PRS-Reporting Standards for the manuscript "A Genomic Risk Score Identifies Individuals at High Risk for Intracerebral Hemorrhage"

	Reporting Item	**Minimal Reporting (MR)**	**Highly Recommended (HR)/Supp Details**	**Study Stage** - For items that are reported separately for development and evaluation	**"A Genomic Risk Score Identifies Individuals at High Risk for Intracerebral Hemorrhage"**
Risk Score Background	**Study Type**	Specify whether authors are **developing a risk score** and/or **externally validating a previously published PRS**. When externally validating or combining previously published PRS, include identifier(s) of original PRS (PMID, PGS catalog ID).			Was MR met?: Yes (clear in **Methods and Supplemental Methods**) Details: - **Introduction:** "In this study, we sought to investigate whether combining genetic liability for possible ICH risk factors and traits reflecting pathologies underlying ICH into a meta-Genomic Risk Score (metaGRS) could improve our ability to predict ICH events among individuals of European ancestry." - **Methods**, **Trait-specific GRS and ICH metaGRS construction** subsection: "We used GOCHA (436 ICH cases and 405 controls) and EUR/ISGC (577 ICH cases and 523 controls) as training datasets to develop GRS for 21 traits associated with ICH risk." - **Supplemental Methods**, **Construction of the main ICH meta-Genomic Risk Score (metaGRS)** subsection: "In order to generate an ICH metaGRS, we followed a standard meta-analytic approach, creating a weighted average of the trait-specific optimized GRS **(Table S23)**."
	Risk Model Purpose & Predicted Clinical End Outcome	Specify what the risk model is intended to predict and the purpose: • Will it be used in risk prediction, diagnostic, prognostic, or therapeutic modalities? • What is the end outcome predicted by	Specify in advance what the goal will be in predicting this outcome, with context of what indicates a "good" prediction (e.g. by presenting AUC from clinical risk models in other studies).		Was MR met?: Yes Was HR provided?: Yes Details: - **Introduction:** "In this study, we sought to investigate whether combining genetic liability for possible ICH risk factors and traits reflecting pathologies underlying ICH into a meta-Genomic Risk Score (metaGRS) could improve our ability to predict ICH events among individuals of European ancestry." - **Supplemental Methods, ICH metaGRS performance and clinical evaluation in GERFHS** subsection

		the risk model? If the predicted outcome is a clinical feature or endpoint within a specific disease, state the disease. If the risk model is developed using an outcome other than the intended end outcome, state why the surrogate measurement was used. • What current models for risk prediction are available, if pertinent?			- **Supplemental Methods**, **External validation of the metaGRS in UKBB** subsection
Study Populations *Many risk score studies involve multiple populations and cohorts that can be used in different stages of PRS and risk score development and evaluation. Each of the populations used (e.g. training, validation, subgroup analysis samples) in the manuscript should be defined using this common set of descriptors.*	**Study Design & Recruitment**	For each of the populations used in the current study describe the type of sample (e.g., cohort, case control, cross sectional), recruitment details and setting (e.g. method and years), and follow-up. State whether the data are primary or secondary data. If secondary analysis, include a reference to the original study.	Performance should not be investigated in case-control studies. Justify why studying case-control data is clinically relevant. The calculation of risk derived from a case-control versus a longitudinal cohort can have different interpretations and therefore these details should be detailed and justified in the manuscript. Explain when prediction of prevalence is justified / clinically relevant.	Development	Was MR met?: Yes Was HR provided?: Partially Details: - **Methods**, **Study design and participating studies** subsection: "As our primary data source […] (EUR/ISGC);" - **Methods**, **Study design and participating studies** subsection: "GOCHA and EUR/ISGC were the training datasets, […]" - **Supplemental Methods**, **Ascertainment of cases and controls** subsection - **Supplemental Methods, Participating Studies** subsection

				Validation	Was MR met?: Yes Was HR provided?: Partially Details: - **Methods**, **Study design and participating studies** subsection: "[…] and the Genetic and Environmental Risk Factors for Hemorrhagic Stroke (GERFHS) study […] spontaneous ICH in the Greater Cincinnati region." - **Methods**, **Study design and participating studies** subsection: "[…] whereas GERFHS was our primary validation dataset. Furthermore, we performed an external validation […] without a prior history of ICH." - **Supplemental Methods**, **Ascertainment of cases and controls** subsection - **Supplemental Methods, Participating Studies** subsection
	Ancestry	Include the ancestral background distribution of each sample population used during PRS development and validation (including those from any GWAS summary statistics that were included), and the data source of this ancestry information (e.g., self-report, genotyping). Ancestry information should be reported using the standardized framework developed by the NHGRI-EBI GWAS Catalog with detailed information beyond this when available. When combining samples from multiple studies, aggregate ancestral distribution information is sufficient. The method of ancestry inference should be	Authors should provide ancestry information by case/control status, if applicable. Geographic location is helpful to include in the absence of known ancestry information and should be explicitly stated as location, not ancestry. If principal components are utilized, plots should be presented both with known publicly available reference panels (such as the 1000 Genomes Project), as well as the study alone. It should be explicitly stated in the limitations if ancestry is not known or able to be disclosed. Avoid ethnocultural descriptors unless they provide information about the underlying genealogy.	Development	Was MR met?: Yes Was HR provided?: N/A Details: - **Methods**, **Study design and participating studies** subsection: "As our primary data source, […], a prospectively collected case-control study of European ancestry subjects aged > 55 years with primary ICH18; the European member sites contributing ICH cases and controls to the International Stroke Genetics Consortium (EUR/ISGC) - Also, for the trait-specific genomic risk scores utilized to construct the ICH metaGRS, we utilized GWAS data from European-only populations, as reported in **Methods**, **Trait-specific genomic risk scores (GRS) construction** subsection: "We leveraged publicly available GWAS summary-level data from international consortia, as detailed in **Table S1.** For all traits, we used data from European-only populations […]"
				Validation	Was MR met?: Yes Was HR provided?: No Details: - **Supplementary Tables**: In "**Table S26.** Clinical characteristics of the GERFHS validation dataset for ICH cases and ICH-free controls." it is reported that 99.9% and 100% of ICH cases and controls were white, respectively. - **Supplementary Tables**: In "**Table S36.** Baseline characteristics of the external UK Biobank dataset for individuals who developed incident ICH over a median 11.3-year period of follow-up and ICH-

		provided - genomic methods to determine ancestry are preferred, (e.g. principal component analysis).	For founder populations, include reference to the broader genetic background. In admixed populations, explicitly state the ancestral backgrounds that contribute to the admixture.		free controls." It is reported that 84.1% and 83.9 of ICH cases and controls were white, respectively.
	Participant Demographics – Age	Include the age distribution of the total data set used to generate a single PRS (whether a single sample set, or the summary of combined samples) using the mean, standard deviation and range. Provide the age distribution by case/control status, if applicable.	If intended use is targeted for a specific age range, provide additional statistics focused on that age range and representation in sample.	Development	Was MR met?: No Was HR provided?: N/A Details: - **Methods**, **Study design and participating studies** subsection: "[…] (GOCHA) study, a prospectively collected case-control study of European ancestry subjects aged > 55 years with primary ICH"
				Validation	Was MR met?: Yes Was HR provided?: N/A Details: - **Supplementary Tables: "Table S26.** Clinical characteristics of the GERFHS validation dataset for ICH cases and ICH-free controls." and **"Table S36.** Baseline characteristics of the external UK Biobank dataset for individuals who developed incident ICH over a median 11.3-year period of follow-up and ICH-free controls."
	Participant Demographics - Sex	Include the sex distribution of the total data set used to generate a single PRS (whether a single sample set, or the summary of combined samples) using the counts and percentages of total sample. State if sex was inferred from self-report or genetic information. Provide the sex distribution by case/control status, if applicable.	If study explicitly refers to gender instead of sex, details should be provided to differentiate the definitions and relevance to study goals. Address limitations of self-report, which more accurately reflects gender identity than biological sex assigned/defined at birth.	Development	Was MR met?: No Was HR provided?: N/A
				Validation	Was MR met?: Yes Was HR provided?: N/A Details: - **Supplementary Tables: "Table S26.** Clinical characteristics of the GERFHS validation dataset for ICH cases and ICH-free controls." and **"Table S36.** Baseline characteristics of the external UK Biobank dataset for individuals who developed incident ICH over a median 11.3-year period of follow-up and ICH-free controls."

	Genetic Data	Provide method for acquiring genetic information (sequencing vs. genotyping) in the PRS sample, including information about genome build and technical details of the assay. If imputing, specify the populations on the imputation panel, and provide the imputation quality for SNPs included in PRS. Report any imputation quality filters to exclude low quality imputation SNPs. If parameters were selected from another study, include reference (PMID, GWAS catalog ID).	Explicitly mention if imputed. State whether imputed SNPs were experimentally validated. If data acquisition differed across combined samples, explicitly state this.	Development	Was MR met?: Yes Was HR provided?: Yes Details: - **Methods**, **Study design and participating studies** subsection: "As our primary data source, we used genotype and phenotype data from 1,861 ICH cases and 1,722 ICH-free controls from three independent GWAS datasets: […]" - **Supplementary Methods**, **Imputation of main GWAS datasets** subsection provides details on SNP imputation and filtering criteria for both training and validation datasets - For the trait-specific genomic risk scores: **Methods**, **Trait-specific GRS and ICH metaGRS construction:** "We leveraged publicly available GWAS summary-level data from international consortia, as detailed in **Table S1.** For all traits, we used data from European-only populations and excluded duplicate and ambiguous AT/GC SNPs and SNPs with MAF≤1%." - For the trait-specific genomic risk scores, GWAS details, including references are included in Table S1.
				Validation	Was MR met?: Yes Was HR provided?: Yes Details: - **Methods**, **Study design and participating studies** subsection: "As our primary data source, we used genotype and phenotype data from 1,861 ICH cases and 1,722 ICH-free controls from three independent GWAS datasets: […]" - **Supplementary Methods**, **Imputation of main GWAS datasets** subsection provides details on SNP imputation and filtering criteria for both training and validation datasets.
	Non-Genetic Variables	Define any non-genetic variables that were included in the risk model, provide inclusion and exclusion criteria to define each variable, along with data source for that information (e.g., ICD codes, e-phenotyping	Include justification for predictor variables used to fit the risk model.	Development	Was MR met?: No Was HR provided?: No Details - **Supplementary Methods**, **Ascertainment of cases and controls** subsection: "We included only primary ICH cases, after applying previously described methods of enrollment and inclusion/exclusion criteria." - Some details regarding inclusion and exclusion criteria for cases and controls in the development datasets are described in **Supplemental Methods, Participating Studies** subsection.

		algorithms, chart review, self-report). Indicate the scale of each variable, e.g. dichotomous, continuous, categorical, or ordinal. Explicitly state which variables are included in the final model in the integrated risk model fitting sections.			
				Validation	Was MR met?: Yes/Incomplete Was HR provided?: Yes Details: - **Supplemental Methods**, **ICH metaGRS performance and clinical evaluation in GERFHS** and **External validation of the metaGRS in UKBB** subsections detail non-genetic variables included in the risk models, methods for deriving them, and justifications for including them in risk prediction models. - **Table S28** also describes the significant clinical predictors of ICH in the validation dataset after backward elimination - **Supplemental Methods, Participating Studies** subsection describes inclusion and exclusion criteria for the GERFHS validation dataset.
	Outcome of Interest	Define the predicted outcome of interest of the risk model, as stated in the introduction, and report distribution. If the predicted outcome is a clinical feature or endpoint within a specific disease, provide the criteria used to define that disease membership. Include details on how information was ascertained (e.g., ICD codes, e-phenotyping algorithms, chart review, self-report). Transformation of continuous data into binary, ordinal, or categorical outcomes should be detailed with justification. For integrated risk models, state whether	In a validation study, if the predicted outcome differs from the phenotype of interest in score development, justify this decision.	Development	Was MR met?: Yes Was HR provided?: N/A Details: - Details regarding ICH status adjudication in the development datasets are described in **Supplemental Methods**, **Participating Studies** and **Ascertainment of cases and controls** subsections.
				Validation	Was MR met?: Yes Was HR provided?: N/A Details: - Details regarding ICH status adjudication in the validation datasets are described in **Supplemental Methods**, **Participating Studies, Ascertainment of cases and controls**, and **External validation of the metaGRS in UKBB** subsections.

		the predicted phenotype of the polygenic score is the same or different than the predicted outcome of the risk model. Provide justification for differences, if applicable.			
	Missing Data	Authors should explicitly state how missing data were handled for all variables included in the model, genetic and non-genetic.		Development	Was MR met?: Yes Details: - **Supplemental Methods**, **Ascertainment of cases and controls** subsection: "For the purposes of the current study, we excluded patients with missing data on ICH status, age, sex and principal components (PCs) reflecting ancestry." - Details on imputation of genotype data are described in **Supplemental Methods**, **Imputation of main GWAS datasets** subsection
				Validation	Was MR met?: Partially Details: - **Supplemental Methods**, **Ascertainment of cases and controls** subsection: "For the purposes of the current study, we excluded patients with missing data on ICH status, age, sex and principal components (PCs) reflecting ancestry." - Details on imputation of genotype data are described in **Supplemental Methods**, **Imputation of main GWAS datasets** subsection
Risk Score Development & Application *Describe the relevant methods used to form the final PRS and/or risk model.*	**Polygenic Risk Score Construction & Estimation**	Describe how genetic data were included in the risk model. Authors should detail inclusion/exclusion criteria for all variants. If individual risk variants are combined into a PRS that is subsequently included	Statistical procedures for selecting variants (e.g. from a GWAS) for inclusion in the final PRS should be provided. State if model was adjusted for covariates. If the PRS was made using GWAS Summary Statistics: provide a reference for		Was MR met?: Yes Was HR provided?: Yes Details - **Supplemental Methods, Trait-specific genomic risk scores (GRS) construction** and **Construction of the main ICH meta-Genomic Risk Score (metaGRS)** subsections detail information required by the minimal reporting standards.

Samples used in this stage of the analysis should be referred to as "Score Development" or "Training" samples, and be described according to the items in the Study Populations section. *Specify if the application of the risk score differs between the development and validation samples.*		in the model as a single variable, define how the variants were selected, weighted and combined into a single score. If the PRS was derived from another study include the reference (PMID, PGS Catalog Score ID).	discovery GWAS and whether any adjustments were performed in the GWAS. If an alternative to GWAS significant SNPs (e.g. p-value thresholds) were used, for instance Bayesian re-weighting of variant effects, explicitly state this and describe/cite the computational method and relevant samples and/or parameters used. Common methods include: LDpred, LD-Pruning and p-value Thresholding (P+T), lassosum, meta-scoring approaches, etc. If the PRS was constructed using variants and weights derived from individual-level genetic data: make sure that the training samples and variant selections are clearly described along with the computational methods and parameters used. Common methods include: snpnet, BLUP-based methods, regularized regression (e.g. LASSO/ridge), stepwise regression. Provide unique identifiers including strand information and which is the affected allele and what are the alternate alleles; allele frequency.		- **Supplemental Material**, **Tables S1-S23** detail information on how genetic data were included and contains references from relevant trait-specific GWAS studies. - Also, **Supplemental Methods, Sensitivity analyses with alternative metaGRS** subsection details information about how specific alternate metaGRS were constructed.
	Risk Model Type	Detail statistical methods used to estimate risk, either relative or absolute, from the continuous	Justify clinical relevance of risk period.		Was MR met?: Yes Was HR provided?: Partially Details

		risk score distribution. Authors should detail if risk is cumulative or cross-sectional, as well as the appropriate comparison groups if relative risk presented. Report time until predicted risk (e.g. 5-year, 10-year, lifetime). In a relative hazard model, the study period or follow up time may be used. In an absolute risk model, state the time until predicted event and the prevalence/incidence of the predicted outcome in the general population.	If applicable, justify why the model type differs between training and validation sets.		- **Supplemental Methods**, **ICH metaGRS performance and clinical evaluation in GERFHS** subsection contains information required by the minimal reporting standards. - **Supplemental Methods**, **External validation of the metaGRS in UKBB subsection** contains details on models in UKBB where a different model for risk estimation was utilized (Cox proportional hazards model).
	Integrated Risk Model(s) Description and Fitting	State the fitting procedure utilized to select the final version of the model (including non-genetic and/or genetic [PRS or variants] variables). If model was selected for optimal performance, describe measures used to assess performance. Explicitly state all terms used in the final risk model, including PRS/variants and any non-genetic variables.	When evaluating models for the optimal PRS, provide metrics (calibration, discrimination, etc) of the individual models compared. This can be included in the supplement. Describe if/how ethnicity or ancestry are accounted for in the model (common methods involve the inclusion of genetic principal components). When applicable, methods appropriate to admixed ancestry exemplified by the African American and Hispanic populations should be used and described in enough detail to reproduce.		Was MR met?: Yes Was HR provided?: Yes Details - MR and HR information is described in **Supplemental Methods**, **ICH metaGRS performance and clinical evaluation in GERFHS** and **External validation of the metaGRS in UKBB** subsections

Risk Score Evaluation Outline the results and procedures utilized to validate the risk score, specifying whether the validation was performed on internal or with an external validation samples. Performance results should be described for both the development and validation samples.	**PRS Distribution**	Include a general description of the distribution of the risk score, as well as model fit measures. This details the continuous distribution output directly from the risk model.		Development	N/A
				Validation	Was MR met?: Yes Details: - **Figure 2. Odds for intracerebral hemorrhage (ICH) across the metaGRS distribution.** - **Supplemental Material**, **Figures S5, S6**
	Risk Score Predictive Ability	Describe and report metrics of overall performance (proportion of variance explained; R2) and estimates of risk (such as odds or hazards ratios from regression models) used to evaluate the PRS and/or risk models. Describe the set of genetic/non-genetic variables included in the analysis.	Authors should state explicitly the summary statistics their algorithm produces (for instance Hazard Ratio (HR), Odds Ratio (OR), and/or Beta). When stating this, authors should state any reference levels used (for instance: bottom third polygenic risk vs top third polygenic risk). See So & Sham, 2010 for details.	Development	Was MR met?: Yes Was HR provided?: No Details - **Supplemental Material, Figure S1B** depicts association estimates between trait-specific GRS and ICH in training datasets
				Validation	Was MR met?: Yes Was HR provided?: Yes Details: - **Results**, **Associations between the metaGRS and ICH in the validation dataset** subsection contains information required by the MR and HR standards. - Effect size estimates and confidence intervals for ICH risk in higher thresholds of the metaGRS distribution are presented in **Figure 2**.
	Risk Score Discrimination	Describe and report metrics (such as ROC or Precision-Recall (AUROC/AUPRC) and the Concordance statistic (C-index) for survival models) used to assess the discrimination of evaluated risk models and whether any non-genetic variables were included beyond a PRS in this analysis.	Provide this information as a visual or graphical display for cases and controls separately, showing overlap in distributions.	Development	N/A
				Validation	Was MR met?: Yes Was HR provided?: Partially Details - **Results**, **Predictive performance of metaGRS for ICH in comparison with clinical risk factors** and **Validation of the metaGRS in the UKBB population** subsections contain information required by the MR standards. - **Figure 3** provides a graphical display of the MR standards, as well as **Figure S8** for the different versions of the metaGRS.

		Evaluation of potential clinical utility of models requires evaluating tail-based measures, such as proportions of populations and cases exceeding specified clinically relevant risk thresholds and measures of reclassfications (e.g. NRI) at such thresholds for comparison of models.			
	Risk Score Calibration	Describe and report metrics used to assess the calibration of the risk score and whether any variables were included beyond the risk score in this analysis.	Please state metrics used to test calibration of the constructed prediction model. This cannot be done for case-control validation cohorts.	Development	N/A – Not evaluated
				Validation	N/A – Not evaluated
	Subgroup Analyses	Subgroup size, demographics and clinical characteristics should be given. Relevant evaluation methods and measures (distribution, predictive ability, discrimination, calibration) should be described for each subgroup analysis.		Development	N/A
				Validation	Was MR met?: Yes Details: - **Results**, **Predictive performance of metaGRS for ICH in comparison with clinical risk factors** subsection contains information on analysis on the GERFHS validation dataset by ICH location (lobar and non-lobar) and with adjustment for *APOE* status. - **Tables S30-S35** provide details of above analyses. **- Results, Validation of the metaGRS in the UKBB population** subsection contains information on analysis in the UK Biobank validation dataset regarding high- versus low-risk individuals.
Translation Discussing the broader context of the study and risk score	**Risk Model Interpretation**	Summarize the risk score in terms of what it predicts, how well, and in whom. The predicted outcome	**Comparisons to Conventional Risk Models** Give AUC and/or relevant performance metrics for all models tested, and provide		Was MR met?: Yes Was HR provided?: No Details:

		predicted should be consistent with the introduction. **Comparisons to Conventional Risk Models** Explicitly mention the performance of the PRS and/or combined risk model in comparison to conventional risk models. Conventional risk models might include demographic (age, sex), disease-specific risk factors, and/or family history of disease.	changes in metrics relative to the risk model being compared to. Common comparisons: - Does the PRS/risk model outperform family history of disease? - Does the PRS/risk model improve currently utilized risk prediction tools? What are the implications of these improvements (e.g. reclassification metrics, proportion of the risk or phenotypic variance explained) - Comparing to existing high-impact mutations		- **Discussion**: "We found the derived metaGRS to be significantly associated with the odds of ICH in an independent validation dataset of 842 ICH cases and 796 ICH-free controls. The metaGRS was independent of traditional clinical risk factors of ICH and improved model performance in prediction of ICH. Furthermore, the score was significantly associated with incident ICH risk in a population-based cohort study of 480,000 individuals followed-up for a median of 11 years (1,500 incident ICH events)." - **Discussion**: "Second, the metaGRS improved risk discrimination for ICH when compared to classical clinical predictors. Specifically, it was associated with ICH risk independently of vascular risk factors and was found to have a predictive value superior to all predictors except for education."
	Limitations	Outline limitations in interpreting results, discuss the impact of these limitations on the interpretation of the risk score and any downstream replication needed. Common considerations include: study design restrictions, ascertainment biases, the distribution participant-level traits (ancestry, age, comorbidities), accuracy/specificity of phenotype data, and any statistical considerations. Make note of and discuss the impact of any unknown reporting	Explicitly state any overlap in samples between GWAS, testing, and validation datasets. Ideally there should be none. For combined samples, discuss variability between and across combined samples in terms of study and participant-level traits. Explain how this affects the confidence in prediction, how it influenced the methods utilized in the study, and any other caveats this creates relevant to interpretation. If data acquisition differs across combined samples, explicitly state this. Expanding on weaknesses in study design: include biases in sample ascertainment due		Was MR met?: Yes Was HR provided?: Partially Details: - **Discussion:** "Second, ICH is a phenotypically heterogeneous disease, with the most common etiologies being hypertensive small vessel disease (typically in non-lobar locations) and cerebral amyloid angiopathy (typically in lobar locations). To maximize the power of our approach, we have pooled cases, which could have negatively impacted the predictive performance for specific ICH etiologies. While our score was predictive for both non-lobar and lobar ICHs, developing etiology-specific scores might be of more relevance for specific clinical scenarios." - For HR: **Discussion**: "Third, while the metaGRS showed significant associations with risk of incident ICH in the UKBB, we could not explore its effects in concert with other clinical predictors, because the metaGRS was generated using associations with these predictors in datasets including data from the UKBB. Therefore, independent validation either of a score trained in an entirely UKBB-independent dataset or of the described metaGRS in another external cohort would be necessary."

		items from previous sections.	to recruiting method (e.g., convenience sampling.) and recruitment setting (clinic vs. research vs. healthy populations), especially if these methods impact disease prevalence metrics or the possibility of secondary outcomes. Discuss whether any biases influence the target audience for using the PRS. If the risk period is not known, this limitation should be explicitly stated and why.		
	Generalizability	Discuss which populations this score may be applied to and explicitly address any issues with generalizability beyond the included populations. Discuss whether the risk score has been externally validated, or if the sample is limited with respect to ancestry, age, or other variables.	Discuss what population this might be able to be applied to and explicitly address any issues to generalizability beyond that. It should be explicitly stated if ancestry is not known or able to be disclosed. Discuss whether the score replicates previous findings or has been externally validated. Authors should address any limitations in generalizability of their results.		Was MR met?: Yes Was HR provided?: Yes Details - **Discussion**: "While it remains to be clarified how these individuals would benefit from potential primary preventive interventions, this information could be useful both for screening for hypertension, the main clinical risk factor for ICH, and early initiation of antihypertensive treatment, as well as for decision making when considering initiation of antiplatelet or anticoagulation treatments that might increase ICH risk. These risk stratification strategies based on genomic information are increasingly important as millions of persons in the US and around the world have been genotyped by direct-to-consumer genotyping companies." - **Discussion**: "The metaGRS was associated with a higher risk of ICH even among individuals with evidence-based control of relevant risk factors, who were not actively smoking, had blood pressure of 140/90 mmHg or less, no evidence of diabetes, normal BMI, and who reported no use of anticoagulants. While such analyses are restricted by lack of power, our results suggest that for specific individuals with a high genetic risk, the recommended treatment targets for modifiable risk factors might not be sufficient for primary ICH prevention. The importance of this observation lies on the fact that the genomic information is available long before vascular risk factors are present and could thus be used for earlier risk stratification in otherwise low-risk individuals. Concomitantly, the metaGRS was also associated with a higher risk of ICH even among a high-risk group of individuals using antithrombotic medications, indicating its potential utility among a relevant group of patients for

					whom bedside calculation of ICH risk might be particularly relevant to clinical care." - **Discussion**: "Fourth, the metaGRS was constructed solely on the basis of data from individuals of European genetic ancestry, and may thus not be applicable for individuals of other ancestries. Larger multi-ethnic GWAS studies of ICH currently underway will facilitate the generation of ancestry-specific GWAS datasets."
	Risk Model Intended Uses	Discuss whether there is an intended clinical use or utility to the risk model. If so, discuss the "clinic readiness" and next steps with respect to the interpretation, limitations, and generalizability of the model. Discuss how the predictive ability of the model is benchmarked against current standard of care or other published work (such as existing PRS) on predicting the outcome of interest.	Only discuss actionability if the study was set up such that the relevant clinical population is the target audience of the PRS study design. Discuss the incremental value of the PRS on top of an established risk model for the disease assessed (e.g., Gail Model, 10-year CHD risk ACC/AHA pooled cohort equations). To what extent did the PRS lead to meaningful (e.g., meeting treatment thresholds) risk reclassification?		Was MR met?: Yes Was HR provided?: No Details: - **Discussion**: "A post-hoc analysis of trial data showed that among patients with atrial fibrillation and a CHA2-DS2-VASc score of 2, a high genomic risk score for ischemic stroke led to an absolute ischemic stroke risk equivalent to those with a higher score. Whether integration of a genomic risk score for ICH in such analyses could lead to a more precise assessment of the risk-benefit ratio for specific patients remains to be determined. Along these lines, the several clinical trials currently evaluating anticoagulation as a secondary prevention strategy after ICH constitute a unique opportunity for genomic-based risk-stratification, as a portion of them have built-in biobanks that are collecting DNA samples."
Data Transparency and Availability		Information sufficient to calculate the PRS and/or risk model on external samples should be made available. For genetic variables this would include information about the variants (e.g., rsID, chromosomal location, effect allele, and the effect weight) that comprise the score; PRS with this information can be published in the PGS	PRS intended for downstream clinical use should strive to meet stringent validation requirements outlined in PMID: 29154853, most notable including the evaluation of sensitivity, specificity and positive predictive value, to more easily facilitate clinical translation. Authors should provide sufficient data for external groups to validate findings, including reference scores calculated on control samples, ideally ones that are publicly available. Authors		Was MR met?: Yes Was HR provided?: No Deails: - **Table S23** contains the tuning parameters for the construction of the trait-specific GRS. - **Table S25** contains the weights of the different trait-specific GRS included in the metaGRS versions. - **Methods**, **Data availability statement subsection: "**MetaGRS single nucleotide polymorphism (SNP)-specific weights will be made publicly available at The Polygenic Score (PGS) Catalog."

		Catalog for findability and to promote re-use and comparison with other established scores. Weights for non-genetic variables should also be provided to make the risk model calculable in the same way.	should provide information on how to access this data.		

Abbreviated version of PRS-Reporting Standards for the manuscript "A Genomic Risk Score Identifies Individuals at High Risk for Intracerebral Hemorrhage"

Reporting standard		Page Number(s) or Sections
Background	**Study type**	7
	Risk model purpose and predicted outcome	6,7
Study population and data	**Study design and recruitment**	7,8; Suppl Mat 4-7,12; Table S1
	Participant demographics and clinical characteristics	Tables S26,S36
	Ancestry	Tables S26,S36
	Genetic data	7,8; Suppl Mat 6,7; Table S1
	Non-genetic variables	Suppl Mat 10-12; Table S28
	Outcome of interest	Suppl Mat 4-7,11,12
	Missing data	Suppl Mat 6,7
Risk model development and application	**PRS construction and estimation**	8,9; Suppl Mat 7-9, 11,12; Fig S1-S4; Tables S1-S25
	Risk model type	9; Suppl Mat 10-12
	Integrated risk model(s) description and fitting	9; Suppl Mat 7,8,10-12
Risk model evaluation	**PRS distribution**	Figure 2; Fig S5,S6
	Risk model predictive ability	10-12; Fig S5-S7; Tables S27,S28
	Risk model discrimination	10,11; Figure 3; Fig S7,S8; Tables S28,S29
	Risk model calibration	-
	Subgroup analyses	11,12; Figure 4; Tables S30-S35
Limitations and clinical implications	**Risk model interpretation**	12-14
	Limitations	15-17
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Data transparency and availability		7; Tables S1,S23,S25