How to misinform using medical research

Scary stories about our health, supported by alarming statistics, feature regularly in newspapers and scientific papers. It is surprisingly easy to take a piece of good (or bad) research and sensationalise the results. Postgraduate research student Stephanie Shoop investigates some of the most common tricks used to misinform people about scientific research

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Key words

Extrapolation
Sample size
Cancer
Diabetes
Diet

There is only one goal in scientific research — to find the truth. But the truth is not always easy to come by. Sometimes the truth is let down by methods. If a scientist recruits only one person to give their opinion on giving blood, and if that opinion is that 'giving blood is a waste of time', it is likely that this opinion will not reflect that of everyone in the country. On the other hand, the methods could be excellent but the result gained might not be novel or surprising. The scientific community or the general public may not deem the results interesting. But in the pursuit of publication, there are some simple ways to bend these results, making them seem novel, scarier and therefore more exciting.

Bending the truth

It is not difficult to twist facts into any shape you deem appropriate. You could choose to ignore most of the evidence, leaving a strong one-sided argument for your cause. It especially helps if you use studies with imperfect methods, so that '100% of people surveyed thought that giving blood was a waste of time'. You could choose to exaggerate results so wildly that cell death in a petri dish becomes full-blown extinction of the human race. You could point randomly around you and claim that whatever you're left pointing at *definitely* caused your current headache despite a perfectly reasonable alternative explanation. This bending of facts and research can have devastating consequences, including the rise of anti-vaccination campaigners and the related rise of measles infection in the UK. This article covers four of the methods most commonly used to twist and tangle scientific data so that almost any conceivable conclusion can be 'proved'.

Cherry-picking

Let's start with a fairly uncontroversial statement. 'Eating fruit is good for human health.' But does eating more fruit lower your risk of dying from cancer? You could just Google your question and discover a scientific paper by someone called Hertog who agrees with the statement. But how do we know this research is reliable? If we really want the

What are the chances that the whole orchard contains cherries as tasty as these?

to ensure ordered bundle organisation through a number of mechanisms. For example, we showed that the Short stop (abbreviated 'Shot') protein can guide the extension of newly forming microtubules along actin at the axon surface (B in Figure 3), thus laying them out into regular bundles. Another protein sits at the axon surface and, if microtubules leave their bundle and go off-track, it can capture and eliminate them (C in Figure 3), thus correcting any errors that occur during Shot-mediated guidance. Another set of proteins cross-links microtubules with one another and stabilises them, thus maintaining bundles once they are formed (D in Figure 3).

Neurodegenerative diseases

Our fly-derived model predicts that different mechanisms work together towards one common goal: the maintenance of microtubule bundles. Since nothing biological is perfect, there is a possibility that this machinery will fail and cause harmful axon swellings with disorganised, curled microtubule arrangements where mitochondria get trapped, leading eventually to axon degeneration (see Figure 3). Axon swellings are frequently found in the ageing brain. This offers one explanation as to why we lose 50% of our axons as we age. We predict that such swellings become more frequent if the microtubule machinery is weakened by mutations in microtubule regulators, potentially explaining why several of these mutations cause paralysis through nerve degeneration (see Figure 3). For example, mutations in the microtubule regulators spastin (which cleaves microtubules — F in Figure 3), kinesin or dynein (two microtubule-associated motor proteins driving transport and generating forces — E in Figure 3) cause **hereditary spastic paraplegias** or **Charcot-Marie-Tooth disease**. Mutations in dynactin (which partners with dynein) cause **motor neurone disease**, and mutations in dystonin cause **hereditary sensory and autonomic neuropathy** (dystonin is the human protein that corresponds to *Drosophilia* Shot — B in Figure 3) and, as in *Drosophila*, dystonin-deficient mice show microtubule disorganisation. A mutation of human dystonin affecting its interaction with microtubules was recently shown to cause the same type of neurodegeneration as shown in mice, and our model offers a plausible explanation.

In conclusion, our model derived from work in flies predicts that microtubule disorganisation may be a potential common disease mechanism for mutations in microtubule-regulating genes. Using flies, we test, challenge and refine this model, and then perform focused experiments in mice to test whether our ideas hold true in higher animals. Even if future work proves aspects of our model wrong, work in the fly will have provided innovative ideas to influence and advance concepts of nervous system ageing and degeneration.

This is just one example of how *Drosophila* remains an important pillar in the process of scientific discovery and continues to spearhead new research trends as a constant generator of ideas and conceptual understanding.

Further reading

http://tinyurl.com/jbs52y3 Two 'Small fly, big impact' YouTube movies describing the origins and importance of fly research (part 1 — 'Why the fly?') and how research in flies can help us to understand disease and find potential treatments (part 2 — 'Making research fly').

https://droso4schools.wordpress.com The 'Why fly?' page explains the advantages of *Drosophila* in research. The 'Organs' page compares tissues and organs of flies and humans with helpful overview images; the L1 tab explains the use of flies for neurodegeneration research; the L3 tab explains the working of nerve cell networks. Other tabs on this site provide curriculum-relevant biology sample lessons, as well as information on the biology of alcohol and statistics.

www.flyfacility.ls.manchester.ac.uk/forthepublic The Manchester Fly Facility has put together additional information for the public and school teachers: the 'Why the fly?' tab complements the information on droso4schools, providing simple facts, non-specialist books and over 80 lay articles about fly research; the 'Outreach Resources' page provides many other exciting links to *Drosophila*-specific information and resources.

www.prokop.co.uk/Research/LAYMAN/1-brain-intro.html An eight-page layman's guide to principles of neuronal circuits and synapses, also explaining how flies are used to study them.

www.youtube.com/watch?v=E_r-mfMc610 A short film explaining the axon model of local homeostasis.

http://tinyurl.com/z5bu8hc This blog explains why *Drosophila* is not only great for research but also a powerful teaching tool for biology lessons.

Brookes, M. (2001) *Fly: the Unsung Hero of Twentieth-Century Science*, Ecco; explains the history and importance of *Drosophila*.

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Key points

- *Drosophila* has been used as a model organism in biomedical research for over 100 years, leading to seven Nobel prizes in physiology or medicine.
- *Drosophila* has advanced our understanding of fundamental biology in many areas, most of them highly relevant for understanding important diseases.
- Axons are the cables that wire the brain. They are actively maintained to prevent nerve degeneration.
- The mechanisms maintaining axons can be studied in flies. These studies have led to a novel concept of local axon homeostasis.

Terms explained

Biomarker A biological measure that can be used to indicate a disease state, for example high blood pressure.

Confounder Something that accounts for the relationship between two events. It must be related to both the exposure event and the outcome event.

Extrapolation Extending your argument beyond what you actually know.

Meta-analysis Review that combines data from all previous work to make an overall conclusion.

Systematic review Study where results from every paper on a specific subject are summarised.

answer, we should look for a **systematic review** (see Box 1). It's a massive undertaking to find and read every paper ever written on a specific subject, so scientists frequently write and read summaries of all related work. A scientific review published in 2014 assessed data from seven different studies about people's fruit consumption, when they died and what caused their death. One research study (the Hertog article) showed that people who ate more fruit had a lower risk of dying from cancer. However, the other six found that, no matter how much fruit people ate, it didn't change their risk of dying from cancer. Unsurprisingly, when you consider the data from all the studies, it doesn't seem that eating fruit changes your risk of dying from cancer.

Sometimes journalists write articles based on one scientific article, perhaps stating that eating fruit protects you against cancer. This is called cherry-picking, because when you go picking cherries you choose only the tastiest cherries. In all fairness, the study you've cherry-picked may be very high quality. People rarely question whether anything contradictory has been published and are then surprised when foods are presented as life-savers one week and killers the next.

A real-life example of cherry-picking comes from the *Daily Mail*. In April 2015, the *MailOnline* published an article about foods that prevent potentially fatal diseases such as heart disease and cancer. What is particularly ironic about this piece is that they championed the cherry in a story that cherry-picks evidence. According to the *Mail*, eating more cherries can reduce inflammation, and eating cranberries improves heart health. But there have been relatively few studies comparing different types of fruit and health outcomes, and so far it looks as though it is the quantity of fruit you eat and not the type that affects your health. The *MailOnline* example states that a molecule called an 'antioxidant' gives these fruits health benefits. This is an example of our next technique, **extrapolation**.

Extrapolation to the general population

A lot of research is done in vitro, meaning 'in glass' — that is, not conducted in a whole body but in a cell culture or a tissue sample (see pp. 34–36, this issue). These studies can be informative and

Box 1 A guide to systematic reviews and meta-analyses

The methods for a systematic review can be easily split into three sections: search, extract and compare.

Search

- Using online databases, and sometimes even trawling through paper copies in dusty libraries, the first step is to make a list of all scientific papers containing **key words** for your research question. For a research question on 'cherry picking', you would search for all papers containing fruity words, such as 'fruit' or 'berry' and some deadly words, such as 'cancer death' or 'cancer mortality'.
- Next, look at paper summaries and fully read all the relevant ones. Yes, you read that correctly. It's hard work being a scientist sometimes!
- Before you allow any papers into the review, you have to assess each one for quality. For example, the researchers might have engineered their results so that anyone who died of cancer after eating fruit was omitted from the study and forgotten. Ergo, eating fruit saves lives. Here, you have the right to retaliate in kind and omit them from the review for cheating.

Extract

- Extract all the relevant information and/or data from each study.

Compare

- If the information is not numerical, for example, papers asking the question, 'How well do you feel after eating fruit?', with answers, 'Poorly', 'No different' or 'Much better', the results of each paper are described with how many found positive, neutral or negative results.
- If the results are numerical, for example, the number of people who died of cancer after eating fruit, the review gets upgraded to a meta-analysis. A meta-analysis pools all the data to create one combined result. It's often displayed in a forest plot like Figure 1.1.

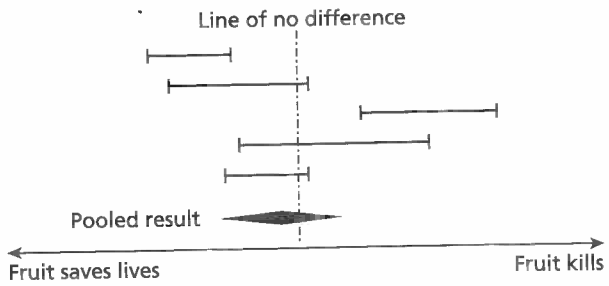
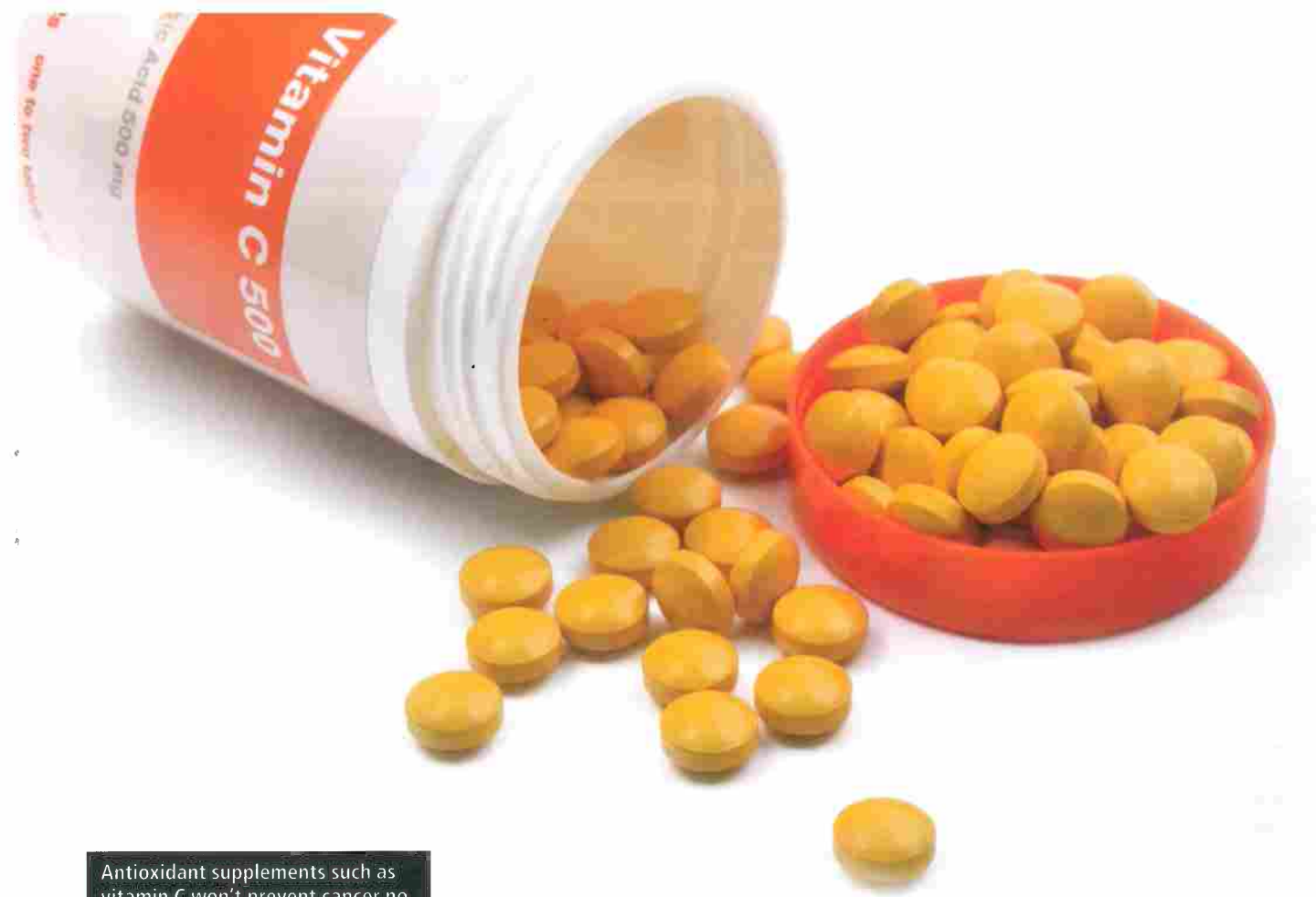


Figure 1.1

In Figure 1.1, if the line is on the left, the study showed that fruit saves lives. If it's on the right, it showed that fruit kills. However, if the line crosses the 'line of no difference', the study found no relationship between fruit and cancer death. The 'pooled result' diamond combines all the data from all the studies. The diamond crosses the line so overall there is no effect of eating fruit on death from cancer.



Antioxidant supplements such as vitamin C won't prevent cancer no matter how hard we extrapolate

are widely used by researchers, largely because they help clarify the direction of future research into new treatments that will be undertaken in whole organisms.

In early 2015 the *Daily Telegraph*, the *Independent* and *The Times* reported health benefits of consuming antioxidants. You might conclude that taking antioxidant supplements prevents cancer. Antioxidants include vitamins A, C and E and beta-carotene. They play vital roles in our bodies, including protection from a damaging state called 'oxidative stress', which is an inevitable result of breathing oxygen. Oxidative stress has been linked to cancer. It is sometimes said that antioxidants protect against a state that causes cancer and therefore antioxidants prevent cancer. However, this is extrapolation — extending the argument beyond what is actually known. Antioxidants also limit blood clot formation. So we could also extrapolate that 'antioxidants cause uncontrolled bleeding'. Extrapolation is purely guesswork. Indeed, when research moved from cell culture in a petri dish to studies of healthy people, taking antioxidant supplements had no effect on the risk of cancer.

We can even extrapolate when our study starts in a living animal. It takes a long time and a lot of money to see if something genuinely reduces your risk of cancer or heart disease, because these conditions tend to happen later in life. Researchers have therefore developed studies that look at intermediate disease states as the outcome. For example, instead of looking at whether a drug lowers the risk of heart disease, we could instead look at whether it reduces high blood pressure, which sometimes leads to heart disease. Here, high blood pressure is a proxy or marker for heart disease, more technically called a **biomarker**. However, even if something affects your biomarker, it does not mean it will affect

Further reading

If you are interested in learning more about how to scaremonger and want some great examples, read *Bad Science* by Ben Goldacre.

Summary of antioxidants: **http://tinyurl.com/mgugs2q**

Even more reasons to ignore the MMR autism paper: **http://tinyurl.com/ks9pvjz**

Newspaper examples from this article:

- the *Daily Mail* article on superfoods: **http://tinyurl.com/nv7y2vf**

Stories championing antioxidants:

- *Daily Telegraph*: **http://tinyurl.com/lrm55wu**
- *Independent*: **http://tinyurl.com/qd3bjnn**
- *The Times*: **http://tinyurl.com/lm4ztb5**

BBC Guinness and dogs story: **http://tinyurl.com/y3qhh3s**

Review on the MMR vaccine: **http://tinyurl.com/6uzr89q**

Box 2 The MMR controversy

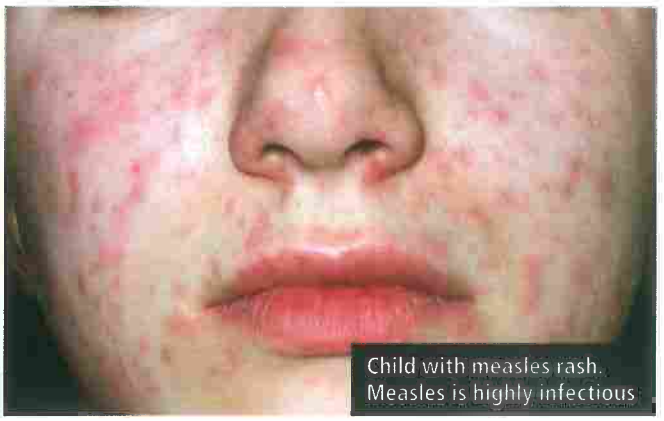
The MMR vaccine was introduced in the UK in 1988 to protect against three highly infectious and potentially life-threatening diseases: measles, mumps and rubella. Before the use of vaccination, measles alone caused over 2.5 million deaths worldwide every year.

It is important to continuously monitor the safety of all drugs over time, and 10 years after the MMR vaccine was introduced, a research paper was published in *The Lancet*, a highly regarded journal, associating the MMR vaccine with 12 children's autism. It asked parents and doctors of 12 children what they thought the cause of their child's communication problems was. For 11 children, the MMR vaccine was mentioned.

In itself, this study did not produce enough evidence to suggest that the MMR vaccine causes autism for the following reasons:

- There was no comparison between children who had taken the vaccine and those who had not.
- The paper only looked at 12 children. With such a small sample size, results could be chance findings.
- The MMR vaccine is extremely common. In any group of children, regardless of whether they have autism or not, it is not surprising when the majority have had the vaccine.

However, the media steadily began whipping up a frenzy, with celebrities joining in the 'MMR causes autism' debate. This media attention has had devastating consequences, with a drop of more than 10% in vaccine rates. Because of this, three serious diseases began to rise again in the UK with the number of measles cases climbing from 56 in the year of *The Lancet* paper to just under 1000 in 2007.



Child with measles rash. Measles is highly infectious

Celebrities and the media consistently failed to present the truth.

- *The Lancet* paper was retracted for unethical conduct and lies about where the children had been recruited from.
- The lead author had submitted a patent for a vaccine that would compete with the MMR vaccine.
- The majority of the authors on *The Lancet* paper have stated that their paper did not provide a link between the MMR vaccine and autism.

The evidence for the MMR vaccine being safe is overwhelming and comprehensive.

your disease. For example, in 2003, the BBC News reported on a research study where dogs were given Guinness. The study showed that the dogs that were given Guinness had lower blood clotting than dogs given light beer. Since blood clots can sometimes lead to heart attacks, the BBC then linked drinking Guinness with preventing heart attacks in humans. This is extrapolation not just from one biological process to a serious disease, but also across species.

Sample size and power

In any experiment, we need to appreciate that the number of samples studied might affect the significance of our results. If we have enough samples, then our study is said to have enough power, which is the probability that we can distinguish between a real effect and chance. What is important is not the actual number of samples but how many we need to answer our question. So power can be increased with bigger sample sizes. For example, suppose you want to know what proportion of students in your school have blood group O. If you ask only five students, by chance there might be no students with blood group O, and you might panic about the lack of universal blood donors at the school. However, if

The more people in a study, the less likely we will find something by chance

you ask 200 students, you will be more likely to get the right answer — around 50%.

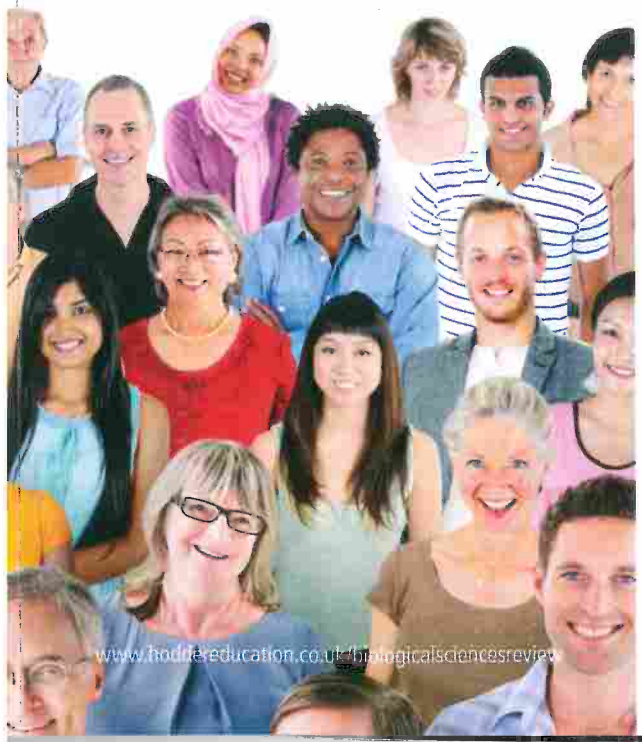
Power can also be increased by looking for larger effects. For example, if nearly everyone that ate broccoli died immediately and we gave two groups of people real broccoli and fake broccoli (such as a cauliflower painted green), we wouldn't need a big sample size to determine whether or not there was some sort of broccoli-related death rate (hardly ethical, however — see pp. 34–36, this issue).

A scary example is the once-supposed link between the MMR vaccine and autism (see Box 2). Since the media storm, a much larger sample size has been studied, which showed that the life-saving MMR vaccine is not linked to autism.

Confounding

Our final misuse of statistics — **confounding** — is common. To illustrate this, let's focus on ecological studies, which often have very large data sets and focus on populations rather than individual people. Let's consider some data from the UK government website (**data.gov.uk**), which contains freely available national information. Figure 1 is a scatter plot with the regional percentage of people on job-seekers allowance from 2007 plotted against the prevalence, or proportion, of people living with diabetes in England in the following year. The higher the percentage of people on job-seekers allowance, the higher the prevalence of diabetes. One interpretation might be that being on job-seekers allowance causes diabetes.

This interpretation fails at many levels. It uses three different types of misinterpretation. First, relationships at a population level don't necessarily apply to individuals. Second, a correlation between two events does not mean that one causes the other. Third, the issue is confounding — something else



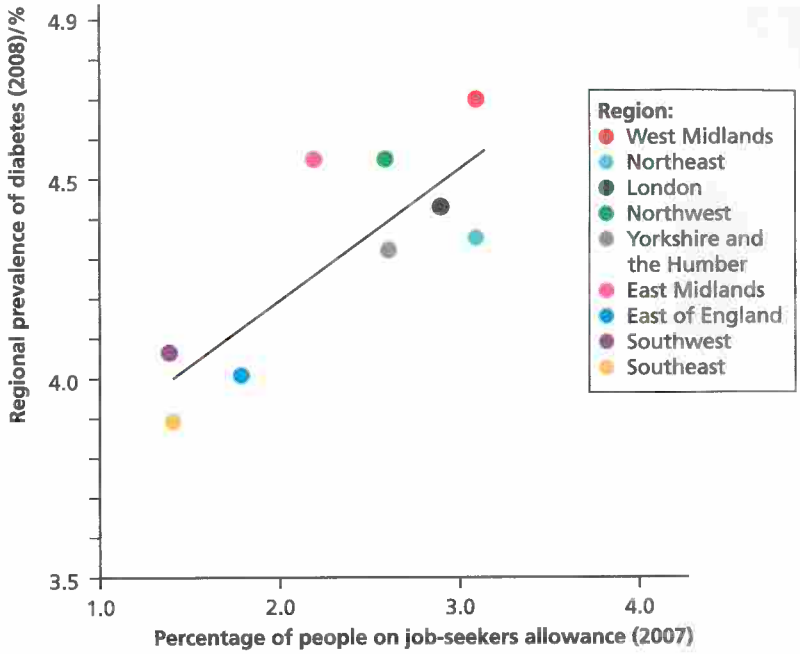


Figure 1 Percentage of people on job-seekers allowance in 2007 and prevalence of diabetes in 2008 in English regions (from data.gov.uk)

could account for this relationship. What if people that are on job-seekers allowance are more likely to buy cheaper 'fast' foods? Or, what if they have less time to exercise because they are looking for jobs? Since either diet or exercise could account for this relationship, they are confounders. Confounders have to be related to both our exposure 'job-seekers allowance' and our outcome 'diabetes'.

Using our MMR example, we can spot a massive potential confounder. The MMR vaccine is given to children at around the age that many autistic children develop symptoms. Therefore 'age', which is related to our exposure (MMR vaccine) and our outcome (autism), confounds the relationship.

Things to do

There are many more ways that medical data can be distorted and the examples highlighted are not the worst, or even the newest. Pick up any newspaper today, go to the 'health' or 'lifestyle' section, and see whether you can spot any of the issues raised in this article. Better still, next time someone tells you a study proves that sun cream causes skin cancer, ask what the sample size was or whether hours spent in the sun could be a confounder.

Stephanie Shoop is a PhD student in epidemiology (the study of diseases: trends, causes and cures) at The University of Manchester. She is currently looking at what can predict remission in children with arthritis, and loves pulling apart bad science.

Key points

- It is easy to take good quality evidence and distort the results.
- Newspapers frequently misinterpret evidence.
- Four simple ways to misuse medical evidence are:
  - selecting only those papers that agree with you
  - exaggerating results from tissue samples to whole humans
  - using studies with so few people that the results may occur by chance
  - ignoring other factors that may account for the relationship seen