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An analysis of reporting pain and distress recognition and alleviation in scientific journal publications

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Abstract
Pain and distress in animal research adversely affects animal welfare and scientific quality, as well as erodes public support for research. Journal requirements for inclusion of detailed information on animal welfare in submitted manuscripts, including how animal pain and distress were addressed, would likely increase scientist attention to pain and distress and thus improve science and animal welfare. In order to examine this issue further, we analyzed and compared thirty nine journals for instructions to authors in regards to animal pain and distress. The analysis also sought to determine the extent to which pain and distress information is reported in these journals and whether journal reporting requirements and animal use policies influence this reporting. Two randomly selected articles involving animal use that potentially caused pain and/ or distress were chosen from recent issue(s) of each journal and examined for inclusion of pain and distress information. The data show that instructing authors to report pain and distress information influences authors to include pain and distress information in articles. Having an animal use policy or statement that mentions pain and distress also encourages reporting of pain and distress information.

Keywords: animal use, journal, pain and distress, reporting, literature

Introduction

Tens of millions of animals are used in biomedical research, testing and education per year worldwide. The use of animals for such purposes involves various stakeholders, each with ethical and legal responsibilities to minimize the pain and distress that the animals experience. Journals that publish animal research are stakeholders and can play an important role in improving animal welfare due to their "enormous influence on the quality of experimental design and planning." (Boisvert, 1997).

Results from studies involving animal pain and/or distress submitted for publication in peer-reviewed journals should clearly indicate steps that were taken to monitor, recognize and, if needed, alleviate pain and distress. Inclusion of this information in published papers would demonstrate attention to animal welfare and quality of science. This information would also allow others to reproduce the methods used and ensure proper interpretation of results by readers.

Journals are also one of few sources of information regarding animal research that are accessible to the public. Since public support for animal research decreases as the amount of pain and distress caused to the animals increases (HSUS 2001), reporting information relating to pain and distress in articles would show scientists' attention to animal welfare—and specifically pain and distress—and could prove beneficial to the public's outlook on animal research.

Scientists have also voiced their support for including information on animal pain, distress and welfare in published journal articles, including in a recent article and letters that appeared in *Nature* and a blog on *Nature's* website. One scientist pointed out that slight changes in a "laboratory animal's environment or husbandry can have profound influences on its biological functioning…and that variables such as these…should be reported in published papers as an essential component of the accurate reporting of science." (Sherwin, 2007). Another response further recommended that there should be a "3Rs section in the methods section of published papers." (Würbel, 2007).

The role of journals in addressing animal welfare was also a point of discussion at the Second World Congress on Alternatives and Animal Use in the Life Sciences, held in 1996. For example, Boisvert (1997) then pointed out a recent increase in regulations,

guidelines and editorial policies of journals regarding animal use. He thus sought to analyze whether journals required authors to certify that animal use met an established standard (Boisvert, 1997). It was found that only 24 of a sample of 46 journals had such requirements. It was further examined whether articles from five journals that had stringent animal welfare requirements actually included the required information. Of the 85 articles examined, 25 "provided no evidence of meeting an established standard." A sample of 63 articles also demonstrated that scientific information regarding animals, husbandry or welfare information was largely absent. The results demonstrated that despite editorial policies regarding animal use, information regarding animal use and welfare was still not being included in the publication.

Festing and van Zutphen (1997) also held a workshop of experts, including journal editors, to discuss the influence of journals on experimental design and implementation of the Three Rs (refinement, reduction and replacement). The participants agreed that journals should include a statement in the instructions to authors regarding the ethical use of animals, should ensure that the policy is implemented, and that authors should sign a declaration or include a statement in the paper indicating compliance with the policy.

The analysis to be discussed here sought to examine the current status of journal requirements for authors to include detailed information on animal pain and distress, as well as the extent to which those requirements lead to actual reporting of animal pain and distress information. General animal use policies or statements regarding animal pain and distress and the extent to which inclusion of these policies influence reporting of pain and distress was also analyzed. Based on these results, recommendations on what journals can do to improve animal welfare and quality of science will be discussed.

Materials and methods

Journal Selection

Eight mainstream laboratory animal science journals currently in print were selected based on whether or not they contained publications of original research that involved the use of animals. An additional 32 journals were selected using the Institute for Scientific Information's Impact Factors List for 2005, which is a measure of the frequency with which the average article in a journal has been cited in that year. Journals were selected based on high impact factor and whether the main focus of the journal was an area of research involving potential animal pain and distress (i.e. toxicology).

Once a journal was chosen, a database search was done on PubMed (a database of peer-reviewed literature maintained by the National Library of Medicine at www.pubmed.com) in order to determine if the journal included studies involving original animal research. If the journal contained no articles with original animal research, it was eliminated. The search was terminated when there were a total of 32 journals. It was later determined that one of the journals actually didn't meet requirements for inclusion in the analysis and was eliminated. Overall, a total of 39 journals (taking into account the eight laboratory animal science journals), were used for the analysis (See Table 1).

Article Selection

Two articles from each of the 39 journals were chosen by searching the PubMed database for all

Table 1. Names of journals used in the analysis

Laboratory Animal Science Journals

1. Animal Welfare
2. Comparative Medicine
3. Journal of Applied Animal Welfare Science
4. Journal of the American Association for Laboratory Animal Science
5. Journal of the American Veterinary Medical Association
6. Journal of the Federation of American Societies for Experimental Biology
7. Lab Animal
8. Laboratory Animals

Other Journals

1. Cancer Cell
2. Cancer Research
3. Cell
4. Circulation
5. Developmental Cell
6. Environmental Health Perspectives
7. Genes and Development
8. Immunity
9. Investigative Ophthalmology and Visual Science
10. Journal of Applied Physiology
11. Journal of Clinical Investigation
12. Journal of Dental Research
13. Journal of Experimental Psychology: Animal Behavior Processes
14. Journal of Infectious Diseases
15. Journal of Pharmacology and Experimental Therapeutics
16. Journal of the American College of Cardiology
17. Journal of the National Cancer Institute
18. Lancet
19. Molecular Cell
20. Nature
21. Nature Biotechnology
22. Nature Cell Biology
23. Nature Genetics
24. Nature Immunology
25. Nature Medicine
26. Nature Neuroscience
27. Neuron
28. Pain
29. Plos Biology
30. Science
31. Toxicology and Applied Pharmacology

articles published by each journal between June 2006 and June 2007 and containing original animal research. A list was generated in chronological order, with the most recent article first. The abstracts for the articles were read and it was determined whether they involved original animal research that potentially caused animal pain and/or distress. The two most recent articles that met these criteria were selected. Once all of the abstracts were selected, the full text of each article was obtained. In analyzing the full text of the articles, two articles were excluded because they did not use animals and/or did not involve potential pain and/or distress to the animals used. Therefore, a total of 76 articles were used for the analysis.

Journal reporting requirements

In order to determine whether journals required reporting of certain information by authors, the *Instructions to Authors* for each of the 39 journals were located on each journal's website. Once located, these instructions were analyzed and labeled as falling into one of three categories: 1.) requirements regarding general reporting of animal use hereafter referred to as "Basic Reporting Requirements"; 2.) requirements regarding reporting of how pain and distress were addressed hereafter referred to as "P&D Reporting Requirements"; or 3.) No requirements regarding reporting of information on animal use, hereafter referred to as "No Reporting Requirements." See Table 2 for examples of each of these categories.

The number of journals that fell into the Basic Reporting Requirements category was much higher than the other categories. In order to adjust for this, deviation from expectation was used for each calculation. Details regarding each calculation will appear throughout this paper.

Reporting of pain and distress information in publications

We were interested in whether specific issues related to animal pain and distress were reported in manuscripts, regardless of whether this specific information was required by journals. As a result, we created four factors relevant to pain and distress assessment and alleviation for examination:

1.) Anesthetics, analgesics, or other drugs used to relieve pain and/or distress (AAOD);

2.) Humane endpoints (HE);

3.) Method of pain/distress assessment (MOA); and

4.) Other methods to relieve pain and distress (OM).

Each of the 76 articles was read and analyzed for reporting of information related to each of these four factors. The corresponding journal instruction type (Basic Reporting, P&D Reporting, No Reporting) was then examined in order to determine whether some kind of pain and distress reporting requirements promote actual reporting of pain and distress information by authors.

Percent deviation from expectation was calculated by subtracting the percent of articles that would be expected to report specific information for each type of journal requirement from the number of articles that actually did report each factor. A positive percent deviation was translated as more articles than expected reported a given factor, while a negative percent deviation meant fewer articles than expected reported a given factor.

We then compiled the four factors and calculated the percent of articles that reported *at least one* of the four pain and distress factors per reporting requirement category. The percent of articles that we would expect to report *at least one* of the factors for each type of reporting requirement was subtracted from the number of articles that actually reported at least one factor in order to calculate percent deviation from expectation. A positive percent deviation was translated as more articles than expected reported at least one factor, while a negative percent deviation meant less articles than expected reported at least one factor.

Of the 76 articles, 25 of them referred to supplemental information, for which separate analyses were conducted in order to determine whether supplemental information would influence results.

Compliance with pain and distress reporting requirements

In order to determine whether authors complied with specific journal requirements, each article that corresponded with a journal that had pain and distress reporting requirements was analyzed to see if the specific requirements were followed. For example, if a journal required authors to report the name and dosage of anesthetics and analgesics, the two articles from that journal were examined to determine if the name and dosage of anesthetics and analgesics were actually mentioned. This procedure was performed

Table 2. Journal reporting requirements: categories used for the analysis and examples of each

Category: reporting requirements	Examples of reporting requirement
Basic Reporting Requirement	"Authors must include in the methods section (or for contributions without methods sections, at the end of the text), a brief statement identifying the institutional and/or licensing committee approving the experiments."
P&D Reporting Requirement	"Any study involving experiments with animals must state that their care was in accord with institution guidelines. Where applicable, the dose and schedule of anesthetics and analgesics should be reported."
No Reporting Requirement	No reporting requirement mentioned

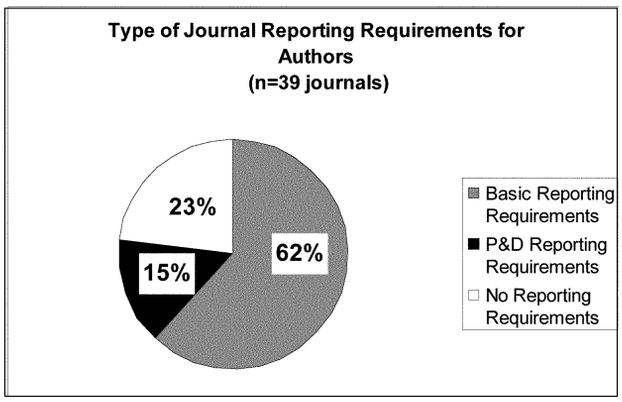

Fig. 1. Type of Journal Reporting Requirements for Authors

for all 12 articles from journals with P&D Reporting Requirements. If an item required to be reported by the journal was not applicable to the corresponding article, it was not included as being required. A compliance percentage was calculated for each article by dividing the total number of required items to be reported by the number actually reported in the article. The average compliance percentage for all twelve articles was determined by calculating the mean of the percents for each of the twelve articles.

Journal policies regarding animal use

The *Instructions to Authors* of each journal were also analyzed for policies regarding the use of animals. Journal animal use policies were labeled as falling into one of three categories: 1.) basic policy regarding animal use, "Basic Policy"; 2.) policy regarding animal use that specifically mentions pain and distress, "P&D Policy"; or 3.) no policy regarding animal use, "No Policy." See Table 3 for examples of each of these policy categories.

As with reporting requirements, the number of journals with basic policies was much higher than the other policy categories. In order to adjust for this, deviation from expectation was determined for each calculation.

The impact of animal use policies on actual reporting of pain and distress was determined by examining reporting of each of the four pain and distress factors and determining the corresponding animal use policies. A similar calculation was done in regards to reporting of *at least one* of the four pain and distress categories. For example, the percent of articles that we would expect to report at least one of the factors for each type of journal policy was subtracted from the number of articles that actually reported at least one factor, to calculate percent deviation. A positive percent deviation was translated as more articles than expected reporting at least one factor, while a negative percent deviation meant less articles than expected reported at least one factor.

Of the 76 articles, 25 of them referred to supplemental information, for which separate analyses were conducted in order to determine whether supplemental information would influence results.

Results

Journal reporting requirements

The majority (62 percent) of the 39 journals had requirements regarding general reporting of animal use, or "Basic Reporting Requirements" in their *Instructions to Authors*. Only 15 percent of the journals had requirements regarding reporting of animal use that specifically requires mention of information on how pain and distress were addressed, or "P&D Reporting Requirements" (See Fig. 1).

Reporting of pain and distress information in publications

Since two articles were acquired from each journal (regardless of type of author requirements), this meant that the majority of the 76 articles were from journals with Basic Reporting Requirements—46 articles with Basic Reporting requirements, 12 with Pain and Distress Reporting Requirements, and 18 with No Reporting Requirements.

The 76 articles were first analyzed for reporting of each of the four pain and distress factors discussed in the Methods section. Fig. 2 demonstrates that each factor was reported in 50% or fewer articles. The method of assessing animal pain and distress was most frequently reported, being mentioned in 50% of articles. Information regarding AAOD was reported in 39% of articles, OM in 30% and HE in 25%.

Correspondence between each of the four pain and distress factors and the journal reporting requirements was then examined (See Fig. 3). The articles from journals with P&D Reporting Requirements reported all four factors more than expected—AAOD, HE, MAA and OM (OM was the factor most reported by those articles), with no factor being reported below expectation.

Articles from journals with Basic Reporting Requirements reported less than expected for all factors except for AAOD. Articles from journals

Table 3. Journal policies/statements regarding animal use: categories used for the analysis and examples of each

Category: type of policy	Examples of policy type
Basic Policy	"All experiments on live vertebrates or higher invertebrates must be performed in accordance with relevant institutional and national guidelines and regulations."
P&D Policy	"[Name of Journal] will not include papers based on work that involves unnecessary pain, distress, suffering or lasting harm."
No Policy	No mention of animal use policies

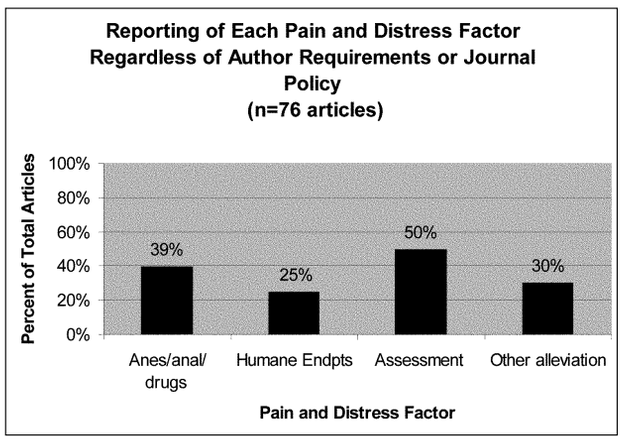

Fig. 2. Reporting of each pain and distress factor in published articles, regardless of author requirements or journal policies

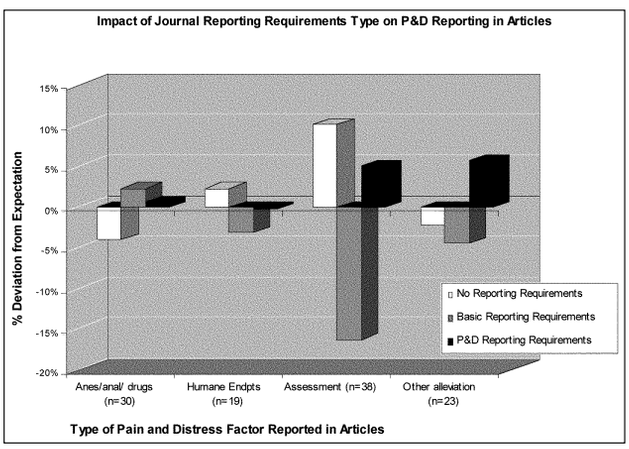

Fig. 3. Impact of journal reporting requirements on reporting of pain and distress information in articles: four pain and distress factors

with No Reporting Requirements reported less than expected for two factors (AAOD and OM) and more than expected for HE and MAA.

In some cases Basic Reporting Requirements or No Reporting Requirements had a higher positive deviation from expectation than P&D Reporting Requirements, however, articles from journals with P&D Reporting requirements were the only ones that reported at or above expectation for all four pain and distress factors.

It was found that supplemental information did not have an impact on results.

Articles were then analyzed for having reported *at least one* of the four pain and distress factors (See Fig. 4). It was found that articles from journals with P&D Reporting Requirements reported pain and distress more often than expected, with a deviation of +7%. Articles with No Reporting Requirements also reported more often than expected, at +1%. Articles with Basic Reporting Requirements reported pain and distress below expectation, at – 9%.

It was found that supplemental information did not have an impact on results.

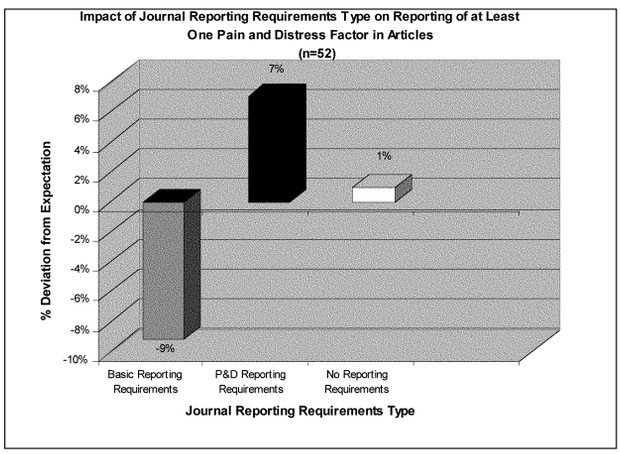

Fig. 4. Impact of journal reporting requirements on reporting of at least one of four pain and distress factors

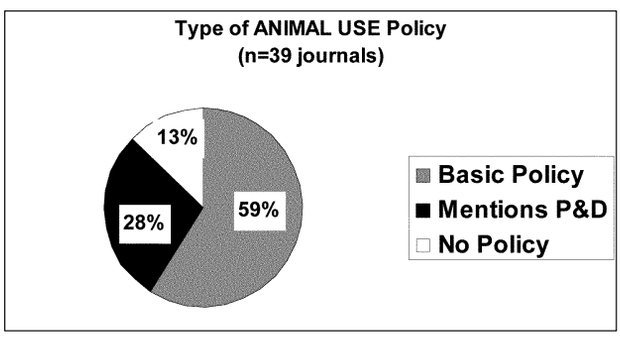

Fig. 5. Type of animal use policies in journals

Compliance- Articles with pain and distress Reporting requirements

When examining whether the authors followed the specific instructions required by each journal with P&D Reporting Requirements, it was found that the average compliance for the articles (n=12) was 87.5%, meaning that the vast majority of the articles included information that was specifically required.

Animal use policies regarding pain and distress: Analyses

Journal policies regarding animal use

The majority (59%) of the 39 journals had basic policies regarding animal use, or "Basic Animal Use Policies" in their *Instructions to Authors*. Twenty-eight percent of the journals had policies regarding animal use that specifically mention pain and distress, or "P&D Animal Use Policies" and 13% had No Policy (See Fig. 5). Overall, the majority (40) of the 76 articles were from journals with a Basic Policy, 24 with a P&D Policy, and 12 with No Policy.

Reporting of pain and distress information in publications vs. animal use policy type

When the articles were analyzed for reporting of the four factors relating to pain and distress (see Fig. 6), articles coming from journals with a P&D Policy reported three factors more than expected, with

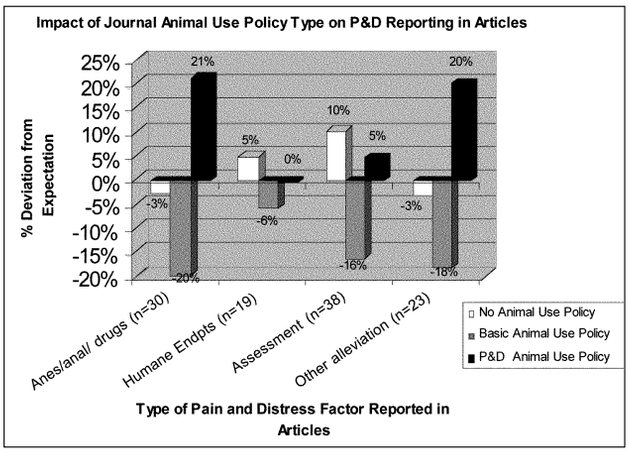

Fig. 6. Impact of journal animal use policies on reporting of pain and distress in articles

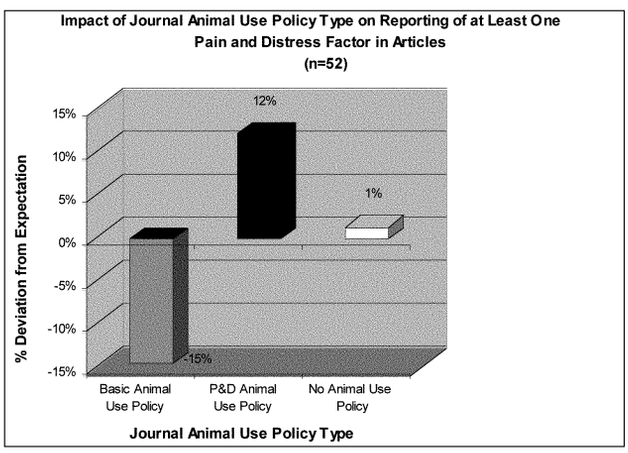

Fig. 7. Impact of journal animal use policy type on reporting of at least one of four pain and distress factors

HE being reported only slightly less than expected. AAOD and OM were the two factors most reported above expected in journals with a P&D Policy at 21% and 20% respectively. Articles from journals with a Basic Policy reported far less than expected for all four factors, while articles from journals with No Policy reported less than expected for two factors (AAOD and OM) and more than expected for the other two factors (HE and MAA).

Articles were then analyzed for reporting of *at least one* of the four pain and distress factors. Overall, articles from journals with a P&D Policy reported pain and distress more often than expected, at 12%. (See Figure 7). Those articles with No Policy also reported pain and distress above expectation, at 1%. Those with a Basic Policy reported significantly below expectation at -15%. When the same analysis was performed on the articles *and* articles' supplemental information, the addition of the supplemental information did change the results.

Discussion

It has long been argued that inclusion of animal pain and distress information in published articles would be beneficial to scientists, animal welfare, and quality of science. This current analysis sought to determine the status of reporting of pain and distress information in published articles and whether journal requirements for inclusion of such information or general policy statements made by journals that convey concern about animal pain and distress influence the extent of this reporting. The results of this analysis assist in drawing conclusions about what influences reporting of pain and distress information.

Table 4. Previous Studies on Journals' Author Reporting Requirements

Study and year	n=? journals	Percent with reporting requirements regarding animal use
Boisvert 1997	46	52%
van Zutphen (unpublished) 1998-1999	83	41%
Gomez & Conlee (current analysis)	39	77%

When interpreting the results of our analyses, it is important to take some things into consideration. In regards to the analyses of whether four specific factors relevant to pain and distress were reported in articles (namely, anesthetics/analgesics or other drugs; humane endpoints; method of animal pain and distress assessment; and other methods to alleviate pain and distress), it is important to recognize that all four pain and distress factors may not apply to each study. For example, if a paper was about an animal model of infectious disease, anesthetics or analgesics wouldn't address the distress caused by the disease and therefore wouldn't have been applicable. As a result, some of the trends in reporting by authors may appear to be weaker than they actually were.

Furthermore, while this analysis only included information reported in articles and the corresponding supplemental information, it did *not* include references to past papers. For example, if a methods section said "See xx paper from 1998 for a detailed explanation of the methods used", the information in the 1998 paper was not analyzed. Because the articles are journal-specific, reporting was limited to what was published by *that journal*. We believe that journal editors should not be satisfied with references to other journal's articles for an explanation of methods used.

We reported here that 77 percent of the journals examined had some kind of reporting requirements or policy related to animal use , which is higher than has been found in the past (See Table 4.). These statistics may be an indicator that requirements regarding reporting of animal use information have increased over time, likely due to proactive efforts on this issue. Despite this increase, the results from our analysis demonstrate that pain and distress assessment and

alleviation is still often not reported in published articles. While this was a disappointing finding, it highlights the need for stakeholders to take more proactive measures to increase attention to animal pain and distress.

Our most important finding was that journal requirements for authors to report pain and distress information do positively impact whether authors report such information. Interestingly, having an animal use policy regarding pain and distress (i.e. a general statement that conveys concern or expectations about animal use but doesn't actually require inclusion of information in the manuscript) also encourages reporting of pain and distress information.

While it is clear that journal policies and reporting requirements regarding pain and distress drive reporting of pain and distress information, "basic policies" and "basic reporting requirements" as well as those journals that have no policies or reporting requirements, presented some interesting findings. Journals that fall into the category of Basic Policy or Basic Reporting Requirements seem to actually discourage reporting of pain and distress information by authors. While this seems counterintuitive, one explanation may be that if authors are required to make a statement that all animal welfare laws were followed, for example, it may lead them to decide that additional information regarding animal pain and distress isn't necessary. This seems to be an unintended consequence of efforts by some to push for journals to adopt basic policies. Basic policies or reporting requirements may still draw attention to welfare issues and may improve welfare in general, but still have an overall negative impact on inclusion of information regarding animal pain and distress in published articles.

The results of journals with no animal use policies or reporting requirements were varied, but resulted in reporting of animal pain and distress slightly above expectation. While our analysis revealed that having no policy or reporting requirements was favorable over a basic policy or basic reporting requirements, it must be emphasized that pain and distress reporting requirements and policies were the most beneficial in terms of reporting information on pain and distress assessment and alleviation.

As a result of our findings, journals should consider adopting pain and distress reporting requirements and should make strong policy statements regarding the welfare of animals used for research purposes. Once such requirements and policies are adopted, reviewers and editors should ensure compliance with the requirements and also measure the impact of these changes.

One obstacle faced today is the purported lack of space in journals, but this can be overcome by the use of online supplemental information. Our analysis demonstrated that supplemental information currently isn't being used for reporting of pain and distress information, but it could be if journals encouraged authors to do so. Journals should move in this direction and require that all welfare information be easily accessible either online or in the hard copy of the journal.

In addition to individual journals, journal editor associations could also play an important role in regards to animal welfare. Alfaro (2005) recommended that animal use reporting requirements "[be incorporated] into the International Committee of Medical Journals Editors (ICMJE) and, later, into the Instructions for Authors of peer-reviewed journals." Maybe if ICMJE adopted requirements for reporting pain and distress information in articles it would further hasten journals to adopt these requirements. While the current study focused on pain and distress, other aspects of animal welfare, such as housing and environmental enrichment, are important as well and should be incorporated into reporting requirements as well.

For future study, a more extensive analysis with a larger sample size would be beneficial. This study also only used high impact journals, whereas a larger overview of journals should be conducted. It is likely that the need for pain and distress requirements would be even more evident than was found here.

The careers of scientists often depend upon publication of their work, therefore journals can, undoubtedly, play a leadership role in information sharing and ensuring that animal pain, distress and welfare are properly addressed.

Acknowledgements

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