Review on uses of animals in scientific research

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Abstract: It is true that animals are used in a variety ways of in biological and biomedical research. The contributions of animal research to medical science and human health are undeniable. Scientific expertise, consensus and facts on the use of animal research must be weighed accordingly to have a honest, public discussion. Animal experimentation is necessary for scientists and different researchers at the current level of knowledge for studying the pathogenesis of different disease undertake drug trials, generate a variety of biological such as immunodiagnostics, vaccines to alleviate suffering in the human and animals themselves. Animals that are used for investigation and qualification of experiments and biomedical research are the base for different purposes of scientific studies we must use in a responsible and reasonable manner with no stress, pain and discomfort when we conduct studying with them based on the role and regulation of ethical arguments.
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Introduction

From time immemorial, peoples were depended on animals for their survival, either as food (cattle, sheep, pigs, poultry etc.) or for competition and companionship (horse, dog, cat, parrots etc). As they knew more about their surroundings, they extended this dependence to acquisition of knowledge, dating back to the days of the great physician Galen (129-200 AD), who used animals to demonstrate that arteries contained blood and not air. We have come a long way since then and specially breed laboratory animals consisting of mice, rats, hamsters, guinea pigs, rabbits, cats, dogs, monkeys, higher farm animals and a variety of birds and other lower forms are now integral part of biomedical research. The use of animals in research is one of many investigative methods used in science today, and has played a crucial role in development of modern medical treatments. Use of animals in research will continue to be necessary as long as researchers seek new improvement and information. Faced with irrefutable causal links between animal studies and medical breakthroughs, opponents of animal research typically respond with a claim and a demand of their own. The claim is that such research represents work performed decades ago (Shanks and Pyles, 2007).

On one hand, they accept that about the respiratory, circulatory and digestive systems from animals that has been relevant for human health. There is little or nothing left to be understood about basic biological function from animals that is relevant to human conditions. In other words, the entire field of animal research is declared to be exhausted of fundamental results (Greek, 2011).

Animal models of disease are only one way in which animals are used in science. A substantial amount of research is aimed at understanding the basic biological processes of life and disease, so-called basic research. The function of cells, how they communicate, how they develop, how they age and how they die are all part of the foundations of biological science. Some have characterized this research as “knowledge for knowledge’s sake”, the benefits of which, we are told, are so unlikely to materialize that one cannot possibly justify the use of animals in this type of work. However, it is precisely such basic knowledge, from the abstract geometric theorems of ancient Greece, to the physical models of atoms and subatomic particles, to the inner workings of cells and organs that are responsible for our greatest scientific advancements. The mission of the National Institutes of Health (NIH) recognizes this fact in its opening statement, NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life and reduce the burdens of illness and disability (NIH, 2011). Therefore the main objectives of this paper are to Review:-.

- ✓ The application of animals in scientific research.
- ✓ Interaction and ethical issues between scientist and animals.
- ✓ The aim of laboratory animals on both animal and human health.

2. Literature Review

2.1. Use of animals in experiments

Each year more than 20 million animals are used in biomedical research projects, with more than 90 percent of them being mice, rats, and other rodents. Of the other animal species, about 65,000 dogs, 23,000 cats, and 55,000 primates were used for research purposes in the United States between October 1, 2003 and September 30, 2004. In most cases, these animals are specifically breed for research purposes and are purchased from animal breeders. Every major medical advance of this century has depended on animal research (Troll and Charles, 1987). Importance of Animals in Research involving laboratory animals is necessary to ensure and enhance human and animal health and protection of the environment. In the absence of human data, research with experimental animals is the most reliable means of detecting important toxic properties of chemical substances and for estimating risks to human and environmental health. Research animals must be used in a responsible manner. Scientifically-valid research designed to reduce, refine or replace the need for laboratory animals is encouraged (AMA, 2003*)*.

Assessing the scope of their use in biomedical research*,* Charles and Wise, states that there's never been a medical therapy developed without animals. It is true that animals are used in a variety of ways in biological and biomedical research. Certainly, many fundamental biological discoveries in the past three centuries were made by studying animals. Moreover, animal studies continue to be of important scientific value in the context of basic biological and biomedical research (AHA, 2001). Research in reality, involves three facts: acquisition of new knowledge, use of animals in teaching exercises, and the testing of compounds, chemicals or devices for safety and effectiveness. There must be reasonable expectation that research involving animals will contribute significantly to present and future knowledge, which may eventually lead to the protection and improvement of the health and welfare of either humans or animals. Laboratory animals have organs and body systems similar to humans and other animals. In many cases, they are susceptible to the same diseases that affect humans. Because of this, the data derived from research on these animals can be applied directly to humans and to other animals as well. While not all biomedical research involves the use of animals, animals are essential in many areas (Beyene, 1970).

World over, new drug research as well as tests meant for assuring the quality and efficacy of pharmaceutical products /vaccines/biological are based on experiments involving animals. Toxicological studies especially those performed in rodents and dogs are the essential link between the pre clinical phase and clinical development of the drug molecule. No new drug can be introduced in clinical practice or even for the matters into clinical research unless it passes the battery of toxicity tests in animals (Salsburg, 2005). Scientists also use animals for toxicological studies. Toxicology is the study of how chemical substances interact with living systems and affect normal processes, and the use of this information to predict safe exposure levels. Toxicological research and testing helps us to live safely and to derive benefit from natural and synthetic substances while avoiding harm. Toxicologists are involved in the evaluation of household products, medicines and the effects of incidental and occupational exposure to natural and manufactured substances. Toxicology also helps us develop the best treatments in the event that accidental overexposure dose occurs. Toxicologists conduct basic research, using both whole animals and in vitro methods, to learn how various chemicals and dosages interact with living systems (Weinshilboum, 2003). Basic research is necessary to understand mechanisms that maintain living organisms and to determine baselines for physiological processes. For many chemicals that enhance the quality of our lives, the mechanism that produces the beneficial effect is the same mechanism that makes the chemical toxic. For example, aspirin reduces pain and fever by reducing the activity of enzymes in the body that normally increase production of compounds associated with pain and distress. However, acute toxicity can occur when the aspirin dose is so high that inhibition of similar enzymes in the heart interferes with normal function. Animal studies help determine the ratio between the beneficial dose and the toxic dose of medications. Toxicologists determine which levels of substance cause harm by conducting safety studies which progress from the test tube to animal studies and, in some cases, to human trials. Safety testing is needed to identify the crossover points between no impact, beneficial effects and harmful effects. For example, when alcohol is taken directly into the bloodstream and blood levels rise in direct proportion to consumption (Young, 2005).

Animals play a crucial role for experiment and biomedical research:-Cancer research uses animal experiments to develop methods for treatment and diagnosis, an animal model is also used to investigate a long list of diseases in humans and animals, the use of transgenic animals (animals that have had their genes modified by technical intervention has increased exponentially), testing new surgical techniques is often done on animals, New medicines and vaccinations are often tested on animals before they are used on humans and other animals. Animals are used in production of antibodies that are used in diagnosis of diseases in humans and animals and in cancer

research, diagnosis of physiological and pathological conditions can be obtained by a diagnostic methods (WHO,2001).

2.1.1. Fundamental biological and medical research

This is necessarily to be undertaken as to unravel the secrets of nature. If we essentially know how different tissues and organs are kept healthy, we can then find out what goes wrong when disease strikes. Fundamental research in biology and medicine are basic foundations on which future discoveries are based (Houdebine, 2007).

2.1.2. Developing new treatments for diseases

To conquer disease, a lot of work needs to be put into, by way of developing better medicines, perfecting surgical operations as well as making vaccines and finding other ways of preventing diseases. Even though much of this work is for humans, many of them are applicable to animals as well, and even some are exclusively for animals. There are many diseases which are yet to have a proper cure like multiple sclerosis, certain cancers, as well as new diseases like AIDS, Alzheimer disease etc. All these need initial input in terms of animal experiments (Grass and Sinko, 2002).

2.1.3. Preparations of natural products used in medical research and treatment

Animals can produce useful medical substances in their blood or milk, like antibodies, vaccines and hormones which are important for diagnostic tests, medical treatments, and basic research. May be at a later date, we can produce all these synthetically, but at present, most of them are produced using animals (Eds *et a*l., 1984).

2.1.4. Safety testing of chemicals and drugs

A wide range of chemicals and medicines which are used in day-to-day life, as household products, in farming, industry etc need to be tested for their safe use in humans as well as in animals. Such preliminary testing is very much essential for avoiding pollution and associated health hazards and proper healthy maintenance of the environment (AVMA, 1987).

2.1.5. Study of genetic disorders

There are many diseases which are inherited fully or partially and are caused by basic faults in a person's genetic code. Some of the animals also have similar genetic fault as humans do. There are mutant strains like dystrophic mice which have the same faulty gene as the muscular dystrophic patients. The animal thus plays a vital role in understanding and treatment of such genetic diseases. Scientists have now made such progress in molecular biology that they can now alter genes and breed strains of mice and other animals with particular genetic diseases. This may ultimately lead to treatments in genetic disorders like cystic fibrosis, sickle cell anemia and other diseases which run in families (Goldstein, 2003).

2.1.6. Development of new diagnostic tests for diseases

If the treatment of a disease is to be effective, an accurate and quick diagnosis is essential. Animal experiments are vital in this area, which include scanning of unborn babies for identifying cancers, diagnose heart diseases etc. Animal tests have paved the way for many blood tests for the diagnosis of infectious diseases (Beynen *et al.*, 1987).

2.1.7. In biology and medical education

The animals are to be used in teaching biology in schools and colleges in understanding the basic anatomy and physiology of man and other animals (Schivndaman *et al.*, 1983). There are some benefits of animals in medical research at present which are listed below in table 1.

Table 1: Contributions of animals to medical research.

No	species	Contributions
1.	Cats	Studies of AIDS, eye and ear disorders, and the nervous system.
2.	Dogs	Coronary bypass surgery; artificial heart valve insertion; pacemaker implantation; hip and other joint replacement surgery.
3	Fish	Studies of vision, liver cancer, bacterial diseases, temperature regulation, and skin tumors.
4	Mice	Studies of cancer, aging, AIDS, immunology, and genetics; embryo transfer techniques in humans and domestic and endangered animal species.
5.	Nonhuman Primates	Treatments for polio and studies of HIV and AIDS, cancer, heart disease, neurological disorders, and infectious diseases such as malaria.
6	Pigeons	Study of coronary heart disease.
7	Pigs	Burn treatments; human heart valve replacements.
8	Rabbits	Corneal transplants; drugs that lower blood cholesterol and help to stop the development of hardening of the arteries.
9	Rats	Studies to find treatment for paralysis caused by nerve damage; product safety tests; causes of some cancers; understanding tissue rejection.

Source**: (**Lafollette and Shanks, 2002).

2.2. Ethical issues for the uses of animals in biomedical research

Through biomedical research, scientists strive to better understand the causes of disease; to develop new drugs, vaccines, or procedures to prevent or treat diseases; and to test the safety of products we use every day of our lives. Through the similarities between humans and laboratory animals we can possibly justify the use of animals in this type of work (WHO, 2001).

2.2.1. Responsibility of Scientists in biomedical research

Experimental animals must be managed and cared for through the application of uniform acceptable standards, in facilities designed for animal holding, in caging which provides for comfort and safety. As well the animal's social and behavioral need must be addressed. Unnecessary pain and stress should be avoided, but may be caused by inadequate caging or animal facilities, or improper handling by personnel. Humane painless handling of animals, humane treatment of all experimental animals including proper maintenance of living conditions and minimization of distress constitutes a hall mark ethic of a civil and democratic society. The scientists should be deeply concerned about the rational and humane use of animals in research. Ethics committee should be functional in institutions. They should be concerned about avoiding unnecessary pain or suffering or injury to animals during holding, experimentation and post – experimentation period by monitoring and improving their housing, environment, feeding and veterinary care. This can be achieved by providing accreditation services to laboratories by constituting, national accreditation board of testing and calibration laboratories having membership of the international laboratory accreditation cooperation (Schivndaman *et al.*, 1983).

Animals free of clinically recognizable or latent disease and of appropriate genetic stock of strain should be chosen. Whoever the supplier, they must understand the importance of genetic quality and breeding techniques, recognize disease and maintain healthy stocks of animals. In the use of animals in research, it must be recognized that contrary to human experimentation, consent can never be given; therefore, the animal knows no reason nor sees any benefit that may be derived from its use. Although man and other animals are known to be beneficiaries of research, it is the animal on experimental study which experiences the pain and the results of the procedures, and does not know when the pain might end or be relieved (Evans and McLeod, 2003).

Both the public and policy makers need to understand not only the scientific justification for our work but also, in some cases, why we deem our studies to be morally justifiable (Alberts *et al.*, 2002).

2.2.2. Ethical arguments of scientists

The fundamental pragmatic value of biomedical enquiry to both humans and other animals is the relief of human and animal suffering and the enhancement of opportunities for individual activity and well being'. The scientists involved in biomedical research have a duty to perform and the Institutions are maintained by public funds for this purpose. The production of animal models, in terms of natural mutants, or transgenic as long as they are for pursuing a higher scientific goal need not be denied to the scientists. However, several ethical dilemmas arising from the very nature and limitations of science are inescapable. For example, it has been well argued by animal researchers that animal experimentation leads to important theoretical and practical results, benefiting both humans and animals. There is difficulty in judging prospectively which particular experiments will lead to significant results and which will prove useless. Even with calculations of probability of success, it is difficult ethically to face this not so productive use and harming of animals (Pandora *et al.*, 2004).

An area in which scientists usually face ethical dilemma is the toxicity testing on animals. Toxicity tests are routinely employed in laboratories around the world for testing new chemicals (intermediates in industrial process and chemical ingredients used in cosmetics) and new commercial products (pharmaceuticals and pesticides). These tests are intended to identify which organs of the body may be susceptible to damage by a particular chemical. Such tests are usually required for statutory regulations designed to protect health welfare of both workers/manufacturers and consumers and they generally aim at establishing the degree to which new chemical compounds have potentially toxic or irritant effects. Also all drugs intended for clinical use should undergo toxicity testing in a rodent, carnivore and a primate before it is taken for human trials. Such tests need to go on along with the ethical conflict it produces in the minds of the users as well as testers (Anon, 2000).

Another moral dilemma which the scientists face is when they have to use higher mammals more close to them like cats, dogs and primates. To pursue a particular scientific goal, the scientists should have the same consideration for all the models they use, be it a mouse or monkey. In fact, many of the animal welfare movements have its roots in the handling of these higher forms by scientists. Too many cats and dogs are more than a companion and the use of these and primates evoke a sense of empathy even to scientists.

But if special ethical consideration has to be given to the use of the higher forms then it would halt potentially significant basic or applied research (Sabourdy, 1988).

2.2.3. The balancing act between animals and scientists

The lay public often gets confused by the rigid postures assumed by the animal activists on one hand and the animal researchers on the other. After all, the general public is the beneficiary for whose benefit the war is fought by both the sides. A proper balancing seems to be necessary, where each side understand and appreciate the view point of the other. The animal activists contend that animals have rights just as human being do, and animal experimentation is a violation of these rights. Rights and responsibilities always go hand in hand. Human beings have the rights, and thus they have a responsibility towards non-human beings surrounding them. No responsibilities are attributed to non-human beings and intrinsically, they cannot have the same right as enjoyed by human beings (Richmond and Scan, 2000).

On a large scale the balancing act can be achieved by minimizing the use of animals in scientific research; testing and education by resorting to the three `R' principles of Replacement, Reduction and Refinement advocated by British Zoologist William M.S. Russel and the microbiologist Rex L. Burch in 1959. The three R`s explains how we can diminish and remove inhumanity, and define the search for alternatives to animal experiments. The ultimate goal of any animal welfare measure is the elimination of all experiments on animals that are likely to cause pain or distress. But this can be only a dream, at present since new and new disease (s) keep propping up and sometimes eliminating one may provide for another one to flourish. So the next best measure is to think of strategies that can eliminate the use of higher mammal's altogether or at least reduce the number as much as possible. The importance of their approach lies in its combination of animal welfare considerations along with good science and best practices. They defined the 3R's in the following way. 'Reduction' as a means of `lowering the number of animals used to obtain information of a given amount and precision, 'refinement' as any development leading to a decrease in the incidence of severity of inhumane procedures applied to those animals, which have to be used' and, 'replacement' as any scientific method `employing non-sentient material which may replace methods which use conscious living vertebrates (Russel and Burch, 1959).

Animal sharing an internal system adopted by any laboratory wherein whenever the animal (s) is sacrificed at the end of the experiment, the organ, tissues or body fluids not needed for that project can be shared amongst other researchers. Culling of morbid or very old animals (especially rodents) is a normal practice in many animal facilities. Replacement is the ultimate in animal welfare measures, where given purpose is achieved without conducting experiments or other scientific procedures on protected live animals. The replacement can be absolute or relative, direct or indirect, total or partial. Based on the various terms of replacements described above, different approaches can be practiced by researchers. Some of the important strategies are as follows: Avoid unnecessary repetition of experiments, and use alternatives where ever possible by seeking access to on-line data base; which give up to date lists of published research in all areas of science, use immunochemical systems to replace bioassays for detecting bacterial toxins, study enzyme structures and mechanisms of action or computer linked mannequin for teaching basic principles of medicine and applied techniques, use mathematical and computer modeling like molecular modeling, physiologically based pharmacokinetic modeling and specified computer programs to study anatomy, physiology and other processes for education and training purposes, use invitro methods which include sub-cellular fractions, tissue-slices, cell suspensions and perfused organs, and tissue culture proper (cell and organotypic cultures), including human tissue culture, in toxicity testing and for preliminary screening, use lower organisms those not protected by legislation controlling animal experiments which include invertebrates plants, fungus, bacteria and viruses. Some of them are useful as pre-screen system, especially for agrochemicals and environmental pollutants, and also for genotoxic studies and endotoxin detection, use early developmental stages of vertebrates before they reach a point at which their use in experiments and other scientific procedures is regulated, use human tissues and volunteers, wherever possible to avoid the problem of inter specific extrapolation from animals to humans and to get more mechanistic information. In nutrition studies, and sometimes for dermal toxicology, human volunteers can be sought (Richmond and Scan, 2000).

2.2.4. Need for guidelines and provision of professional training

Every country which uses animals for research has come out with a set guideline for the care and use of laboratory animals, which include housing, feeding and humane caring. The guidelines are uniform throughout the world, and strict adherences to these guidelines are made compulsory by appropriate animal welfare laws. These guidelines insist on standard environmental conditions to be provided to the animals in terms of light, temperature, humidity, ventilation standard nutritive diet etc. Enrichment can

take a variety of different forms depending on the animal. It can for example, involve to bedding and nesting materials, novel feeding techniques or social interactions. This is more true for higher mammals like cat, dog and primates (Solas, 2006).

Unlike rodents they should not be caged singly for long periods, and for their well being they should have the freedom of moving periodically into larger areas (runs) enriched with stimulating objects for exploration and group interactions. National bodies are set up in many countries for the proper care and use of experimental animals and there is an International Committee for Laboratory Animal Science (ICLAS) (currently the office of the President of ICLAS, based in USA), with a membership of about 100 countries. The ICLAS has taken up the job of setting up international guidelines for animal husbandry, experimental procedures, teaching and training of researchers and professionals in the field were published by Indian National Science Academy (Lafollette and Shanks, 2002).

The most important scientific goals and well designed protocols are worthless, if those who handle the animals are improperly trained or unskilled. Professional bungling and inadequacy of animal care with ensuing animal distress can skew experimental data and render a particular experiment useless. Attention to the training of personal concerned with animals' upkeep, and the researchers who use these animals should be the prime concern of any institution using animals (Mukerjee, 1997).

Laboratory animal science is a nascent science which mainly encompasses the fields of biosciences, medicine and veterinary and other disciplines. Its basic aim is the know-how of animals used in research (mostly rodents, rabbits, cats, dogs, primates and a variety of other species) and the appropriate way to handle them for various experimental procedures. They have to learn hands on procedures, proper anesthesia, and specification of inbreed strains and so on, as well as the three R's. Assessments of pain and distress to animals during upkeep and experimental procedures is an integral part of this training, and have to be familiar with physiological and behavioral signs of pain, control and alleviation of pain through environmental and behavioral measures and through drugs. Professionals need to be familiar even with euthanasia procedures when and wherever they are applicable (Lindl *et al.*, 2005).

2.2.5. A critical look at the use of animals in medicine

In medical research many laboratory animals are model animals, animals that are altered through genetic manipulation, surgery or injections to model human conditions. Human data is often interpreted according to data obtained from non human animals (Johnston, 2000).

Indeed there are several examples from the past where animal research has delayed rather than helped medical research. For example In the case of lung cancer studies had suggested a correlation between smoking and lung cancer as early as in 1963. However almost all animal experiments failed to show that tobacco could cause lung cancer. As a result, health warning was delayed for years (Coulston and Shubick, 1980).

In the case of polio research, animal models led to a misunderstanding of the mechanism of infection. Monkey experiments led the researchers to believe that the polio virus was transmitted through the respiratory organs. The polio virus in humans is actually transmitted through the digestive route; this misunderstanding caused failed preventing measures and delayed the development of a vaccine (Staprans and Feinberg, 2004).

Taking into account the crucial genetic, molecular, immunologic and cellular differences between humans and other animals, unwarranted focus on animal models may prevent progress in many important medical research areas. Animal models are extensively used in research on cancer, AIDS, psychology/drug abuse and genetic diseases. However the contribution of animal models to these disciplines can be disputed (Evans and McLeod, 2003).

Animal experiments are still being repeated, for good reasons or not. It's generally accepted that important findings should be successfully reproduced by independent scientists/institutions before it can be accepted as a scientific fact. However in toxicology and safety testing one might argue that more repeating of animal testing than strictly necessary is conducted. There is little sharing of information among manufacturers and regulators, and different test requirements between nations and regions can cause obstacles for mutual recognition of data. This may cause supplementary testing to satisfy different regulators. Sharing of data and equal test requirements between nations can reduce repeated animal Testing (Smith, 2009).

2.2.6. Opposition to animal use for research

In spite of the advancement in biomedical research, and the benefits derived by the society through them, the opposition to animal experiments always existed. Opposition to use animals for research draws attention to the poor quality of science on animals and some of them maintain that animal experiments have not led to significant advances in human and animal medicine. They also contend that pure scientific enquiry cannot be justified because it is simply a question of curiosity (Greek and Greek, 2004).

The other scientific opposition is the use of cell cultures has turned out to be both effective and accurate when producing vaccines. Hormones and vaccines manufactured in cell cultures are purer than those made within the animals. This reduces the need for animal test to check for the safety of the vaccines. This technique has given dramatic changes in the use of monkeys in polio vaccine production in the Netherlands. What used to be 5000 monkeys annually has been reduced to the cell cultures of only 10 monkeys, and these ten monkeys produce enough polio vaccine to supply the whole country. The usefulness of cell-cultures will increase as our knowledge about body cell improve. The interest for different aspects of medical science has varied over time. An increase in interest for cell- and molecular biology resulted in a decrease in interest for animal models. Now that the medical science has obtained more knowledge about the details about the human organism, the interest for animal models, as an intermediate, has once again grown. These fluctuations have resulted in a failing knowledge about animals, because more scientists are specialists and not generalists. As a result of these change in scientific trends with more specialists, there is a need for close co-operation between grouping of scientists like molecular biologists and veterinarians (Barnard and Neal, 1997).

3. Conclusion And Recommendations

Many medical breakthroughs have been a result of animal research, and animals have been used in experiments and it must be emphasized that use of animals in research is inevitable and cannot be abandoned in the interest of human and animal welfare. Animal experimentation is necessary at the current level of knowledge for studying the pathogenesis of different disease, undertake drug trials, and generate a variety of biological such as immunodiagnostics, vaccines to alleviate suffering in the human and animals themselves. In vitro alternate methods cannot replace animal experimentation totally but can work only as together and reduce the number of animals to the extent possible. This is why the use of animals continues to be mandatory to meet the statutory requirements. However, efforts to develop alternate methods should continuously be made so that the day will be reached when no more animals are used for experimentation. Therefore based on the above conclusions the following recommendations are forwarded:

- Animals are the base for examination of animal and human health in biomedical research.
- Scientists should use animals in a reasonable and applicable ways when they are needed and whenever they are used in order to keep their ethical argument.
- Ethical issues must be taken into consideration while using animal for biomedical research.
- Every research institute or Veterinary faculties etc, which are using animal for demonstrations / research, must have an Animal ethical committee, which should follow the guidelines of international standards. No research should be allowed to proceed without the permission from Institutional ethical committee.

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