frontiers

Research ethics checks

Guidelines for editors and reviewers

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1 Introduction

For studies involving human or animal participants, it is of utmost importance that the studies have been **conducted ethically and with appropriate documentation in place**. This guide has been created with the intention of assisting editors/reviewers in determining that the studies they are evaluating conform to these requirements.

1.1 Ethics checks at Frontiers

How are study ethics checked at Frontiers?.

- The research integrity (RI) team checks the submissions that are flagged to them by AIRA for various reasons before they proceed to review.
- We rely on the editors and reviewers to check that manuscripts include the appropriate ethics and consent statements. Additionally, RI rely on the expertise of editors and reviewers for more complex ethics issues.
- When the reviewers' reports have been finalized, editors are required to run a final check to ensure that the appropriate statements are included.

1.2 Frontiers are a member of COPE

As a member of the Committee on Publication Ethics (COPE), **Frontiers reserves the right to reject any manuscript that does not uphold the highest ethical standards**.

2 Your assessment

During your initial assessment of the manuscript, please consider whether or not the research adheres to ethical standards and research quality in the field.

2.1 Studies that require ethics approval and/or written informed consent for participation/publication

The most fundamental requirement for a study involving human and/or animal participants or material is the **presence of statements** reporting :

a. The presence of ethics approval from an appropriate ethics committee, institutional review board, institutional animal care and use committee or other relevant body. Ethics approval should have been obtained *before* the study commenced.

b. The collection of written informed consent from participants, or from a parent/guardian if the participant is below the local age of consent. Written informed consent is required for the following:

- Participation in a study
  If a patient is enrolled in a study, or samples are collected from them for intended use in research, informed consent needs to be collected before the study commenced or procedure performed;

- Publication of identifiable information
  For the publication of a case report, or other identifiable information or images, consent for publication needs to be obtained from the subject (this consent can be collected at any time before publication of the manuscript).

2.2 Studies that may not require ethics approval and/or written informed consent for participation/publication

There are certain types of study involving humans or animals that may not require ethics approval; if this is the case, the authors should include a statement specifying this, along with justification of why ethics approval / written informed consent was not obtained or why the ethics committee waived the requirement for approval / written informed consent.

2.2.1 Country or region specific requirements

There are also certain country or region specific requirements that may apply; several prominent animal research ethics frameworks are linked in section 4.4, while the US Department of Human and Health Services hosts an International Compilation of Human Research Standards.

2.2.2 Examples of studies exempt from ethics approval

Some studies may not require ethics approval.

a. Retrospective studies involving the analysis of previously collected data, such as information in a hospital database, typically do not require ethics approval (studies involving retrospective analysis of tissues, such as in a hospital tissue bank, may still require approval). It is advised for authors to check with their institutional ethics body to confirm that their study is exempt from ethics approval before commencing the study.

b. Studies using information in the public domain, such as public databases or datasets shared in a publicly accessible online repository, typically do not require ethics approval, although ideally the authors of the original study in which such datasets were generated should have obtained ethics approval.

c. Clinical audits and service evaluations are typically not considered to constitute research, and therefore may not require ethics approval; however, the legislation of the country/region in which the audit/evaluation was conducted should have been followed, and informed consent may be required.

d. Case reports typically only require ethics approval if the case study involves some form of intervention that deviates from standard practice; however, consent for publication is still required.

e. Studies that involve the use of animal tissues obtained post mortem from animals sacrificed for non-scientific purposes (such as obtaining bovine bone tissue from a slaughterhouse) do not require ethics approval.

2.3 Concerns about ethics or consent statements

If there is any doubt about whether a statement provided by an author is appropriate, or there is doubt regarding the authenticity of an ethics approval/consent statement, you can request supporting information from authors. However, approval or consent forms should not be routinely requested, and patient confidentiality should be protected in the event that proof of consent is required.

2.4 Studies that do not uphold the highest ethical standards

It is important to acknowledge that even with ethical approval, a study may not be ethical. Decisions to not consider manuscripts reporting practices that are widely considered to be unethical can be taken independent of the presence of an approving ethics committee or previously published studies using the same technique; such procedures include the use of overdose with chloral hydrate, ether, or chloroform as a method of animal euthanasia.

We encourage authors to specify any regional or national guidelines that their study was conducted in accordance with; for human experiments, this is typically the Declaration of Helsinki, while there are various guidelines available for animal studies (please see section 4.4).

IMPORTANT
You are at liberty to request ARRIVE checklists (for animal experiments), CARE checklists (for case reports), or any other documentation you consider necessary to evaluate the above.

2.5 Red flags to look out for

If you notice any of the following, it may be a 'red flag' for you to ask for more information from the authors:

a. **Verbal consent**
Informed consent must always be written. Verbal consent is insufficient and will only be considered in circumstances where the study was not in any way invasive or sensitive and the ethics committee that approved the study deems verbal consent sufficient.

b. **No clear ethics committee name**
The ethics committee that approved the study must be clearly stated. Approved by 'the local ethics committee', for example, is insufficient.

c. **Ethics committee not at any of authors' affiliations**
There may be a valid reason for this, but please ask the authors why that is.

3 Further information: human studies

3.1 Considerations for studies on humans

For ethical standards related to human experiments, please always consider the following:

- Is ethical approval and/or written informed consent needed? If so, does the manuscript contain the appropriate statement, and has any necessary ethics approval been issued by an appropriate committee/organization?
- If the manuscript uses human samples, does the manuscript clearly state where these samples were obtained?
- Does the manuscript mention that experiments were performed according to the Declaration of Helsinki?
- Does the manuscript contain a clear description of the procedures performed on the human subjects?

Please refer to the human studies checklist below to assist you in these checks.

3.2 Human studies checklist

Mandatory checks

- ○ Ethics committee approval and full name of the ethics committee provided
- ○ If ethics committee approval was not required, a statement specifying this, along with justification of why ethics approval was not obtained or why the ethics committee waived the requirement for approval, is provided
- ○ Written informed consent and approval obtained from legal guardians in case of minors
- ○ Case report contains written informed consent for publication (separate from written informed consent for participation)
- ○ There is written informed consent for the publication of human images when identifiable
- ○ Data from questionnaires/surveys are deidentified

Additional checks

- ○ Adherence to Declaration of Helsinki
- ○ Source of cells is clearly stated (if human cells are used and no further information provided)
- ○ Clinical trial registration number is provided for a clinical trial
- ○ Sensitive images in the manuscript: they are necessary to understand the scientific content of the manuscript and have been adjusted to cover the most sensitive areas

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3.3 Guidance table for common ethics issues in human studies

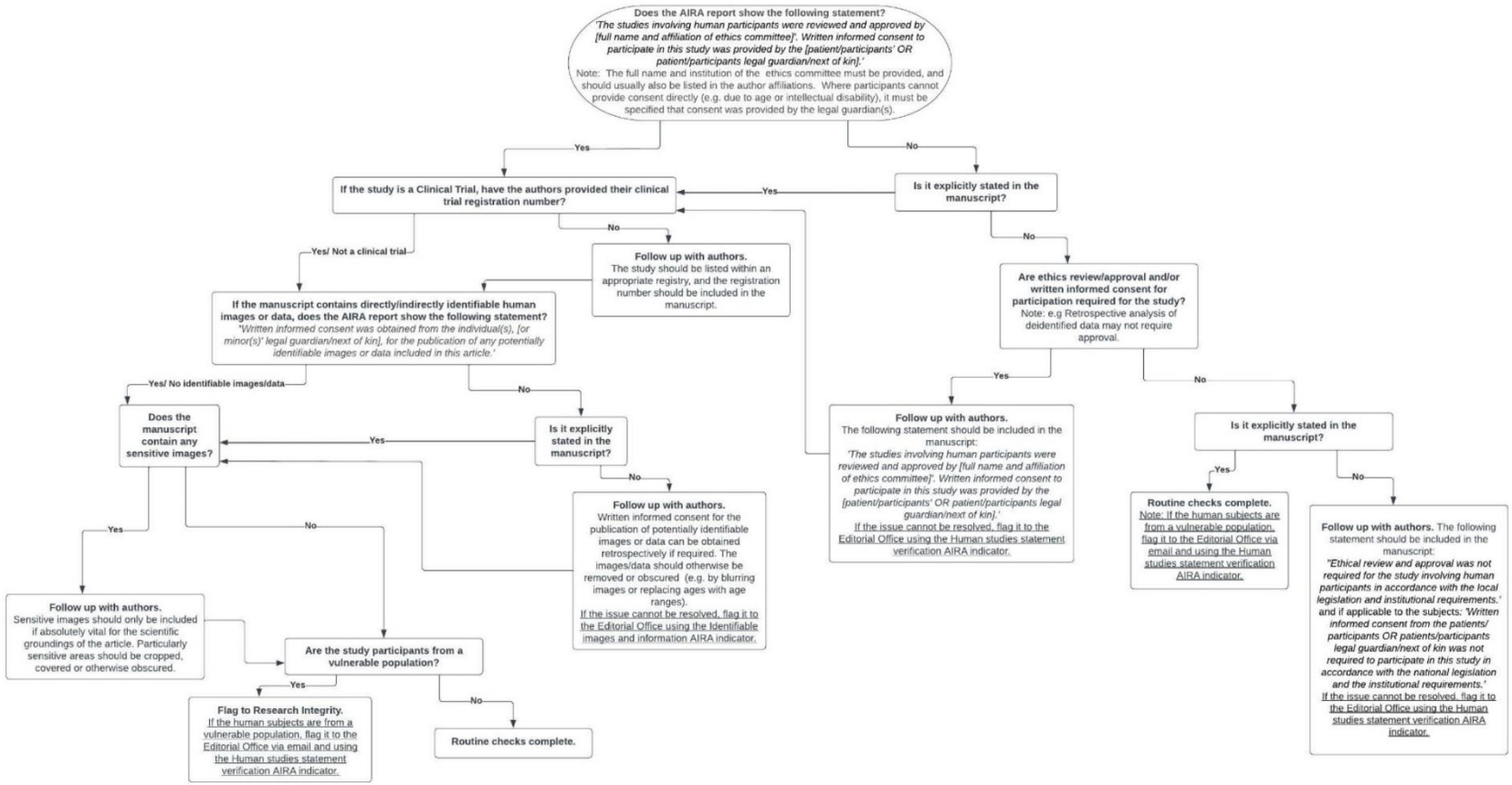
Issue	Action needed
No ethics approval and written informed consent for participation	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following ethics statement in their manuscript: 'The studies involving human participants were reviewed and approved by [full name and affiliation of ethics committee]'. Written informed consent to participate in this study was provided by the [patient/participants' or patient/participants legal guardian/next of kin].' If the authors state that ethics approval or specific consent procedures were not required for this study, request further evidence. If the issue cannot be resolved, flag it to the editorial office using the human studies statement verification AIRA indicator.
No ethics approval	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following ethics statement in their manuscript: 'The studies involving human participants were reviewed and approved by [full name and affiliation of ethics committee]'. If the authors state that ethics approval was not required for this study, request further evidence. If the issue cannot be resolved, flag it to the editorial office using the human studies statement verification AIRA indicator.
No written informed consent for participation	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following statement in their manuscript: 'The patients/participants [legal guardian/next of kin] provided written informed consent to participate in this study'. If the authors state that specific consent procedures were not required for the study, request further evidence. If the issue cannot be resolved, flag it to the editorial office using the human studies statement verification AIRA indicator.
No written informed consent to publish a case report	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following statement in their manuscript: 'Written informed consent was obtained from the [individual(s) AND/OR minor(s)' legal guardian/next of kin] for the publication of any potentially identifiable images or data included in this article'. If written informed consent was not obtained for the publication of this case report, please advise the authors that this can be obtained retrospectively. If the issue cannot be resolved, flag it to the editorial office using the identifiable images and information AIRA indicator.

No written informed consent to publish identifiable image(s)	Please use your 'Editor' tab in the review forum to ask the authors to either: 1) Please complete and include the following statement in their manuscript: 'Written informed consent was obtained from the [individual(s) AND/OR minor(s)' legal guardian/next of kin] for the publication of any potentially identifiable images or data included in this article.' or 2) If the authors did not obtain written informed consent from the participants for the publication of this identifiable image/s, advise them that this can be obtained retrospectively or ask them to remove the image/s or edit to disguise identity. If the issue cannot be resolved, flag it to the editorial office using the identifiable images and information AIRA indicator.
No written informed consent to publish identifiable data	Please use your 'Editor' tab in the review forum to ask the authors to either: 1) Complete and include the following statement in their manuscript: 'Written informed consent was obtained from the [individual(s) AND/OR minor(s)' legal guardian/next of kin] for the publication of any potentially identifiable images or data included in this article'. or 2) If the authors did not obtain written informed consent for the publication of the data, advise them that this can be obtained retrospectively, or that they can amend any possible data into ranges, such as age (for example change 26 years old to 25-30 years). If the issue cannot be resolved, flag it to the editorial office using the identifiable images and information AIRA indicator.
No clinical trial registration number	Please use your 'Editor' tab in the review forum to ask the authors to confirm whether or not their study has been registered with an appropriate registry (https://www.who.int/clinical-trials-registry-platform/). If the study has been registered with an appropriate registry, please ask the authors to include the trial registration number in their manuscript. If the issue cannot be resolved, flag it to the editorial office using the human studies statement verification AIRA indicator.
Vulnerable population studied	Flag this to the editorial office using the human studies statement verification AIRA indicator and send an email to [journalname].editorial.office@frontiersin.org (please see https://www.frontiersin.org/about/contact for the correct email address) to alert them to the study on vulnerable population(s). The RI team will request more documents from the authors.

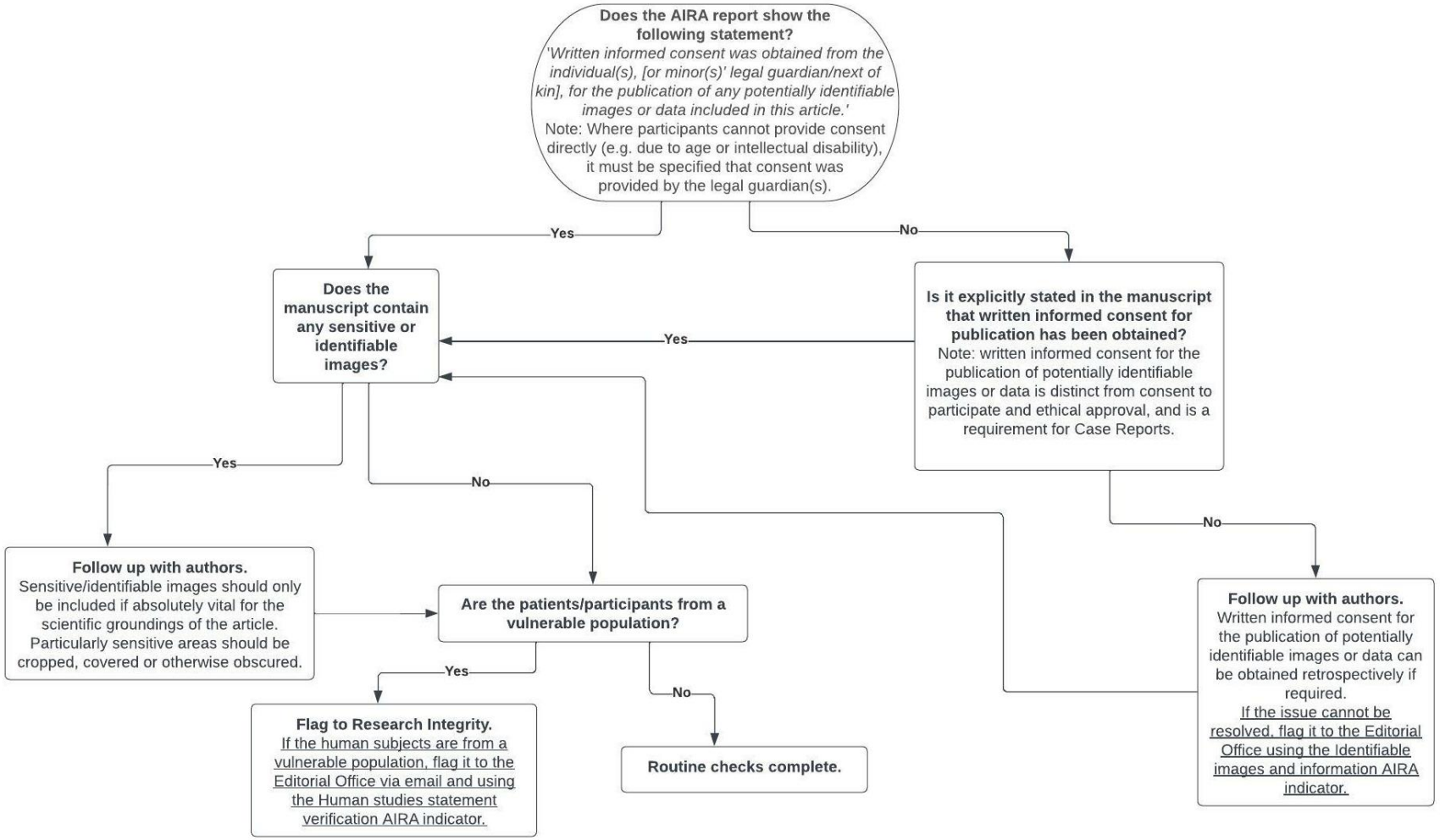
Sensitive images	Please use your 'Editor' tab in the review forum to ask the authors to verify that the inclusion of the image(s) is absolutely necessary for the scientific groundings of the manuscript, and if necessary, to crop or cover areas of a sensitive nature.
Ethics statement is correct in the manuscript file but not the review forum	Please resolve the indicator as 'OK' but use your 'Editor' tab in the review forum to advise the authors to update their ethics statement(s) in the review forum when they resubmit their manuscript. If they do not do this, please still proceed with the manuscript – if the ethics statements in the manuscript are sufficient it should not be held.
Ethics approval not required but no statement	Please use your 'Editor' tab in the review forum to ask the authors to change their ethics statement to: 'Ethical review and approval was not required for the study of human participants in accordance with the local legislation and institutional requirements' and if applicable to the subjects: 'Written informed consent from the patients/participants OR patients/participants legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements'.
Committee name not provided	Please use your 'Editor' tab in the review forum to ask the authors to include the full name of the ethics committee that approved the study, for instance: 'The studies involving human participants were reviewed and approved by [full name and affiliation of ethics committee].'
Source of cell line	Please use your 'Editor' tab in the review forum to ask the authors to include the source of the cell line used in their manuscript: 1) If the cell line was commercially obtained or from a repository such as a biobank, please request that the following statement is completed and included in the manuscript: 'The cell lines present in this study were obtained from [full name of the company or repository].'2) If the cell line was obtained from human participants and the authors obtained ethics approval, please request that the following statement is completed and included in the manuscript: 'The studies involving human participants were reviewed and approved by [full name and affiliation of ethics committee]'.3) If the cell line was obtained from human participants but the authors state that ethics approval was not required for this study, ask the authors to provide further evidence and/or flag to the RI team
Samples isolated from humans	Please use your 'Editor' tab in the review forum to ask the authors to update their manuscript to include more information about the samples used. Samples/isolates may not require ethical approval if they were: 1) gifted from another research group; 2) primarily isolated as part of the authors' previous study for which ethical approval was obtained; 3) a by-product of routine care or industry; or 4) deidentified. In these cases, please request more information. If the issue cannot be resolved, flag it to the editorial office using the human studies statement verification AIRA indicator.

3.4 Flowchart for human studies

3.4.1 Human studies flowchart



3.4.2 Case report flowchart



3.5 Useful information on human studies

3.5.1 Vulnerable populations

A vulnerable population is a subtype of vulnerable group, specifically an ethnic group which requires greater consideration than standard against the potential risks of participating in research (children are a vulnerable group but not a vulnerable population and the Rohingya are both a vulnerable group and a vulnerable population).

When the research integrity team receives a manuscript on/including a vulnerable population, we ask for the following from the authors: how the participants were recruited and the rationale for using that population; a blank version of the consent document participants read and signed; and the study protocol that was approved and approval certificate (all with English translations if necessary). The specialty chief editor will make the final decision on whether a manuscript on a vulnerable population can proceed to review/publication. If you notice a study on a vulnerable population, please flag this to the RI team and they will confirm that they have checked the above documents.

3.5.2 Cells from human samples

In contrast to cell lines, primary cells are cells directly isolated from human tissue, such as bone marrow and blood. Samples taken prospectively from humans require ethical approval.

On the other hand, cells lines are derived from primary cultures; if the authors used cell lines that were obtained from a commercial entity, ethical approval is generally not required. However, the source where the authors obtained the cell lines from needs to be clearly stated in the manuscript.

3.5.3 Human embryos

Ethical review and approval is required for all studies involving human embryos. If the study methods include details on how the embryos were acquired, written informed consent should also be stated.

3.5.4 Non-identifiable sensitive images

Clinical photographs that are of a private nature, but are non-identifiable, ie they do not contain any identifiable features or faces and do not require written informed consent to publish, should only be included if deemed absolutely necessary for the scientific groundings of the study. If you notice images that are of a private nature and are unnecessary, please ask the author to remove these from the manuscript.

3.5.5 Examples of identifiable data

a. **Scans and x-ray images**
X-ray images are not considered to be identifiable as it is highly unlikely that a participant will be able to identify themselves from these images. However, if any identifiable clinical markers, such as age and gender, are included on the scan image written consent to publish would be required.

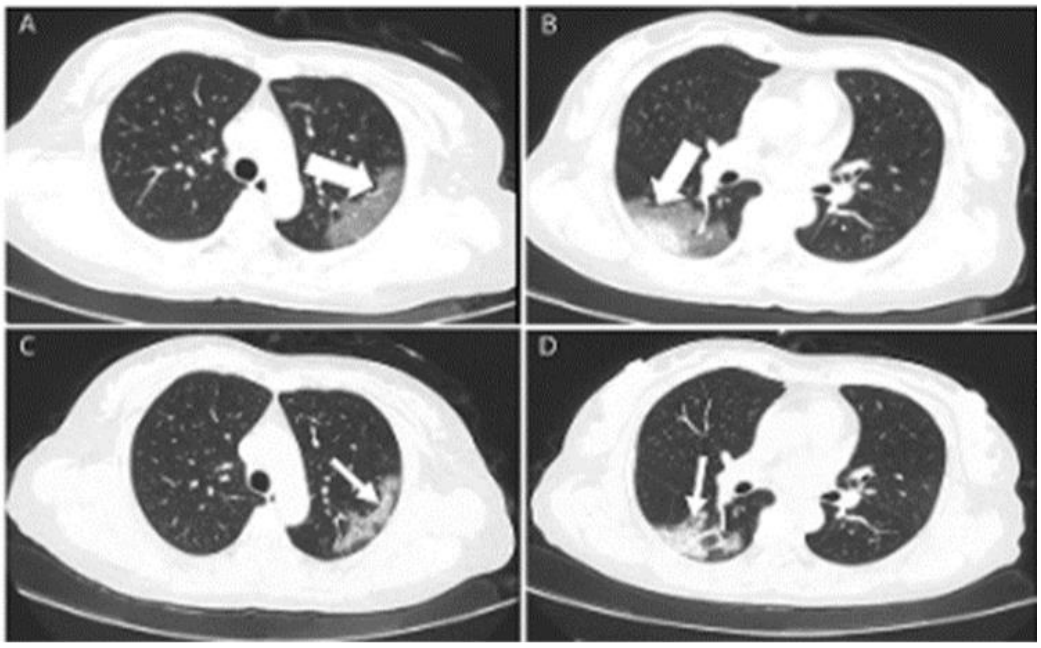


Figure 1
Zhao, W., He, L., Tang, H., Xie, X., Tang, L. and Liu, J., 2020. The relationship between chest imaging findings and the viral load of COVID-19. Frontiers in Medicine, 7, p.558539.

b. **Images that have not been sufficiently cropped or censored**
Any image that includes distinguishable features of a participant where they are likely to recognize themselves requires written informed consent to publish. Images that include the faces of participants need consent to be published, please note covering up the eyes is not sufficient enough to waiver consent for publication.

Please see Figure 1 of this Frontiers article as example:
https://www.frontiersin.org/articles/10.3389/fmed.2022.902716/full

c. **Combination of indirect identifiers in a table**
As the exact age, gender and specific clinical data of each participant is included the likelihood of a patient being identified is high. Therefore, written informed consent to publish this data is required.

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	45	34	22	36	29
Gender (M/F)	M	F	M	M	M
Country of origin	Congo	Somalia	Sierra Leone	Somalia	Somalia
BMI (kg/m^2)	29.5	29.8	26.7	22.7	21.1
Insulin dose (U/d)	82	186	34	22	26
Initial HbA_{1c} (mmol/mol)	132	101	153	77	82
Ketosis	++++	+++	+++	++	++
Stimulated C-peptide (nmol/L)	1.44	0.676	"Low"	1.07	1.17
Autoantibodies	Negative x 3	Negative x 2	Negative x 3	Negative x 2	Negative x 2
LDL-cholesterol (mmol/L)	3.7	4.2	5.2	2.9	3.4
Treatment	Sitagliptin	Synjardy Semaglutide	Janumet	Qtern	Sitagliptin
Follow-up					
HbA_{1c} (mmol/mol)	57	37	46	40	44
Insulin dose (U/d)	0	18	0	0	0

M, male; F, female.

Figure 2
Sjöholm, Å., 2019. Ketosis-prone type 2 diabetes: a case series. Frontiers in Endocrinology, 10, p.684.

d. Interview quotes

The below interview quotes contain personal information, such as childhood experiences and family background, inferring that identification of the participant is likely. Written informed consent for the publication of these extracts is required.

The participants described early access to the outdoors as a gateway into sport. Andreas specialized early for ski-jumping (e.g., progressing to Ski-Flying) and others engaged in more of a multi-sport approach but typically were in outdoor sports by approximately 8 years of age. At this age, adult support in addition to peer learning is often required.

Parental influence was instrumental for Andreas Küttel who recalled that:

> *My dad was a physical coach for the ski jumping team so I was very in touch with it and the ski jumping center is in my home town.*

This provided him with an opportunity to access the ski-jumps, observe both peers and expert performance, receive coaching, all with the support of his father. Sibling support was noted as influential for Tehillah McGuinness who noted:

> *I think I was quite a Tom-Boy – I mean growing up we were all incredibly close – my mum kind of had us in pairs – so my brother and I when we were younger, we were a year apart so I would do everything with him and his friends.*

Interestingly, Rosie Foley, who had grown up in the midst of a patriarchal rural Irish society, highlighted those influencers who had overcome social barriers to facilitate early childhood opportunities for participation regardless of gender. She recalled how a local swim teacher had introduced her to swimming in the river Shannon:

> *Peter Lacey was a gentleman renowned in this area and he used to teach people in the Pier Head how to swim with a kind of a homemade leash structure that he'd hold onto people [they were tethered] and that's how he got them going.*

Figure 3
MacIntyre, T.E., Walkin, A.M., Beckmann, J., Calogiuri, G., Gritzka, S., Oliver, G., Donnelly, A.A. and Warrington, G., 2019. An exploratory study of extreme sport athletes' nature interactions: From well-being to pro-environmental behavior. Frontiers in Psychology, 10, p.1233.

e. Case descriptions

As we have several indirect identifiers for a single participant and a detailed description of their medical history, written informed consent to the publication of this case description is required.

Case Description: We update the clinical course and report new treatment outcomes of a 32-year-old man with ADP managed for many years with weekly prophylactic hemin infusions. He has developed evidence of iron overload and was more recently found to have compensated cirrhosis. The patient was started on givosiran (Givlaari™, Alnylam), a small interfering RNA (siRNA) therapeutic that is effective in preventing frequently recurring attacks of acute intermittent porphyria (AIP), the most common type of AHP.

Figure 4

Graff, E., Anderson, K.E. and Levy, C., 2022. Case Report: Lack of Response to Givosiran in a Case of ALAD Porphyria. Frontiers in Genetics, p.1601.

f. Summary of direct and indirect identifiers that require written informed consent to publish

We follow the British Medical Journal's guidelines on identifiable data, which are summarized below.

Directly identifiable data that require consent	Examples of indirectly identifiable data that require consent if used in combination
Names/initials	Combination of age, gender, location
Address/email	Rare disease and treatment
Facial images/audiotapes	Socioeconomic data
Biometric data or medical identifies	Transcripts or description of an event

4 Further information: animal studies

Frontiers follows the International Association of Veterinary Editors (AVMA) guidelines for the publication of studies including animal research: https://www.frontiersin.org/guidelines/policies-and-publication-ethics/.

4.1 Considerations for studies on animals

For ethical standards related to animal experiments, **please always consider the following**:

- Is ethical approval and/or written informed consent from the owners of the animals needed? If so, does the manuscript contain the appropriate statement, and has any necessary ethics approval been issued by an appropriate committee/organization?
- If the manuscript uses animal samples, does the manuscript clearly state where these samples were obtained?
- Does the manuscript mention that experiments were performed according to the named location or national guidelines?
- Do all procedures performed on animals described in the manuscript appear to conform to internationally accepted standards? Please see section 4.4 for more details.
- Does the manuscript contain a clear description of the procedures performed on the animal subjects, including any details of any anesthesia or euthanasia performed?

Please refer to the animal studies checklist below to assist you in these checks.

4.2 Animal studies checklist

Mandatory checks

- ○ Ethics committee approval and full name of the ethics committee provided – for all vertebrates and higher invertebrates
- ○ If ethics committee approval was not required, a statement specifying this, along with justification of why ethics approval was not obtained or why the ethics committee waived the requirement for approval, is provided
- ○ All procedures performed on animals described in the manuscript appear to conform to internationally accepted standards or named local standards
- ○ Euthanasia was necessary and the methods were humane

Additional checks

- ○ The dose of anesthesia is provided and conforms to approved standards
- ○ Animal/organ cells are used and the origin is clearly stated in the manuscript
- ○ If zebrafish were used, ethical approval was provided (except for embryos and larvae up to five days old)

4.3 Guidance table for common ethics issues in human studies

Issue	Action needed
No ethics approval	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following ethics statement: 'The studies involving animals were reviewed and approved by [full name and affiliation of ethics committee].' If the issue cannot be resolved, flag it to the editorial office using the animal studies statement verification indicator.
The word 'euthanasia'/'anesthesia' (or similar) has flagged but the methods are not clearly stated	Please use your 'Editor' tab in the review forum to ask the authors to clearly state the methods used in the manuscript.
Written informed consent from the owners of the animals included but not required	Please use your 'Editor' tab in the review forum to ask the authors to remove the unnecessary consent statement.
No written informed consent from owners of animals (but required)	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following statement in their manuscript: 'The patients/participants [legal guardian/next of kin] provided written informed consent to participate in this study.' If the issue cannot be resolved, flag it to the editorial office using the animal studies statement verification indicator.
Ethics statement is correct in the manuscript file but not the Review Forum	Please resolve the indicator as 'OK' but use your 'Editor' tab in the review forum to advise the authors to update their ethics statement(s) in the review forum when they resubmit their manuscript. If they do not do this, please still proceed with the manuscript – if the ethics statements are sufficient in the manuscript, it should not be held.
Ethics approval not required but no statement	Please use your 'Editor' tab in the review forum to ask the authors to change their ethics statement to: "Ethical review and approval was not required for the study of animals in accordance with the local legislation and institutional requirements."
Committee name not provided	Please use your 'Editor' tab in the review forum to ask the authors to include the full name of the ethics committee that approved the study, for instance: 'The studies involving animals were reviewed and approved by [full name and affiliation of ethics committee].'
Source of cell line	Please use your 'Editor' tab in the review forum to ask the authors to include the source of the cell line used in their manuscript:

	1) If the cell line was commercially obtained or from a repository such as a biobank, please request that the following statement is completed and included in the manuscript: 'The cell lines present in this study were obtained from [full name of the company or repository].' 2) If the cell line was obtained from an animal(s) and the authors obtained ethics approval, please request that the following statement is completed and included in the manuscript: 'The studies involving animals were reviewed and approved by [full name and affiliation of ethics committee]'. 3) If the cell line was obtained from animals but the authors state that ethics approval was not required for this study, ask the authors to provide further evidence. If the issue cannot be resolved, flag it to the editorial office using the animal studies statement verification indicator.
Samples isolated from animals	Please use your 'Editor' tab in the review forum to ask the authors to update their manuscript to include more information about the samples used. Samples/isolates may not require ethical approval if they were: 1) gifted from another research group; 2) primarily isolated as part of the authors' previous study for which ethical approval was obtained; 3) or a by-product of routine care or industry. In these cases, please request more information. If the issue cannot be resolved, flag it to the editorial office using the animal studies statement verification indicator.
No ethics approval	Please use your 'Editor' tab in the review forum to ask the authors to complete and include the following ethics statement: 'The studies involving animals were reviewed and approved by [full name and affiliation of ethics committee].' If the issue cannot be resolved, flag it to the editorial office using the animal studies statement verification indicator.

4.4 Useful information on animal studies

Please ensure that all procedures performed on animals described in the manuscript appear to conform to internationally accepted standards. For example:

- The revised Animals (Scientific Procedures) Act 1986;
- The Directive 2010/63/EU in Europe;
- The Breeding of and Experiments on Animals (Control and Supervision) Rules, 1998 in India;
- The NIH Guide for the Care and Use of Laboratory Animals in the USA.

If not, do the authors provide some form of justification for this procedure being ethical (eg including a citation to another study using this protocol)?

4.4.1 Principles of 3Rs and ARRIVE

Frontiers endorses the 3Rs (replacement, reduction and refinement) framework for humane animal research, as well as the ARRIVE guidelines for reporting animal research. Editors and reviewers are at liberty to request relevant documentation pertaining to these guidelines (e.g. ARRIVE checklist) if they have concerns regarding animal experiments reported in a manuscript.

4.4.2 Higher invertebrates

All research involving regulated animals (that is, all live vertebrates and **higher invertebrates**) must have been reviewed and approved by an ethics committee prior to commencing the study, and performed in accordance with relevant institutional and national guidelines and regulations.

Higher invertebrates are animals without a backbone but with a coelomic cavity. Please find phyla belonging to higher invertebrate families in the table below.

Family	Examples
Phylum Annelida	Earthworms and leech
Phylum Arthropoda	Insects, prawns, crabs, spiders, scorpions, millipedes, and centipedes
Phylum Mollusca	Snails, clams, oysters, octopus, and squid
Phylum Echinodermata	Starfish
Phylum Chordata	Hemichordata

4.4.3 Anesthesia

If an animal study has involved induction of anesthesia in subjects, it is encouraged for authors to provide specific details of these procedures. This includes the type of anesthetic used, the route of administration and the dose administered. There are an array of different institutional resources that can provide information over whether an anesthetic dose is appropriate, such as those provided by the University of Colorado, Albert Einstein College of Medicine, and the University of Iowa. If anesthetic doses stated in manuscripts appear to fall outside the accepted ranges stated by these or similar guidelines, ask the authors to provide justification for their dose, as otherwise this may represent a case of unethical research.

4.4.4 Euthanasia

If an Authors are encouraged to provide a clear description of the method(s) of euthanasia used to sacrifice animals at the end of any study involving animal research, or to clarify the fate of these animals if they were not sacrificed. The American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals (2020) are recommended as a tool for determining whether euthanasia protocols described in a study are acceptable. Editors and reviewers are at liberty to ask for any necessary supporting information or documentation in order to determine whether animals were humanely euthanized during the course of an animal study. Of note, Frontiers will not consider manuscripts reporting the use of euthanasia protocols widely considered to be unethical, such as overdose using chloral hydrate, ether or chloroform.

4.4.5 Non-standard protocols

Due to the diversity in background and discipline of authors submitting manuscripts to Frontiers, it is expected that some studies will report protocols that deviate from common practice. If editors or reviewers harbor ethical concerns regarding non-standard protocols described in submissions that they are handling, they are at liberty to ask authors to provide the approved ethics application detailing the use of this protocol, as well as to provide citations to other reputable studies using this protocol or details of how animal welfare was protected during the course of the study. In cases where editors or reviewers are not satisfied that a protocol is ethical, they can recommend a manuscript for rejection.

4.4.6 Animal embryos

Ethical review and approval on animal embryo research vary between countries. In the UK, research using animal embryos that are more than two thirds of the way through gestation requires ethical approval. This rule may not apply for all countries; please follow up with the authors to confirm that their ethical protocols meet the national regulation standard.