



Ottawa Hospital
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Does interpretation of the principle of reduction by ethics committees lead to underpowered studies?

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The Dilemma

- Too many
 - Animals lives are wasted
- Too few
 - May lead to type II error (false negative)
 - Animals lives are wasted



Reduction

“Reduction means reduction the numbers of animals used to obtain information of given amount and precision.”



Sample size calculations in randomised trials: mandatory and mystical

Kenneth F Schulz, David A Grimes





Preclinical

- Few studies report use of sample size calculations
 - e.g. [Kilkenny et al 2009](#)
- Evidence of poor reporting



Increasing value and reducing waste in biomedical research regulation and management

Rustam Al-Shahi Salman, Elaine Beller, Jonathan Kagan, Elina Hemminki, Robert S Phillips, Julian Savulescu, Malcolm Macleod, Janet Wisely, Iain Chalmers

“...few ethics review panels require investigators to increase the number of animals used in a proposed research programme... suggests that the principle of reduction takes precedence over the need for optimum experimental design.”



In Canada...

- “...the number of animals to be used must be optimized to the greatest extent possible consistent with sound scientific and statistical standards, i.e., not below or in excess of the number required to produce statistically valid experimental data.”
- “...to emphasize reduction of animal use within an appropriate experimental design, while ensuring that sufficient numbers of animals will be used to fulfill requirements for statistical significance/scientific validity in the case of research projects...”



Question

- How do individuals on ethic review panels view Reduction and optimum experimental design?



Survey of Canadian Animal Care Committee (ACC) Members

- Online Survey
- 15 Questions on Practices and Perceptions
 - Reduction
 - Sample Size Calculations
- Population
 - 132 ACC Co-ordinators contacted
 - 440 ACC members received survey from co-ordinators
 - ~97 Institutions (Academic, Government, Industry)
- Responses
 - 34% response rate (n=149)



When evaluating whether the proposed number of animals in an ethics protocol submission is appropriate, what factors does your local Animal Care Committee consider?

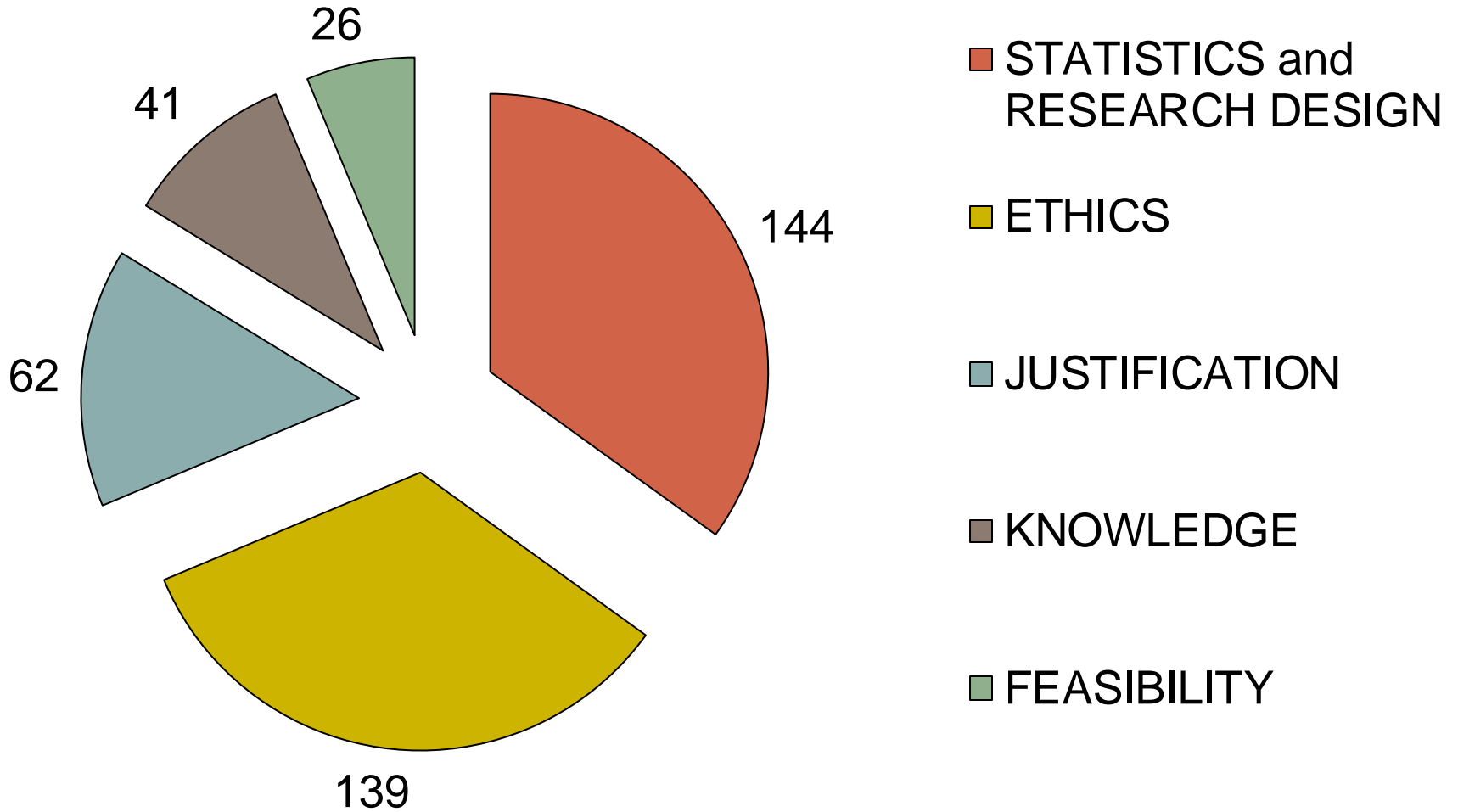
149 Participants Responded (100%)

412 Codes Identified (Open Coding)

5 Categories

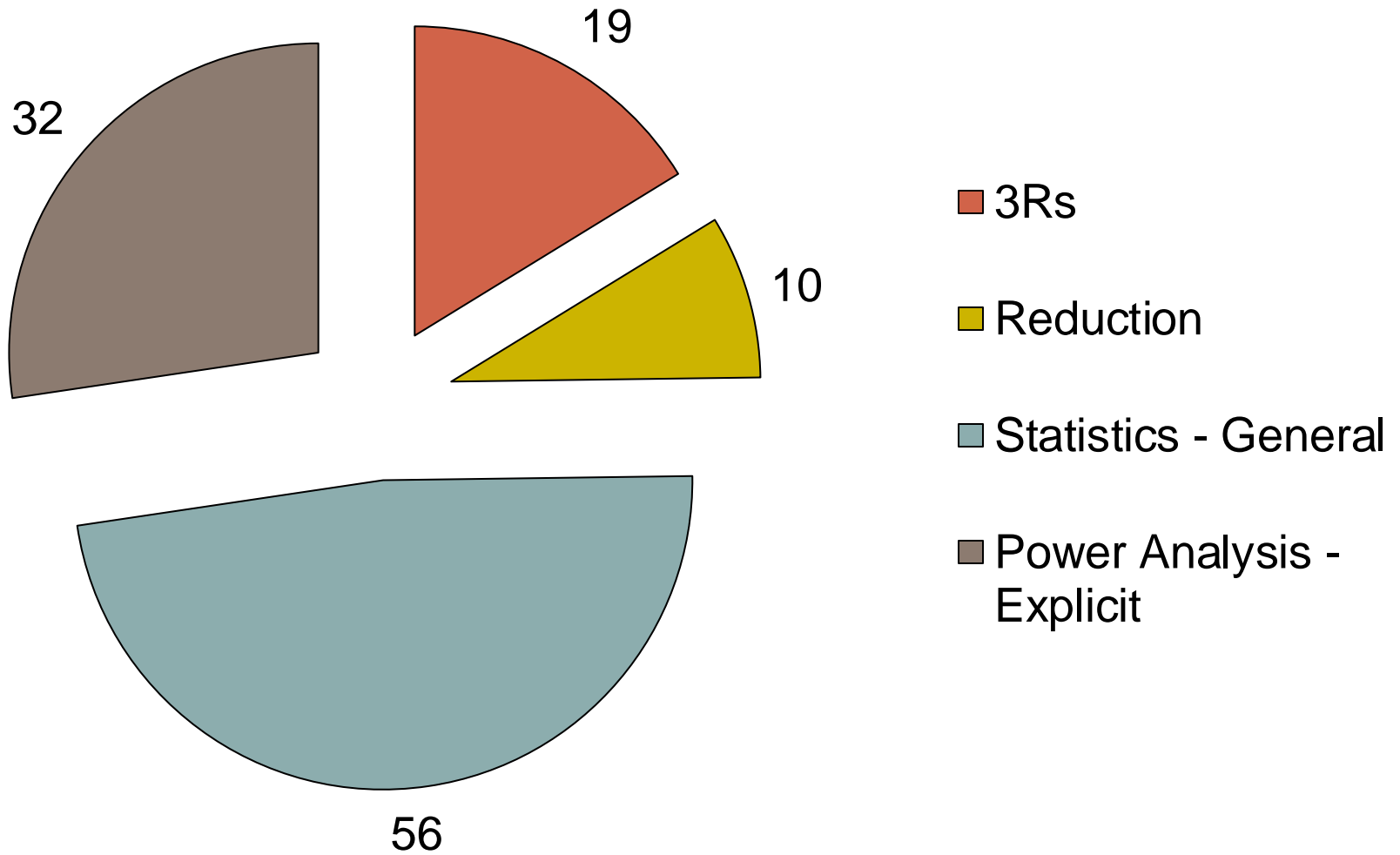


Five Categories



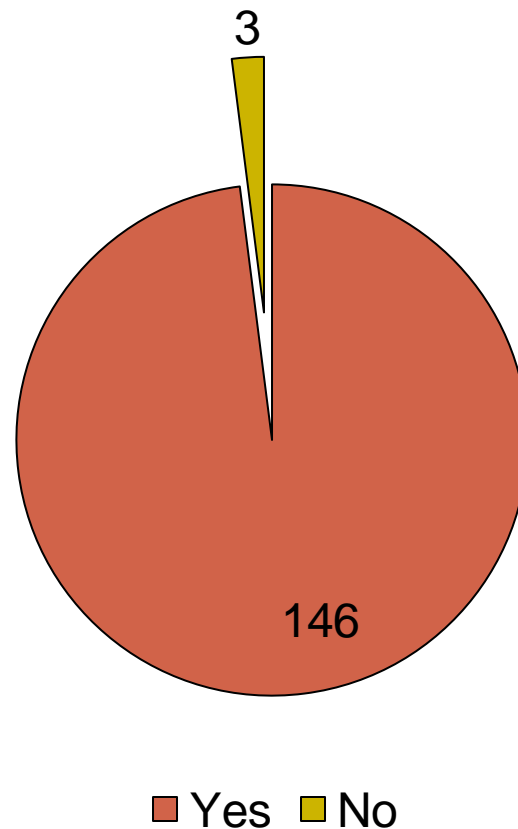


Four Codes Related to Reduction and Sample Size Calculations



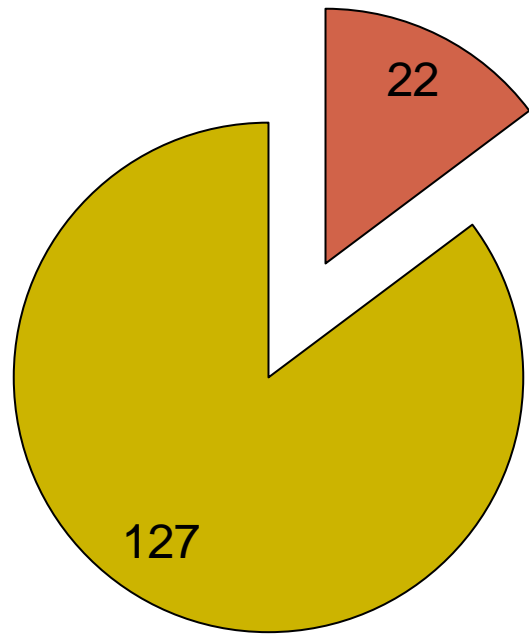


When evaluating whether the proposed number of animals is appropriate; does the ACC consider the principle of Reduction?





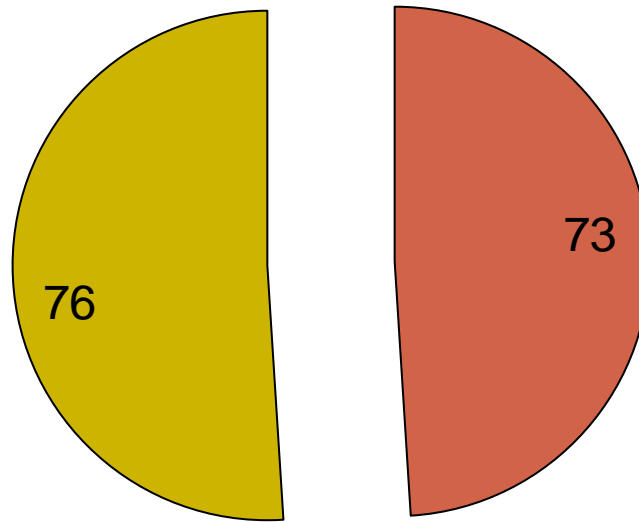
Do you consider that the principle of Reduction is in conflict with using sample size calculations to determine the number of animals needed for experiments?



■ Yes ■ No



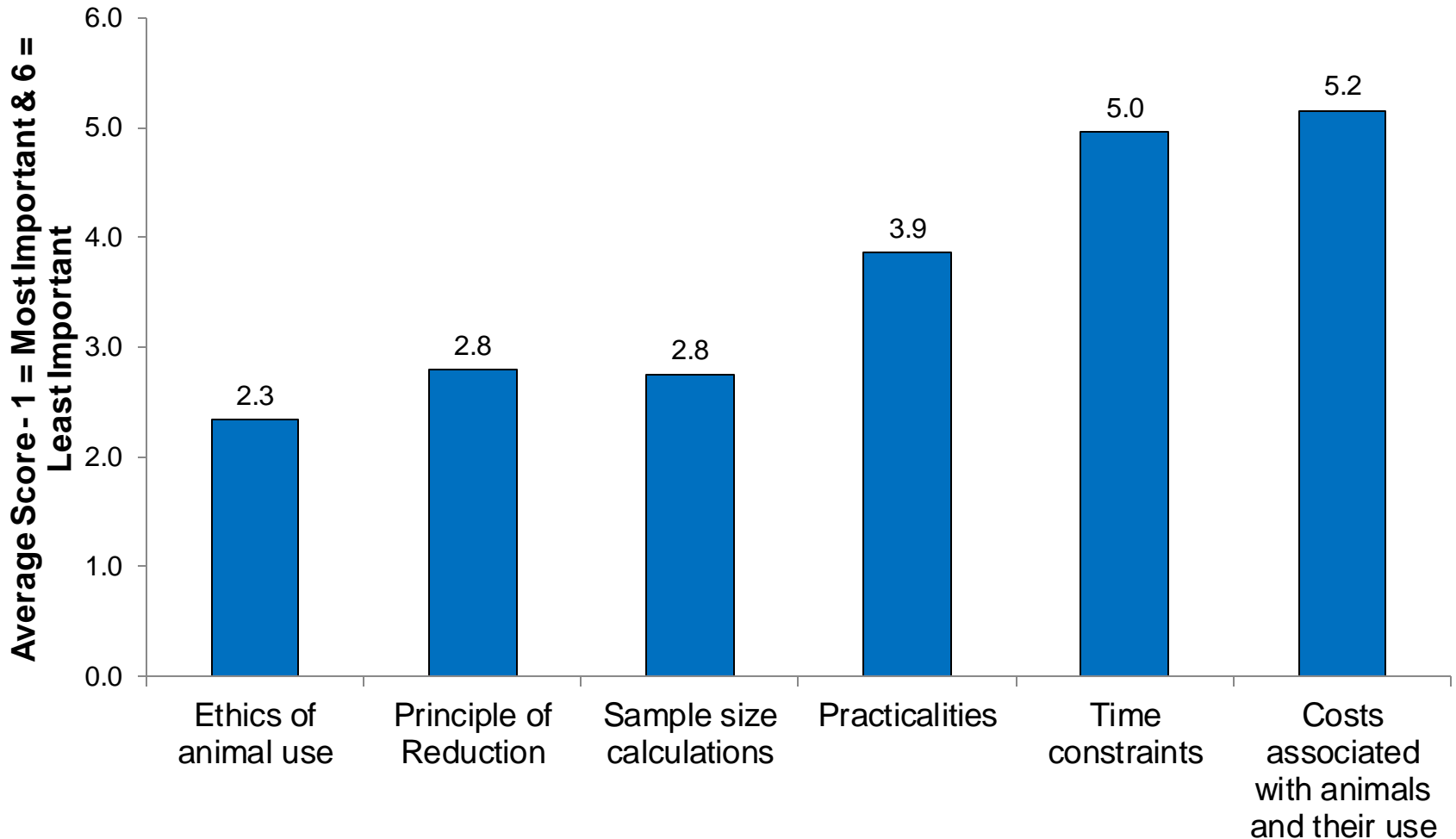
Are you aware of any occasion when the ACC has asked for an increase in the number of animals proposed because they were considered insufficient?



■ Yes ■ No

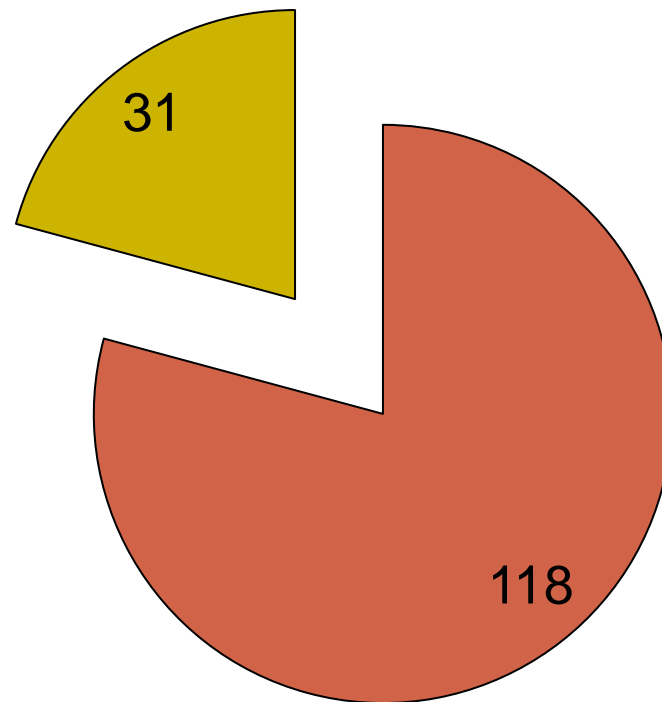


Please rate these factors from most to least important for determining the appropriate number of animals for an individual experiment (1 Most, 6 Least):





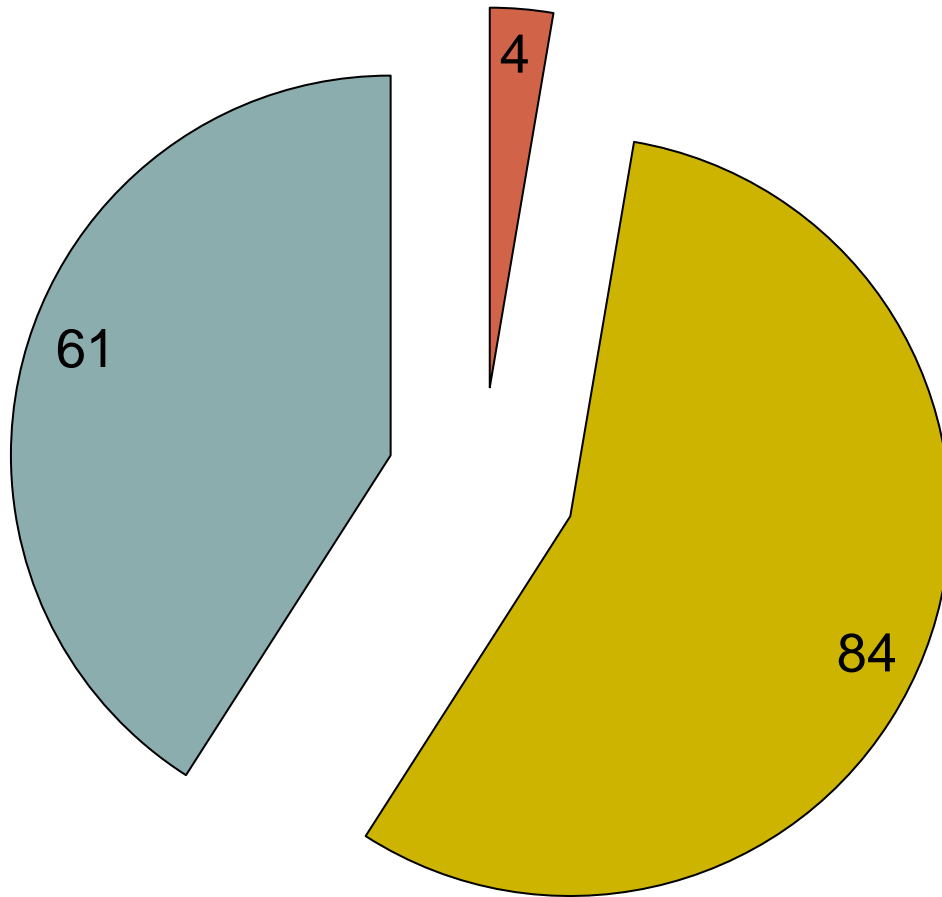
Does the Animal Care Committee evaluate the research design of individual experiments within ethics protocol submissions?



■ Yes ■ No



Which of the following statements do you think is most important?



- Minimizing the total number of animals used in the experiments
- Minimizing the number of animals needed to achieve worthwhile research objectives
- Minimizing the suffering of animals even if that means using more animals in experiments



Summary

- Generally, no perceived conflict between Reduction and optimal experimental design or sample size calculations
- Half of members recall cases where animal numbers are increased
- Minimizing the number of animals is important, but not at the expense of optimal experimental design



Limitations

- Practice and perception may differ
- Sample size samba
- Generalizability (Canadian system)



Future Directions

- Animal Use Protocols (AUP)
 - What reporting on reduction and sample size is required (national standards)?
 - What differences exist between Universities AUP protocol templates?
 - How frequently are sample size calculations included in AUPs (direct evidence)?



Support



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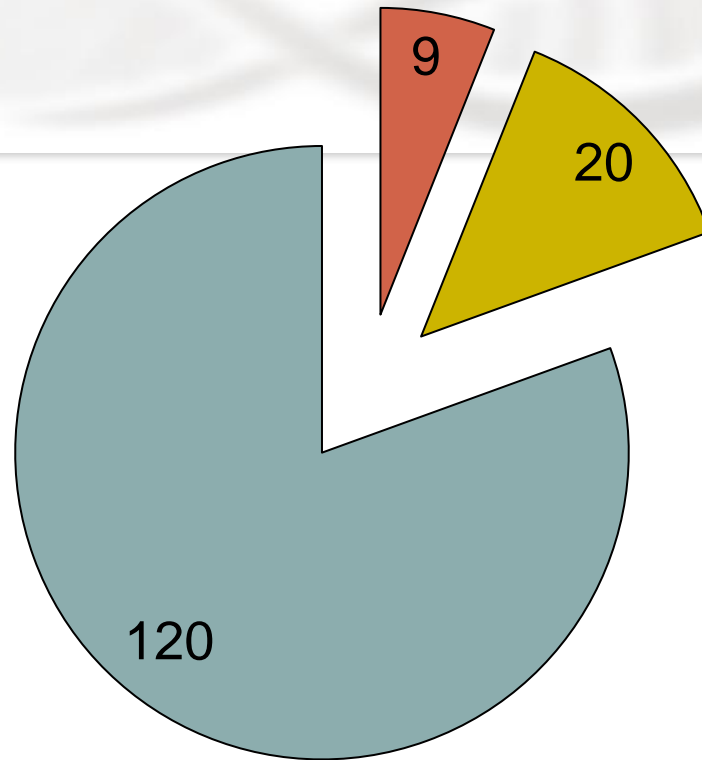
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- Ensure that the number of animals to be used must be optimized to the greatest extent possible consistent with sound scientific and statistical standards, i.e., not below or in excess of the number required to produce statistically valid experimental data
- Emphasize reduction of animal use within an appropriate experimental design, while ensuring that sufficient numbers of animals will be used to fulfill requirements for statistical significance/scientific validity in the case of research projects
- Both ensure optimisation and emphasise reduction as in a and b above