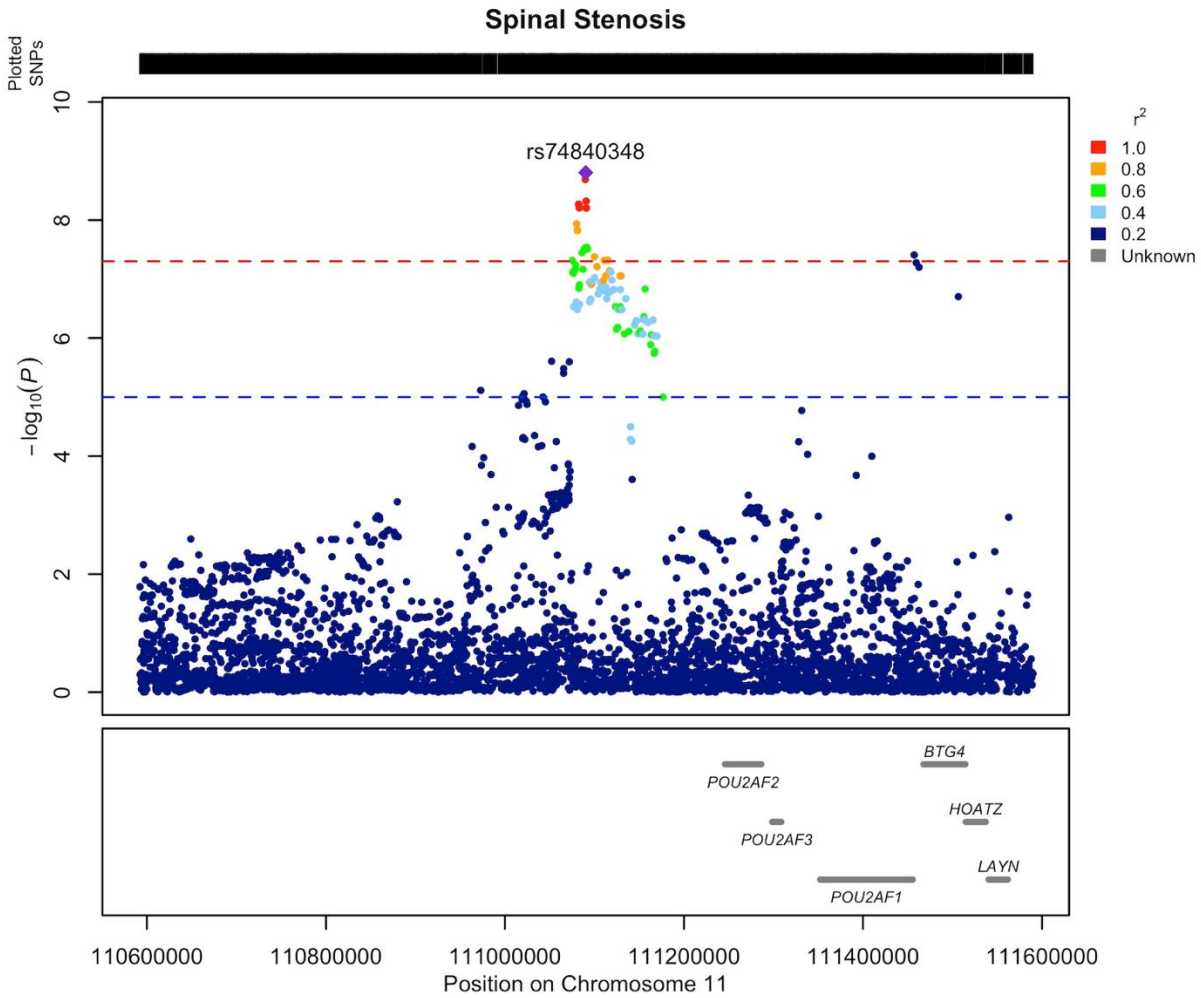

Fig S42. Regional association plot of previously unreported LSS association on chromosome 11 area of 110.6-111.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *LAYN (layilin).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

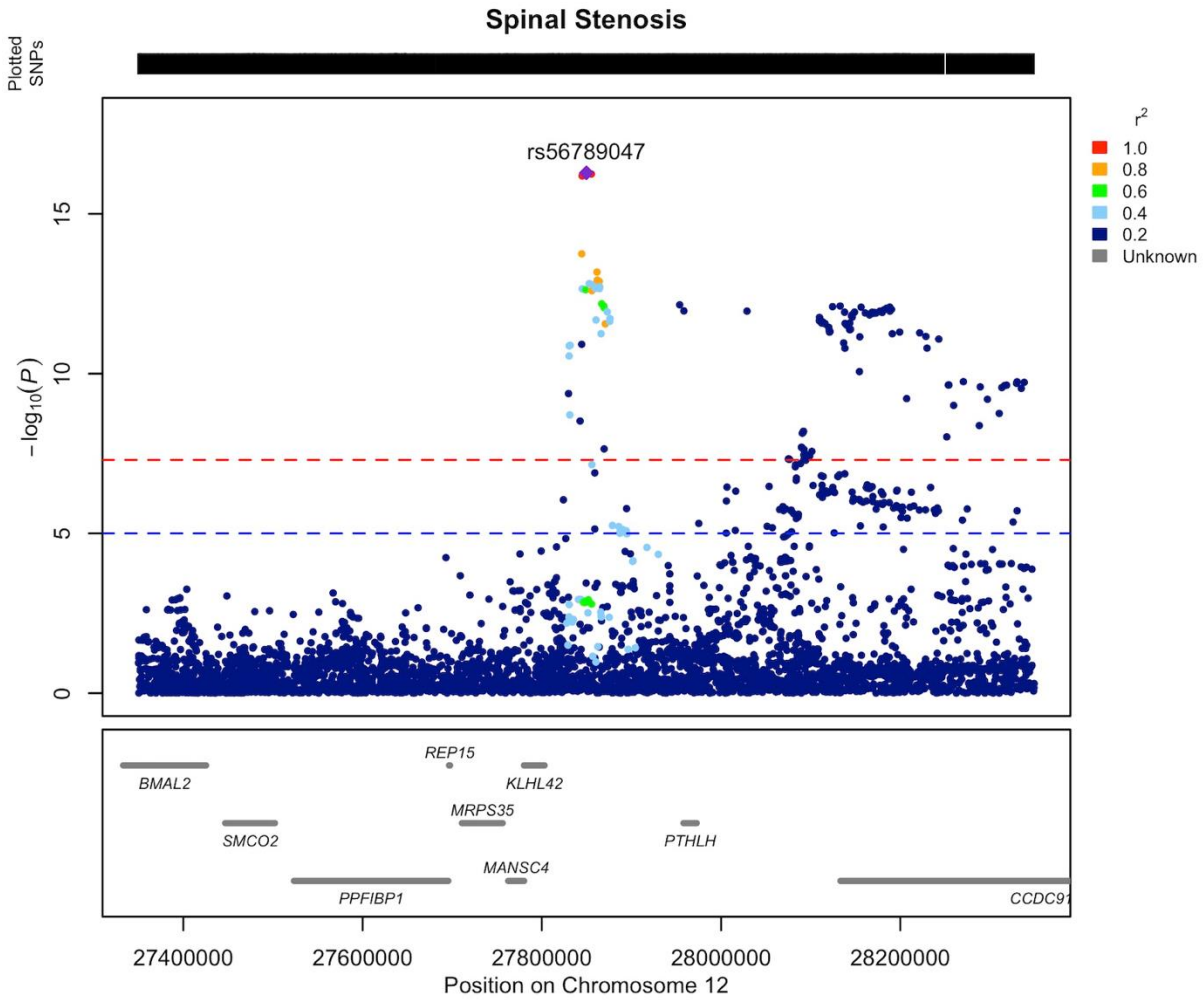

Fig S43. Regional association plot of previously unreported LSS association on chromosome 12 area of 27.4-28.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *CCDC91* (*coiled-coil domain containing 91*). The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

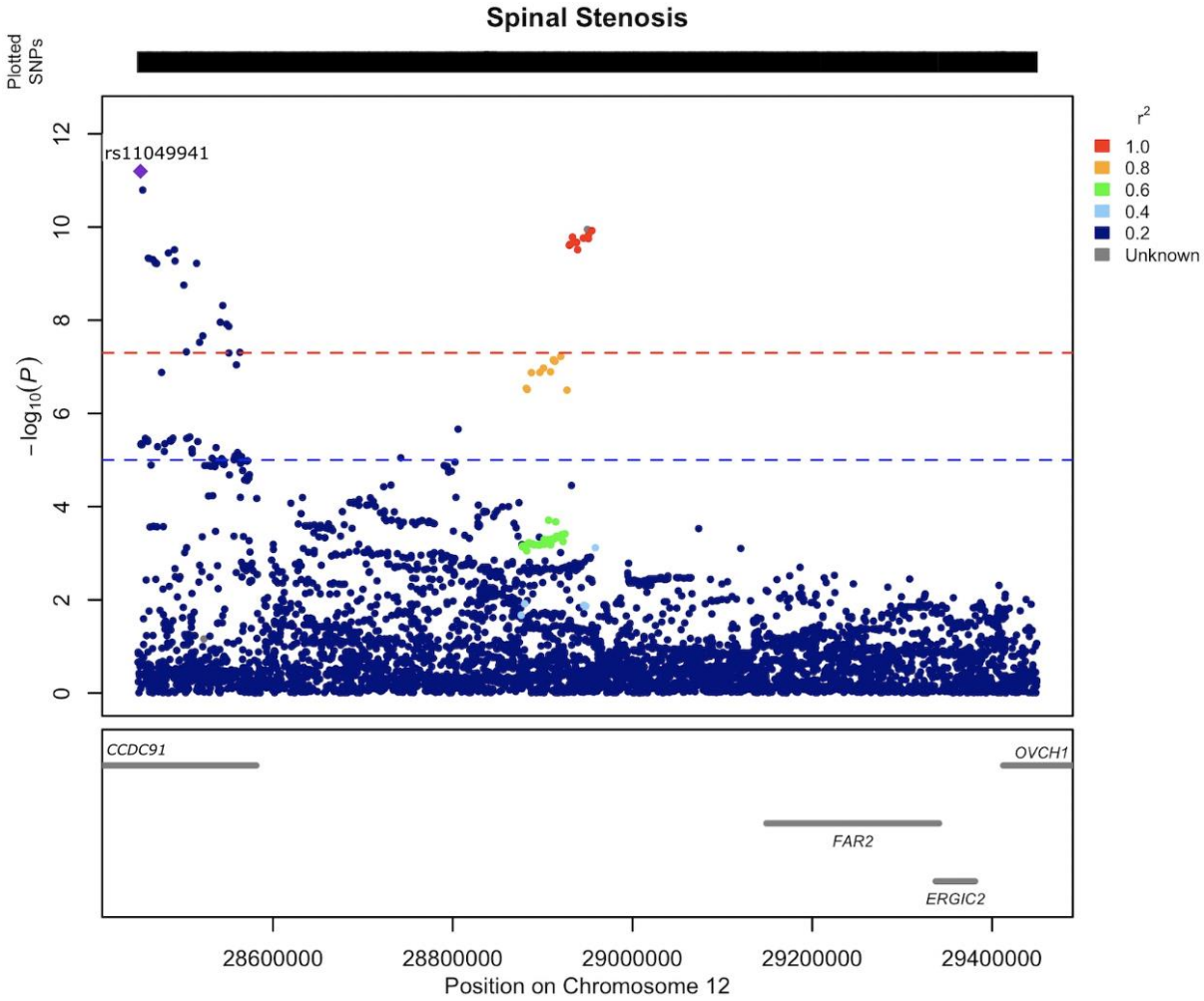

Fig S44. Regional association plot of previously unreported LSS association on chromosome 12 area of 28.4-29.4MB. Our findings indicate that the gene responsible for the locus's association is most likely *CCDC91* (*coiled-coil domain containing 91*). The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

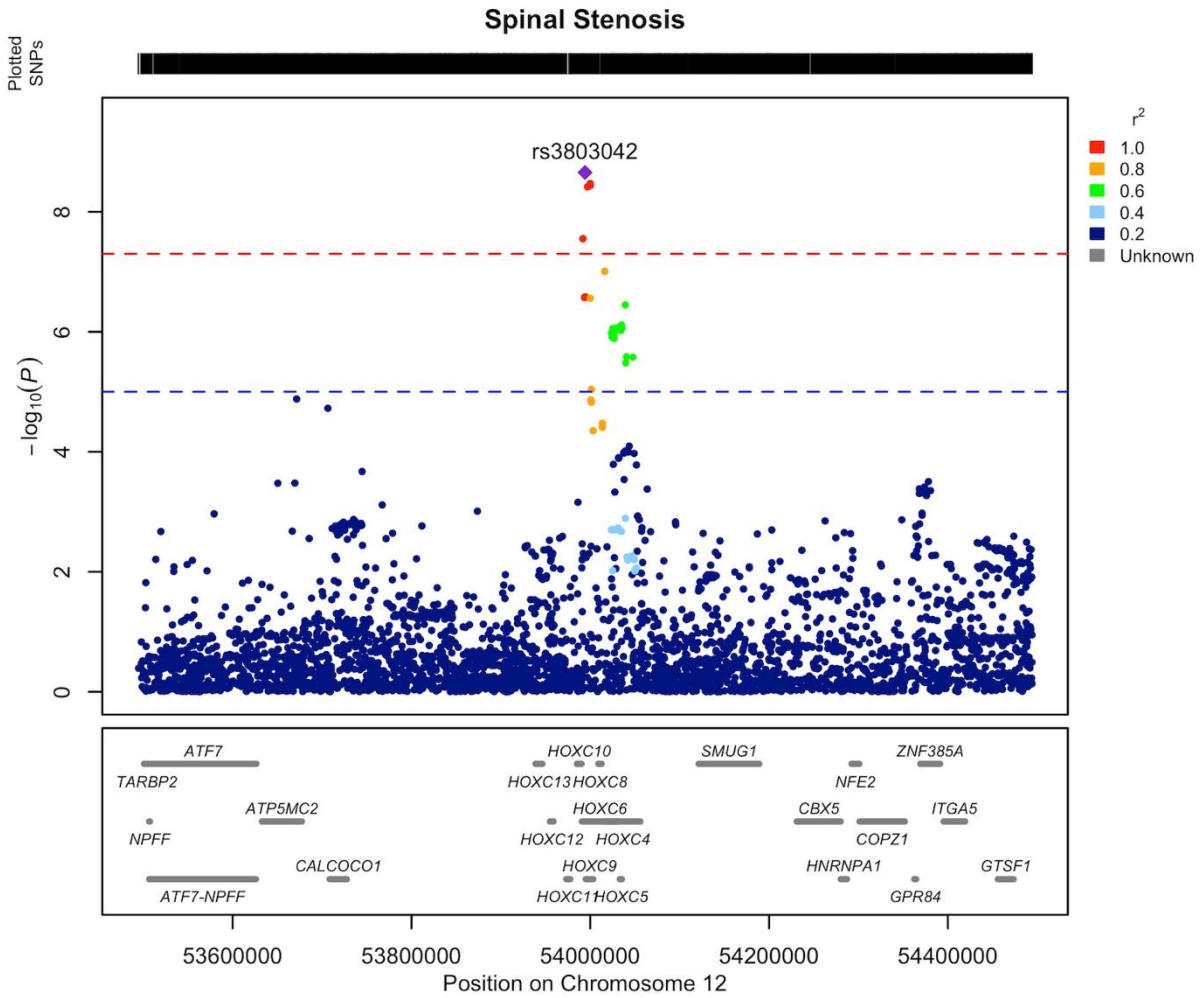

Fig S45. Regional association plot of previously unreported LSS association on chromosome 12 area of 53.5-54.5MB. Our findings indicate that the gene responsible for the locus's association is most likely *HOXC10* (*homeobox C10*). The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

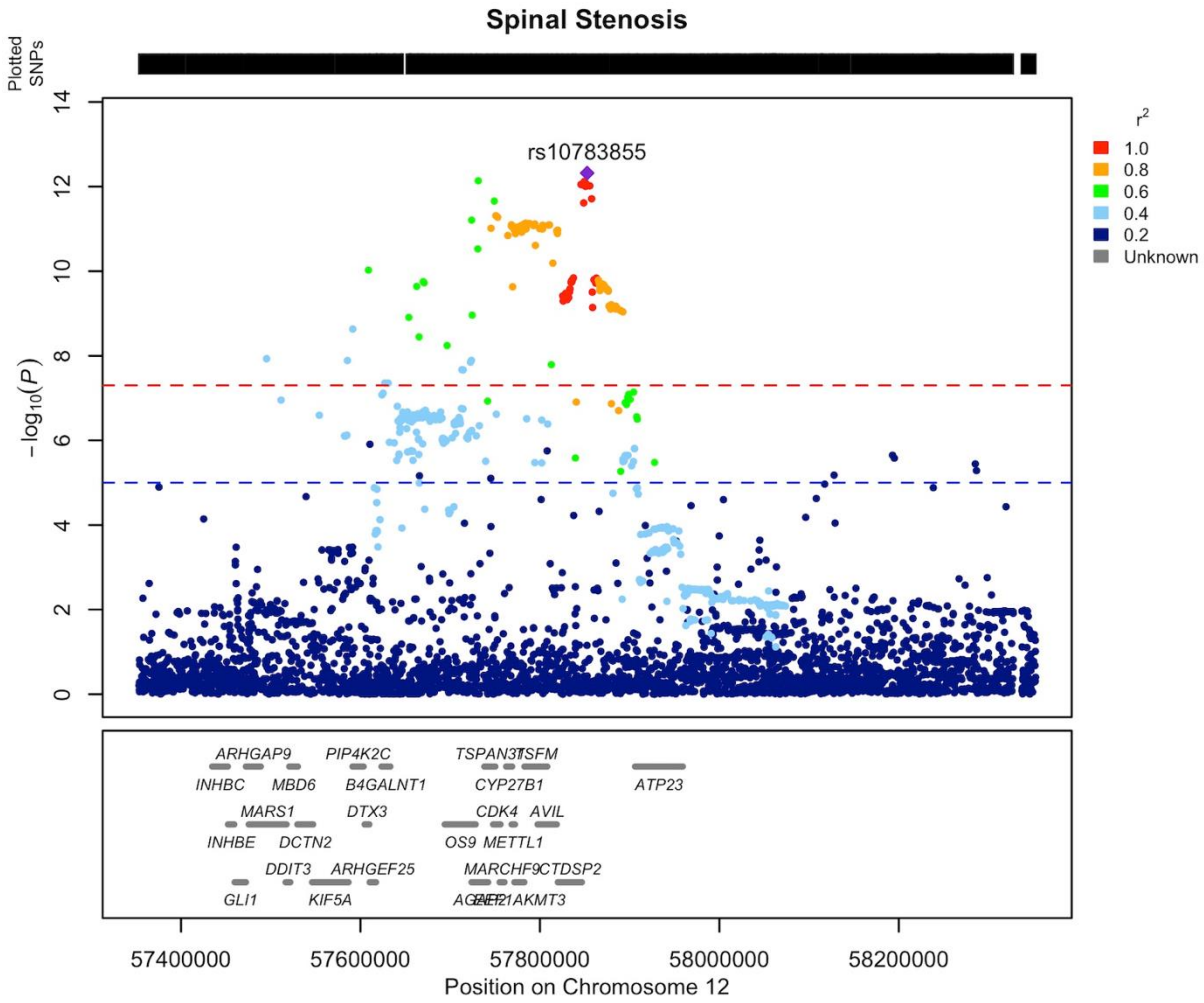

Fig S46. Regional association plot of previously unreported LSS association on chromosome 12 area of 57.3-58.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *GLI1 (GLI family zinc finger 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

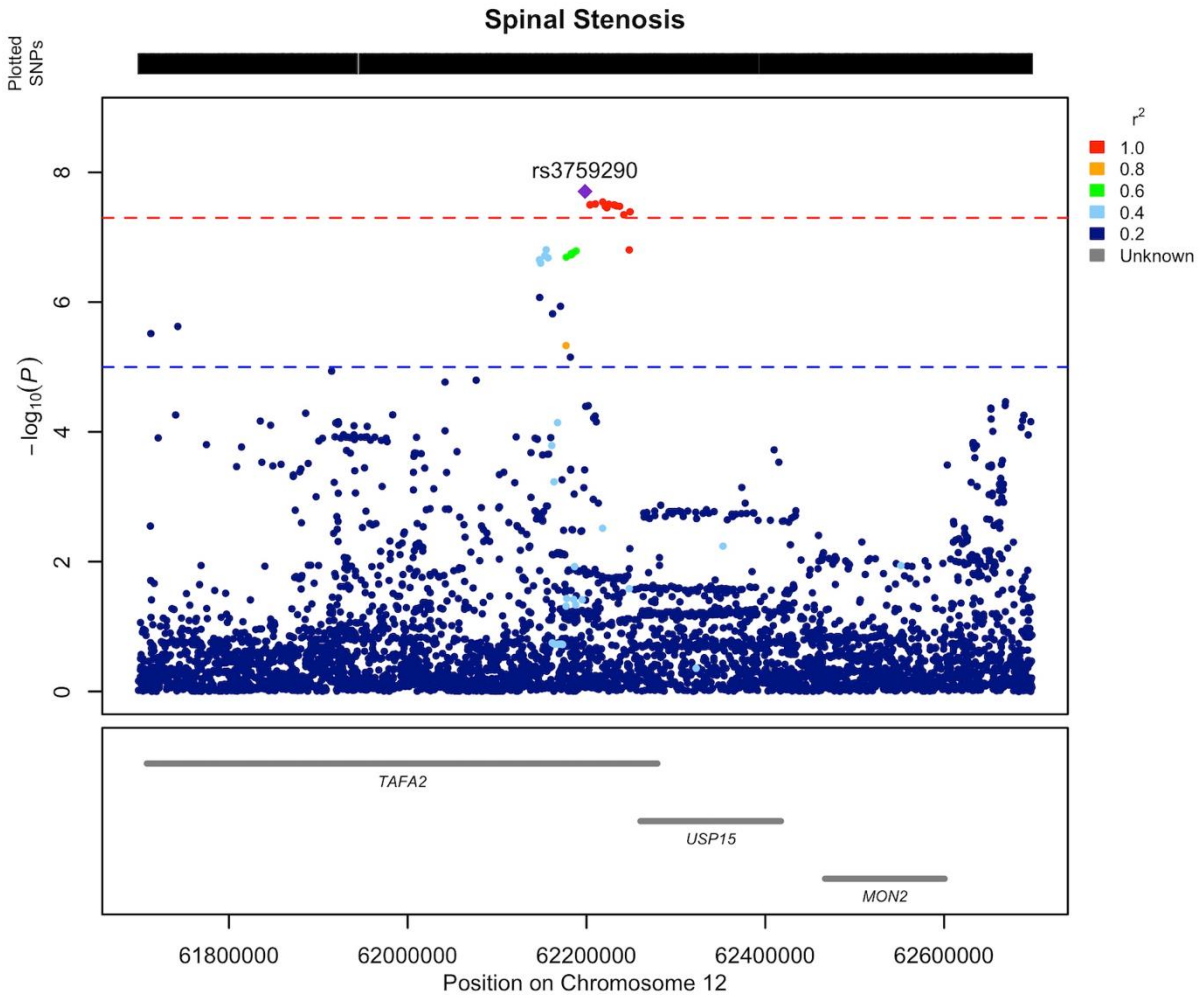

Fig S47. Regional association plot of previously unreported LSS association on chromosome 12 area of 61.7-62.7 MB. Our findings indicate that the gene responsible for the locus's association is most likely *USP15 (ubiquitin specific peptidase 15).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

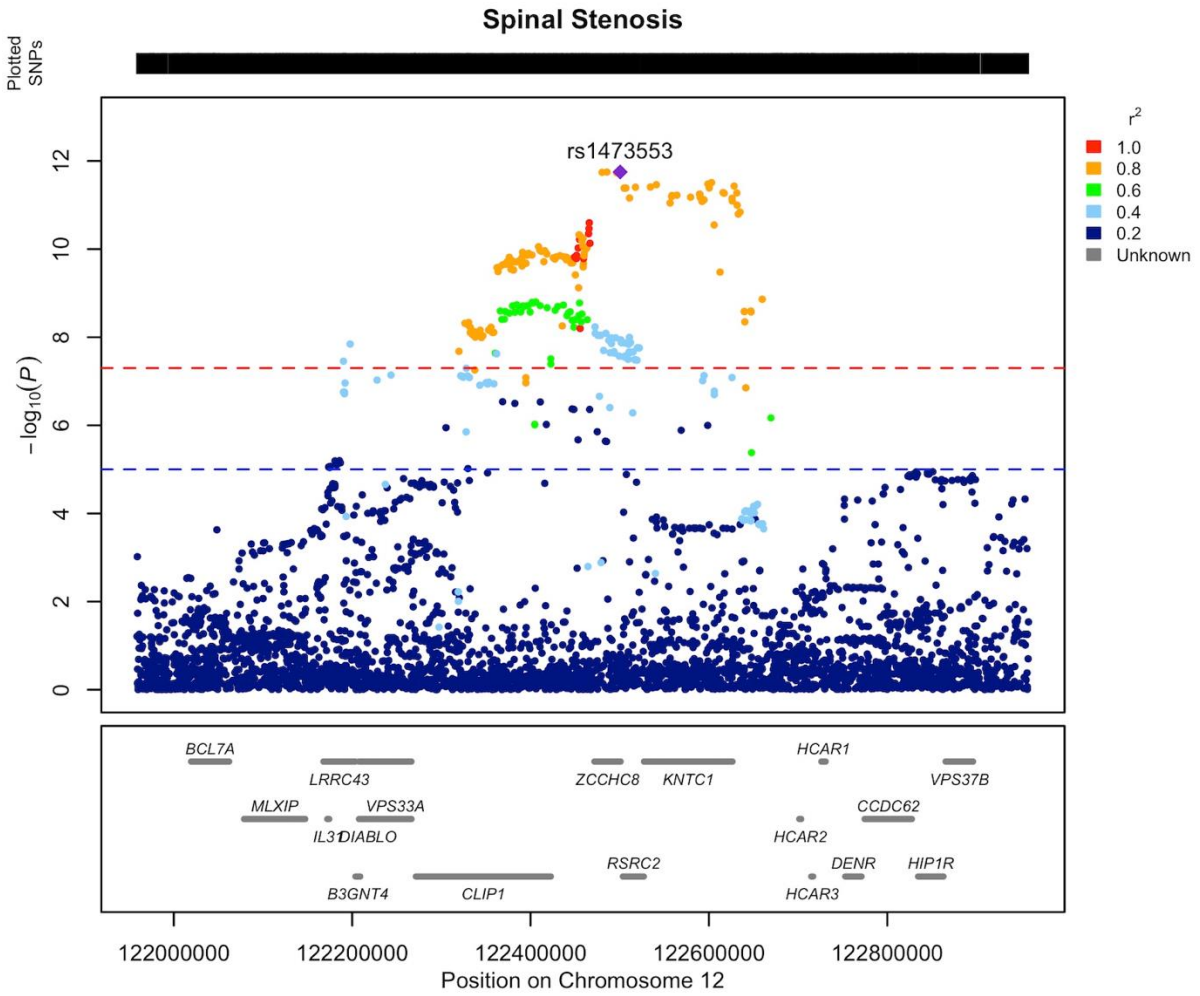

Fig S48. Regional association plot of previously unreported LSS association on chromosome 12 area of 121.9-122.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ZCCHC8 (zinc finger CCHC-type containing 8).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

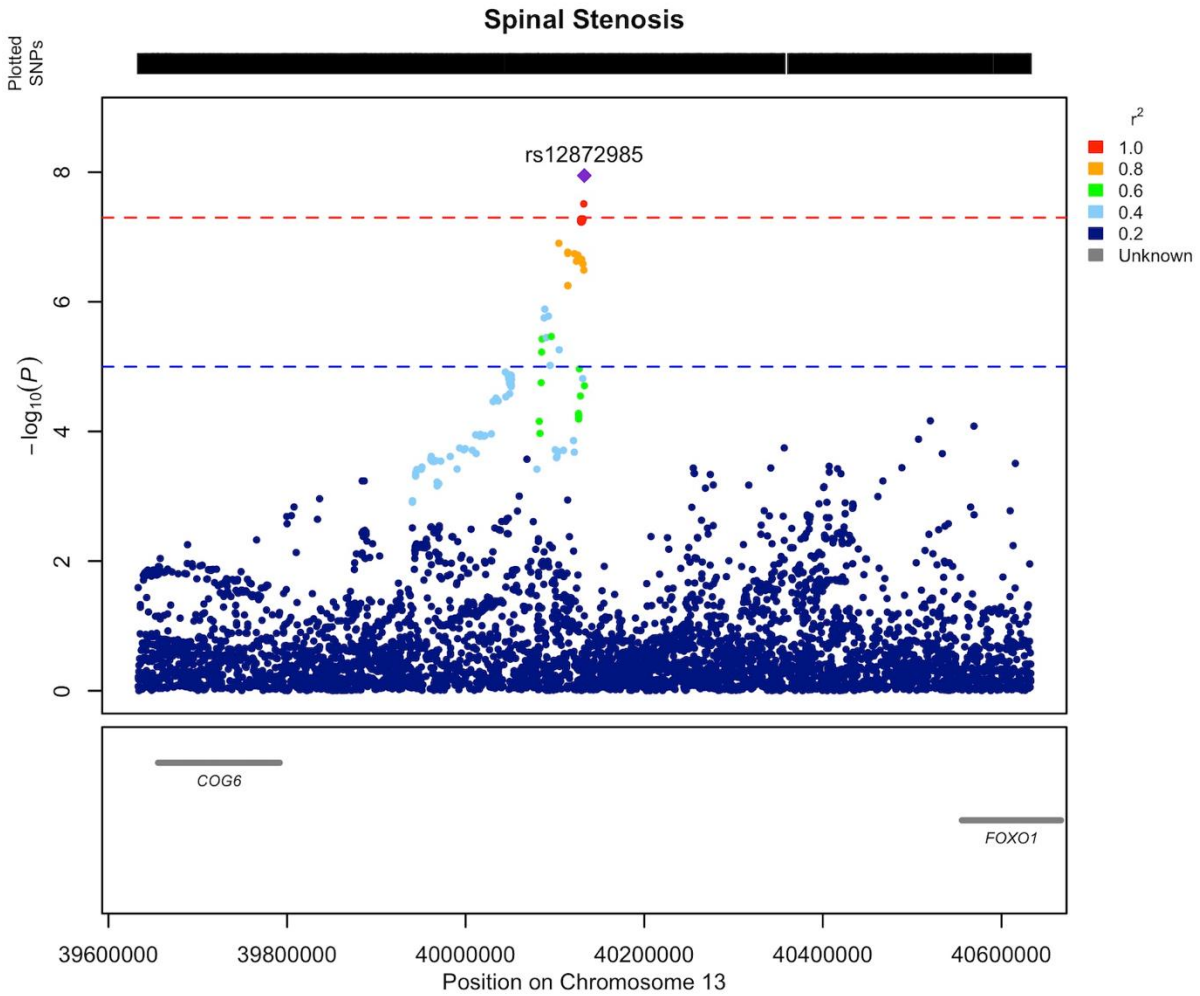

Fig S49. Regional association plot of previously unreported LSS association on chromosome 13 area of 39.6-40.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *FOXO1 (forkhead box O1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

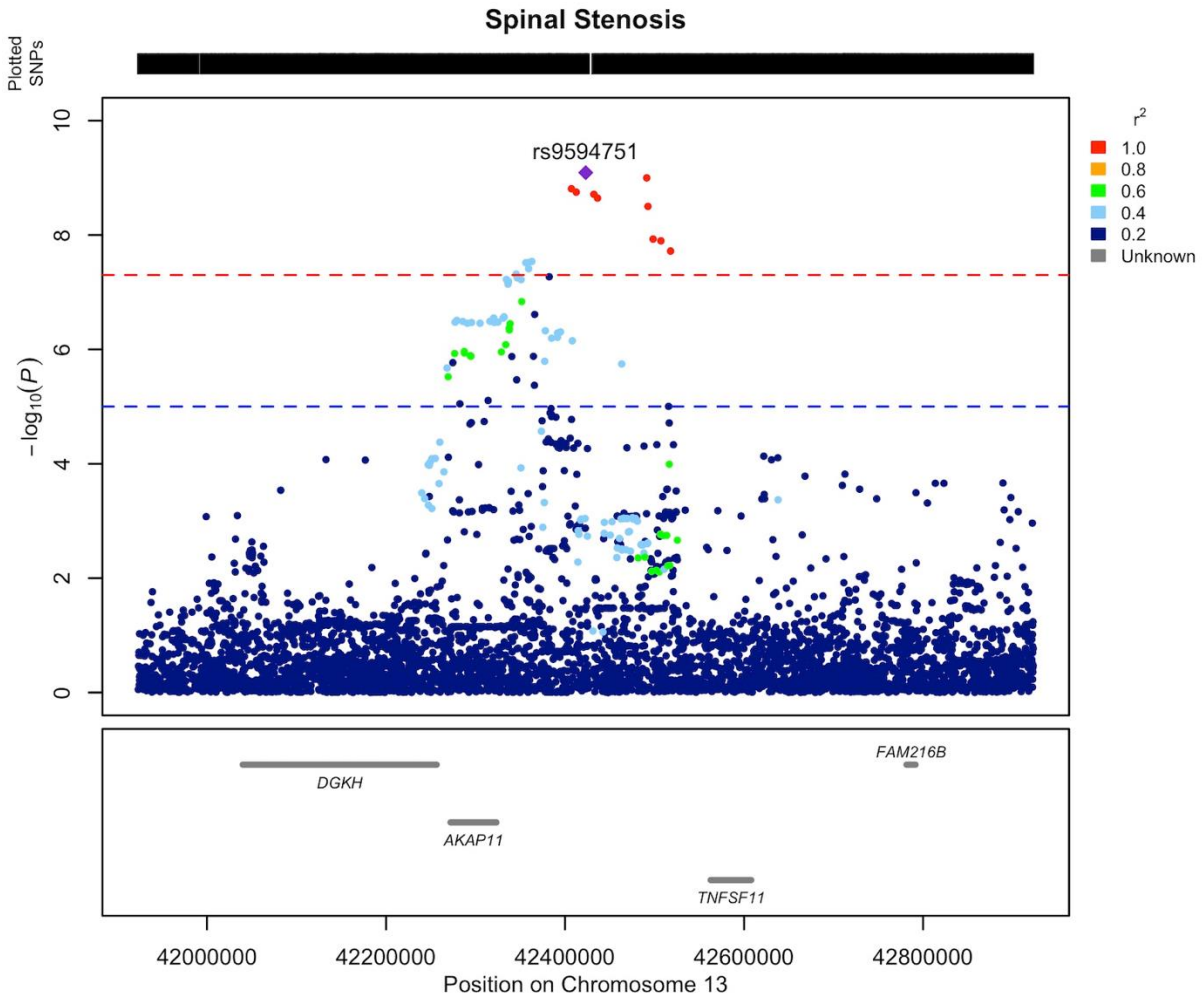

Fig S50. Regional association plot of previously unreported LSS association on chromosome 13 area of 41.9-42.9 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TNFSF11 (TNF superfamily member 11).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

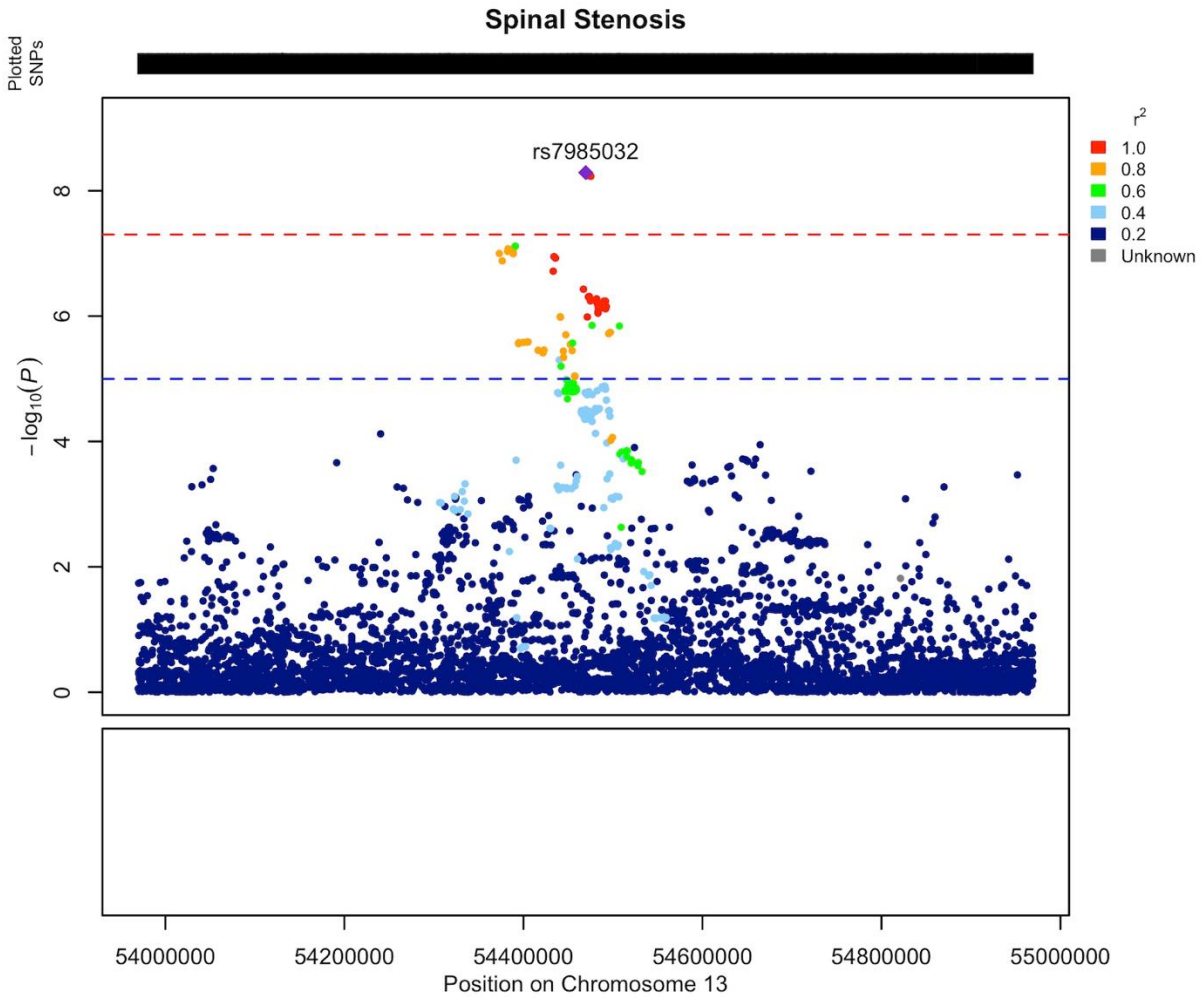

Fig S51. Regional association plot of previously unreported LSS association on chromosome 13 area of 54.0-55.0 MB. There was not any protein coding gene in this locus, so it was classified as *RPL13AP25 (ribosomal protein L13a pseudogene 25).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

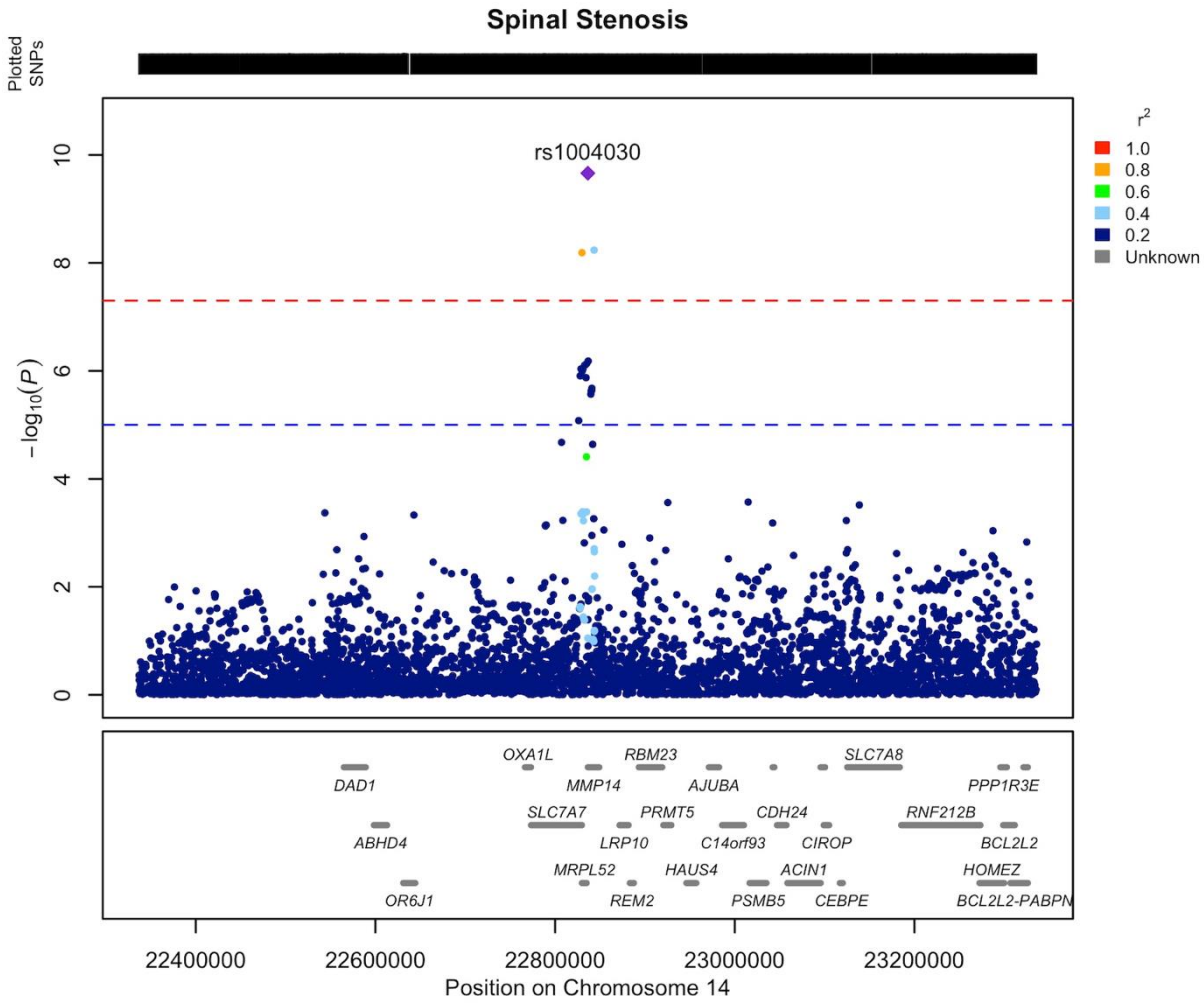

Fig S52. Regional association plot of previously unreported LSS association on chromosome 14 area of 22.3-23.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *MMP14 (matrix metallopeptidase 14).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

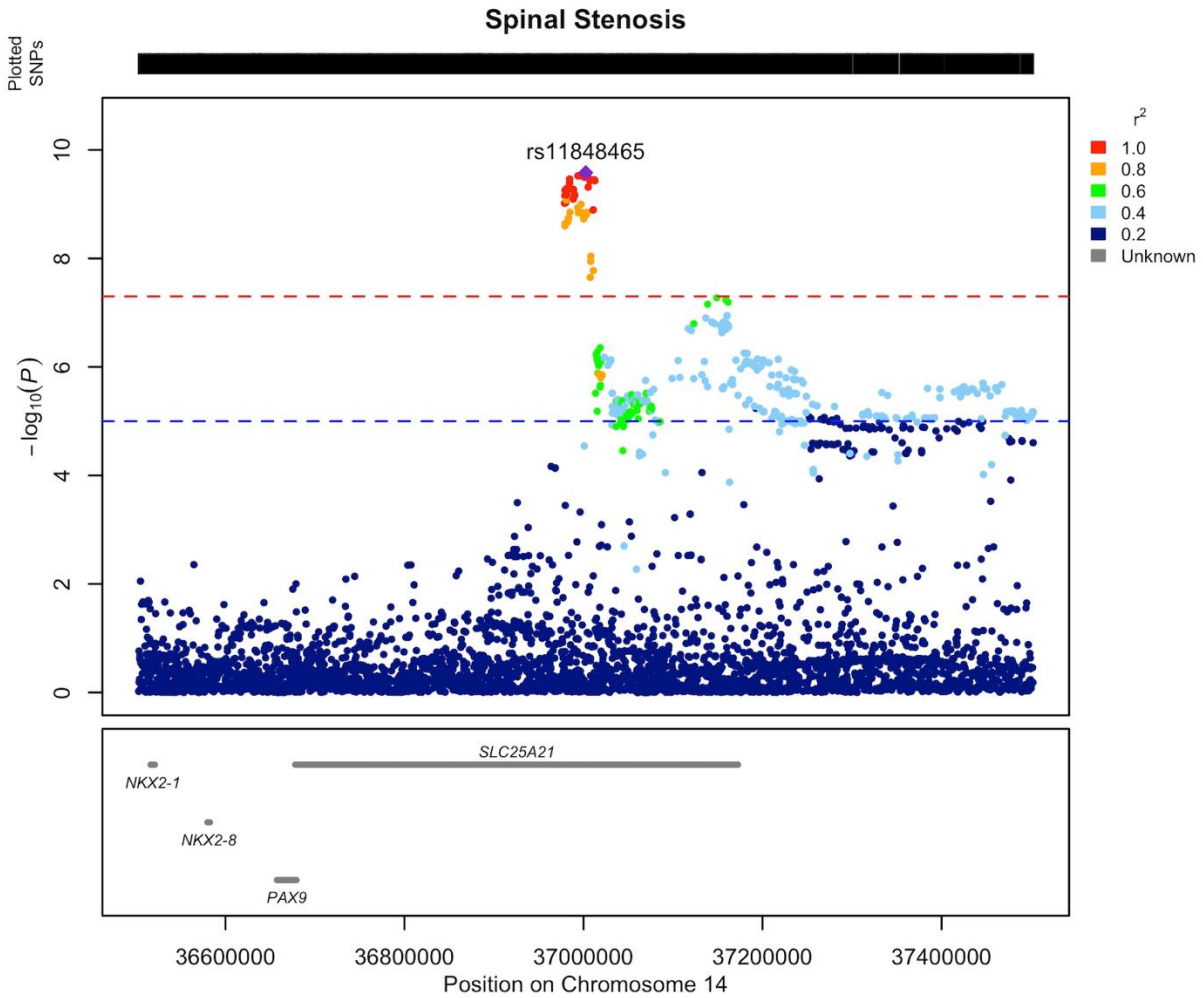

Fig S53. Regional association plot of previously unreported LSS association on chromosome 14 area of 36.5-37.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *PAX9 (paired box 9).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

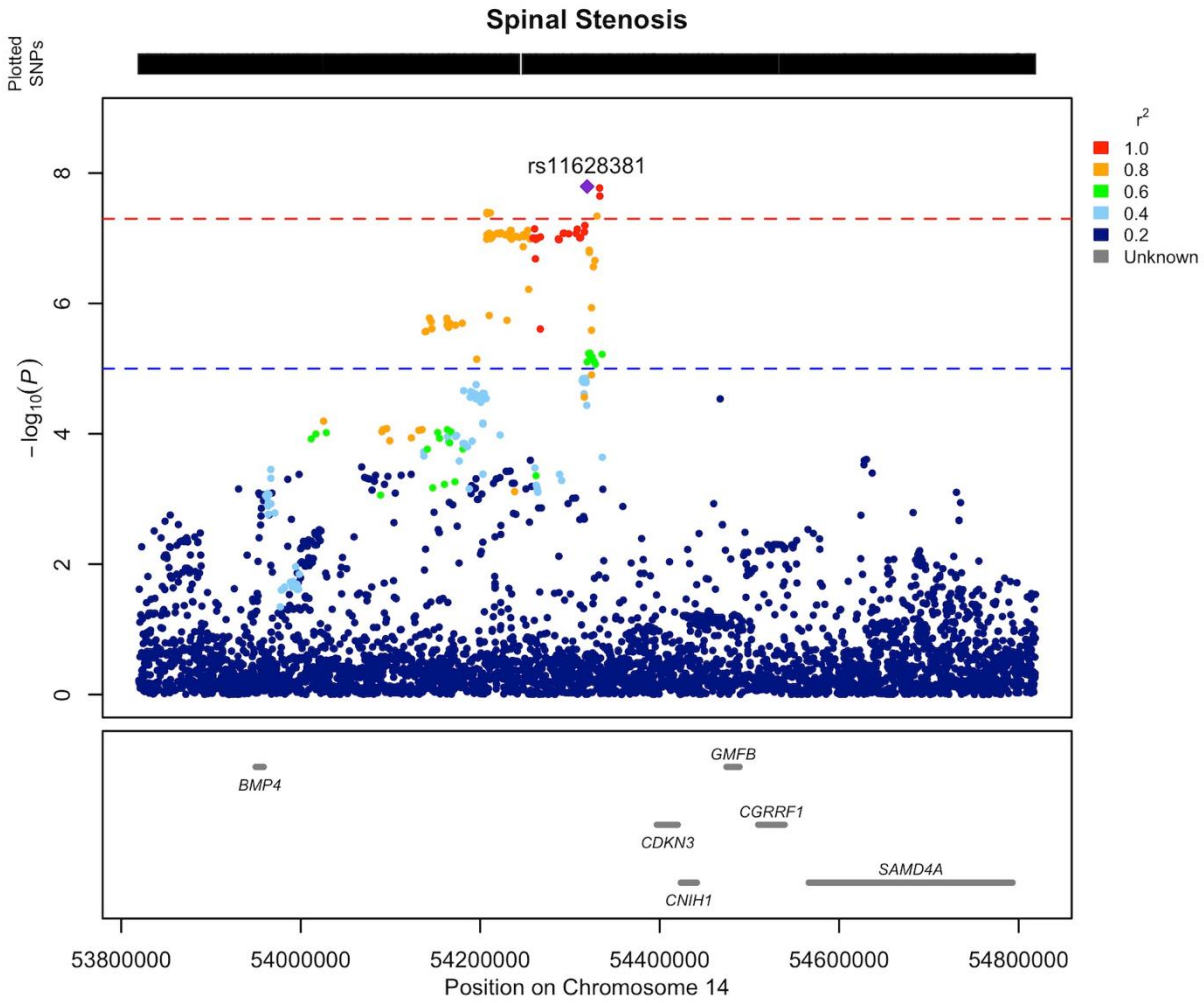

Fig S54. Regional association plot of previously unreported LSS association on chromosome 14 area of 53.8-54.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *BMP4 (bone morphogenetic protein 4).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

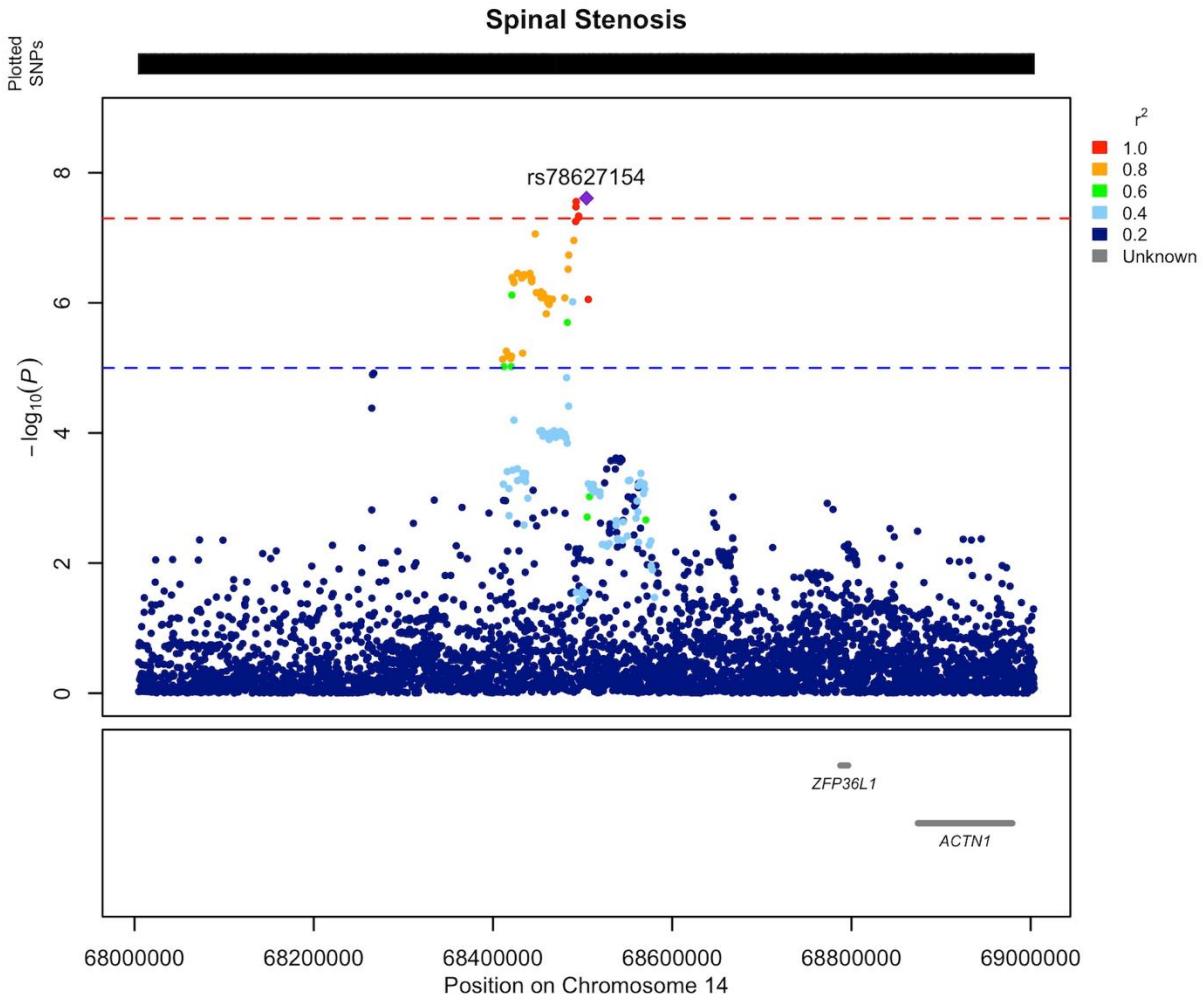

Fig S55. Regional association plot of previously unreported LSS association on chromosome 14 area of 68.0-69.0 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ZFP36L1 (ZFP36 ring finger protein like 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

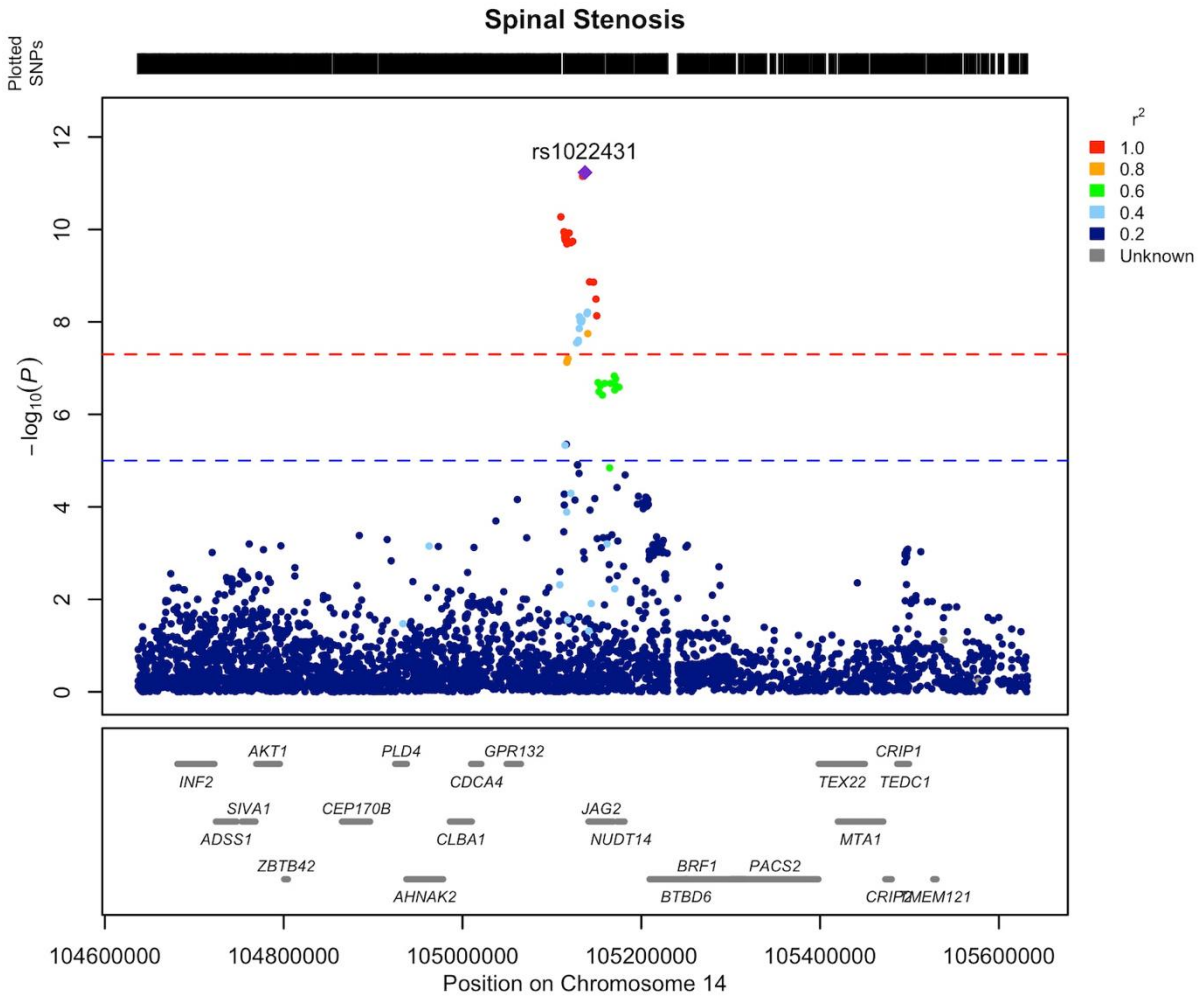

Fig S56. Regional association plot of previously unreported LSS association on chromosome 14 area of 104.6-105.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *GPR132 (G protein-coupled receptor 132).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

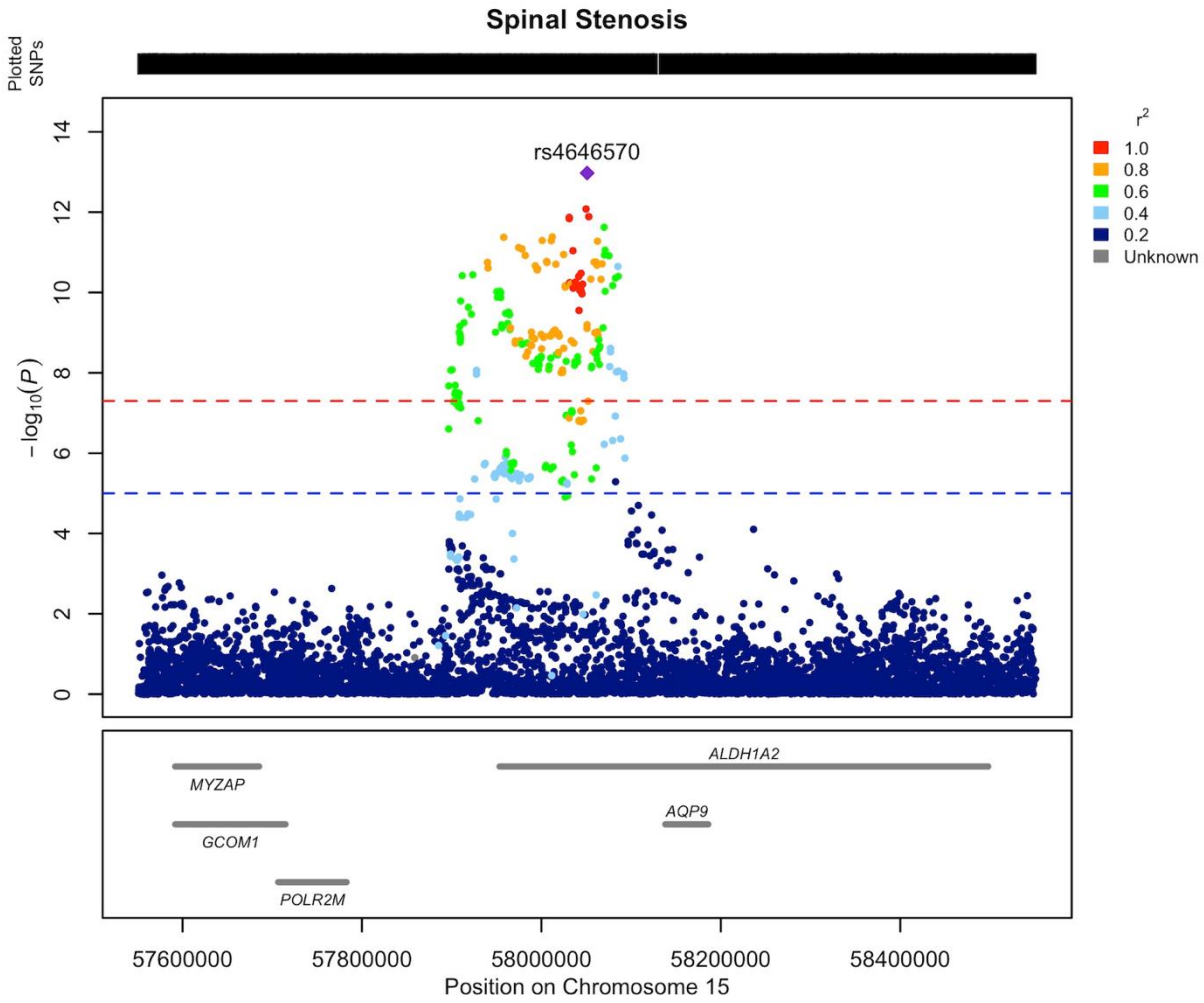

Fig S57. Regional association plot of previously unreported LSS association on chromosome 15 area of 57.6-58.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ALDH1A2 (aldehyde dehydrogenase 1 family member A2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

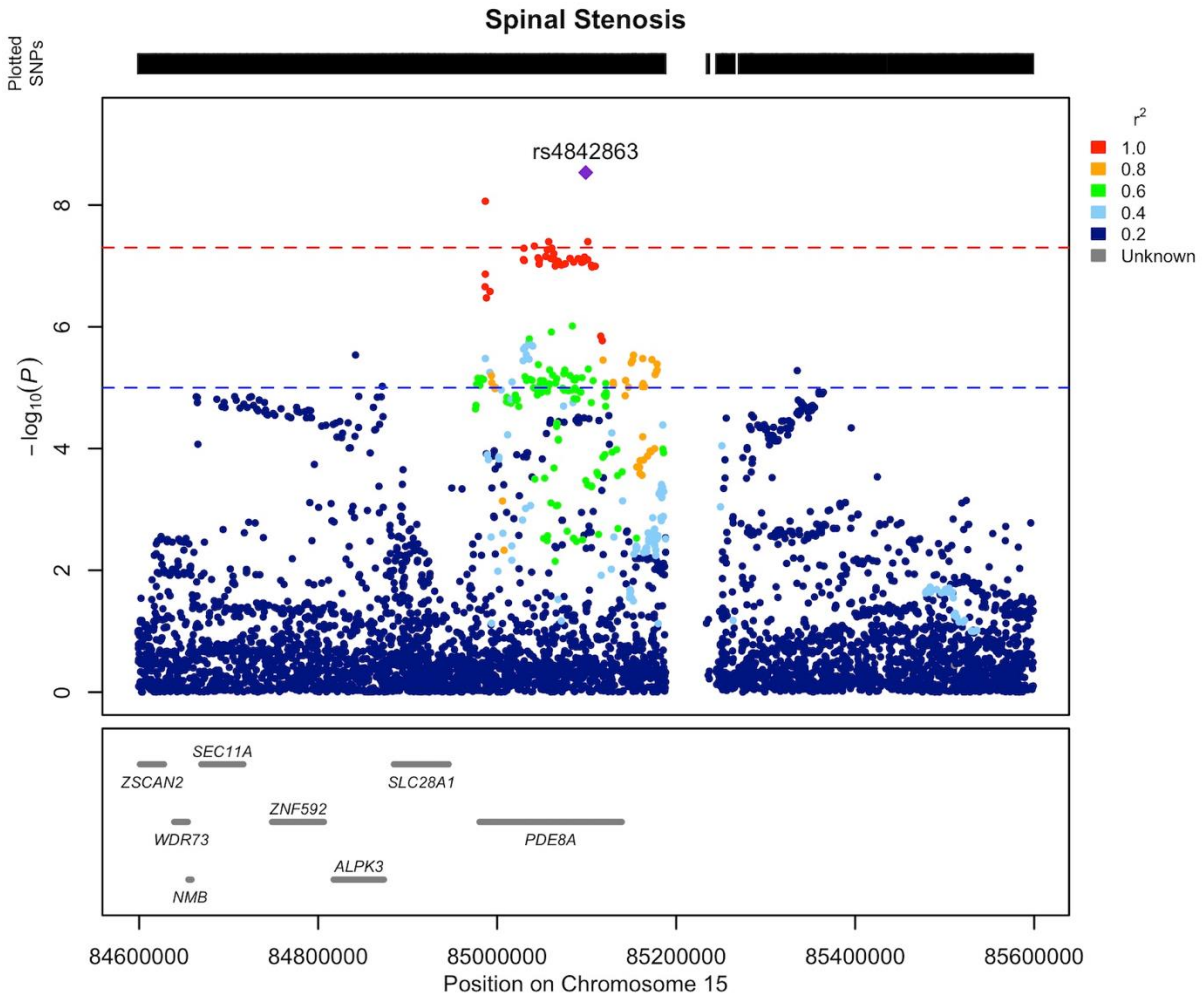

Fig S58. Regional association plot of previously unreported LSS association on chromosome 15 area of 84.6-85.6 MB. Our findings indicate that the gene responsible for the locus's association is most likely *PDE8A (phosphodiesterase 8A).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

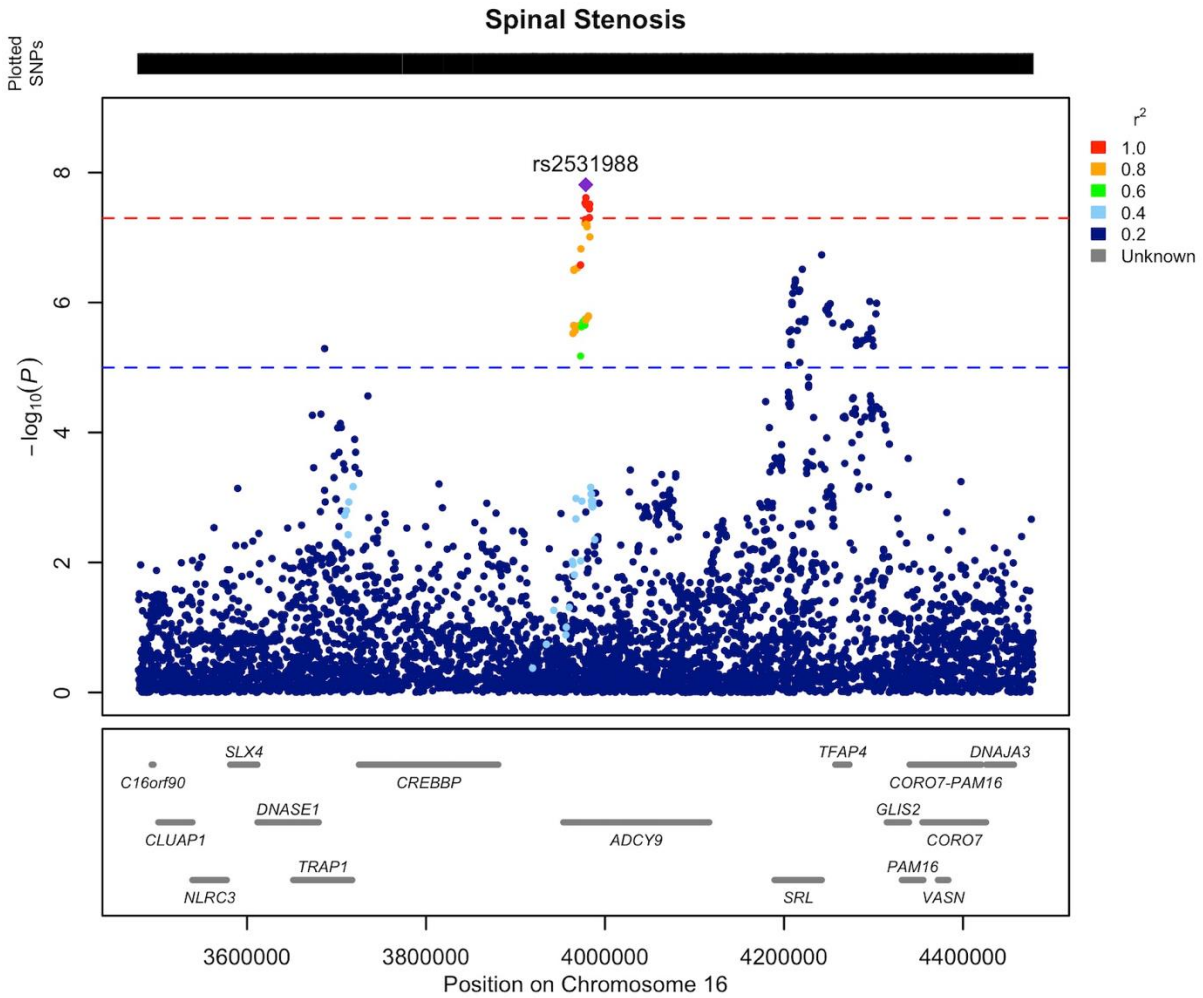

Fig S59. Regional association plot of previously unreported LSS association on chromosome 16 area of 3.5-4.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *CREBBP (CREB binding lysine acetyltransferase).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

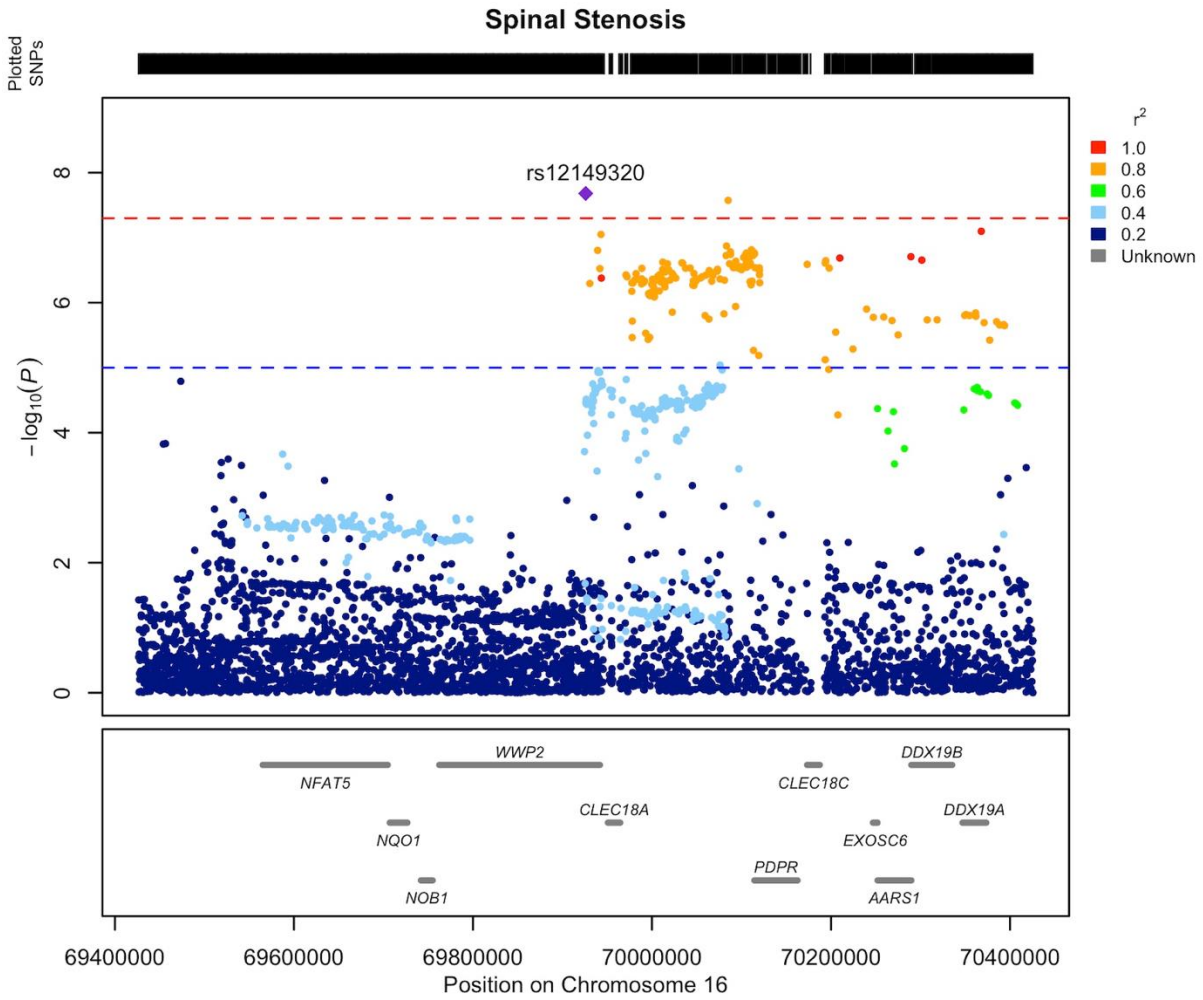

Fig S60. Regional association plot of previously unreported LSS association on chromosome 16 area of 69.4-70.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *WWP2 (WW domain containing E3 ubiquitin protein ligase 2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

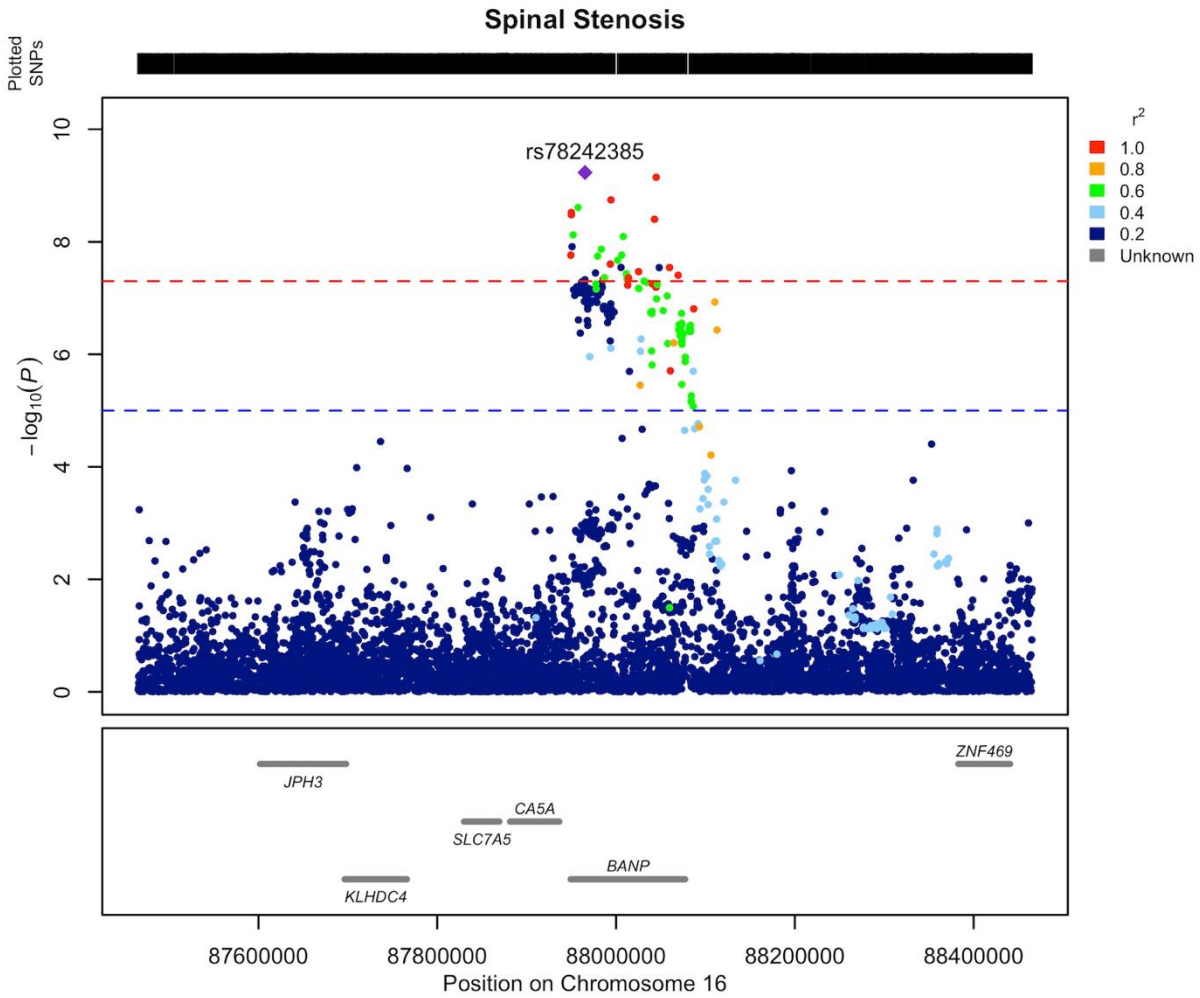

Fig S61. Regional association plot of previously unreported LSS association on chromosome 16 area of 87.5-88.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *SLC7A5 (solute carrier family 7 member 5).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

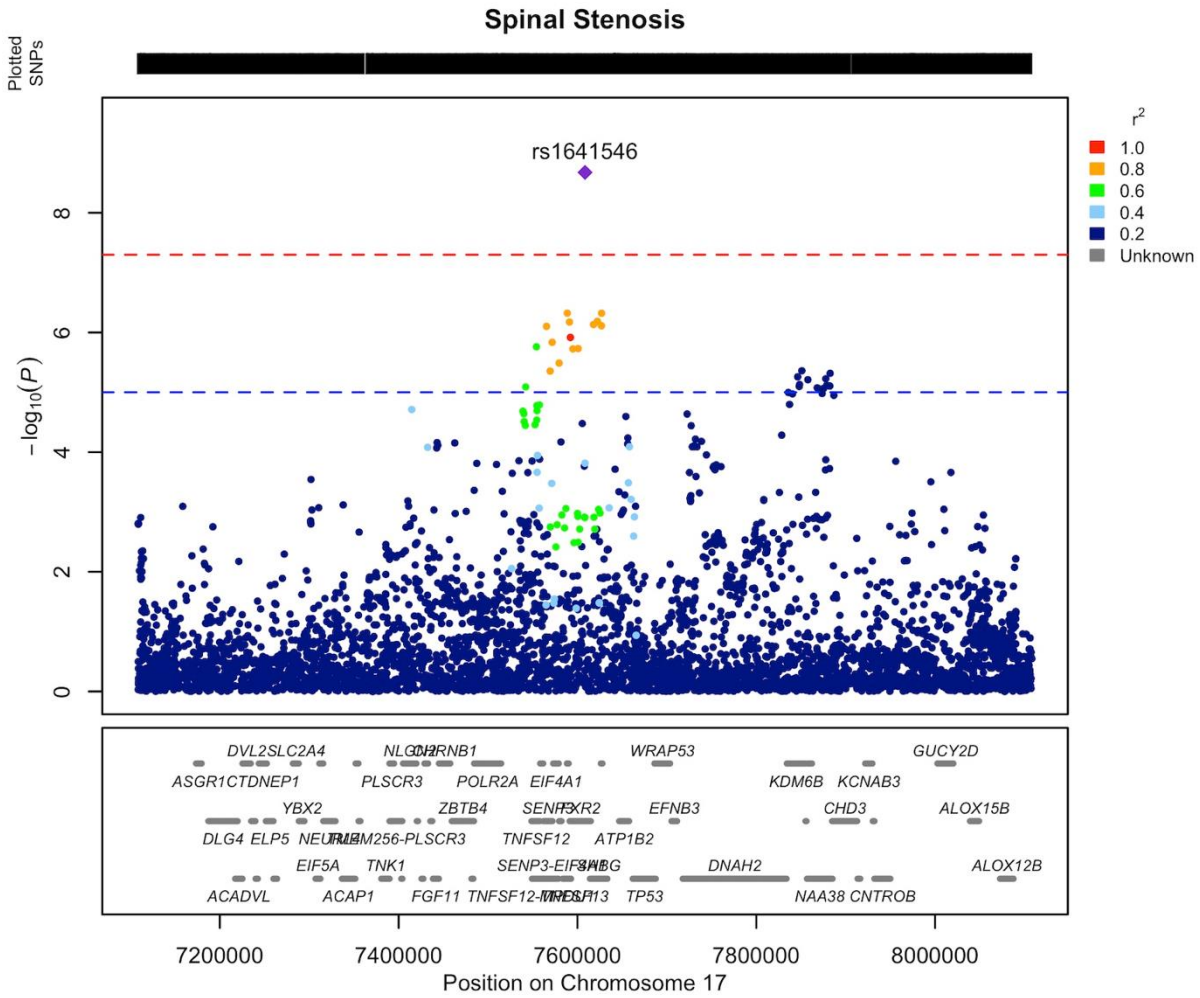

Fig S62. Regional association plot of previously unreported LSS association on chromosome 17 area of 7.1-8.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *TNFSF12 (TNF superfamily member 12).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

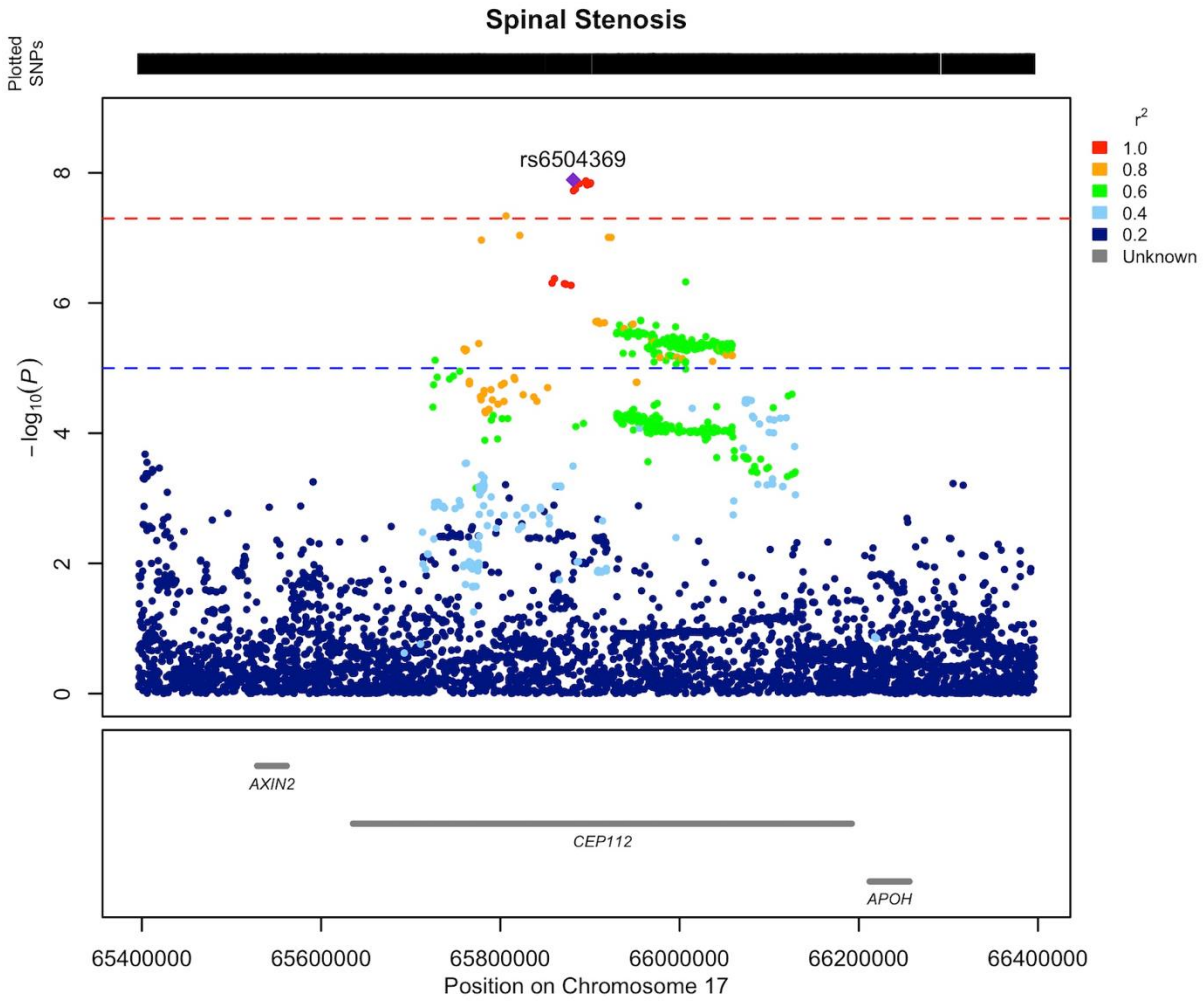

Fig S63. Regional association plot of previously unreported LSS association on chromosome 17 area of 65.4-66.4 MB. Our findings indicate that the gene responsible for the locus's association is most likely *AXIN2 (axin 2).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

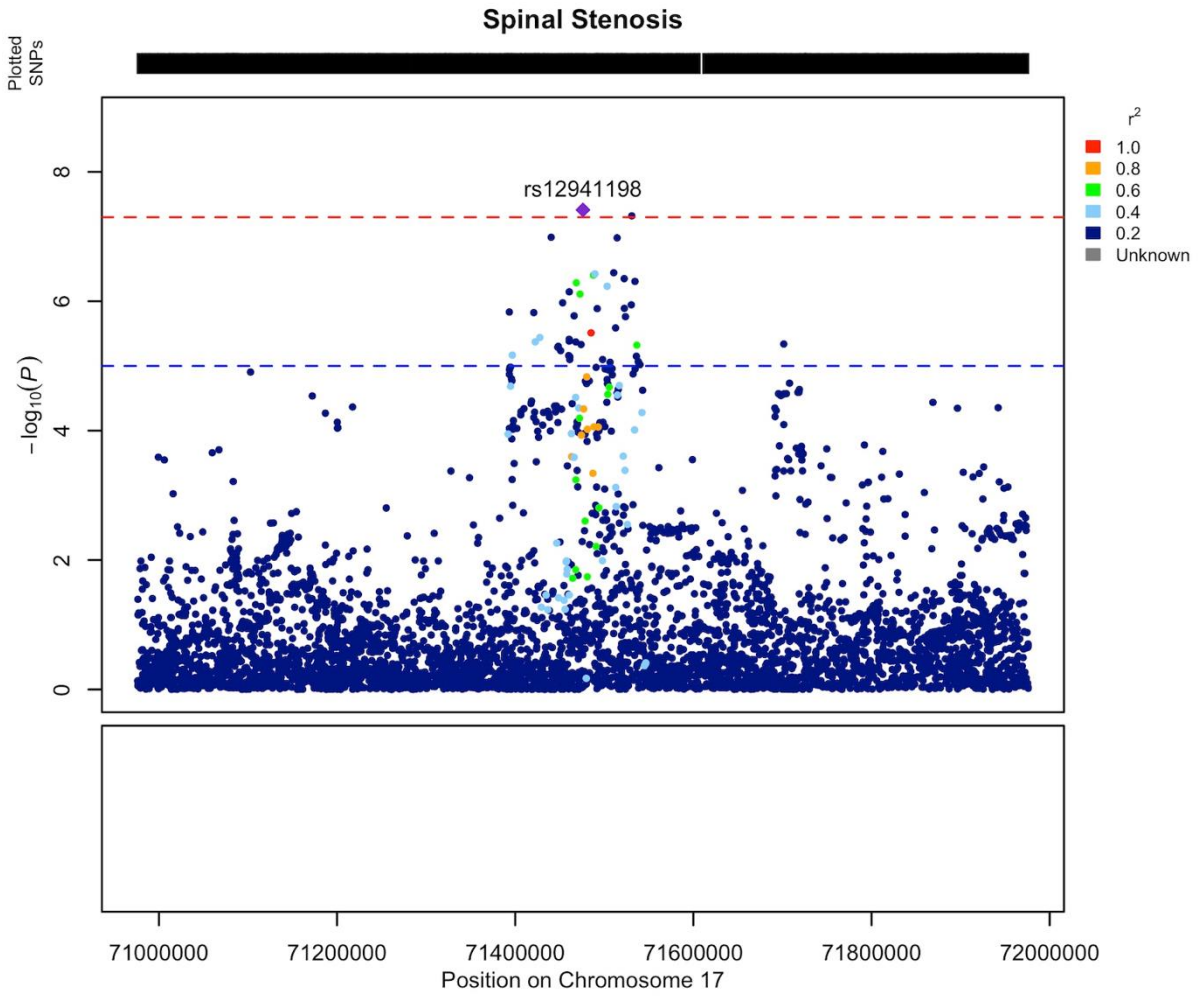

Fig S64. Regional association plot of previously unreported LSS association on chromosome 17 area of 71.0-72.0 MB. There was not any protein coding gene in this locus, so it was classified as Empty. The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

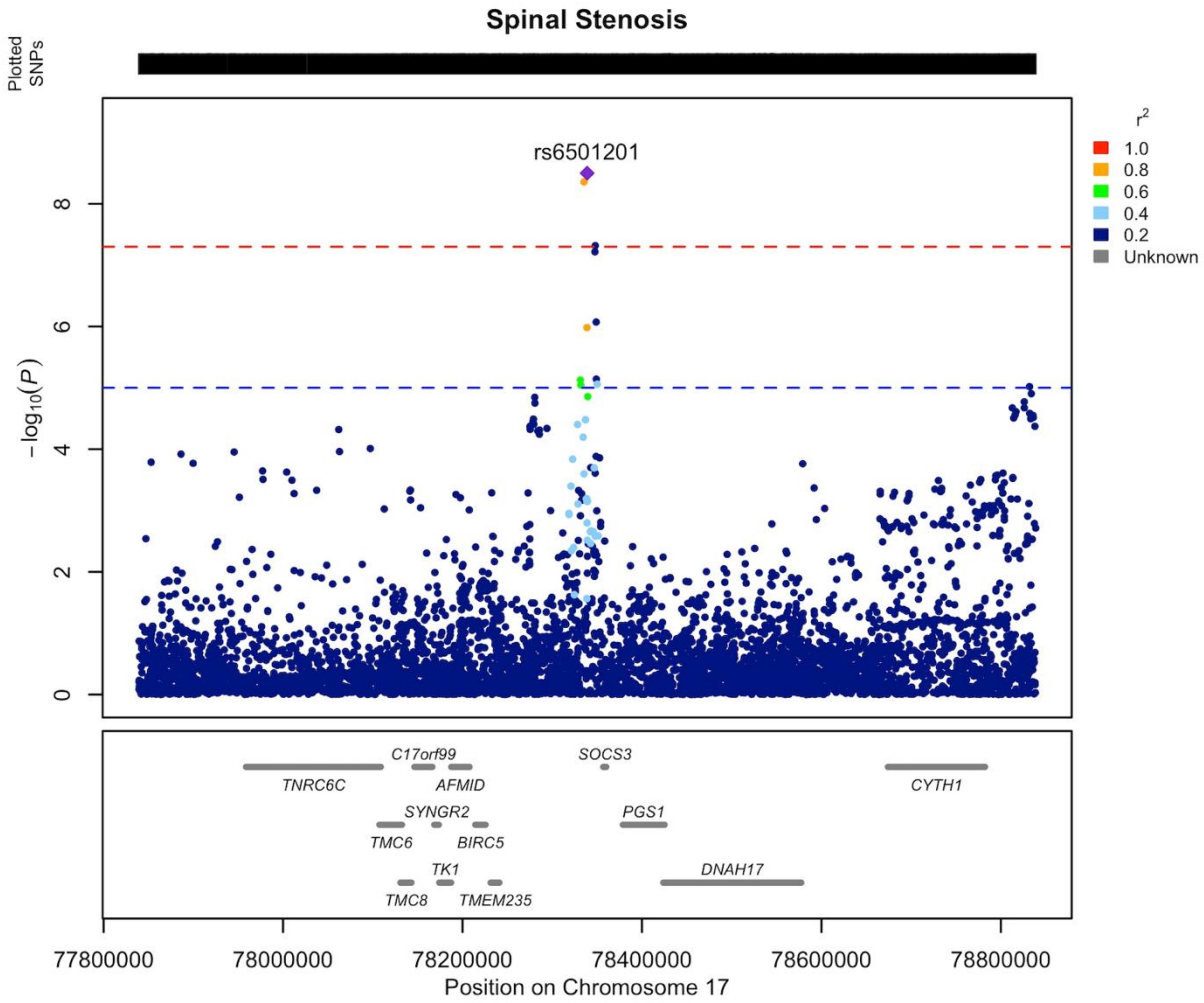

Fig S65. Regional association plot of previously unreported LSS association on chromosome 17 area of 77.8-78.8 MB. Our findings indicate that the gene responsible for the locus's association is most likely *SOCS3 (suppressor of cytokine signaling 3).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

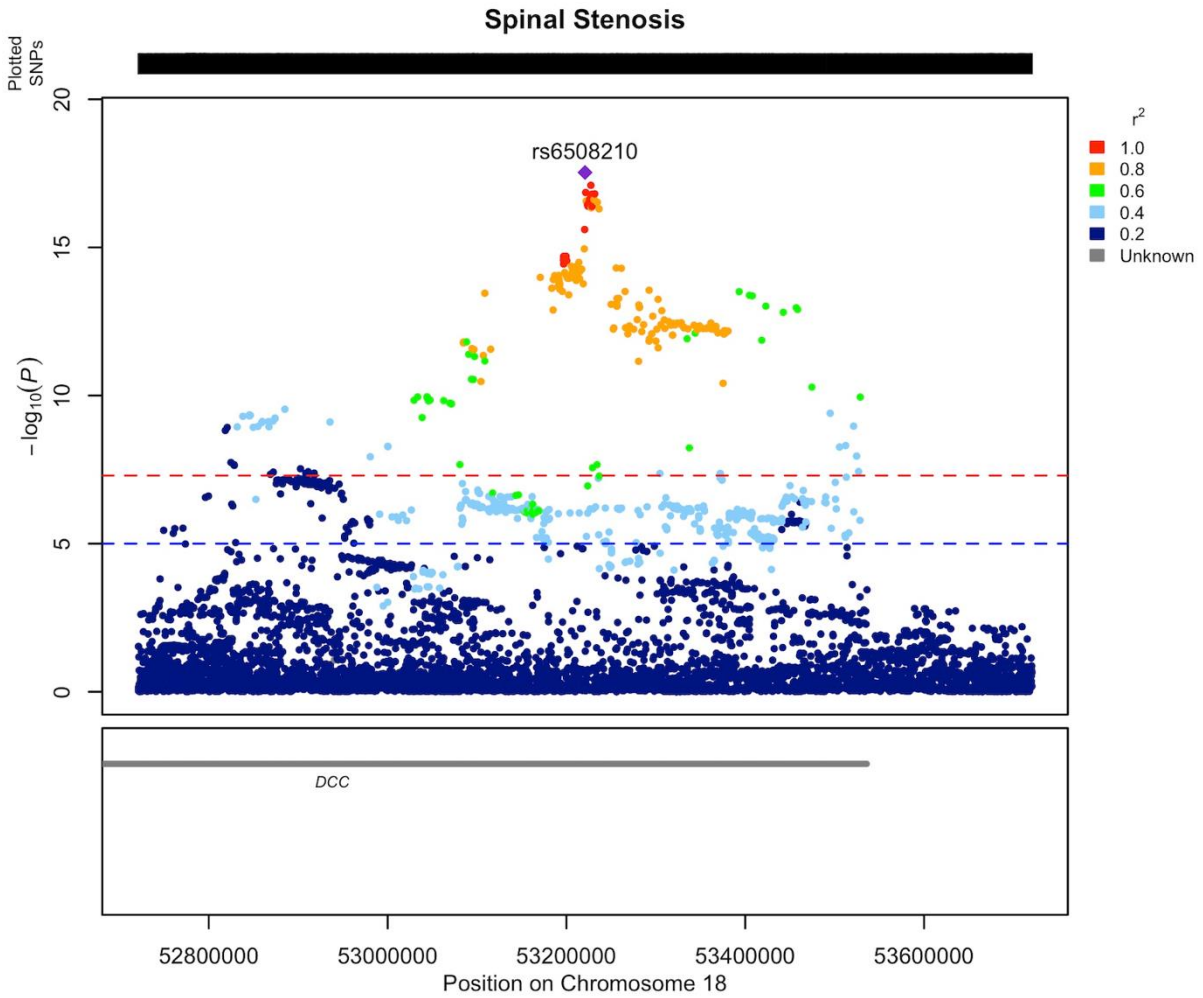

Fig S66. Regional association plot of previously unreported LSS association on chromosome 18 area of 52.7-53.7 MB. Our findings indicate that the gene responsible for the locus's association is most likely *DCC (DCC netrin 1 receptor).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

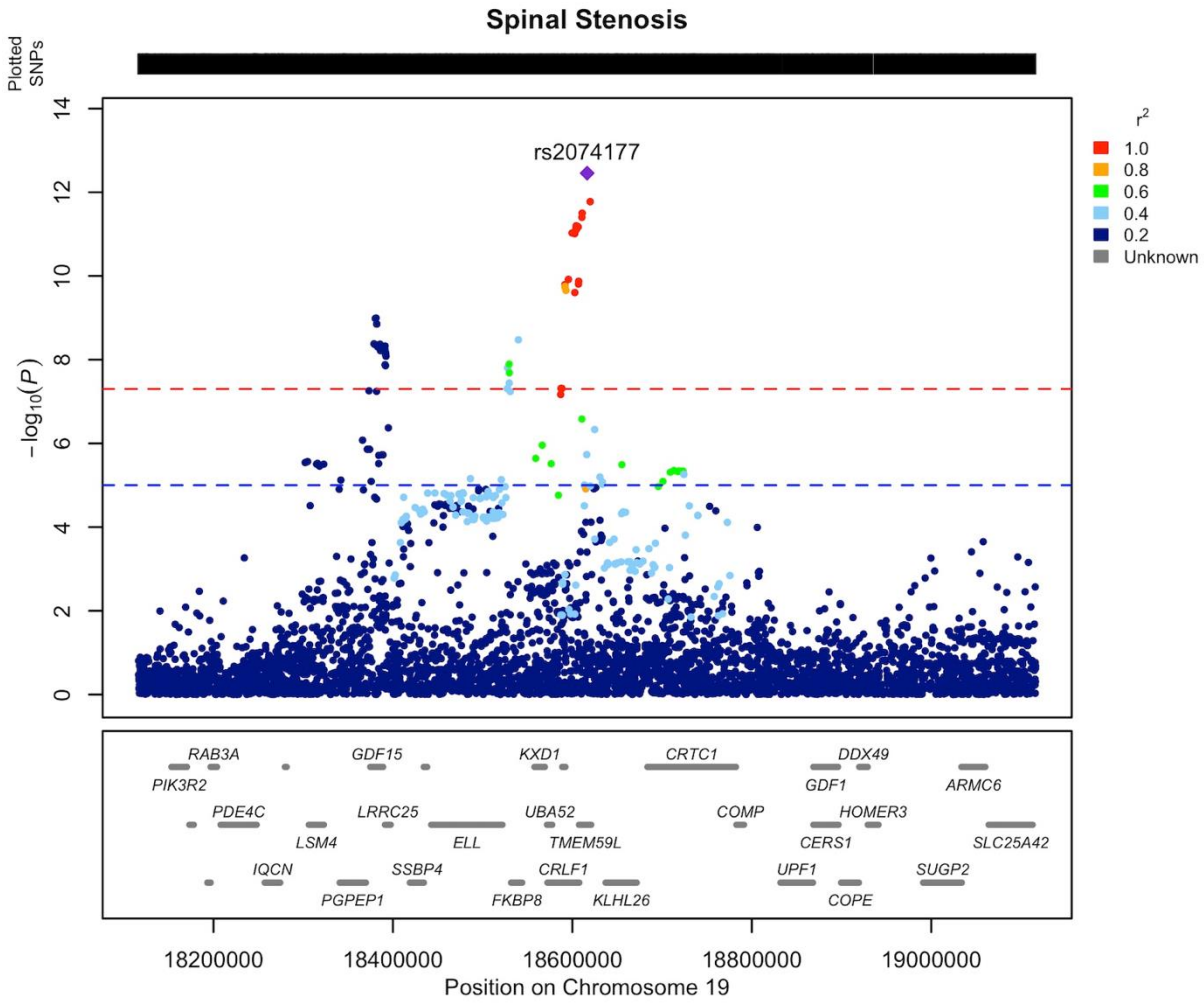

Fig S67. Regional association plot of previously unreported LSS association on chromosome 19 area of 18.1-19.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *CRLF1 (cytokine receptor like factor 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

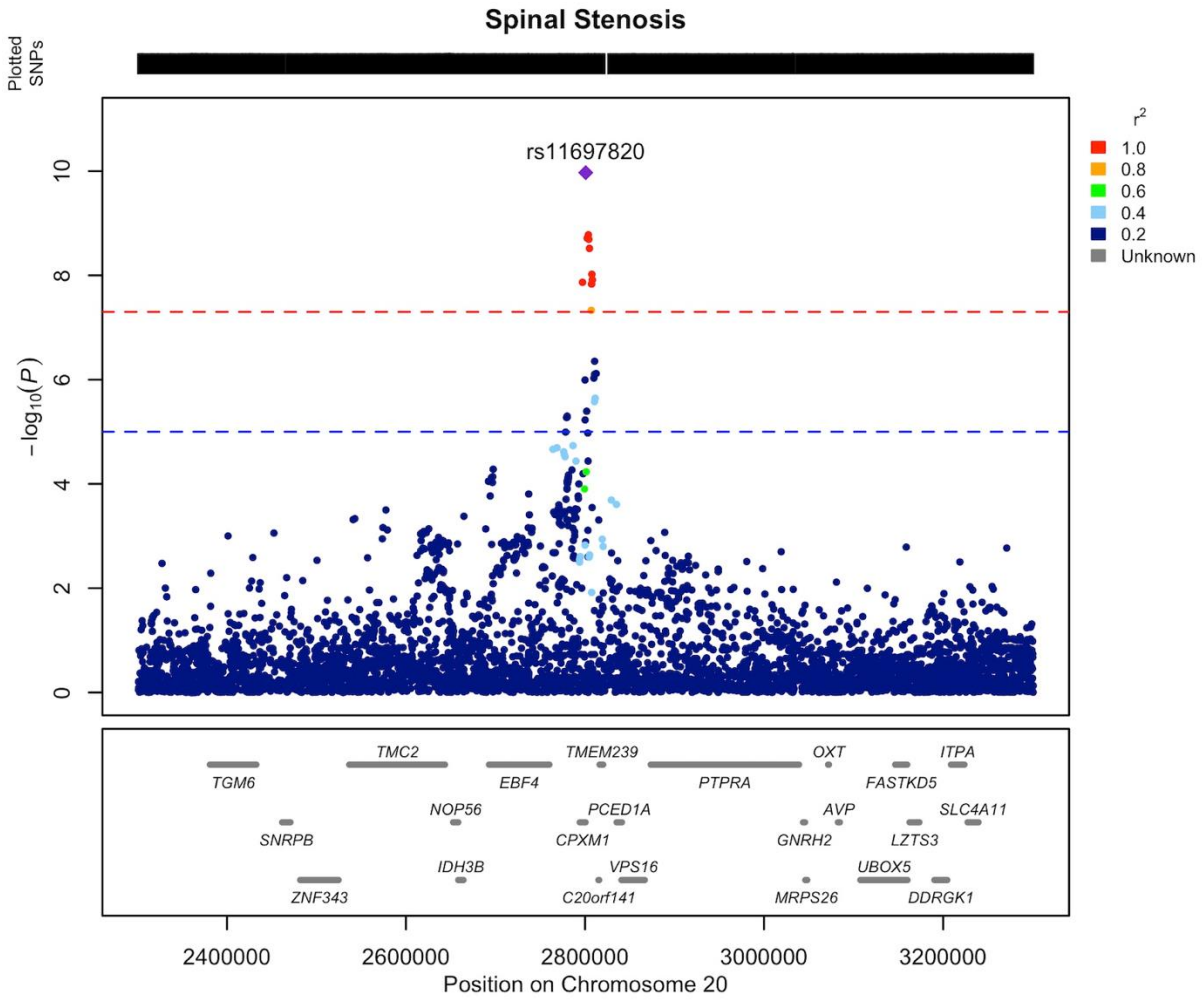

Fig S68. Regional association plot of previously unreported LSS association on chromosome 20 area of 2.3-3.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *DDRGK1 (DDRGK domain containing 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

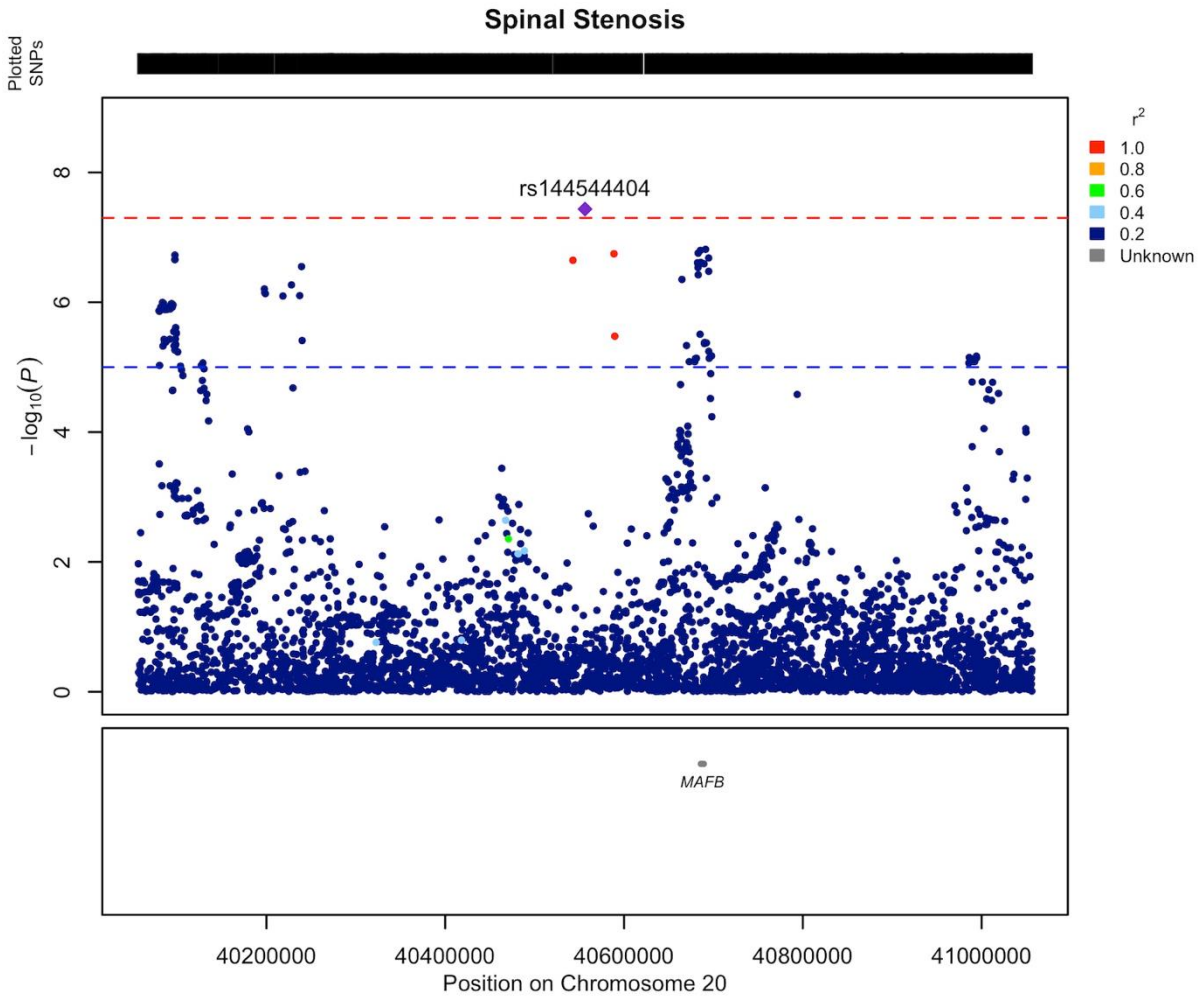

Fig S69. Regional association plot of previously unreported LSS association on chromosome 20 area of 40.1-41.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *MAFB (MAF bZIP transcription factor B).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

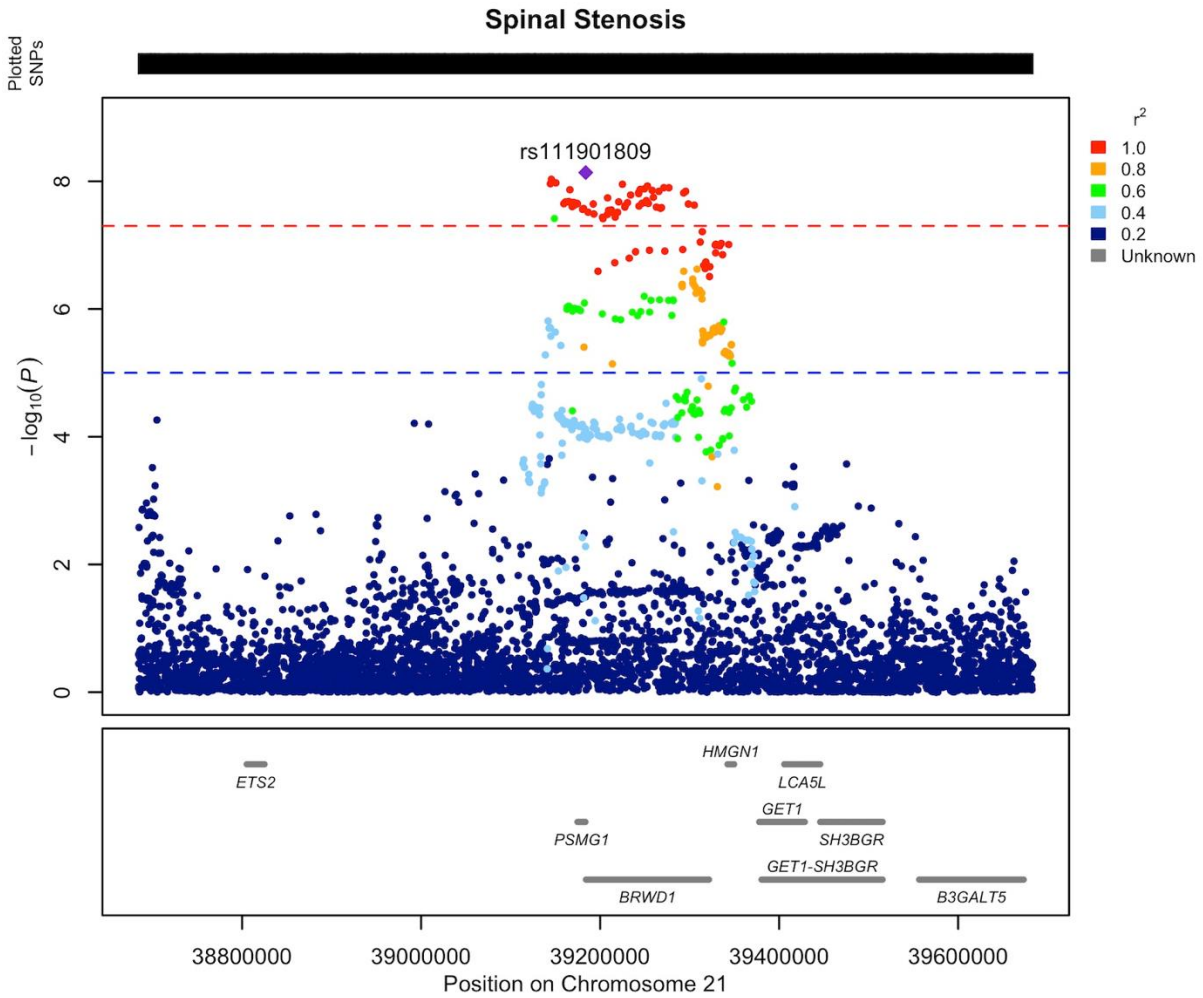

Fig S70. Regional association plot of previously unreported LSS association on chromosome 21 area of 38.7-39.7 MB. Our findings indicate that the gene responsible for the locus's association is most likely *ETS2 (ETS proto-oncogene 2, transcription factor).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

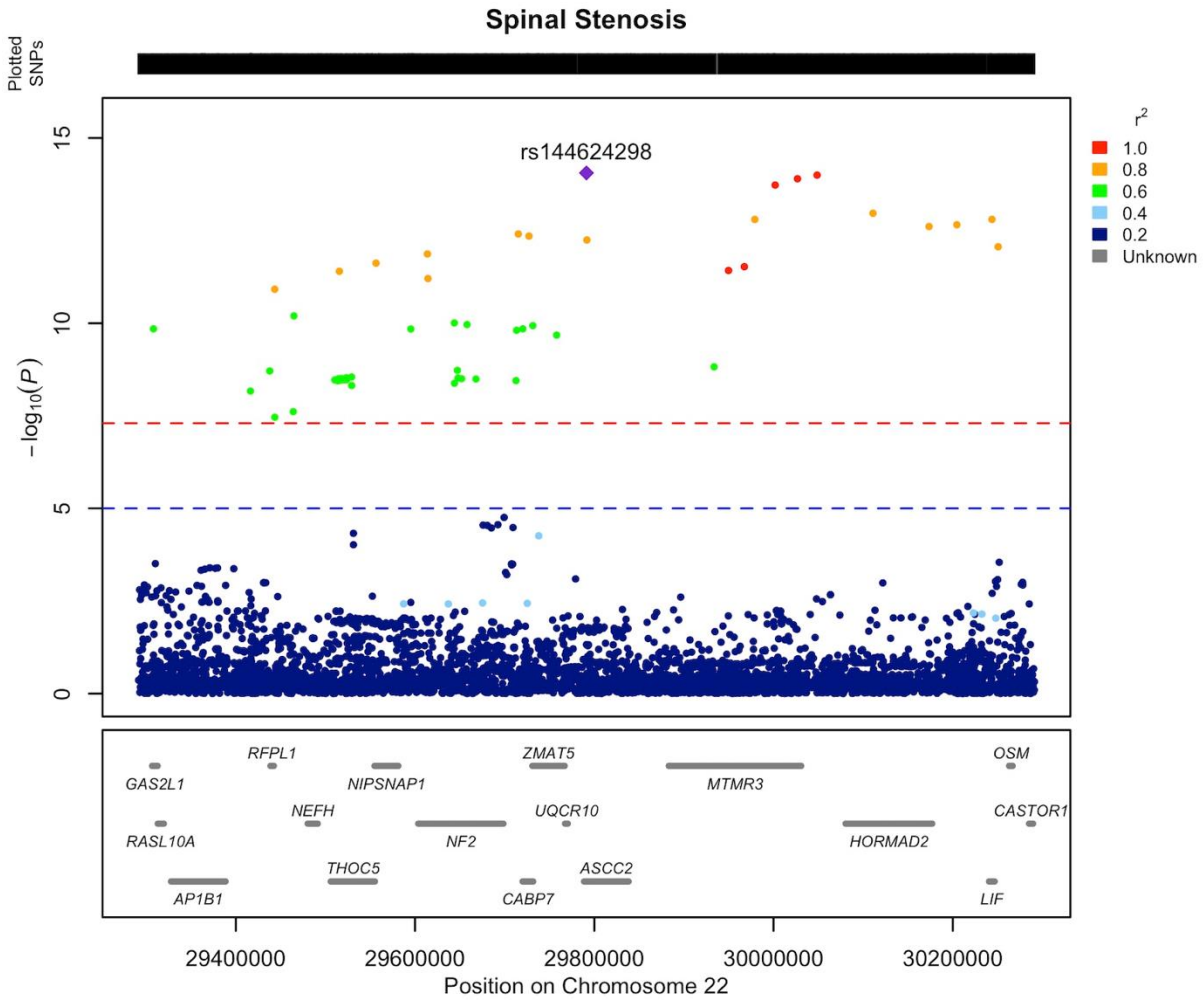

Fig S71. Regional association plot of previously unreported LSS association on chromosome 22 area of 29.3-30.3 MB. Our findings indicate that the gene responsible for the locus's association is most likely *OSM (oncostatin M).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

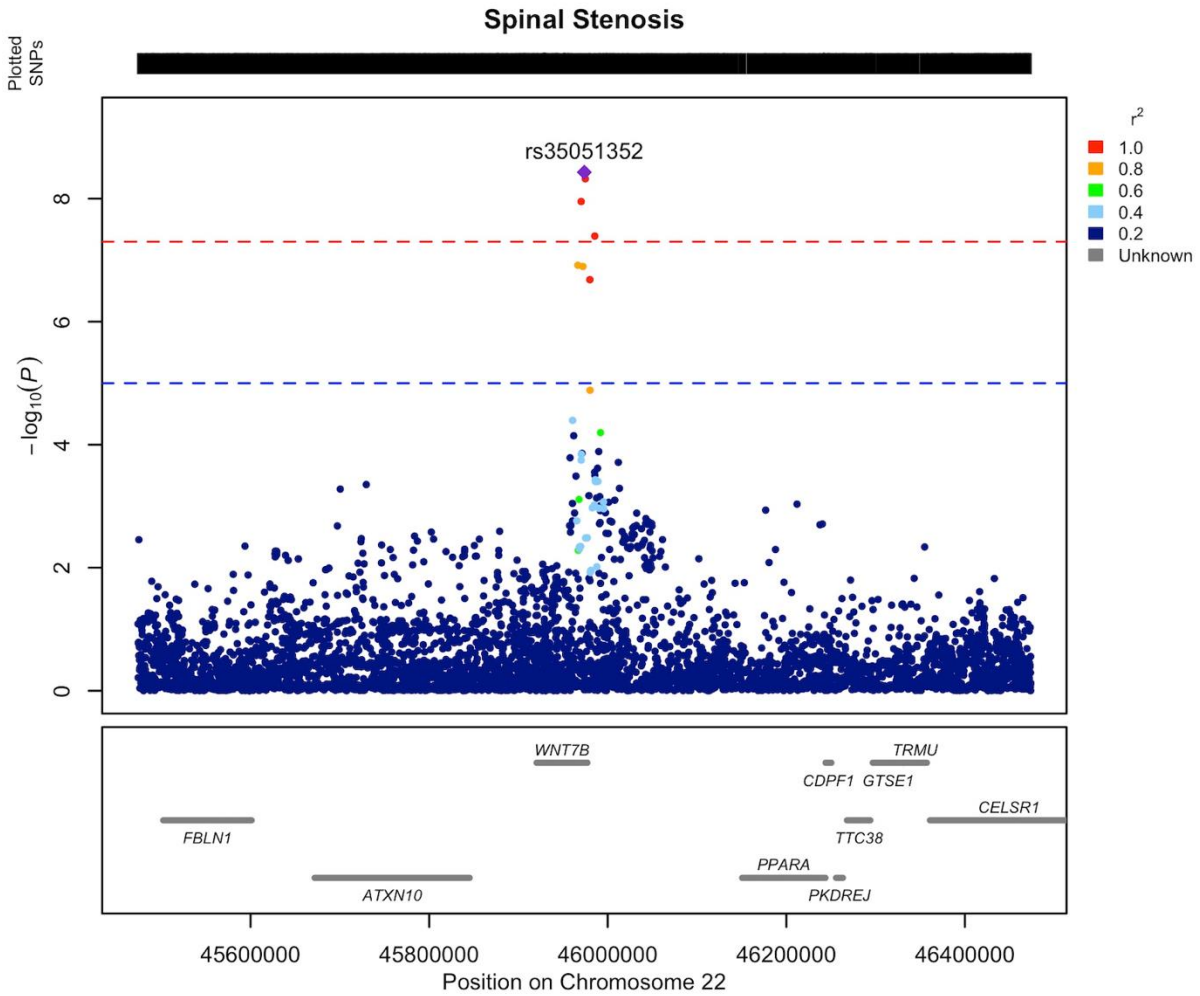

Fig S72. Regional association plot of previously unreported LSS association on chromosome 22 area of 45.5-46.5 MB. Our findings indicate that the gene responsible for the locus's association is most likely *WNT7B (wnt family member 7B).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list.

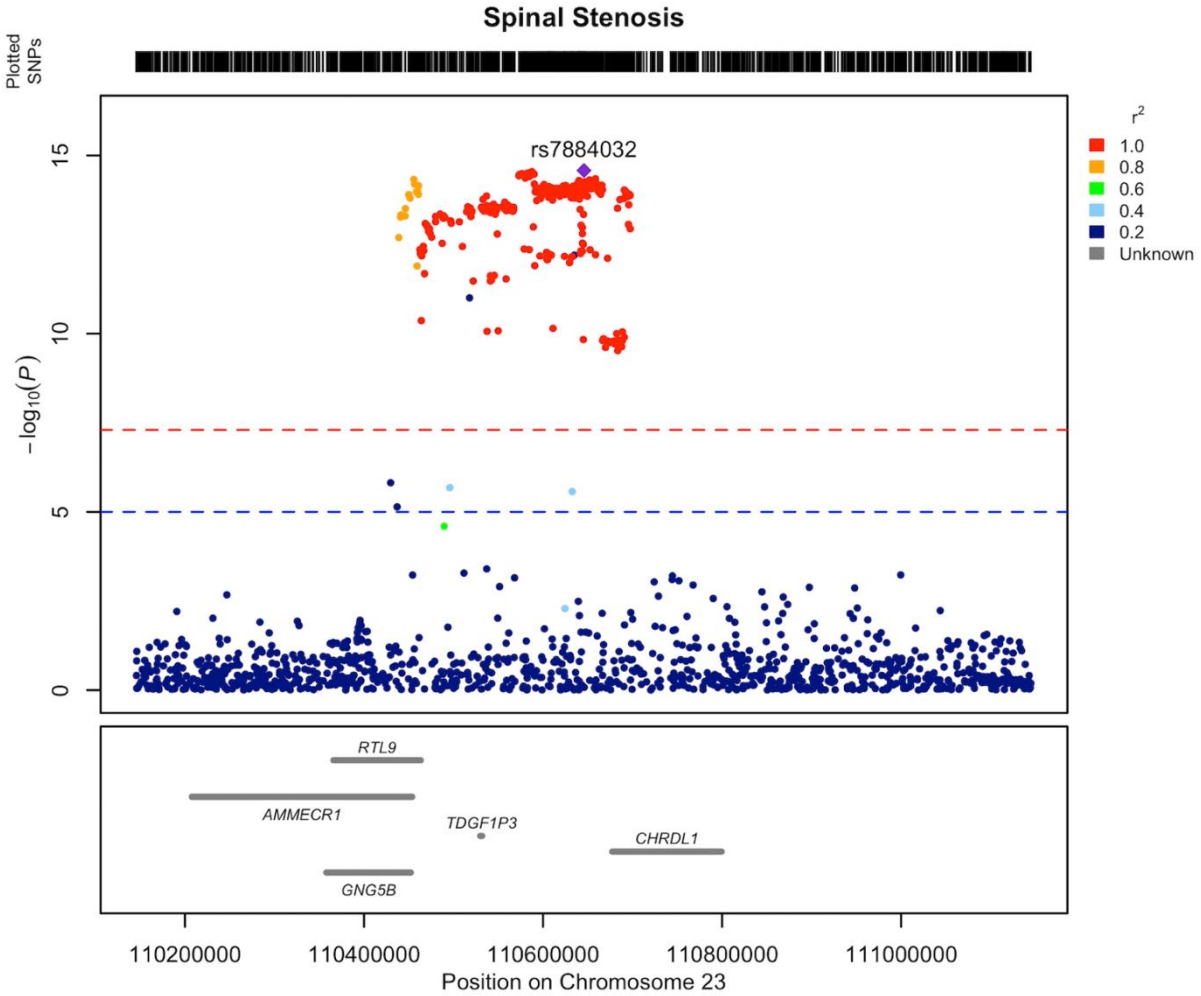

Fig S73. Regional association plot of previously unreported LSS association on chromosome X area of 110.1-111.1 MB. Our findings indicate that the gene responsible for the locus's association is most likely *CHRDL1 (chordin like 1).* The LD structure of the plot does not fully represent the meta-analysis as it was calculated using FinnGen. The Locuszooms (https://github.com/Geeketics/LocusZooms) R package was used to generate the plot, and the Ensembl archive (https://jul2023.archive.ensembl.org) was used for the gene list. Both sexes were included in the LD calculation.

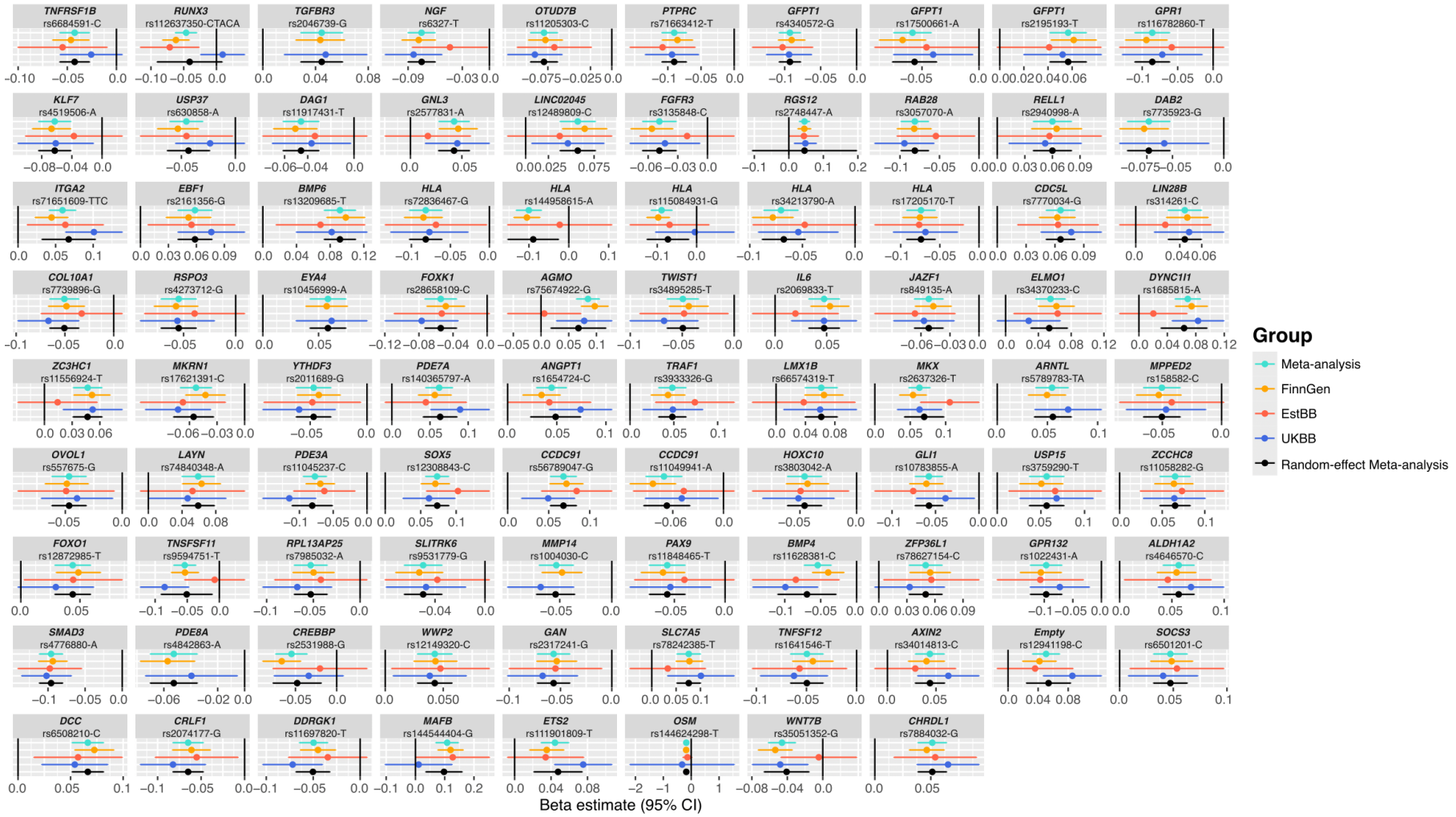

Fig S74. The forest plot displays the effect estimates and 95% confidence intervals for LSS-associated lead variants in the meta-analysis (Ncases= 40 303, Ncontrols=741 468, [green]), as well as each dataset separately in FinnGen (Ncases=26 090, Ncontrols=353 224, [orange]), Estonian Biobank (Ncases=6019, Ncontrols=65 258, [red]), and UK Biobank (Ncases=8194, Ncontrols=322 986, [blue]). Also, since some of the observed effects appeared to be heterogenous we also performed random-effect meta-analysis as a sensitivity analysis (Ncases= 40 303, Ncontrols=741 468, [black]). Candidate gene, rsid and effect allele were used as variant identifiers. Supplementary Data 4 displays the cohort level odds ratios and effect allele frequencies. Source data are provided as a Source Data file.

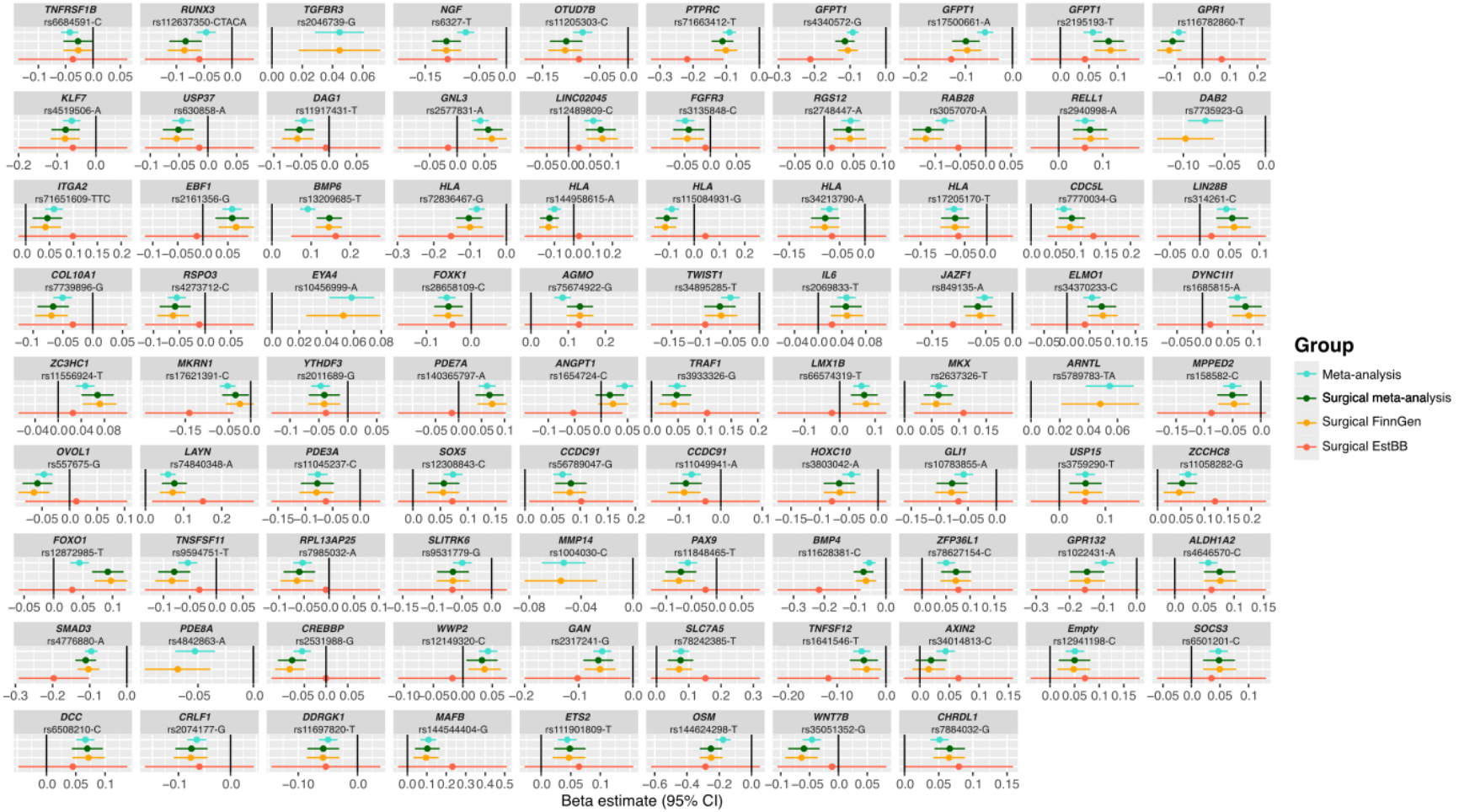

Fig S75. A comparison of the effect sizes of the lead variants discovered in the original meta-analysis (Meta-analysis, ICD-10:M48.0 [skyblue], Ncases= 40 303, Ncontrols=741 468) and in sensitivity analysis with LSS patients requiring surgery (Surgical meta-analysis, *Nomesco v1.15*: ABC36, ABC56, ABC66, ABC99, NAG61, NAG62, NAG63, NAG66, NAG67, and NAG99 [green], Ncases=12 784, Ncontrols=418 246) as well as each dataset separately: Surgical GWAS FinnGen (Ncases=11 747, Ncontrols=352 997, [orange]), Surgical GWAS Estonian Biobank (Ncases=1037, Ncontrols=65 249, [red]),. Between meta-analysis and surgical GWAS we observed statistically significant effect differences for *RUNX3, NGF, GFPT1, BMP6, AGMO* and *FOXO1* variants (Fig. 1B). Results of the effect differences and p-values for difference can also be seen from Supplementary Data 9. Source data are provided as a Source Data file.

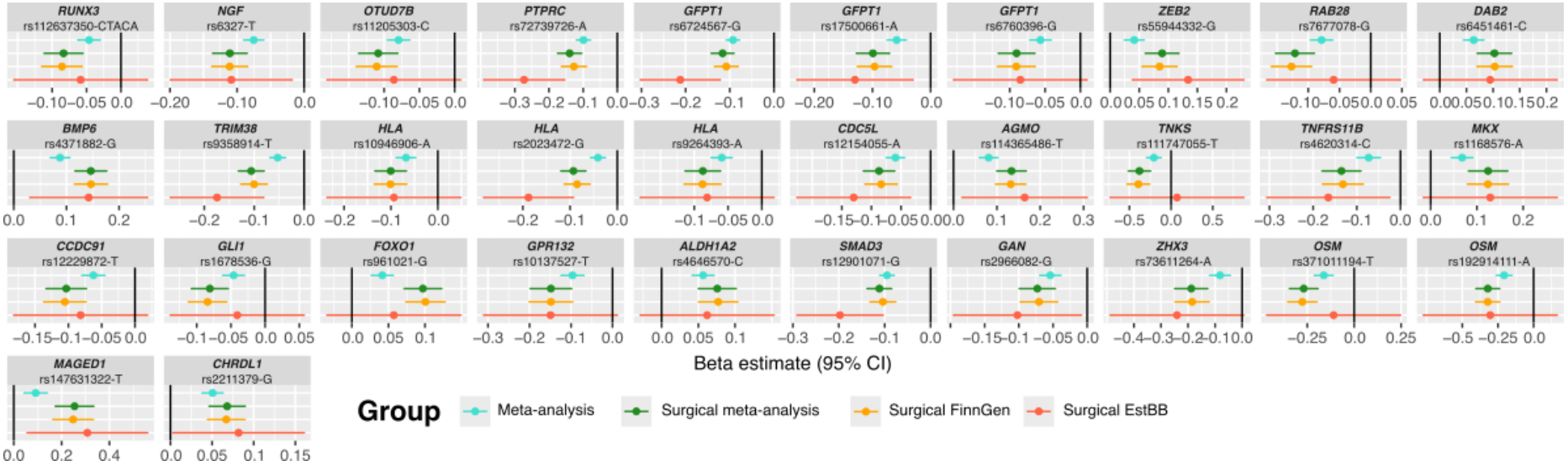

Fig S76. The forest plot displays the effect estimates and 95% confidence intervals for surgical LSS-associated lead variants in the original meta-analysis (Ncases=40 303, Ncontrols=741 468, [skyblue]) and in surgical meta-analysis (Ncases=12 784, Ncontrols=418 246, [green]), as well as each dataset separately: Surgical GWAS FinnGen (Ncases=11 747, Ncontrols=352 997, [orange]), Surgical GWAS Estonian Biobank (Ncases=1037, Ncontrols=65 249, [red]). The surgical meta-analysis involved patients with LSS who had undergone surgery (NOMESCO version 1.15, ABC36, ABC56, ABC66, ABC99, NAG61, NAG62, NAG63, NAG66, NAG67, and NAG99). Potential candidate gene, rsid and effect allele were used as variant identifiers. Supplementary Data 7 contains more information about the associated variants and Supplementary Data 8 displays the cohort level odds ratios and effect allele frequencies. Source data are provided as a Source Data file.

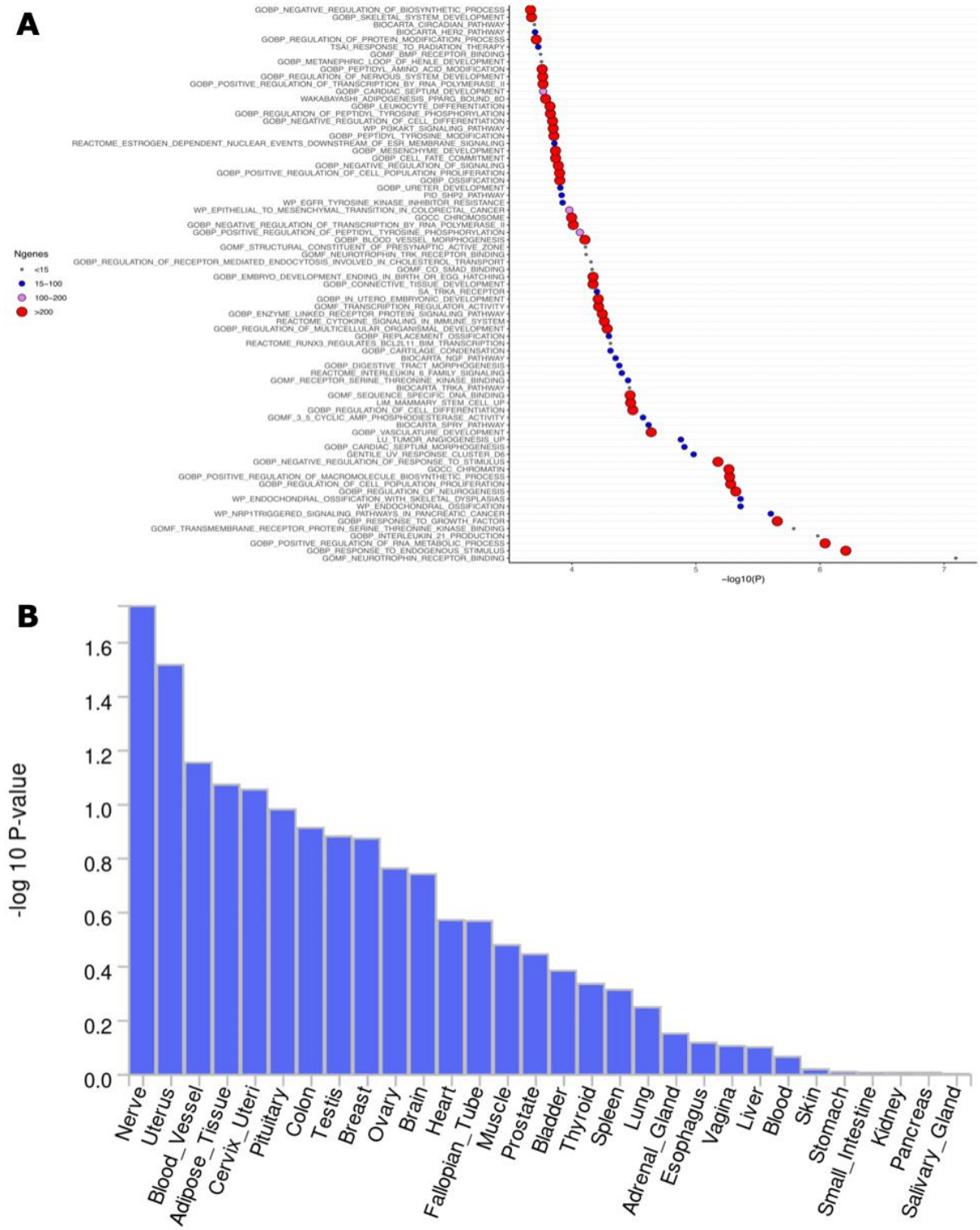

Fig S77. MAGMA gene-set and tissue expression analysis[1] results. A) Shows significantly enriched pathways (pFDR < 0.05), curated gene sets, and GO-annotations ranked by significance (-log10(P-value)). The circle size refers to the size of the gene set. Small gray <15, blue 15–100, violet 100-200, and red >200 genes. No genome-wide significant results were observed in tissue expression analysis. B) No tissues showed statistical significance above the threshold of $-\log_{10}(2.78)$ ($-\log_{10}(0.05/30)$) after Bonferroni correction for testing 30 tissues (dashed line). y-axis, -log 10 P-value; x-axis, tissues (GTEx Output-General tissues). The analysis was done using FUMA[2], and the gene sets and GO annotations included in the analysis are from MSigDB[3]. Source data are provided as a Source Data file.

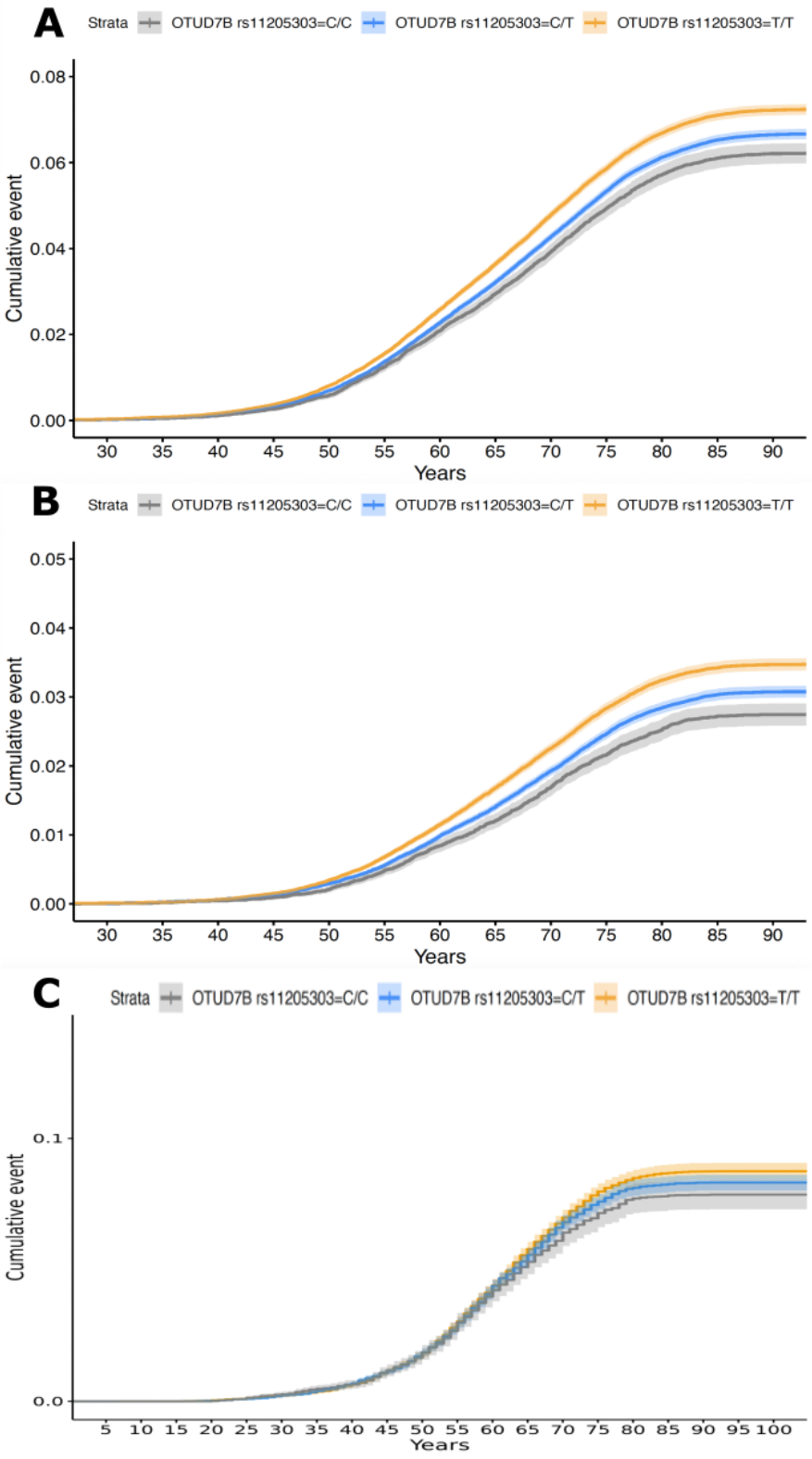

Fig S78. Kaplan-Meier plots for the LSS-associated variant located near *OTUD7B*. For this variant, we observed that the cumulative incidence of LSS differed between homozygotes already at the age of 34. The graph A) is based on FinnGen results, B) is based on FinnGen surgical results and C) is based on Estonian Biobank replication. Age in years is on the x-axis, and the corresponding fraction of the cases is on the y-axis. The grey line depicts homozygotes for the effect allele, the orange homozygotes for the other allele, and the blue line corresponds to heterozygotes having one copy of each allele. The heterozygote differences were not tested and are just shown for illustration. Source data are provided as a Source Data file.

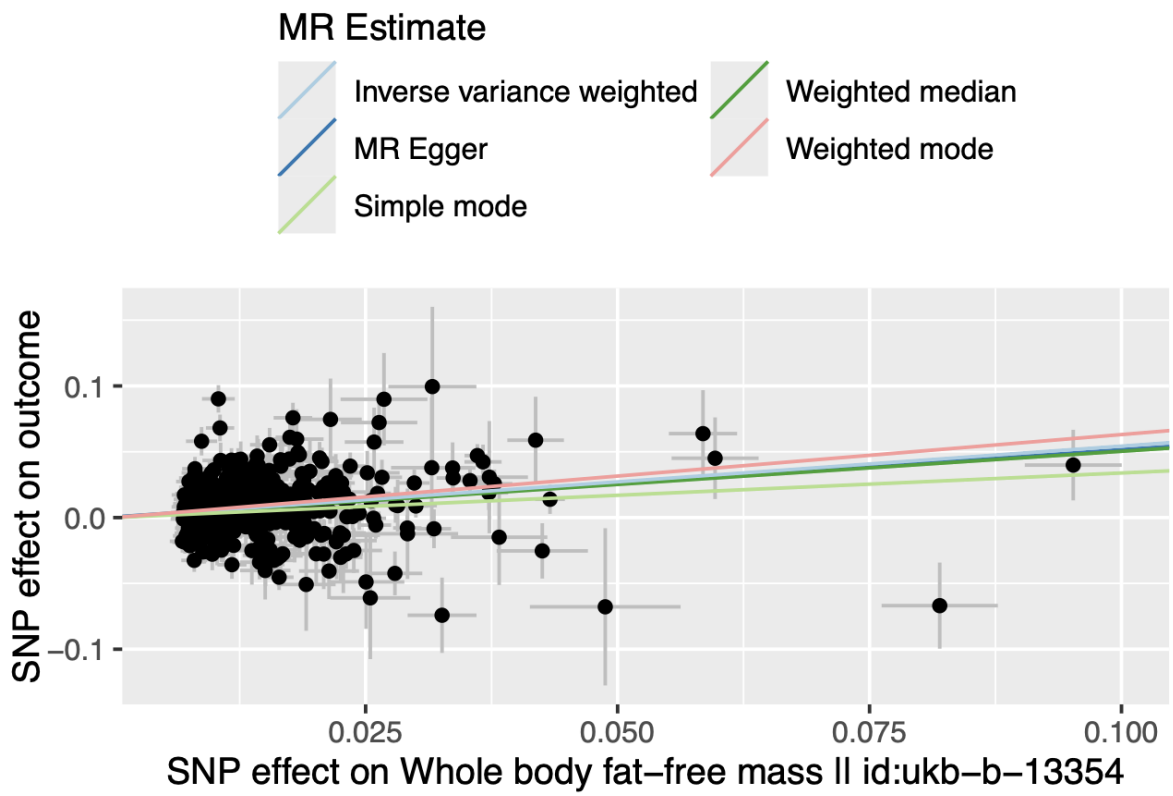

Fig S79. Scatterplot for whole body fat-free mass that could potentially be causal for LSS. Genetic instruments for LSS were extracted from FinnGen. For "Whole body fat-free mass" (id:ukb-b-13354, n= 454 850) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

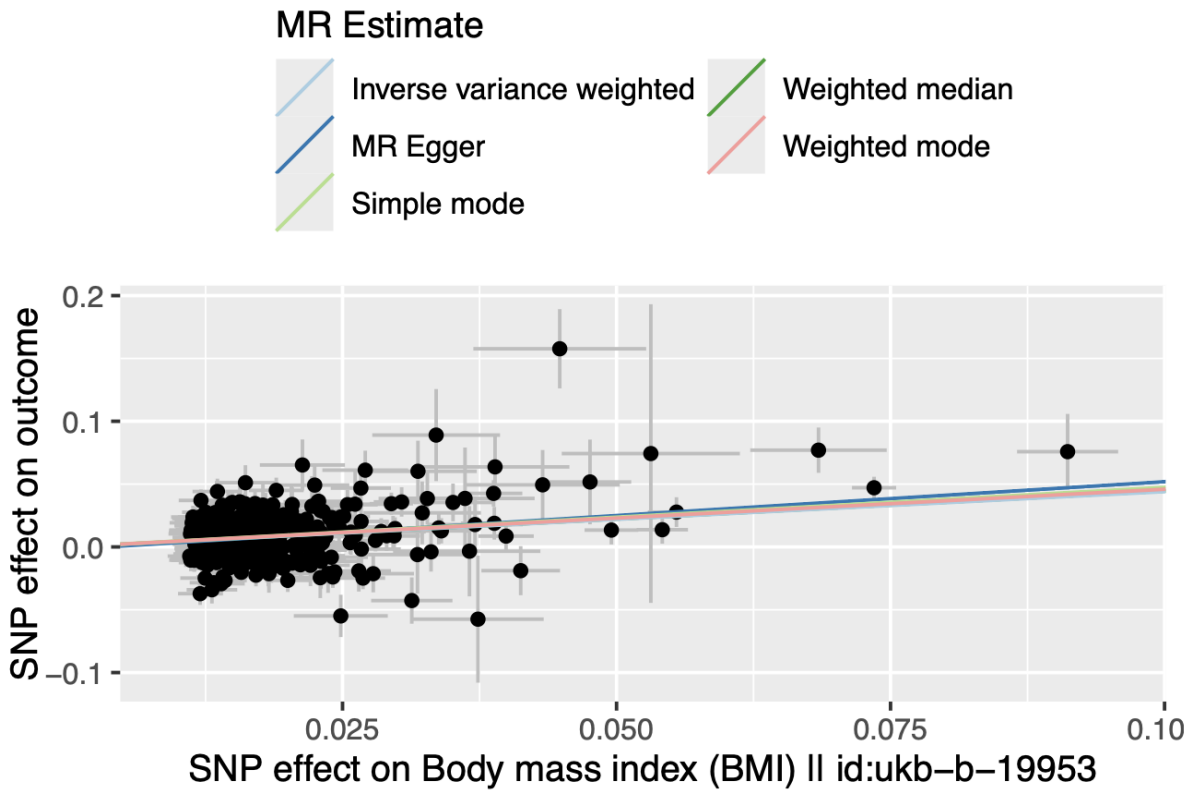

Fig S80. Scatterplot for body mass index (BMI) that could potentially be causal for LSS. Genetic instruments for LSS were extracted from FinnGen. For "Body mass index (BMI)" (id:ukb-b-19953, n= 461 460) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

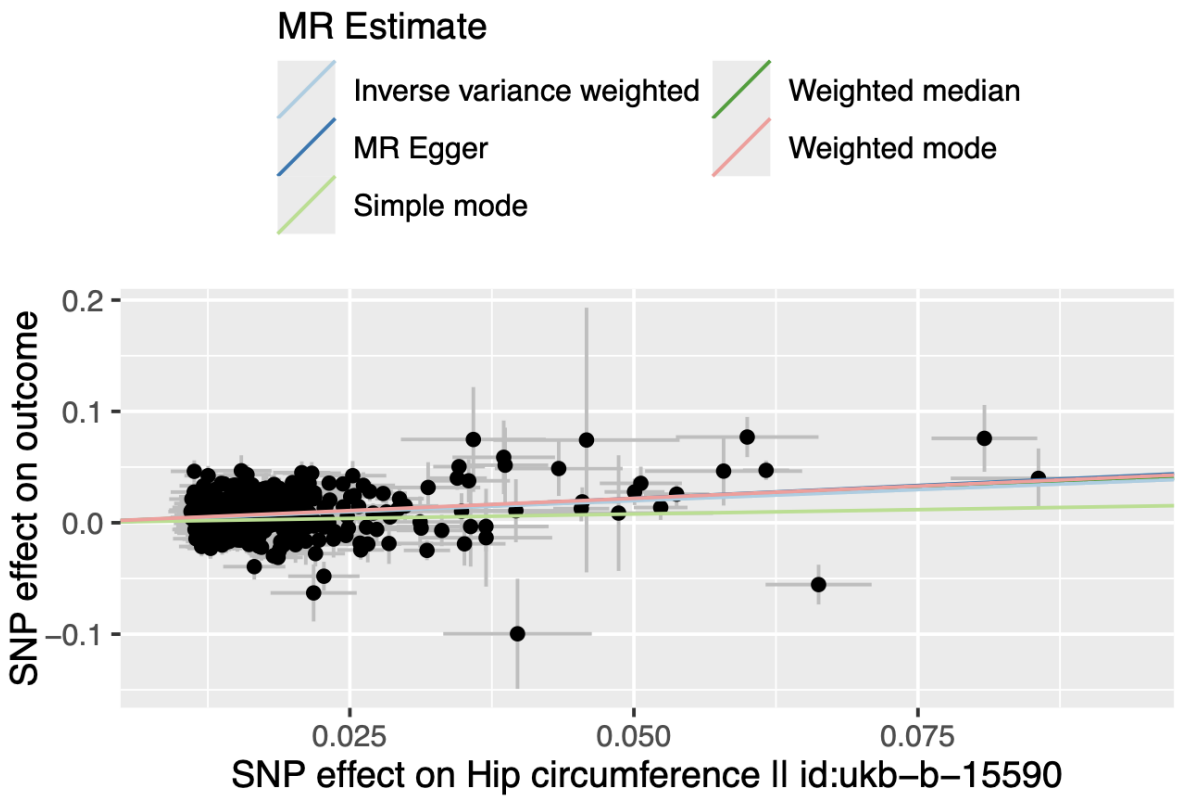

Fig S81. Scatterplot for hip circumference that could potentially be causal for LSS. Genetic instruments for LSS were extracted from FinnGen. For "Hip circumference" (id:ukb-b-15590, n= 462 117) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

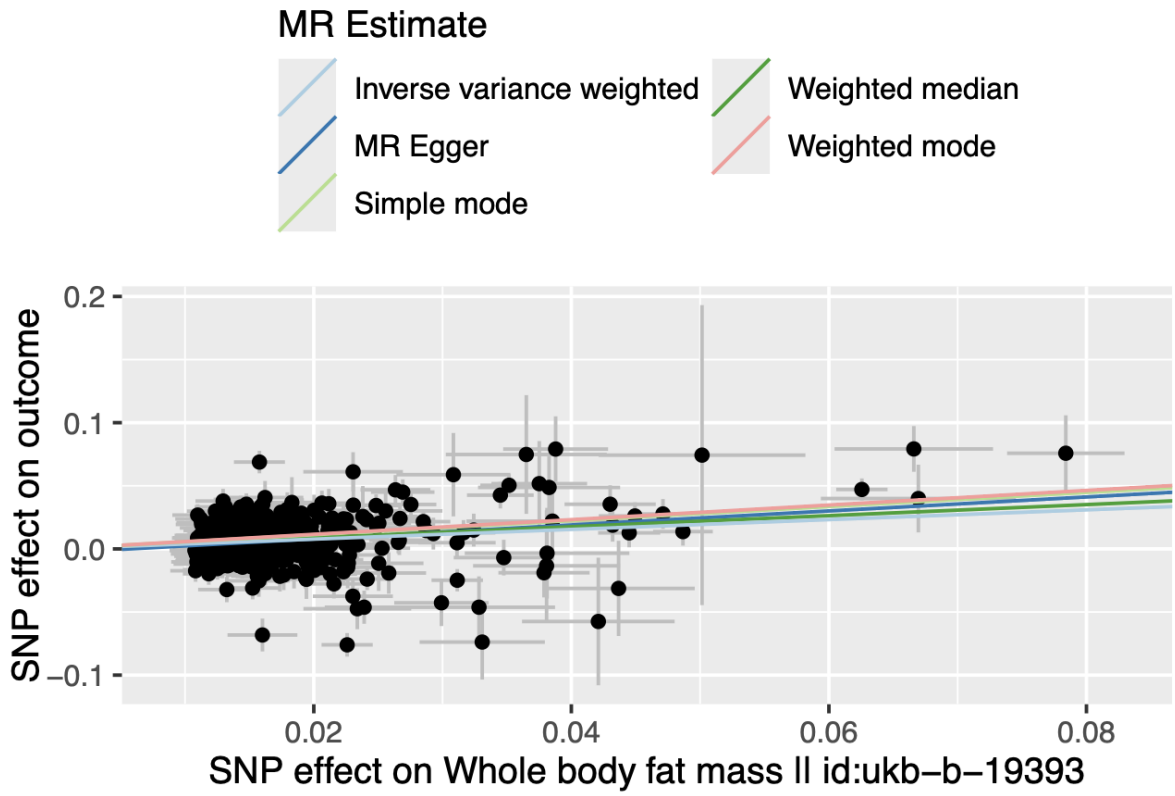

Fig S82. Scatterplot for whole body fat mass that could potentially be causal for LSS. Genetic instruments for LSS were extracted from FinnGen. For "Whole body fat mass" (id:ukb-b-19393, n= 454 137) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

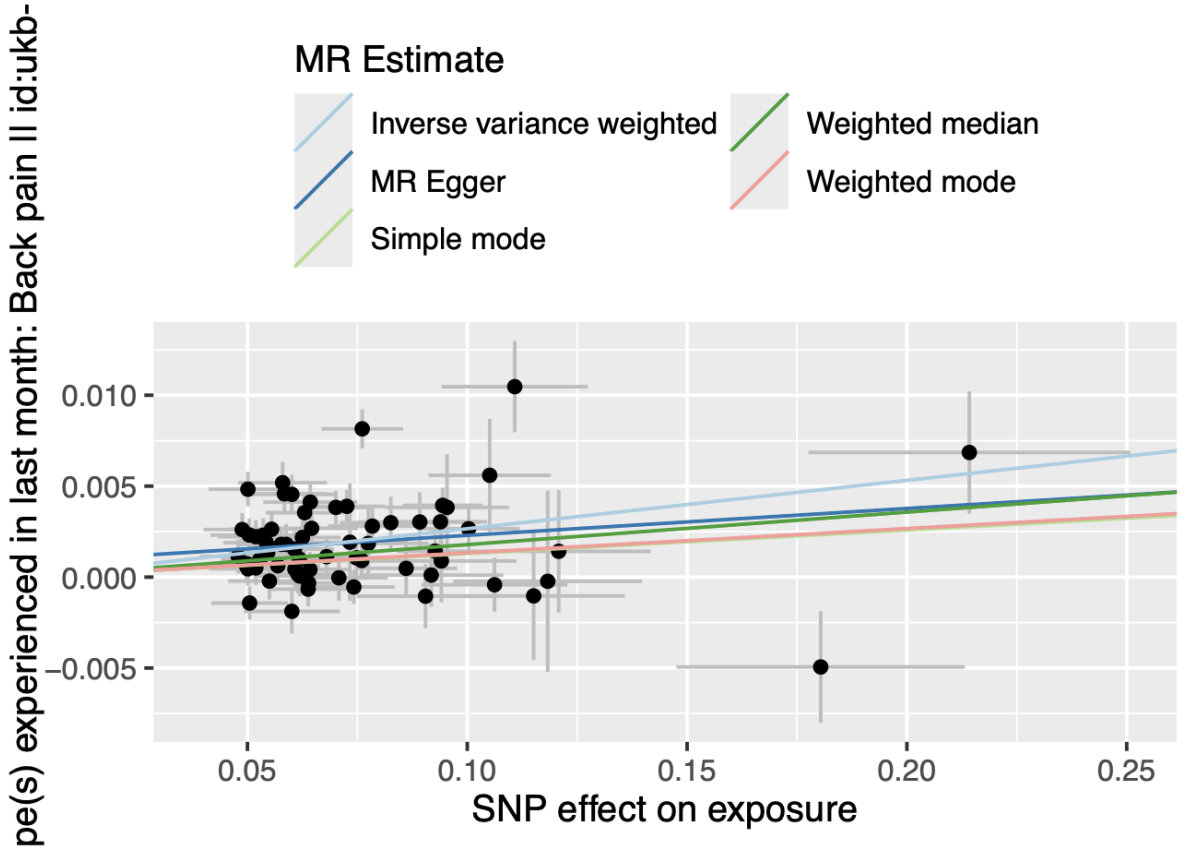

Fig S83. Scatterplot for back pain for which LSS is potentially causal. Genetic instruments for LSS were extracted from FinnGen. For "Pain type(s) experienced in last month: Back pain" (id:ukb-b-9838, n= 461 857) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

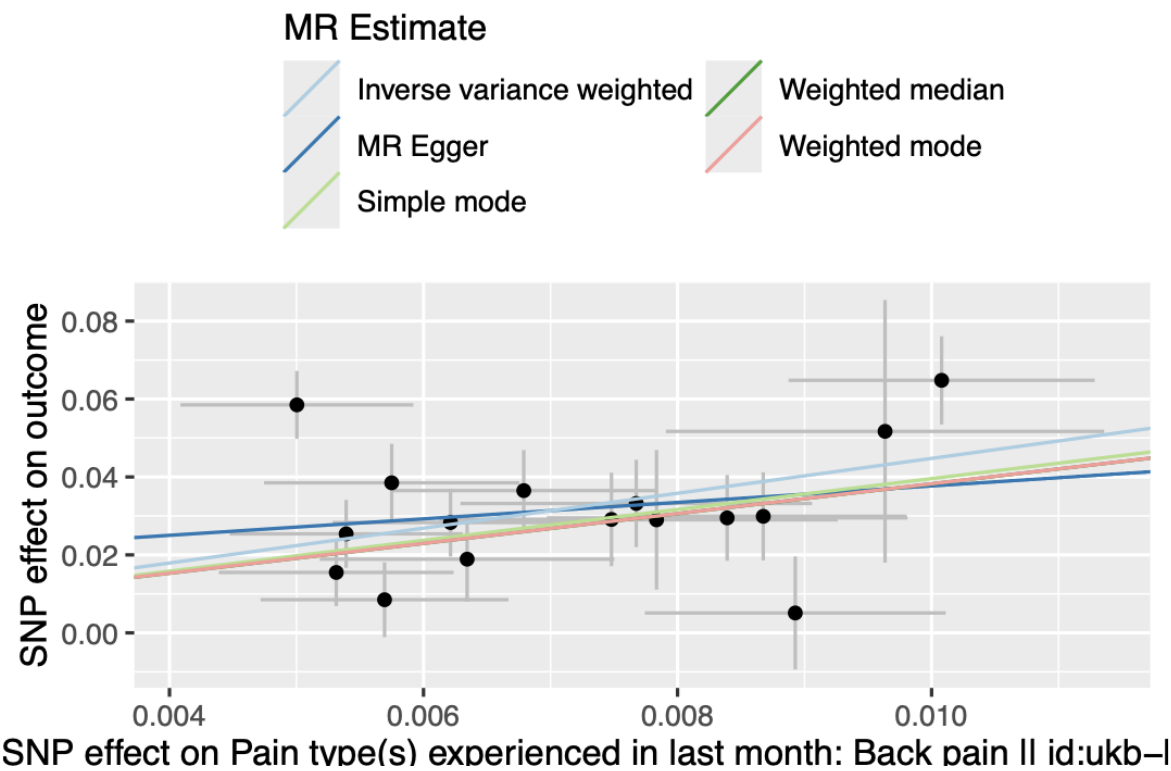

Fig S84. Scatterplot for back pain that could potentially be causal for LSS. Genetic instruments for LSS were extracted from FinnGen. For "Pain type(s) experienced in last month: Back pain" (id:ukb-b-9838, n= 461 857) from the GWAS database provided by the MRC-IEU, which is integrated in the TwoSampleMR R library. European population references was utilised in LD pruning, with thresholds of r2=0.001 and clumping window of 10kb. The error bars indicate the 95% confidence intervals of the SNP effects. Source data are provided as a Source Data file.

References

1. de Leeuw, C. A., Mooij, J. M., Heskes, T. & Posthuma, D. MAGMA: Generalized Gene-Set Analysis of GWAS Data. *PLoS Comput Biol* 11, e1004219 (2015).
2. Watanabe, K., Taskesen, E., van Bochoven, A. & Posthuma, D. Functional mapping and annotation of genetic associations with FUMA. *Nat Commun* 8, 1826 (2017).
3. Liberzon, A. *et al.* Molecular signatures database (MSigDB) 3.0. *Bioinformatics* 27, 1739–40 (2011).