Original Research:

General research

A maximum of 12000 words in the whole document including 50 references. In animal studies, describe animal experiments in detail according to the full ARRIVE guidelines and submit a completed version of the ARRIVE author checklist with your manuscript. Indicate the species and, where appropriate, the strain of the animal; the total number of animals used throughout the study; the number of animals per experimental group; the experimental design including statistical design and analysis; randomization and blinding methods; other pertinent details relating to the lifetime experience of the animals, including housing and care; refinements of experimental procedures to reduce suffering; pain management; humane endpoints; and euthanasia methods.

- Do not list animals as materials.

- Indicate which institutional and national guidelines for the care and use of laboratory animals were followed.

- Confirm that the study went through a process of ethical review prior to the study commencing, indicate which ethics committee approved the study and provide the associated permit number(s).

- If ethical approval was not required, include a statement of this and the reason.

- Confirm that the potential for application of the 3Rs was rigorously researched prior to starting, and every opportunity was taken during the course of the study to implement each of them.

- Confirm that animal husbandry and care was in accordance with contemporary best practice and all individuals involved with the care and use of animals were trained and skilled to an acceptable level of competency, with euthanasia carried out according to contemporary best practice.

JARO recommends following the PREPARE guidelines (<u>https://norecopa.no/PREPARE</u>) in planning studies using animals to ensure that the above requirements are met, and the respective information is documented during the study. JARO further recommends the use of the Experimental Design Assistant (https://www.nc3rs.org.uk/experimental-design-assistant-eda) for the design of experiments using animals to ensure that they use the minimum number of animals consistent with their scientific objectives, methods to reduce subjective bias and appropriate statistical analysis.

Randomized Controlled Trials

A maximum of 12000 words in the whole document including 50 references. In accordance with guidelines issued by the <u>ICMJE</u>, *JARO* requires registration of clinical trials in a public trials registry at or before the time of first patient enrolment. A clinical trial is defined as any research project that prospectively assigns people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome. Health-related interventions are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioral treatments, dietary interventions, quality improvement interventions and process-of-care changes. Health outcomes are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events.

Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

The ICMJE accepts registration in any registry that is a primary register of the <u>WHO International</u> <u>Clinical Trials Registry Platform</u> or in <u>ClinicalTrials.gov</u>. The trial registry number should be included at the end of the Abstract.

Reports of randomized controlled trials should include the checklist items set out in the <u>CONSORT</u> <u>guidelines</u>, as well as a <u>patient flow diagram</u>. See the <u>CONSORT website</u> for further details. Authors must submit a completed <u>CONSORT 2010 checklist</u>, along with the original trial protocol (including statistical analyses to be undertaken). For reports of non-pharmacological treatment interventions, please use the appropriate <u>extension of the CONSORT statement</u>.

For secondary analyses of randomized controlled trials or observational studies, please complete either a <u>CONSORT</u> or a <u>STROBE</u> checklist, as appropriate. Reference can be made in the checklist and the current paper to previous publications that describe the study in more detail. Any sections of the checklist that do not apply to the current study can be marked 'not applicable' (NA). Please note that a STROBE checklist might be more suitable where a cohort from a previous randomized controlled trial is used to answer a different research question.

Genetic Association Studies

A maximum of 12000 words in the whole document including 100 references. There is a widely accepted need to improve the robustness of published genetic association findings. We also need to provide the readership of the journal with information that allows a more complete assessment of the biological significance of the findings reported in these kinds of manuscripts. Submissions to *JARO* should, therefore, pay careful attention to the following fundamental issues of study design. It is not intended that these represent absolute criteria for publication in *JARO* (we do not want to block otherwise interesting studies that fail to meet one or another of these). However, these guidelines set out the main factors that we expect our reviewers and Associate Editors to use in evaluating the quality of the manuscripts we receive. Submissions to *JARO* should, therefore, pay careful attention to the following: size, multiple testing, functional data, whole gene studies, replication, phenotypes and other technical requirements.

Size Studies should include sufficient samples to have power to detect effect sizes that are reasonable given current understanding of the genetic architecture of complex traits. Power calculations should be included that make explicit the effect sizes that the study was powered to detect; such power calculations should guide the interpretation of the data. Wherever possible, all available samples should be typed: results based on only a portion of a larger sample are of limited interest.

Multiple testing Genetic association studies often involve testing of a large number of hypotheses (e.g., multiple single nucleotide polymorphisms [SNPs] or haplotypes; multiple phenotypes; multiple analytical models; testing of multiple strata such as male/female, lean/obese). Manuscripts should feature explicit discussion of the consequences of multiple hypothesis testing for the interpretation of the findings. Assessments of the significance of the findings should be related to the study-wide (or genome-wide) significance.

Functional data Functional data (e.g., demonstration that a SNP alters expression) can strengthen association findings, but the functional assays must have demonstrable relevance to the phenotype showing the association. Good functional data do not compensate for a poor association study.

Whole gene studies Single SNP studies are acceptable where the SNPs typed have strong prior claims for involvement in the trait of interest. However, where feasible, studies should attempt to examine genome sequence variation across a gene.

Replication Replication is highly desirable for all association studies, particularly for studies where extensive multiple testing means that study-wide significance is not clear. However, replication should only be claimed when it addresses the same variant, phenotype and genetic model (all too often other phenotypes or variants within a gene are offered as evidence of replication).

Phenotypes Authors should explicitly justify why the samples typed are well-suited to address the particular hypothesis posed. Care needs to be taken in the definition of cases using standardized criteria, and in the selection of appropriate control samples.

Positive/negative studies Well-performed association studies that represent "significant negative" findings are welcome provided the gene examined has clear relevance to disease pathogenesis (or has been implicated on the basis of prior association data).

Technical requirements The information provided by a manuscript can be improved if certain technical requirements are observed. Where relevant, we ask that authors:

- Provide rs numbers for all variants reported (these are quite easy to obtain for novel variants). Where these are provided, details of the assay (primer sequences, PCR conditions) can be kept brief;
- Provide explicit details of the measures taken to ensure genotyping accuracy (including, for example, % successful genotype calls, number of duplicated genotypes, % correspondence);
- Provide approved HUGO gene names in the appropriate case and italics;
- Use standard terminology for variants (see http://www.hgvs.org/mutnomen/);
- Describe LD relationships between typed variants;
- Provide information on departures from Hardy–Weinberg equilibrium (HWE), not only as a check for possible genotyping errors, but also because methods assuming HWE may be employed in the downstream association analyses (e.g., haplotype inference using the EM algorithm/single-point analyses testing the multiplicative model);
- Provide raw genotype frequencies (i.e., allele frequencies alone are not sufficient);
- Provide the criteria they have used to select tagSNPs. Authors should also carry out association analyses consistent with the tagging method employed, e.g., if an aggressive multimaker tagging approach has been followed, appropriate analyses are required to retrieve all the information captured;
- Denote the boundaries they have considered when studying a gene of interest (e.g., 5 kb upstream of transcription initiation, etc.) and indicate which portions of the gene have been examined (e.g. exons and exon / intron boundaries).

Database Studies

A maximum of 12000 words in the whole document including 100 references. For studies that involve the use of patient data from databases, or routinely collected health data, authors should complete either a <u>STROBE checklist</u> or a <u>RECORD checklist</u>. Where data are collected for a more-or-less specific research purpose, STROBE is the most appropriate, whereas RECORD is more suitable for routinely collected data.

Meta-analyses

A maximum of 12000 words in the whole document including 100 references. We recommend that authors register their study in a publicly accessible database and submit the study protocol as supplementary material. There is no need to contact the Editor-in-Chief before submitting a meta-analysis; please upload at https://www.editorialmanager.com/jaro/ in the usual way.

For meta-analyses of randomized controlled trials, follow the <u>PRISMA reporting guidelines</u> — include a <u>flow diagram</u> in your manuscript and submit a completed <u>PRISMA checklist</u>. For metaanalyses of observational studies in epidemiology, follow the <u>MOOSE reporting guidelines</u> and submit a completed <u>MOOSE checklist</u>.

Systematic Reviews

A maximum of 12000 words in the whole document including 100 references. Authors must register their study in a publicly accessible database (e.g., PROSPERO, Open Science Framework, Research Registry), and include the registration number in the manuscript. *JARO* will refuse to consider systematic reviews that have been registered after data extraction has begun. The study protocol should be submitted as supplementary material, or its reference included in the methods. There is no need to contact the Editor-in-Chief before submitting a systematic review; please upload the manuscript in the usual way, along with a <u>PRISMA</u> or <u>MOOSE checklist</u>