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Research to Promote Longevity and Healthspan in Companion Dogs: A Pediatric Perspective.

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This proposed rapamycin trial in companion dogs raises the question of the social value of research designed to increase healthy lifespan (or “healthspan”) in animals. Concerns have been raised about the appropriateness of promoting “longevity” as a goal of the research. This broad question is enduring and is related to the distinction between health and disease and the goals of medicine. It evokes a recurrent theme in literature from Wilde (*The Picture of Dorian Gray*) to Thomas (“Do not go gentle into that good night”) about our acceptance of aging. While it is beyond the scope of this commentary to explore this concern in detail, we think that efforts to extend the duration of healthy life of humans and companion animals through the prevention and treatment of conditions of aging, including cardiovascular disease, cancer, and immune decline are suitable goals for medicine. Of course, another *complementary* goal of medicine is also to assist patients and families making deliberative choices towards the end of life, and appreciating that death, while often tragic and sad, is part of what makes us human (or canine, as the case may be).

The case also raises the question about the appropriateness of the dogs’ participation. While the inclusion of animals in research is typically viewed in the context of laboratory-based animal research, the companion dogs in this study are being enrolled as “study participants,” making the situation bear striking similarities to pediatric research in which parents enroll their children. The medical care of companion animals and children shares another common feature: much is done without evidence from randomized controlled trials. Just as there has been an increase in pediatric clinical research over the past decade, there has also been an increase in the availability of clinical trials for companion animals. Most notably this has occurred in oncology and, as with pediatric medicine, such research is typically done in the *context of providing medical care* for companion animals. In fact, it is precisely the ongoing use of clinical interventions without evidence that provides the strongest ethical justification for conducting clinical research in both populations. And just as it is important to think deliberately about how best to engage and respect parents when they are asked permission to enroll their young children in clinical research, it is necessary to think deliberately about

how best to engage and respect the “owners” when they are asked permission to enroll their companion animals in research.

The Pediatric Research Ethics Framework

Thus, the framework that has been developed for pediatric research under the federal regulations (Department of Health and Human Services, 2009) can be a useful starting place in guiding both researchers and those charged with oversight for companion animal research. A key component of this framework is the concept of parental permission, which is distinct from consent as it is a decision made by a surrogate on behalf of a participant who cannot make a decision for themselves (Katz, Webb, Committee on Bioethics 2016). A related aspect of this framework is the importance of independent assessments of benefits and risks, before parents are even given an opportunity to give permission (Freedman, Fuks, Weijer 1993). A third aspect of this framework is the useful distinction between research activities that offer a prospect of direct benefit, and those that are justified on the basis of the advancement of scientific knowledge (Roth-Cline and Nelson 2015).

The proposed rapamycin trial offers a prospect of direct benefit to extend life span based on previous animal studies. Within the context of the pediatric regulations, such a study would also have a balance of benefits and risks such that the risks are justified by the anticipated benefits, and that the balance is as favorable as that provided by available alternative approaches. It is beyond the scope of this commentary to assess the risks and benefits of this trial, other than to suggest that it is plausible for such a trial to meet these criteria.

One challenge for the rapamycin study will be to develop a sound recruitment and permission process. This is especially important given the likely motivation of owners to extend the healthy lifespan of their own companion animal rather than being motivated to ask their dog to sacrifice for the pursuit of generalizable knowledge. Further, given the natural lifespan of dogs, we can anticipate that a proportion of the enrolled animals will die during the study. This reinforces the importance of developing materials and communication approaches to set realistic expectations. It may also be valuable to empirically evaluate owners’ motivations and experiences to inform future recruitment approaches.

Approaches to Oversight

Another opportunity to borrow from the world of human subjects’ protection is to consider what approaches for independent oversight of clinical trials for companion animals should be used. While the Institutional Animal Care and Use Committee is an important starting place for oversight for the use of animals in research, Institutional Review Boards, would be involved in this study since data is collected from the owners, making them research subjects themselves. In pediatric research, IRBs also consider not only the interests of children, but also consider the rights and welfare of the parents, as decision-makers for their children. However, an IRB would not typically be involved in overseeing how veterinary researchers interact with owners as the surrogate decision-makers for their dogs. In this case, *since the IRB is already involved because of the data collection from owners, the IRBs could also*

consider how the researchers interact with the owners as the responsible party for the companion animals.

Having IRB expand their focus to consider the owners as *in loco parentis* may be useful for those studies designed to offer a prospect of direct benefit and especially when the prospect of direct benefit is either more tenuous or is not the primary goal, as would be the case for phase I oncology studies or studies like the rapamycin study. The IRB could review recruitment and promotional materials to ensure that the owners have appropriate expectations for the trial.

A data monitoring committee is another important oversight mechanism of clinical research that may play a valuable role here even though there are not typically external requirements for such an oversight process in companion animal research. Committee members could be selected to have the relevant expertise to assess study design, clinical risks and benefits, statistics, and ethics. Further, the committee would have access to interim data to ensure the appropriate and timely evaluation of adverse events, as well as determining stopping rules for such a trial.

Conclusion

The overarching relevance of the pediatric framework for studies to improve health span in companion animals, as in the rapamycin study, is to consider the impact on the dogs, as well as the indirect impact on owners serving as surrogate decision makers. Researchers should aim to treat both with respect and dignity, and to value their contribution to scientific discovery. Empirical social science research about owners' experience in this study can advance the evidence-base, so that future research can be conducted appropriately.

References

- Department of Health and Human Services. 2005 "Protection of Human Subjects (The Common Rule): Additional Protections for Children Involved as Subjects in Research. 45 CFR 46.401-409". Available at: <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#subpartd> (Accessed June 6, 2018).
- Freedman B, Fuks A, and Weijer C. 1993 "In loco parentis. Minimal risk as an ethical threshold for research upon children." *Hastings Center Report* 23 (2): 13–9.
- Katz AL, Webb SA, and Committee on Bioethics. 2016 "Informed Consent in Decision-Making in Pediatric Practice." *Pediatrics* 138 (2): e20161485. [PubMed: 27456510]
- Roth-Cline M, and Nelson RM. 2015 "Ethical Considerations in Conducting Pediatric and Neonatal Research in Clinical Pharmacology." *Current Pharmaceutical Design* 21(39): 5619–5635. [PubMed: 26323417]