PHOENIX ZONES INITIATIVE

A Journalist's Resource Guide to Reporting on Science, Health, and Medicine

Frequently asked questions, questions to ask, and useful resources.

FAQS AND SOURCES OF DATA

Q: How are national medical and public health research priorities determined?

Numerous studies have documented the fact that people in the United States tend to have higher disease rates and poorer health outcomes than those in many other high-income countries, despite increased spending.

Yet the US still lacks an evidence-based national research agenda to guide public health systems and practices. In the US (and other countries) systematic determination of medical and public health research priorities is limited by infrastructure gaps, disparate financing mechanisms, and data constraints.

Currently, many health research priorities are guided by the political and practical priorities of several agencies of the US Department of Health and Human Services (HHS), including the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA). Though these agencies have overlapping goals, their distinct missions differ.

For example, the National Institutes of Health is an agency of the US Department of Health and Human Services focused on medical and behavioral research. Its 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 illness and disability."

In comparison, the Centers for Disease Control and Prevention (also an agency of HHS) is focused on protecting the US from health, safety, and security threats.

And the Food and Drug Administration is focused on protecting and advancing public health, including by ensuring safe drugs, food, and biological products and medical devices.

The private sector and nonprofit organizations also set medical and public health research priorities that are determined by their various missions and stakeholders. Additionally, the government, academia, and industry often work in collaboration to determine research priorities.

Q: What is the allocation of funding for medical and public health research in the US?

In 2020, an estimated $717 billion was spent on research and experimental development (R&D) in the US alone.

The federal budget for research and development within the Department of Health and Human Services (HHS) was about $51 billion in 2022. About 97 percent of HHS R&D is allocated to the National Institutes of Health (NIH).

In fiscal year 2022, the NIH received approximately $45 billion toward medical research, approximately 47 percent of which was spent on animal research. The NIH is the largest public funder of animal research.

Far less funding is spent on prevention research.

For example, a 2019 cross-sectional study discovered that, across more than 11,000 research projects, the leading risk factors and causes of death and disability were significantly underrepresented in NIH research relative to their burden, with only 34 percent of NIH research projects addressing any of the top 10 risk factors for death, which account for 57.3 percent of the leading causes of death.

Up to half of all premature deaths in the US are attributable to preventable factors.

Diseases such as heart disease and cancer are now the top killers in the US. And poor diet has now surpassed tobacco use as the largest preventable cause of death.

Many behavioral causes of death are related to social, economic, legal, political, and environmental determinants of health, such as access to social and economic opportunities, safe homes, quality education, clean air and water, and nutritious food.

Q: What is the process and timeline for drug and device development and approval in the US?

The Food and Drug Administration (FDA) outlines five steps to the drug development and approval process in the US. This process takes an average of 10-12 years.

The five steps include

1. Discovery and Development

Discovery and development involves a range of approaches, including animal experiments, in vitro methods, microphysiological systems, computational modeling, and observations made in human medicine and other areas of research.

Once researchers identify a promising compound, they conduct further experiments to gather information on how it's absorbed, distributed, metabolized, and excreted, as well as any information they can gather on potential toxicity.

Researchers also look at a compound's potential benefits and mechanisms of action as they try to identify the best dosage and the best way to deliver the drugs, such as by mouth or injection.

2. Preclinical Research

Preclinical research has historically required tests on two nonhuman species, usually rodents and non-rodent species such as dogs or nonhuman primates.

The FDA Modernization Act 2.0 has removed the requirement that drug developers test on animals, enabling the inclusion of new approach methods and other innovations.

3. Clinical Research

Usually, clinical research starts with a Phase 1 study —small studies of 20 to 100 healthy volunteers or people with the condition to test safety and dosage.

About 70 percent of these studies move forward to Phase 2 studies, which include hundreds of people with the disease. They may take months to years to test efficacy and side effects.

About a third of these studies move forward to Phase 3 studies, which include hundreds to thousands of people with the disease over about one to four years to test efficacy and adverse reactions. About a quarter of these studies move forward.

4. FDA Review

Typically, after a Phase 3 study, the FDA reviews company data for a New Drug Application (NDA).

5. Post-Market Safety Testing

If the FDA moves forward with the new drug application and it's approved, the drug is released, and post-market surveillance (and sometimes additional Phase 4 testing) begins.

Q: What types of research do physicians use to help inform their treatment of patients?

When making daily medical decisions with patients, doctors follow a hierarchy of medical evidence in recommending lifestyle changes, medicines, vaccines, surgery, and other medical interventions.

The top level of evidence includes systematic reviews and meta-analyses—filtered information that draws together unfiltered information from other types of medical studies, such as randomized controlled trials and cohort studies.

Lower on the hierarchy are case-controlled studies, case studies, and expert opinion.

Q: How does preclinical (nonclinical) research translate in relation to clinical trials?

When doctors and scientists have examined how animal experimentation translates to human outcomes, they have found serious problems. When researchers have analyzed published animal studies through systematic reviews and meta-analyses, they have shown that animal studies do not reliably match human data.

In drug development, for example, animal data does not correspond well with human data.

Studies in animals repeatedly show that there is no clear relationship between human bioavailability (the proportion of a drug that enters the bloodstream and can have an effect) and animal bioavailability, including in dogs, nonhuman primates (such as monkeys), and rodents—all animals who are commonly used in research.

As a result of the mismatch between human and animal data, high rates of false negatives (a wrong negative result) and false positives (a wrong positive result) are common, which increases the risk for harmful events in humans and delays in drug discovery.

Researcher Daniel Hackam conducted a citation analysis of seven leading science journals that regularly publish animal research. He looked at the most-cited animal research to see if it translated into human studies. He looked at 2,000 studies and chose 76 that met established selection criteria. Of those, 11 percent were subsequently approved for human use.

In another analysis, Pablo Perel and colleagues did a comparison of treatment effects between animal experiments and clinical trials and discovered that only about half were concordant in terms of their results, and half were discordant. Their analysis illustrated the difficulties with accurately predicting whether human and animal studies will have similar or disparate results.

In 2019, Cathalijn Leenaars and colleagues conducted a systematic scoping review, which also demonstrated a lack of predictability in the translation of animal research to human clinical research.

Although some researchers have advocated for more systematic reviews and meta-analyses that evaluate translation rates across different areas of research, they are still relatively rare. Even when published, they do not reliably inform future research strategies.

Q: What are the ethical principles that guide human research and animal research?

There are several codes of ethics that guide human research, including

- The Nuremberg Code (1947)
- The Belmont Report (1979)
- The Council for International Organizations of Medical Science
- The Declaration of Helsinki

These codes and regulations work to advance principles such as respect for autonomy, beneficence (doing good), nonmaleficence (avoiding doing harm), and justice.

These principles have laid the groundwork for informed consent, risk-benefit analysis, the fair selection of research subjects, and the protection of vulnerable populations.

The codes that govern research on animals include

- The Institute for Laboratory Animal Research
- The Principles of Humane Experimental Technique by William Russell and Rex Birch (1959)
- The Council for International Organizations of Medical Science's Guiding Principles for Biomedical Research Using Animals
- Public Health Services Policy on Humane Care and Use of Laboratory Animals

Q: What are the laws and regulations that govern human research and animal research?

Human research in the US is commonly governed by certain federal or state regulations, institutional policies, and/or accreditation regulations.

One such regulation is the Common Rule, initially adopted in 1991 and revised in 2017. The Common Rule is meant to protect people who participate in research, including by requiring informed consent.

The Department of Health and Human Services (HHS) has additional regulations that offer further protections for certain vulnerable populations. And the Food and Drug Administration has regulations for human research that fall under its jurisdiction.

HHS also maintains an International Compilation of Human Research Standards. Such standards haven't prevented all abuses against humans, but if these guidelines are violated, they can cost researchers funding, employment, and professional status.

Some research, such as that conducted or paid for by a private company or wealthy individual, does not come under the Common Rule. However, other regulations may provide protections for human research subjects in these situations.

The primary US law governing the use of animals in research is the Animal Welfare Act. This federal law (first passed in 1966) "regulates the treatment of animals in research, teaching, testing, exhibition, transport, and by dealers." However, it does not recognize animals such as mice and rats—considered to be the most commonly used animals in research—and certain birds as an "animal," and thus does not cover them.

There are other regulations that address the treatment of animals used in laboratories, but as research shows, those regulations fail to offer significant protections.

There are no standards for animals that are comparable to those that apply to human subjects under *The Belmont Report* and the Common Rule.

Researchers who engage in human and/or animal research are also governed by US Public Health Service regulations, which exist to promote objectivity in research and to ensure no financial conflicts of interest.

Q: How many (nonhuman) animals are used in research each year?

It is impossible to precisely state how many animals are used globally for research. Only 37 countries publish national statistics, and the definitions of "research" and "animal" both vary domestically and abroad.

And although researchers try to standardize the definition of "animal" when compiling data, it's not always possible to compare data sets between countries—or even between US research facilities.

Using reports from the 37 reporting countries, and additional prediction modeling, experts estimate that roughly 192.1 million animals were used for scientific purposes worldwide in 2015.

Based on the increase in the numbers of animals used in research from 2005 to 2015, it is possible that the number of animals used in research each year continues to grow.

Q: Which species of animals are used in medical research?

In the US, almost any species of animal can be used in research.

In 2015, after decades of invasive chimpanzee research, the US joined other nations in ending the use of chimpanzees in medical research.

Today, other nonhuman primates, cats, dogs, pigs, sheep, horses, and many other animals are all still commonly used in federally registered research facilities. The most commonly used animals in research include invertebrates, mice, rats, rabbits, fishes, reptiles and amphibians, birds, guinea pigs, and hamsters.

Q: How are animals used in medical research?

Animal experiments conducted within the context of medical research generally fall into two categories: basic research (e.g., curiosity-driven experiments focused on discovery) and applied research (e.g., drug, device, and vaccine research and development, and toxicity and safety testing).

Research is conducted in both the private and public sectors. Animals can be used in research without any limit to the amount of pain they might endure, or any limit to the extent of permanent physical and psychological damage the experimentation might cause. Animals are typically killed after an experiment (or series of experiments) is concluded.

Q: If nonhuman animals aren't used in research, what does that mean for humans?

The history of human research is fraught with examples of unethical practices that exploited vulnerable populations. As adjustments have been made to the prevailing ethical framework, researchers have found new ways to engage with science.

Just as research has shifted within the last century to improve protections for human research subjects, research can shift to improve protections for animals while still producing knowledge that is beneficial to humans.

QUESTIONS TO ASK AND DATA INTERPRETATION

When looking at a research study, consider:

- What is the study question and how does it relate to real-world problems?
- Was the study question evaluated appropriately throughout the publication, including in the conclusion?
- Who approved the study? What standards, regulations, and/or principles were in place to guide approval?
- Who funded the research? How might the funding source(s) affect study bias?
- Who performed the research?
- What assumptions have the researchers made? What are their conflicts of interest, and how were they addressed?
- What ethical guidelines related to those used in the study were followed?
- What population(s) were included in the study, how many individuals, and why?
- What comparison group(s) were used? If a control group was used, what did they receive?
- What intervention was completed, and how? What are the details of the study or experiment?
- What are the strengths and limitations of the study design?
- Does the study establish causation?
- Are the findings statistically significant? How do the reported results compare with previous studies?
- Was the study peer reviewed?
- How generalizable is the research to pressing medical and public health issues?

Some general questions to consider:

- What are the differences between human research standards and standards for animals used in research?
- What are the current laws that exist to regulate the use of animals in research? What animals are covered by those laws, and what are the specific allowable and unallowable research practices? How well are these laws applied and enforced?
- How does the ability to justify causing harm in medical research hamper our ethical and scientific growth and ability to innovate?
- Is it ever ethical to expose individuals, particularly those who can’t consent, to significant risks, including for the benefit of others? And, if it is okay in certain conditions, what are the requirements that should be satisfied for such research to go forward?

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