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Estimates of Worldwide Laboratory Animal Use

127 Million Non-human Vertebrates Used Worldwide for Scientific Purposes in 2005

Dear Editor,

Taylor and colleagues are to be commended for their exceedingly informative estimates of national and worldwide laboratory animal use in 2005.[1] Reasonably accurate assessments of animal use, both in specific countries, and globally, over time, are fundamental when assessing compliance with Three Rs strategies of Replacement, Refinement and Reduction of animal use,[2] or when seeking to identify regions in which implementation is relatively advanced or particularly poor.

After adjusting official data for 37 countries to match EU definitions of animals and experimental procedures, and other relevant EU criteria,[3] Taylor and colleagues estimated that a total of 50,425,021 animals were used in 2005. By demonstrating a highly significant, positive linear correlation between animal use in these countries and animal study publication rates the following year, they were able to predict that 7,914,951 additional animals were used in 142 remaining countries for which only publication figures were available. They included all nations with a human population greater than 200,000. In total, they estimated that 58,339,972 living non-human vertebrates were subjected to fundamental or medically-applied biomedical research, toxicity testing, or educational use, within these 179 countries, in 2005.

Additional animal use

Although not included within these EU definitions, animals killed for the provision of experimental tissues, animals used to maintain established genetically-modified (GM) strains, or bred for laboratory use but killed as surplus to requirements, also give rise to serious bioethical concerns, and are important when considering the merits of laboratory animal use. When these additional categories were included, the estimate increased by 97.6%, to a total of 115,279,785 non-human vertebrates used worldwide.

Substantial though these estimates are, they nevertheless appear to have been overly conservative, because they relied on 'arithmetic,' or unweighted, rather than 'weighted', means. Consider, for example, the case of animals used to maintain GM strains. As reported by Taylor and colleagues, data was available for only two countries:

— In Great Britain (GB), data were available for 2005. 1,874,207 animals were used for experimental purposes as defined within the EU (GB_{EU}), and an additional 630,755 procedures were conducted to maintain GM strains (GB_{GM}; in this case, the number of procedures was likely to equal the number of animals used). $GB_{TOT} = GB_{EU} + GB_{GM} = 2{,}504{,}962$, and $GB_{TOT}/GB_{EU} = 1.337$. Hence, an extra 33.7% of animals were used to maintain GM strains.

— In The Netherlands (NL), NL_{GM} was unknown for 2005, but was 3,834 in 2006. So, for 2005, Taylor and colleagues assumed an identical NL_{GM} of 3,834, which they used in conjunction with the 2006 NL_{EU} of 523,956, to maintain the 2006 proportion. $NL_{TOT} = NL_{EU} + NL_{GM} = 527{,}790$, and $NL_{TOT}/NL_{EU} = 1.007$. So, an extra 0.7% of animals were used to maintain GM strains.

By according an equal weighting of 0.5 to both the GB and NL proportions of 1.337 and 1.007, respectively, Taylor and colleagues derived an arithmetic mean of 1.172, representing an additional 17.2% of animals used to maintain GM strains in 2005. However, the contributions of GB and NL were not equal, because $GB_{TOT} = 2{,}504{,}962$ is quantitatively far more significant than $NL_{TOT} = 527{,}790$.

Weighted means accord an importance or 'weight' to each contributing element that accurately reflects its proportional contribution to the whole. The derivation of weighted means is described at the statistical website http://www.statistics.com/resources/glossary/w/wmean.php, and elsewhere. In this case, the contribution of GB should be accorded greater weighting than that of NL. The correct weighting factor for GB is $GB_{TOT}/(GB_{TOT} + NL_{TOT}) = 0.826$, and the correct weighting factor for NL is $NL_{TOT}/(GB_{TOT} + NL_{TOT}) = 0.174$.

Hence, whereas the arithmetic mean = $[0.5 \times GB_{TOT}/GB_{EU}] + [0.5 \times NL_{TOT}/NL_{EU}]$, the weighted mean = $[\{GB_{TOT}/(GB_{TOT} + NL_{TOT})\} \times GB_{TOT}/GB_{EU}] + [\{NL_{TOT}/(GB_{TOT} + NL_{TOT})\} \times NL_{TOT}/NL_{EU}] = [0.826 \times 1.337] + [0.174 \times 1.007] = 1.280$, or, without introducing rounding approximations into the formula, 1.279. This represents an increase of 27.9%, rather than 17.2%, when animals used to maintain GM strains are considered.

Similarly, weighted means can be derived to estimate the number of animals killed for the provision of experimental tissues (21.6%), and bred for laboratory use but killed as surplus to requirements (68.1%) (Table 1).

Table 1: Proportional increases in laboratory animal use

Animal Use	Arithmetic Mean	Weighted Mean
Provision of tissues	21.1	21.6
Maintenance of GM strains	17.2	27.9
Surplus to requirements	59.3	68.1
Total	**97.6**	**117.6**

Worldwide animal use in 2005

Hence, in addition to the 58,339,972 living non-human vertebrates predicted by Taylor and colleagues, approximately 68,607,807 animals (117.6%) may have been killed for the provision of experimental tissues, used to maintain established GM strains, or bred for laboratory use but killed as surplus to requirements. This results in a grand total of almost 127 million non-human vertebrates used worldwide in 2005.

Estimate limitations

As stated by Taylor and colleagues, however, the very limited number of countries for which data were available markedly limits the reliability of these additional estimates. Numbers of animals killed for the provision of experimental tissues were available for six countries, while numbers of animals used to maintain GM strains, or bred for laboratory use but killed as surplus to requirements, were available for only two countries, in each case. On the other hand, the EU countries involved often used very large numbers of animals, somewhat increasing the reliability of the estimations derived.

Furthermore, in each of these three cases, the proportions of animals used in 2005 were not directly available for some countries, and so were assumed to be identical to those derived by using figures from the closest available years. For those instances for which data were available, the errors introduced by such assumptions appeared to be small. For example, when compared to the 2005 NL_{EU} of 531,199, the 2006 NL_{EU} of 523,956 was only 1.4% lower. Nevertheless, as acknowledged by Taylor and colleagues, these estimates include a number of significant approximations. Despite these, they are considerably more reliable than previous estimates, which have largely been based on varying expert opinions, or very limited surveys.

Despite their magnitude, it appears likely that these estimates remain highly conservative. As identified by Taylor and colleagues, for example, their estimate of 17.3 million living vertebrates used within the USA is very significantly less than a 2000 US Animal Plant Health Inspection Service estimate of 31–156 million, based on extrapolation from the results of a survey of only 50 of 2,000 research institutions.[4] Furthermore, these estimates exclude several other categories of concern, such as some invertebrate species now understood to have advanced capacity for suffering, including certain cephalopods, and studies on advanced fetal developmental stages.

Conclusions

Despite the conservatism of these estimates, and the exclusion of some categories of concern, the total approximation of 127 million laboratory animals used worldwide in 2005 remains enormous, by any reasonable standard. It clearly demonstrates the need for considerably greater compliance with the Three Rs — which are universally recognised as an essential component of good laboratory animal practice, both for ethical reasons, and to increase the quality of the research and the robustness of subsequent results.

To increase the reliability and international comparability of laboratory animal estimates, thereby facilitating governmental and public scrutiny of the utility of social expenditure on associated research, considerably greater reporting and harmonisation of laboratory animal statistics internationally is also required. The overwhelming majority of countries that currently fail to provide adequate official statistics, should begin to do so, in a coordinated fashion.

Where laboratory animal use is large overall, or disproportionally large in comparison to countries with similar research budgets or publication rates, or is increasing over time, mechanisms to increase compliance with the Three Rs are likely to be particularly necessary.

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Estimates for Worldwide Laboratory Animal Use in 2005: Authors' Response

Dear Editor,

We thank Andrew Knight for his comments on our paper.[1] He suggests the use of weighted means as an alternative way of calculating the animal-use figure that includes extrapolations for animals killed only for tissue supply, to maintain genetically-modified strains and animals bred for laboratory use but considered as surplus to requirements. Neither we nor our reviewers suggested the use of weighted means and, whilst it might be an appropriate approach, it adds little to the reliability of our extrapolations. Consultation with a senior, independent statistician has confirmed this position.

The final extrapolations leading to our "more-comprehensive" global total of 115.3 million were based on the average percentage of animals reported by only five countries for animals killed only for tissue supply; by two countries for animals used to maintain breeding colonies; and by two countries for animals bred for laboratory use but considered as surplus to requirements.[1] Given this less than ideal sample size, any mean (no matter how calculated) does not command complete confidence, a caveat given in our original paper.

We could have presented our headline figure of 115.3 million animals within a range, placing the mean in its correct context. The range could be derived by adding the final figure derived from the model (58,339,972) to the sum of the smallest percentage for each of the three additional animal uses and the sum of the largest percentage for each of the three additional animal uses (see Table 1). This results in a final range figure of 82,434,380 to 154,075,866 animals used in 2005 worldwide (82 to 154 million). This range would encompass Andrew's weighted mean estimate and the possibility that animal use by countries such as USA and China has been underestimated by our approach — a possibility strongly suspected by estimates provided by both those working with laboratory animals[2] and surveying their use.[3]

We reiterate our assertion that what is now needed is more complete and accurate statistics from more countries, especially those who use animals heavily. Our estimates for global animal use remain the best to date, although we acknowledge they are frustratingly incomplete.

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Table 1: Calculating the range for the final extrapolated figure for animal use

Additional animal use	Smallest percentage	Largest percentage
Provision of tissues	2.4% (Norway, 2005)	50.1% (Sweden, 2005)
Maintenance of GM strains	0.7% (The Netherlands, 2006)	33.7% (Britain, 2005)
Surplus to requirements	38.2% (Norway, 2005)	80.3% (Britain, 2005)
Total percentage (extrapolation factor)	**41.3%** (1.413)	**164.1%** (2.641)
Final estimate (total of 58,339,972 plus extrapolation factor)	**82,434,380**	**154,075,866**

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