Reviewer #1 (Patrick Gonin):

This paper gives a short opinion about animal ethics review committees, encompassing a lot of jurisdictions and fields of research.

The title asks "*Are more ethics review committees the solution?*". We could as well wonder what is the relevance of the question. Indeed, in general, increasing the number of ethics committees is surely not a good solution since it will mechanically increase the variability and discrepancy between assessments (and that's the main argument of the European Commission against high numbers of ethics committees in member states).

The question is related specifically to the first half of the title, i.e. would an increase in ethics review committees ensure that animal (welfare) research is ethical? – the answer, we argue, and you agree, is no, but that is not the point of view of all colleagues and stakeholders. We chose the title to be simple and slightly provocative, and also to allow us to concentrate on this specific issue (i.e. why more committees do not solve the problem), condensing the manuscript and thereby increasing the likelihood that (busy) researchers would actually read it.

Lin. 33 To the question *What do ethics committees do?* the authors could have also considered the work of the FELASA-AAALAS working group (Bronstad et al, 2016, Laboratory animals). The paragraph is very concise. In addition, precisely, depending on the jurisdiction, ethics committees may do much more than that (training, disseminating culture of care, in-house inspection (US), etc.).

We acknowledge that the paragraph is concise, which – as also explained in our response to Reviewer #2 – was a conscious choice to reflect that it is not (at least on the surface) a complex task that the review committee undertakes. But your observations are important, and in the revised version, we have emphasised that it is not the only task (lines 36, 43 – 45).

Line 41 and next. To the question *"When ethics approval is needed?"* Researchers are not and should not be on their own. In Europe, they have to ask to the Institutional Animal Welfare Body (which has also to assess whenever it is needed, about the "needle prick" criterion). In other places, researchers may and should consult animal welfare specialists, veterinarians (specialists in laboratory animal science and medicine) and experimented colleagues.

Although we agree that it would be better if all researchers had access to an ethics committee, in reality this is not the case. And this is the whole point of our article, namely that it is easy for researchers working in different countries, cultures, and jurisdictions to take for granted that what they are used to is also how it is globally. We highlight this in the examples of Scandinavian countries where the national ethics committee does not touch below-threshold protocols (lines 92-96), and for researchers in countries or institutions where access to an ethics committee is limited or non-existent (lines 96-101). We have also moved the reference to an independent, available ethics committee to here (lines 102-104). One of our main points (which we have tried to explain better (lines 136-139) in the revised manuscript) is that we should all carry out harm-benefit analyses on the work we do. This is not the same as saying that review committees should not be involved, but simply that ethics should be at the forefront of any researcher's mind from the outset, before any experimental subjects (animals or humans) are involved.

The next paragraph makes a point which is very right about all which relates to ethology studies, farm animals, agricultural, wildlife research. Some regulatory work has to be done here; some loopholes exist.

The paragraph from line 74 is interesting, but a little amazing since in some other European countries, officially approved ethics committees are allowed and encouraged to review projects which are not mandatorily reviewed and not subjects to official authorization.

Which is exactly the point we are trying (but perhaps failing) to get across: if a researcher works in one country (jurisdiction), they are not aware of the regulations in other countries (jurisdictions). In some, even many, research institutes, local ethics review committees are being set up. Although this is commendable, it adds to the variability (as also highlighted by you in your first comment). It also does not overcome the issues faced by our colleagues in the global south. No matter whether it is allowed or encouraged, not all officially approved ethics committees accept reviewing projects not subject to official authorization, leaving the researchers in challenging situations.
We have moved this paragraph to the next section (lines 92-101) and elaborated on this in lines 115-116 and lines 119-120.

A lot of researchers criticize the ethics approval system saying that ethical assessments sometimes differ between committees. The main reason is that the animal ethics committees, in their current formats and duties are quite new in a lot of geographic areas. In addition, one could also answer that when a research paper is being sent to 3 or more reviewers, each review will be different. So, yes training of ethics committee members is very important, but also the ethics committees should have the right size and the right resources for operating smoothly and efficiently.

We agree and have made this clearer in the revised manuscript (lines 186-189).

When *"the available committee does not have competence in the proposed research area"*, it should of course ask for external help, under a confidentiality and impartiality agreement.

Another good point. Unfortunately, it is not always clear to the committee that a protocol is outwith their (usual) competence, such as when humans are being surveyed in studies of animal welfare. But we have included your suggestion as one of the improvements that could be made (lines 189-191).

Line 103, as stated above, this is a very important point that would need more insight and review of literature. Indeed, resources are one of the main points. Some countries allow pay-per-assessment, and some other settings depending on the country (in some, ethics committees are official state or region official bodies).

Yes, the increase in committees is likely to happen by institution and, just like reviewing scientific articles, it should be something that counted/was appreciated officially. We have specified that in lines 184-186.

Line 104: *"Whereas influential researchers may be able to convince their institutions to establish their own committees,"* This is definitely not the right way to go. This may work correctly in very big institutions, but overall, it is way better when ethics committees are either external to the institution (see Switzerland, Sweden, Germany), or multi-institutions so that the risk of bias is very low.

We agree, but reality is that national committees, although aiming to ensure homogeneity in assessment, are more difficult to operate (and may refuse to assess certain protocols, as is the case in Scandinavia). Although individuals from different institutions may populate a local committee, some institutional committees (e.g. in France) assess only protocols carried out in their own experimental facilities, because they have visited these facilities. We have tried to make this clearer in this paragraph (lines 114-120).

Lines 109 and next: *"reviewing all protocols independently of severity"*: please explain why you raise this point. This is unusual.

We think this is a misunderstanding and have reworded the statement (line 127). We did not mean that severity should not be reviewed, we were merely referring to the assessment of protocols that where below the severity (needle-prick) threshold for requiring approval (i.e. no or minor harm).

Line 117 to 130: a lot of wishful thinking and obvious statements, which could be summed up better by citing the culture-of-care paradigm.

We have indicated that we may be stating the obvious (line 144) but, unfortunately, there are still a large number of researchers with a lot of influence on younger colleagues who are dismissive of the suggestions we are making. Ethics is more than culture-of-care (now added in line 134), and too often young researchers think that application of the 3Rs constitutes a complete ethical justification. So rather than being wishful thinking, we would argue that early career scientists need to read this, thereby having something concrete to refer to and share with colleagues.

Line 126 "*We may be stating the obvious, but far too often animal research protocols are constrained by existing housing facilities and management procedures. Researchers, including the authors, may make use of the model species that happens to be available, without sufficient consideration for their suitability for the question asked or whether it is the species and experimental approach which will incur the least harm.*" Well, this is also what animal facility managers, ethics committees and veterinarians criticize. Researchers should always try to find the best animal model for their studies (which means the species and the techniques/ interventions/ procedures), regardless of what is in-house. Then they should either implement it there or go elsewhere for learning the required skills or for performing their experiments, if this is not possible. On an ethical standpoint, using an animal model just because "it is here" is not acceptable.

*We couldn't agree more. Unfortunately, a lot of research is planned around the capacity of the animal facility, and the '*we have always done it like that*' mentality. When more senior colleagues have already published results using protocols that may not be appropriate (either statistically or ethically), it can be difficult for younger colleagues to break the tradition. It is easy to be scathing of others when they do wrong, but the best way to solve these issues is to raise them before they happen. This article is aiming to do so, and we have expanded this section to reflect the above (lines 145-148).*

Line 131 to 138: This would be like publishing all the ethical review, so that it can be checked and redone by editors, reviewers and readers? It would be far better and productive to publish all raw data of studies (Open Science, Diedrich et al, https://doiorg.proxy.insermbiblio.inist.fr/10.1371/journal.pbio.3001810). In addition, this implies a lack of confidence in ethics committees.

*No, it is not a suggestion to publish the full ethical review. It is to encourage researchers to inform and educate each other on the ethical thoughts they had themselves, and how they adjusted their protocols to accommodate this – using a few sentences (Publishing raw data (albeit very commendable and may reduce future use of animals) is a different issue, as the animals have already been used). We have made this clearer in lines 159-161. It is also meant to expose more clearly the existing difference between ethics committees and, as we say further down in the article: "*That an ethics committee has approved a study should not lead to reviewers omitting to consider the ethical implications of the protocol being assessed, in the same way as they assess the scientific quality of the study." *Unfortunately, papers are published which has been given ethical approval by a committee (according to the article), but which are ethically questionable (e.g. a study where dogs were fitted with 3D-printed artificial plastic eyes; Park et al., 2020). The fact that ethics committee documentation is usually confidential and in the vernacular means that they remain largely inaccessible, and bringing the essence of ethics practice into the open would help increasing trust in both research and ethics committees.*

Line 150 *"It can be discussed whether this suffices on its own or whether an ethics committee also needs to be involved"*. This is not relevant. In many places, fortunately, the ethics committee review is mandatory anyway.

It is a suggestion that would lead to a reduction in the number of times a protocol needs to be seen by competent authorities. If the (scientific) reviwers assessing a protocol (submitted as a Registered Report) also had ethical training, then this would not only save work for the busy scientists, but also prevent that unethical research is carried out as the assessment is done prior to the experimental work, and either adjustments can be made, or the project rejected. We would argue that this is a better system than the current one. We have included this in lines 174-179.

Line 153. Since I do not think that the overall question of the paper is relevant: the number of committees is not an issue at all, and it should not be increased (except of course in places where there are no animal ethics assessments).

We respectfully disagree about the relevance of the question. We have discussed some of the other issues you raise in a previous paper (Olsson et al, 2022), which we refer to in line 28), and as the two other reviewers have no issue with the question we raise, we have chosen to leave it as is.

Line 156 "*We also need to find ways of ensuring ethics committees are more harmonized across regions, by means of training, global guidelines (Petkov et al., 2022), and communication between ethics review bodies"* There have already been a lot of work on this topic (see above, Bronstad et al). Overall, when it comes to the ethics assessment part of the committees, the same requirements and values are already here. However, differences exist regarding the composition of ethics boards, training of their members and their roles. As always when harmonization is sought, it is a lot way to go. Indeed, everyone has to do small steps and a lot of people in the working parties tend to try to impose their values and ways.

We have inserted (line 84) the reference by Brønstad et al. (2016), as well as Part 2 of the same study (line 188), which gives recommendations on how to standardize better across committees (Laber et al., 2016). In addition, we have added two references on the use of the 3Rs (lines 140-141).

Line 166 *"we recommend always explaining the ethical reasoning for a study in the scientific article(s) arising from it, whether or not an ethical approval has been/needs to be obtained. This will demonstrate the ethical thoughts behind the chosen protocol, making comparisons easier, and educate us on where the thresholds for approval are placed across jurisdictions. By reducing the number of requests ethics committees get, the more time they will have for the studies that really need a diligent review"* This part is really difficult to translate into concrete actions.

Please see our response below.

Line 168: *"This will demonstrate the ethical thoughts behind the chosen protocol, making comparisons easier, and educate us on where the thresholds for approval are placed across jurisdictions"* As stated above, researchers should not be on their own to determine the thresholds. I do not agree with this part. It is not a solution to "demonstrate ethical thoughts" and then decrease requests for ethics committees (which would then work swiftly and have more time). The solution is to have well-dimensioned ethics committees, with the relevant resources. These committees should also be officially supervised by a national authority (which is mandatory in Europe member states, even if their attributions may differ a little between countries).

We are not advocating that researchers should be on their own to determine thresholds, and this is not what is written either. It is what we have said earlier, that one of our main points (which we have tried to explain better (lines 136-139) in the revised manuscript) is that we, as researchers, should all carry

out harm-benefit analyses on the work we do. This is not the same as saying that review committees should not be involved, but simply that ethics should be at the forefront of any researcher's mind from the outset, before any experimental subjects (animals or humans) are involved. By also including (briefly) these considerations in the published article – and some journals encourage this, e.g. Animal Welfare – it will educate us all, as editors, reviewers, researchers, and members of ethics committees.

Conclusion of the review: From the authors experience, and this is known to be true, in general, animal ethics committees are not very well suited to ethology, agricultural, wildlife and animal welfare research. The paper would have been far more interesting if clearly focused on these areas. Indeed, there are a lot of general statements which are not relevant for most research using animals. If the paper is a general overview about ethics committees, their number and relevance in research using animals, it brings few new contributions.

Although some ethics committees may find certain aspects of ethology, agricultural, wildlife and animal welfare research difficult, we know of many examples where this is not the case. Not least because many of the authors of this article are involved as members of ethics committees (as well as being editors, reviewers, and researchers). On the contrary, we think that many of the general statements made in the article are highly relevant for all animal researchers and ethical committees. This paper is not a general overview of ethics committees but is highlighting the many issues that may not be apparent to individual researchers working in their own facility/culture/bubble, and which only become obvious when dialogue happens. This article is a result of discussions among the authors and with other researchers. We would strongly argue that it brings important new information to a range of people involved in animal science, and particularly for animal behaviour and welfare protocols.

I suggest that the paper be therefore refocused and expanded on this particular interesting topic: animal ethics committees for ethology, agricultural, wildlife and animal welfare research, especially for non-laboratory animal species (there is only a hint in the title to the scope of the paper: "Ensuring animal welfare research", but animal welfare research for laboratory animals exists too). What are the specific questions and differences? What does not work with the existing ethical review system? How could this be improved? Some elements are included here, but most statements are too general and do not apply to most cases.

Please see our previous reply as well as our previous paper on ethics (Olsson, I.A.S., Camerlink, I., Pongrácz, P., Ceballos, M.C., Nielsen, B.L., Golledge, H.D.R., Chou, J.-Y., and Whittaker, A.L. (2022). An international perspective on ethics approval in animal behaviour and welfare research. Applied Animal Behaviour Science 253: 105658. https://doi.org/10.1016/j.applanim.2022.105658).

Reviewer #2 (Leon Borgdorf):

General Feedback: Overall, the authors provide a solid argument that increasing the number of ethics review committees alone does not suffice to address all ethical problems that come with animal experiments. Aside from the accessibility of ethics review committees, the authors refer to questionable criteria upon which such committees act, regional differences, and biases within committees. They propose creative and promising solutions, such as integrating the ethical decision-making process in the final paper and introducing committees that review the research plan before the experiment is conducted. Although the arguments provided by the author consistently show that both solutions would help address several shortcomings of the current ethical review process, the authors could make an even more convincing case by considering the objections raised below.

Evaluation of the various components of the article

Title: The title is attractive and already suggests that there is more to ensuring ethical animal welfare research than simply increasing the number of ethics review committees. Some of the solutions proposed in the article would probably require a significant increase in ethical review committees, so increasing the number of committees would be part of it, but the authors properly address the benefits of increasing the number of ethics review committees as well.

Thank you – due to comments from Reviewer #1 we have now further emphasised (lines 180 onwards) that an increase in number of ethical committees is still part of the solution (but that it does not solve other problems highlighted in our article).

Introduction: The function of ethical review committees is properly explained. One could maybe highlight that such committees endorse a utilitarian way of reasoning by weighing the benefits against the harms caused by the experiment rather than rights-based views, which exist in the literature, and generally question animal use.

Thank you for this suggestion. We have inserted a reference to the utilitarian approach to clarify this (lines 41-43).

Problem Analysis: The problems associated with ethics approval are adequately explained. One might still consider listing the international differences and the resulting unequal access to ethical review under this section rather than as part of the section explaining the functioning.

Thank for this suggestion. We have moved that paragraph to the next section (now lines 92-101), and added the information on the independent ethics committee here (lines 102-104).

Main Argument: The proposed solution of training researchers and reviewers in ethics and including an ethical justification in the article, is highly sensible and helps address problems, which cannot be tackled by increasing the number of committees. This would indeed lead to increased transparency and more engagement of the researchers with the ethical questions behind it.

Thank you, we are glad you like the suggestion.

At some point, the dialectic is missing. The paper would be stronger if it included objections to the proposed solutions. How can be ensured that researchers and have access to a proper ethics training? How can biases inherent in the discipline be prevented? It could be the case that researchers working with lab animals are less sceptical of animal experimentation than members of an ethics committee. The idea of implementing methodological review boards or registered is an interesting addition as well. Indeed, prevention is better than correction. Here as well, some objections could be dealt with to make a stronger case for this measure. Previously, the authors argued that demanding that all studies undergo ethics review bears the risk of ethical review becoming a box-ticking exercise. This objection might also hold for the proposal. Furthermore, many of the accessibility and effort-related objection towards ethical review committees might apply to such boards as well.

These are valid points, but the notion of differences in attitude may be better discussed elsewhere so as not to dilute our main message. We have expanded on and clarified our possible solutions (e.g. lines 137-139; 159-161; 174-179) whilst continuing to acknowledge that we do not have all the answers.

Conclusion: Overall, the arguments and conclusions reached in this paper are adequately summarised. Qua structure, the final paragraph of the previous section already reads like a conclusion, which leads to some redundancy in this section. It might be considerable to combine both paragraphs into one final conclusion.

We see the paragraph before the conclusions as reflecting on an increase in ethics committees, whereas the conclusions relate to how we can best ensure only ethical animal research is carried out. For this reason, we have left the Conclusion paragraph as a stand-alone section.

References: The referencing style is consistent and relevant sources are included.

Thank you – we have also now added three additional relevant articles.

Reviewer #3 (Christian Nawroth):

It was a pleasure to review this thoughtful commentary on the limitations and challenges of (animal) ethical review boards. I very much liked the outlining of the problems and the discussion about the proposed solutions, but in some cases, those fall a bit short and/or put too much effort on the individual researchers, rather on systematic changes. In other cases, coherence in arguments was lacking.

Thank you for the kind words, and the suggestion to encourage more systemic changes to the ethical approval process, which we have now included in the revised version (lines 186-189).

I have a few questions and potential recommendations that will hopefully prove helpful and will make the case (and the arguments) of this piece even stronger.

1. Initial argument / Setting the stage: First, it appears as the phrase "Are more ethics review committees the solution" is a reference to a previous argument being made (taken from another publication, a blog, on social media, etc) but is never referenced as such. This way, it reads a bit artificial as the reader does not understand the contextual setting of the article. Second, the same phrase is a bit misleading, as it is not clear whether this refers to the type of committee, the number per institution, the number in general; what is a "solution" needed for, etc. I understand the placative writing to increase engagement with the text, but am wondering whether a different, more concise title, would help the reader to identify the main arguments earlier.

*Thank you for this suggestion, as it highlights that we have not been as clear as we wanted to be. The reference was, indeed, to the first part of the title, and we have tried to at least make that more apparent by using now the word 'ensure' (line 26) to reflect this, also now underlined in line 180. We would argue that the sentence "*If enough ethics review committees are available to allow assessment of each and every scientific protocol involving animals then, surely, we can ensure that no unethical animal research will be carried out" *makes it sufficiently clear. In addition, we have inserted more specific descriptions of the committees in lines 186-191.*

2. Clarify key audience: Who is the supposed main audience of the manuscript? From the title, it suggests animal welfare researchers. However, many of the examples and challenges are also faced by scientists working with animals without a welfare background. I would recommend aligning this throughout the manuscript, as it right now artificially narrows the target audience as the statements in the manuscript can be of wider relevance. It should also be clarified whether the main focus is on animal ethics boards (needle-prick criteria), or also human ethics boards (which are stated frequently in the text). This mix of general vs narrow audience statements makes it sometimes a bit hard to identify the main challenges and solutions from the text.

Very good point. The article was, at its outset, aimed at animal welfare science researchers, but it should also include applied and fundamental ethologists. However, it is relevant for anyone working

with animals in research, but medical and pharmaceutical research is (almost) always above the threshold for ethical approval. We have tried to make the audience clearer in lines 31-33.

3. Putting the responsibility on the individual researcher: The manuscript, directly or indirectly, hints that it may be up to the researchers to make a decision on whether a study protocol needs ethical review (line 47, lines 166-168). Although I understand this reasoning from the point of having only limited resources for ethics committees, many researchers do not have ethics training and might not be able to judge this appropriately. This makes it even more difficult when the authors suggest that authors should outline their reasoning, in particular when approval was not obtained, in their manuscript – in that case, data has already been collected (e.g., it is too late to amend the design). This procedure might only work out in the case of RRs, as the authors appropriately stated (lines 147-152). Wouldn't the most obvious solution be to enable those review boards themselves to assess whether a study protocol would need review or not (i.e., via initial screening, without going through the full procedure)? In some countries with national ethics committees, it is possible to get a procedural number in the case that the ethics review was waived (although I might be a bit biased here). On a final note, I fully understand the argument of adding additional information about the harms and benefits of the study protocol, but this might extend a scientific manuscript considerably – maybe an additional/alternative solution would be to add this information as ESM or link to a repository – this can even be the text that has been submitted (and evaluated) by the ethics committee! I understand that many of these suggestions stand and fall with differences in national and institutional jurisdictions, but so do most of the other solutions.

Yes, it is not ideal whenever researchers themselves need to assess whether their protocol needs ethical approval, but the example of the systematic review of published literature that had ethics approval (Samet et al., 2023) illustrates the caricature of never trusting the researchers to do this assessment. The establishment of internal ethical boards needs to be better implemented (with systematic and international guidelines, as you suggested previously) – this has now been added in lines 186-191. We have also tried to emphasise that researchers should always do their own harm-benefit analysis (before anything else) which should not differ from that of any ethics committee (lines 136-139). In addition, we have added a clearer explanation of what we suggest to include in articles (lines 159-161) and expanded on how the RRs can reduce the workload (lines 174-179).

I also have some rather minor comments:

Lines 34-39: this part falls a bit short on the details of an ethical review process – it might be good to elaborate – e.g., also stating some guidelines, international recommendations, etc

In the revised manuscript, we have included that the work of an animal ethics committee is more complex, and we have also mentioned the utilitarian approach used by ethics committees (lines 41-45).

Line 59: please explain 3Rs here (as they have not been introduced before) and provide a reference

Oops- 3Rs are now explained and referenced (lines 65-66).

Lines 74-80: this part does not really fall beyond the scope of "when is ethical approval needed" as it rather highlights limitations to having access to review committees per se

Point taken – the paragraph has been moved to the next section (lines 92-101) and we have also added the information on the independent ethics committee here (lines 102-104).

Lines 83-106: half of this part focuses on human participants – although relevant, this might be a bit heavy for an article arguing about ethical approval in animal (welfare) research. E.g., you could

elaborate on other criteria than the needle-prick criterion, how psychological stress might be difficult to assess, etc

Thank you for pointing this out. During the recent COVID-19 pandemic, many surveys were carried out by many animal scientists for the first time due to limited access to animals, revealing a lack of access to (and appropriate understanding of) ethical assessment when humans are involved. We have now moved the reference to the independent ethics committee in the UK to a previous paragraph, and focused this paragraph on studies involving human participants (lines 105-113), where we note that surveys and interviews are indeed relevant tools in animal welfare research, since assessing stakeholders' knowledge and attitudes is often of interest. (lines 109–111).

Lines 89-92: I think elaborating here would help the reader to further understand why one decision of one ethics committee might different to the decision of a different committee. Where in the decision process does national jurisdiction end, where does subjective judgement start, etc.

This is such a delicate subject, and we have toned it down a little (lines 88 and 90). It's a bit like medical doctors – we know some are more competent than others, but they (should) all possess a certain level of skill.