Relevant participants

From: Key Concepts for assessing claims about treatment effects and making well-informed treatment choices (Version 2022)

3.1c Consider the relevance of fair comparisons in laboratories, animals, or highly selected people.

Explanation

Studies that only include animals, or only a selected minority of people, may not provide results that are relevant to most people.

Here are some examples of misleading extrapolation from animals or a selected minority of people, found in news reports *[Haneef 2015 (RS)]*:

Quote from news reports	Basis for the quote
"Researchers have shown that contact lenses laced with medicines are an effective way of treating glaucoma patients."	A study that showed the effect only in rabbit eyes.
"It could treat phobias and perhaps even post-traumatic stress disorders."	A before-after study in 15 healthy volunteers without any phobia.
"Broccoli slows arthritis".	A study in mice of a sulphoraphane compound present in cruciferous vegetables, including broccoli.
"The results of the trial – the first in humans – could offer hope to one in five people who are resistant to statins. It could also be offered to patients who suffer ill-effects from the drugs, or those whose cholesterol remains high even after statins are prescribed."	A study in healthy volunteers with high cholesterol levels who had received no lipid-lowering treatment in the past 30 days and were not statin resistant.
"Everyone should have at least 10-15 minutes of exposure to the sun every day to ensure that vitamin D levels are adequate."	A study in rats that assessed dietary vitamin D deficiency leading to elevated tyrosine nitration in the brain, which may promote cognitive decline.

Basis for this concept

It has been estimated that 11% of agents tested in humans are ultimately licensed, and only 5% of high-impact basic science discoveries claiming practical relevance are successfully translated into approved agents within a decade *[Henderson 2013 (SR)]*. Testing so many agents is potentially harmful to individuals in trials, and wastes resources. Animal studies are used to screen drugs and other treatments prior to testing in humans. A reason that so many animal studies fail to predict effectiveness or safety in humans is the use of treatments, animal models, or outcome assessments that are poorly matched to people – for example, using an acute disease model in animals to represent a chronic disease in humans. Another is when the pathophysiology underlying the disease in humans is not the same as in animals. A third reason is poorly designed and conducted animal studies. Several systematic reviews have documented major shortcomings of animal studies that limit their usefulness, including being too small, being badly reported and poorly summarised and interpreted in systematic reviews, being inconsistent, having a high risk of bias, and using animal

models that cannot be generalised to humans *[Avey 2016 (SR), Bahadoran 2020 , Grüter 2020 (SR), Korevaar 2011 (SR), Kringe 2020 (SR), Lamontagne 2010 (SR), Moja 2014 (SR), Mueller 2014 (SR), Roberts 2002 (SR), Xiao 2021 (SR)]*.

Reviews that have compared the results of animal studies to studies in humans have found success rates that range from 0% to 100% *[Leenaars 2019 (SR)]*. This wide range suggests that the potential of animal studies to predict successful treatments in humans is unpredictable.

Implications

Results of systematic reviews of studies in animals, or highly selected groups of people, may be misleading.

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Systematic reviews

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